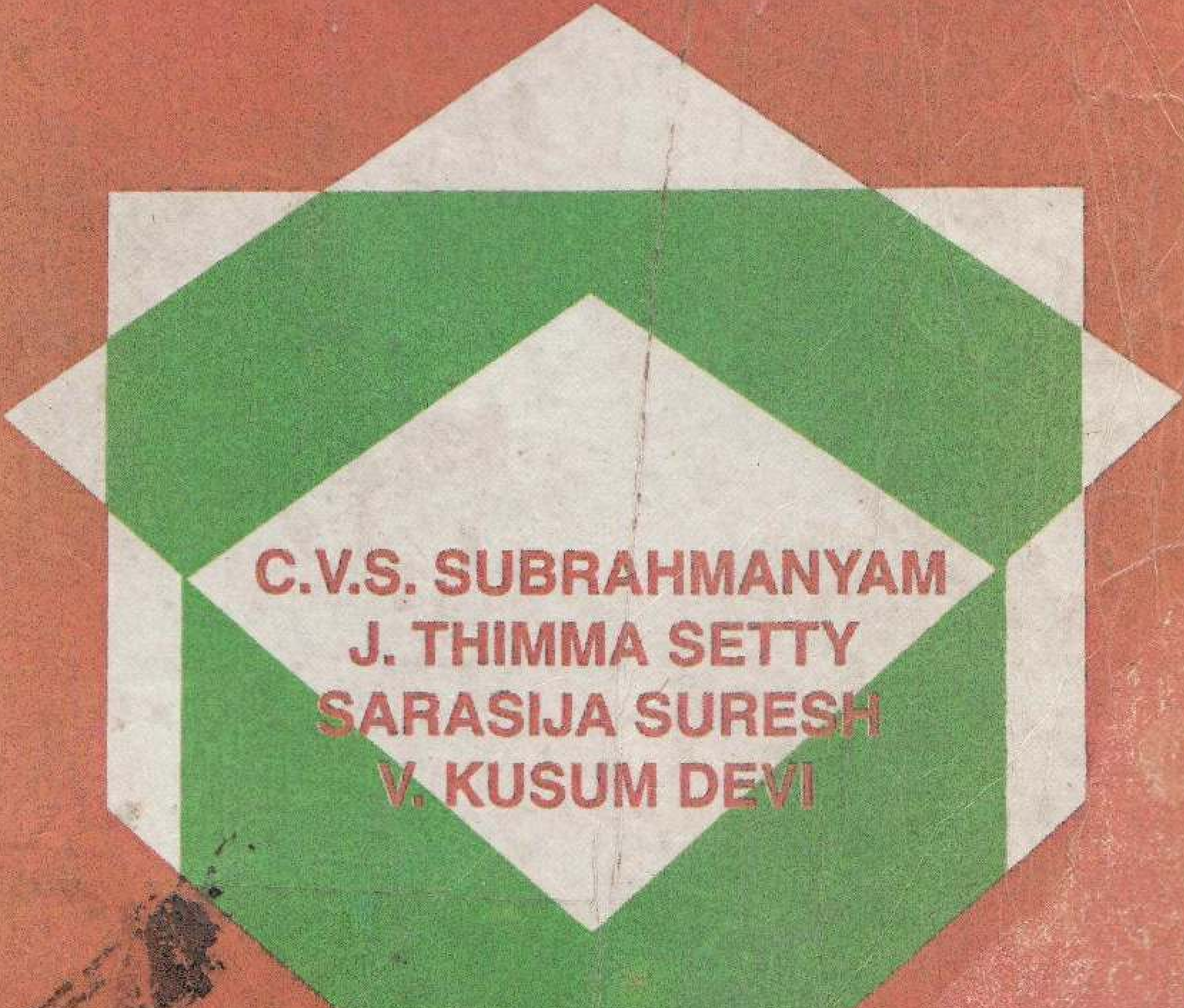
Compiled By Chinmay Kulkarni

PHARMACEUTICAL ENGINEERING

PRINCIPLES AND PRACTICES



C.V.S. SUBRAHMANYAM
J. THIMMA SETTY
SARASIJA SURESH
V. KUSUM DEVI

Pharmaceutical Engineering

(*Principles and Practices*)

C.V.S. Subrahmanyam
M.Pharm., Ph.D

J. Thimma Setty
M.Pharm.

Mrs Sarasija Suresh
M.Pharm., Ph.D.

Mrs V. Kusum Devi
M.Pharm., Ph.D.

DELHI
VALLABH PRAKASHAN

Dedicated to
Dr P. Gundu Rao
(Retired Professor and Principal of
College of Pharmaceutical Sciences, Manipal)
Director, Divi's Laboratories, Hyderabad.

ISBN 81-85731-27-6
VPBN 52

First Edition	2001
Reprint	2002
Reprint	2003
Reprint	2004
Reprint	2005
Reprint (Aug)	2005

Published by
M K Jain for VALLABH PRAKASHAN
AP-53A, Pitampura, DELHI-110088
Phone : (011)-27317755
e-mail : vallabh@vsnl.com

Printed at
New Gyan Offset Printers, Delhi

Preface

Pharmaceutical Engineering is concerned with the study of industrial processes required to convert raw material into value added pharmaceuticals such as drugs and excipients. It is a subject of importance both to the industrial pharmacist and the undergraduate students. Over the years, students of pharmacy have been feeling the need for a simple book, yet in sufficient depth to enable them to handle industrial operations with understanding of the principles involved therein. This book is an attempt to meet these twin objectives.

This book consists of 18 chapters: introduction to basic principles in engineering, fluid flow, liquid material transport, solid conveying, heat flow, size reduction, size separation, mixing (solids, liquids and semisolids), filtration, centrifugation, distillation, evaporation, crystallisation, drying, humidification and dehumidification, corrosion, plant materials of construction and other related aspects of pharmaceutical industry.

This book deals with unit operations and processes utilised in the production of bulk drugs, dosage forms and biological products. There is a proper blend of physical, chemical and engineering principles. One model equipment has been selected for explaining all the principles and general working though many variations and varieties of the same may be available. Hopefully this book will provide strong foundation subject, and for in-house training of technical personnel in the industry.

Special emphasis is laid on the following:

- Application of principles, practice and pharmaceutical examples.
- Illustrations and diagrams explaining the working of equipment.
- Units have been described in SI system.
- Question bank.

Suggestions and criticism are welcome.

Davangere
15th June, 2001

Authors

Reprinted after necessary corrections and improvement

Acknowledgements

We place on record our thanks to Prof. K.V. Jayadevappa, B.E., M.Sc.(Engg), Professor and HOD, and Mr. Y.J. Jagadeesh, Lecturer, Department of Mechanical Engineering, Bapuji Institute of Engineering and Technology, Davangere, for reviewing the manuscript. Thanks are due to Prof. K.S. Muralikrishna, Professor, and Mr. S.M. Vijayendra Swamy, Lecturer, Bapuji Pharmacy College, Davangere, for sharing their thoughts and critical comments on the manuscript. Thanks are also due to Mr. Giriraj Kulkarni, Lecturer, JSS College Pharmacy, Ooty for his valuable suggestions on the manuscript.

We express our thanks to Prof. Y.R. Prabhakara, Principal, BEA's School of Pharmacy, Davangere, and Prof. B.G. Shivananda, Principal, Al-Ameen College of Pharmacy, Bangalore, for their continued support in the preparation of this edition.

We thank Mr. Kiran Shenoy, Artist, Audio-Visual Section, J.J.M. Medical College Library and Information Centre, Davangere, for the preparation of figures, graphs, and artwork. We acknowledge the support extended by Miss Ranjeetha H.S., Pradeep Xerox and DTP Centre, Davangere, in the preparation of electronic script.

The authors thank their respective parent associations namely, Bapuji Educational Association, Davangere, and Al-Ameen Educational Society, Bangalore, for their encouragement in this educational endeavour.

The authors are grateful to the Curriculum Development Cell, All India Council for Technical Education, Government of India, at Indian Institute of Science, Bangalore, for the financial assistance provided for the preparation of this book. We thank them profoundly.

We also express thanks to Mr. Manish K. Jain of M/s. Vallabh Prakashan, Delhi, for his painstaking efforts to bring out this edition.

Davangere
15th June, 2001

Authors

A

Contents

1

Industrial Processing and Basic Principles

Unit Operations—Unit Processes
Unit Operations—Scientific Foundations
Dimensions, Units, Systems and Inter-Conversions
Dimensions—Formulae, Equations and Analysis
Stoichiometric Equations—Balancing

Pharmaceutical engineering is concerned with the study of industrial processes in which raw materials are changed or separated into pharmaceutically useful products such as drugs and excipients. A wide variety of processes are involved in these conversions. Some of them are as follows.

1. **Production of dosage forms :** Conversion of drugs (chemicals as raw materials) into medicines (*dosage forms*), which are suitable for use by the patient. Example is conversion of diclofenac sodium into dosage forms such as tablets, capsules, suspensions and injections.

2. **Production of bulk drugs :** Chemicals (raw materials) are converted into drugs. For example, salicylic acid is acetylated to obtain acetylsalicylic acid (aspirin). This area is known as production of *Bulk Drugs*. Conversion of chemicals into intermediates, which in turn are used for production of drugs in commercial scale, is also included in this area.

3. **Production of antibiotics :** Manufacture of drugs (antibiotics) using microbes with the aid of precursors is another area of interest to the pharmacist. This area is known as *fermentation technology*. For example, penicillin G is produced using *Penicillium chrysogenum* with the aid of precursor, phenylacetic acid.

4. **Production of biologicals :** Extraction of drugs from animals, plants and minerals from native raw materials into purified (or semi-purified) products are of interest to the pharmacist. Some examples are vaccines, insulin, streptokinase and recombinant DNA technology products.

Each process is developed systematically from a laboratory scale to pilot scale and finally to an industrial scale. In each case, process is undertaken by employing a number of equipment. The areas of interest with reference to equipment are:

- design
- fabrication
- assembly
- operation
- maintenance

Similarly, each process has to be followed scrupulously in terms of:

- effectivity
- efficiency
- validity
- safety
- economy

Effectiveness refers to the quality of what is to be actually accomplished. *Efficiency* means accomplishing tasks with a minimum of wasted material, time and money. In the popular management cliché, efficiency is doing things right, while effectiveness is doing right things.

Validation is defined as a procedure that demonstrates the ability of consistently producing a product with the established specifications under ideal conditions.

Safety refers to the protection of products, personnel, factory etc. Prevention of accidents and protection from fire constitute important aspects. Sufficient care should be exercised so that human factor is removed from the hazards by making protection a permanent and automatic.

Economy refers to the protection of factory from financial problems. The industrial activity essentially involves the conversion of raw materials into value added products. The steps are initiated for the optimization of parameters for an operation and process, so that economy works out for the factory as well as customer (or consumer). Standard Operating Procedures (SOPs) are helpful to obtain a quality product coupled with economy.

Therefore, a broad understanding of the basic principles involved in a process, knowledge about the construction, working and skills in handling them are of vital importance. This chapter provides the basic information and prerequisites that are necessary for understanding pharmaceutical engineering.

UNIT OPERATIONS AND UNIT PROCESSES

Normally, every process involves a series of steps. Each step is performed individually. This approach is an economical way of organizing a given task.

Unit Operations

Each chemical process frequently consists of a fewer number of distinct individual steps. Each step is called *unit operation.*

Each unit operation is based on one type of scientific principle. A few examples of unit operations and underlying principles are listed below.

Drying : It is a unit operation used to remove liquid or moisture from solids by evaporation with the aid of heat. For example, drying process is employed to remove excess moisture (above equilibrium moisture content) from the wet granules in the production of tablets.

Size reduction : This is a unit operation in which drugs (vegetable or chemical origin) are reduced to smaller pieces, coarse particles or fine powder. This process is extensively used in the manufacture of talcum powders and tooth powders (cosmetic industry).

Distillation : It is a unit operation of converting liquid into vapour by heating and reconverting vapour again into liquid by condensing the vapour. This unit operation is used for obtaining essential oils from various parts of the plants. Example is lemon-grass oil (perfume industry).

Evaporation : It is a unit operation which involves free escape of vapour from the surface of a liquid below its boiling point. For example, evaporation technique is extensively used for concentrating the syrup in the manufacture of sugar (sugar industry).

The **advantage** is that each unit operation is a common technique and employed in diverse chemical and pharmaceutical industries. For example, the operation of mass transfer is involved in humidification, evaporation, distillation, extraction and drying. The unit operation of drying is used in the following industries.

(1) **Pharmaceutical industry :** In the production of tablets, the powdered mass is converted into wet mass, which is subsequently dried in order to obtain free flowing dry granules.

In the manufacture of herbal drug extracts, a large number of plants are used. The plant extracts are dried in order to extend the shelf life. Otherwise, the product may deteriorate. For example, in the preparation of belladonna dry extract IP, liquid extract of belladonna is dried completely. Otherwise it gets deteriorated.

(2) **Food industry :** Grapes, cashew, almonds and other types of fruits are dried to obtain dry fruits. These products have extended storage life.

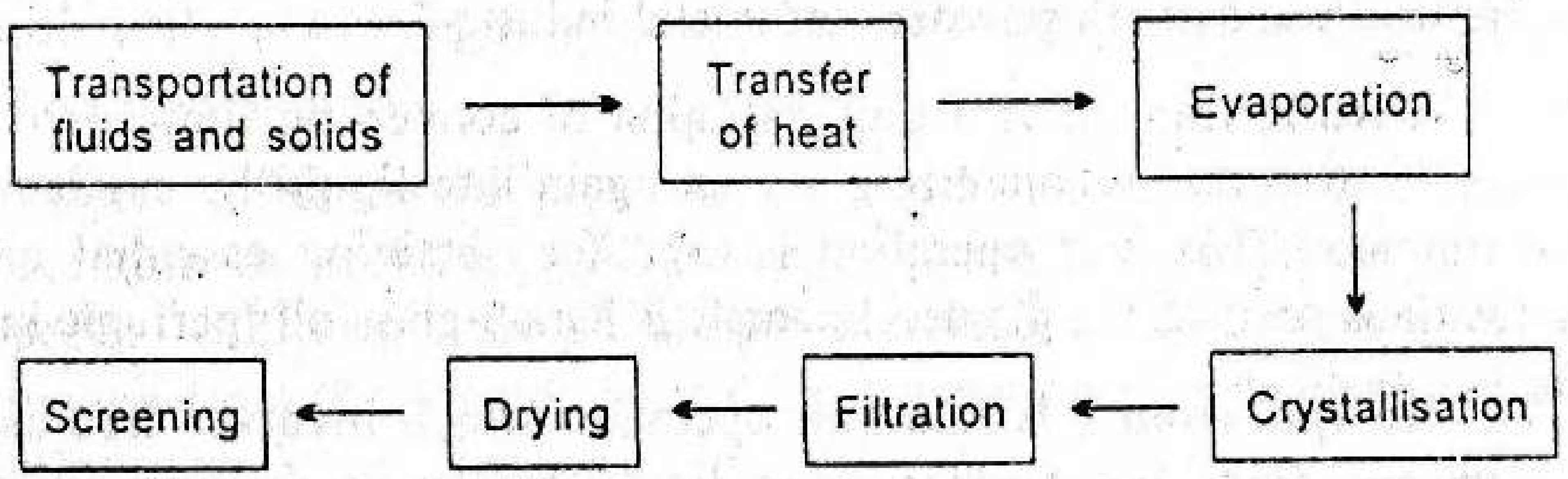
(3) **Sugar industry :** The crystals of sugar are dried to remove residual water, so that the sugar will be dry and free flowing.

Unit operations are based on both science and experience. The theory and practice must be combined judiciously for achieving proficiency in handling equipment.

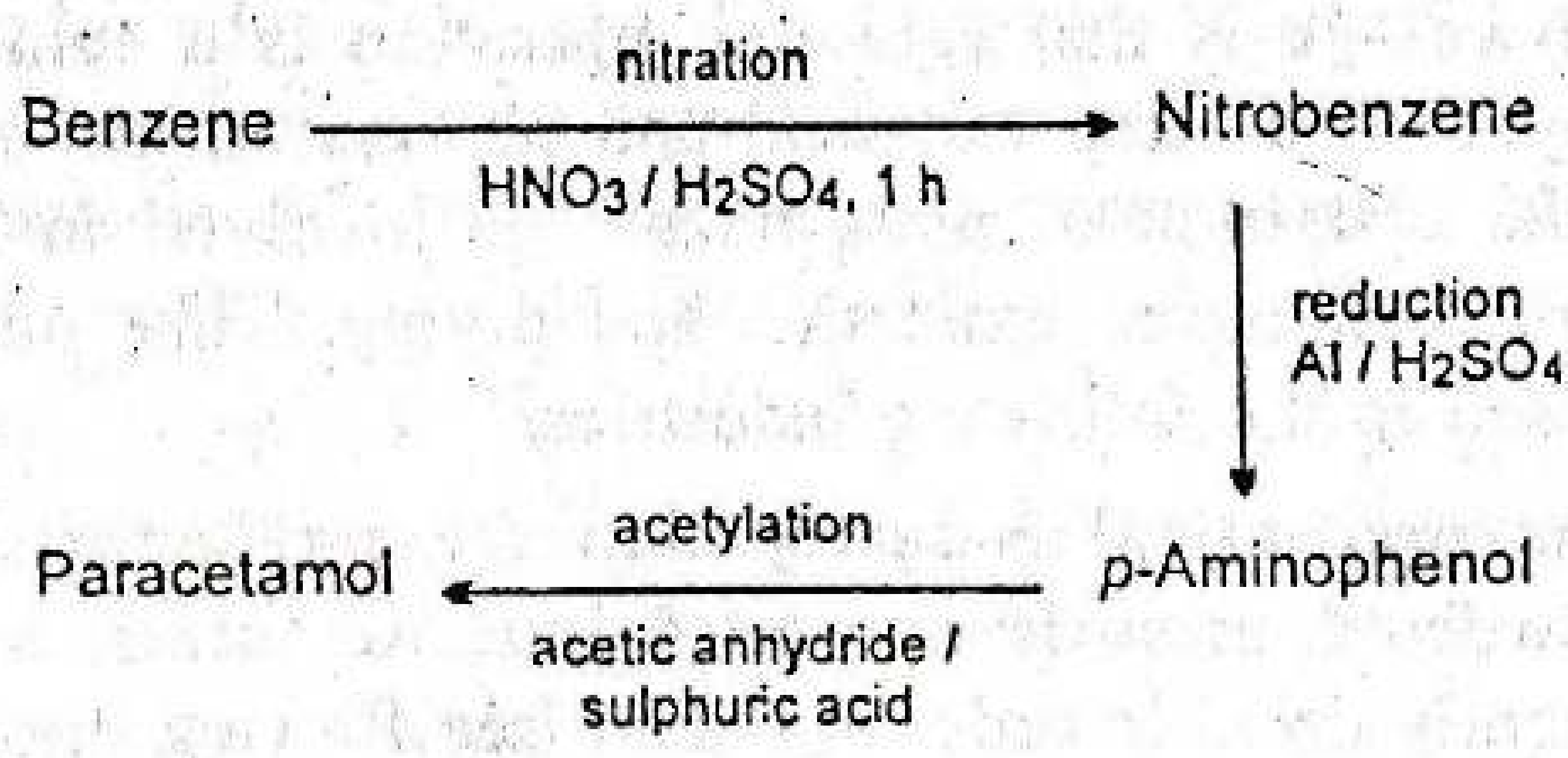
Unit Process

Unit process is defined as the one in which several unit operations are combined in a sequence to achieve the objectives of a chemical or physical process.

Unit process-Physical process : Consider the example of manufacture of common salt. The unit operations involved are:

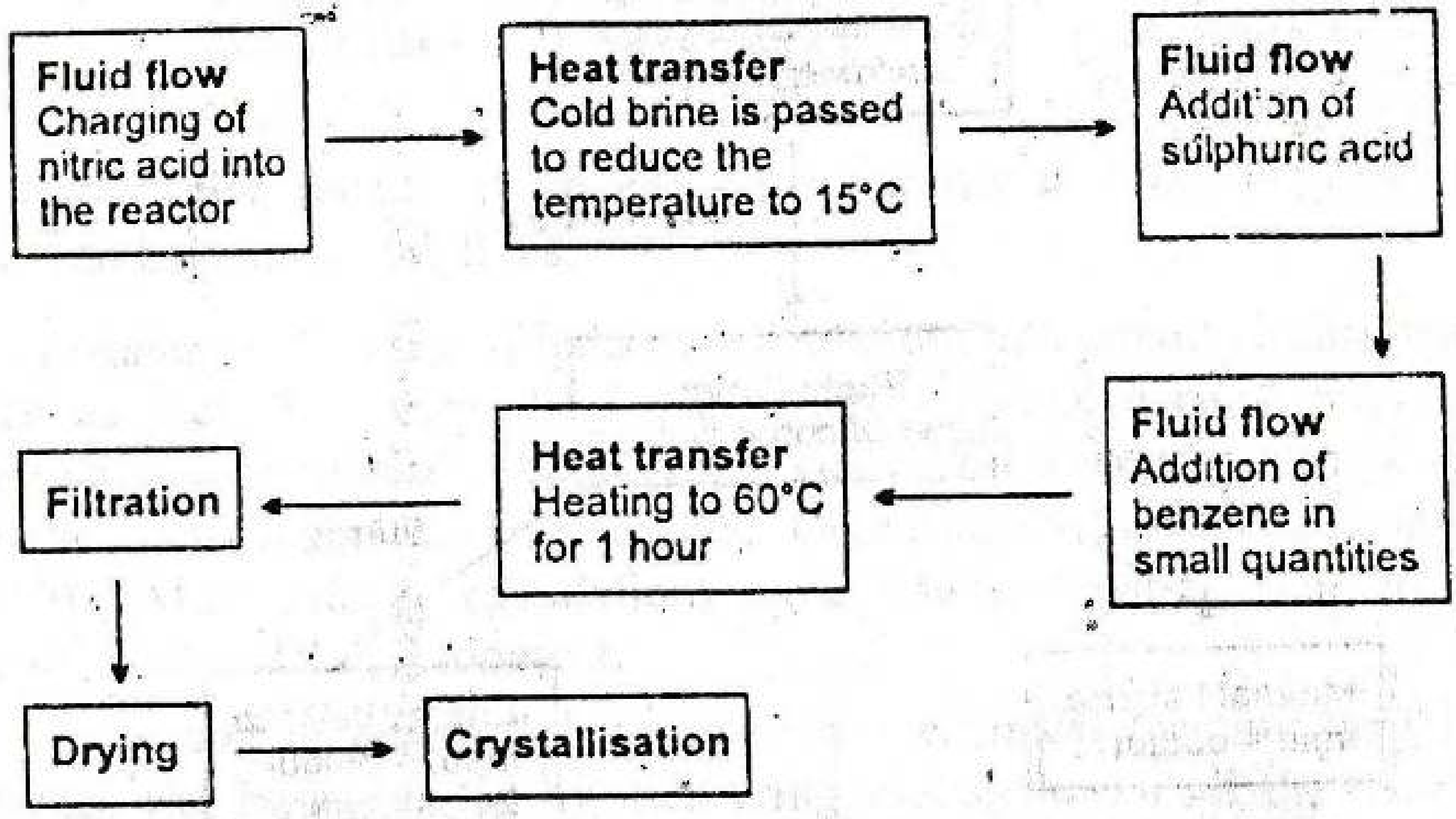


Unit process—Chemical process : Consider the production of paracetamol from benzene.



Sequence of reactions for the production of paracetamol (or acetaminophen).

In the above process, three unit processes are involved. These are nitration, reduction and acetylation. Each unit process is in turn made of a number of unit operations. For example, in the nitration of benzene to nitrobenzene, the unit operations involved are:



These examples illustrate that unit operations are largely used to conduct the physical steps such as:

1. Preparation of the reactants,
2. Separation and purification of the products,
3. Recycling of the unconverted reactants.
4. Controlling of the energy transfer into or out of the chemical reactor.

Thus, several steps are carried in a sequential order to achieve a process efficiently and economically.

UNIT OPERATIONS—SCIENTIFIC FOUNDATIONS

A large number of unit operations are simultaneously handled in a chemical process. Hence, the knowledge of the elementary physical and chemical laws (Figure 1-1) is essential for the application of scientific principles and techniques. Some of these laws are:

Basic laws: Laws of conservation of matter.
Laws of conservation of energy.

Special laws: Universal gas laws (Ideal gas equation).
Dalton's law of partial pressures.

Special laws are discussed in detail in different books mentioned in bibliography. The basic laws are highlighted below.

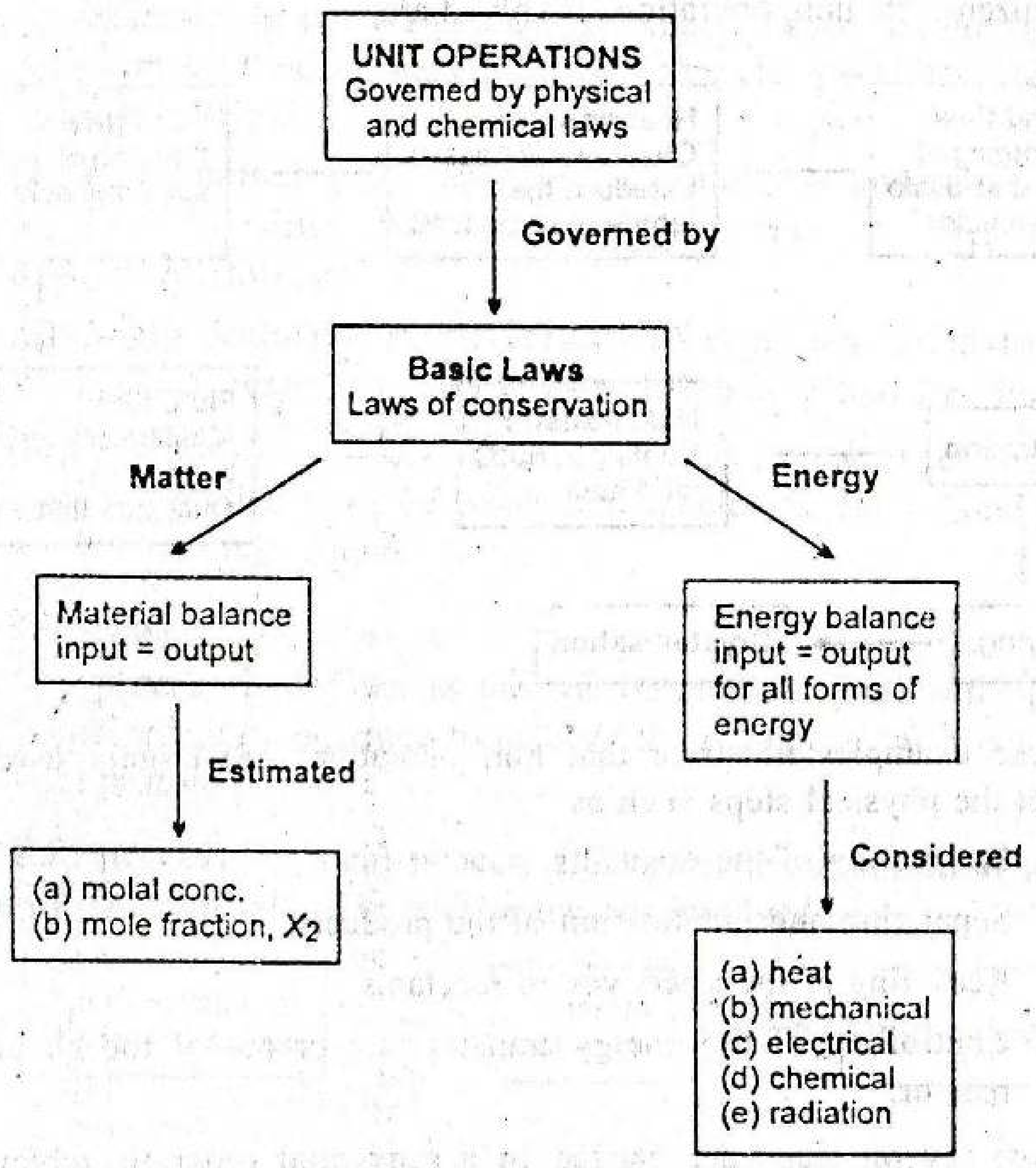


Figure 1-1. Scientific foundations in unit operations. Basic laws are included.

Basic Laws

The general law of conservation can be applied to any process. It is employed in engineering in the form of:

(a) Material balance

(b) Energy balance

Material balance : *The law of conservation of matter* states that material cannot be destroyed or created, it can be changed from one form to another.

In other words, the material entering a process must either accumulate or leave the process. The given input must be accounted for an output. The principle of material balance can be applied to an equipment, or to the entire process or any part of it. A simple account of material balance

INPUT	=	OUTPUT		
Amount of raw materials		Amount of changed materials	+	Amount of unchanged materials

Radioactive process is an exception because it does not obey the material balance calculations.

Advantages : The mass balance calculations can provide information such as yield value (practical and theoretical) and percent recovery. Currently, validation of processes and equipment has become important in the certification of International Organisation for Standardisation (ISO). Mass balance calculations have assumed central place in the current industrial development.

Estimation of material balance : In a chemical reaction, material balance can be accounted by measuring the amount of all the components (constituents). Normally, the amount is expressed in concentration units; moles/litre, molal units, mole fraction units, % w/v, % w/w etc. Some of them are reported for ready reference.

Mole : In a chemical reaction, the molecular unit is *gram mole* or *pound mole*. Some important expressions are molal units and mole fraction units.

In the mass balance calculations, mole is a better term and used frequently. For an individual component, mole is defined as quantity of that substance whose mass is numerically equal to its molecular weight.

$$\textit{Gram-moles of a substance} = \frac{\text{mass in grams}}{\text{molecular weight}} \qquad (1)$$

These values are useful while selecting the amount of each ingredient to be added to the reaction mixture based on the stoichiometric equation and coefficients. For example, x grams of oxygen gas has been mathematically expressed as:

$$\textit{Number of moles} = \frac{x \text{ grams of oxygen}}{\text{molecular weight of oxygen}} = \frac{x \text{ grams}}{32}$$

Average molecular weight: When a mixture of substances is involved in a reaction, the average molecular weight of the mixture may be written as:

$$\textit{Average molecular weight of mixture, } m = \frac{W_a + W_b + W_c + \dots\dots}{\frac{W_a}{M_a} + \frac{W_b}{M_b} + \frac{W_c}{M_c} + \dots\dots} \qquad (2)$$

where W_a, W_b, W_c etc. are the weights of individual components *a, b, c,* etc. M_a, M_b, M_c etc. are the molecular weights of components *a, b, c,* etc.

Molality : For individual components, molality is expressed as:

$$\textit{Molality, } m = \frac{\text{number of moles of substance}}{\text{number of kg of medium (solvent)}} \qquad (3)$$

The unit is mol kg^{-1}. It is designated as m. Molality (molal) notation is frequently used in theoretical studies. The **advantages** are enumerated below.

(a) It does not change with temperature, i.e., contraction or expansion of a liquid with temperature does not affect the calculations.

(b) The weight of solvent (reaction medium) is considered. Volume has no influence, since it is not precisely known always.

Mole fraction : For individual component, mole fraction is expressed as:

$$\textit{Mole fraction of A, } X_A = \frac{\text{number of moles of one constituent}}{\text{total number of moles of all constituents}}$$

It is designated as *X*. One constituent may be solute. Total number of moles of all the constituents refers to moles of solutes and solvents. It is in general notations as:

$$\textit{Mole fraction of A, } X_A = \frac{\frac{W_a}{M_a}}{\frac{W_a}{M_a} + \frac{W_b}{M_b} + \frac{W_c}{M_c}}$$

$$= \frac{n_a}{n_a + n_b + n_c + \dots} \qquad (4)$$

where n_a, n_b, n_c etc., are the number of moles of individual components a, b, c, etc.

The sum of the mole fractions of all components must be equal to unity. Mole fraction is used frequently in experiments involving theoretical considerations. The **advantage** of mole fraction notation is that it expresses the relationship between the reactants and other components in a simple and direct way.

Energy balance : *Energy* is the capacity to exert a force through a distance and manifests itself in various forms.

The unit of energy in SI system is J (Joule). The energy per unit mass is known as *specific energy*, which has the unit of J/kg. Engineering processes involve: (a) conversion of energy from one form to another (b) transfer of energy from place to place (c) storage of energy in various forms utilizing a working substance. The first law of thermodynamics is a statement of conservation of energy. It expresses the fact that energy cannot be created or destroyed, though energy can be transported from one kind to another.

The *law of conservation of energy* states that the energy output must be same as the energy input in a chemical process.

The energy balance equation must include all types of energies.

* heat
* mechanical
* electrical
* chemical
* radiation

When one kind of energy is destroyed or consumed, an equal amount of another kind must be formed.

Applications : The principle of conservation of energy is applied in a number of instances. A few of them are mentioned here.

(1) In the study of fluid flow, Bernoulli's theorem is applied, which is a special case of the law of conservation of energy.

(2) Energy is converted from one form to another. This principle is used in the working of a pump wherein kinetic energy is converted into pressure head for pumping the liquids.

(3) Energy losses due to friction can be accounted, while a fluid is flowing through pipes. It is also helpful for adopting suitable measures to reduce losses.

(4) Since efficiency and economy are important parameters for any process (chemical or physical), energy calculations and balancing have assumed importance. When energy is obtained from non-renewable sources, balancing of energy will be a critical factor.

Some Basic Concepts

Rate of a process or reaction : The rate of a reaction can be understood by studying the time course changes in the concentration. In general, rate is expressed mathematically as a differential equation:

$$\textit{Rate of reaction} = \frac{dQ}{dt} = \frac{dF}{R} = \frac{\text{driving force}}{\text{resistance}} \qquad (5)$$

where Q = quantity being transferred or reacted

t = time

F = driving force

R = resistance

According to equation (5), the rate at which a system approaches equilibrium may be expressed as the combined effect of two factors. These are:

(*a*) *Potential factor* : It indicates the driving force necessary to make (proceed) the reaction.

(*b*) *Resistance factor* : It indicates the capacity to impede the speed for a given potential.

In the example of heat transfer from the hotter end of the iron rod to the colder end, the driving force is the difference in temperature (ΔT). At the same time, iron also offers certain amount of resistance to heat flow, on account of poor thermal conductivity.

Steady state and unsteady state : In a system, if the operating conditions are varying with time, then such a system is said to be in *unsteady state* or *transient state*.

For example, consider a tank of cold water. A coil in which constant pressure of steam is maintained is immersed in the tank. During the heat transfer through the coil, the operating conditions such as temperature difference between the coil and water do not remain same with time. Similarly, thermal resistance between the coil and water changes with time.

A system is said to be at *steady state*, if the conditions do not vary with time.

For example, consider water in a pipe is flowing under two conditions. (A) Water entering the tank at constant temperature and flow rate. (B) A jacket in which steam is maintained at constant temperature surrounds the pipe. Condition may vary from section to section along the pipe, but at any one cross section, it does not vary with time.

DIMENSIONS, UNITS, SYSTEMS AND INTER-CONVERSIONS

For the purpose of measurement (dimensions), three systems have been used, namely:

Cgs system (centimetre-gram-second)—Also known as metric system

Fps system (foot-pound-second)—Also known as British system

Mks or SI (metre-kilogram-second)—Modern system

The basic quantities identified for this purpose are length, mass, time etc. These are expressed in various ways in different systems. Some of the important principles in dimensions are given in Figure 1-2.

The units mentioned in any system for expressing the physical quantities are known as *fundamental units* or *primary units*.

For example, length is expressed as centimetre in cgs system, foot in fps system and metre in mks system. The official international system of units is the SI system (Systeme Internationale d'Units) and commonly employed in engineering and science. The basic units in SI system are given in Table 1-1. Primary units are the basis for obtaining derived units.

Secondary units or *derived units* are those that are made by the inclusion of primary units.

For example, acceleration is a secondary unit. It is expressed as length/time^2. Other examples of derived units in SI units are given in Table 1-2. For these units, alternative base units are given in B part of Appendix II.

TABLE 1-1
Basic Units in SI System

Measurement/Quantity	*Unit*	*Symbol*
Length (L)	Metre	m
Mass (m)	Kilogram	kg
Time (t)	Second	s or sec
Amount of substance	Mole	mol
Temperature	Kelvin	K
Electric current	Ampere	A
Luminous intensity	Candela	cd

All physical quantities consist of two parts.

1. **Unit** : It indicates about the quantity and gives the standard by which it is measured (examples are centimetre, foot, second, pound, grams).
2. **Number** : It denotes the number of units needed (examples are one, two, three etc.).

These two parts together they make a physical quantity. It is essential to specify both the parts, whenever a physical quantity is expressed in the engineering.

Supplementary units : Two supplementary units are at present defined, the radian and the steradian, which are the units of plane and solid angles, respectively.

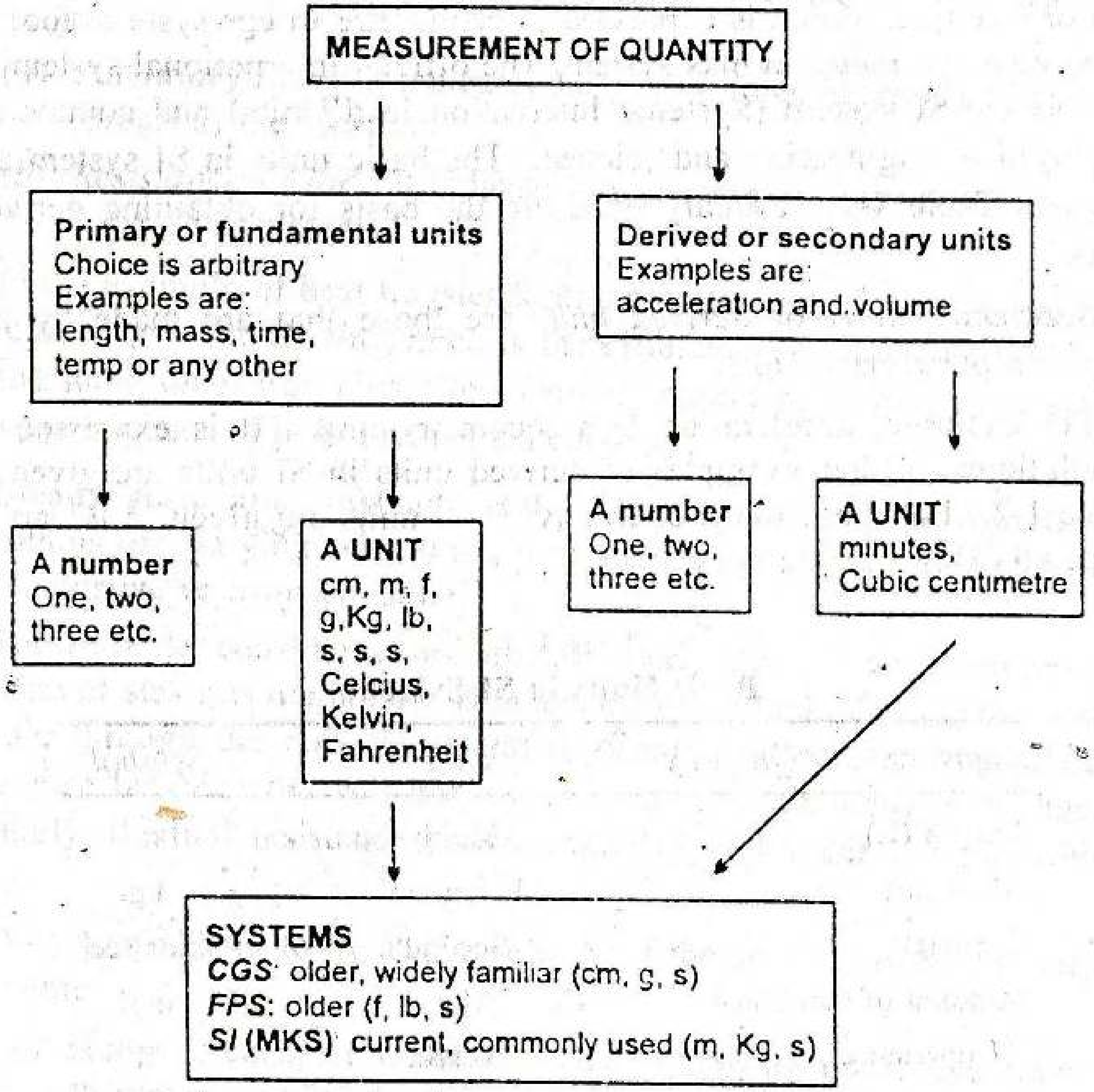


Figure 1-2. Unit systems and relevant ways of expressing a quantity.

Applications : It is essential to be conversant with all the systems and also their inter-conversions. In pharmaceutical engineering, it is necessary to handle a large number of physicochemical data, while selecting the right kind of materials for a process. Most of the literature data are available in the older systems such as cgs and fps systems. Therefore, it is necessary to be expert in all the systems of units.

TABLE 1-2

Some Derived Units in SI System

Measurement/ Quantity	*Unit*	*Symbol*
Force	newton	N
Energy	joule	J
Power	watt	W
Pressure	pascal	Pa
Frequency	hertz	Hz
Electric charge	coulomb	C
Electrical potential	volt	V
Electrical resistance	ohm	Ω

Inter Conversions

Any quantity can be converted from one system to other by the use of conversion factors.

Conversion factor is a pure number and simply the ratio of the magnitude of the unit in one system to that of the corresponding unit in the other system.

Conversion factors are simply multiplication factors. For example, the length expressed in fps system is 10 feet. To convert it from fps to SI system, the conversion factor is 0.3048, i.e., 1 foot = 0.3048 metre.

Hence, 10 feet = 0.3048 × 10 = 3.048 metre

It is always better to make a mental-picture of a unit, which will give a large figure (i.e., number). Then the conversion factor should be applied as direct proportionality or inverse proportionality. This can be illustrated here.

In the above example, the conversion factor is 0.3048. Metre (mks system) has higher magnitude compared to feet (fps system). Therefore, metre has a small number compared to the corresponding number in feet. Hence, foot has to be multiplied by the conversion factor to get metre.

10 feet = 10 x conversion factor = 10 × 0.3048 = 3.048 metre

Conversely, metre should be divided by conversion factor to obtain feet. For example,

$$3.048 \text{ metre} = \frac{1}{0.3048} \times 3.048 = 10 \text{ feet.}$$

Inter-conversion between SI system and cgs system is simple, because both use same standards for time and temperature. Mass can be converted from one system to the other. Some conversion factors for primary and secondary units between different systems are in tables 1 and 2 of Appendix III.

Temperature is normally denoted in degrees by Celsius (°C), or Fahrenheit (°F) or Kelvin (K) scale. The thermodynamic temperature scale is called the Rankine scale, in which the temperature is denoted by degrees Rankine. Their relationships are given in Table 3 of Appendix III.

Practice Problem 1-1. The unit of viscosity in the cgs system is the poise, which is equal to 1 dy.s/cm². If the fluid has a viscosity of 0.20 poise, calculate the corresponding value in SI units (Pa·s).

Solution: Data–The units are:

$$\text{Poise} = \frac{\text{dy.s}}{\text{cm}^2} = \frac{\text{g}}{\text{cm·s}}$$

The viscosity in SI units and its conversion into base units may be written as:

$$\text{Viscosity} = \text{Pa·s} = \frac{\text{N·s}}{\text{m}^2} = \frac{\text{kg·m·s}}{\text{s}^2\text{·m}^2} = \frac{\text{kg}}{\text{s·m}}$$

The conversion factor can be determined as follows. From the conversion Table of Appendix III, the following factors are obtained.

1 g = (1/1000) kg; 1 cm = (1/100) m;

By substituting the above terms for units

$$\frac{\text{g}}{\text{cm.s}} = \frac{(1/1000)\text{ kg}}{\text{s} \times (1/100)\text{ m}} = \frac{100\text{ kg}}{1000\text{ m} \times \text{s}} = \frac{1\text{ kg}}{10\text{ m.s}} = 0.1\text{ kg/m·s}$$

$$0.20 \text{ poise} = 0.2 \times 0.1 \text{ Pa·s} = 0.02 \text{ Pa·s}$$

Practice Problem 1-2. The density of talc is reported as 2.7 g/ml. Express the same in SI system (kg/m³).

Solution: The given unit of density is g/ml is to be converted to kg/m³. g/ml is also equal to g/cm³. From the conversion Table 1 of Appendix III, the following factors are obtained.

1 g = (1/1000) kg; 1 cm³ = (1/100) m³.

The conversion factor may be obtained as follows.

$$\frac{\text{g}}{\text{cm}^3} = \frac{(1/1000)\text{ kg}}{(1/100)^3\text{ m}^3} = \frac{1000000\text{ kg}}{1000\text{ m}^3} = \frac{1000\text{ kg}}{\text{m}^3} = 1000\text{ kg/m}^3$$

The conversion factor = 1000

2.70 g/ml = 1000 × 2.7 kg/m³ = 2700 kg/m³.

Practice Problem 1-3. In the literature, mass transfer coefficients in the gas phase are often reported in terms of lb·mol/h·ft²·atm. Determine the conversion factor by which the above must be multiplied in order to obtain the corresponding value of kg·mol/s·m²·Pa.

Solution: The given units units into which converted

$$\frac{\text{lb·mol}}{\text{h·ft}^2\text{·atm.}} \qquad \frac{\text{kg·mol}}{\text{s·m}^2\text{·Pa}}$$

From conversion Table 1 of Appendix III, the following conversion factors can be obtained.

lb = 0.4536 kg; ft² = 0.093 m²; h = 60 × 60 s; atm. = 1.01325×10⁵ Pa.

Substituting the values in the equation gives:

$$\frac{\text{lb·mol}}{\text{h·ft}^2\text{·atm.}} = \frac{0.4536\text{ kg·mol}}{0.093\text{ m}^2 \times 60 \times 60\text{ s} \times 1.01325 \times 10^5\text{ Pa}}$$

$$= \frac{0.4536\text{ kg·mol}}{0.093 \times 3600 \times 1.01325 \times 10^5\text{ m}^2\text{·s·Pa}} = \frac{0.4536\text{ kg·mol.}}{339.236 \times 10^5\text{ m}^2\text{·s·Pa}}$$

$$= 1.337 \times 10^8\text{ kg/m}^2\text{·h·Pa.}$$

The conversion factor for lb/ft²·h·atm. = 1.337 x 10⁸ kg/m²·h·Pa.

Practice Problem 1-4. The overall coefficient of heat transfer is 200 Btu/h·ft²·F. Convert the same into SI units [W/m².K].

Solution:

The given units of $\frac{\text{Btu}}{\text{h.ft}^2\text{·F}}$ into units of $\frac{\text{W}}{\text{m}^2\text{·K}}$

The Btu's equivalent in SI units is J/s, while J/s is equal to W. Therefore, J/s is considered in place of W for obtaining conversion factor.

$$\frac{\text{Btu}}{\text{h·ft}^2\text{.°F}} \text{ to } \frac{\text{J}}{\text{s·m}^2\text{·K}}$$

From the conversion tables 1 & 3 of Appendix III, the following relationships can be obtained.

1 Btu = 1.0551×10³ J; 1 h = 60 × 60 s; 1 ft² = 9.290×10⁻² m²; 1°F = (1/1.8) K

Substituting the above conversion factors into the above equation gives:

$$\frac{\text{Btu}}{\text{h.ft}^2\cdot{}^\circ\text{F}} = \frac{1.0551\times10^3\ \text{J}}{60\times60\times9.290\times10^{-2}.1/1.8\ \text{s}\cdot\text{m}^2\cdot\text{K}}$$

$$= \frac{1.0551\times10^3\ \text{J}\times1.8}{3600\times9.290\times10^{-2}\ \text{s}\cdot\text{m}^2\cdot\text{K}} = \frac{1899.18\ \text{J}}{334.44\ \text{s}\cdot\text{m}^2\cdot\text{K}}$$

$= 5.6787\ \text{J/s}\cdot\text{m}^2\cdot\text{K}$

Since J/s = W, it can be included in the above expression to get units 5.6787 $\text{W/m}^2\cdot\text{K}$. Therefore, the conversion factor = 5.6787.

$200\ \text{Btu/h}\cdot\text{ft}^2\cdot{}^\circ\text{F} = 200\times5.6787\ \text{W/m}^2\cdot\text{K} = 1135.74\ \text{W/m}^2\cdot\text{K}$

DIMENSIONS–FORMULAE, EQUATIONS AND ANALYSIS

Dimensional Formulae

A dimensional formula is a formula that explains the way in which fundamental units enter into the operation.

Dimensional formula expresses the quantity in secondary units. For example, the dimensional formula for acceleration is:

$$[a] = l\cdot t^{-2} \qquad (6)$$
$$= \text{length}\times\text{time}^{-2}$$

Equation (6) can be explained as follows. Acceleration is defined as velocity per unit time.

$$[a] = \frac{\text{velocity}}{\text{time}} \qquad (7)$$

Velocity is defined as a distance per unit time. Therefore, acceleration can be written as:

$$[a] = \frac{\text{Distance (length)}}{\text{time}\times\text{time}} = l\cdot t^{-2} \qquad (8)$$

The symbol $[a]$ means the dimensional formula of the quantity of 'a'.

Applications : Dimensional formulae are used in order to convert the secondary units of one system into another. In these calculations, conversion factors are used cautiously. Then, the physical quantity is obtained in another system.

The dimensionless equations are derived from basic laws mathematically, no matter however complicated they may be. An equation in which all terms have same dimensions is known as *dimensionally homogeneous equation.*

For example, consider equation for Reynolds number.

$$Re = \frac{Du\rho}{\eta} \qquad (9)$$

where D = diameter of the pipe, m
u = velocity of flow, m/s
ρ = density of the fluid, kg/m^3
η = viscosity of the fluid, Pa·s

Consider the units in the numerator in equation (9)

$$Du\rho = \text{m}\times\frac{\text{m}}{\text{s}}\times\frac{\text{kg}}{\text{m}^3} = \frac{\text{kg}}{\text{s}\cdot\text{m}}$$

Consider the units in the denominator in equation (9).

$$\eta = \text{Pa}\cdot\text{s} \qquad (10)$$

Since, Pa = $\text{kg/m}\cdot\text{s}^2$, it can be substituted in equation (10)

$$\eta = \frac{\text{kg}\times\text{s}}{\text{m}\times\text{s}^2} = \frac{\text{kg}}{\text{m}\cdot\text{s}}$$

Therefore, equation (9) may be written as:

$$Re = \frac{\text{kg/m}\cdot\text{s}}{\text{kg/m}\cdot\text{s}} = \text{dimensionless number}$$

Hence equation (9) is considered as dimensionless equation.

Consider another equation as a variation. For example, falling of a body in time, t, can be expressed as:

$$S = ut + (^1/_2)gt^2 \qquad (11)$$

where S = vertical distance, length
u = initial velocity, distance/time
t = time
g = acceleration due to gravity, distance/time^2

In equation (11), first and second terms are expressed separately as follows:

$$ut = \text{velocity} \times \text{time} = \frac{\text{distance (length)}}{\text{time}} \times \text{time} = \text{distance (length)}$$

$$\frac{1}{2}gt^2 = \frac{\text{distance (length)}}{\text{time}^2} \times \text{time}^2 = \text{distance (length)}$$

Each term has the units of length. Equation (11) can be made dimensionless by dividing by 'S'.

$$I = \frac{ut}{S} + \frac{I}{2} \bullet \frac{gt^2}{S} \qquad (12)$$

In equation (12), the dimensions get cancelled and each term is dimensionless.

The **advantages** of dimensionless equations are:

1. Unit of any system (cgs or fps or SI) can be used without introducing conversion factors. For example, length in either metres or feet can be substituted in equation (11).
2. Dimentionless equations are based on theoretical principles. They contain variables affecting the physical process.

Dimensional Equations

Dimensional equation is defined as an equation, which contains terms of varying dimensions as it is obtained by empirical methods.

Experimental results are correlated by empirical means. Therefore, dimensional consistency is ignored. Such equations are also known as *dimensionally non-homogeneous equations.*

For example, the rate of heat loss (by conduction and convection) from a horizontal pipe to the atmosphere may be written as:

$$\frac{q_c}{A} = 0.5\,\frac{(\Delta t_s)^{1.25}}{(D'_o)^{0.25}} \qquad (13)$$

where q_c = loss of heat, Btu/h

A = pipe surface, ft^2

Δt_s = excess of temperature of the pipe wall over that of atmosphere, °F

D'_o = diameter of the pipe, in

The quantities substituted for the terms must be expressed in the units mentioned above. For example, D'_o may be substituted only in inches, not in feet. The reasons are that the numerical coefficients such as 0.5, 1.25 and 0.25 are applicable for those units.

The **disadvantage** of this equation is that it has limited applications. It is particularly used for calculations of a system under specified conditions.

Dimensional Analysis

In the pharmaceutical engineering, many physical problems have been solved completely by theoretical and mathematical methods. On the other hand, there are still many situations wherein empirical relationships have been established over a period of time; since theoretical relationships have failed to satisfy experimental results. Common examples related to these problems are - fluid flow, heat flow and mass transfer.

Dimensional analysis is an important tool to convert the empirical relationships into theoretical principles on a rational basis.

Dimensional analysis assumes that there must exist a relationship among all the factors affecting a process. This technique involves the following steps.

(1) All the factors are to be identified, which are important in the problem. Initial stages, empirical relationship may be adequate.

(2) These factors are grouped together into fewer numbers and expressed as dimensionless groups.

(3) Such groups are entered into final equation.

(4) Such equations are correlated to the possible physical laws.

(5) A possible mathematical solution is obtained.

In the above analysis, the first step is to consider the units for the verification of factors. For example, in the experiments on the fluid flow, the factors involved are listed below.

- pipe diameter (D), m
- velocity (u), m/s
- viscosity (η), Pa·s
- density (ρ), kg/m^3

These factors are varied as one at a time. Then the results are combined. It is shown by dimensional analysis that these factors must appear in a dimensionless group as shown below.

$$\frac{Du\rho}{\eta} \text{ or } \mathrm{m}\,\frac{\mathrm{m}}{\mathrm{s}} \bullet \frac{\mathrm{kg}}{\mathrm{m}^3} \bullet \frac{1}{\mathrm{Pa{\cdot}s}} = \frac{\mathrm{kg}}{\mathrm{s{\cdot}m{\cdot}Pa}} = \frac{\mathrm{m{\cdot}s^2{\cdot}kg}}{\mathrm{m{\cdot}s^2{\cdot}kg}}$$

This equation is expressed as Reynolds number, which has no dimensions. This example illustrates the success of the dimensional analysis. But heat transfer experiments on fluids involve about 11 factors. A total of five different expressions are obtained. Still dimensional analysis could provide a satisfactory equation to describe the heat transfer process.

Advantages : (1) Dimensional analysis reduces drastically the number of independent variables that effect the problem.

(2) This analysis does not yield numerical values in the equation.

(3) This helps in constructing dimensionless (dimensionally homogeneous) equation.

(4) Very useful for any system of units (cgs or fps or SI).

Disadvantages : Dimensional analysis is a difficult process, if enough knowledge is not available about the physics of the situation.

STOICHIOMETRIC EQUATIONS—BALANCING

Stoichiometry means carrying out of calculations based on quantitative relationships.

The numerical problems involving the use of stoichiometric equations are known as *stoichiometric calculations.*

A chemical reaction is a symbolic representation of a chemical change. Each chemical reaction is expressed in the form of an equation. This is obtained by balancing the atoms of each of the species involved in the reaction. The initial constituents that take part in the reaction are called the *reactants*, and the final constituents that are formed by the reaction are called the *products*. For example, hydrogen and oxygen react to form water. This reaction is expressed as:

$$\text{Skeleton equation: } H_2 + O_2 \longrightarrow H_2O \qquad (14)$$

In equation (14), two hydrogen atoms are present on each side. On the left side, two oxygen atoms are present and on right side one oxygen atom is present. Moles can be multiplied or divided by smallest possible integer to obtain a balanced equation. Hence, equation (14) may be balanced as:

$$H_2 + (^1/_2)O_2 \longrightarrow H_2O \qquad (15)$$

$$\text{Balanced equation: } 2H_2 + O_2 \longrightarrow 2H_2O \qquad (16)$$

Equation (16) indicates that one mole of hydrogen and half mole of oxygen combine to form one mole of water. The reaction may also takes place in reverse direction. The coefficients 2, 1 and 2 in equation (16) are called *stoichiometric coefficients.*

According to the law of conservation of mass, total mass of reactants must be equal to the total mass of products in a reaction. In other words, the number of atoms of each kind in the reactants and products must be the same.

A *balanced chemical equation* indicates the exact number of various elements participating in the reaction.

Balancing is done by inspection. Balanced chemical equations are quantitative expressions of chemical changes. Hence, they enable us to work out the masses of substances reacting together. A few examples are given below.

Applications : (1) Stoichiometric equations (and balancing) helps in understanding the quantitative relationship between different reactants. For example, the ratios 2:1 (equation 16), 1:1 (equation 14) etc.

(2) The amount of reactants to be added for carrying out a reaction can be determined theoretically.

Practice Problem 1-5. Nitrogen combines with hydrogen under suitable conditions to form ammonia. Write the equation and balance it.

Solution: Nitrogen and hydrogen are bi-atomic molecules. The formula of ammonia is NH_3. The reactants and products can be written as:

$$\text{Skeleton equation: } N_2 + H_2 \longrightarrow NH_3 \qquad \text{(i)}$$

Nitrogen atoms on both sides of equation (i) can be balanced by multiplying NH_3 by 2. In the next step, hydrogen atoms can be made equal both sides by multiplying H_2 by 3. Now, the balanced equation becomes:

$$\text{Balanced equation: } N_2 + 3H_2 \longrightarrow 2NH_3 \qquad \text{(ii)}$$

Practice Problem 1-6. Carbon combines with oxygen to give carbon dioxide. Write chemical equation and balance it.

Solution: Carbon normally exists in mono-atomic state (C). Oxygen exists as diatomic (H_2). Carbon dioxide is represented by CO_2. Then the skeleton equation may be written as:

$$\text{Skeleton equation: } C + O_2 \longrightarrow CO_2 \qquad \text{(i)}$$

The number of elements present on the left-hand side of equation (i) is equal to the right-hand side of the equation. Therefore, balanced equation is same as the skeleton equation.

Practice Problem 1-7. Write the balanced equation for the combustion of ethane.

Solution: Combustion means complete oxidation of a substance in the presence of air (oxygen). The products of combustion are normally carbon dioxide and water. Therefore, the equation of the combustion of ethane may be written as:

$$\text{Skeleton equation:}\quad C_2H_6 + O_2 \longrightarrow H_2O + CO_2 \qquad \text{(i)}$$

On the left side of equation (i), the number of carbons is two, while on right hand-side the number of carbon is one. Therefore, multiply CO_2 by 2. Then, equation (i) can be changed with respect to carbons as:

$$C_2H_6 + O_2 \longrightarrow H_2O + 2CO_2 \qquad \text{(ii)}$$

On the left hand-side of equation (ii), the number of hydrogen atoms is six, while on the right hand-side, hydrogen atoms are two. Therefore, multiply H_2O by 3. Then equation (ii) changes with respect to hydrogen as:

$$C_2H_6 + O_2 \longrightarrow 3H_2O + 2CO_2 \qquad \text{(iii)}$$

On left hand-side of equation (iii), the number of oxygen atoms is two, while on the right hand-side, the oxygen atoms are seven (3 + 4). Therefore, multiply O_2 by 7/2. Then, equation (iii) can be changed with respect to hydrogen as:

$$C_2H_6 + (7/2)O_2 \longrightarrow 3H_2O + 2CO_2 \qquad \text{(iv)}$$

The equation (iv) is balanced. But fractions can be removed by multiplying the entire equation by 2. Then, the balanced equation is:

$$\text{Balanced equation:}\quad 2C_2H_6 + 7O_2 \longrightarrow 6H_2O + 4CO_2 \qquad \text{(v)}$$

The above examples illustrated the methods of balancing chemical equations.

Practice Problem 1-8. Calculate the mass of oxygen obtained by the complete decomposition of 5.0 g of potassium chlorate (K = 39.1; Cl = 33.5; O = 16).

Solution: The equation for the given reaction may be written as:

$$KClO_3 \longrightarrow KCl + O_2$$

Balancing of equation can be with respect to the number of moles of oxygen.

$$2KClO_3 \longrightarrow 2KCl + 3O_2$$

In other words, 2 moles of $KClO_3$ yield 3 moles of oxygen.

2[39.1 + 35.5 + 3(16)] g of $KClO_3$ yields 3(2 x 16) g of oxygen

245.2 g of $KClO_3$ yield 96 g of oxygen

5.0 g of $KClO_3$ yield ? g of oxygen

$$\frac{96 \times 5.0}{245.2} = 1.958 \text{ g of oxygen}$$

The mass of oxygen obtained is **1.958 g.**

Glossary of Symbols

A = Pipe surface, ft²
cgs = Centimetre-gram-second.
D = Pipe diameter, m.
η = Viscosity, Pa·s.
F = Driving force.
fps = Foot-pound-second.
g = Acceleration due to gravity, m/s².
M = Molecular weight of individual components.
mks = Metre-Kilogram-second.
n = Number of moles.
R = Resistance.
R = Rankine.
ρ - Density, kg/m³.
S = Vertical distance, m.
SI = Systeme Internationale.
u = Velocity, m/s.
t = Time, s.
W - Weight of individual components.

QUESTION BANK

Each question carries 2 marks

(1) Describe the principle of stoichiometry with a suitable example.
(2) Highlight the importance of unit operations in pharmaceutical engineering
(3) Describe the molecular concept of stoichiometry.
(4) Give an expression to calculate the average molecular weight of a mixture.
(5) How is the rate of a reaction expressed?
(6) Distinguish between steady state and non-steady state.
(7) Distinguish between equilibrium and steady state.
(8) Define the term 'dimensionless equation' with the help of an example.
(9) Define dimensional equation. What are its limitations?
(10) Define the term 'dimensionless equation'. What are its advantages?

Each question carries 5 marks.

(1) Describe 'unit operation' and 'unit process'. Give two examples each.

(2) Explain the term 'unit operation'. Describe the basic principles of various unit operations used in pharmaceutical and other associated industries.

(3) Explain the term 'mass balance' and 'energy balance'. What are its applications?

(4) Give an account of unit systems and their inter-conversions.

2

Flow of Fluids

Fluid Statics
Fluid Dynamics
Bernoulli's Theorem
Energy Losses
Measurement of Rate of Flow of Fluids

Fluid flow may be defined as the flow of substances that do not permanently resist distortion.

This definition covers the flow of liquids and gases. Fluid is considered to be a mass of a substance formed by a series of layers. When an attempt is made to change its shape, the layers of fluid slide over one another, until a new shape is attained. At the end, the fluid is relieved off the stresses that it encountered during the flow.

Flow of fluids is observed while handling materials.

(a) **Handling of liquids :** Transportation of materials such as solvents, solutions and suspensions is simpler, cheaper and less troublesome than handling of solids in industrial operations.

(b) **Handling of solids :** Solids are handled in a finely divided state in the form of suspension of fluids, so that transportation becomes easy. This two-phase mixture is known as *'fluidised solids'*.

During the handling process, the behaviour of liquids changes transiently. Such changes have profound influence on heat transfer process, energy losses during pumping, energy changes in pumping etc. Therefore, fluid flow is treated independently.

Flow of fluids is involved in a number of areas of pharmaceutical industries. Some of them are:

Passing of reactants (liquids or gases) into the reaction system.
Transferring of air, nutrient broth into the fermenter.
Bottling of liquid (dosage forms) medicaments into suitable containers.

Transporting of sterile air and sterile water in the production of parenterals.
Mixing of solids and liquids in case of suspensions.
Packing of semisolids in containers.

The nature of flow influences the type of equipment used for handling. Flow characteristics through pipes and channels are relevant. At the same time, the measurement of rate of flow is necessary for the quantification of additives (reactants) into a process.

The subject of fluid flow can be divided into fluid statics and fluid dynamics.

- *Fluid statics* deals with fluids at rest in equilibrium.
- *Fluid dynamics* deals with fluids in motion.

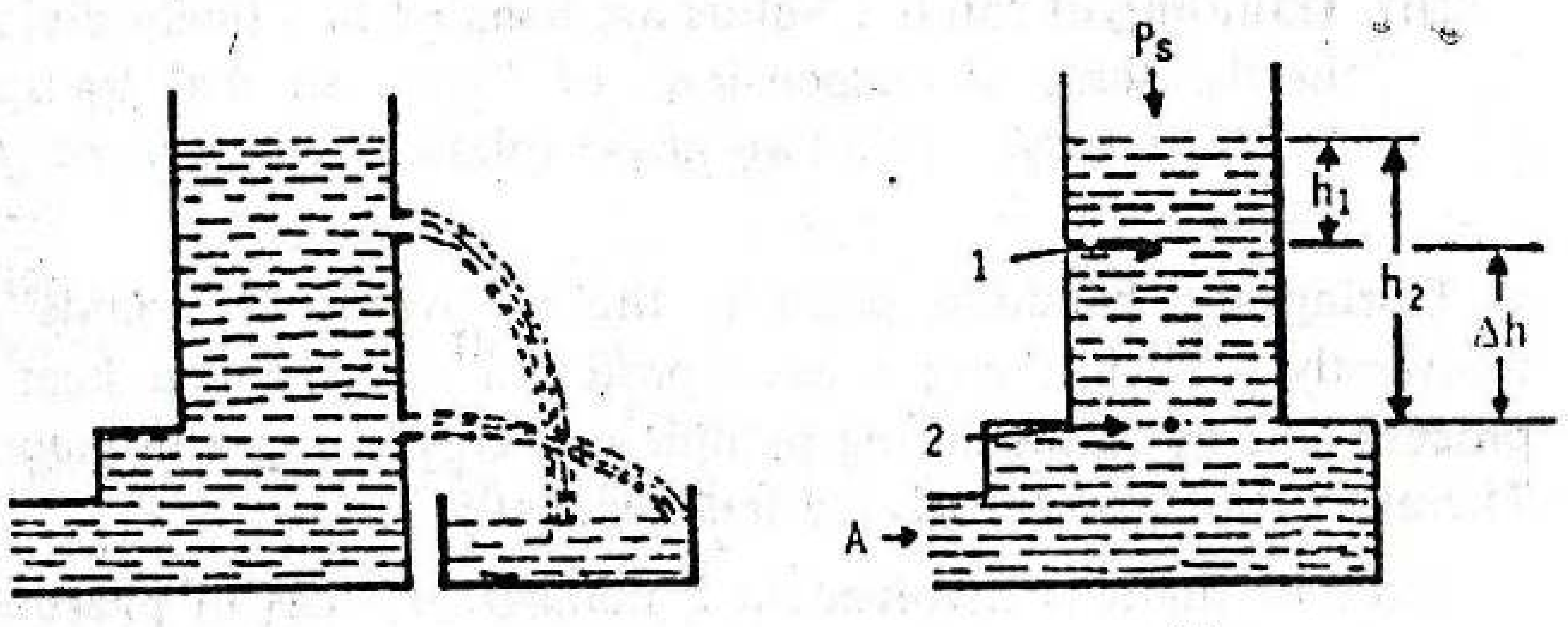
FLUID STATICS

Fluid statics deals with the fluids at rest in equilibrium. The behaviour of a liquid at rest, the nature of pressure it exerts and the variation of pressure at different layers in the liquid are some of the relevant aspects in the pharmaceutical engineering.

Pressure Difference Between Layers of Liquids

Consider a column of liquid as shown in Figure 2-1(a). Two openings are provided to the wall of the vessel at different heights. The rate of flow from these openings is different (Figure 2-1a). This is due to the differences in the pressures exerted at different heights. This behaviour can be quantitatively expressed as follows.

Consider a stationary column of fluid as shown in Figure 2-1(b). The pressure P_s pascals is acting on the surface of the fluid. The stationary column is maintained at constant pressure by applying pressure, P pascals at point A.



(a) (b)

Figure 2-1. Hydrostatic pressure observed at different layers of a stationary column.

Let the cross-section of the column be S metre square and is uniform from top to bottom. The force (further pressure) acting on the liquid at different levels of the liquid column can be determined. The forces (newton) acting on each side (horizontal components) of the point 1 are mutually nullified. The forces in newtons acting below and above the point 1 are evaluated.

Force acting on the liquid at point 1 = force on the surface + force exerted by the liquid above the point 1 (1)

Substituting the force with pressure × area of cross section (S) in equation (1) gives:

Pressure at point 1 × surface area = (Pressure on the surface × surface area) + (mass × acceleration) (2)

$$P_1S = P_sS + \text{volume} \times \text{density} \times \text{acceleration due to gravity}$$
$$= P_sS + \text{height} \times \text{area} \times \text{density} \times \text{acceleration due to gravity}$$

$$P_1S = P_s\,S + h_1S\rho g \quad (3)$$

Since cross sectional surface area is same, equation (3) may be written as:

$$P_1 = P_s + h_1\rho g \quad (4)$$

Similarly, the pressure acting on the liquid at point 2 may be written as:

$$P_2 = P_s + h_2\rho g \quad (5)$$

The difference in the pressure may be obtained by subtracting equation (4) from equation (5) as:

$$P_2 - P_1 = g\,(P_s + h_2\rho) - (P_s + h_1\rho)g$$
$$\Delta P = (P_s + h_2\rho - P_s - h_1\rho)g$$
$$\Delta P = (h_2 - h_1)\rho g$$
$$= \Delta h\rho g \quad (6)$$

Therefore, the pressure difference (ΔP pascals) between any two points can be measured by the distance between those points in a fluid. If the density of fluid (ρ kilogram per metre cube) varies with variation of pressure, an average density could be used. The variation in densities is quite negligible for liquids and gases. Since the difference in the heights (Δh metre) is necessary for the measurement, height can be measured from the bottom of the stationary column.

Applications : The principle of fluid statics is employed in the working of manometers. In such cases, the pressure difference (ΔP) is measured in terms of difference in the heights of the liquid column. It is also applied for quantification of fluid flow as in Bernoulli's theorem.

Manometers

Manometers are the devices used for measuring the pressure difference. Three different manometers are available. These are:

1. Simple
2. Differential
3. Inclined

The principles and applications of these manometers are discussed in the following sections.

Simple manometer : This manometer is the most commonly used. The construction of a simple manometer is shown in Figure 2-2. It consists of a glass U tube filled with a liquid (A) of density, ρ_A kilogram per metre cube. Above liquid A, the arms are filled with liquid B of density ρ_B kilogram per metre cube. The liquids A and B are immiscible and the interface can be seen clearly.

If two different pressures are applied on the two arms, the meniscus of liquid A will be higher in one arm than the other (Figure 2-2). Let the pressure at point 1 is P_1 pascals in left hand-side of the limb. Let the pressure at point 5 is P_2 pascals in the right hand-side of the limb. From the principles of fluid statics, the pressure at point 2 can be written as:

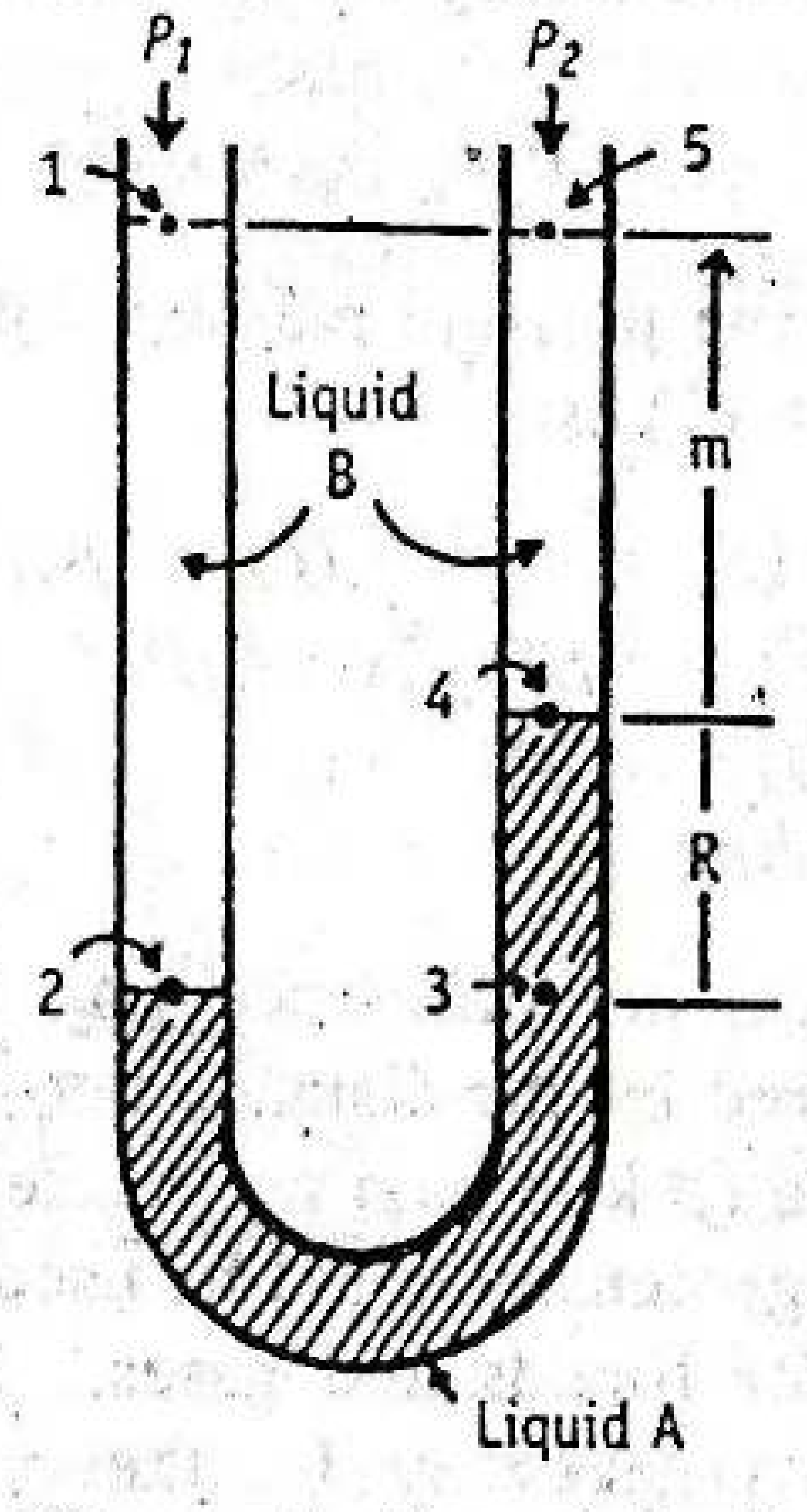


Figure 2-2. The construction of simple manometer.

$$\text{Pressure at point } 2 = P_1 + (m+R)\rho_B g \qquad (7)$$

where (m+R) = distance from points 3 to 4 + distance from points 4 to 5.

Since, points 2 and 3 are at the same level, the pressure at point 3 may be written as:

$$\text{Pressure at point } 3 = P_1 + (m+R)\rho_B g \qquad (8)$$

The pressure at point 4 can be written from the right hand-side of the limb (from P_2) as:

$$\text{Pressure at point } 4 = P_2 + gm\rho_B \qquad (9)$$

In another manner, the pressure at point 4 can be written from point 3 (i.e., from left hand-side) as:

$$\text{Pressure at point } 4 = P_1 + \rho_B(m + R)g - \rho_A Rg \qquad (10)$$

Equations (9) and (10) represent the pressure at point 4 only. Hence, these equations should be equal. This relationship may be written as:

$$P_1 + g\rho_B(m + R) - \rho_A R\, g = P_2 + gm\rho_B$$
$$P_1 - P_2 = gm\rho_B - \rho_B(m + R)g + \rho_A Rg$$
$$\Delta P = m\rho_B g - m\rho_B g - R\rho_B g + R\rho_A g$$
$$\Delta P = R(\rho_A - \rho_B)g \qquad (11)$$

The important conclusions drawn from equation (11) are:

(1) It is easy to measure R value (metres), i.e., the difference in the levels of liquid A in the two limbs.

(2) The value ΔP pascals is independent of the value of m and also the dimensions of the U tube.

When wide ranges of pressure are applied, the sensitivity of liquids employed in the measurement is important. If the pressure differences are large, mercury (high density, liquid A) can be used as manometric liquid. If the pressure differences are small, liquids such as alcohol, water (for gases) and carbon tetrachloride are used.

Applications: (1) Simple manometer helps in measuring the consumption of gases in the chemical reactions. (2) Manometers are used in conjunction with flow meters for the measurement of flow of fluids. For example, venturi meter and orifice meter are used for the measurement of pressure head using a manometer. Pitot tube measures the velocity head using a manometer.

Differential manometers : Differential manometers find occasional applications. This manometer is suitable for measurement of small pressure differences. It is a sensitive device and useful for measuring even small gas pressures (heads).

The construction of a differential manometer is given in Figure 2-3. The differential manometer is also known as *two-fluid U-tube manometer*. It contains two immiscible liquids A and B having nearly same densities. The U tube consists of enlarged chambers on both limbs. Hence, the meniscus of the liquid in these enlarged chambers does not change appreciably with changes in the reading *R*.

Using the principle of simple manometers, the pressure difference (ΔP pascals) can be written as:

$$\Delta P = P_1 - P_2 = R(\rho_C - \rho_A)g \qquad (12)$$

Equation (12) indicates that the smaller the difference ($\rho_C - \rho_A$), the larger will be reading on the manometer (R metres) for a given value of ΔP.

Micromanometers based on the liquid column principle are available commercially. They measure the reading with extreme precision and sensitivity. These are free from errors due to capillarity and require no calibration, apart from checking the micrometer scale.

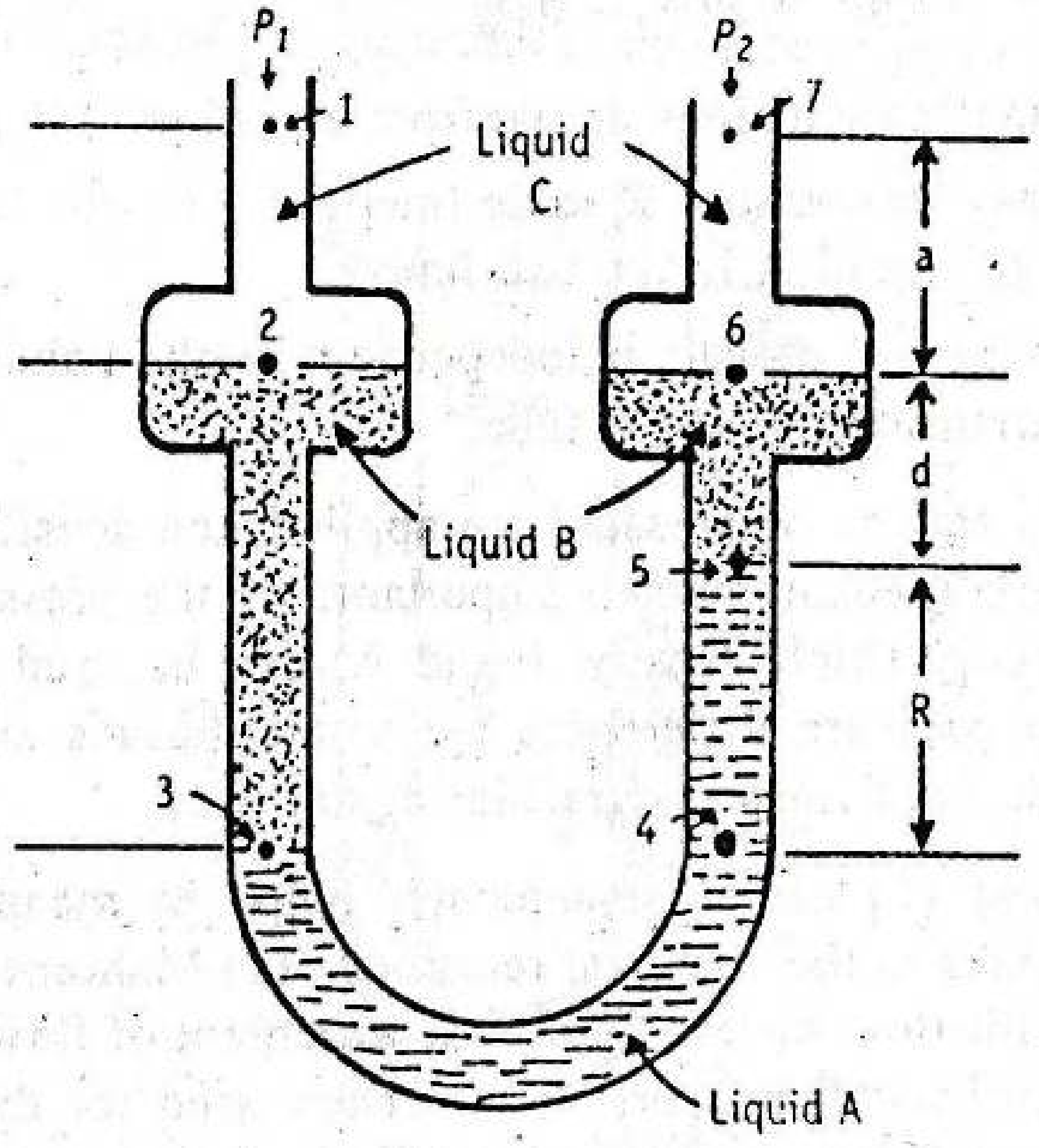


Figure 2-3. Construction of a differential manometer.

Inclined manometers : They have limited applications and, therefore, not discussed here.

FLUID DYNAMICS

Fluid dynamics deals with the study of fluids in motion.

Study of flow properties of liquids is important for pharmacists working in the manufacture of dosage forms, such as simple liquids, gels, ointments, creams and pastes. These systems change their flow behaviour, when exposed to different stress conditions in the following situations.

(1) **Manufacture of dosage forms :** Materials undergo processes such as mixing, flowing through pipes and getting filled in the containers. Flow related changes influence the selection of mixing equipment.

(2) **Handling of drugs for administration :** The syringeability of the medicines, pouring of the liquids, extrusion of ointment from tubes etc., depend on the changes in flow behaviour of dosage forms.

Thus, flow behaviour of liquids is of relevance in pharmacy. Performance of a product depends on the net effect of all the above mentioned processes. Therefore, flow properties are used as important quality control tools to maintain the superiority of the product and to reduce the batch to batch variations.

In general, engineering of fluid flow considers the macroscopic properties. The molecular level interactions are beyond the scope of this book (Refer the book *Physical Pharmaceutics* by C.V.S. Subrahmanyam, Vallabh Prakashan).

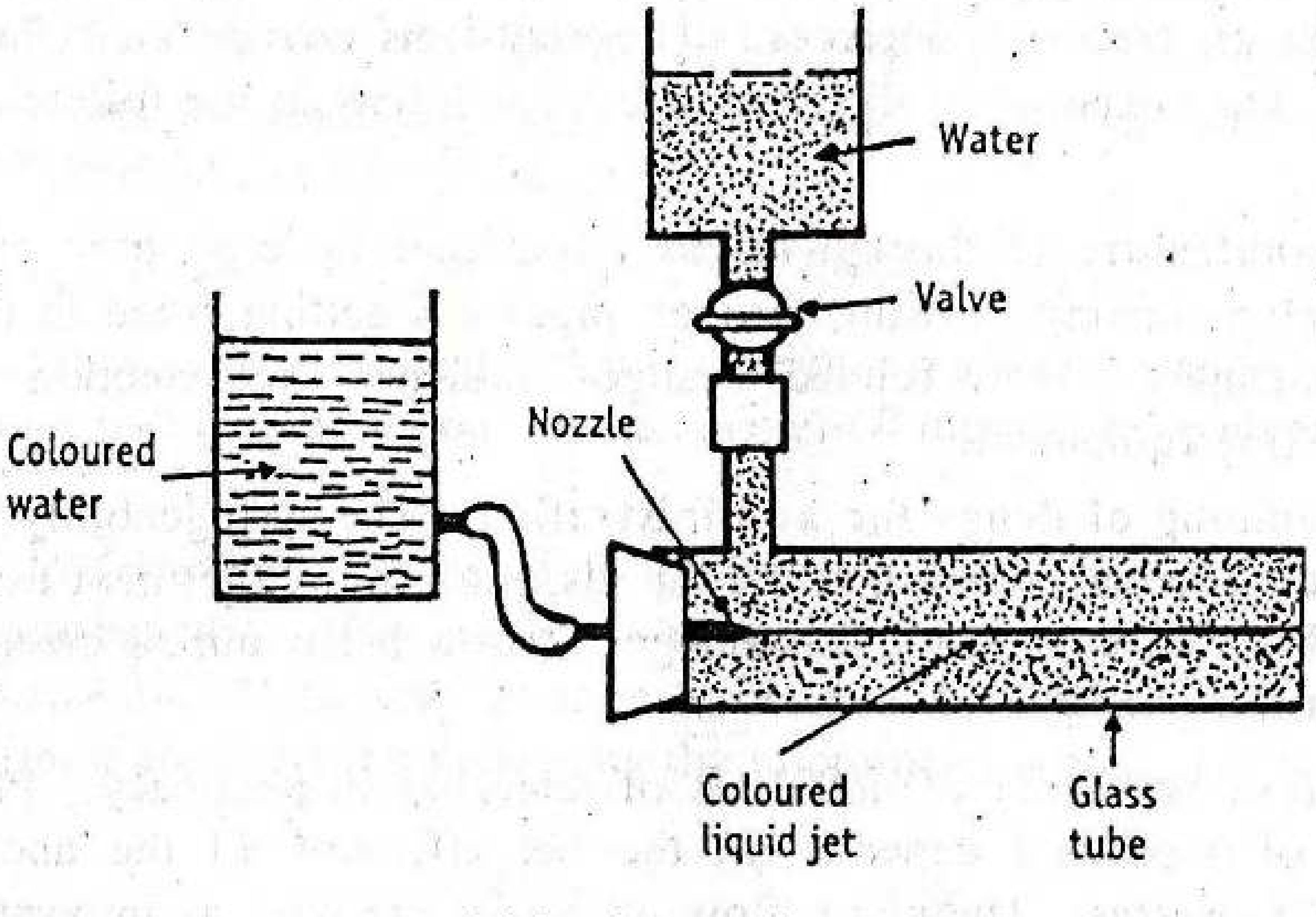
Nature of Fluid Flow–Reynolds Experiment

The flow of fluid through a closed channel (pipeline) can be either viscous or turbulent. These can be observed in the classical Reynolds experiment.

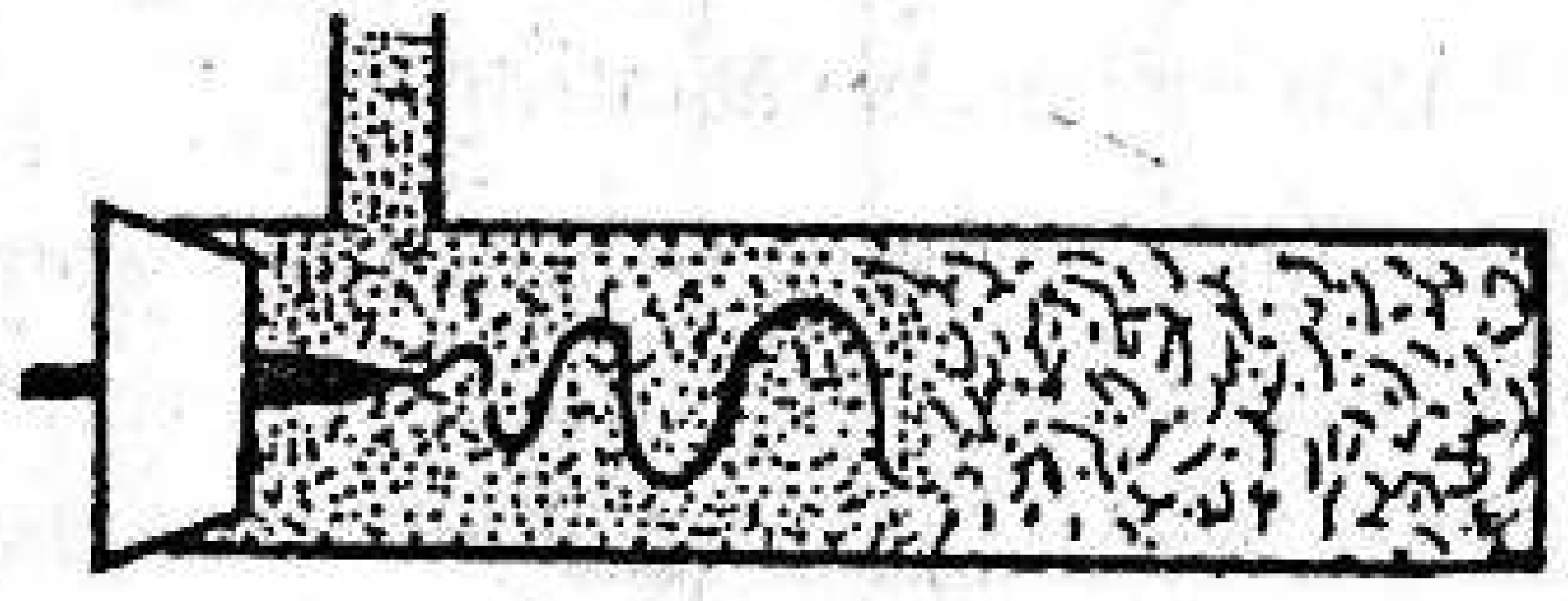
The assembly of the apparatus for the Reynolds experiment is shown in Figure 2-4.

A glass tube is connected to a reservoir of water as shown in Figure 2-4. The rate of flow of water through the tube can be increased or decreased at will through a valve. A reservoir of coloured solution is connected to one end of the glass tube with the help of nozzle(s). Therefore, coloured solution can be introduced into the glass tube as a fine stream. From this experimental setup, the following observations may be made and conclusions can be drawn.

(a) When the velocity of water is low, the thread of coloured water maintains its identity throughout the tube. By introducing similar jets of coloured water at different points in the cross section of the glass tube, it can be noted that no part of the tube exhibits the signs of mixing. In other words, the colour streams are seen as parallel lines. The flow of water is considered to be *viscous or streamline or laminar.*



(a) Laminar or viscous flow.



(b) Turbulent flow.

Figure 2-4. The assembly of the apparatus of the Reynold's experiment.

A *laminar flow* is one in which the fluid particles move in layers or laminar with one layer sliding over the other. Therefore, there is no exchange of fluid particles from one layer to the other. Hence, transfer of lateral momentum to the adjacent layers is not observed.

(b) When the velocity of water is increased (by increasing the flow rate), the threads of coloured water disappear and the entire mass of water gets uniformly coloured. It indicates complete mixing of solution. Then, the flow of water is considered to be *turbulent.*

When the flow attains a certain velocity, it no longer remains steady and eddy currents appear. All the fluid particles are disturbed and get mixed up with each other. Thus, there is a continuous transfer of momentum to adjacent layers. Such a diffused flow is called *turbulent flow.*

(c) The change over of the flow from viscous to turbulent is a critical factor.

Critical velocity is defined as average velocity of any fluid at which viscous flow changes into turbulent flow.

Reynolds number : In Reynolds experiment, the flow conditions are affected by four factors.

Diameter of pipe, m (D)
Average velocity, m/s (u)
Density of liquid, kg/m^3 (ρ)
Viscosity of the fluid, Pa·s (η)

These factors are grouped into a particular expression as given below.

$$\text{Reynolds number, } Re = \frac{Du\rho}{\eta} \qquad (13)$$

Reynolds number is obtained by the following equation.

$$\text{Reynolds number, } Re = \frac{\text{inertial forces}}{\text{viscous forces}} = \frac{\text{mass} \times \text{acceleration of liquid flowing}}{\text{shear stress} \times \text{area}}$$

Inertial forces are due to mass and the velocity of the fluid particles trying to diffuse the fluid particles. The viscous force is the frictional force due to the viscosity of fluid, which makes the motion of fluid in parallel layers.

Therefore, at low velocities, the inertial forces are less when compared to the frictional forces caused by the viscosity. The resulting flow will be viscous in nature, i.e., the particles move in parallel layers. For this reason, laminar flow is sometimes known as *viscous.* On the other hand, when inertial forces are predominant, the fluid layers break up due to the increase in velocity, hence, turbulent flow takes place.

It is a dimensionless group, because the units of factors mutually get cancelled. If $Re < 2000$, the flow is said to be laminar and if $Re > 4000$, the flow is said to be turbulent. If Re lies between 2000 to 4000, the flow changes from laminar to turbulent.

Applications : (1) Reynolds number is used to predict the nature of flow (viscous or turbulent) in a particular set of experimental conditions. (2) The physical stability of suspensions (or emulsions) depends on the rate of settling of particles (or globules). For the study of sedimentation of particles, Stokes' law is used. In this study, rate of sedimentation of particles must not be too rapid to create turbulence. Therefore, type of flow (whether laminar or turbulent) is important. Accordingly Stokes' equation is modified to include Reynolds number. (3) The rate of heat transfer in liquids also depends on the flow, whether viscous or turbulent.

Variation in the Velocity of Flow Across the Cross-Section

When the local velocity of the fluid is plotted against distance from the wall (Figure 2-5), the following conclusions can be drawn.

- The flow of fluid in the middle of the pipe is faster than the fluid nearer to the wall.
- The velocity of fluid approaches zero as the pipe-wall is approached.
- At the actual surface of the pipe-wall, the velocity of the fluid is zero.

Since variations are observed in velocity of flow across the cross section, there should be some means of estimating average velocity.

- In viscous conditions, the average velocity over the whole cross section is 0.5 times the maximum.
- In turbulent flow, the average velocity over the whole cross section is 0.8 times the maximum.

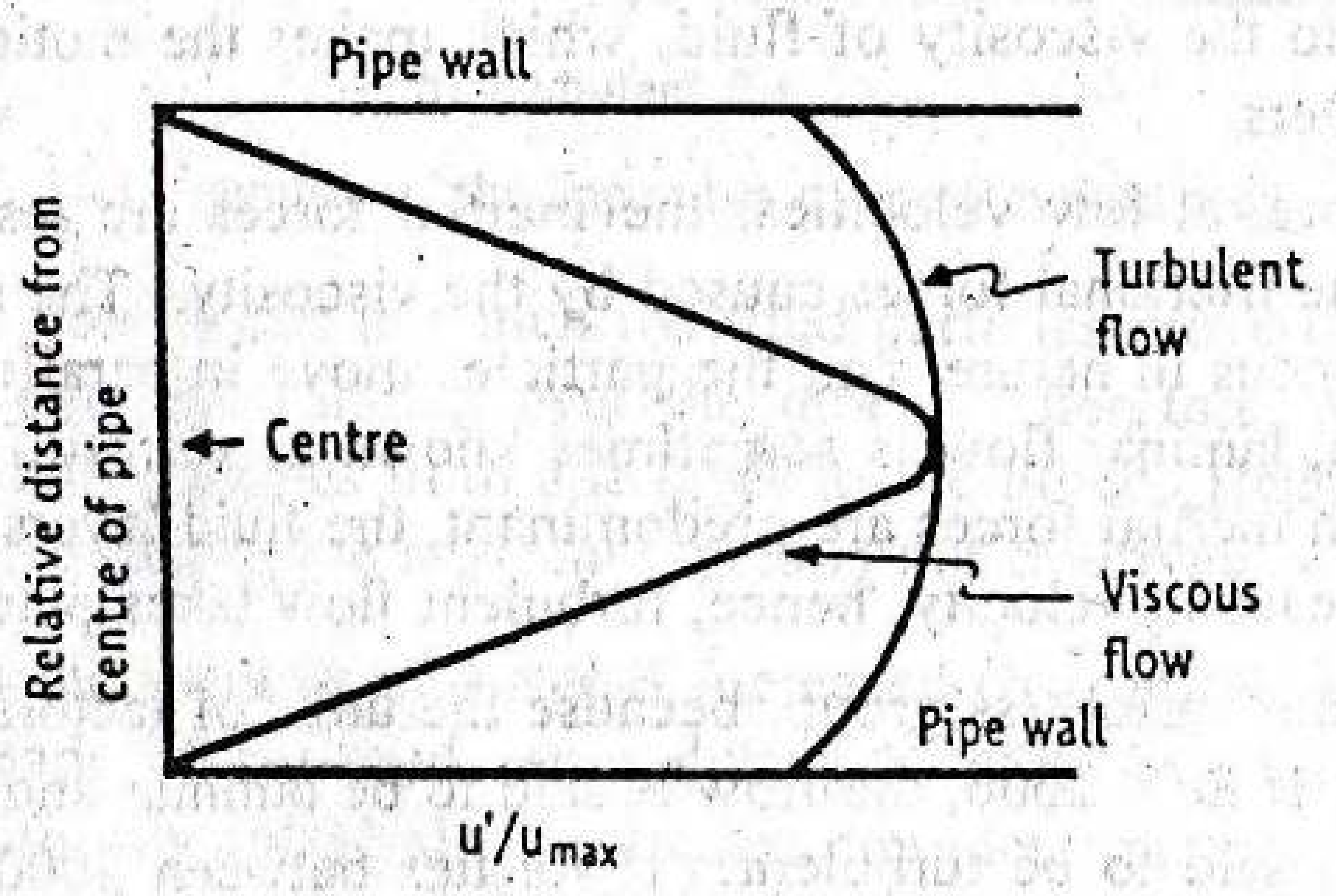


Figure 2-5. Distribution of fluid velocities across the cross section of a pipe

- Since the velocity of the fluid is zero at the wall surface, there should be some layers in viscous flow near the pipe-wall, which acts as a stagnant layer.
- Even if the flow is turbulent at the centre (of the pipe) and viscous at the surface of the wall, a buffer layer exists.
- A gradual transition from one region to another, there exists a boundary layer which is known as buffer layer. This buffer layer oscillates between viscous flow and turbulent flow.

It must be emphasized that boundary layer can never be eliminated. Increasing the velocity of the fluid over the surface will reduce the thickness of the layer, but it will be never eliminated entirely.

Applications : (1) Though the general principles are mentioned above, considerable variation in velocity distribution may be possible with changes in roughness, direction, temperature or cross section of the pipe. Due to these reasons, the shape of curves may be changed. (2) The nature of flow of liquids in pipes determines the rate of heat transfer. The buffer layer in turbulent flow and stagnant layer in viscous flow offer resistance to heat transfer. Further discussion on rate of heat transfer is dealt in Chapter 5 'Flow of Heat'.

BERNOULLI'S THEOREM

When the principle of conservation of energy is applied to the flow of fluids, the resulting equation is called Bernoulli's theorem.

Pumps generally supply energy for conveying liquids from one point to another. Consider such a pump working under isothermal conditions between points A and B, as shown in Figure 2-6.

Bernoulli's theorem states that in a steady state ideal flow of an incompressible fluid, the total energy per unit mass, which consists of pressure energy, kinetic energy and datum energy, at any point of the fluid is constant.

At point A, one kilogram (unit mass) of liquid is assumed to be entering. At this point, liquid experiences pressure energy, kinetic energy and potential energy, which are obtained as follows.

Since liquid is flowing through the pipe at certain pressure, pressure energy in joules may be written as:

$$\text{Pressure energy} = \frac{P_A}{g\rho_A} \qquad (14)$$

where P_A = Pressure at point A, Pa
g = acceleration due to gravity, m/s
ρ_A = density of the liquid, kg/m^3

Potential energy (datum energy) of a body is defined as the energy possessed by the body by virtue of its position or configuration. The point A is considered at a height of X_A metres above the horizontal datum plane. The potential energy for one kilogram of liquid may be written as:

$$\textit{Potential energy} = X_A \tag{15}$$

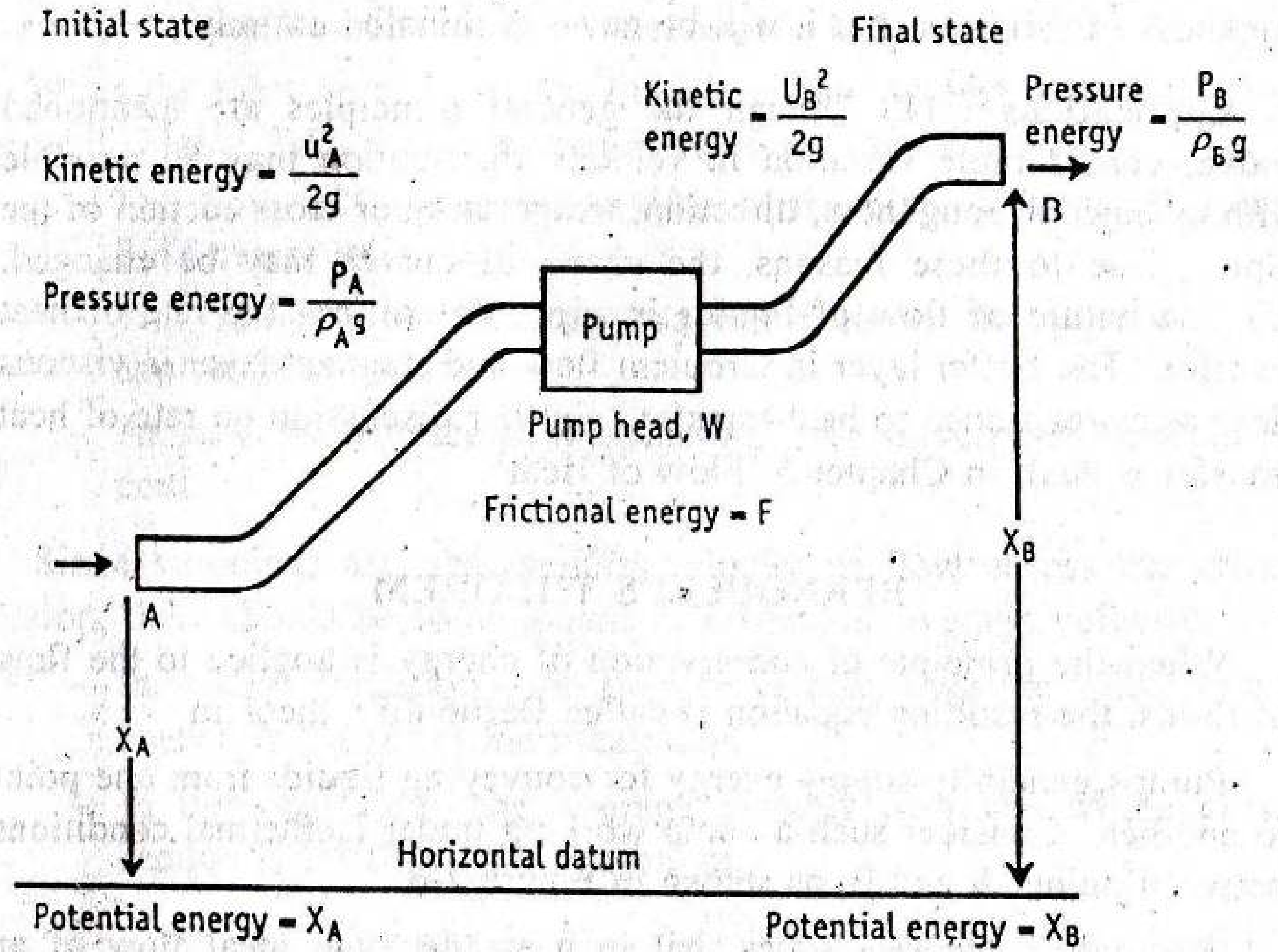


Figure 2-6. Development of Bernoulli's theorem.

Kinetic energy of a body is defined as the energy possessed by the body by virtue of its motion. Since liquid is under motion, the velocity of liquid may be designated as u_A metre per second at point A. The kinetic energy may be expressed as:

$$\textit{Kinetic energy} = \frac{u_A^2}{2g} \tag{16}$$

The total energy at point A may be summarised by combining equations (14), (15) and (16) as:

Total energy = pressure energy + potential energy + kinetic energy

$$\textit{Total energy at point } A = \frac{P_A}{g\rho_A} + X_A + \frac{u_A^2}{2g} \tag{17}$$

According to Bernoulli's theorem the total energy at point A is constant. Therefore, equation (17) is:

$$\textit{Total energy at point } A = \frac{P_A}{g\rho_A} + X_A + \frac{u_A^2}{2g} = \text{constant} \tag{18}$$

After the system reaches the steady state, whenever one kilogram of liquid enters at point A, another kilogram of liquid leaves at point B. Therefore, energy content of one kilogram liquid that is being displaced at point B may be written (Bernoulli's theorem) as:

$$\textit{Total energy at point } B = \frac{P_B}{g\rho_B} + X_B + \frac{u_B^2}{2g} = \text{constant} \tag{19}$$

where X_B = height from the datum to the pipe, m
u_B = velocity at point B, m/s
P_B = pressure at point B, Pa
ρ_B = density at point B, kg/m^3

If there is no gain or loss of energy, the principle of conservation of energy may be applied to the two points A and B.

INPUT = OUT PUT

Total energy at point A = Total energy at point B

$$\frac{P_A}{g\rho_A} + X_A + \frac{u_A^2}{2g} = \frac{P_B}{g\rho_B} + X_B + \frac{u_B^2}{2g} \tag{20}$$

Theoretically all kinds of energies involved in fluid flow should be accounted. In the transportation of fluid, the pump has added certain amount of energy, which can be written as:

$$\textit{Energy added by the pump} = + wJ \tag{21}$$

During the transportation of liquid, some energy is converted to heat due to frictional forces and it is inevitable. The energy loss may be written as:

$$\textit{Loss of energy due to friction in the line} = FJ \tag{22}$$

The energy balance between points A and B can be accounted by including equations (21) and (22) in equation (20). This complete equation representing such energy may be written as:

$$\frac{P_A}{g\rho_A} + X_A + \frac{u_A^2}{2g} - F + W = \frac{P_B}{g\rho_B} + X_B + \frac{u_B^2}{2g} \qquad (23)$$

Equation (23) is called *Bernoulli's equation.* Bernoulli's theorem, although derived here over two ends of a system, it is applicable between any two points in a system.

Equation (23) is numerically correct. But it is not correct theoretically, since each of the terms in equation (23) is actually energy term and should be measured in the units of joules per unit mass. In practice, these terms are always referred as the heights and often measured in terms of height of a column of liquid.

Applications: (1) Bernoulli's theorem is applied in the measurement of the rate of fluid flow using orifice meter, venturi meter etc.

(2) Bernoulli's theorem is applied in the working of centrifugal pumps. In these pumps, the kinetic energy is converted into pressure head, which helps in pumping the liquids.

(3) It is easy to measure heights and apply them as energy terms, which is a contribution of Bernoulli's theorem.

Concept of Head (Pressure Head)

The terms in Bernoulli's equation represent energy and supposed to have the units of energy. But numerically these terms give the units of metre. Therefore, energy terms can be measured in the units of metre, which is a unit of height. Hence these terms are known as *heads.*

The *pressure head* is defined as the height of a column of liquid of known density, which is numerically equal to pressure energy term.

The units of height can be obtained by considering the pressure energy term, i.e. equation (14).

$$\textit{Pressure energy} = \frac{P_A}{g\rho_A} = \frac{\text{pressure}}{\text{acceleration due to gravity} \times \text{density}}$$

Consider the units for equation (14).

$$\text{Pressure energy} = \frac{\text{N}}{\text{m}^2} \cdot \frac{1}{(\text{m/s}^2)} \cdot \frac{1}{(\text{kg/m}^3)}$$

$$= \frac{\text{N} \times \text{s}^2 \times \text{m}^3}{\text{m}^2 \times \text{m} \times \text{kg}} = \frac{\text{N}\cdot\text{s}^2}{\text{kg}} \qquad (24)$$

But N (newton) = kg·m/s². Substituting this term in equation (24) gives:

$$\text{Pressure energy} = \frac{\text{kg} \times \text{m} \times \text{s}^2}{\text{s}^2 \times \text{kg}} = \text{m}.$$

Thus, pressure energy is in metre, i.e., as a height. Therefore, the height is termed as head in the discussion of hydraulics. Hence, pressure energy is called pressure head.

In an analogous manner, there are different heads in the Bernoulli's equation (18), namely:

potential heads (X)
velocity heads ($u^2/2g$)
pressure heads ($P/g\rho$)

Similarly, F is known as friction head and W is the head that is added by the pump.

ENERGY LOSSES

Bernoulli's equation includes the term 'loss of energy' in the pipe. According to law of conservation of energy, energy balances have to be properly accounted. Therefore, it is necessary to calculate the energy losses. Fluids experience energy losses in several ways while flowing through a pipe. Some of them are:

1. Friction losses
2. Losses in fittings
3. Enlargement losses
4. Contraction Losses

These are discussed in the following sections.

Friction Losses

During the flow of fluids, frictional forces cause a loss in pressure (ΔP_f pascals). The fluid flow can be either viscous or turbulent, which also influences the losses. In general, the pressure drop (ΔP_f) due to friction in a fluid is:

- directly proportional to the velocity of the fluid (u), m/s
- directly proportional to the density of the fluid (ρ), kg/m³
- directly proportional to the length of the pipe (L), m
- inversely proportional to the diameter of the pipe (D), m

These relationships are proposed in *Fanning equation* for calculating the friction losses, irrespective of the nature of flow (viscous or turbulent).

Fanning equation:
(viscous or turbulent)

$$\Delta P_f = \frac{2fu^2L\rho}{D} \qquad (25)$$

where f = friction factor
ΔP_f = pressure drop, Pa

Equation (25) considers the friction losses when the fluid is passing through a straight pipe. The value of f depends on:

- Nature of flow of the fluid (turbulent or viscous).
- Roughness of the inner surface of the pipe. The roughness factors for some conditions of pipes are given below.

Condition of pipe	*Roughness factor*
Smooth brass, copper or lead pipe	0.6
New steel or cast-iron pipe	1.0
Old steel pipe	1.6
Badly rusted cast-iron pipe	2.5

The numerical values reported in the above table give a rough estimate of the magnitude of the effect, which contributes to the friction factors. Frictional loss can be reduced by the addition of soluble, high molecular weight polymers in low concentrations.

In practice, fluids are rarely handled in viscous flow. For viscous flow, *Hagen-Poiseuille equation* could be employed for calculating the pressure drop due to friction.

Hagen-Poiseuille equation:
(*viscous flow*)

$$\Delta P = \frac{32Lu\eta}{D^2} \qquad (26)$$

where η = viscosity of the liquid, Pa·s
ΔP_f = pressure drop, Pa

If the viscosity (η) is known, Hagen-Poiseuille's equation permits the calculation of pressure drop due to friction. However, equation (26) is normally used to calculate the viscosity, by experimentally estimating ΔP.

Friction losses are permanent, since potential and kinetic energies are converted into heat.

Losses in Fittings

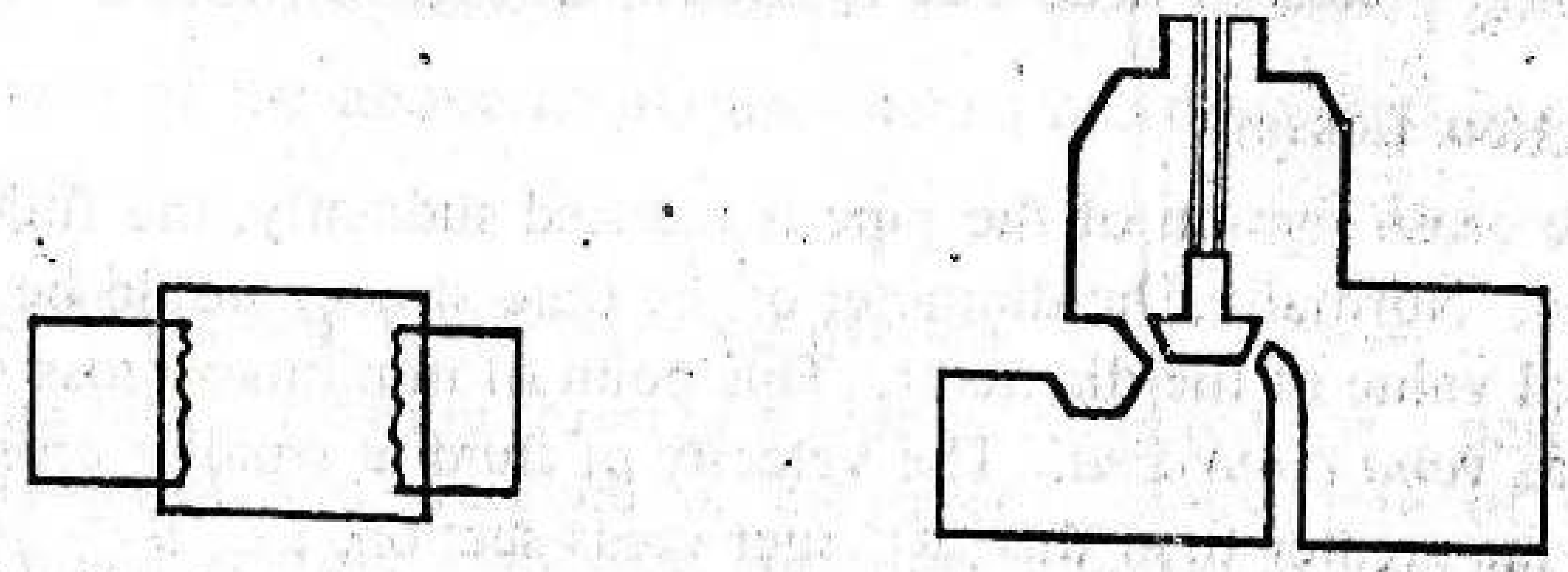
Normally, a large number of fittings are included in a pipeline (Figure 2-7). For a liquid passing through a straight pipe, Fanning equation is applicable for the losses. When fittings are introduced into a straight pipe, they cause disturbances in the flow, which results in additional loss of energy. It is difficult to specify the loss due to each type, because of varying types of fittings.

- Losses in fittings may be due to
  - change in direction, for example elbow fittings,
  - change in the types of fittings, for example, coupling, union, valve or meter.

Losses in fittings, by convention, is expressed in terms of an **equivalent length of straight pipe**, which is given as a certain number of pipe diameters.

Elbow 90 fitting
Equivalent length: 32

Tee fitting
Equivalent length: 90



Coupling fitting
Equivalent length: negligible

Globe valve coupling
Equivalent length: 300

Figure 2-7. Friction losses in fittings of a new screwed pipe.

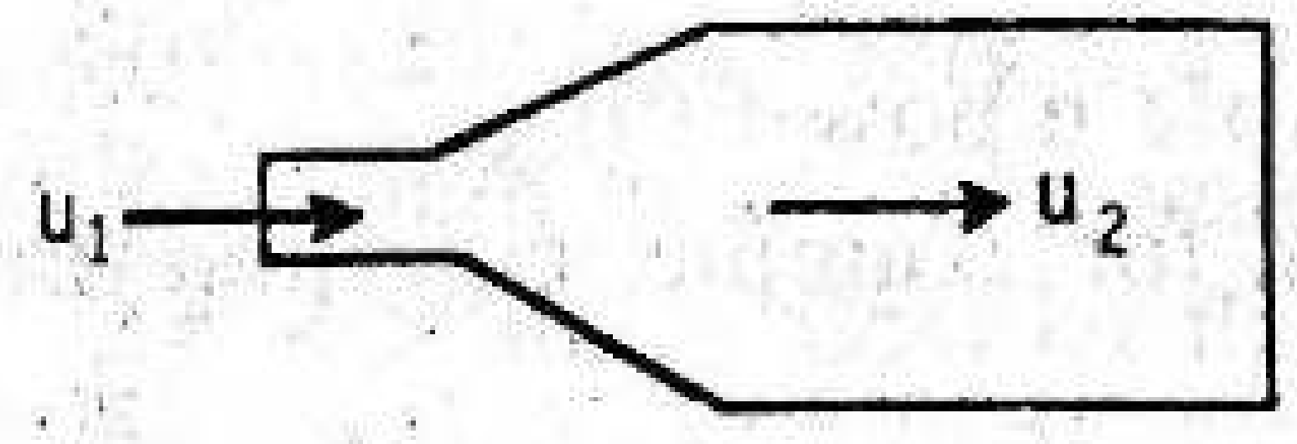
Equivalent lengths for a few screwed fittings are shown in Figure 2-7. For example, a globe valve is fitted in a pipeline having an internal diameter of 50 millimetres. Globe valve has an equivalent length of 300. Then,

Equivalent length of this fitting = 300 × 50 = 15000 mm or 15.0 m.

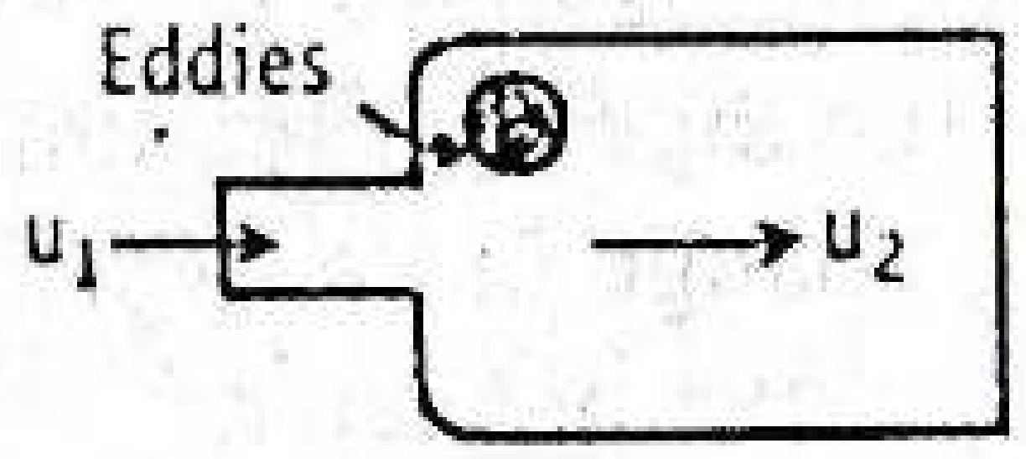
That means the contribution of a globe valve is equivalent to 15 metres of a straight pipe towards the losses. This length is added to the straight section of the pipe and substituted in the Fanning equation (25) to obtain energy losses due to fittings.

Enlargement Losses

If the cross section of the pipe enlarges *gradually*, the fluid adapts itself to the changed section without any disturbance. Therefore, there is no loss of energy at this point.



(a) Gradual enlargement
No loss of energy



(b) Sudden enlargement
Loss of energy

If the cross section of the pipe changes suddenly, loss of energy is observed due to eddies. These are greater at this point than straight pipe. Due to these disturbances, the loss of head will be observed. In sudden enlargement, the velocity of flow at larger cross-section is less than the velocity at smaller cross-section, i.e., $u_2 < u_1$. For sudden enlargement, the loss is represented by:

$$\textit{Sudden enlargement losses:}\quad \Delta H_e = \frac{(u_1 - u_2)^2}{2g} \tag{27}$$

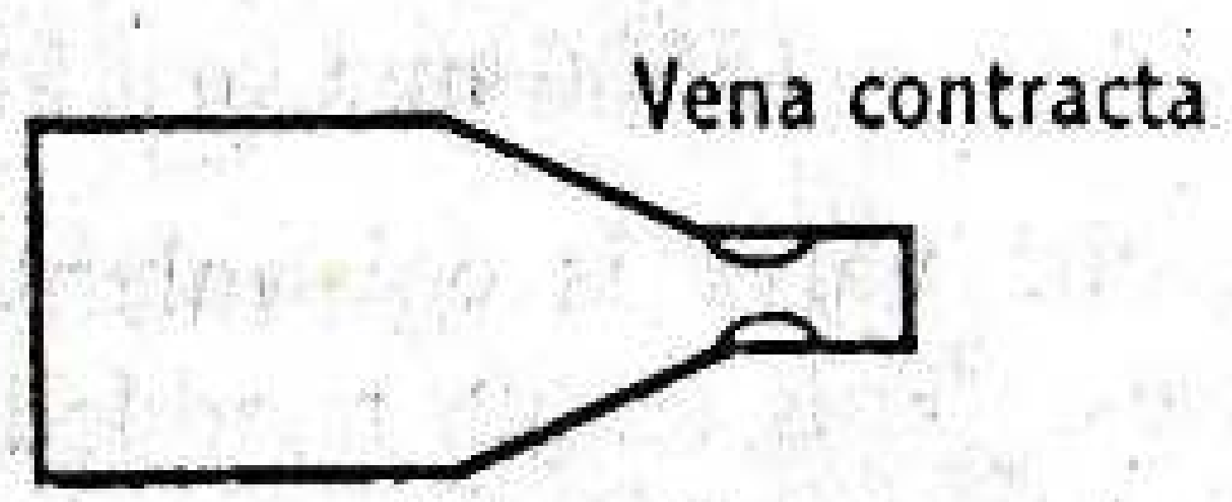
where ΔH_e = loss of head due to sudden enlargement, m.

Contraction Losses

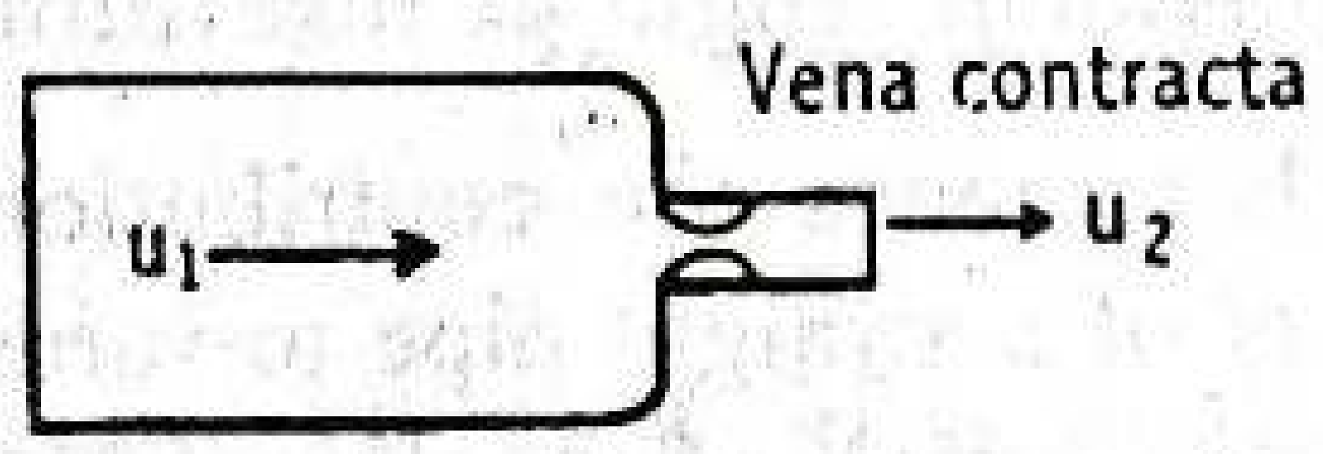
If the cross section of the pipe is reduced suddenly, the fluid flow is disturbed. Normally, the diameter of the fluid stream would be less than the initial value of the diameter. This point of minimum cross section is known as *vena contracta*. The velocity of fluid at smaller cross-section will be far greater than that at larger cross-section, i.e., $u_2 > u_1$. Then, u_1 may be considered negligible. The losses due to additional eddying are observed. Such contraction losses can be expressed as:

$$\textit{Sudden contraction losses:}\quad \Delta H_c = \frac{K u_2^2}{2g} \tag{28}$$

where ΔH_c = loss in head due to sudden contraction, m
K = constant
u_2 = velocity, m/s



(a) Gradual contraction
No loss of energy



(b) Sudden contraction
Loss of energy

The constant K depends on the relative areas of two sections. For example, when the ratio of the areas is 0.5, K is equal to 0.3. For rounded entrance, K value for turbulent flow is about 0.04. For laminar flow, the loss is negligible.

MEASUREMENT OF RATE OF FLOW OF FLUIDS

Whenever fluids are used in a process, it is necessary to measure the rate at which the fluid is flowing through the pipe. This is required for optimization of process parameters in a chemical industry. Measurements are required for the calculation of auditing (for example, town planning of water supply) and cost of usage (for example, cost of water used in the houses). Methods of measurement may be classified as:

1. Direct weighing or measuring
2. Hydrodynamic methods
    (a) Orifice meter
    (b) Venturi meter
    (c) Pitot tube
    (d) Rotameter
3. Direct displacement meter

Some of the above mentioned meters are discussed in the following sections.

Direct Weighing or Measuring Meters

The liquid flowing through a pipe is collected for a particular period at any point and weighed or measured. Thus, rate of flow can be determined. Gases cannot be weighed. On commercial scale, it is not convenient to weigh the liquids. Therefore, these methods are impracticable.

Orifice Meter

Principle : The orifice meter is a thin plate containing a narrow and sharp aperture. When a fluid stream is suddenly allowed to pass through the narrow constriction, the velocity of the fluid at the orifice meter increases compared to the velocity of the fluid in the upstream. This results in corresponding decrease in the pressure head. Bernoulli's theorem provides the basis for correlating the increase in the velocity head with the decrease in the pressure head between two points. The difference in the pressure head (ΔH) may be read from a manometer. If the diameter of the orifice is small compared to the diameter of the pipe, velocity of the fluid at the point before entering the orifice may be considered negligible. In such cases the manometer reading directly gives the velocity of the fluid.

The velocity of the fluid at the thin constriction may be written as:

$$u_o = C_o\sqrt{2g.\Delta H} \qquad (29)$$

where u_o = velocity of fluid at the point of orifice meter, m/s

C_o = a constant

ΔH = difference in head from manometer, m

The ΔH can be measured using a manometer, which is connected to the pipe section between the initial stage and the orifice section. It can be substituted in equation (29) in order to get the velocity of the liquid flowing through the orifice. When cross-section of the pipe is known, the volume of the liquid flowing per hour can be determined.

Construction : The orifice meter is considered to be a thin plate containing a sharp aperture through which a fluid flows. Normally, orifice plate is placed between long straight pipes, so that other fittings do not alter the flow rate that is being measured. Although it is possible to place orifice meter in the side or bottom, for the present discussion, the plate is introduced into the pipe (Figure 2-8). A manometer is connected at points A and B as shown in Figure 2-8.

Working : Orifice meter is referred to as *variable head meter*, i.e., it measures the variation in the pressures across a fixed constriction placed in the path of flow consisting of a constant area.

When fluid stream is allowed to pass through the cross-section of the orifice, the velocity of fluid at point B increases at the expense of pressure head. As a result, the pressure at point A is higher than at point B. Bernoulli's equation provides the basis for correlating the increase in velocity head with the decrease in pressure head. The difference in pressure (ΔH metres) may be read from a manometer, connected to the points A and B as shown in Figure 2-8.

Bernoulli's equation may be applied for two points (A and B) for the given experimental conditions, as given below:

$$\sqrt{u_o^2 - u_A^2} = C_o\sqrt{2g.\Delta H} \qquad (30)$$

where u_o = velocity of fluid at the point of orifice meter, m/s

u_A = velocity of fluid at the point A, i.e., before orifice meter, m/s

C_o = a constant

ΔH = difference in head, m

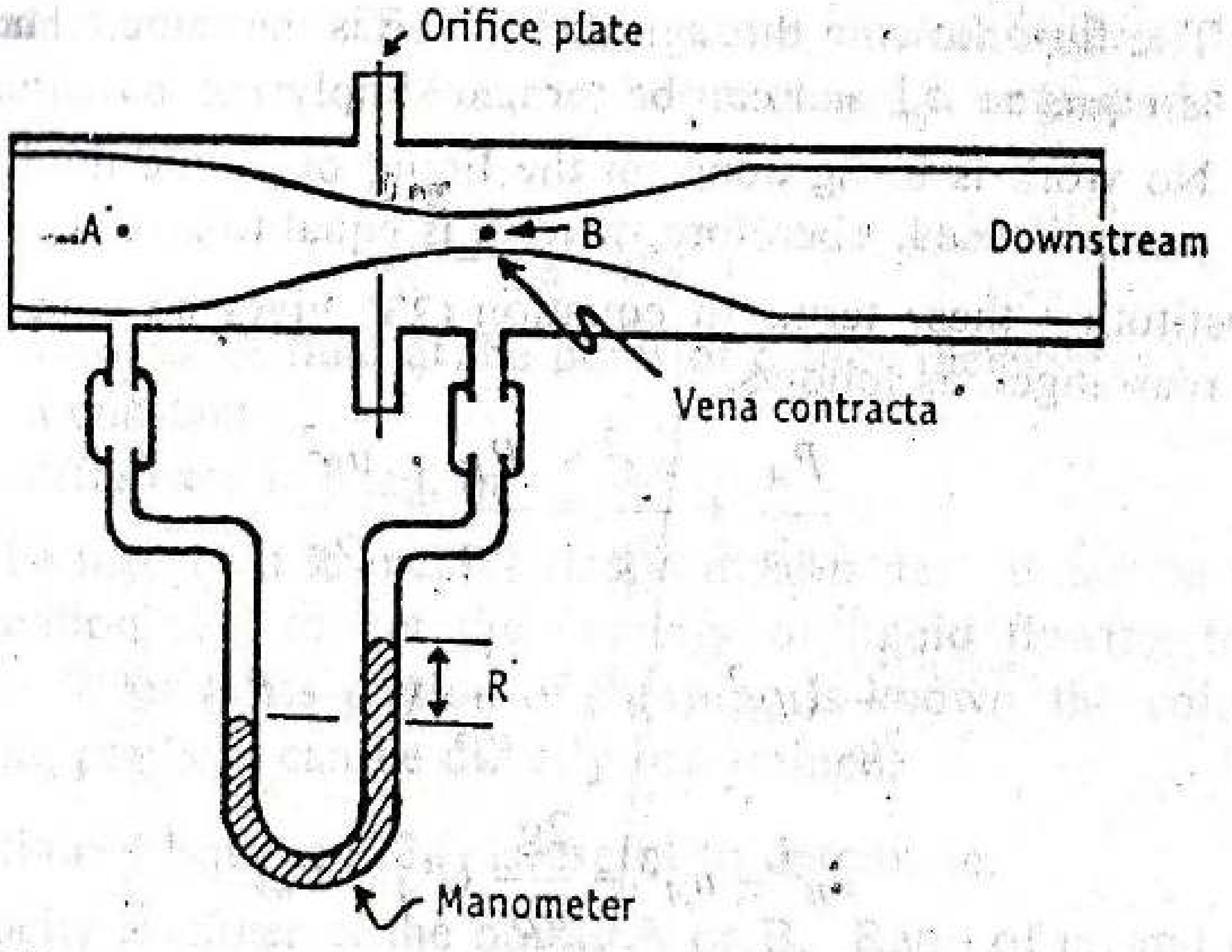


Figure 2-8. Construction and assembly of orifice meter.

If the diameter of the orifice is 1/5th of the pipe diameter or less, u_A is small compared to u_o. Then, u_A term may be neglected. Then equation (30) becomes:

$$u_o = C_o\sqrt{2g.\Delta H} \qquad (29)$$

ΔH can be measured using a manometer. It can be substituted in equation (29) in order to get the velocity of liquid flowing through orifice pipe. When cross-section of the pipe is known, the volume of liquid flowing per hour can be directly determined.

Mathematical treatment : Consider a fluid flowing through a pipe at a certain velocity (u_A). If the edge of orifice is sharp, fluid does not lose the velocity at once, while passing through the orifice. Two points A and B on either side of the orifice meter are chosen and Bernoulli's equation is applied. The Bernoulli's equation is:

$$\frac{P_A}{g\rho_A} + X_A + \frac{u_A^2}{2g} - F + W = \frac{P_B}{g\rho_B} + X_B + \frac{u_B^2}{2g} \qquad (23)$$

In equation (23), the following assumptions may be made based on the working of orifice meter (Figure 2-8).

(1) Let the sections of pipe be horizontal, so that the heights (metres) of the points A and B are same (Figure 2-8). Then, two X terms are identical and get cancelled.

(2) Let the friction losses will not be appreciable and considered negligible. Then, F term becomes zero.

(3) The fluid flowing through the orifice is the same. Therefore, ρ_A is equal to ρ_B, and can be termed simply ρ.

(4) No work is being done on the liquid or by the liquid, since no pump is used. Therefore, w term is equal to zero.

Substituting these terms in equation (23) gives an equation, which can be rearranged as follows.

$$\frac{P_A}{g\rho} + \frac{u_A^2}{2g} = \frac{P_B}{g\rho} + \frac{u_B^2}{2g}$$

$$\frac{1}{2g}(u_B^2 - u_A^2) = \frac{1}{g\rho}(P_A - P_B)$$

$$u_B^2 - u_A^2 = \frac{2g}{g\rho}(P_A - P_B) \qquad (31)$$

$$u_B^2 - u_A^2 = \frac{2g}{g\rho}\Delta P \qquad (32)$$

From the principles of statics, $(\Delta P/g\rho) = \Delta H$ in metres. Introducing this term in equation (32) gives:

$$u_B^2 - u_A^2 = 2g.\Delta H$$

$$\sqrt{u_B^2 - u_A^2} = \sqrt{2g.\Delta H} \qquad (33)$$

Normally, the diameter of the fluid stream would be less than the diameter of the orifice (Figure 2-8). This point of minimum cross section is known as the *vena contracta*. Though the pipe is full of liquid on both sides of the orifice, still the *vena contracta* exists and is surrounded by swirling liquid. Point B is chosen at the *vena contracta*.

In practice, the diameter of the stream at the *vena contracta* is not known, but that of the orifice diameter is known. A constant, C_o, is, therefore, included in equation (33) in order to correct the differences between velocities at orifice and at *vena contracta*. Therefore, equation (33) may be modified in terms of the velocity through the orifice (u_o).

$$\sqrt{u_o^2 - u_A^2} = C_o\sqrt{2g.\Delta H} \qquad (30)$$

The constant C_o also includes some losses due to friction. It depends on the construction (ratio of the orifice diameter to the pipe diameter and position of the orifice taps) and the nature of flow of liquid (Reynolds number).

If the diameter of the orifice is 1/5th of the pipe diameter or less, u_A is small compared to u_o. Then, u_A term may be neglected. Then equation (30) becomes:

$$u_o = C_o\sqrt{2g.\Delta H} \qquad (29)$$

where u_o = velocity of fluid at the point of orifice meter, m/s
C_o = a constant
ΔH = difference in head, m

ΔH can be measured in metre using a manometer. It can be substituted in equation (29) to get the velocity of liquid flowing through orifice pipe. When cross-section of the pipe is known, the volume of liquid flowing per hour can be directly determined.

Applications : Equation (30) is useful to determine:

(1) velocity at either of the points A or B. Ratio of u_o and u_A can be related to ratio of the area of the orifice to the area of the pipe, which is normally known.

(2) volume of the liquid flowing per hour when u_A and cross-section of the pipe are known.

Venturi Meter

Principle : Venturi meter consists of two tapered sections in the pipeline with a gradual constriction (throat) at its centre. When fluid stream is allowed to pass through the narrow throat, the velocity of the fluid increases at the venturi compared to the velocity of the upstream. This results in corresponding decrease in the pressure head. Bernoulli's theorem provides the basis for correlating the increase in the velocity head with the decrease in the pressure head between two points. The difference in the pressure head (ΔH) may be read from a manometer. If the diameter of the venturi is small compared to the diameter of the pipe, velocity of the fluid at the point before entering the venturi may be considered negligible. In such cases, the manometer reading directly gives the velocity of the fluid.

The velocity of the fluid at the narrow constriction (throat) may be written as:

$$u_v = C_v\sqrt{2g.\Delta H} \qquad (34)$$

where u_v = velocity at the throat of the venturi, m/s
C_v = coefficient of the venturi meter
ΔH = difference in head from manometer, m

ΔH can be measured using a manometer. It can be substituted in equation (34) in order to get the velocity of the liquid flowing through the venturi. When the cross-section of the pipe is known, the volume of liquid flowing per hour can be determined.

Construction : A venturi meter consists of two tapered sections inserted in a pipeline (Figure 2-9). Normally, venturi meter is placed between long straight pipes, so that other fittings will not alter the flow rate that is being measured. The upstream cone is normally shorter than the down stream. The tapers are smooth and gradual. Therefore, eddies in the down stream are absent and no power loss is observed. In addition, the cross-section of the high velocity part of the stream is well defined. A manometer is connected at points A and B as shown in Figure 2-9.

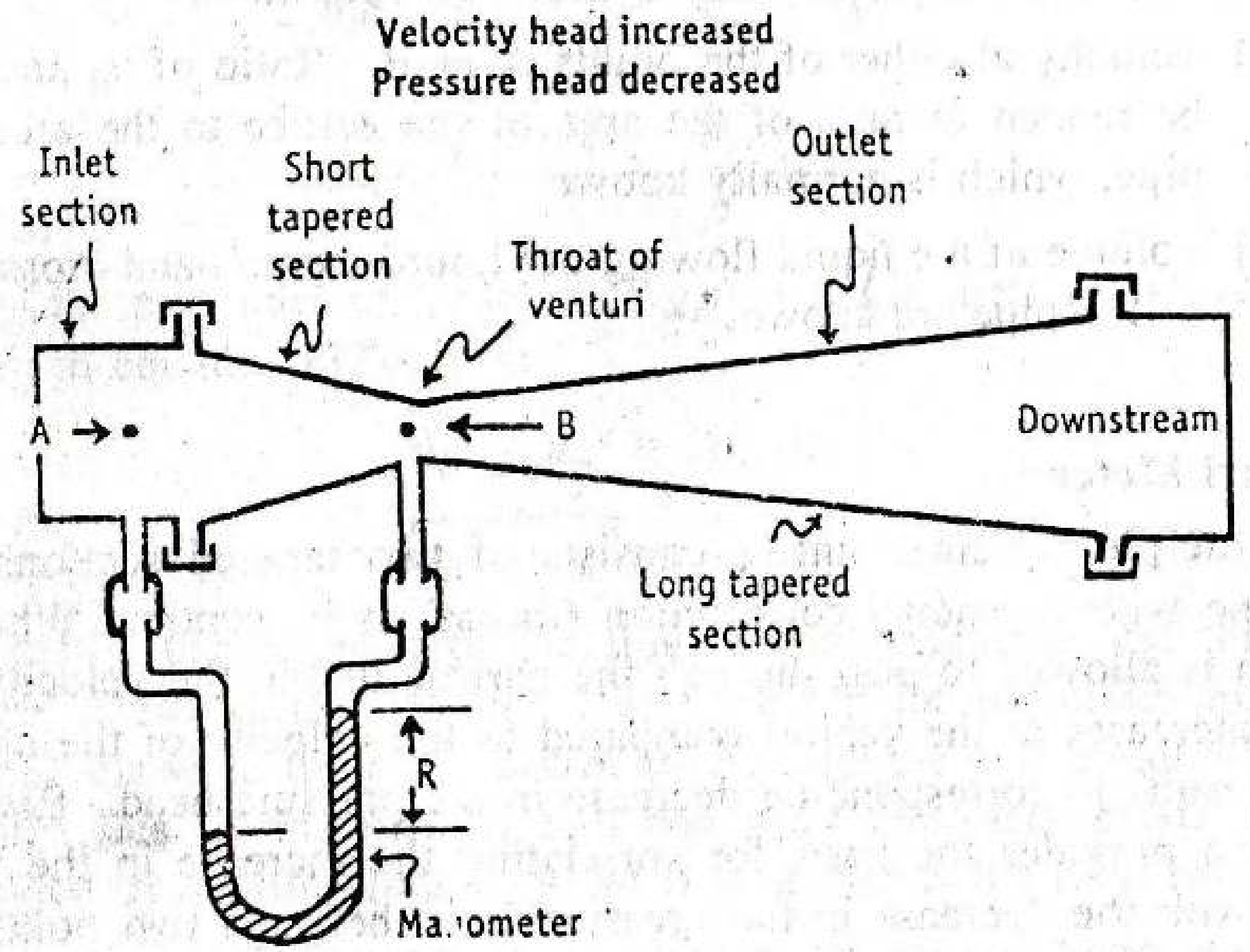


Figure 2-9. Construction of a venturi meter.

Working : Venturi meter is referred to as *variable head meter*, i.e., it measures the variable differential pressure across a fixed constriction placed in the path of flow consisting of a constant area. In a venturi meter, the velocity of the fluid is increased at the throat, due to the constriction. This results in decreased pressure in the up-stream cone. The pressure drop in the upstream cone is utilised to measure the rate of flow using a manometer. Venturi meter nearly confirms the theoretical equations obtained for an orifice meter. On similar lines of equation (30), an equation for venturi meter may be written as:

$$\sqrt{u_v^2 - u_A^2} = C_v\sqrt{2g.\Delta H} \qquad (35)$$

where u_v = velocity at the throat of the venturi, m/s
u_A = velocity at point A (venturi throat), m/s
C_v = coefficient (= 0.98)

If the diameter of the smaller section is one-fifth of the pipe diameter or less, u_A^2 is considered to be small compared to u_v^2. Therefore, u_A^2 term may be disregarded. A simplified form of equation (35) is:

$$u_v = C_v\sqrt{2g.\Delta H} \qquad (34)$$

The difference in pressure (ΔH) can be read in metres directly from the manometer. Thus velocity of the flow may be measured. The value given by the venturi meter is average velocity of the flow. The velocity then decreases and the original pressure is recovered in the down stream cone.

Applications : Venturi meter is commonly used for liquids, especially water. It can also be used for the measurement of gases.

Disadvantages : (1) Venturi meter is expensive. (2) Venturi meter occupies more space. (3) The ratio of throat diameter to pipe diameter cannot be changed.

TABLE 2-1

Differences Between Orifice Meter and Venturi Meter

Orifice meter	*Venturi meter*
(1) Cheap	Expensive
(2) Easy to install	Fabrication is highly technical
(3) Construction can be made at home	It should be purchased from the instrument dealer
(4) Head losses are more	Head losses are insignificant
(5) Power losses are more particularly on fluid that is carried for long periods of time	Power losses are less
(6) Normally used for testing purposes, for example, steam lines etc.,	Used in on-line installation
(7) Greater flexibility	Not flexible, permanent
(8) Reading of the orifice meter is larger under identical conditions	The reading of venturi meter is comparatively smaller under identical conditions

Differences between orifice and venturi meters: The differences between orifice and venturi meters are explained in Table 2-1.

Pitot Tube

Principle : Pitot tube consists of a sensing element with a small constriction compared to the size of the flow channel. When the sensing element is inserted at the centre of the stream, the velocity of flow is increased. This results in decreased pressure head. Tube at right angles to the flow measures pressure head only. The tube that pointed upstream measures pressure head and velocity head. The difference in the above readings indicates the velocity head.

Accordingly to Bernoulli's equation, velocity head of the fluid may be obtained using equation (33).

$$\Delta H_p = \frac{u^2}{2g} \qquad (36)$$

where u = velocity of the flow at the point of insertion, m/s
ΔH_p = difference in head from manometer, m

Therefore, the reading (R) of the manometer measures the velocity head in metres.

Construction : The construction of a pitot tube is shown in Figure 2-10. Pitot tube is also known as *insertion meter*. The size of the sensing element is small compared to the size of the flow channel. The point of measurement may be at the centre of the channel. One tube is perpendicular to the flow direction and the other tube is connected parallel to the direction of flow. The two tubes are connected to the legs of a manometer or a suitable device.

Working : Two tubes are inserted into the pipe in the manner shown in Figure 2-10. Pitot tube is used to measure the *velocity head* of the flow. In this tube, the velocity of fluid is increased at the narrow constriction. This results in decreased pressure. Tube at right angles to the flow measures pressure head only. The tube that points upstream measures pressure head and velocity head. The difference in the above readings indicates velocity head. Therefore, the reading (R) of the manometer measures the velocity head.

As seen in the Bernoulli's equation, velocity head of the fluid (ΔH_p) may be obtained from an equation similar to equation (29), which can be represented as:

$$u^2 = 2g.\Delta H_p$$

This is the theoretical velocity. Actual velocity is given by:

$$u^2 = C_v\sqrt{2g.\Delta H_p} \qquad (36)$$

where C_v = coefficient of pitot tube.

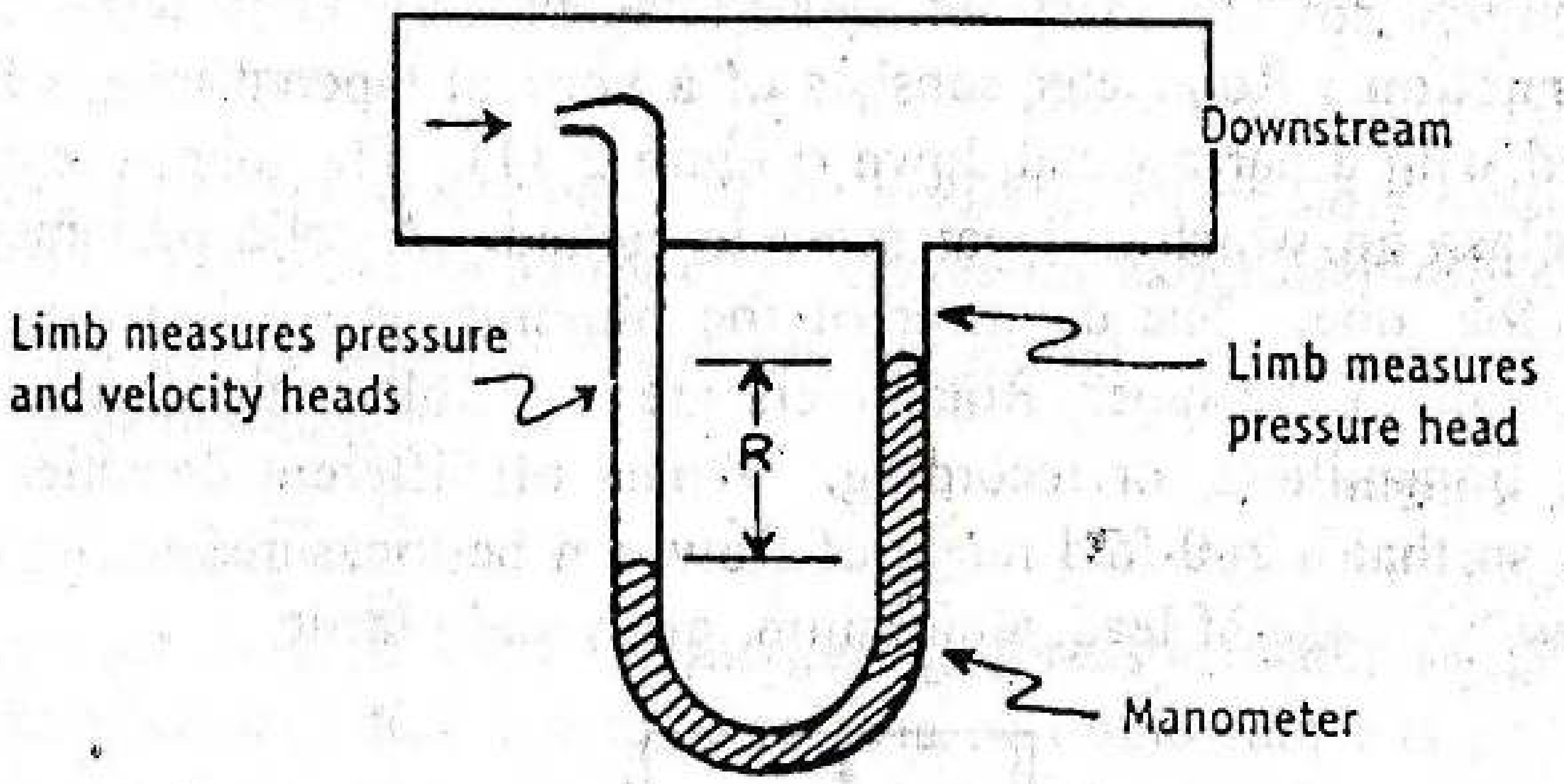


Figure 2-10. Construction and assembly of pitot tube.

Normally, pitot tube measures the velocity at one particular point, i.e., at the point of insertion. The average velocity (across the cross section of the pipe) may be obtained by either ways.

(a) Pitot tube may be inserted at the centre of the pipe and it measures the maximum velocity. Average velocity may be calculated from this maximum by means of calibrated charts.

(b) Adjustable pitot tube may be used to take readings from different points in the cross section. Mean velocity may be found by graphic integration. It is a difficult process.

Advantage : Pitot tube measures the velocity at one point only.

Disadvantages : (1) The pitot tubes themselves cause more disturbance. Eddies within the pressure tube disturb the readings.

(2) They do not give average velocity directly.

(3) For gases, the reading is extremely small. For gases working on low pressure, some form of multiplying gauges must be used.

Rotameter

Rotameter is a variable area meter, i.e., it measures the area of flow, so as to produce a constant head differential. Therefore, rotameters are known as *area meters*.

Principle : Rotameter consists of a vertical, tapered and transparent tube in which a plummet is placed. During the fluid flow through the tube, the plummet rises and falls because of variation in flow. As a result, the area of the annular space between the plummet and the tube varies. The head loss across the annulus is equal to the weight of the plummet. The upper edge of the plummet is used as an index to note the reading on the tapered tube. This value indicates the flow of the fluid.

Construction : Rotameter consists of a vertical tapered tube, which is mounted with a narrow end down (Figure 2-11). The tube is usually made of glass on which a linear scale is etched. A solid plummet is placed in the tube. The diameter of the plummet is smaller than the narrowest part of the tube. Rotameters are available with electric and electronic transmitters for recording. Floats of different densities are available, so that a 200-fold range of flow can be measured accurately. Floats may be made of lead, aluminium, glass and plastic.

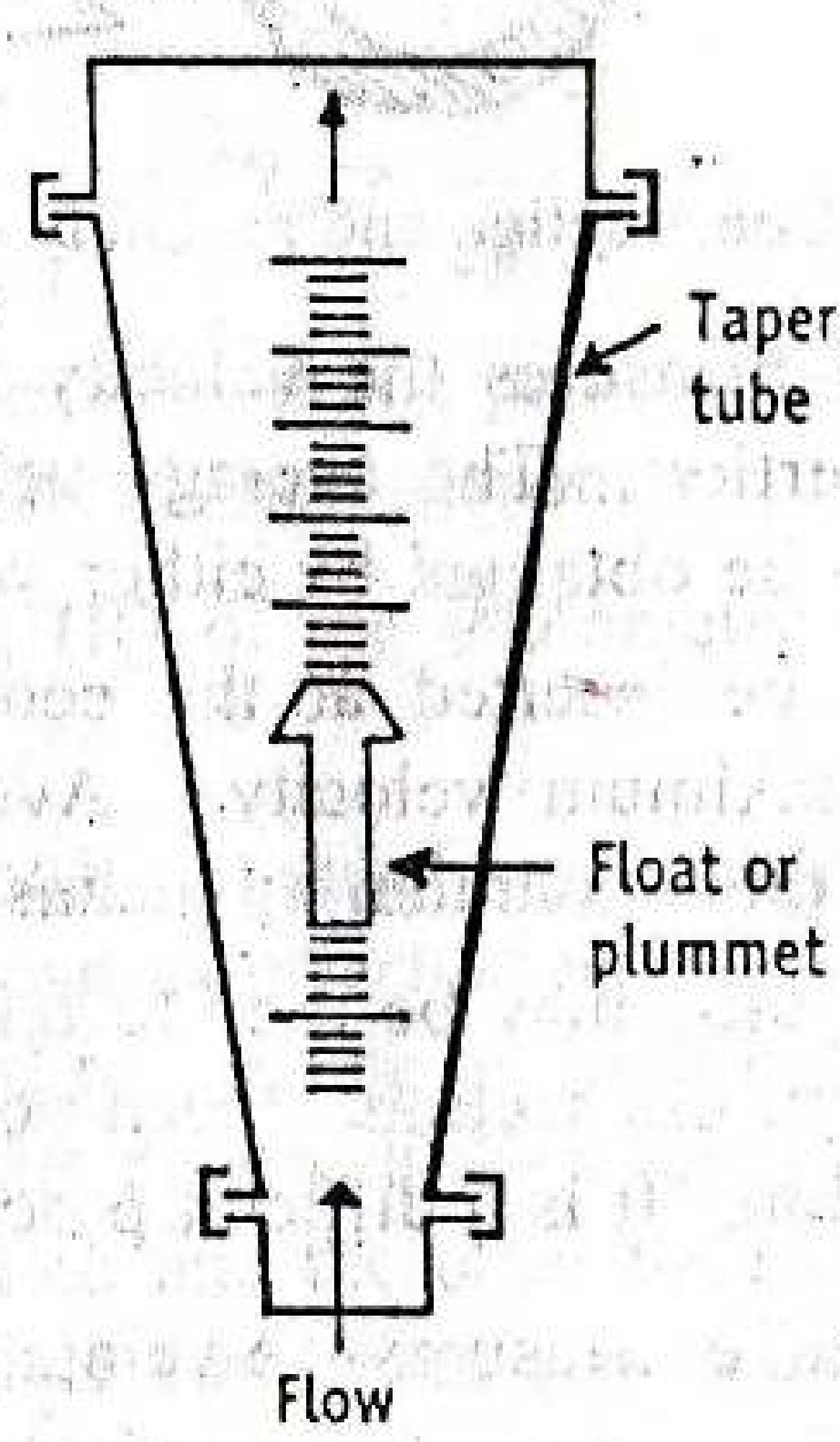


Figure 2-11. The Construction of a rotameter.

Working : As the flow is upward through a tapered tube, the flow of fluid varies. The plummet, which is surrounded by the fluid, rises and falls depending on the rate of flow. The greater the flow rate, the higher the plummet rises in the tube. In rotameters, the pressure drop is constant or nearly constant.

During the fluid flow, the area of the annular space between the plummet and the tube varies. Therefore, the head loss across the annulus is equal to the weight of the plummet. The flow may be read using the upper edge of the plummet as an index. The area is properly calibrated to the flow rate. The reading may be transmitted for recording, integrating and controlling.

Normally, manufacturers supply the necessary data and charts along with the meter while purchasing the instruments.

Uses : Rotameters are extensively used in chemical industries, such as bulk drugs. In the fermenters, the supply of air is controlled through rotameters. Rotameters are satisfactory both for gases and for liquids at high and low pressures.

Advantages : (1) Operator has a direct visual index of flow reading. It is satisfactory for manual control of processes for experimental work.

(2) It does not require the condition that straight pipes should run before and after the meter.

Direct Displacement Meter

Displacement meter is used for measuring domestic water supplies. This has the advantage that the total volume of liquid that has passed can be read directly.

Principle : Displacement meters are used for measuring the flow rate of fluids in small lines. In these meters, a stream of water enters the meter and strikes the moving member (disc as in disc meters or buckets as in current meters). The rate of rotation of the moving member is proportional to the velocity of water passing through the meter. The displacement of moving member is transmitted through a train of gears to the counting dial, which is present in the top of the member.

Advantages : The displacement meters have an advantage over venturi or orifice meters in the sense that the reading represents the total volume of fluid that has passed. This volume divided by a definite period gives the flow rate.

Glossary of Symbols

C_0 = Constant for the orifice meter.
C_v = Constant for the pitot tube.
C_V = Constant for the venturi meter.
D = Diameter of the pipe, m
η = Viscosity of the liquid, Pa·s.
f = Friction factor.
g = Acceleration due to gravity, m/s^2.
h_1 = Height of the liquid column at a point, m.
ΔH = Loss of head, m.
ΔH_e = Loss of head due to sudden enlargement, m.
ΔH_c = Loss of head due to sudden contraction, m.
ΔH_p = Difference in head from manometer in pitot tube, m.

Δh = Height difference between two points, m.

L = Length of pipe, m.

P = Pressure, Pa.

P_s = Pressure on the column of a liquid, Pa.

ΔP_f = Pressure difference due to friction, Pa.

Re = Reynolds number.

ρ = Density of the liquid, kg/m^3.

S = Surface area of the liquid column, m^2.

u = Velocity of the fluid in pipes, m/s.

w = Energy head added by the pipe, J.

X = Height of the liquid pipe from horizontal datum, m.

QUESTION BANK

Each question carries 2 marks

1. Draw a labeled diagram of pitot tube and explain the working of the same.
2. What is the use of a pitot tube? Write its advantages and disadvantages.
3. Write the Fannings equation and explain the terms. What is its importance?
4. Express the Hagen-Poiseuille's relationship. What is its importance?
5. Explain the term 'head'. List the different heads in the Bernoulli's theorem.

What is meant by 'equivalent pipe length? What are its applications?

What is Reynolds number? Describe its importance.

8. List the advantages and disadvantages of rotameter.
9. How are losses of energy due to enlargement in cross section measured? Give relevant equation and explain the terms.
10. Give Reynolds number and explain the symbols used therein.
11. What is a 'differential head meter'? Name some devices under this category.
12. What is a pressure head? How is it calculated?
13. What are vertical head meters? Describe one such meter.
14. Differentiate between constant pressure and constant area meters. Give examples of devices under each category.

Each question carries 5 marks

1. Describe the types of flow patterns exhibited by liquids in motion.
2. Differentiate between fluid statics and fluid dynamics. Name the fluid flow meter, which gives point velocity.
3. Write Bernoulli's equation and explain the symbols used therein with a labeled diagram.

4. Describe Reynolds classic experiment elucidating different types of flow patterns, when a liquid flows through a closed channel.
5. Explain the characteristics of different types of flow. Add a note on Reynolds number.
6. Compare and contrast the advantages and disadvantages of pitot tube and rotameter.
7. What are the merits and demerits of venturi meter over orifice meter?
8. What is the condition of hydrostatic equilibrium? Obtain the barometric equation.

Each question carries 10 marks

1. Deduce relevant equations for calculation of flow rates using orifice meter.
2. Derive Bernoulli's equation stating the assumptions.
3. Give a neat sketch of two fluid manometers and explain its working principle.
4. Explain the working principle and construction of venturi meter. Write the expression for the volumetric flow rate of fluid through it.
5. Explain the energy losses that occur when a fluid flows through a pipe with relevant equations.

3

Transportation of Fluids

Valves
Pumps
Reciprocating pumps
Rotary pumps
Miscellaneous pumps

The transportation is involved in handling of the raw materials, materials in manufacture and finished products. Transportation is also important in mixing, conveying them for filtration, filling into the containers, sealing etc. Transportation of fluids is more convenient and economical than transportation of solids. The importance of transportation of fluids is highlighted in the following areas.

1. **Bulk drugs :** Specified quantities of reactants are transported to the reactor. For example, gases such as chlorine and hydrogen are passed (in chlorination and hydrogenation) into the reaction system. Similarly, large quantities of water are transported to heat or cool the reaction vessels.
2. **Fermentation products :** Medium constituents are transported to the fermenter. For example, sterile air, nutrient broth etc., are passed into the fermenter.
3. **Liquid oral pharmaceuticals :** Production of dosage forms, such as solutions and elixirs, employ fluid flow. In the production of liquid orals, production operations are conducted in the first floor. The bottling and packing are carried out in the ground floor. Therefore, fluid flow in this case involves gravity.
4. **Suspension dosage forms :** In the production of suspensions, fluid flow is obtained with the help of a pump. Normally, it is a mixing process. When suspended solids settle at the bottom of the tank, these are pumped to the top of the vessel continuously.

5. **Semisolid pharmaceuticals :** In case of semisolid preparations (ointments, pastes etc.), fluid flow is obtained by passing them through a hot jacketed pipes, because it is easy to handle them in *fluidised* state under molten conditions.
6. **Injection dosage forms :** In the production of injections, sterile air and sterile water are transported from the place of production to the site of manufacturing operations.

In this modern age, wherein automation is the order of the day, pharmaceutical industry has evolved a number of innovative handling techniques.

VALVES

Valves are used to control the rate of flow of fluids in a pipeline.

Valves are placed between pipes. During maintenance of pipes, valves can be removed and repaired without disturbing the other connected units. Valves are designed in such a manner that they should withstand the following effects:

- Pressure of flow.
- Temperature changes.
- Strain from connected pipes.
- Distortion from the sealing surfaces.

Normally, valves are made of materials such as brass, iron, bronze, and cast iron, depending on the nature of materials that may come in contact. A number of valves have been designed. Some of them are:

(1) Plug cock valve
(2) Globe valve
(3) Gate valve
(4) Diaphragm valve
(5) QO (quick opening) valve
(6) Check valve

These are discussed in the following sections.

Plug Cocks

The construction of a plug cock valve is shown in Figure 3-1. Essentially plug cock consists of a body casting in which a conical plug is fitted. The plug has an opening (cylindrical bore) through which the liquid passes. Some packing materials are included around the stem to close it. The sides of the plug should not be parallel or tapered too much. These valves are used when either complete opening or complete closing is desirable.

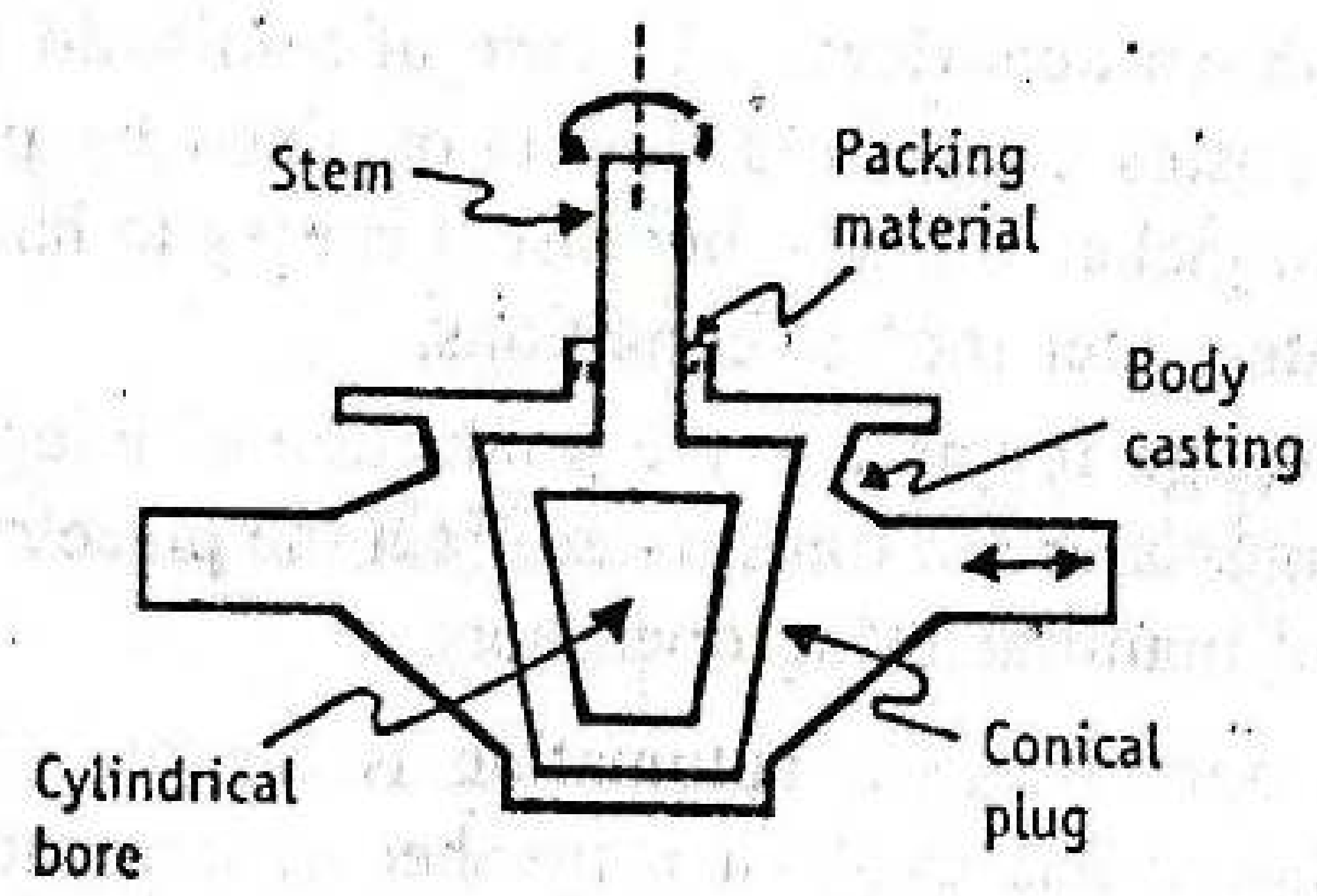


Figure 3-1. Construction of plug valve.

Cocks of wider designs are available with specially shaped openings, where the opening is nearly proportional to the angle through which the plug is turned.

Special design valves include lubricants at the stem of the cock. This lubricant is transmitted to the working faces through small holes drilled through the body of the plug.

Uses : (1) Plug cock valves are used for handling compressed air.

(2) These are used for the purpose of wide opening or complete closing conditions.

Disadvantages : Though it is simple, it has several disadvantages. These are:

(i) Plug cock valves are not suitable for steam or water, because of the cock material.

(2) It is difficult to turn the valves when the plug gets easily wedged in the body firmly. This problem is observed when the sides of the plug are too nearly parallel.

(3) Sometimes the plug comes out of its seat, if the plug sides are tapered too much.

(4) It is difficult to regulate the flow. In normal designs, the area of opening changes rapidly even with slight rotation of the stem. Similarly, flow does not change appreciably when the valve is opened fully.

Globe Valves

The construction of a globe valve is shown in Figure 3-2. A globe valve consists of a globular body with a horizontal internal partition. The passage of fluid is through a circular opening, which can be opened or closed by inserting a disc in the opening.

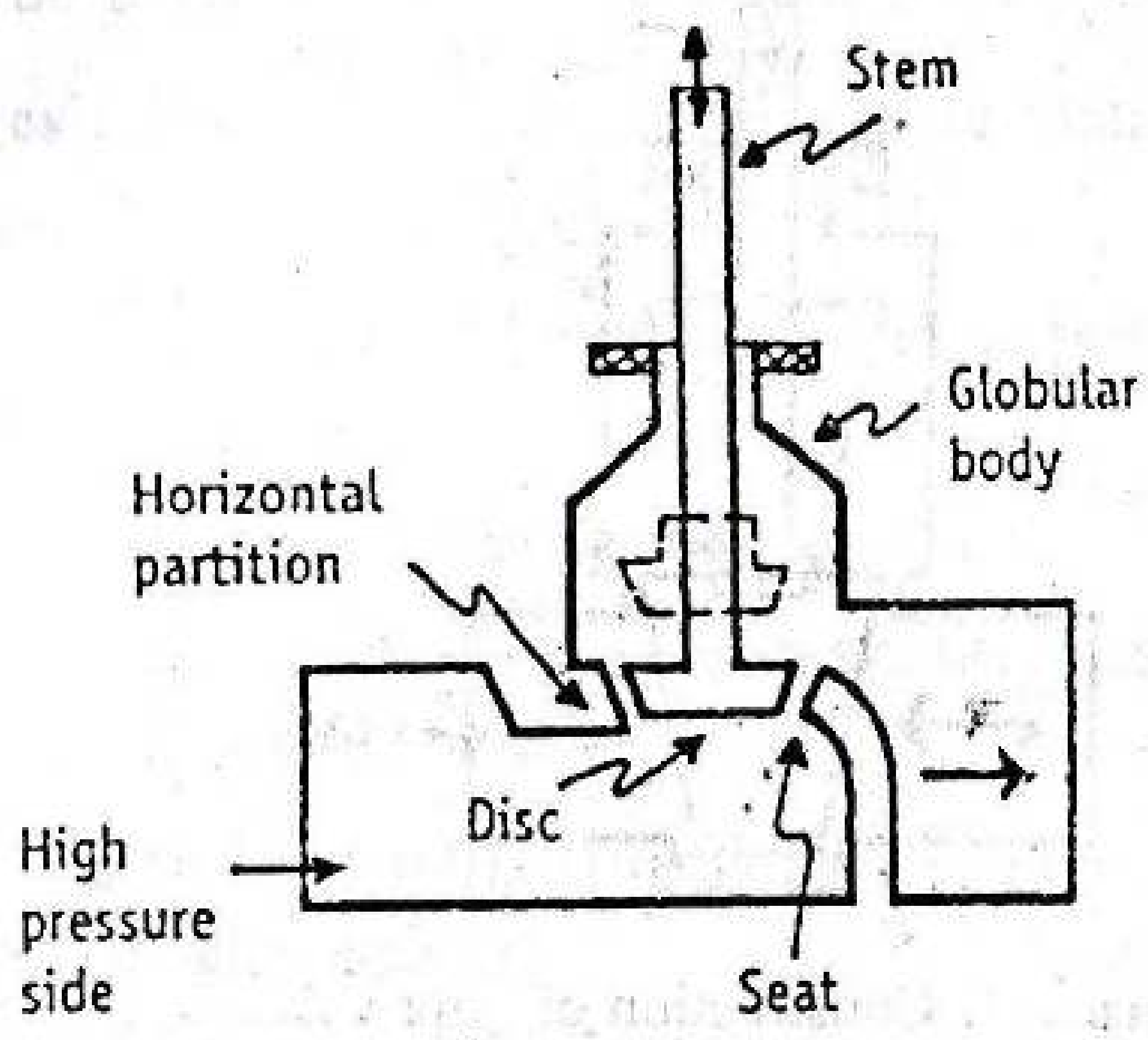


Figure 3-2. Construction of globe valve.

The disc is positioned on the ring, which is known as *seat ring*. The disc can be rotated freely on the stem. Globe valve is installed in the high-pressure side connecting the narrow portion of the disc. Globe valves can be connected in horizontal lines as well as in vertical lines.

The main difference in the variety of globe valves is the construction of the valve, namely disc and valve seat. Normally, cheaper valves have no separate seat ring. Good valves have the seat ring, which permits the ease of renewal. Angular valve is a modification in which an elbow fitting and a globe valve are combined in one compartment.

Uses : Globe valves are mainly used in pipes with sizes not larger than 50 millimetres. In horizontal lines, these valves prevent complete drainage.

Disadvantages : Rust, scales or sludge prevent the opening of the valve.

Gate Valves

The construction of a gate valve is shown in Figure 3-3. A wedge-shaped, inclined-seat type of gate is most commonly used. The pressure on the gates is controlling factor in large valves.

Two types of gate valves are available. In non-rising stem valve, the thread of the valve stem engages the gate. The gate can be raised and lowered without the movement of stem through the stuffing box. The advantage is that the overall length of the stem required is less. In the rising stem valve, the length of the stem is more, since the stem and gate are a single piece.

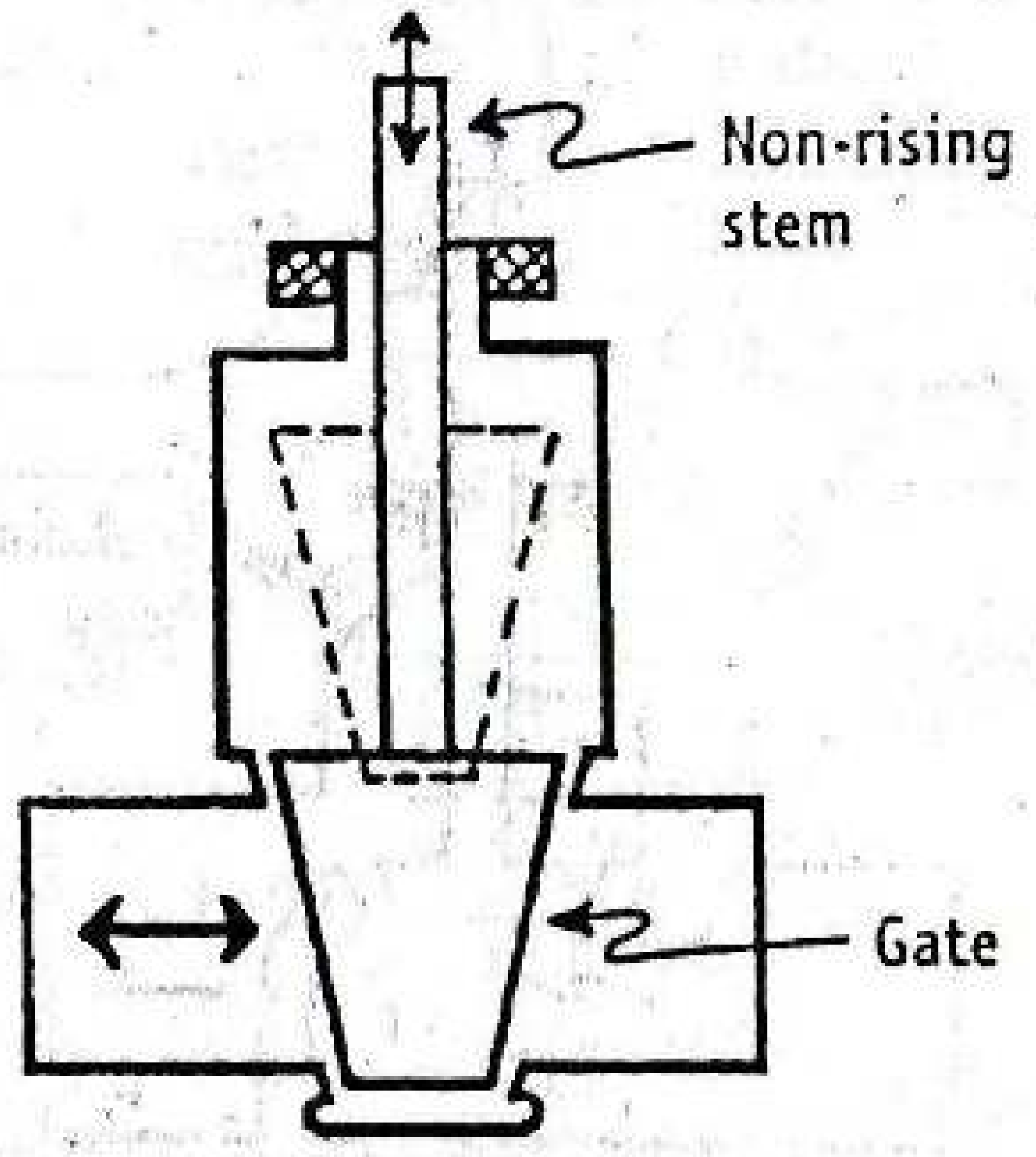


Figure 3-3. Construction of gate valve.

Advantages : (1). Gate valves are available in large sizes.

(2) These are available in a variety of designs to suit the conditions.

(3) Gate valves minimise the differential pressure during opening and stopping the flow.

Diaphragm Valves

The construction of a diaphragm valve is shown in Figure 3-4. Diaphragm is a flexible physical barrier. These valves are made of fabric reinforced, natural rubber and/or synthetic rubber faced with Teflon, a flurocarbon resin.

Special grades of rubber diaphragms coated with PTFE (polytetrafluoroethylene or teflon) are resistant to repeated steam sterilisation.

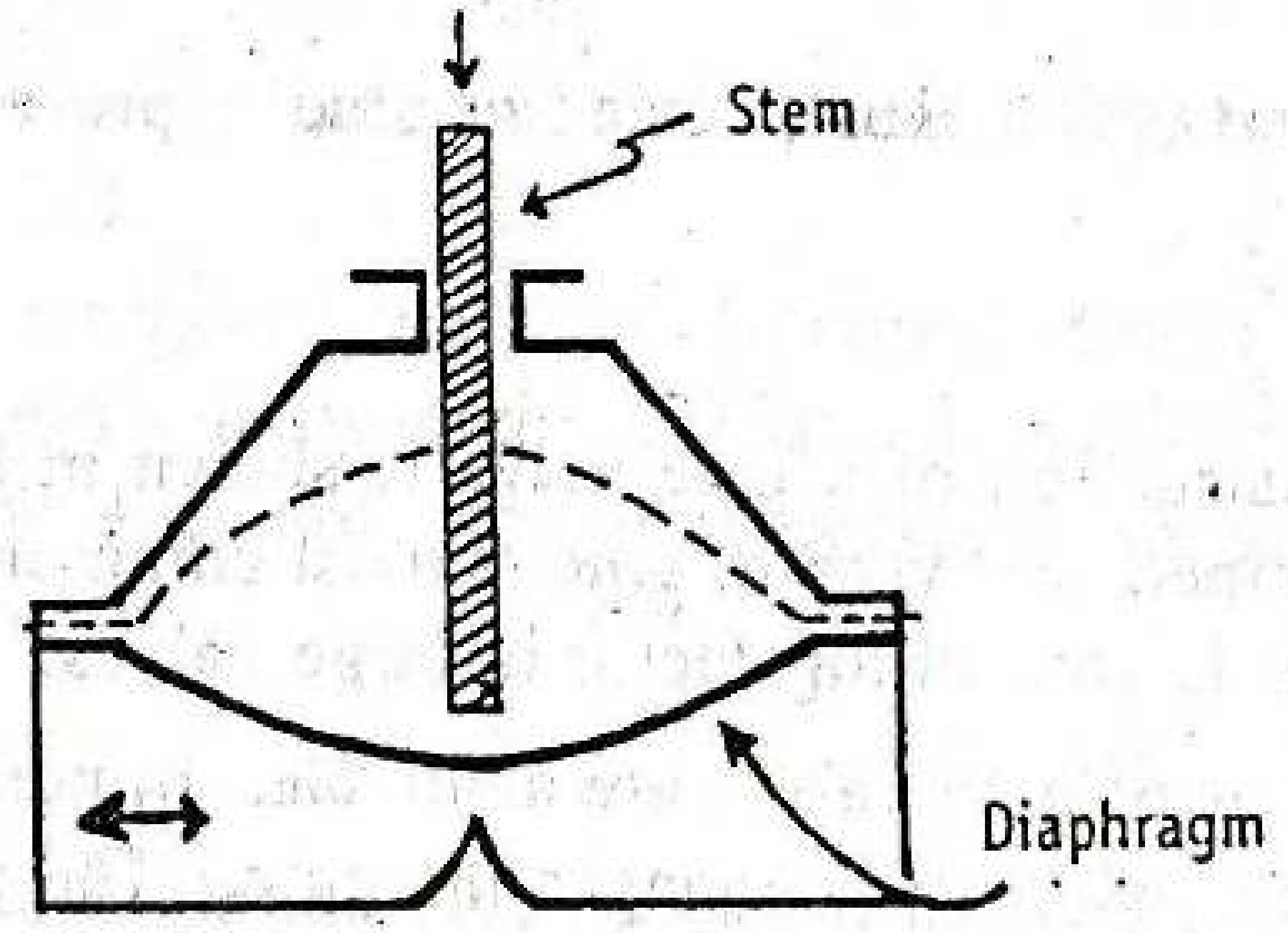


Figure 3-4. Construction of a diaphragm valve.

Uses : Diaphragm valves are more suitable for fluids containing suspended solids. Special types of diaphragms can be easily sterilised so that they can be used in the production of sterile products.

Advantages : (1) Diaphragm valves can be installed in any position.

(2) Pressure drop is negligible.

(3) Complete draining in horizontal lines is possible.

(4) Simple.

(5) Excellent operation (performance).

(6) Replacement of diaphragm is easy, there is no need to remove the valve from the line.

Disadvantages : (1) Diaphragm valves are applicable to pressures of approximately 340 kilopascals.

(2) Maintenance cost increases because of replacement of faulty diaphragms.

(3) These valves are expensive.

Quick Opening Valves (QO Valves)

In the gate valve, stem is threaded. Therefore, a number of turns are necessary to close the valve completely. QO valves have smooth stems and are opened or closed by lever handle in a simple operation. These are convenient, but involve the danger of water hammer.

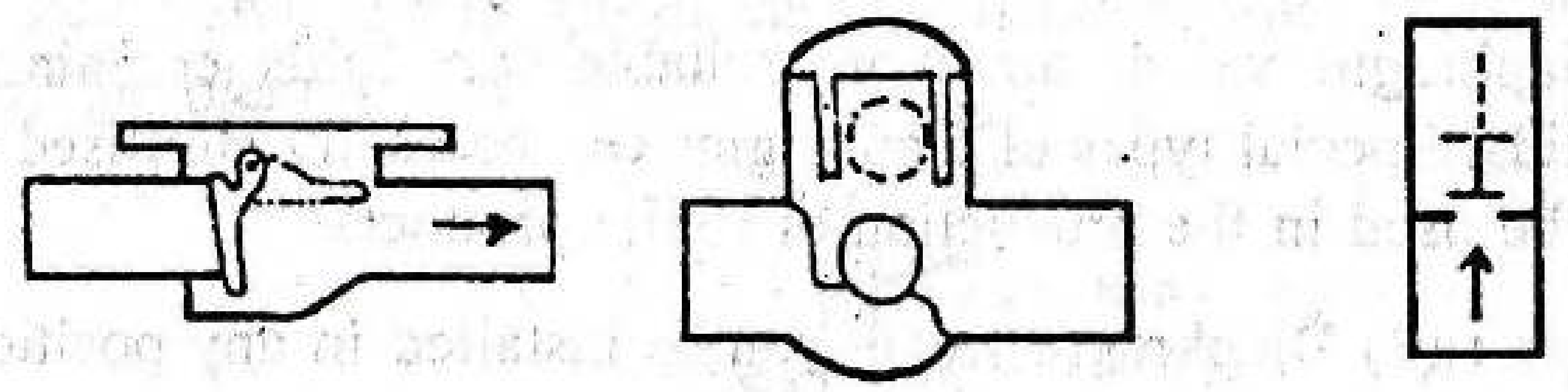
Water hammer : When a liquid is flowing in a pipe, it is associated with considerable kinetic energy due to its mass and velocity. When such a flow is suddenly stopped, the velocity is suddenly destroyed. Since liquids are incompressible, the energy appears as an intense shock. Sometimes, this shock can be about 60 times the velocity of the fluid. Hence, QO valves are used only in short lines. On large lines, the valve should be closed slowly.

Check Valves

These valves are used when unidirectional flow is desirable. Protective mechanism is included to prevent the reversal of flow. These are automatically opened, when the flow of fluid builds up the pressure.

(a) Swing check
(b) Ball check
(c) Lift check, vertical.

The construction of check valves is given in Figure 3-5.



(a) Swing check (b) Ball check (c) Lift check vertical

Figure 3-5. Construction of check valves.

Valves are classified depending on their functions. These are:

Reducing valves : These valves are used in order to maintain uniform pressure in one part of a system lower than the pressure in another part of the system. These valves are merely a special case of regulating valves.

These valves are installed in a high pressure steam line to give a constant, but lower pressure of steam in a steam coil.

Regulating valves : These valves are used to control the flow so as to maintain some other variables such as temperature and concentration at constant values.

PUMPS

Pump is a mechanical device to increase the pressure energy of a liquid. In most of the cases, pump is used for raising fluids from a lower level to a higher level. A number of pumps have been developed to meet a variety of operating conditions. Their principles of working and construction are widely different. The classification of pumps are:

Reciprocating pumps, examples are piston pump, plunger pump and diaphragm pump.

Rotary pumps, examples are centrifugal pumps and gear pumps.

Miscellaneous pumps, example is peristaltic pump.

Some of them are discussed in the following sections.

RECIPROCATING PUMPS

In *reciprocating pumps*, the pumping element moves in forward and backward directions in a cylinder. This cylinder is known as *water cylinder*, since it is usually used for pumping of water. In a simple reciprocating pump, the pumping element moves forward (down stroke or delivery stroke) to push the liquid out as a discharge (output), later it recedes (suction strike) to draw the liquid in as an input. Normally, the pumping element is either a piston or a plunger.

The reciprocating pump is a positive acting type, i.e., a displacement pump. The pump creates pressure and lifts the liquid by the displacement of a moving member.

Uses : These are used for injection of small quantities of inhibitors in polymerisation units and corrosion inhibitors to high pressure systems. These are also used for boiler feed water applications.

Any form of power may be utilised to drive the piston rod. The movements may be applied through a piston rod or a crankshaft using either steam (*steam pumps*) or power (*power pumps*).

Steam reciprocating pumps : In these pumps, the steam cylinder contains a piston, which is directly connected to a piston rod of the water cylinder. This is the most common in reciprocating pumps. Steam pumps can have one steam cylinder with piston (simplex pump at steam-end) or two cylinders each having separate piston (duplex pump at steam-end). Normally, these two cylinders are mounted side by side in the same casing.

Power reciprocating pumps : The power pumps include all forms of reciprocating pumps, in which the piston is actuated by some form of energy other than steam. An example is an electric motor. The movement of the crankshaft is usually through gears by a belt from a line shaft using an electric motor. The common form of such a pump is the vertical, single-acting triplex power pump.

In general, the reciprocating pumps are classified based on the construction of water cylinders. These are two types.

(a) Piston Pumps
(b) Plunger Pumps

These are discussed in the following sections.

Piston Pumps

In *piston pumps*, the piston reciprocates in the enclosed space of the water cylinder. The piston carries the packing material along with it. As the piston moves, the packing material also moves along with it. The general classification of piston pumps is given in Figure 3-6.

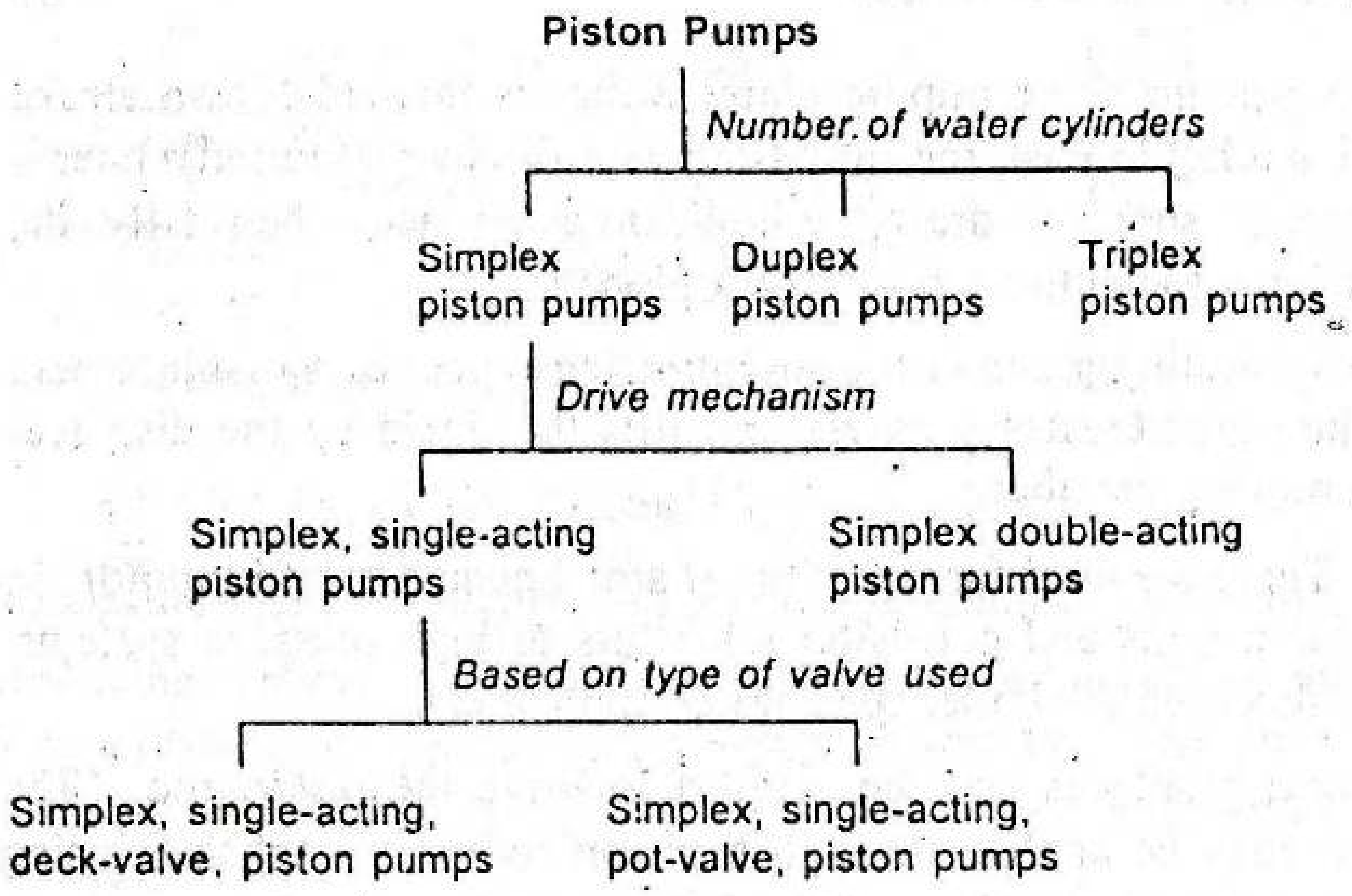


Figure 3-6. Classification of piston pumps. Further classification for duplex and triplex piston pumps follows the same sequence as that of simplex pump branching.

Piston pumps are classified based on the number of water cylinders.

Number of cylinders	*Name*	*Connecting system from steam end to water end*
One	**Simplex**	piston rod is joined
Two	**Duplex**	piston rods are joined separately
Three	**Triplex**	piston rods are joined separately

In a duplex pump, two water cylinders are arranged separately side by side in the same frame. Their piston rods are connected separately to two steam cylinders, which are also arranged side by side in the same frame in the steam end. Connecting several cylinders has an advantage of making the discharge more uniform and free from pulsation.

Each water cylinder may have different drive mechanisms and further classified as:

1. Single-acting piston pumps
2. Double-acting piston pumps

1. Single-acting piston pumps : These displace water on one half of the cycle of the piston movement, normally during the down-stroke. During the other half of the cycle (backward-stroke), the cylinder receives the fluid. Such a pump requires a minimum of two valves: one for receiving the liquid into the cylinder and the other for pumping the liquid out of the cylinder. Single-acting pumps have limited capacity in handling liquid and the discharge is pulsated.

2. Double-acting piston pumps : These displace water on both halves of the cycle. Such a pump requires a minimum of four valves. Two valves are used for suction (to receive fluid) and two valves are meant for pumping the liquid out. Several valves are used in order to pump the discharge at high velocity and more volume of water, during one-half of the stroke. The mechanisms of action of these valves are illustrated in the simplex, double-action, steam-driven, deck-valve, piston pump, which is given in the later section.

Since valves are employed in the pumping, the construction of valves is important for its effective functioning. These are classified as follows.

- Deck valve
- Pot valve

Deck valve : In this valve, springs are attached to the stem, which hold the valve disc against the valve seat. The valve is a non-returnable-one way, so that the flow is unidirectional. For high pressures deck valve is not suitable. Some times, bigger sizes of deck valves are necessary to give a high-pressure discharge.

Pot valve : Pot valves usually have metal discs, which are often provided with guide vanes to keep them in right alignment. The valve is a non-returnable-one way, so that the flow is unidirectional. These are required, when fluids are handled at high pressures. In case of viscous liquids and liquids with very high pressures, loose metal balls are used in place of the valve disc, since these are not strong enough to withstand.

The general principles described above are combined and illustrated using a model piston pump given below.

Simplex, Double-Acting, Steam-Driven, Deck-Valve, Piston Pump

Construction : The construction of a simplex, double-acting, steam-driven deck- valve, piston pump is shown in Figure 3-7. In the water cylinder, a piston consists of two discs with rings of packing between them. These are arranged such that outer packing can be drawn up to compress it. The piston may operate in a cylinder bored directly in the pump casting. In some pumps, the piston operates in a removable bronze liner.

This pump has four valves, i.e., double-acting. The lower row valves, E_1 and E_2, are suction valves and the upper row valves, F_1 and F_2 are discharge valves. For this purpose deck valves are used. The valve disc is made of hard rubber or metal. The valve is a non-returnable-one way so that the flow is unidirectional.

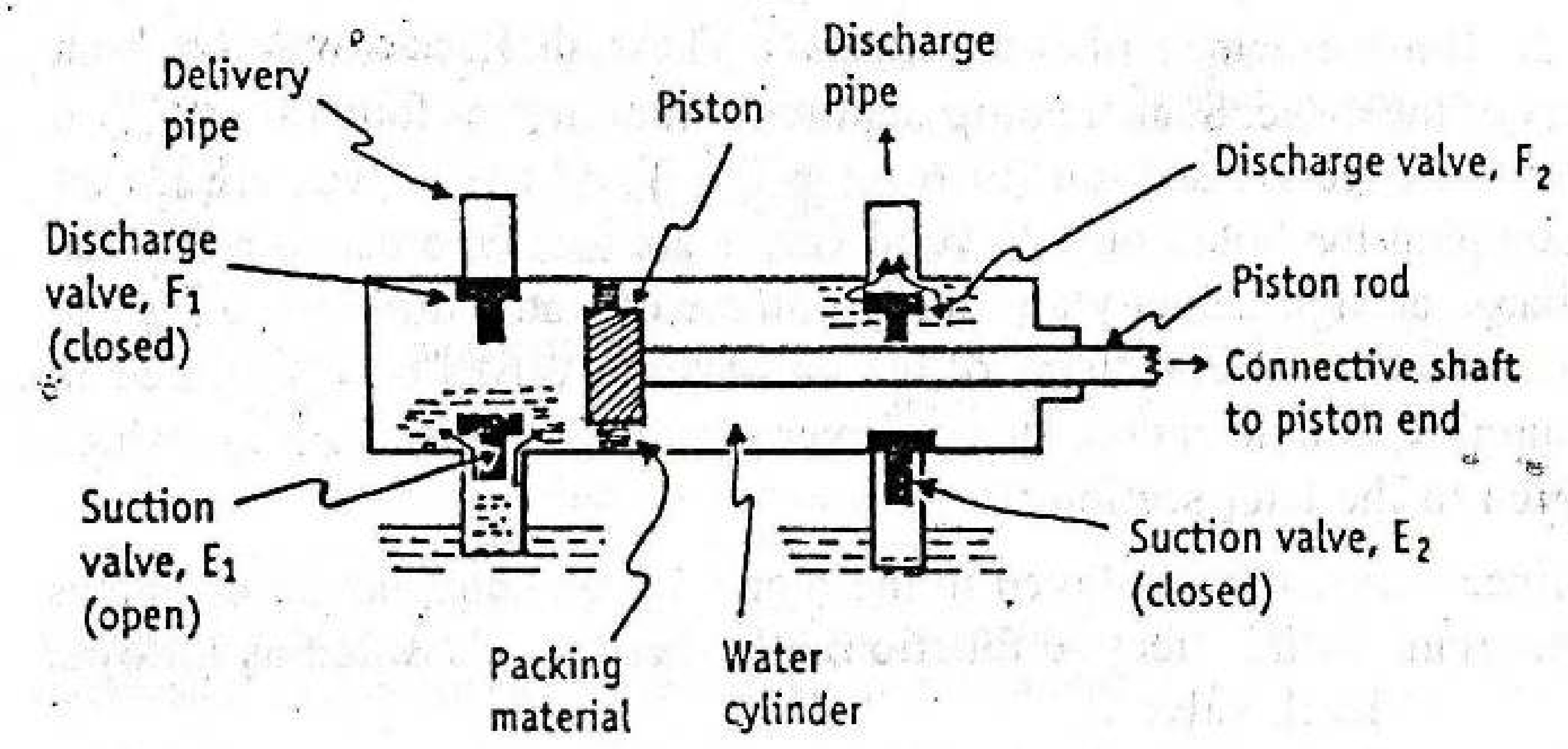


Figure 3-7. Construction of simplex, double-acting, steam-driven, deck-valve piston pump. Working principle is illustrated.

Working : Steam is used at full pressure for the entire stroke in order to maintain a constant pressure on the water end. This enables the pump to produce uniform discharge (output). The steam pressure sets the piston in motion at steam end. This makes piston to reciprocate in the water cylinder.

The valves are unidirectional. The movement of the piston creates vacuum and atmospheric pressure forces the water up through the suction pipe into the cylinder. The liquid pressure in the water cylinder allows the discharge valves (or delivery valves) to open.

When the piston is moving from left to right, the events occur in the following sequence.

Left side cycle	*Right side cycle*
E_1 (suction) valve opens : Water enters the cylinder from left side.	**E_2 (suction) valve closes :** Water does not enter the cylinder due to pressure.
F_1 (discharge) valve closes : Water will not be discharged from this left side.	**F_2 (discharge) valve opens :** Water (that is already present in the water cylinder) goes out through the discharge end.

Therefore, when the piston moves from left to right, water discharges through the valve, F_2. When the piston moves in the reverse direction, i.e., from right to left, it provides discharge from valve, F_1. Thus, the pump is a double-action pump, since it displaces water on both halves of

the cycle. Large volumes of fluids and at high velocity can be transported, since four valves are used.

Uses : Piston pumps are used for heads up to 60 metres. These pumps can be used, if the liquids are not too viscous, corrosive or abrasive. Piston mechanisms are employed in peristaltic and HPLC pumps.

Applications : Piston pumps are extensively used for spray system in sugar coating and film coating operations.

Disadvantages : (1) Piston pumps are relatively expensive.

(2) These are not easy to clean.

(3) Piston pumps induce coagulation of latex coating systems under conditions of significant line pressure.

Plunger Pumps

In *plunger pumps*, a plunger reciprocates in enclosed space of the water cylinder. The term plunger refers to an element, which moves past the stationary packing. The general classification is given in Figure 3-8.

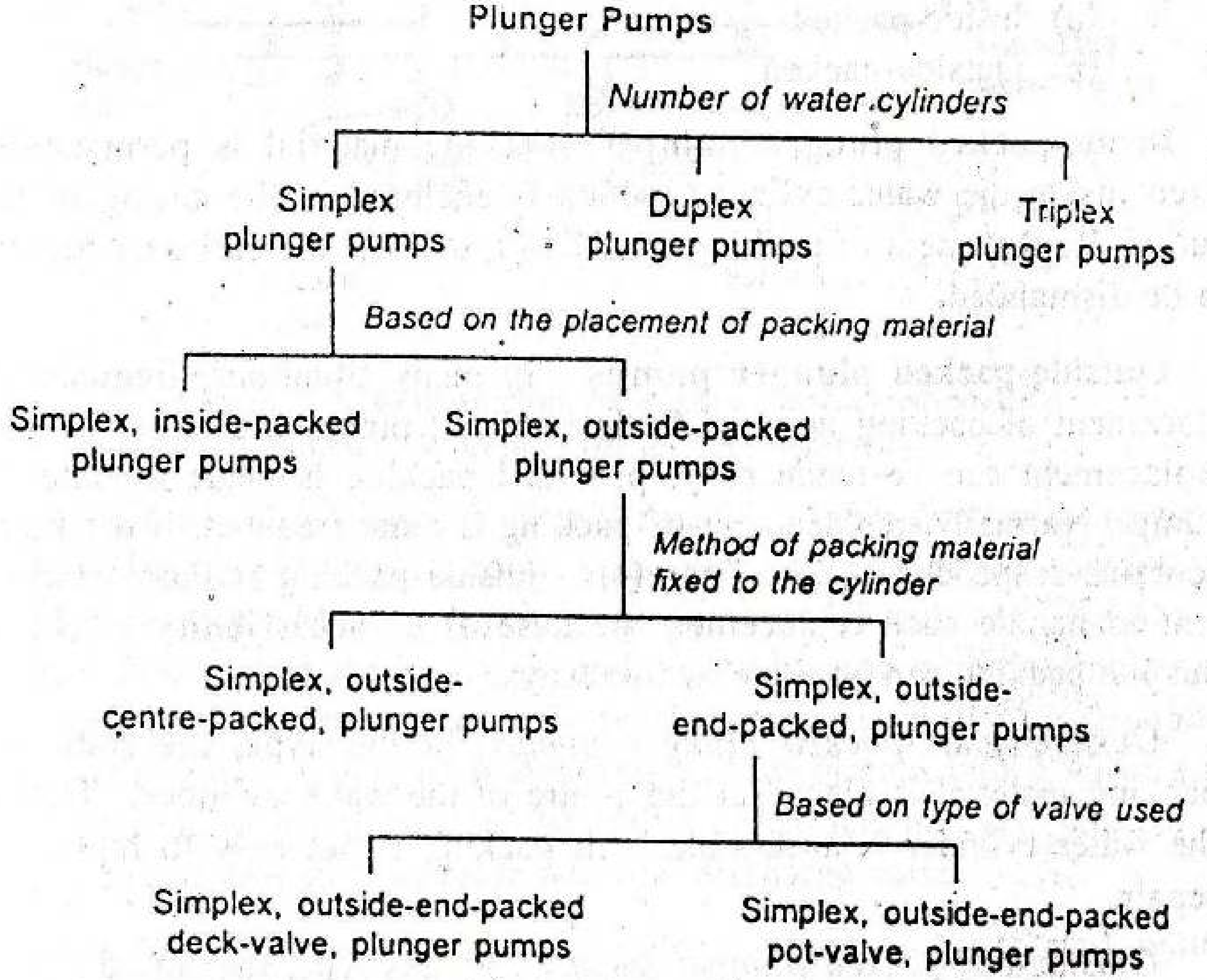


Figure 3-8. Classification of plunger pumps. Further classification for duplex and triplex plunger pumps follows the same sequence as that of simplex pump branching.

Plunger pumps are classified based on the number of water cylinders.

Number of cylinders	*Name*	*Connecting system from steam end to the water end*
One	**Simplex**	plunger rod via shaft
Two	**Duplex**	via crankshaft
Three	**Triplex**	via crankshaft

When the number of cylinders is more, these are connected in parallel to a crankshaft. For example, in a triplex pump, three plungers are connected to a crankshaft at points 120° apart.

Connecting several cylinders has an advantage of making the discharge more uniform and free from pulsation. It is better to use several cylinders each of small size, thereby it is easier to build up high pressure and maintain packing.

Since packing material is permanently fixed in the water cylinder, it can be placed in any position. Based on its placement, plunger pumps are classified as:

(a) Inside-packed
(b) Outside-packed

Inside-packed plunger pumps : Packing material is permanently fixed inside the water cylinder, which is enclosed in the casing of the pump. Replacement of packing is difficult, because the entire casing has to be dismantled.

Outside-packed plunger pumps : In many situations, frequent replacement of packing material is desirable. If pumps are larger in size, replacement can be made easy, provided packing is made outside the pump. Normally, replacement of packing is more frequent, if the liquid contains suspended solids. Therefore, outside packing is more convenient to handle such replacement because of its accessibility. Further, outside packing can be done in two ways.

Outside-centre-packed plunger pumps: In this type, the stationary packing material is placed at the centre of the water cylinder. Though the water cylinder is accessible, still packing is not easy to replace or repair.

Outside-end-packed plunger pumps : In this type, the liquid can be pumped at high pressures, because packing can be more easily maintained. Repairs and detection of leaks are easy, if the packing is outside and end-packed in a water cylinder.

The general principles described above are combined and illustrated using a model piston pump given below.

Duplex Outside-End-Packed, Power-Driven, Pot-Valve, Plunger Pump

Construction : The construction of the water end of a duplex outside-end-packed plunger pump is shown in Figure 3-9. In the plunger pump, a plunger moves past the stationary packing. Since the pump is duplex, the water cylinder is divided into two parts (A and B) by a partition. Two plungers are used. Both halves of the plungers A and B are connected to the same driving mechanism and power supply.

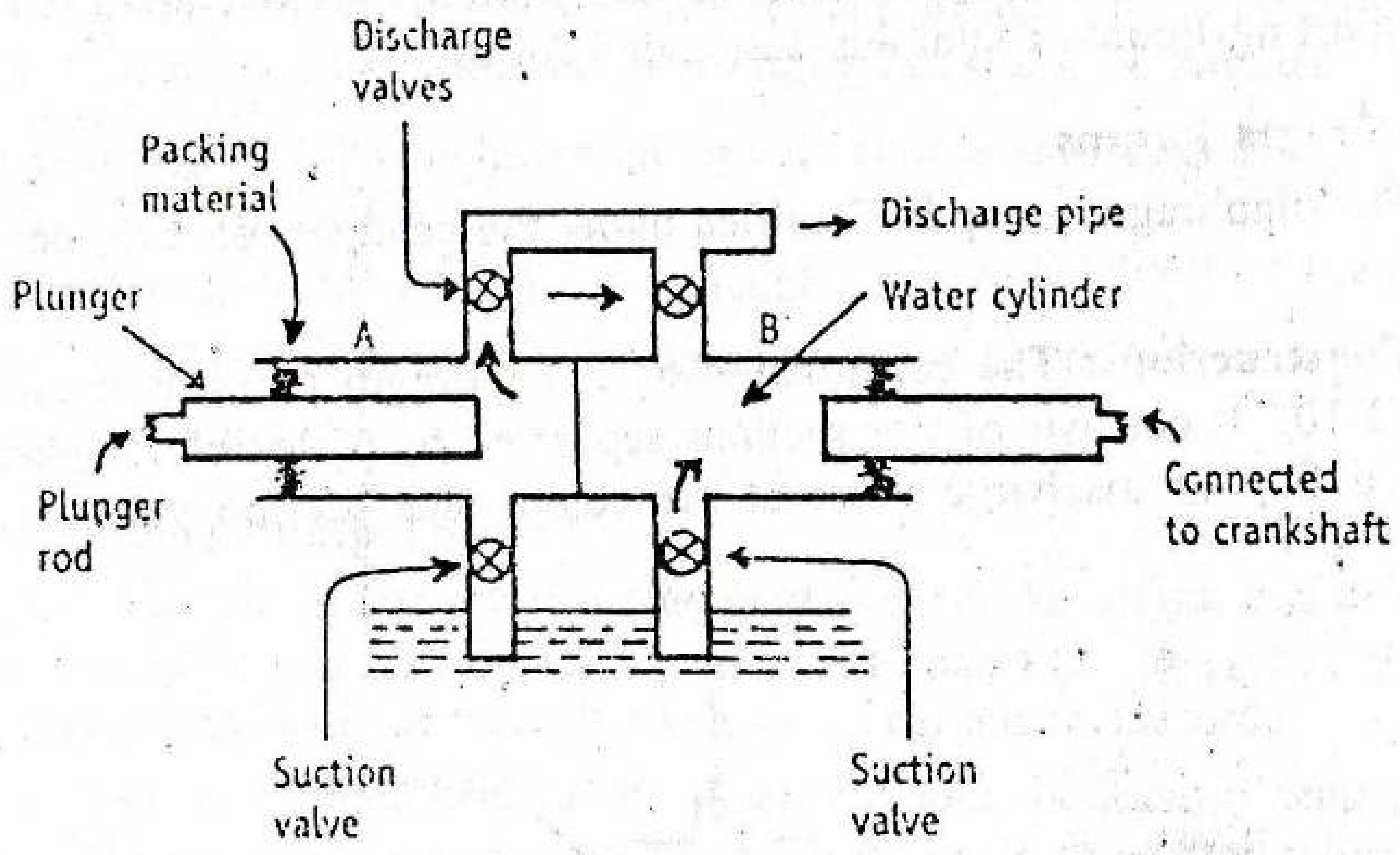


Figure 3-9. Construction of duplex outside-end-packed plunger pump. Working principle is illustrated.

It becomes necessary to replace the packing more frequently, particularly while pumping liquids containing solids. It involves the dismantling of the plunger. Many a times, packing should be checked for leaks. Hence, it is placed at the outside-end due to its ease in replacement and maintenance. The pot valves with metal discs are used. If it is desirable to handle liquids at very high pressures and for viscous liquid, valve disc is replaced by metal ball in the valve construction. Each plunger is connected to one suction valve and one discharge valve.

Working : Through an electric motor the line shaft is rotated, which further rotates the gears through a belt. The gears set the two plungers in motion in the two water cylinders (A and B). Each plunger is connected to one suction valve and one discharge valve.

The valves are one-way so that the flow is unidirectional. The movement of the plunger creates vacuum and atmospheric pressure forces the water up through the suction pipe into the cylinder. The liquid pressure in the water cylinder allows the discharge valves (or delivery valves) to open.

The two plungers are allowed to reciprocate in such a manner that at any moment, water enters into left-side cylinder, while water discharges through the right-side cylinder or vice versa. This ensures continuous pumping of water (non-pulsating). Large volumes of fluids at high velocity can be transported, since four valves are used in this case.

Uses : Plunger pumps are suitable for handling liquids at high pressures. Viscous liquids can be transported. These are used for transporting liquids containing suspended solids.

Diaphragm Pumps

The diaphragm pump is classified under the category of reciprocating pumps.

Construction : The construction of a diaphragm pump is shown in Fig. 3-10. It consists of two sections separated by a flexible diaphragm with a flap of discharge valve at the centre and suction valve at the

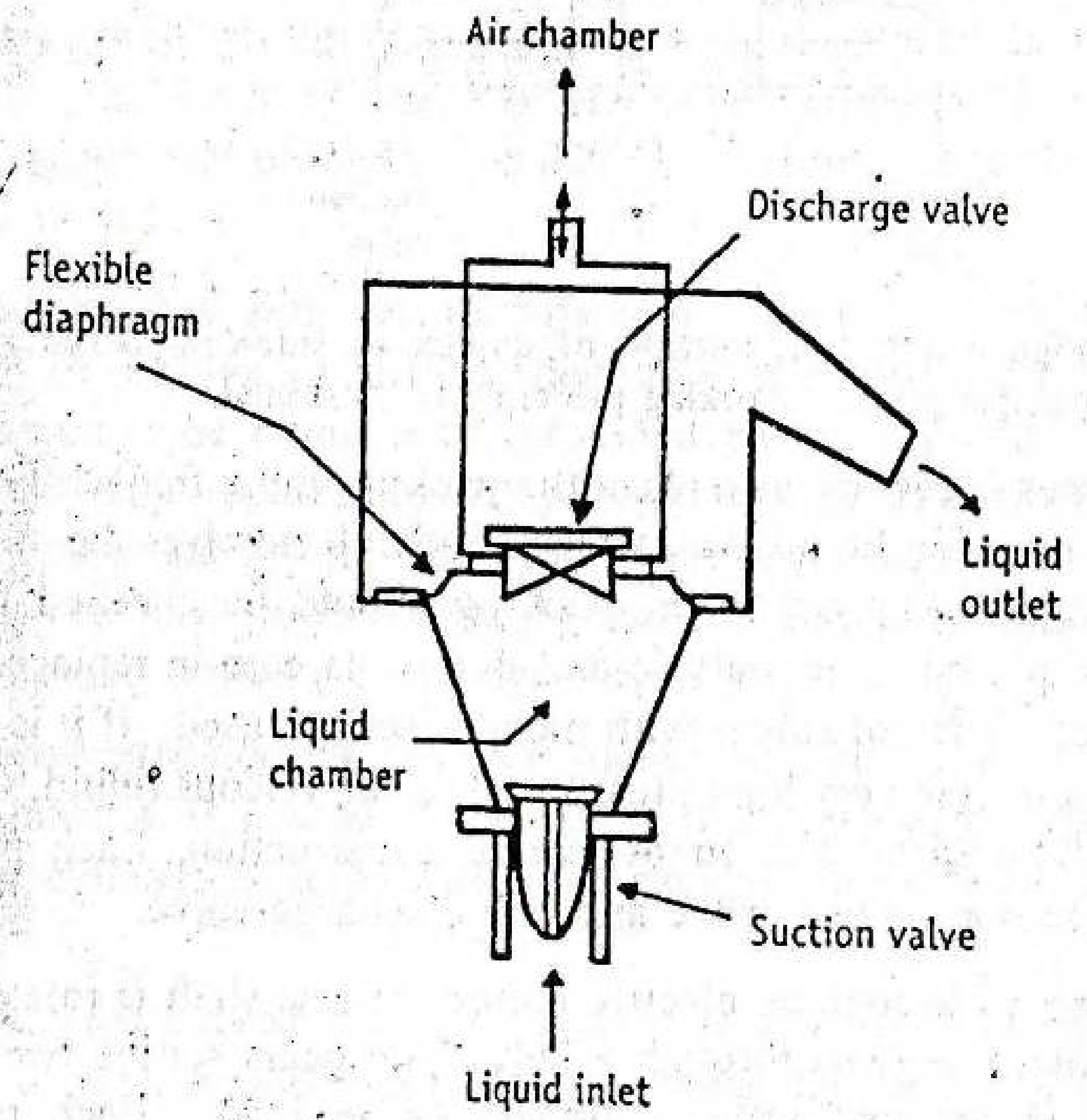


Figure 3-10. Construction of a diaphragm pump.

bottom. Diaphragm is fabricated with the materials such as metal, rubber and plastic.

Working : Through an air chamber, suction is applied so that the flexible diaphragm is pulled up (expanded). As a result, the suction valve is lifted up and the liquid enters the water chamber. When sufficient pressure is built up, the liquid lifts up the discharge valve. Then the liquid flows out. At this stage, both valves are opened so that suction and discharge operate simultaneously. Therefore, non-pulsating discharge is achieved. The stroke can be varied and discharge can be controlled within accurate limits.

Uses : Diaphragm pumps are used in transporting liquids containing solids. Hazardous, toxic and corrosive liquids can also be handled.

Advantages : (1) Diaphragm pumps are simple and rugged.

(2) They can be easily repaired.

(3) The rate of discharge can be regulated.

(4) Packing and seals of the diaphragm pump are not exposed to the fluids.

Reciprocating Pump Theory

As mentioned in the construction of pumps, all specifications of the pump should be mentioned, while procuring a reciprocating pump. Special attention is paid for the following specifications in the order.

1. The size (diameter) of the steam cylinder, because it regulates the pressure to be generated on the piston in the water cylinder.
2. The size (diameter) of the water cylinder, as it controls the desired discharge.
3. The length of travel of the piston.

Since piston displacement is essential for the discharge of fluid, it is necessary to evaluate the water cylinder in quantitative terms of efficiency. The displacement in the water cylinder may be theoretically expressed as:

$$\textit{Theoretical displacement of double-acting pump } (\mathrm{m^3/min}) = \text{piston speed (m/min)} \times \text{area of the piston } (\mathrm{m^2}) \quad (1)$$

$$\textit{Theoretical displacement of single-acting pump } (\mathrm{m^3/min}) = (1/2)\text{ piston speed} \times \text{area of the piston} \quad (2)$$

When the discharge is equal to the theoretical displacement, then displacement is considered as 100%. It is not possible to achieve 100% theoretical displacement, as there are losses during the functioning of a pump. These losses are due to:

- slippage past the piston
- imperfect packing
- leaking of valves
- failure of a valve to close instantly

In practice, the actual discharge could be 50 to 90 % of theoretical displacement. The actual discharge is known as *volumetric or water-end efficiency.* Normally, low-speed pumps are more efficient, provided packing of the material and valves are in good condition. The lower figures of water-end efficiency represent poor packing of pumps and working at high speeds. Such conditions produce excessive wear and tear on:

- valves
- valve springs
- packing

Steam cylinder end : Since steam cylinder is responsible for driving the piston in the water cylinder, the force applied is evaluated as:

$$\text{Force acting on the piston rod in steam cylinder (N)} = \text{steam pressure (Pa)} \times \text{area of steam piston (m}^2\text{)} \qquad (3)$$

Water cylinder end : In the absence of friction, the entire force would be transferred to the piston of the water cylinder. Under ideal conditions, it is expressed as:

$$\text{Theoretical maximum water-end pressure (Pa)} = \frac{\text{force acting on the piston rod (N)}}{\text{area of water piston (m}^2\text{)}} \qquad (4)$$

Normally, it is expected that the piston remains stationary, if the total force on the steam piston is equal to the total force on the water piston. In order to do work on the liquid and to overcome pump friction, total force on the steam piston should be greater than the theoretical force

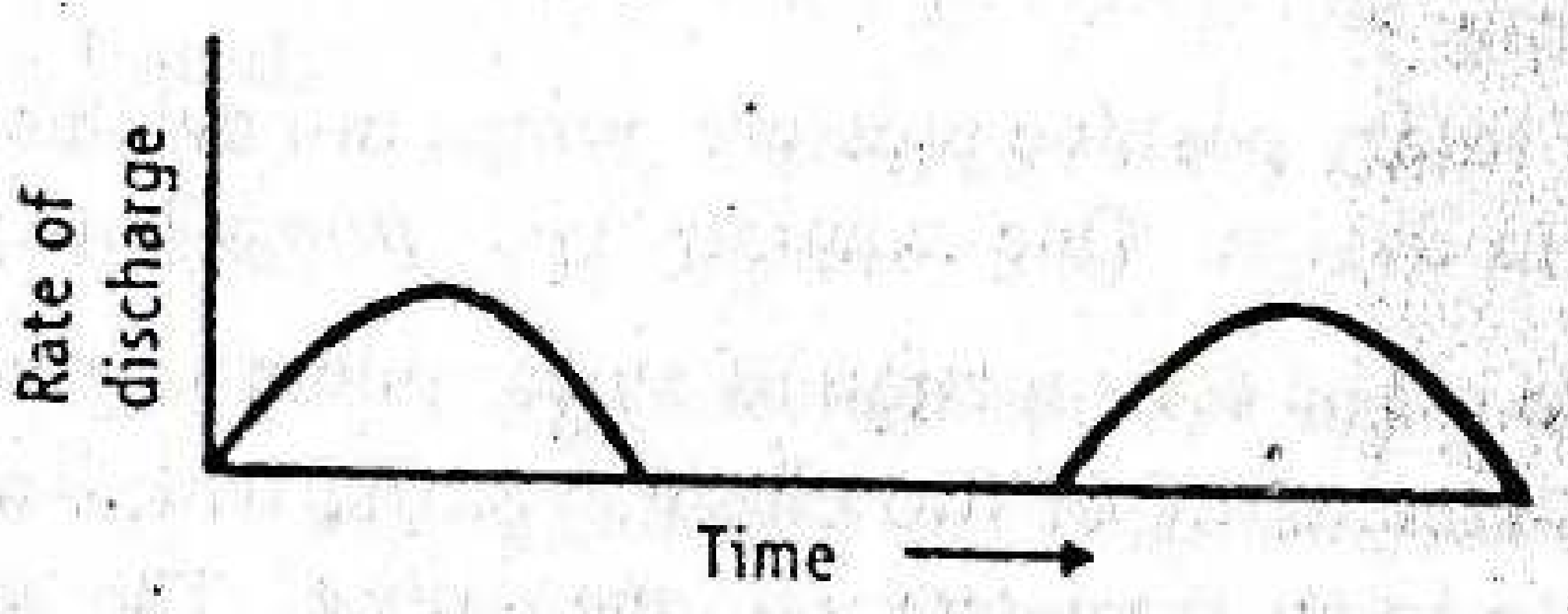
$$\text{Steam-end or pressure efficiency} = \frac{\text{theoretical pressure on the steam piston (Pa)}}{\text{actual pressure needed (Pa)}} \times 100 \qquad (5)$$

This efficiency varies from 60 to 80%.

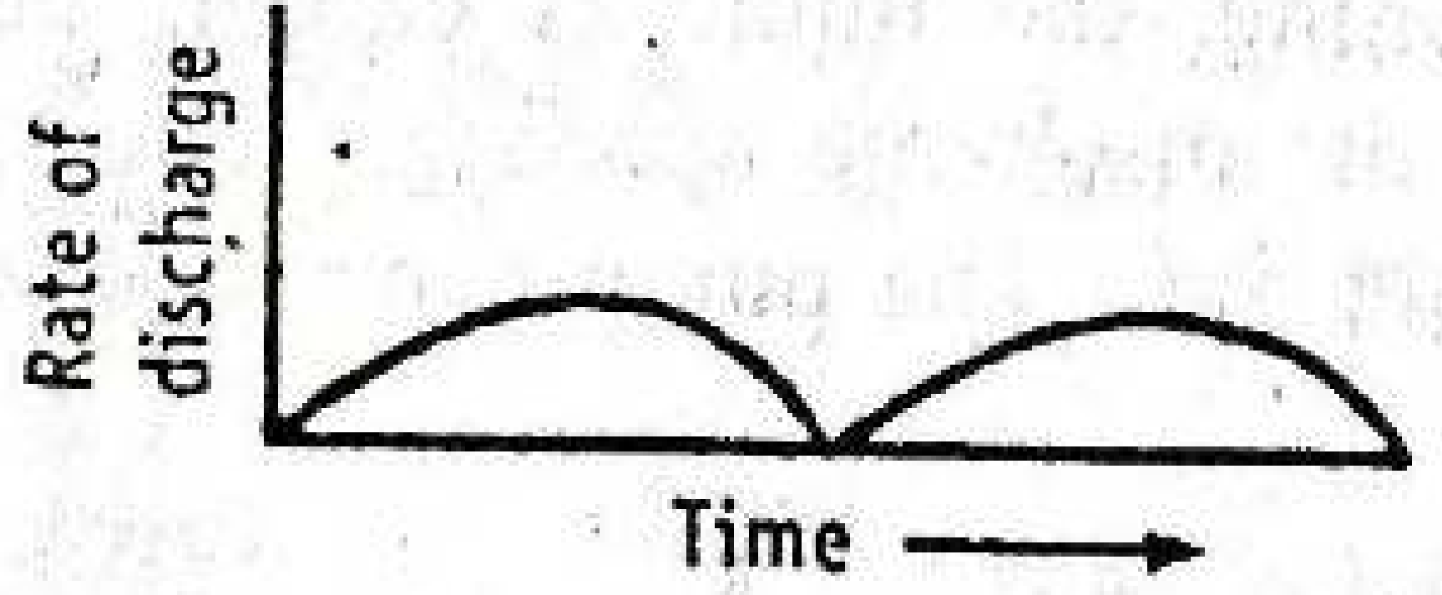
Nature of discharge : The liquid discharge in a single cylinder pump is shown in Figure 3-11. In a single cylinder pump, the discharge is zero at the beginning of the stroke. As the piston reaches full speed at the centre of the stroke, the discharge rises to a maximum. From this point, it decreases to zero at the end of the stroke. Thus the discharge is not uniform, but pulsating (Figure 3-11a).

Several measures may be followed in order to obtain desired nature of discharge as given below.

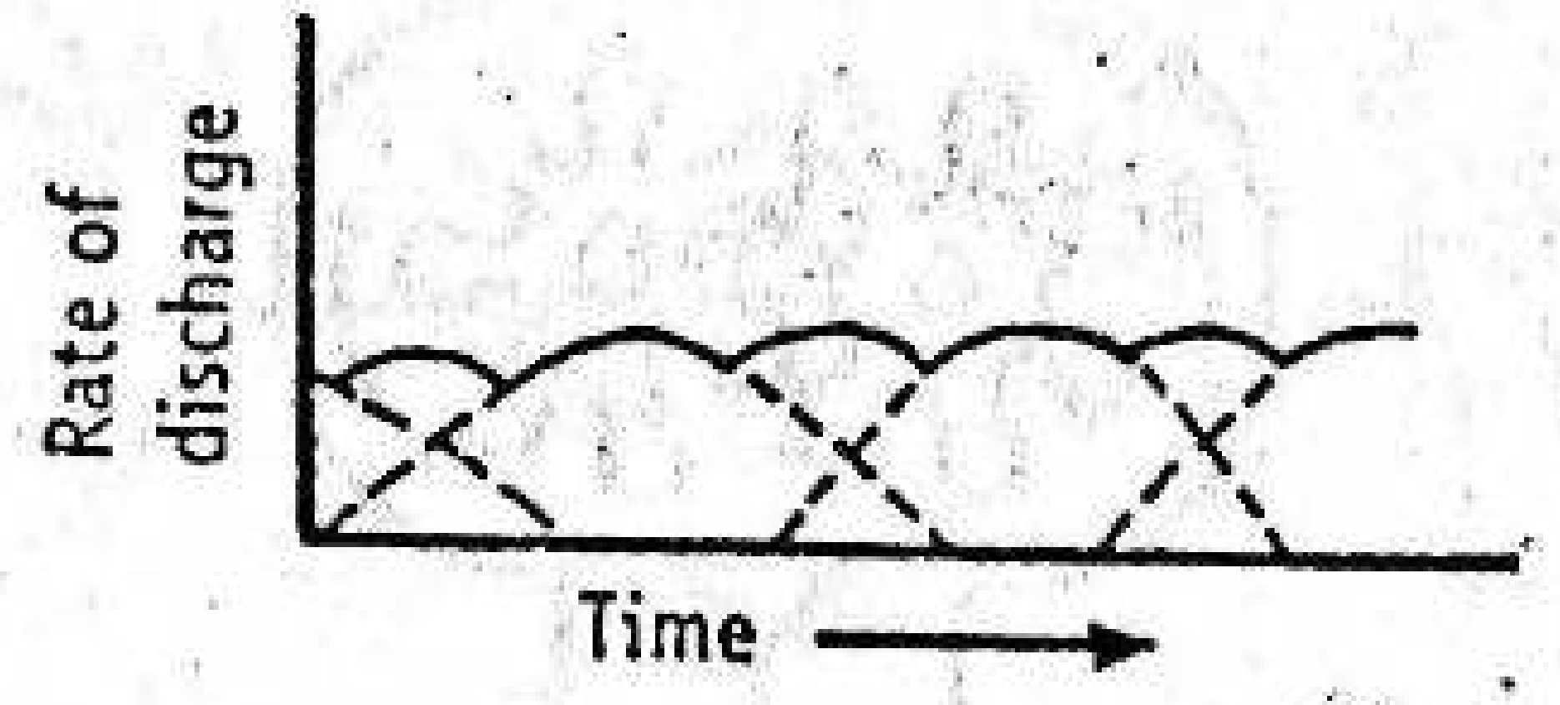
- Pulsating discharge can be removed by using a duplex pump with a piston set half a stroke apart (Figure 3-11b).
- For high pressures, a triplex pump is more suitable, since it avoids shocks and pulsations. The theoretical discharge from a triplex pump is shown in Figure 3-11c.
- For very high pressures, pump with five cylinders on a single crankshaft is employed to make the discharge still more uniform.
- A large air dome connected to the discharge side further reduces the fluctuations. The air in the cylinder will be compressed, when water piston is accelerating and will be expanded when it is decelerating.



(a) Discharge curve of a single acting simplex pump.



(b) Discharge curve of a single cylinder, double acting pump.



(c) Discharge curve of single acting triplex pump.

Figure 3-11. Discharge curves of different pumps.

ROTARY PUMPS

Rotary pump is the one by which the liquid can be transported based on the mechanism of rotation of one or more elements within a stationary casing.

The pump consists of two circular discs with lobes, which are geared to each other or single circular impeller with vanes. In these pumps, the rotary mechanism throws the liquid away from it and pumping is achieved. In general, rotary pumps are classified based on the nature of force applied in pumping. These are:

I. Positive displacement pumps
II. Centrifugal pumps

These are discussed in the following sections.

I. Rotary Positive Displacement Pumps

In *rotary positive displacement pumps*, the liquid is mechanically displaced by the rotation (by pressure) of one or more elements within a stationary housing.

A variety of rotary positive pressure pumps are available with significant variations in design. One example, *gear pump* is explained below.

Gear pumps : The construction of a gear pump is given in Figure 3-12. It consists essentially of two circular gears, which mesh with each other. These run in close contact with the casing. The gears are rotated by some external agency. As spaces between the teeth of the impeller pass the suction opening, the liquid is caught between them, carried around the casing to the discharge opening. The teeth come into mesh, which forces the liquid out. The pump can work without valves also.

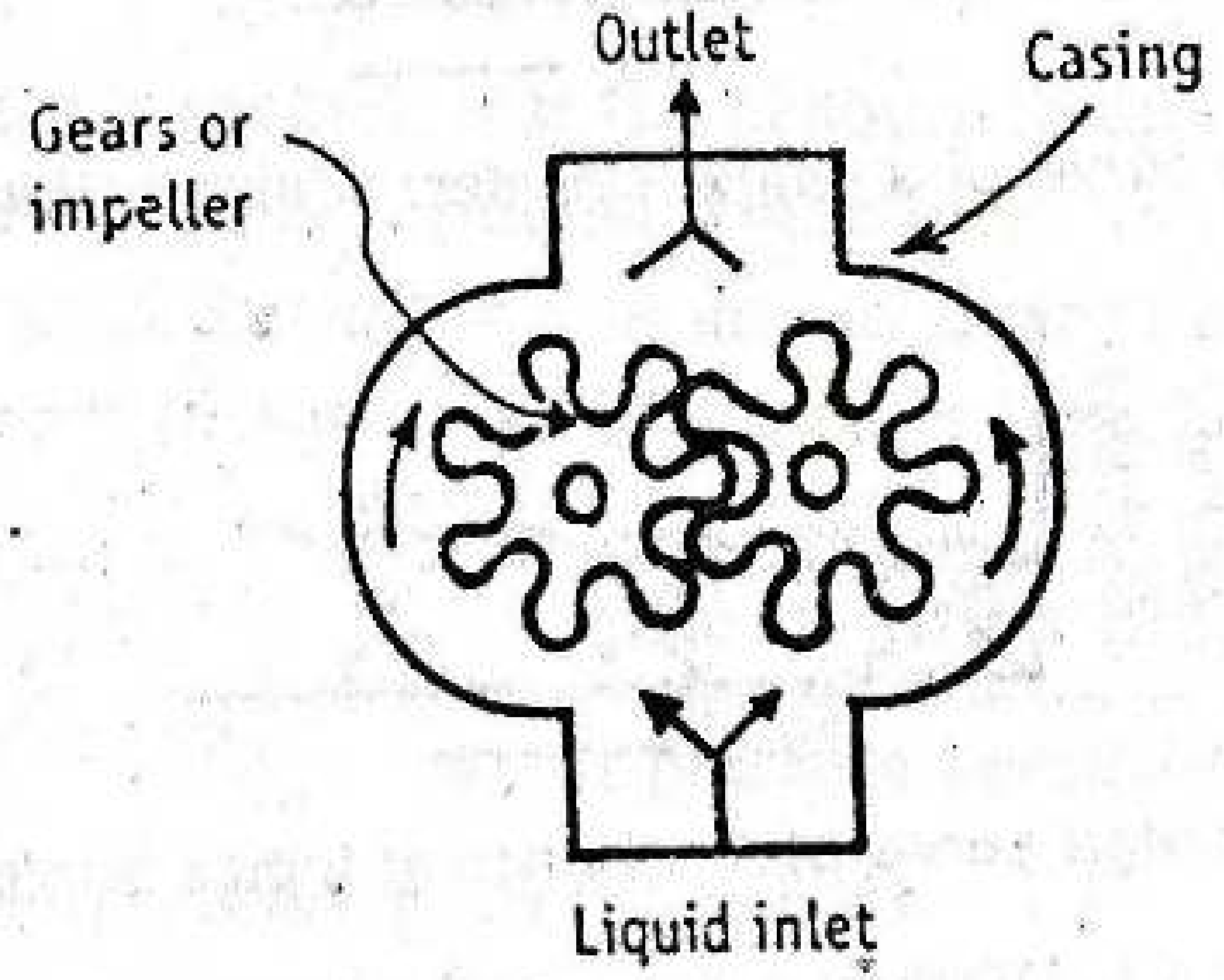


Figure 3-12. Construction of a gear pump.

The number of teeth on each impeller varies from 2, 3 or more. The two or three lobed pumps are generally known as *cycloidal pumps*. If the discharge valve of these pumps is closed while it is running, the pressure is built up inside the pump, which leads to either stopping the pump or breakage. In these pumps, the discharge rate is directly proportional to the speed.

Uses : A gear pump can handle viscous or heavy liquids such as vegetable oil, animal oil, greases, molasses, brine, semisolids and waxes. It is extensively used in aqueous film coating. It can transfer liquids of wide range of viscosities. It is useful when the speeds are not very high. Rotary positive-displacement (gear pump) pump is used to handle liquids that do not contain abrasive material.

Advantages : Gear pumps develop high pressure. It gives a discharge nearly free from fluctuations and independent of pressure.

Disadvantages : Gear pumps are not employed for transportation of solids in suspensions. It requires more complicated clean up procedures. It is likely that latex coating systems coagulate as a result of shear developed as liquid passes through pump head. It is also likely that excessive wear of element occurs while pumping highly pigmented, low viscosity coating liquids.

II. Centrifugal Pumps

The general construction of centrifugal pumps is shown in Figure 3-13. In centrifugal pumps, the blades of impeller rotate by which a reduction in pressure is produced at its centre (Figure 3-13a). This suction draws the liquid into the pump (Figure 3-13b). The basic function of a centrifugal pump is to produce kinetic energy by the action of centrifugal force and then convert this energy partially to pressure by effectively reducing the velocity. Thus liquid is pumped out at high pressure and then transported.

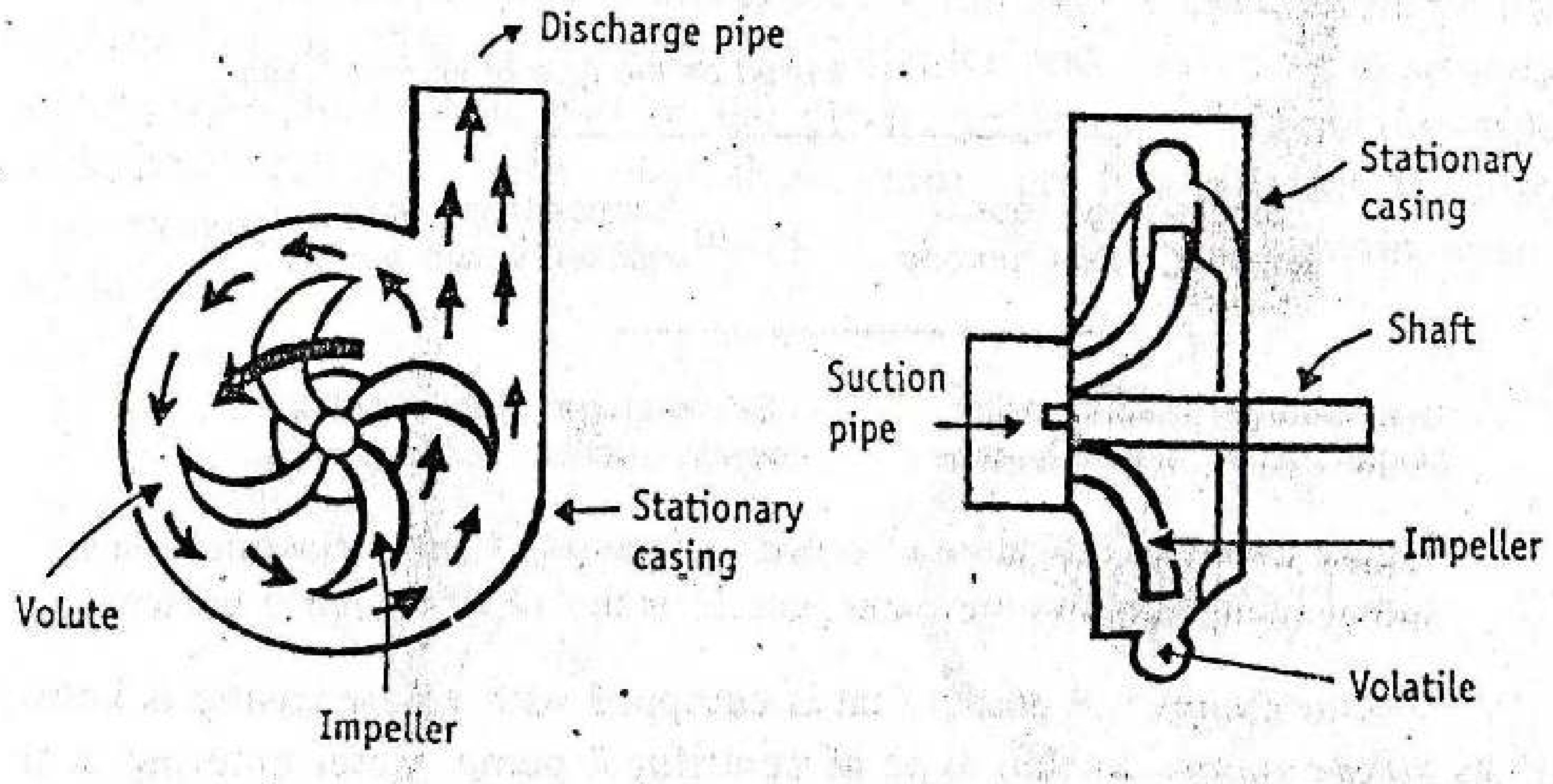


Figure 3-13. The general construction and parts of a centrifugal pump.

In short, the centrifugal pump helps to rise liquids from a lower level to a higher level by creating a required pressure with the help of centrifugal action.

Centrifugal pumps have several advantages such as simplicity, low maintenance requirement, low initial costs, quiet operation and non-pulsating flow. These pumps occupy less floor space. Centrifugal pumps can be built with corrosion resistant materials. These have no limitation on the capacity of the pump. Therefore, centrifugal pumps are found practically in every service.

Classification of centrifugal pumps : Centrifugal pumps are classified based on the type of casing of the pump, volume or diffusion. Such a classification of centrifugal pumps is given Figure 3-14.

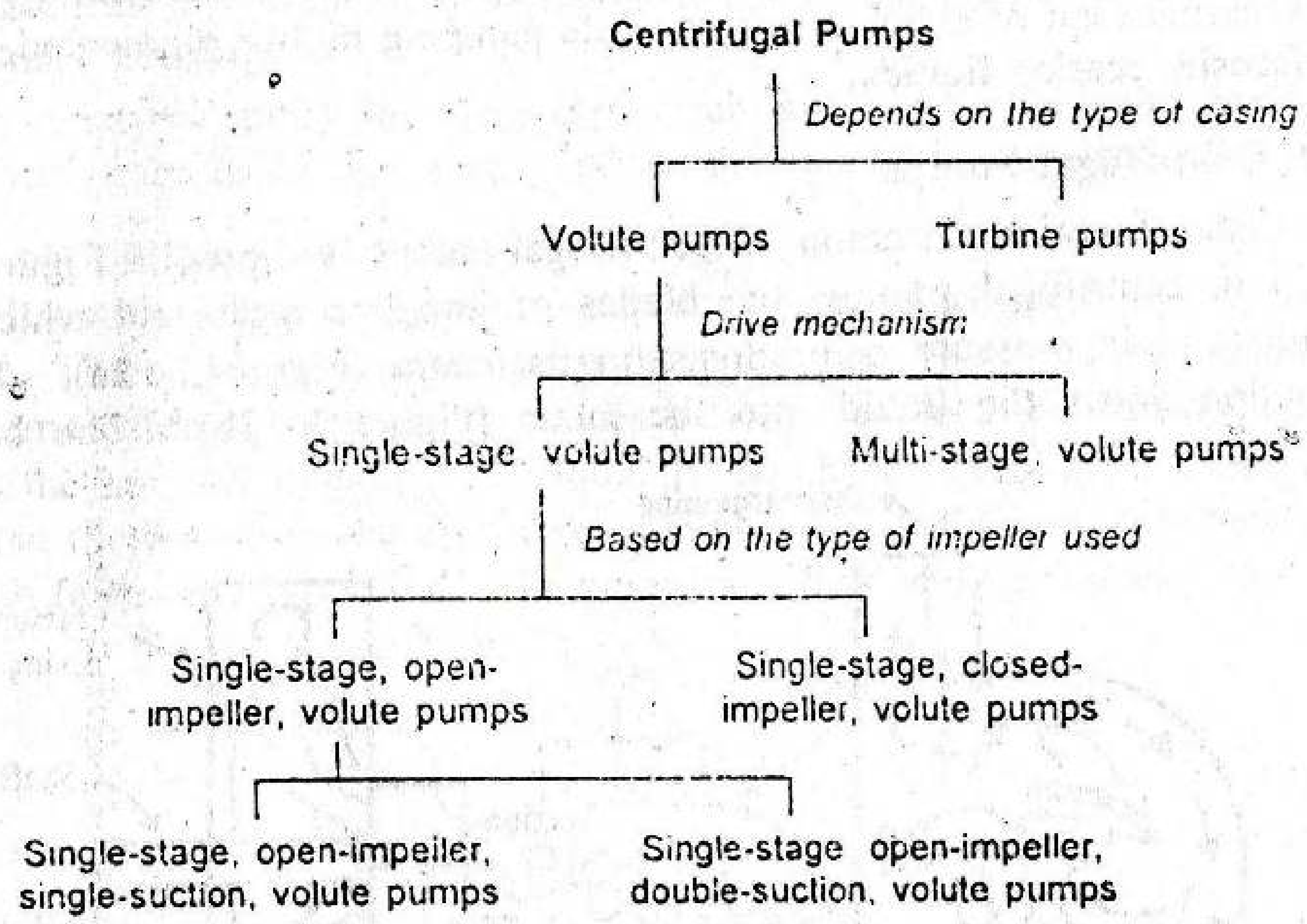


Figure 3-14. Classification of centrifugal pumps. Further classification on turbine pumps follows the same process as that of volute pump branching.

Volute pumps : A pump that is equipped with volute casing is known as *volute pump*. In this type of centrifugal pump, water entering at the suction point is thrown outwards into the volute by the rotation of the curved vanes. As a result, the liquid suddenly changes its direction in the volute, which decreases the velocity head and consequently increases the pressure head. These changes facilitate the pumping of the liquid. The step to change the direction of liquid flow is not smooth. Therefore, these pumps are least efficient. These are also less expensive.

Turbine pumps : A pump in which a diffusion casing equipped with vanes is known as *turbine pump*. In this type of centrifugal pump, a stationary diffusion ring is interposed between the impeller and casing chamber. As a result, the change in the direction is smooth, without shocks during pumping. Therefore, it does not involve energy losses due to eddies as observed in volute pumps. Therefore, turbine pumps are more efficient. However, these are expensive.

Single-stage pumps : In this type, one impeller is employed. Single-stage volute pumps are common and the cheapest. However, their efficiency is the least. The single-stage, turbine pump can generate maximum head of about 90 metres.

Multi-stage pumps : In this type, two or more impellers are placed in series. The liquid from the tip of one impeller is delivered to the inlet of the next impeller with minimum loss. Multi-stage volute pumps are not common, since the losses in each stage would add up leading to a low overall efficiency. In turbine pump, multi-stage can be employed to increase the efficiency of a pump. Heads up to 300 metres may be generated. However, multi-stage turbine pumps are more expensive.

These pumps (volute and turbine) are further classified as follows.

Open-impeller pumps : In this type, the impeller is open to the volute (Figure 3-15a). The fit between the impeller and the casing is usually poor. Therefore, some part of the discharge leaks to the suction-side (i.e., back leakage). As a result, these pumps are less efficient and also less expensive. Many small pumps of general purpose contain open-impeller.

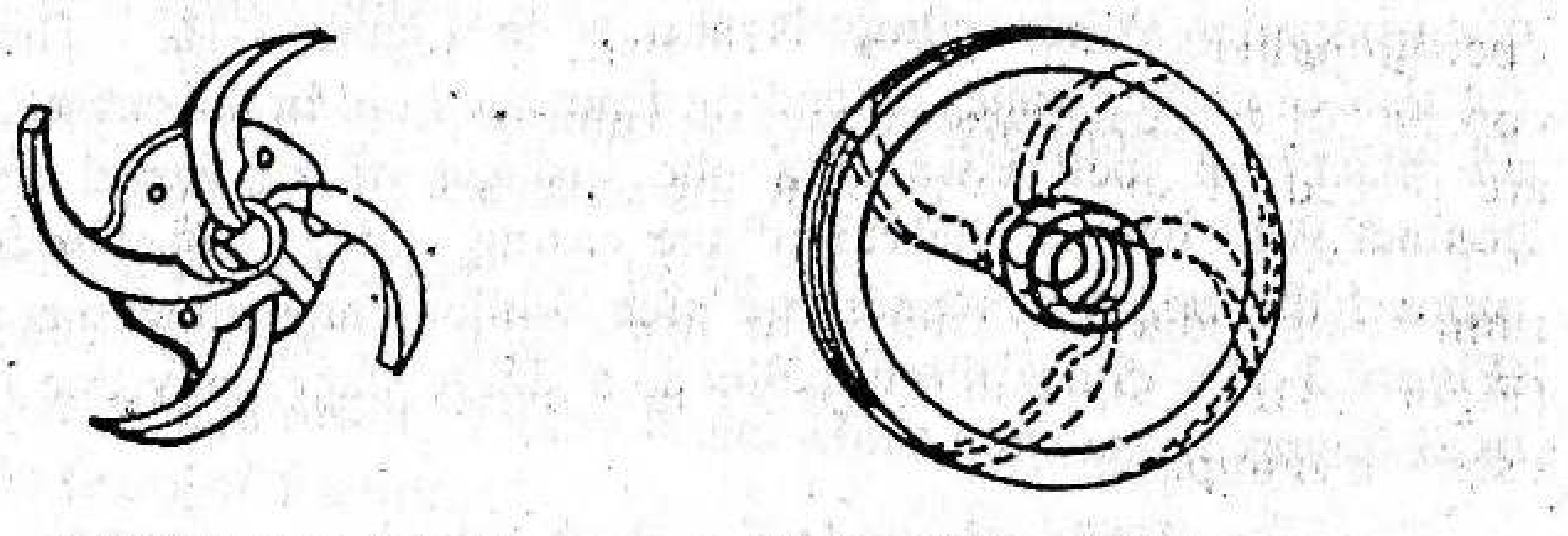

(a) Open impeller (b) Closed impeller

Figure 3-15. Pump impellers.

Closed-impeller pumps : In this type, the impeller vanes are enclosed between two metal sheets (Figure 3-15b). A close fit is maintained between the circumference of the impeller and the entrance of the volute (or between the hub of the impeller and the corresponding point on the casing). Therefore, back leakage of fluid is not observed. These pumps are more efficient and more expensive.

Single-suction pumps : In this type, the liquid enters the impeller from one side only. When such an impeller is allowed to rotate at high speeds, suction is created at its eye (centre), which pulls the impeller away from the shaft. The disadvantage of this pump is the unbalanced hydraulic pressure. As a result, end thrust is produced on the bearings.

Double suction pumps : In this pump, the liquid enters the impellers from both sides. The pump consists of two impellers placed back to back and united in one casing. Therefore, hydraulic pressure is well balanced.

The general principles described above are combined and illustrated using a volute pump given below.

Volute pumps : The space between the edges of impeller and the casing of the chamber is known as *volute*. A pump that is equipped with volute casing is known as *volute pump*.

In this type of centrifugal pump, water entering at the suction connection is thrown outwards by the rotation of the curved vanes into the volute (Figure 3-13). As a result, the liquid suddenly changes its direction in the volute, which decreases the velocity head and consequently increases the pressure head. These changes facilitate the pumping of the liquid. The step to change the direction of liquid flow is not smooth. Therefore, these pumps are least efficient. These are also less expensive.

Single-Stage, Single-Suction, Open-Impeller Volute Pump

Construction : The construction of a single-stage, single-suction, open-impeller volute pump is shown in Figure 3-16. The impeller consists of curved vanes extending from the hub. In the casing, impellers are placed in such a way that the surfaces of the vanes are in close contact with the two halves of the casing. Since impeller is an open runner, the edges of vanes are free without any attachment of rings (Figure 3-16). Since the impeller is a single-stage, only one impeller is used for pumping.

The impeller is attached to a shaft, which is rotated by the use of power from outside. Nearer to the centre (eye) of the impeller, provision is made in the casing to receive the fluid by suction. At the top of casing, an exit for discharge is provided to which volute is exposed.

Working : Power is applied on shaft to rotate. Along with it, the blades of the impeller are also revolved. This results in reduced pressure at the eye of the impeller. Hence, the liquid flows into the impeller through the inlet suction pipe. This liquid is forced outward along the blades at increasing tangential velocity. The liquid leaves the blade tips and passes into the volute chamber. In this process, its velocity head decreases and consequently pressure head is increased. The liquid moves along the casing. Finally, the liquid leaves the discharge pipe.

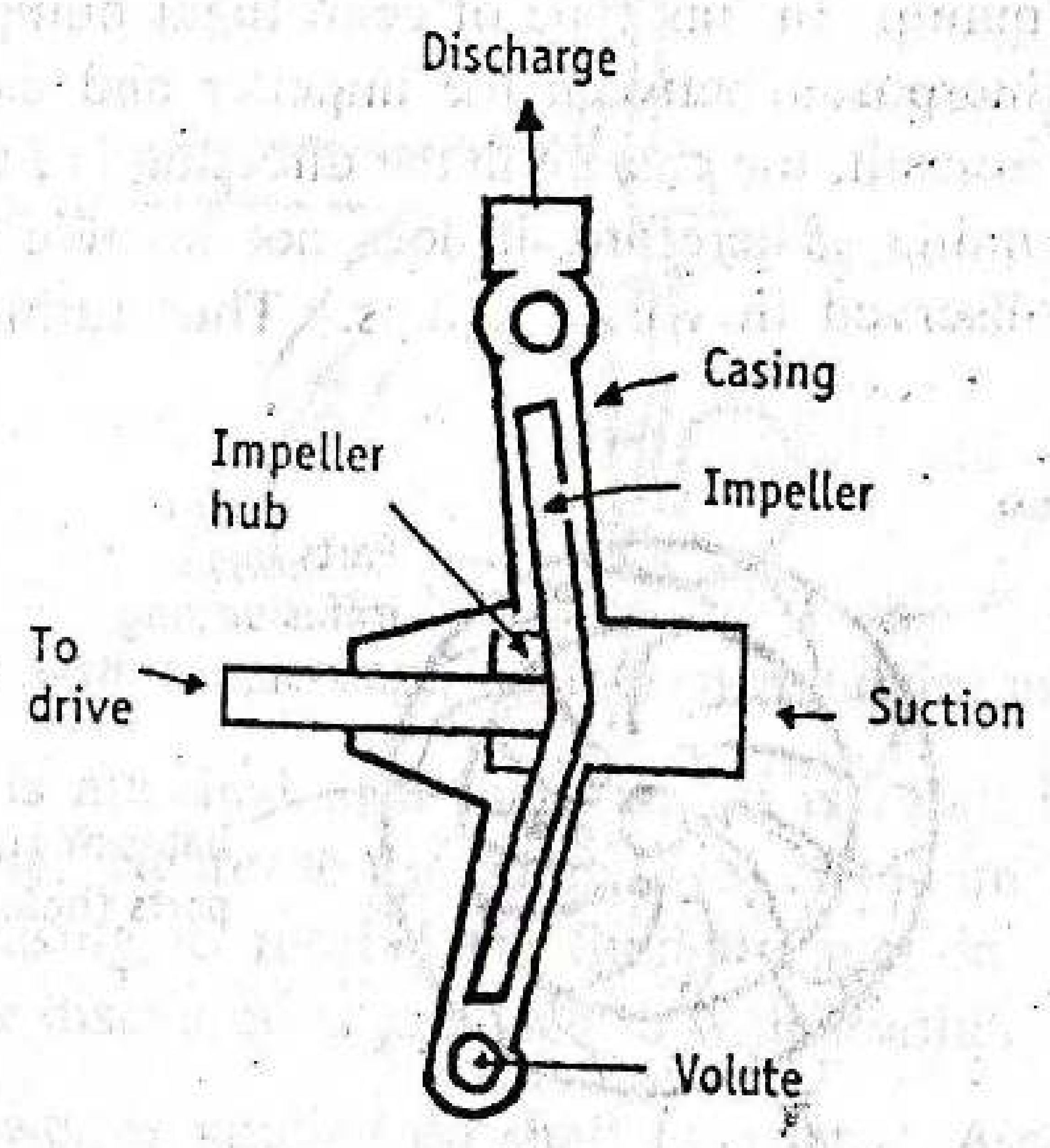


Figure 3-16. Construction of single-stage, single-suction, open-impeller volute pump.

Uses : Volute pumps are used for viscous liquids and liquids containing solid materials. Open impellers are used for this purpose.

Advantages : Volute pumps are cheapest of all centrifugal pumps.

Disadvantages : (1) Volute pumps are the least efficient, because of power losses due to the following reasons.

(a) When water is thrown out by radially moving vanes, it must suddenly change the direction as it enters the volute. Such a sudden change results in turbulence, which consumes some power in the form of friction.

(b) These are cheap pumps, hence not accurately finished. The fit between the impeller and the casing is usually poor. A part of liquid discharge leaks to the suction side. To prevent this back leakage, a closed impeller is used.

(2) In these pumps, the suction side of impeller is under pressure, which is less than the atmospheric pressure. As a result, air may

be drawn into the pump through the stuffing box. This air greatly decreases the rate of discharge or even entirely stops the pump. Sealing the glands can prevent this. A small amount of liquid under the pressure of the discharge is directed through seal pipes to lantern rings in the packing.

Turbine pumps : The diffusion casing equipped with vanes is known as turbine pump. In this type of centrifugal pump, a stationary diffusion ring is interposed between the impeller and casing chamber (Figure 3-17). As a result, the change in the direction is smooth, without shocks during pumping. Therefore, it does not involve energy losses due to eddies as observed in volute pumps. Thus turbine pumps are more efficient.

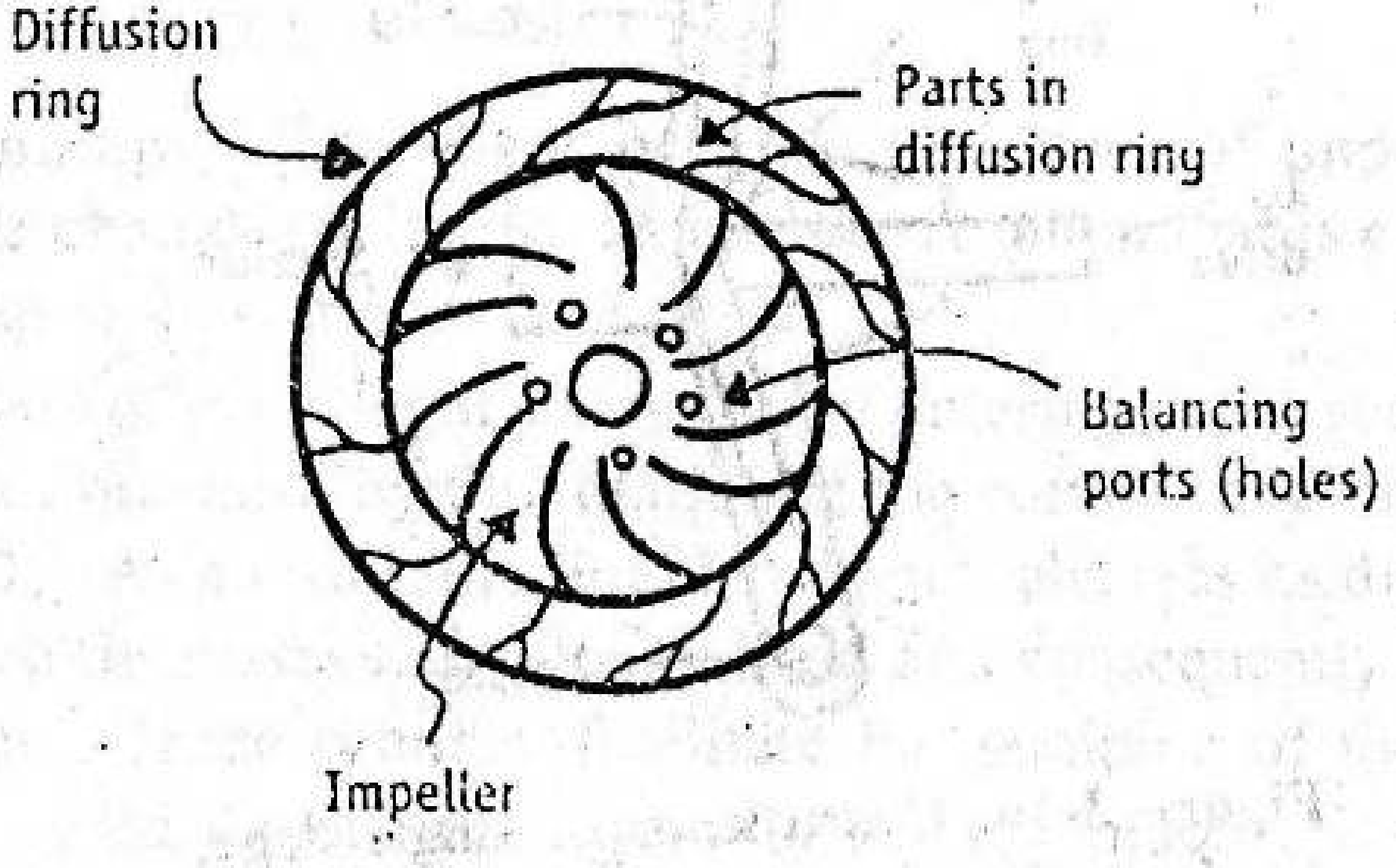


Figure 3-17. Design of impeller in a simple turbine pump.

The design of the impeller and the general construction of the turbine pump is similar to the volute pump. Connecting more number of impellers in series can generate the maximum head. The overall efficiency of such a pump is high, because the liquid from the tip of one impeller is delivered to the inlet of the next impeller with a minimum loss (multi-stage). Therefore, heads up to 300 metres may be generated.

The general principles described earlier are combined and illustrated using a model turbine pump given below.

Single-Stage, Single-Suction, Turbine Pump

Construction : The construction of a single-stage, single-suction, turbine pump is shown in Figure 3-18. The impeller is a pumping mechanism, which consists of curved vanes extending from the hub. In the casing, impeller is arranged in such a way that the two halves of the casing are closely in contact with the surface of the vanes. A diffusion ring contains passages, which change gradually in cross-section and direction. Since the impeller is single-stage, only one impeller is used in the pumping.

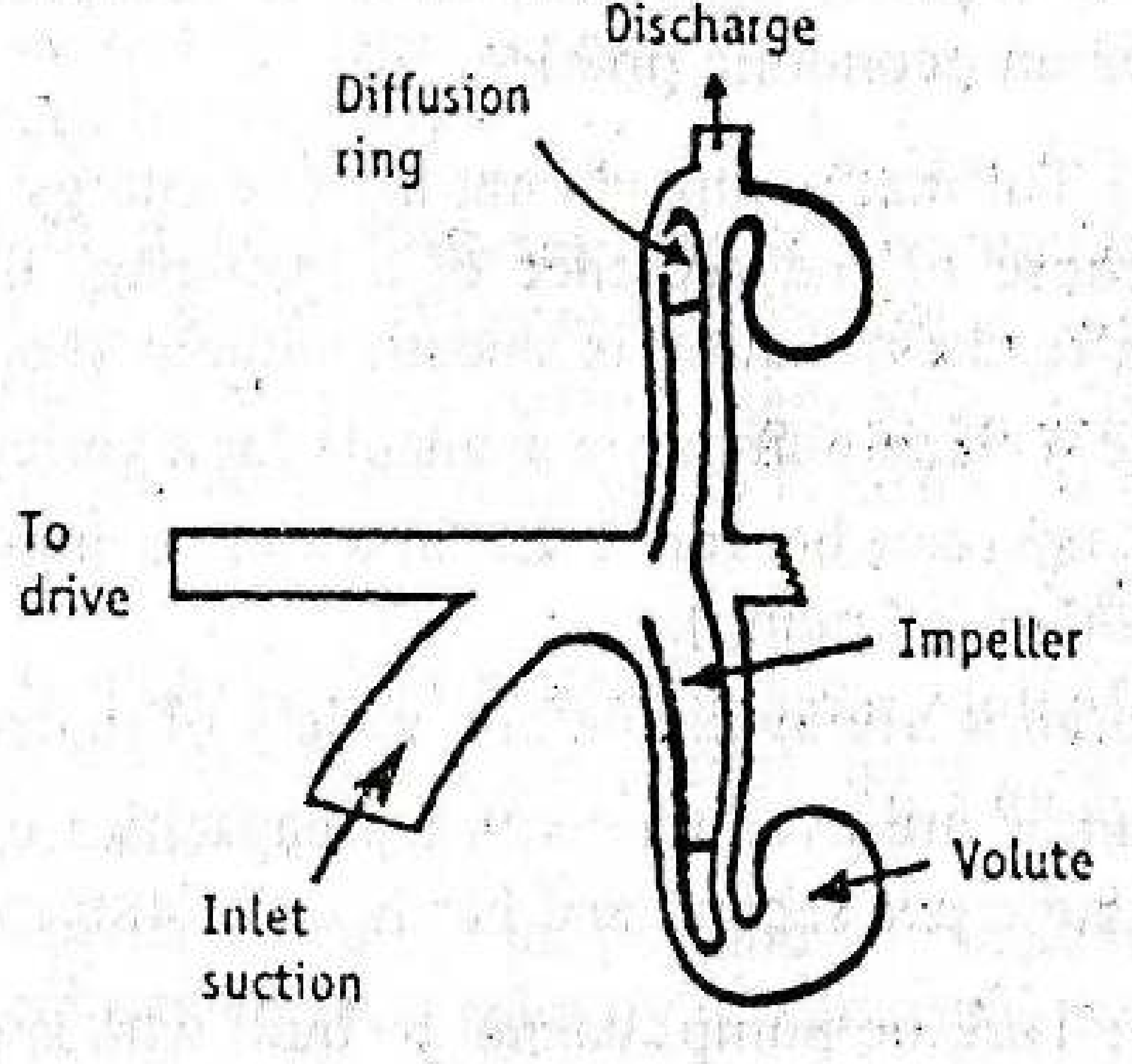


Figure 3-18. Single-stage, single-suction, turbine pump.

The impeller is attached to a shaft, which is rotated by the use of power from outside. Nearer to the centre (eye) of the impeller, provision is made in the casing to receive the fluid by suction. At the top of casing, an exit for discharge is provided to which volute is exposed.

Working : Power is applied on shaft to rotate. Along with it, the blades of the impeller are also revolved. This results in reduction in pressure at the eye of the impeller. Hence, the liquid flows into the impeller through the inlet suction pipe. This liquid is forced outward along the blades at increasing tangential velocity. The liquid released from the tip of the impeller is caught in these passages and turned gradually and smoothly into a discharge valve without shocks and eddies.

In a single suction turbine pump, the impeller produces the end thrust on the shaft, which is partly overcome by holes in the impeller. This partly equalizes the hydraulic pressure behind and front of the impeller. The rest of end thrust is taken up in a thrust bearing.

Uses : Turbine pumps are used in handling of clear, non-viscous and non-corrosive liquids. Vertical turbine pumps, which are particularly suited for pumping water from deep well, are often called *deep-well pumps*.

Double suction, single-stage pumps are used for general water supply and circulating services. Chemical pumps can be used when the liquids to be handled are non-corrosive to iron or bronze.

Turbine pumps are widely used for handling organic solvents, organic heat transfer liquids, light oils, toxic or hazardous liquids or where leakage poses an economic problem.

Advantages : (1) Turbine pumps do not involve energy losses due to eddies, because of the presence of a stationary diffusion ring. The change in the direction is smooth without shocks.

(2) Single-stage turbine pumps are available for a variety of services.

(3) Turbine pumps can be connected in series to improve the efficiency (multi-stage pump).

(4) Chemical pumps are available in a variety of materials.

(5) Turbine pumps are available with the capacities up to and over 400 metre cube per second and heads up to 480 metres.

Disadvantages : Turbine pumps cannot be built with special material. So corrosive liquids cannot be handled.

Air Binding And Self Priming Pumps

When a centrifugal pump is switched on, the fluid does not instantaneously develop pressure. During initial period, air enters the impeller and then fluid follows. The head generated (in metres) by air may be comparable to the head degenerated (in metres) by the liquid. However, the pressure produced by the same air is very small in terms of liquid head. In such situations, the pump practically stops delivering the liquid. This process is known as *air binding.* This is one of the disadvantages of the centrifugal pumps.

Air binding can be prevented by employing some of the following measures.

(1) A check valve is provided in the suction line, so that the suction line and casing will not drain off the liquid, when pump is shut down.

(2) A self-priming pump is provided, so that air can be removed from casing.

(3) Centrifugal pumps are located at a place, so that the pump suction is under a positive heed and thus necessity of priming is eliminated.

Centrifugal Pump—Theory

As mentioned in the working principle of centrifugal pumps, the velocity head of the liquid at the top of the impeller is converted into a pressure head. Such a conversion depends on:

- Angle of the vanes
- Velocity of the liquid at the outer tip of vanes
- Friction and leakage losses
- Changes in viscosity

Performance of a centrifugal pump : The performance of any particular centrifugal pump is expressed by means of curves called *characteristic curves.* These are usually supplied for pumping water by manufacturers. The performance of a pump is measured in terms of four characteristics.

Capacity : It is expressed in metre cube per hour for liquid pumps and in metre cube per minute for gas pumps, for a given inlet temperature and pressure conditions.

If speed of impeller (revolutions per hour) is increased, the rate of discharge also increases correspondingly. This relationship is expressed as:

$$\text{Rate of discharge} \propto \text{speed of the impeller}$$

$$Q \propto N \tag{6}$$

The volume of discharge depends on the cross section of the passages. Therefore, the size of a centrifugal pump is usually specified by the diameter of the discharge connection.

- For high heads and small volumes of discharge, centrifugal pumps having impellers of large diameters, but with narrow slots are used.
- For low heads and large volumes of discharge, centrifugal pumps having impellers of small diameters, but with wide slots are used.

Pressure head : It is the energy supplied to the fluid per unit mass (increase in pressure/fluid specific weight), i.e., head development (metres). The quantity of fluid discharge is increased as a result of the enhanced head developed by the pump. This relationship is expressed as:

$$\text{Head developed} \propto (\text{rate of discharge})^2$$

$$H \propto Q^2 \tag{7}$$

It is generally expressed as column of fluid equivalent to the total pressure differential measured immediately before and after the device, for a given adiabatic condition. Head developed by centrifugal pumps is determined largely by:

- Angle of the vanes.
- Speed of the liquid at the tip of the impeller.

Power : It is the energy consumed by the machine per unit time (kilowatts). High speed of impeller, large head generation and high discharge rate obviously consumes more power. This relationship is expressed as:

Power consumed ∝ Rate of discharge × head developed

$$W \propto Q \times H \tag{8}$$

Or

$$W \propto Q^2 \times Q \propto Q^3 \tag{9}$$

Or

$$W \propto N^3 \tag{10}$$

Equations (6 to 10) are used for the comparison of two pumps.

Efficiency : Energy supplied to the fluid divided by the energy supplied to the machine is referred to as efficiency.

$$\textit{Efficiency of a pump} = \frac{\text{energy supplied to the liquid (i.e., power consumed) (kW)}}{\text{energy supplied to the machine (kW)}} \tag{11}$$

This theoretical relationship is a rough guide to understand the performance of centrifugal pumps.

Power losses : A certain amount of power is lost on account of various reasons, which are listed below:

1. *Mechanical losses* : These are due to friction in bearings, stuffing-box packing etc.
2. *Leakage losses* : These are due to leakage of the liquid from the tip of the impeller back to impeller suction.
3. *Hydraulic losses* : These include:
    - (i) the friction between liquid and casing
    - (ii) the friction between liquid and faces of the vanes
    - (iii) losses due to sudden change in the direction in the volute
    - (iv) losses due to sudden change in cross-section, where liquid leaves the impeller
4. *Recirculation losses*: The velocity of the liquid is not uniform in the space between two adjacent vanes of the impeller. This difference in velocity produces circulation of the liquid within the space between the vanes. Such circulation consumes power.

This can be minimized by:

(a) decreasing the distance between adjacent vanes

(b) putting more vanes on the impeller

Such modifications increase the cost of the pump and enhance the friction losses.

Work done or efficiency : The centrifugal pumps are usually rated on the basis of *head* and *capacity* at the point of maximum efficiency. The work done is expressed as:

Work done = rate of fluid flow × differential height of the column of fluid

$$\textit{Work done}\ (\text{kW·h}) = \text{capacity}\ (\text{m}^3/\text{h}) \times \text{head}\ (\text{m}) \tag{12}$$

Work must be done on the pump system in order to lift any liquid against the gravity. The pump actually raises the liquid and forces it into a pressure vessel or it may provide enough head to overcome the pipe friction. In such cases, the *hydraulic efficiency* is expressed as:

$$\textit{Hydraulic efficiency} = \frac{\text{power of the runner (kW)}}{\text{actual input power (kW)}} \tag{13}$$

It is possible to estimate the theoretical work required of a pump as shown below.

$$\textit{Power output}\ (\text{kW}) = \frac{HQ\rho}{3.670 \times 10^{-5}} \tag{14}$$

where H = total dynamic head of liquid, m
ρ = density of the liquid, kg/m^3
Q = capacity, m^3/h

The dynamic head (H) of a pump can be calculated using the equation (15).

$$H = \text{total discharge head} - \text{total suction head} \tag{15}$$

The power input of a pump should be greater than the power output, because the internal losses resulting from friction, leakage etc. The efficiency of a pump is therefore defined in simple terms as:

$$\textit{Efficiency of a pump} = \frac{\text{power output (kW)}}{\text{power input (kW)}} \tag{16}$$

Reciprocating Pumps Vs. Centrifugal Pumps

A comparison of features of reciprocating and centrifugal pumps is given in Table 3-1.

TABLE 3-1
Comparison of Characteristics of Reciprocating and Centrifugal Pumps

Reciprocating pumps	*Centrifugal pumps*
1. These are designed for higher heads.	These are designed for lower heads
2. The cost of these pumps is lower than centrifugal pumps for the same capacity.	The simplest pumps are cheaper than the simplest reciprocating pumps. For the same capacity, centrifugal pumps are costly.
3. The efficiency of these pumps is constant over a wider range of discharge rates.	In moderate sizes, the efficiency of these pumps is higher.
4. There is no possibility of air binding	Air binding is possible. So special provisions are made for priming.
5. These pumps are more flexible in their operations.	Less flexible in their operations.
6. Discharge of liquid may be pulsating in lower versions.	Deliver liquid at uniform pressure, without shocks and pulsation.
7. Common types are steam driven.	These are commonly power driven
8. Distribution of steam and collection of exhaust are not simple.	Distribution of electric power is simpler.
9. Used for liquids that are not too viscous, corrosive and abrasive.	These can handle suspensions with large solids and corrosive liquids.

MISCELLANEOUS PUMPS

Peristaltic Pumps

Principle : In peristaltic pumps, silicon rubber or other suitable elastic (resilient) tubing is clamped in a U-shaped fashion against a rotating mechanical device (such as 'finger' or 'rollers'). The tubing is compressed in stages by means of rotor. As the rollers rotate, they flatten the tube against the tract at the points of contact. These *flats* move the fluid by positive displacement and the flow can be precisely controlled by the speed of the rotor. The tube quickly recovers its original shape after squeezing.

Uses : Peristaltic pumps are particularly useful for biological fluids where all forms of contact must be avoided. These are increasingly used for pumping emulsions, creams and similar fluids in laboratories and industry, where freedom from glands, avoidance of aeration and corrosion resistance are valuable. In a hospital setup, these are used for pumping parenteral nutrition infusions to the patients and blood pumping in case of surgical operations.

Advantages : (1) Simple and inexpensive (to purchase and operate).
(2) Easy to clean.

Disadvantages : (1) Linearity and often accuracy decreases as the pump speed increases.
(2) Accuracy varies as the tubing wears and fatigues.
(3) Effectiveness is limited by liquid viscosity.

Glossary of Symbols

H = Dynamic head, m.
H = Head, m.
N = Speed of the impeller, r/h.
Q = Rate of discharge, m^3/h.
ρ = Density of the liquid, kg/m^3
W = Power consumed, kWh.

QUESTION BANK

Each question carries 2 marks

1. What type of pump would you recommend for pumping slurries with 40-50% solids? Give reasons.
2. Describe the working of a self priming pump.
3. What is meant by 'air binding' in pumps? How do you overcome the problem?
4. What are the design features and merits of a turbine pump?
5. Write notes on check valves.

Each question carries 5 marks

1. Write the construction and working of a turbine pump.
2. Describe the construction and principle of rotary positive displacement pump for liquid transport.
3. Describe the construction and applications of any one positive displacement pump.
4. Compare the characteristics of centrifugal pumps and reciprocating pumps.
5. Classify reciprocating pumps with descriptions of various terms.
6. Draw the diagram of a piston type of reciprocating pump and explain its operation.

Each question carries 10 marks

1. Describe the principle and construction of a centrifugal pump of your choice. How do you compare a centrifugal pump with reciprocating pump?
2. Describe the construction, working, merits and demerits of a double-action reciprocating pump.

4

Conveying

Belt Conveyors
Screw Conveyors
Pneumatic Conveyors
Chain Conveyors
Bucket Conveyors
Storage of Solids

The term '*conveying*' is applied to the transportation of solids. The transportation of liquids is much simpler, cheaper and less troublesome than handling solids. In many operations, solids are handled in a finely divided state, so that they remain suspended in a stream of fluid. However, such a system is not suitable for handling all types of solids. Therefore, it may be necessary to transport solids as such. This unit operation is important in the storage and handling of raw materials, finished products and packed goods. The advantages and objectives are given below.

Efficient and Effective Conveying—Objectives and Advantages

1. Decreased product costs and increased manufacturing capacity.
2. Decreased cost of raw material. For example, penalty charges are levied when cars are not loaded or unloaded according to schedules. Losses due to spillage or torn containers is reduced.
3. Decreased processing time and conservation of energy.
4. Rigid in-process controls leading to decreased quality control and quality assurance costs.
5. High degree of uniformity, reproducibility of the process and compliance with the cGMP regulations (current good manufacturing practices).
6. Minimum contamination and dust formation.
7. Increased employee safety and reduced labour costs.

If raw materials are not moved as required by production schedules, the manufacturing process will be slowed down. In addition, machine time and operation time will be wasted. As a result in-process inventories will be increased.

Improper handling and storage can lead to damage, outdated and loss of materials. Improper handling of granules, strips, bottles and chemicals can place employees in physical danger. This can often lead to employee frustration and reduced morale due to constant production delays.

In today's world of automation, solid conveying has gained a greater importance. It is often necessary to prevent the contact of material with the persons, in order to avoid contamination (as in case of antibiotics). Similarly working personnel should not be exposed to poisonous and obnoxious substances. Therefore, a closed conveying system is essential. Such a closed circuit manufacturing operation calls for automatic handling systems. The feeding of materials into a reactor is always done mechanically. Similarly, discharge should also be made automatic. Conveyors are used in the production of all dosage forms such as tablets, capsules, liquid orals, injections.

Conveyors are classified into five major groups. These are:

1. Belt conveyors
2. Screw conveyors
3. Pneumatic conveyors
4. Chain conveyors
5. Bucket conveyors

Some important conveyor systems, construction, working and applications are discussed in this chapter.

BELT CONVEYORS

The basic elements of the belt conveyor are:

1. Belt and belt tightening systems
2. Belt drive and power supply
3. Roller supports for belt
4. Feeding arrangements
5. Discharge arrangements

Principle

Horizontally or inclined placed motor driven rotating belt on pulleys convey the material from feeding point to the discharge point.

Construction

The construction of a belt conveyor is shown in Figure 4-1. Belt conveyor consists of a core or carcass (meaning skeleton or backbone for the belt) of several piles of cotton duck, each layer is impregnated and bonded with rubber. The carcass is then covered with a thin layer of rubber that binds the piles together. Both the ends of the belt are joined together, so that the belt can revolve continuously. The belt may run horizontally or slightly inclined from the feed point.

- If the belt is too thin for its width, it will sag between idlers.
- If the belt is too thick, it does not trough properly.

Sometimes, the length of belt is increased due to a variety of factors such as temperature and humidity of the atmosphere. In such cases, it is necessary to keep the belt taut. Hence, tighteners (or take-up) are installed to maintain an even-tension on the belt under all conditions. The simplest take-up consists of a cast iron bed with a travelling block moving along a screw.

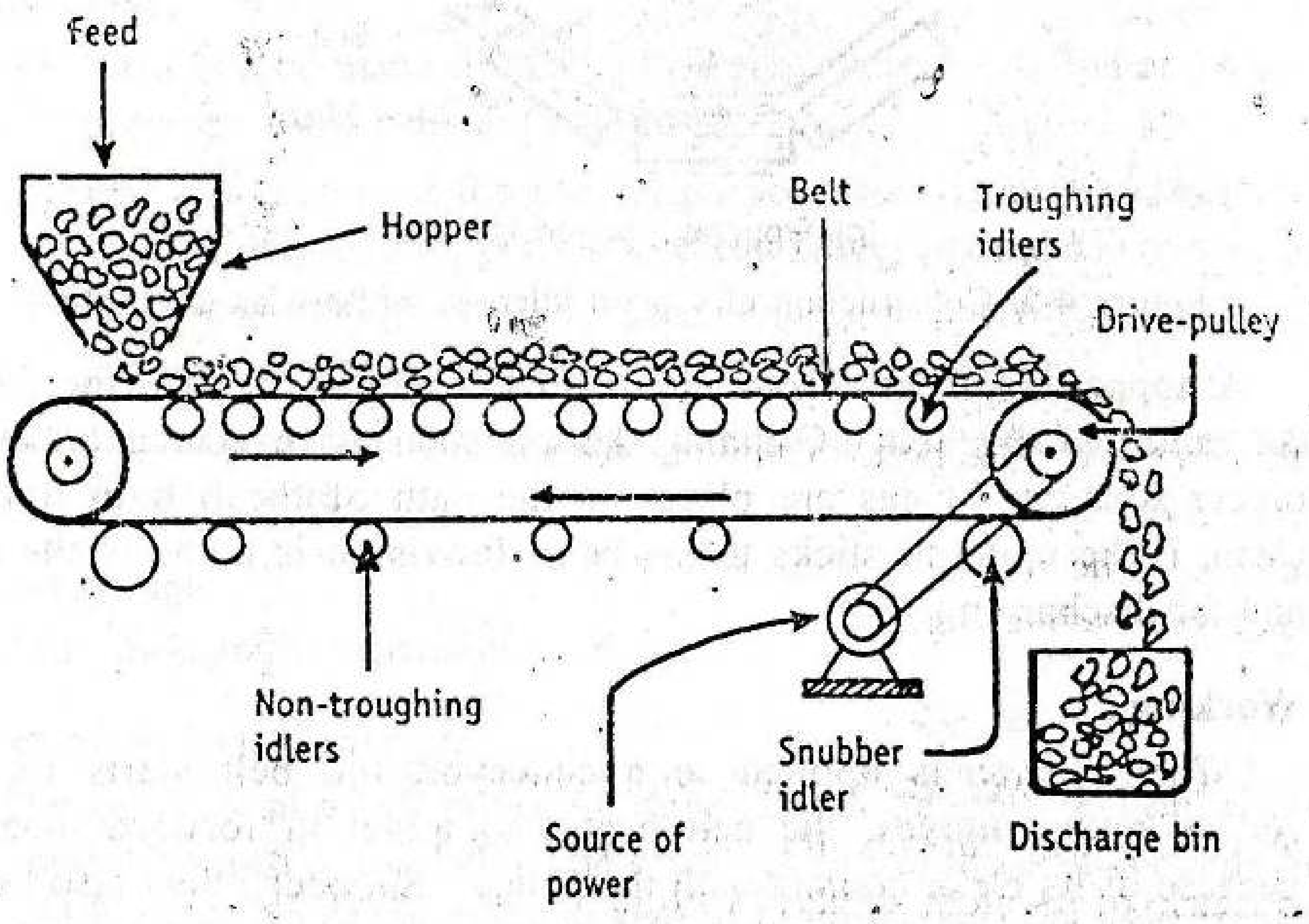
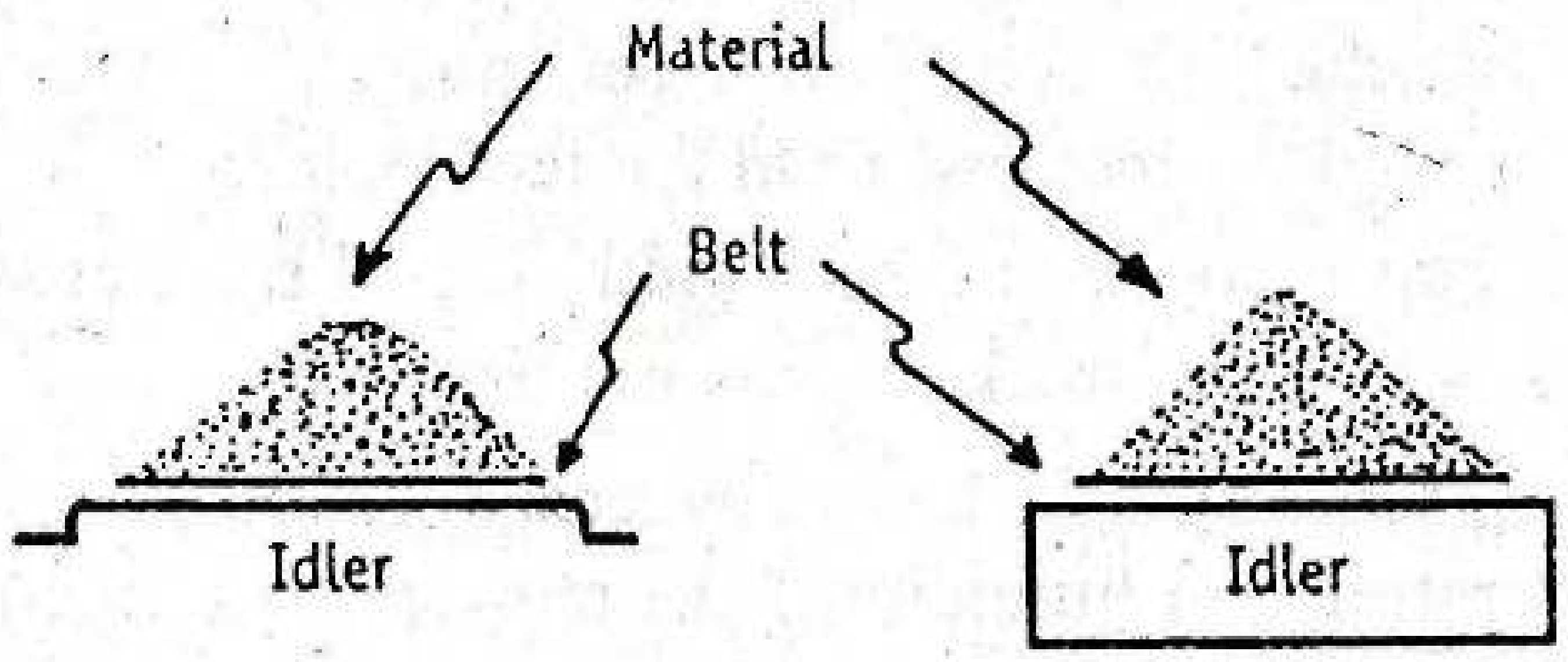


Figure 4-1. Construction of belt conveyor system.

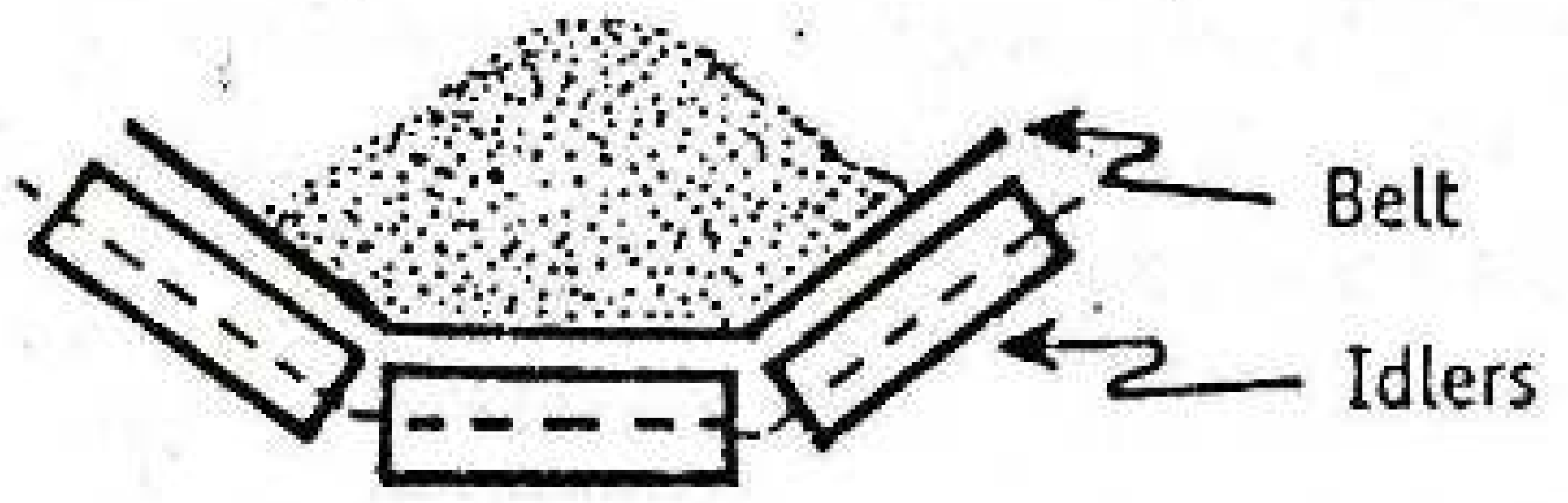
The belt is allowed to move with the help of a *belt drive*. The simplest belt drive is a bare steel pulley actuated with some source of power. The drive of the belt conveyor is fixed at the discharge end (It is rarely arranged at the feed end). There should be appropriate contact between the belt and pulley. Introducing snubber idlers just below the pulley can increase the contact.

The belt is supported by rollers, which are arranged on a shaft. These are called *idlers*. The idlers are carried on bush bearings lubricated with grease-cups. The idlers are generally troughed to depress the belt at the centre and rise at the edges (Figure 4-2c). This permits the belt of a given width to carry more material per linear metre without spillage. The belt returns on ordinary, non-troughing rolls.



(a) Flat belt on continuous plate (non-troughing)

(b) Flat belt on flat belt idlers (or non-troughing)



(c) Troughed belt on 20° idlers.

Figure 4-2. Construction of support idlers in width-wise description.

A hopper is placed at one end in such a manner to load the feed at the centre of the belt. Cleaning devices such as revolving brush and rubber scrapper blades are placed in the path of the belt in order to clean, if the material sticks to the belt. Provision is made at the other end for discharging.

Working

When power is applied to a conveyor, the belt starts rotating. As the pulley moves, the belt begins to travel in forward direction, because of its close contact with the pulley. Snubber idlers also help in maintaining the close contact between the pulley and belt.

The material (to be transported) is loaded on its centre of the belt with the help of a hopper. The material travels above the belt. The belt moves forward on troughing idlers. This permits the belt to carry more material per linear metre without spillage. The amount of feed delivered depends on the width and speed of the belt. At the discharge end, the material may be unloaded manually or mechanically.

Once the material is unloaded, the belt returns on lighter non-troughing rolls to the point of feeding.

Pharmaceutical Applications

Belt conveyors are used in transporting containers for filling, capping, sealing, labelling, pasting, visual inspection etc., in the production of injectables, liquid orals, ointments and jellies.

In the strip and blister packings of tablets and capsules, strips are conveyed on a moving belt. During this process, the strips are packed in the cartons.

Belt conveyors are used in the manufacture of lozenges. It is a continuous process of candy base cookies. When a mass of sugar base is on the conveyor, the water is removed. At the end of the belt, the candy base is mixed, tempered, formed, roped, melted, acidulents and flavours are added, cooled and sized.

Advantages

(1) Belts can be made of asbestos fibres, neoprene, teflon and vinyl polymer. Cord belts are also used.

(2) Belt conveyors are for general purpose installation and available in relatively large sizes. These can travel several kilometres as in case of coal mines.

(3) Routine maintenance of belt conveyor is easy.

(4) Belt conveyor is economical in terms of cost per unit tonne that it can handle.

Disadvantage

Belt conveyor is expensive.

Selection of Belt Conveyor

The capacity of a belt conveyor depends on the cross section of the load and the speed of the belt. The cross section of the load depends on the width and slope of the belt and size of the material. The selection of a belt conveyor depends on:

- Power required.
- Mechanical and tensile strength of the belt system to handle the wider varieties of materials.
- Lump size.
- Troughability of the belt.
- Ability of the belt to support the load between idlers.
- Chemical resistance of the belt to the material to be handled.

Manufacturers of belt conveyors publish charts or formulae for the construction of conveyors, size and power requirements.

SCREW CONVEYORS

The basic elements of the screw conveyor are:

1. Trough system
2. Flights and power supply
3. Feeding arrangements
4. Discharge arrangements

Principle

Horizontally or inclined or vertically placed motor driven screw like flight conveys the material in the trough from the feed point to discharge point.

Construction

The trough is a U-shaped vessel in which the material is enclosed during conveying (Figure 4-3). The trough is usually made of a sheet of steel and available in standard lengths. If a trough of more length is required, then more number of such units are joined together.

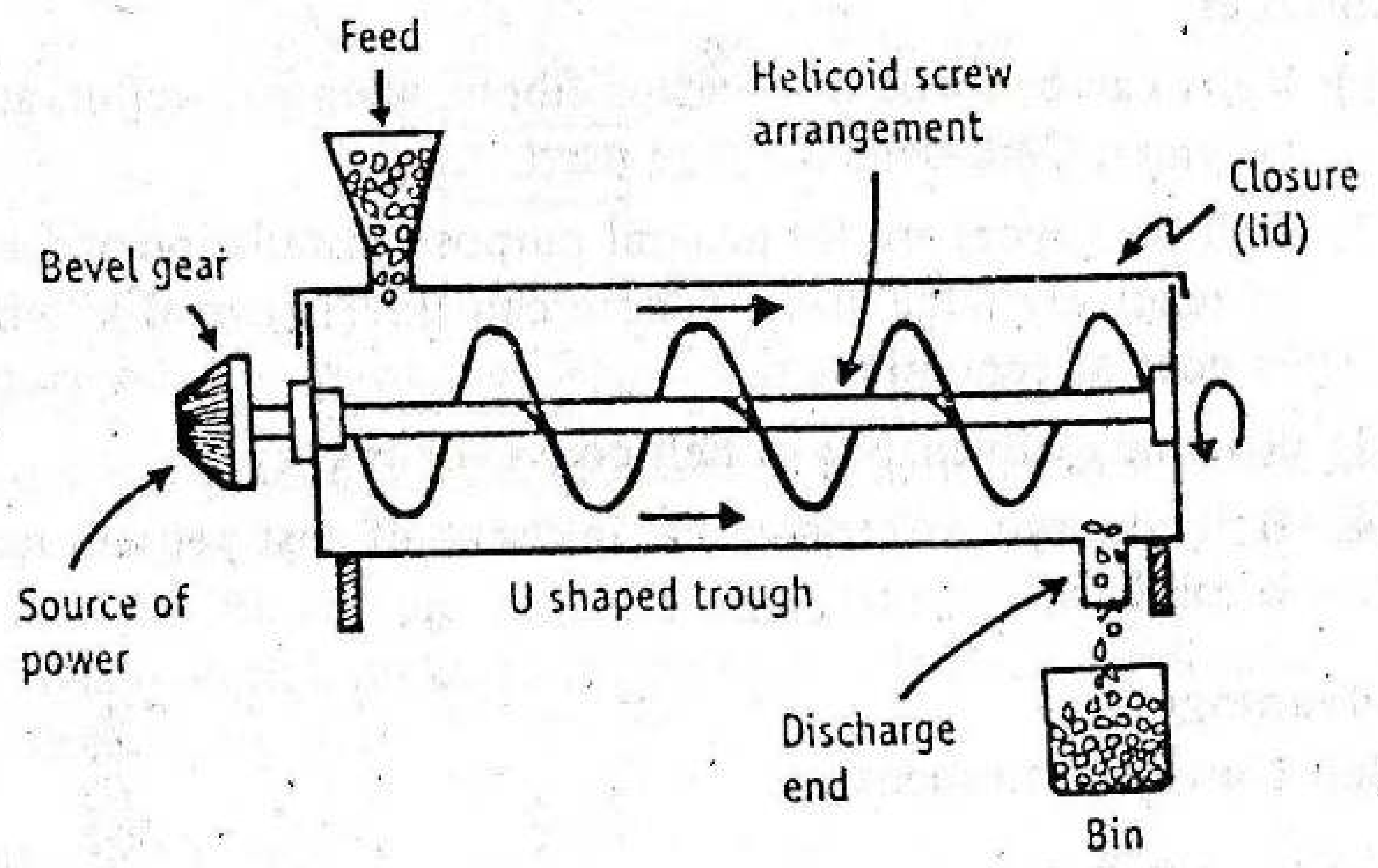


Figure 4-3. Construction of a typical screw conveyor.

Screw element usually consists of a spiral blade (conveying mechanism is like a screw), which is called *flight*. The simplest form of the flight is the sectional conveyor. Helicoid flight is shown in Figure 4-3. It is made of a single long ribbon that is twisted and wrapped into a spiral shape. These standard flights are welded to the central shaft. Alternatively the conveyer element (helicoid flight element) is suspended with the help of hangers along the length of the trough. Usually one hanger is used for each flight section. Hangers contain bushings of white cast iron, so that lubricants need not be used.

The drive end and discharge ends are known as *box-ends*. At the drive end, shaft is connected to the drive by bevel gears. Power is transmitted through the shaft to the flight. The shaft is rotated around an axis and remained nearer to the bottom of the trough. The feed is normally introduced by plain spouts, which gives uniform flow of material. At the discharge end, arrangements are made to receive the material using open-end trough or open-bottom trough.

Working

When power is applied, the drive rotates the shaft through the bevel gears. The screw element starts rotating. The flight is rotated round an axis and remained nearer to the bottom of the trough. Feed is normally introduced by plain spouts. The material will be trapped between the gaps of the spiral blades. As the flight moves, the material also moves forward along the path of the sections. The material is received using open-end trough or open-bottom trough.

Applications

(1) Screw conveyor is used for transporting finely divided solids or pasty solids.

(2) Materials having properties such as light-weight, medium-weight, abrasive, non-abrasive and different densities can be easily handled using screw conveyor. It is a versatile conveyor system.

(3) Special flights and casings are available for operations such as mixing, de-watering, heating and cooling.

(4) It has the capacity to handle the materials of about 280 metre cube per hour.

Advantages

(1) Materials can be conveyed horizontally, vertically or inclined.

(2) Screw conveyors are easy to operate and occupy less space.

(3) Different constructions are available and can be adapted for a variety of materials. Screw conveyors can be fabricated in a variety of materials ranging from cast iron to stainless steel.

(4) Screw conveyor can be operated at positive and negative pressures.

(5) High and low temperatures can be maintained by insulating the casing.

(6) It can be made dust free.

Disadvantages

(1) Screw conveyors operate at relatively low rotational speeds.

(2) Extremely cumbersome handling when conveyor becomes larger.

(3) At high speeds, abrasive problems arise.

(4) Power consumption per unit weight transferred is high.

Selection of Screw Conveyor

The size and speed of a screw conveyor are determined to make a choice of the design. The type of construction depends on the requirements such as:

- Scale of operation
- Severity of service
- Value of the material

PNEUMATIC CONVEYORS

The basic elements of the pneumatic conveyor are:

1. Air supply (or vacuum) system
2. Air slide and pipeline
3. Feed arrangements
4. Discharge arrangements (air and feed separation)

Principle

When a high velocity air is passed through a bed of solid particles, the individual particles are dragged by the air. Finally they are suspended in the air. Such a system is known as *fluidized bed*, which is described as a condition of fully suspended particles. In this condition, the suspension behaves like a dense fluid and can be transported from one point to another in processing plants. At the discharge end, the gas is separated and the solids are recovered.

Construction

The construction of a pneumatic conveyor is shown in Figure 4-4. Fans or cycloidal blowers are connected to the conveying system. An air slide consists of a chute with a porous base through which air passes. The path of material travel may vary from a few metres to several hundred metres. Conveyor mechanism can be operated for horizontal and vertical distances. The material supply (feed) is connected to the air slide through a rotary feeder valve. The other end of the pipeline is connected to a cyclone separator.

Working

The cycloidal blowers (or fans) produce air at pressure about 7.0 kilopascals. This air is passed through the air slide at the rate of 1.5 metre per minute. During this process, the rotary feeder valve rotates and allows the feed to enter the pipeline. These solids are suspended into a stream of air in a *fluidised state* until it reaches the receiving end. The material is then admitted to cyclone separator to remove large particles and fine particles, if any. The large particles are collected into the bin. The fine particles are removed in a bag filter. The gas can be recycled to the blower inlet in a closed system to save the valuable gas. These systems are used for free flowing materials.

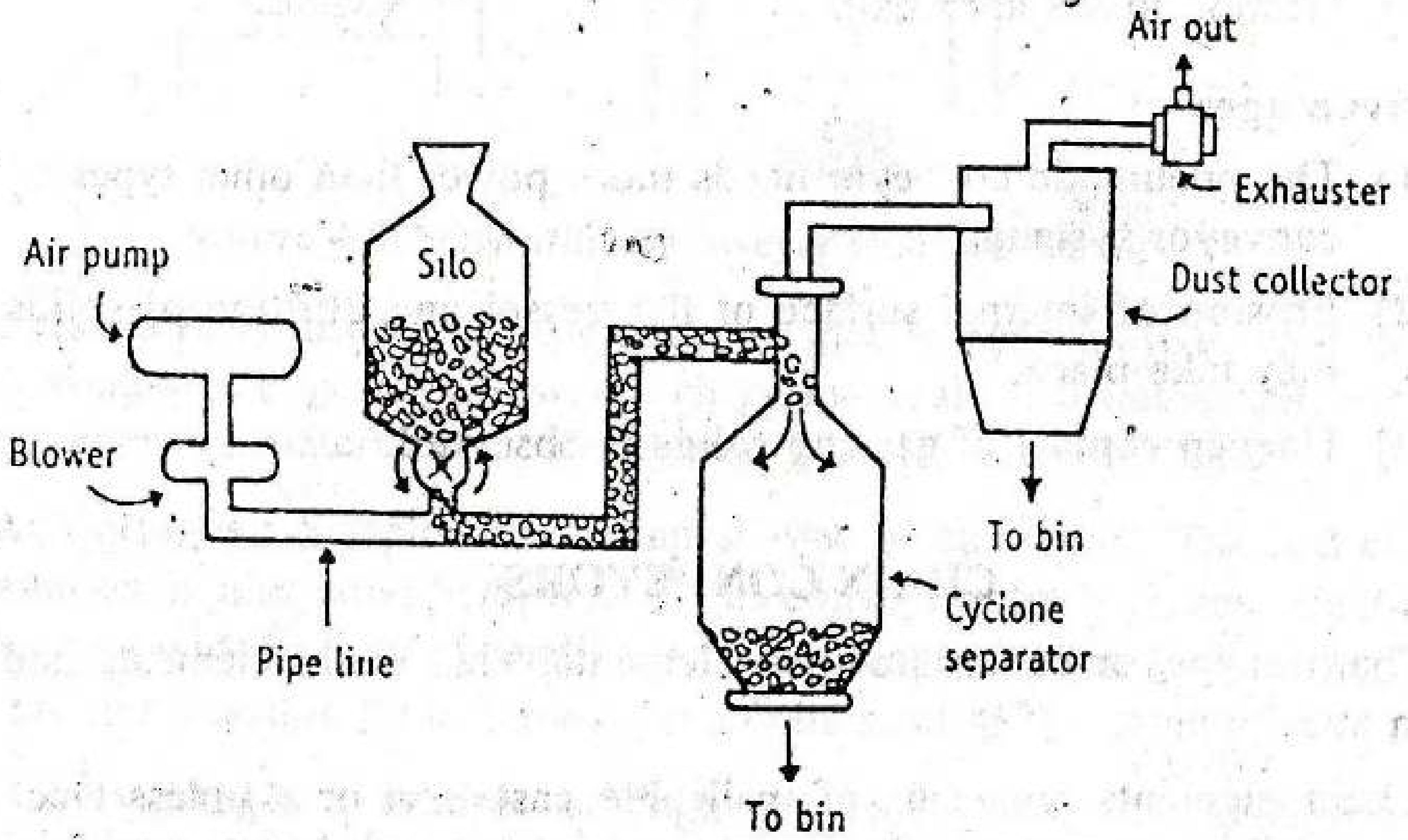


Figure 4-4. Pneumatic conveying system, pressure type.

For the design and satisfactory operation of pneumatic conveying, it is necessary to know about properties of powders such as density, particle size distribution, cohesiveness, angle of friction, angle of repose and fluidization characteristics.

Applications

(1) Pneumatic conveyor is the most important handling technique in chemical industry.

(2) It is used in the formulation of powdered insufflations.

(3) Generally, light and bulky materials such as grains can be transported easily.

(4) Pneumatic conveyor is used for handling of unpleasant and injurious (toxic) materials, since it is a closed system.

(5) Powders containing poisonous constituents can be transported.

(6) Fine powders and pellets having the size up to 6.0 millimetres and bulk densities from 16 to 3000 kg per metre cube can be handled by pneumatic conveyor.

Advantages

(1) While conveying the material, the path involves many turns and lifts. In such cases, other types of conveying become costly.

(2) Pneumatic conveyor is economical compared to other types of conveyors.

(3) Friction losses are small.

Disadvantages

(1) The pneumatic conveyor needs more power than other types of conveyor systems.

(2) Erosion of internal surface of the vessel and attrition of solids may take place.

(3) Uneven contact of gas and solids is observed.

CHAIN CONVEYORS

Chain conveyor consists of two elements, viz., chain elements and chain attachments.

Chain elements are made of malleable cast iron or stainless steel. These links are so cast that they can be assembled and detached without use of tools.

Chains are endless and move continuously. The material is loaded into a suitable container and placed on the chains. These are usually constructed on the job.

Advantages : Chain conveyor is a cheap and simple piece of equipment. It can be adapted to a wide variety of problems.

Scraper/Flight Conveyors

Flight conveyor consists of one or two endless chains passing through a trough or a set of guides. The chains have plates of wood or steel called *flights* attached at regular intervals. The flights are shaped to fit the troughs. The chains pull the flights and the material along the trough and passes over sprockets at the end of the run. One of the sprockets acts as the drive. In an elaborate form, flight conveyor is supported by two chains of roller pintle type (Figure 4-5). Scraper conveyors with speeds of 30 metre per minute are common, but the speed may ranges from 8 to 60 metres per minute.

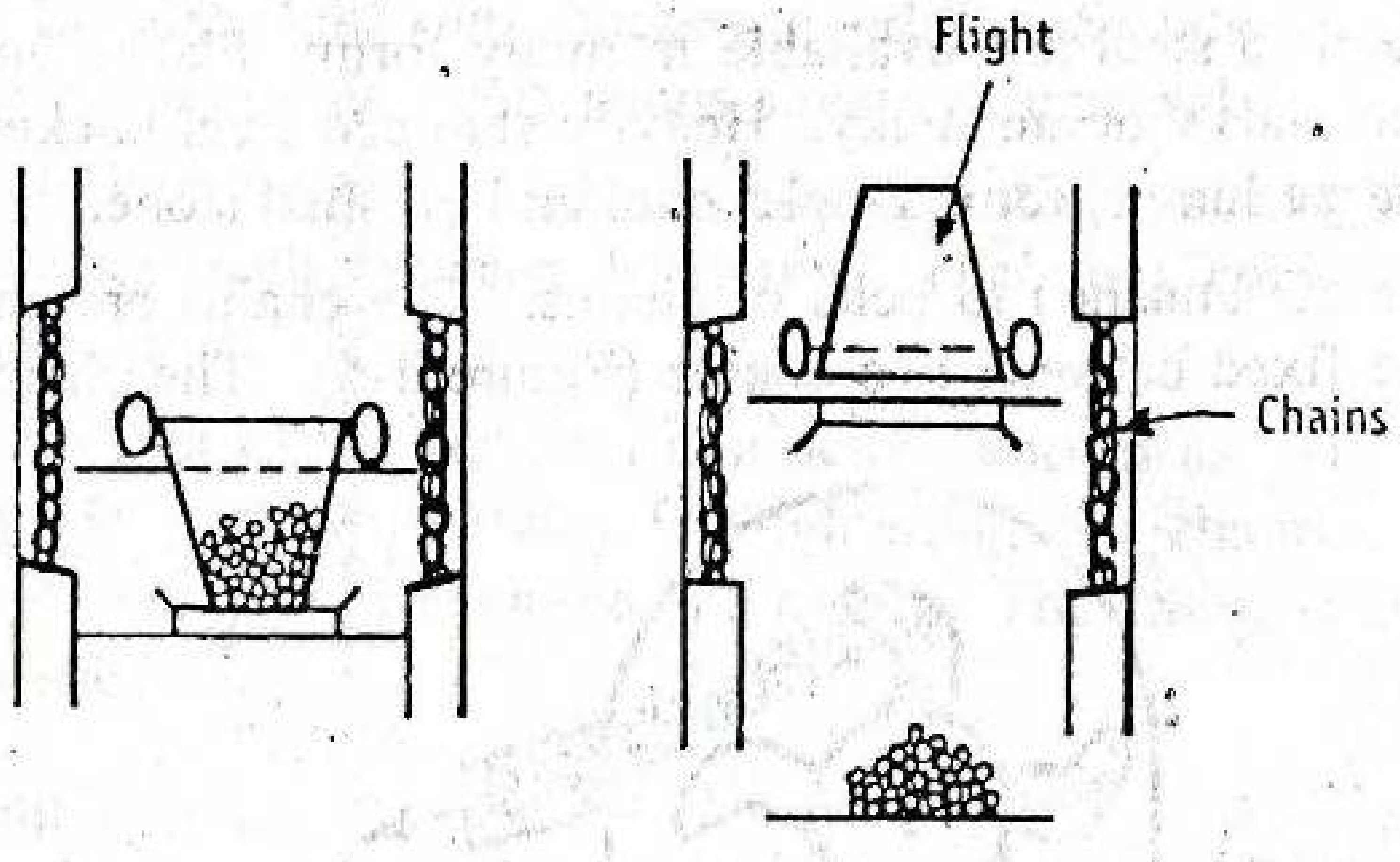


Figure 4-5. Scraper/flight conveyor with two chains.

Uses: Widely used for loose material that is non-abrasive, such as grain, food-waste, garbage, sawdust, chips and coal. It is not suitable for friable abrasive material such as clinkers, gravel and crushed ore.

Advantages : Simplest and cheapest type of conveyor. The cost of installation is also low. Scraper or flight conveyors have greater adaptability to a wide variety of conditions. It is suitable for steeper situations that are not possible by belt conveyor (inclination 45°).

Disadvantages : Scraper or flight conveyor needs heavy power requirements. Repairing charges are high.

Apron Conveyors

Apron conveyors are usually used for heavy loads and short runs. The simplest apron conveyor consists of two endless roller chains, which are connected by double beaded steel pans. The beading prevents the material from slipping backward when conveyor is inclined. Wooden or metal boxes are fixed between the chains and the whole conveyor drags on the support. Apron conveyors are used for

- transporting heavy loads.
- short runs at low speeds.
- conveying material such as lumpy, abrasive and hot, provided that these are not injurious to flexible belts.

BUCKET CONVEYORS

Construction

Buckets are used for loading the materials. The buckets are made of cast iron or stamped steel and available in many forms. Flatter buckets are used for materials that are sticky. Heavily stamped steel buckets are employed for large lumps, for example, coal and crushed stone.

The buckets are attached to belts or chains. The chains are endless and buckets are fixed between two chains (Figure 4-6). The chains are generally long pitch, straight and side type. The buckets are spaced to prevent interference in loading and unloading. For heavier loads, two chains may be used. The attachments are riveted to the ends of the chains. The attachments are slightly above the level of the chain so that the ends of the sprocketed booth do not strike the back of the buckets.

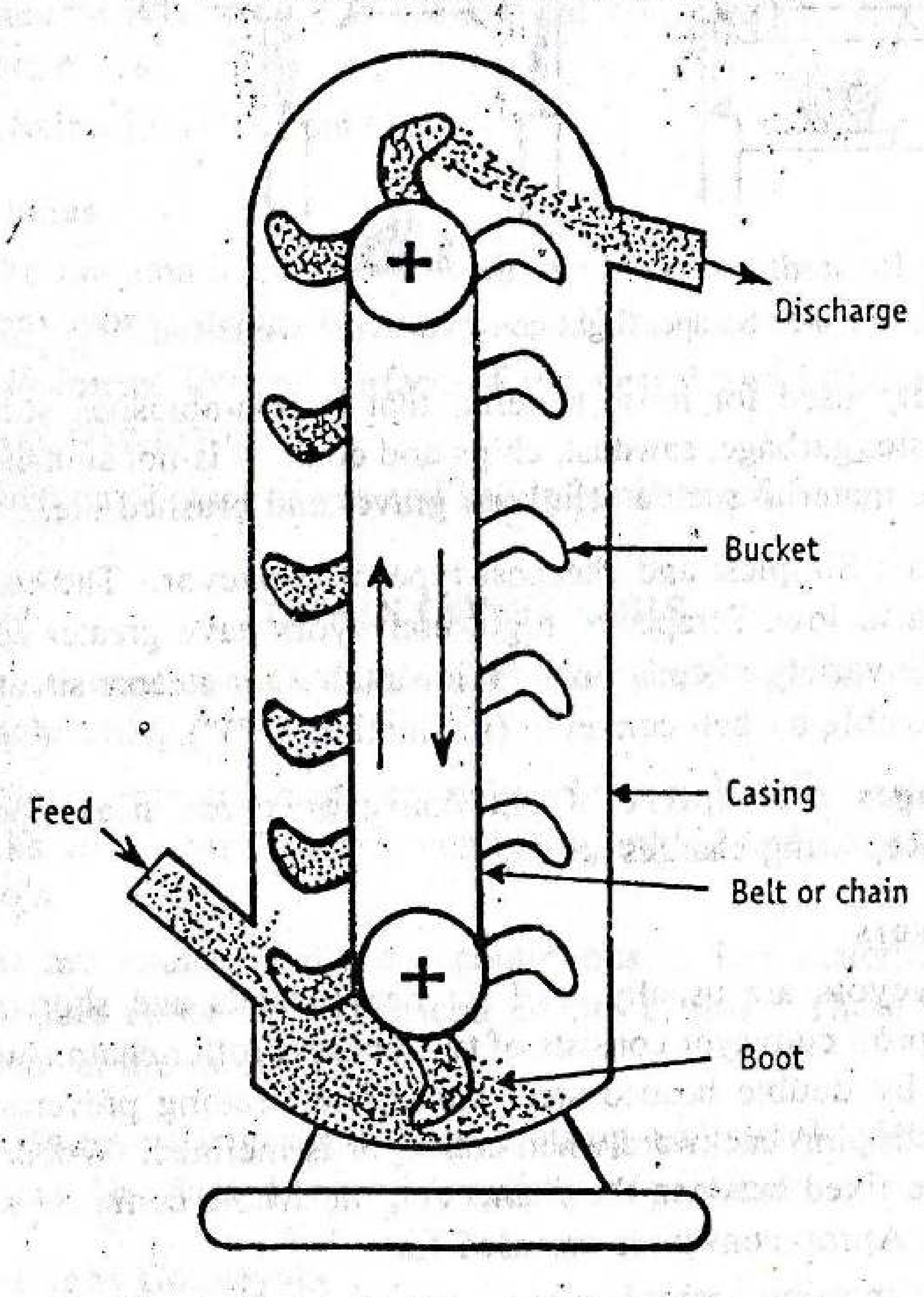


Figure 4-6. Construction of a bucket conveyor.

The weight of the conveyor results in the stretching of the chain under load. Therefore, tightening devices are generally provided for altering the position of the sprocket at the foot of the elevator.

- In *horizontal runs*, buckets overlap each other and the feed is introduced as a continuous stream of material.
- In *vertical lines*, the buckets are pivoted in such a way that they hang freely between the chains. Therefore, conveyor acts as an elevator.

At the foot of the elevator, a structure known as 'boot' is used for feeding the buckets and also for tightening the chains. Buckets are sometimes completely enclosed in a casing. The casing is made of wood or steel sheet.

Working

The elevators are generally driven from the head sprocket. At the foot of an elevator, there is a structure known as 'boot', which helps in feeding. The buckets are normally fed by digging into the materials particularly in case of loose material and granular solids. The buckets maintain their carrying capacity by gravity, but they can convey the material horizontally or vertically or any desired path. Loading can be done by the flow of material through a chute into the buckets. Buckets may be readily discharged at any point by a tripping device, causing each bucket to turn through 90 degrees. The types of discharges are continuous, positive and centrifugal.

Applications

Bucket conveyors are used in transporting coal, crushed stone, grains etc.

Advantage

Bucket conveyors are very flexible.

STORAGE OF SOLIDS

Attention must be paid to the storage of solids. The storage is an important operation, if the material is too valuable or too soluble when exposed to atmosphere as in outdoor piles. The following are used for storing solids.

Bunkers : These are used for storage of pulverised solid material. During plant shut down, the solid material is stored in bunkers. Coarse solids such as gravel and coal are stored outside in large piles, unprotected from the weather. Out door storage can lead to environmental problems such as dusting and leaching.

Hoopers, bins and silos : A *bin* is fairly wide and not so tall. It is a cylindrical or rectangular vessel of concrete or metal. A *silo* is tall and relatively small in diameter. A *hopper* is a small vessel with a sloping bottom. It is used for temporary storage before feeding solids to a process. These containers are loaded from the top by some kind of an elevator and discharged ordinarily from the bottom.

Now-a-days, there have been extensive improvements in the use of solid conveying equipment. For example, granulation and tabletting operations are completely automated and computer controlled. The above system utilizes pumps and bucket conveyors to move materials upward whenever required. Examples are transporting granules and transporting compressed tablets for batching and film coating. These use belt conveyors and pneumatic conveyors to move the material horizontally.

QUESTION BANK

Each question carries 5 marks

1. Illustrate the concept of solid transport by fluidisation.
2. Describe the principle of pneumatic conveyer with a labelled diagram.
3. Describe the different types of conveyors used in pharmaceutical industry.
4. List advantages of screw conveyor and screw elevator. How do you compare these with pneumatic transport of solids?
5. Describe the construction and working of a screw conveyor.

Each question carries 10 marks

1. Describe the construction and working of belt conveyor system for solid transport.
2. Name the devices used for transportation of solids. Describe pneumatic conveyor.

5

Flow of Heat

Mechanisms of Heat Flow
Conduction
Convection
Radiation
Equipment—Heat Exchangers and Heat Interchangers

Heat is a form of energy. According to the principles of thermodynamics, whenever a physical or chemical transformation occurs, heat flows into or leaves the system.

A number of sources of heat is used for industrial scale operations. Steam and electric power are the chief sources to transfer heat. It is essential to convey steam without any losses to the apparatus in which it is used. The study of heat transfer processes helps in designing the plant efficiently and economically.

Applications

A few areas of relevance to pharmaceutical engineering are enumerated here.

Evaporation : Heat is supplied in order to convert a liquid (vehicle) into a vapour, which is subsequently removed. This process is used for preparing vegetable extracts. A construction similar to shell-and-tube heat exchanger is employed in evaporators. The heat flow can be quantified so as to estimate the efficiency of the process.

Distillation : Heat is supplied to a liquid mixture for converting the liquid into vapour so that the individual vapour components are condensed at another place. In case of steam distillation, steam will be in direct contact with the material.

Drying : In the production of tablets, heat is passed through a carrier gas over a bed of wet solid mass for achieving drying. In case of spray drying, heat is supplied to the solutions and suspensions (as in case of production of milk products).

Crystallisation : Saturated solution is heated to bring about supersaturation, which promotes the crystallisation of drugs. On the other hand, removal of heat (cooling) from a saturated solution also facilitates crystallisation, as in case of purification of bulk drugs.

Sterilization : For the sterilization of pharmaceuticals, autoclaves are used with steam as a heating medium. Dry heat is used for the sterilization of glass apparatus and other containers.

In addition, a number of other processes, such as boiling, exsiccation, sublimation and fusion, also use heat.

In a laboratory setup, number of equipment involving heat are used. A few examples are air-ovens, incubators, dryers, refrigerators etc. On industrial scale, equipment are used for applying heat, removing heat and preventing heat loss. The basic principles involved in heat transfer are understood properly for the maintenance and efficient working of the equipment.

MECHANISMS OF HEAT FLOW

Heat flows from a region of high temperature to a region of low temperature. Heat may flow by one or more of the three basic mechanisms.

Conduction

When heat flow in a body is achieved by the transfer of the momentum of individual atoms or molecules without mixing, such a process is known as *conduction.*

For example, flow of heat through the metal shell of a boiler takes place by conduction as far as solid wall or shell is considered. No mixing is involved. Conduction is limited to solids and fluids whose movement is restricted.

Convection

When heat flow is achieved by actual mixing of warmer portions with cooler portions of the same material, the process is known as *convection.*

For example, heating of water by a hot surface (coil type water heater) is mainly by convection. Convection is restricted to the flow of heat in fluids (i.e., liquids and gases). Convection currents of air are set up almost daily in the atmosphere. These are responsible for winds, land and sea breezes, ocean currents etc.

Radiation

When heat flows through space by means of electromagnetic waves, such energy transfer is known as *radiation.*

For example, a black surface absorbs most of the radiation received by it. Simultaneously the absorbed energy is quantitatively transferred into heat. Fused quartz transmits all the radiation that strikes it, while a polished opaque surface or mirror will reflect most of the radiation that strikes it. Solar water heaters, solar cookers, microwave ovens, microwave cookers, sonicator baths etc., are few examples in which radiation is utilized for producing heat.

In general, these mechanisms may operate simultaneously. For example, in ovens hot air is circulated by fan, so as to transfer heat by forced convection. Simultaneously, heat is transferred by conduction from the shelf to the material in contact. Heat also radiates from hot walls of the oven.

CONDUCTION

Heat can flow only when there is a temperature gradient, i.e., heat flows from a hot surface to a cold surface. The rate of conduction through solids can be studied easily, since it is the sole phenomenon. The basic law of heat transfer by conduction can be written in the form of a rate equation as follows:

$$\mathit{Rate} = \frac{\text{driving force}}{\text{resistance}} \qquad (1)$$

The driving force is the temperature drop across the solid surfaces. The greater the temperature drop, the greater will be the rate of heat flow.

The flow of heat will also depend on the conductivity of the materials through which it is flowing. For example, conduction of heat is faster through an iron rod than through a wooden log. This factor is represented by the term resistance, which can be quantitatively expressed by Fourier's law.

$$\mathit{Resistance} = \frac{\text{thickness of the surface (m)}}{\text{mean proportionality constant (W/m·K)} \times \text{area of the surface (m}^2\text{)}} = \frac{L}{k_m A} \qquad (2)$$

Equation (2) for resistance can be obtained from the Fourier's law.

Fourier's Law—Conduction of Heat through a Metal Wall

Fourier's law states that the rate of heat flow through a uniform material is proportional to the area and the temperature drop and inversely proportional to the length of the path of flow.

The Fourier's law may be mathematically expressed as:

$$\text{Rate of heat flow} \propto \frac{\text{area (m}^2) \times \text{temperature difference } (\Delta t)}{\text{thickness (m)}}$$

$$q \propto \frac{A.\Delta t}{L}$$

$$\text{or} \qquad q = \frac{k_m.A.\Delta t}{L} \qquad (3)$$

where k_m = mean proportionality constant, W/m·K.

Derivation : Fourier's law can be applied to a metal wall through which the conduction of heat is taking place (Figure 5-1). The characteristics are as follows.

Area of the wall = A, m^2

Thickness of the wall = L, m

Face of the wall (HH) is maintained at a uniform, definite and higher temperature = t_1, K

Face of the wall (CC) is maintained at a lower, but uniform temperature = t_2, K

The heat flow will be at right angles to the plane A and is assumed to be in a steady state. Consider a thin section of thickness dL at an intermediate point in the wall. This section is parallel to the plane, A. For this section, Fourier's law may be applied as given below.

$$\frac{dQ}{d\theta} = \frac{-k.A.dt}{dL} \qquad (4)$$

where Q = heat transferred, J

θ = time, s

k = proportionality constant, W/m·K

t = temperature, K

The constant, k, is a function of temperature, but independent of length. The '*minus*' sign indicates the decrease in temperature in the direction of flow. In equation (4), (dt/dL) represents the temperature gradient. For a steady state heat transfer, equation (4) changes to:

$$\frac{dQ}{d\theta} = \text{Constant} = q = \frac{-k.A.dt}{dL} \qquad (5)$$

where q = rate of heat transfer, J/s (or W)

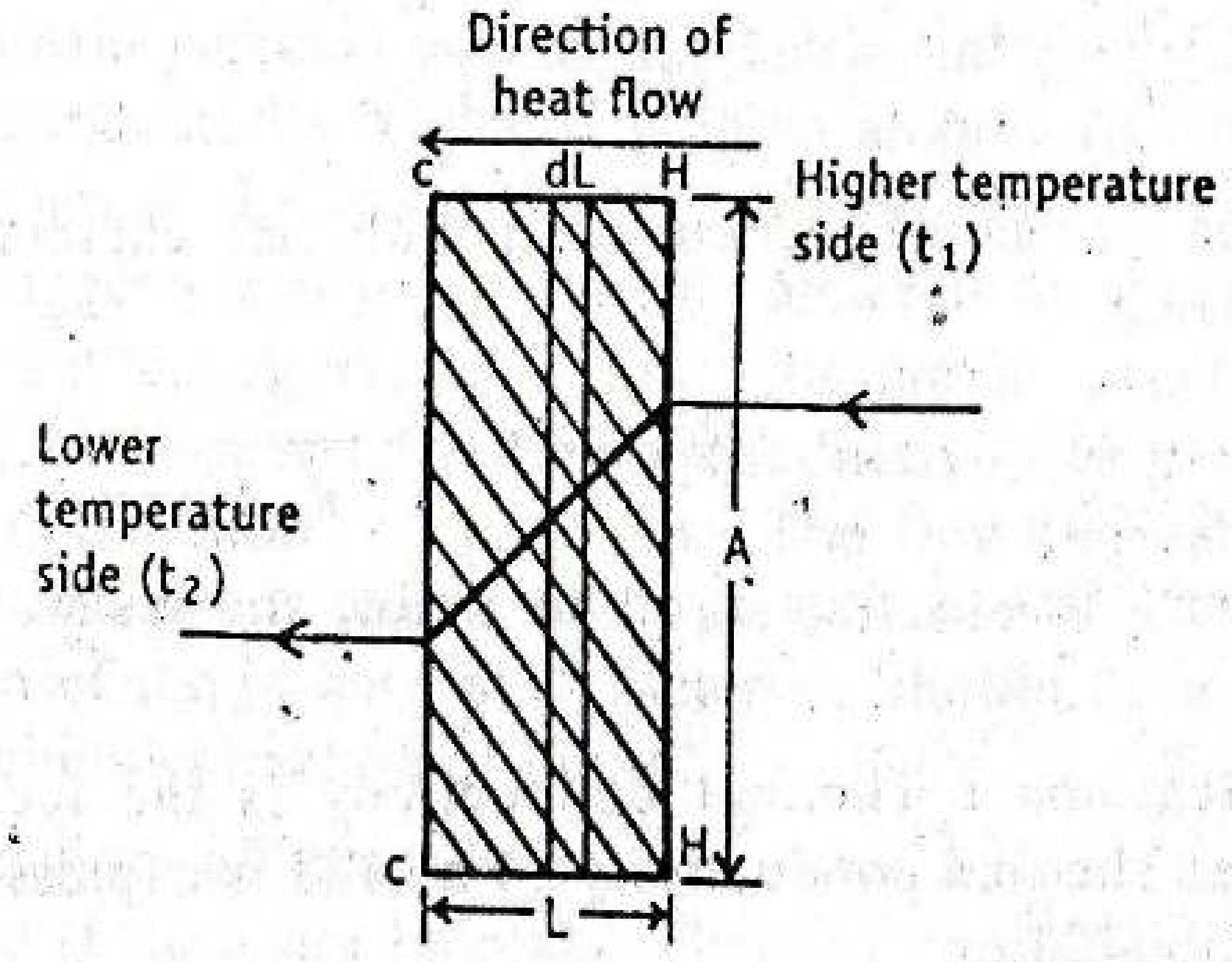


Figure 5-1. Heat transfer through a metal wall by conduction.

The temperature difference in the intermediate section is not known. But temperatures at the two faces of the wall are known. The area, A, may vary with L, but is independent of temperature. By separating the variables, equation (5) can be written as:

$$\frac{q.dL}{A} = -kdt \qquad (6)$$

Integrating equation (6) between the limits

$L = 0$ when $t = t_1$ and

$L = L$ (total thickness) when $t = t_2$,

gives:

$$q\int_0^L \frac{dL}{A} = -\int_{t_1}^{t_2} kdt = \int_{t_2}^{t_1} kdt$$

$$\frac{qL}{A} = k_m(t_1 - t_2) = k_m.\Delta t \qquad (7)$$

Rearranging equation (7) gives:

$$q = \frac{k_m.A.\Delta t}{L} \qquad (3)$$

where k_m = mean proportionality constant, W/m·K

In steady state heat transfer, 'q' remains constant. In equation (3), the term 'Δt' indicates the driving force. Equation (3) may be rearranged to obtain:

$$q = \frac{\Delta t}{\dfrac{L}{k_m \cdot A}}$$

Comparing the above equation with rate expression [equation (1)] indicates that:

$$Resistance = \frac{L}{k_m A} \qquad (2)$$

Fourier's law is thus used to define the resistance in quantitative terms.

Applications : Thermal conductivity is the reciprocal of thermal resistance. Thermal conductivity of a solid is expressed in terms of k as per equation (3).

The *coefficient of thermal conductivity* is the quantity of heat that flows across a unit surface area in unit time, when the temperature drop is unity.

The coefficient of thermal conductivity depends upon the material with which the body is made and upon its temperature. Thermal conductivities of some substances are given in Table 5-1.

TABLE 5-1

Thermal Conductivities of Some Metals

Materials	*Thermal conductivity*, W/m·K
Copper	379.0
Silver	57.0
Steel	43.0
Aluminium	24.2
Stainless steel	17.0
Glass (borosilicate)	1.0
Building bricks	0.69
Water	0.62
Air	0.03

From Table 5-1, the following conclusions can be drawn.

- Thermal conductivities of liquids and gases are very small compared to most of the solids. In other words, the resistance offered by liquids and gases is high as far as the conduction is concerned.
- In case of steam jacketed vessels, the kettle (inner surface) must have good conductivity so that maximum amount of heat passes from the steam to the contents. The high thermal conductivity of copper suggests that it is a suitable material for the construction of the kettle. At the same time, the metal used for jacket (outer surface) must have minimum conductivity to prevent loss of heat by conduction and radiation. The low thermal conductivity of iron suggests that it would be suitable material for the construction of the jacket. Such materials should be resistant to solvent or chemical action of liquid.

For the construction of evaporators and tubular heat exchangers thermal conductivity values are helpful. Thermal conductivity is very sensitive to changes in chemical composition and temperature and, therefore, the above values cannot be applied to all situations. The materials and their usefulness with respect to thermal conductivities are discussed in Chapter 17.

Compound Resistance in Series

Consider a flat wall constructed of a series of layers as in Figure 5-2. The characteristics are:

Thicknesses of the three layers = L_1, L_2 and L_3, m

Conductivities of materials of which layers are made = k_1, k_2 and k_3, W/m·K

Area of the entire wall = A, m^2

Temperature drops across three layers = Δt_1, Δt_2, and Δt_3, K

Resistances of the three layers = R_1, R_2 and R_3

For the above descriptions, the total temperature drop may be written as:

$$Driving\ force,\ \Delta t = \Delta t_1 + \Delta t_2 + \Delta t_3 \qquad (8)$$

The rate of flow of heat through several resistances in series is exactly analogous to the current flowing through several electrical resistances in series. Therefore, the overall resistance (R) is equal to the sum of individual resistances.

$$R = R_1 + R_2 + R_3 \qquad (9)$$

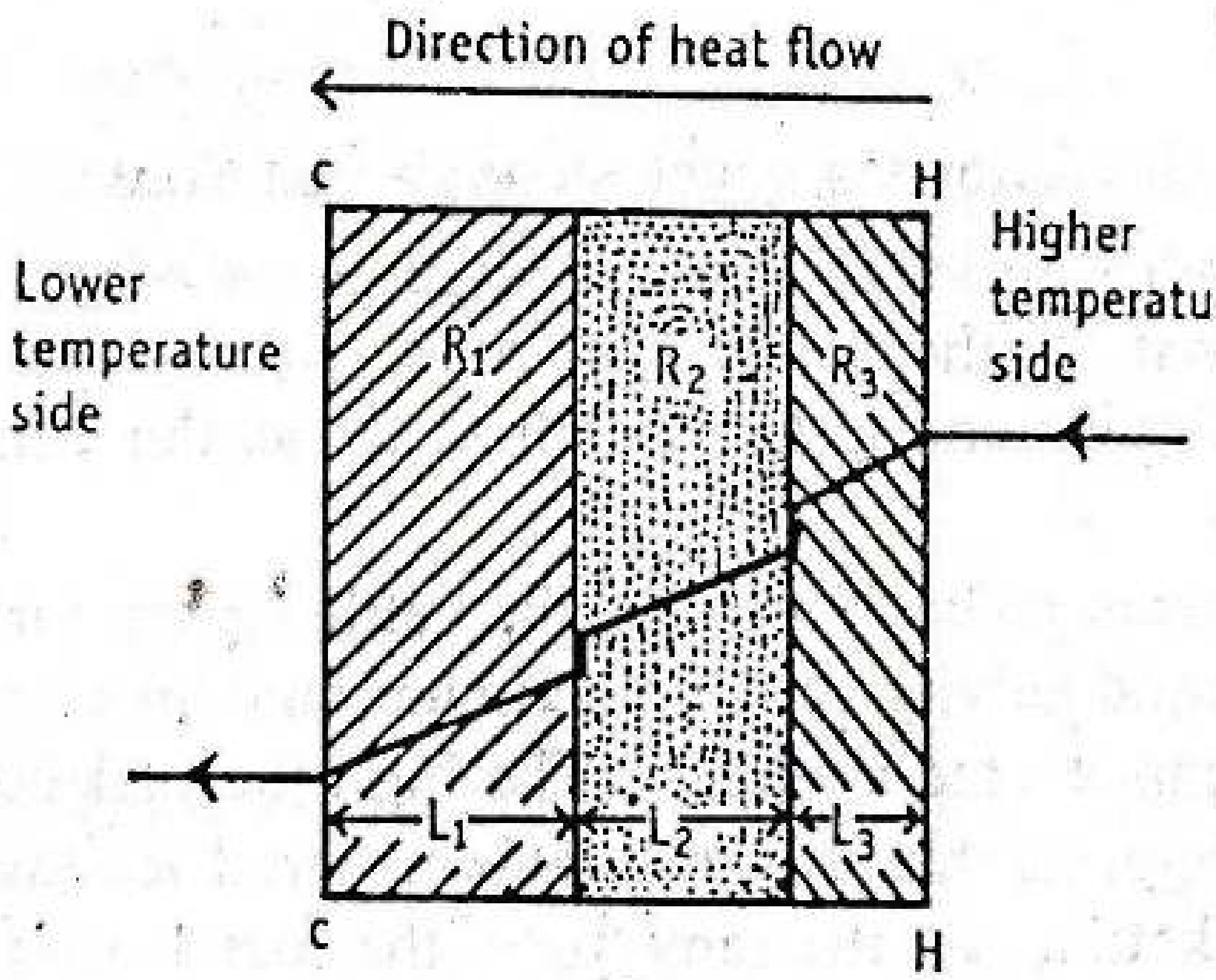


Figure 5-2. Flow of heat through several resistances arranged in series.

According to Fourier's law, individual resistances, are described by equation (2). These are incorporated in equation (9) to get:

$$R = \frac{L_1}{k_1 A} + \frac{L_2}{k_2 A} + \frac{L_3}{k_3 A} \tag{10}$$

Since entire heat must pass through the resistances in series, heat q can be written as:

$$q = q_1 + q_2 + q_3 \tag{11}$$

Using the principles of conduction, the rate of heat transfer, q, may be expressed as:

$$q = \frac{\Delta t}{R_1 + R_2 + R_3} \tag{12}$$

The contributions of temperature drops to the total temperature and individual resistances to the total resistance can be expressed mathematically as:

$$\Delta t : \Delta t_1 : \Delta t_2 : \Delta t_3 :: R : R_1 : R_2 : R_3 \tag{13}$$

Heat Flow through A Cylinder—Conduction

In a heat exchanger, hot fluid or steam is passed through the circular pipe. The hot fluid transfers the heat to the inner surface of the pipe wall. Further heat transfer takes place by conduction through the pipe wall. The rate of heat transfer by conduction through a cylinder may be obtained as follows.

Consider a hollow cylinder as shown in Figure 5-3. The heat is flowing from inside to outside the cylinder. Consider a very thin cylinder at the centre of the pipe. The following characteristics may be enumerated.

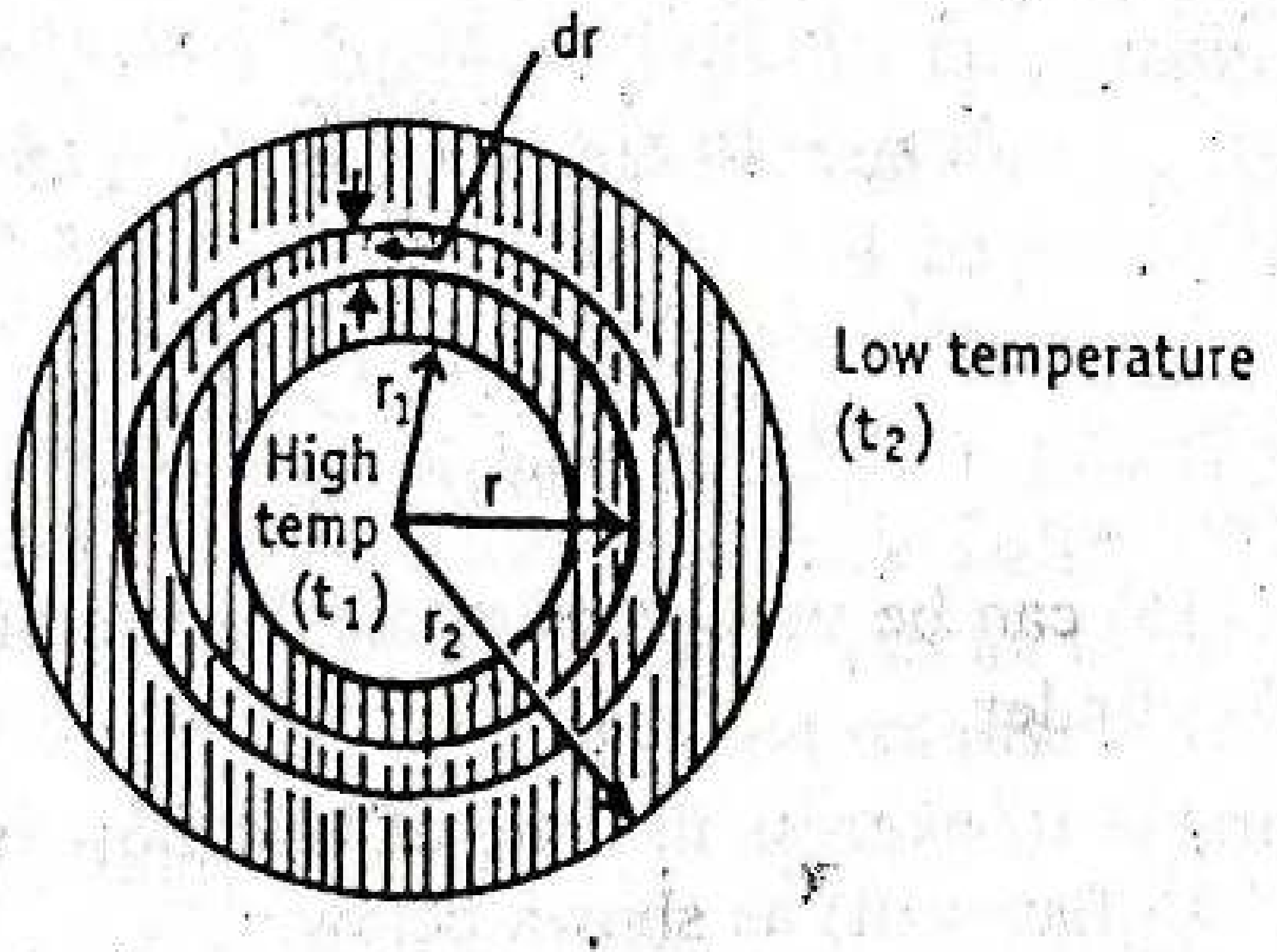


Figure 5-3. Flow of heat through thick-walled cylinder.

Mean thermal conductivity of material of cylinder = k_m, W/m·K
Temperature of the inside surface (higher) = t_1, K
Temperature of the outside surface (lower) = t_2, K
Radius of the thin cylinder = r, m
Thickness of the thin section = dr, m
Radius of the inner wall = r_1, m
Radius of the outer wall = r_2, m
Length of the hollow cylinder = N, m

The heat flow (in watts) is considered as parallel and the rate of heat transfer (q) can be written as:

$$q = -k \frac{dt}{dr} (2\pi r N) \tag{14}$$

where $2\pi r N$ is the area of the heating surface, i.e., the interior of the cylinder. The mean surface area (A_m) may be written as circumference multiplied by length of cylinder.

Considering the variables such as radius and temperature, equation (14) is rearranged to obtain:

$$\frac{dr}{r} = \frac{-2\pi N k}{q} dt \tag{15}$$

Integrating equation (15) within the limits of

$r = r_1$, when $t = t_1$ and
$r = r_2$, when $t = t_2$,

gives:

$$\int_{r_1}^{r_2} \frac{dr}{r} = \frac{-2\pi N}{q}\int_{t_1}^{t_2} k\,dt = \frac{2\pi N}{q}\int_{t_2}^{t_1} k\,dt$$

$$\ln r_2 - \ln r_1 = \frac{2\pi N k_m}{q}(t_1 - t_2)$$

$$q = \frac{2\pi N\, k_m\,(t_1 - t_2)}{\ln (r_2/r_1)} \qquad (16)$$

Equation (16) can be used to calculate the rate of heat flow through a thick walled cylinder.

It is desirable to express the rate of heat flow in a more convenient form (similar to flat wall) as shown below.

$$q = \frac{\text{coefficient} \times \text{area} \times \text{temperature difference}}{\text{length of the metal layer}}$$

$$q = \frac{k_m A_m (t_1 - t_2)}{L} \qquad (17)$$

By equating the right hand-side terms in equations (16) and (17), the area (of surface) term may be obtained as:

$$\frac{A_m}{L} = \frac{2\pi N}{\ln (r_2/r_1)}$$

Since L is the thickness, it is related to thickness of the tube, i.e., $(r_2 - r_1)$ of the cylinder. This value is substituted for L and rearranged to obtain A_m (mean area of a cylinder).

$$A_m = \frac{2\pi N(r_2 - r_1)}{\ln (r_2/r_1)} \qquad (18)$$

A_m, area may be considered as $2\pi r_m N$. From equation (18), mean radius, r_m, may be written as:

$$r_m = \frac{(r_2 - r_1)}{\ln (r_2/r_1)} = \frac{(r_2 - r_1)}{2.303 \log (r_2/r_1)} \qquad (19)$$

In equation (19), the term, r_m, is called *logarithmic mean radius*. Logarithmic mean is less convenient than the arithmetic mean. The arithmetic mean is sufficiently accurate, if the tube is thin walled. This relationship is explained below.

- The value $r_1/r_2 < 3.20$ reflects that the wall is thick. If arithmetic mean radius is used, the result will be within 10 % of that obtained by equation 16 (i.e., logarithmic mean radius is used).
- The value $r_1/r_2 < 1.5$, reflects that the wall is thin. If arithmetic mean diameter is used, the results will be within 1% of that obtained by equation 16 (i.e., logarithmic mean radius is used).

For most cases in practice, arithmetic mean radius is sufficiently accurate, if the cylinder is thin-walled. For thick walled tube, logarithmic mean radius has to be used. The use of either an inner radius or an outer radius does not give sufficiently accurate results.

Conduction through Fluids

Conduction in liquids is usually small and this presents a considerable obstacle for heat transfer. Conductance in fluids is because of eddies setup by the changes in density with temperature, which is observed in the boiling of liquids (as in case of evaporation and distillation of liquids).

Conduction through fluids rarely occurs in practice, except when heat flows through thin films. In these cases, the thickness of the film is not exactly known. Therefore, equations described earlier cannot be applied. This difficulty can be overcome by the use of surface coefficient, which will be discussed later. If a body of fluid is large, both convection and conduction may prevail. This complicates the data analysis and fails to provide accurate predictions.

CONVECTION

When heat flow is achieved by actual mixing of warmer portions with cooler portions of the same material, the process is known as *convection.*

The heat transfer in fluid occurs on account of actual mixing of its layers.

Forced convection : Mixing of fluid may be obtained by the use of a stirrer or agitator or pumping the fluid for recirculation. Such a process in heat transfer is designated as *forced convection.* For example, in some types of tube evaporators, the evaporating liquid is forced through the tubes under pressure. Therefore forced convection is observed.

Natural convection : Mixing of fluid may be accomplished by the currents set up when body of fluid is heated. Such a process is known as *natural convection.* For example, in pan evaporator, convection currents are set up in the evaporating liquid.

In general, fluid flow may be described as either laminar or turbulent. These create problems in the estimations. Some of them are as follows. When heat is passed through the tube, stagnant films are important in determining the rate of heat transfer.

- When fluid exhibits viscous flow, the velocity is zero at the actual surface of the wall. It means that the layer of fluid adjacent to the wall acts as a stagnant film.
- A comparatively stagnant film can be observed even in turbulent flow. At the centre, the fluid is in turbulent flow, while at the surface the fluid exhibits viscous flow. A film of buffer layer oscillates between these types of flow.
- Sometimes, scales are deposited on the surface of the metal wall and heat must be conducted through the scales.
- When steam gives up latent heat, water will condense on the surface of the vessel (or tube). Again the heat must be conducted through this water film.

For heat transfer in a tube, heat must pass through the stagnant film by conduction. Hence, conductivity of these films is important. Normally, thermal conductivities of fluids are low. The conductivity of the stagnant film will be still less. For example, the thermal conductivity of water is less. A film of water has a resistance of about 500 times and that of air film is about 13,000 times greater than a copper sheet of the same thickness. Thus, the resistance offered by these films (though it is thin) is large for the heat flow. Beyond these films, the turbulence brings about rapid equalization of temperature.

Therefore, the resistance offered by the boundary film is of importance in the flow of heat, particularly in the evaporation process.

Forced Convection–Temperature Variation–Individual Heat Transfer Coefficients

Mixing of a fluid may be obtained by the use of a stirrer or agitator or pumping the fluid for recirculation. Such a process in heat transfer is designated as *forced convection.*

Forced convection is obtained in some types of tube evaporators, wherein the evaporating liquid is forced through the tubes under pressure.

In a heat transfer process, the overall coefficient depends upon many variables. It is necessary to break them into individual parts. The temperature distribution across a column of fluid that is being heated (or cooled) is related to the velocity distribution across the same column of fluid.

Consider a case of heat flowing from a hot fluid through a metal wall into a cold fluid. At a specific point, the variation of temperature on each side of the metal wall is depicted in Figure 5-4. Several important facts are evident from Figure 5-4, as listed below.

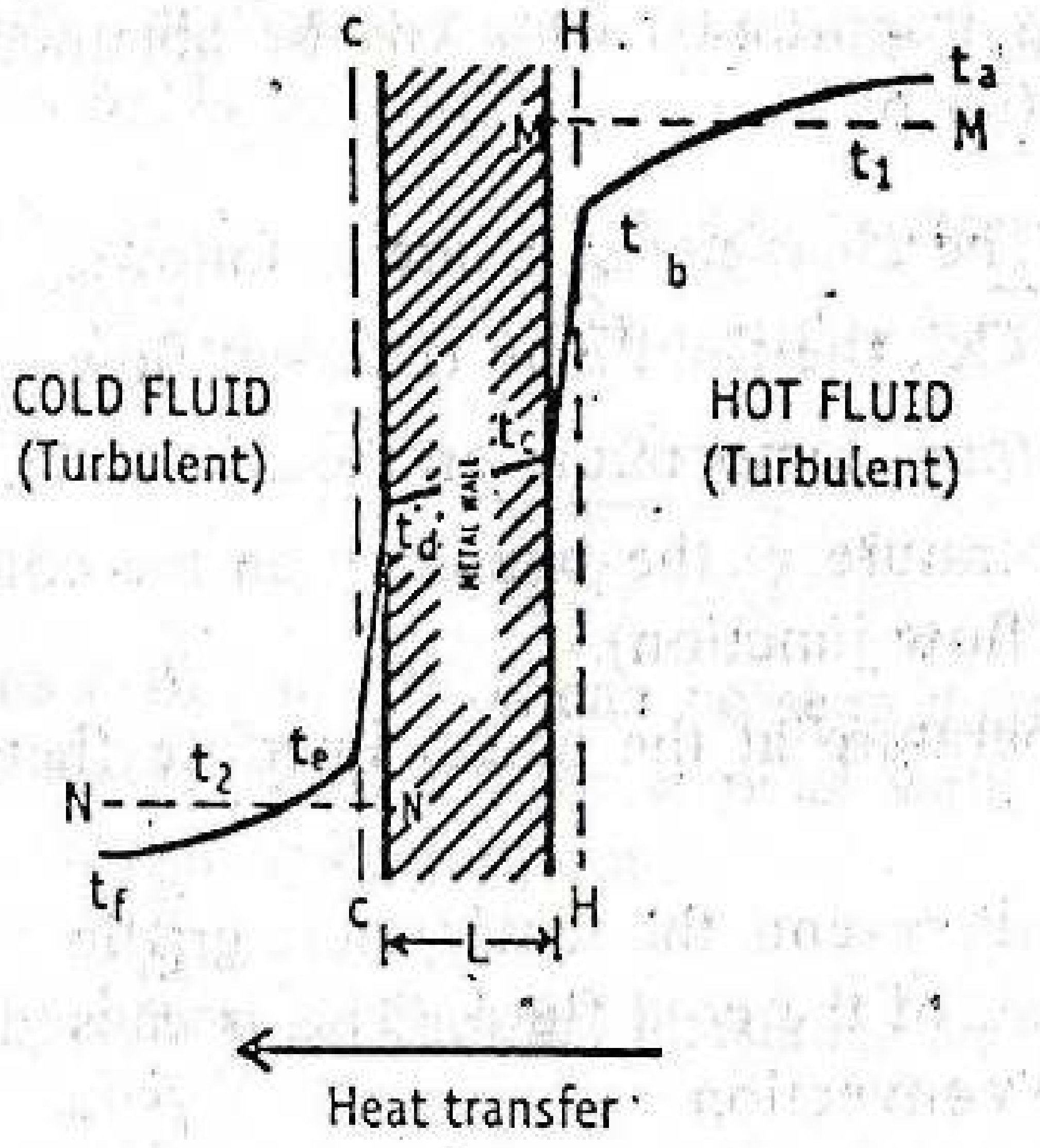


Figure 5-4. Temperature gradients in forced convection, while heat is flowing from a hot fluid to a cold fluid through a metal wall.

Metal wall : The characteristics are as follows.

(1) Dotted lines HH and CC represent the boundaries of the films in viscous flow on the hot and cold sides, respectively, on each side of the metal wall.

(2) The temperature gradient through the line $t_c t_d$ is caused by the flow of heat purely by conduction through the metal whose thermal conductivity is known.

(3) Metal wall thickness is L.

Hot fluid side : The characteristics are as follows.

(1) To the right of HH, the fluid is in turbulent flow on the hot side.

(2) t_a is the maximum temperature in the hot fluid.

(3) t_b is the temperature at the boundary on the hot side (turbulent and viscous flow junction).

(4) t_c is the temperature at the actual interface (between fluid and solid surface).

(5) Curve t_a t_b t_c represents the temperature gradient from the bulk of the hot fluid to the metal wall. This is caused by the flow of heat in forced convection.

(6) t_1 is the average temperature on the hot fluid side represented by the line MM. In general, for heat transfer calculation, average temperature is important. This can be obtained by taking its temperature after mixing.

Cold fluid side : The characteristics are as follows.

(1) To the left of CC, the fluid is in turbulent flow on the cold side.

(2) t_f is the minimum temperature on the cold fluid.

(3) t_e is the temperature at the boundary on the cold side (viscous and turbulent flow junction).

(4) t_d is the temperature at the actual interface (between fluid and solid).

(5) Curve t_d t_e t_f represents the temperature gradient from the metal wall to the bulk of the cold fluid. This is caused by the flow of heat in forced convection.

(6) t_2 is the average temperature on the cold fluid side represented by the line NN. In general, for heat transfer calculation average temperature is important. This can be obtained by taking its temperature after mixing.

Surface or film coefficients : In forced convection, the stagnant films (HH and CC) are of great importance in determining the rate of heat transfer. Though these films are thin, the resistance offered by them is large. Beyond these films, the turbulence brings about rapid equalization of temperature.

Film coefficient is the quantity of heat flowing through unit area of the film for unit drop in temperature.

It is the conductive capacity of the stagnant film for the transfer of heat.

It is difficult to determine the thermal resistances of fluid films, since thicknesses of the films cannot be known precisely. The thickness of the film depends not only on viscosity of the fluid, but also on the fluid circulation level (forced convection). Hence, the resistance offered by these films cannot be individually calculated. Therefore, indirect method of computation of surface coefficients is employed.

Let q watt (joules per second) of heat is flowing from hot fluid to cold one. Same heat must pass through stagnant fluid film on the hot side, through the metal wall and through the stagnant film on the cold side. Let the following be the characteristics.

Area of the metal wall on the hot side = A_1, m^2
Area of the metal wall on the cold side = A_2, m^2
Average area of the metal wall = A_m, m^2

Surface or film coefficient on the hot side : On the hot side, the surface coefficient, h_1, is defined as:

$$\text{Film coefficient on the hot side } (\text{W/m}^2\cdot\text{K}) = \frac{\text{amount of heat flowing (W)}}{\text{area (m}^2) \times \text{difference in temperature (K)}}$$

$$h_1 = \frac{q}{A_1\,(t_1 - t_c)} \tag{20}$$

From equations (20) and (7), it can be seen that surface coefficient (h_1) is analogous to the term, k/L for a metal wall. Since L/kA is the resistance term for metal wall, the term:

$\dfrac{1}{h_1 A_1}$ is known as thermal resistance on hot side.

The thermal resistance is due to the combined effect of the viscous film HH and the turbulent core. This resistance caused the difference in temperature, $t_a - t_b$.

Surface or film coefficient on the cold side : Film coefficient on the cold side can be written on similar lines as:

$$\text{Film coefficient on the cold side} = \frac{\text{amount of heat flowing}}{\text{area} \times \text{difference in temperature}}$$

$$h_2 = \frac{q}{A_2\,(t_d - t_2)} \tag{21}$$

And,

$\dfrac{1}{h_2 A_2}$ is known as thermal resistance on cold side.

Overall coefficient : In the over all heat transfer, three resistance terms are involved in series.

$\frac{1}{h_1A_1}$ is the resistance on the hot fluid side.

$\frac{L}{kA_m}$ is the resistance of the metal wall.

$\frac{1}{h_2A_2}$ is the resistance on the cold fluid side.

Applying the principle of compound resistance in series, the overall heat transfer may be written as:

$$q = \frac{\Delta t}{\frac{1}{h_1A_1} + \frac{L}{kA_m} + \frac{1}{h_2A_2}} \qquad (22)$$

If both numerator and denominator of the right side of equation (22) are multiplied by A_1, equation (23) is obtained.

$$q = \frac{A_1\Delta t}{\frac{1}{h_1} + \frac{LA_1}{kA_m} + \frac{A_1}{h_2A_2}} \qquad (23)$$

Then, the overall heat transfer coefficient U_1 (W/m^2·K) is defined by equation (24)

$$U_1 = \frac{1}{\frac{1}{h_1} + \frac{LA_1}{kA_m} + \frac{A_1}{h_2A_2}} \qquad (24)$$

If equation (24) is compared with equation (23), it is apparent that:

$$q = U_1\Delta tA_1 \qquad (25)$$

Equation (25) states that

Rate of heat transfer = overall heat transfer coefficient ×
area of the heating surface × (26)
temperature drop

For a tubular wall : The above derivation (equation (24)) is based on the metal wall of thickness, L. This relationship may be extended to a tubular metal wall. The heat coefficients may be written in terms of diameter (metre), since area is proportional to the corresponding tube diameter. The overall heat transfer coefficient for a tubular metal wall may be written as:

$$U_1 = \frac{1}{\frac{1}{h_1} + \frac{LD_1}{kD_m} + \frac{D_1}{h_2D_2}} \qquad (27)$$

In some cases, one particular area is more convenient than the other. Suppose $h_2 >> h_1$, the (D_1/D_2h_2) becomes small in comparison to $(1/h_1)$. Similarly, resistance of the tube wall is also small in comparison with $(1/h_1)$. Hence, ratios (D_1/D_m) and (D_1/D_2) have very little significance and can be disregarded. Then, equation (27) becomes:

$$U_1 = \frac{1}{\frac{1}{h_1} + \frac{L}{k} + \frac{1}{h_2}} \qquad (28)$$

Equation (28) can be used in cases of:

(a) thin walled tubes with larger diameter
(b) thin walled plates

In these cases, area A can be used for A_1, A_m and A_2, since errors will be negligible. In such cases,

$$U_1 = U_m = U_2 \qquad (29)$$

When h_1 is very small compared to h_2 and (L/k), $(1/h_1)$ will be larger. Therefore these two terms in the denominator are disregarded. Then

$$U_1 = h_1 \qquad (30)$$

Thus, rate of heat flow from one fluid to another through the retaining wall can be simplified. Hence, numerical value of surface coefficients can be predicted easily.

Factors influencing film coefficients : Several factors influence the surface film coefficients. However, the factors that are widely applied in practice are a few with reference to the processing conditions. These are:

- Thermal conductivity of the liquid
- Specific heat of the film
- Density of the liquid
- Turbulence of the fluid
- Thickness of the film

If the films are thin, their resistances will be reduced. This can be achieved by increasing the speed of the steam on one side and the speed of liquid on other side.

Fluids in Natural Convection

When a fluid is heated, the currents set up may cause mixing of fluid. Such a heat transfer process is known as *natural convection.*

The mechanism of natural convection is depicted in Figure 5-5. Consider a case of single horizontal cylinder. A large volume of fluid is present surrounding the cylinder. When a fluid is in contact with a hot surface, the fluid that is immediately adjacent to the tube absorbs heat. The temperature of this part of the fluid increases, which in turn decreases the density. As a result, the fluid rises from the surface and is replaced by the cold fluid. This process continues thereby effecting the mixing of hot and cold fluids.

Fluid circulation caused by changes in the densities due to temperature differences in the fluid is termed as *natural convection.*

Fluid circulation also changes with:

- geometry of the system, i.e., size, shape and arrangement of heating surface.
- shape of the vessel in which the fluid is enclosed.

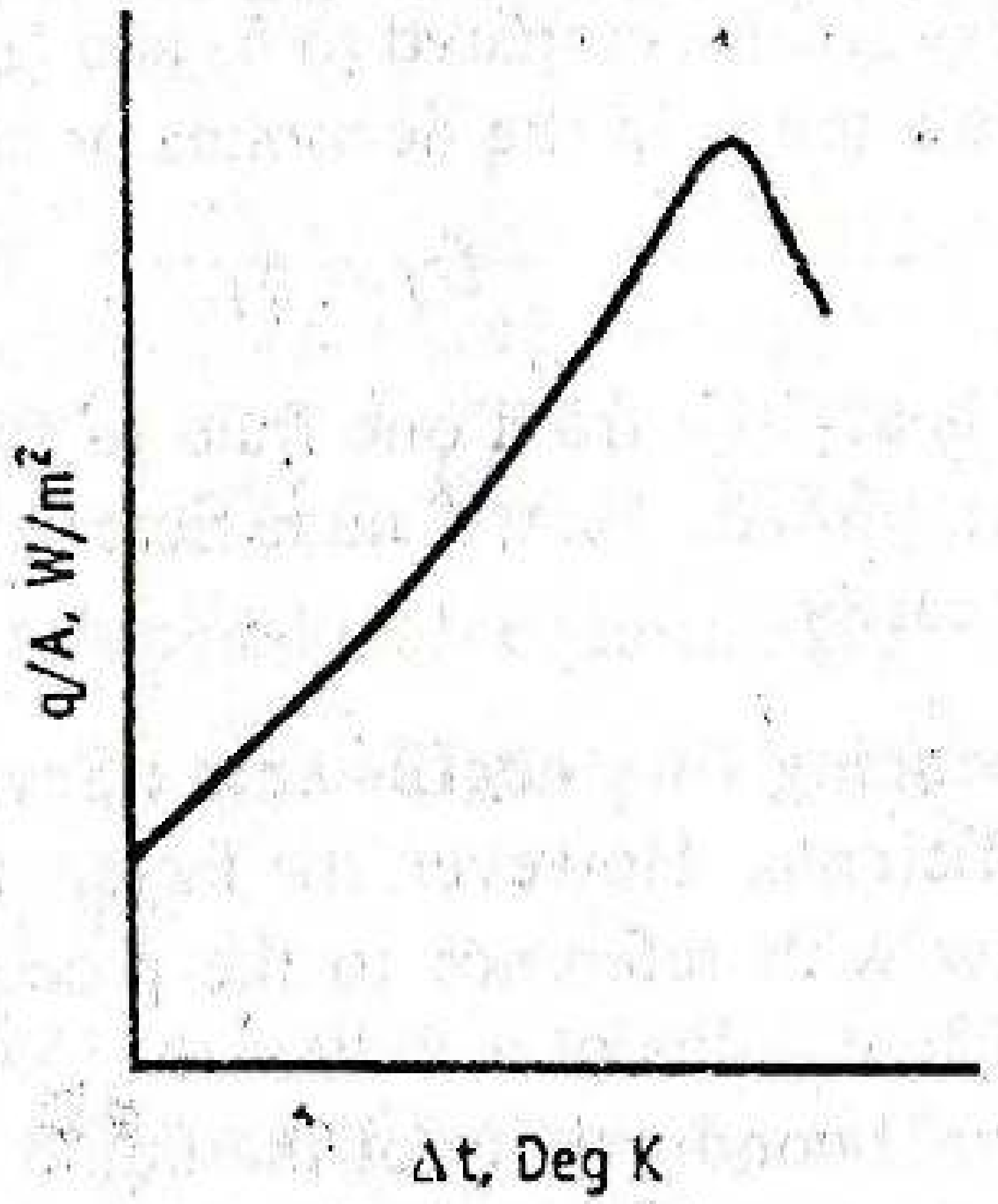


Figure 5-5. Mechanism of heat transfer in natural convection.

The physical properties of the system are individually evaluated at the mean film temperature. Generally, hot bodies lose heat to their surroundings both by radiation and by convection. At lower temperature ranges, convection is more predominant, while radiation is important at higher temperature ranges. In practice, liquid film coefficients may vary from 10 to 200 depending on the arrangement of apparatus and the viscosity of the liquids.

Application : Natural convection is observed when extracts are evaporated in open pans.

Changes in Fluids during Heat Transfer

In heat transfer by convection, two liquids are involved. The hot liquid gives heat, while the cold liquid receives it. Each liquid undergoes changes during heat transfer. Steam condenses to give heat, while the cold liquid boils.

Hot liquid–Steam boiler : Steam is generated in a central boiler house at high pressure. The following are the advantages.

(1) High pressure steam can be used to drive a turbine for generating electric power.

(2) Low pressure exhaust steam is used for process heating.

(3) Central generation is more economical.

(4) More steam is stored in a boiler if high pressure is applied.

(5) High pressure steam means high temperature.

Characteristics of the steam : (1) Steam should be as dry as possible, thereby heat losses can be minimized.

(2) Since the latent heat is the useful heat, steam should be used at the lowest pressure that will give a suitable temperature gradient.

(3) Steam should be pumped at its saturated temperature. Superheated steam should not be used.

(4) Steam should be replaced continuously so that the process proceeds indefinitely.

Hot liquid–condensing of vapour : Steam gives its heat of vaporisation during condensation. This heat is transferred to the cold liquid through a metal wall.

In a heater, steam is passed through the tubes or outside the tubes. In each case, the metal surface of the tube gets heated up. While transmitting heat to a metal surface, the saturated vapour condenses into two distinct forms based on the nature of wetting of the metal surface. These are as follows.

Film type condensation : In this type, the condensed liquid wets the surface on which it is condensing and forms a continuous film of condensate.

If condensation is occurring on the outside surface of a horizontal metal tube (a very common case), this film of condensate drops off beneath the tube. If the tube is vertical, then it runs down the whole length and drops off from the edge. Generally, smooth and clean surfaces tend to form film type. For film type condensation the film coefficients are low. Equations have been proposed for heat transfer calculations.

Drop-wise condensation : In this type, the condensed liquid collects as drops that may range from microscopic size up to drops that are seen with the naked eye.

If the condensed liquid does not wet the surface, the drops grow and then fall off the surface, leaving an apparent bare area on which new drops form. Normally, oily or greasy surfaces tend to induce drop-wise condensation. The coefficients for drop-wise condensation may be double or more than double that of film type under identical conditions. It is difficult to estimate the coefficients of heat transfer for drop-wise condensation.

In general, the film coefficient between condensing vapour and metal wall increases with increasing temperature of vapour. Film coefficients decrease with increasing temperature drop. When steam is employed as a source of heat, it is necessary to remove non-condensable gases. Otherwise, they reduce the film coefficients, because of their accumulation.

Cold liquid–boiling of liquids : When heat is supplied to a liquid, it boils and the vapour pressure increases. This process continues until the vapour pressure is equal to the atmospheric pressure. At this stage, the temperature of the liquid remains constant, which is known as boiling point. Generally, heat is supplied to a liquid through a heater by passing steam.

Consider a horizontal tube, which is immersed in a pool of pure liquid. Steam is passed through the tube. The heat transfer depends on the differences in temperatures on each side of the tube wall. The relationship between temperature differences and heat transfer coefficients in liquids (boiling outside the horizontal tube) is shown in Figure 5-6. Δt may be defined as:

$$\Delta t = \text{tube wall temperature–saturated temperature of liquid } (= \text{vapour pressure in spaces})$$

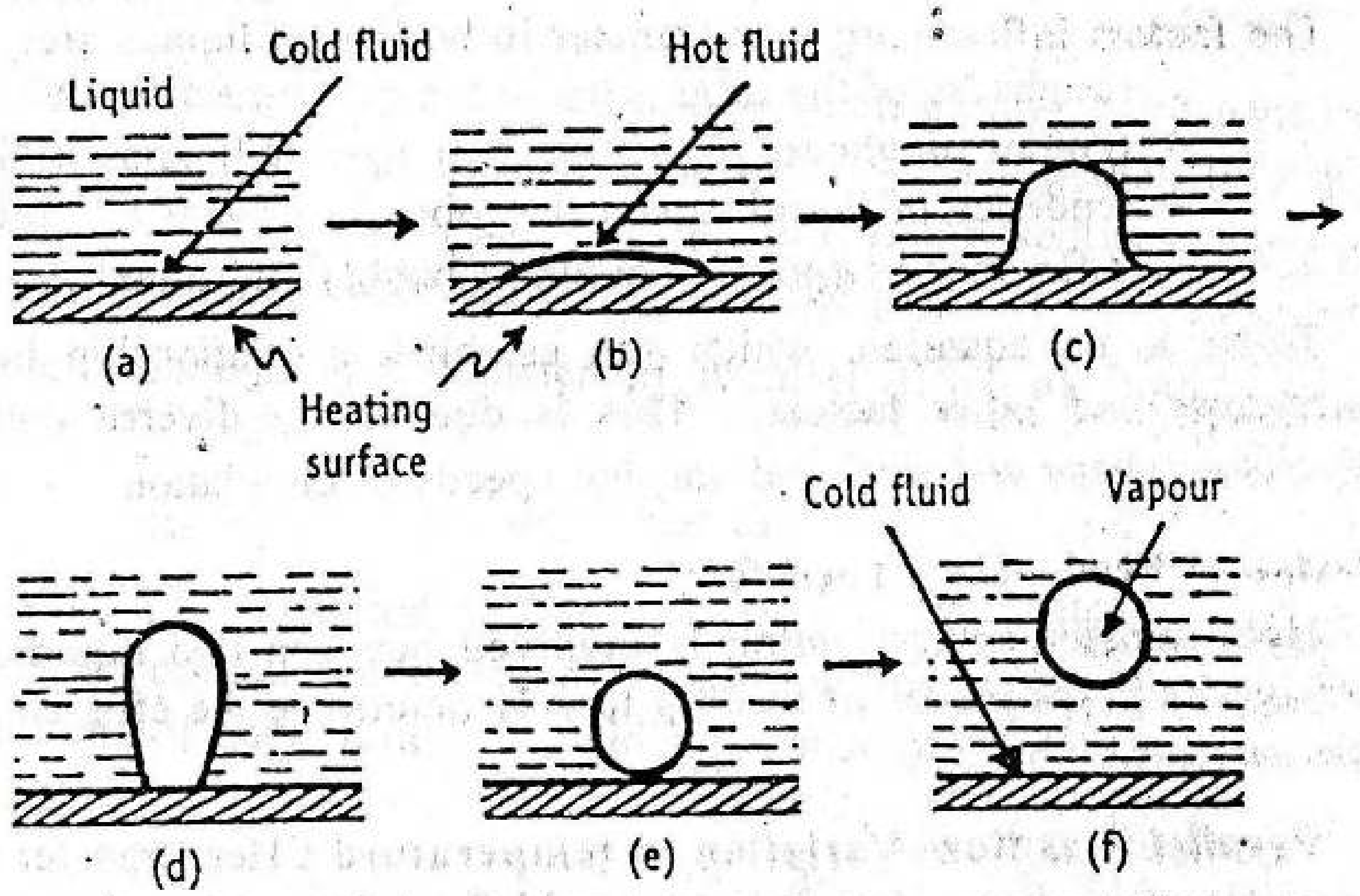


Figure 5-6. Effect of temperature difference on the behaviour of a liquid boiling outside the horizontal tube.

The following conclusions may be drawn from Figure 5-6.

(1) If Δt is very small, the rate of heat transfer (q/A) is not much. Hence, liquid doesn't boil.

(2) If Δt is increased, the rate of heat transfer (q/A) will be increased, because heat transfer coefficient increases rapidly. The mechanism is as follows. The heated liquid at the wall forms bubbles of vapour and gets detached from the surface. These vapour bubbles rise through the liquid. This type of boiling is called *nucleate boiling*. The cold fluid now wets the tube wall. Thus bubbles produce a series of currents, which have a stirring effect.

(3) If Δt is increased further, the surface temperature increases continuously up to a point, where the heat transfer coefficient reaches a maximum. This temperature is known as *critical Δt*. At this stage, the bubbles begin to coalesce into a continuous film of vapour, which insulates the tube.

(4) Beyond critical Δt, further increase in Δt leads to lowering of heat transfer coefficients rapidly. The continuous film of vapour insulates the tube, thereby the effective Δt fails to increase. Thus rate of heat transfer is decreased.

For some organic liquids. the heat transfer coefficient may decrease rather slowly after critical Δt. Therefore, maximum heat flux may occur at higher Δt than the maximum coefficient.

The factors influencing heat transfer in boiling of liquids are:

- roughness of the tube
- type of roughness
- tendency of liquid to wet the tube
- difference in densities between bubble and liquid

There is no equation, which can establish a relationship between coefficient and other factors. This is due to the diverse nature of apparatus (shape and size) and varying speeds of circulation.

Modes of Feed—Heat Transfer

Heat transfer by convection is involved between two liquids. The differences in the modes of feeding largely determine the efficiency of a heat process.

Parallel heat flow–Variation in temperature : Heat transfer across a metal surface from a hot fluid to a cold fluid depends on the temperature gradient (Δt). Generally, it is assumed to be constant for all parts of heating surface.

When the hot fluid and the cold fluid enter the apparatus from the same end, the flow is parallel to each other. This arrangement is known as *parallel flow*.

Consider a heat interchanger. The temperature of the hot fluid inside a pipe decreases from T_1 to T_2 by transferring heat to a cold fluid outside the pipe. As a result, the cold fluid temperature is increased from t_1 to t_2. This condition is represented in Figure 5-7.

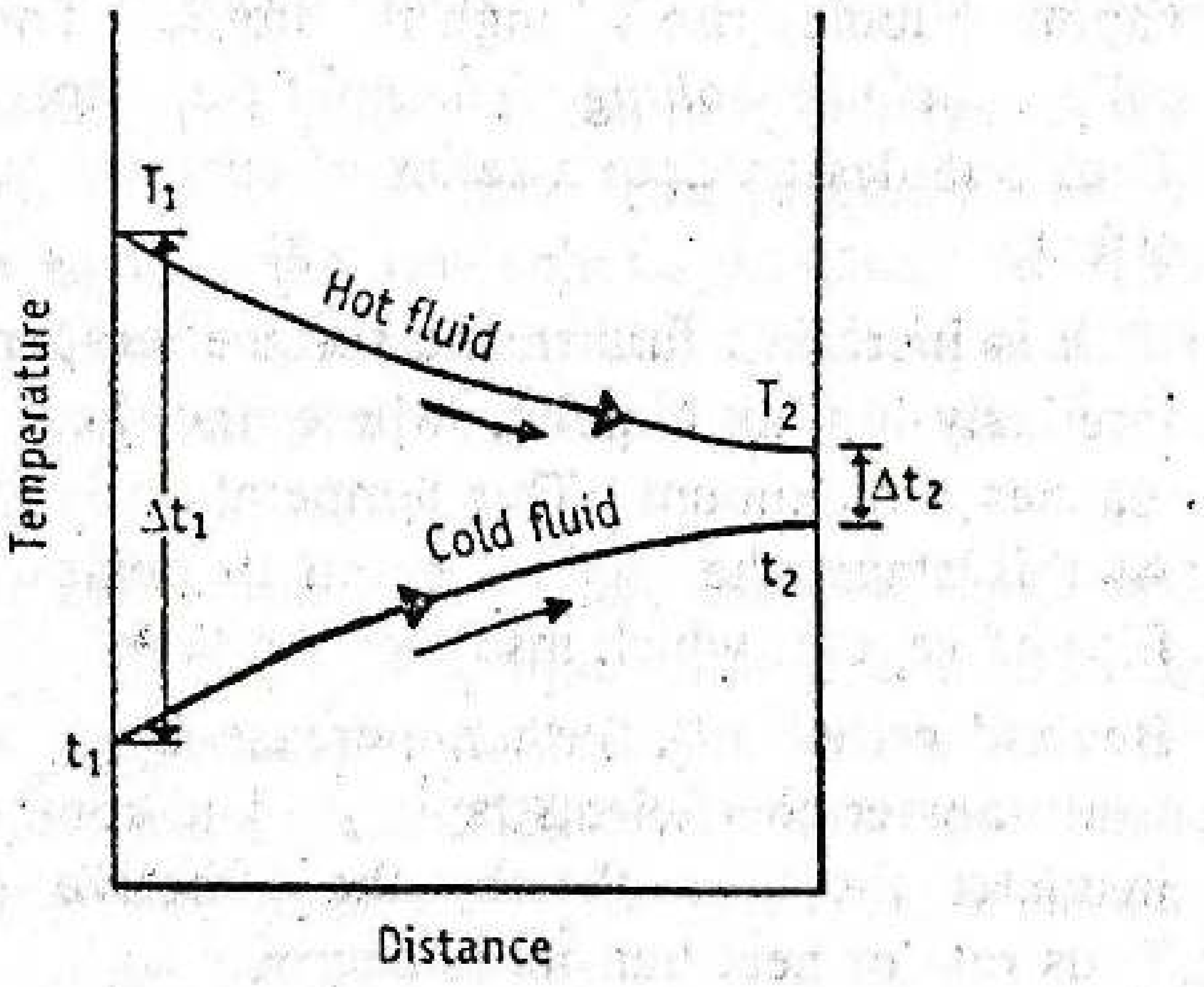


Figure 5-7. Temperature difference in parallel-current heat flow.

The temperature-drop at the left-end is much greater than at the right-end. It means that heat transfer is faster at left-side than that of the right-side. These changes, as occurring in a small section of the pipe, can be considered for the whole length of the pipe.

Mathematically, heat transfer in parallel flow of liquids can be written as:

$$dq = U.A.\Delta t \tag{31}$$

Equation (31) is based on two assumptions. (a) The overall coefficient (U) is considered constant throughout the equipment. (b) The specific heat of each fluid is considered constant. Integrating equation (31) gives:

$$q = UaL\frac{\Delta t_1 - \Delta t_2}{ln\dfrac{\Delta t_1}{\Delta t_2}} \tag{32}$$

where L = length of pipe, m
a = area of the pipe, m^2

Comparing equation (32) with the general equation of heat transfer (equation 25) gives:

$$\Delta t_m = \frac{\Delta t_1 - \Delta t_2}{ln\dfrac{\Delta t_1}{\Delta t_2}} \tag{33}$$

Thus logarithmic mean temperature difference (Δt_m) is used. The total heating surface (A) is equal to aL. Heat transfer equation in parallel flow heat exchanger is:

$$q = UA\Delta t_m \tag{34}$$

The logarithmic mean temperature difference is used to account varying temperature drop in parallel flow. If the temperature drop is nearly equal ($\Delta t_1 \cong \Delta t_2$), then arithmetic average temperature (Δt_m) can be used, which is a general expression for heat transfer.

In parallel heat flow, the heating obtained per unit surface area is much less effective at the fluid exit point compared to it at the point of entrance of the apparatus.

Counter-current heat flow–temperature gradient : When the hot fluid is passed through one end of the apparatus while cold fluid is passed through the other end, fluids pass and by pass each other in the opposite directions. This arrangement is known as *counter-current* or *counter-flow*.

The temperature gradients for the counter-current flow are shown in Figure 5-8.

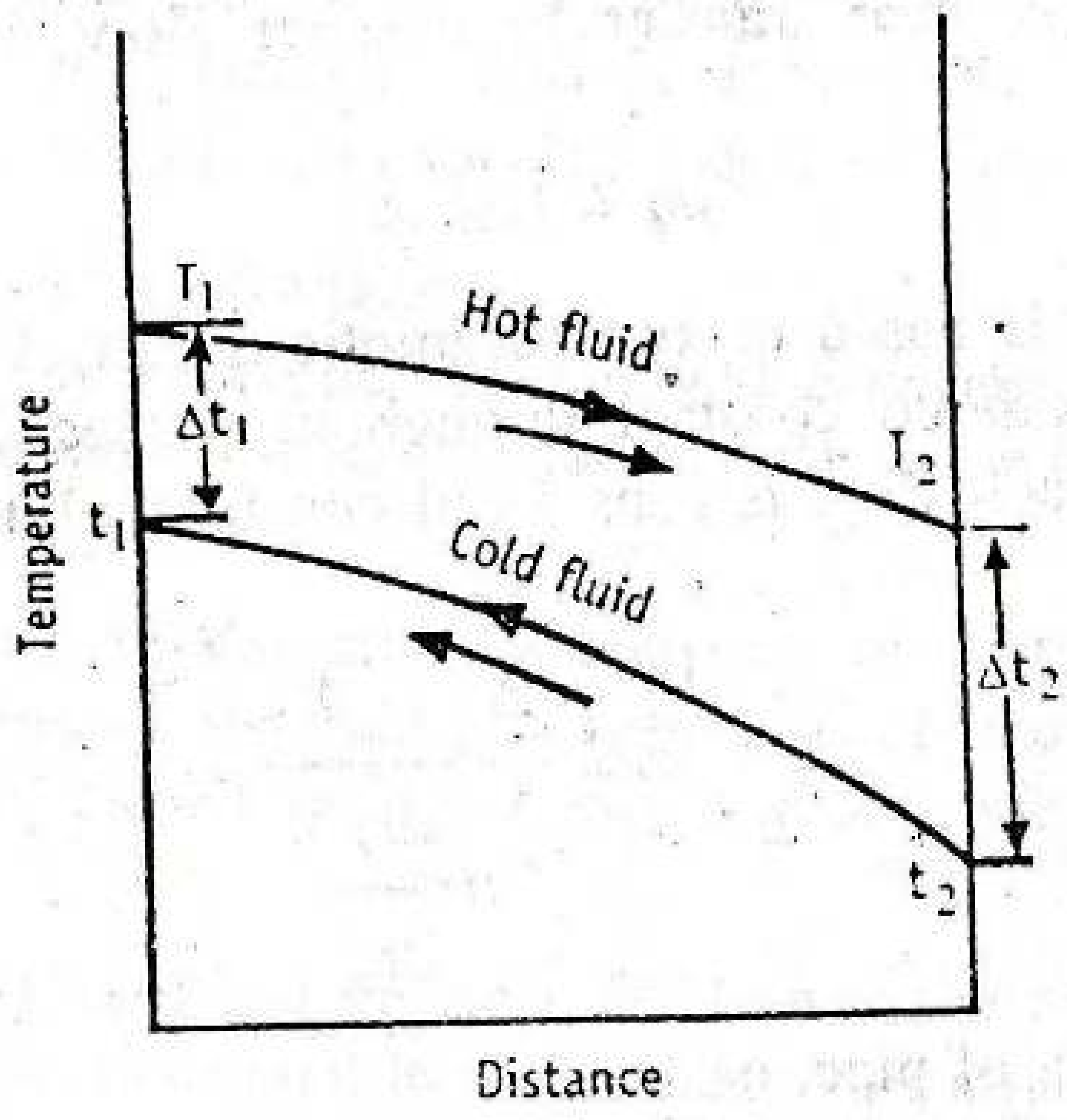


Figure 5-8. Temperature difference in counter-current heat flow.

From the Figure 5-8, it can be concluded that the temperature drop along the length of the apparatus is nearly constant. In other words, amount of heat transfer per unit area is substantially same at both ends. The heating surface is nearly constant throughout the apparatus.

In counter-current heat flow, the exit temperature of the hot fluid is considerably less than the exit temperature of the cold fluid. Hence a large proportion of the heat content of the hot fluid can be extracted for a given entrance temperature of the cold fluid. If $\Delta t_1 \cong \Delta t_2$, temperature ($\Delta t$) can be taken as arithmetic average.

$$\Delta t_{av} = \frac{\Delta t_1 + \Delta t_2}{2} \tag{35}$$

The heat transfer equation for counter-current heat flow can be written as:

$$q = UA.\Delta t_{av} \tag{36}$$

Consider a case, where steam is transferring its heat to a colder body. Let the pressure difference in steam be constant. The temperature difference when steam is in a heat exchanger is shown in Figure 5-9.

Initially steam cools down to the condensing temperature as indicated by AB in Figure 5-9. Then condensation occurs at constant temperature (section BC), and may further be allowed to cool (section CD). Here large errors would be introduced, if AF and DE are taken for Δt_1 and Δt_2, respectively. Separate heat transfer calculations must be done for the three sections in Figure 5-9 and then are added.

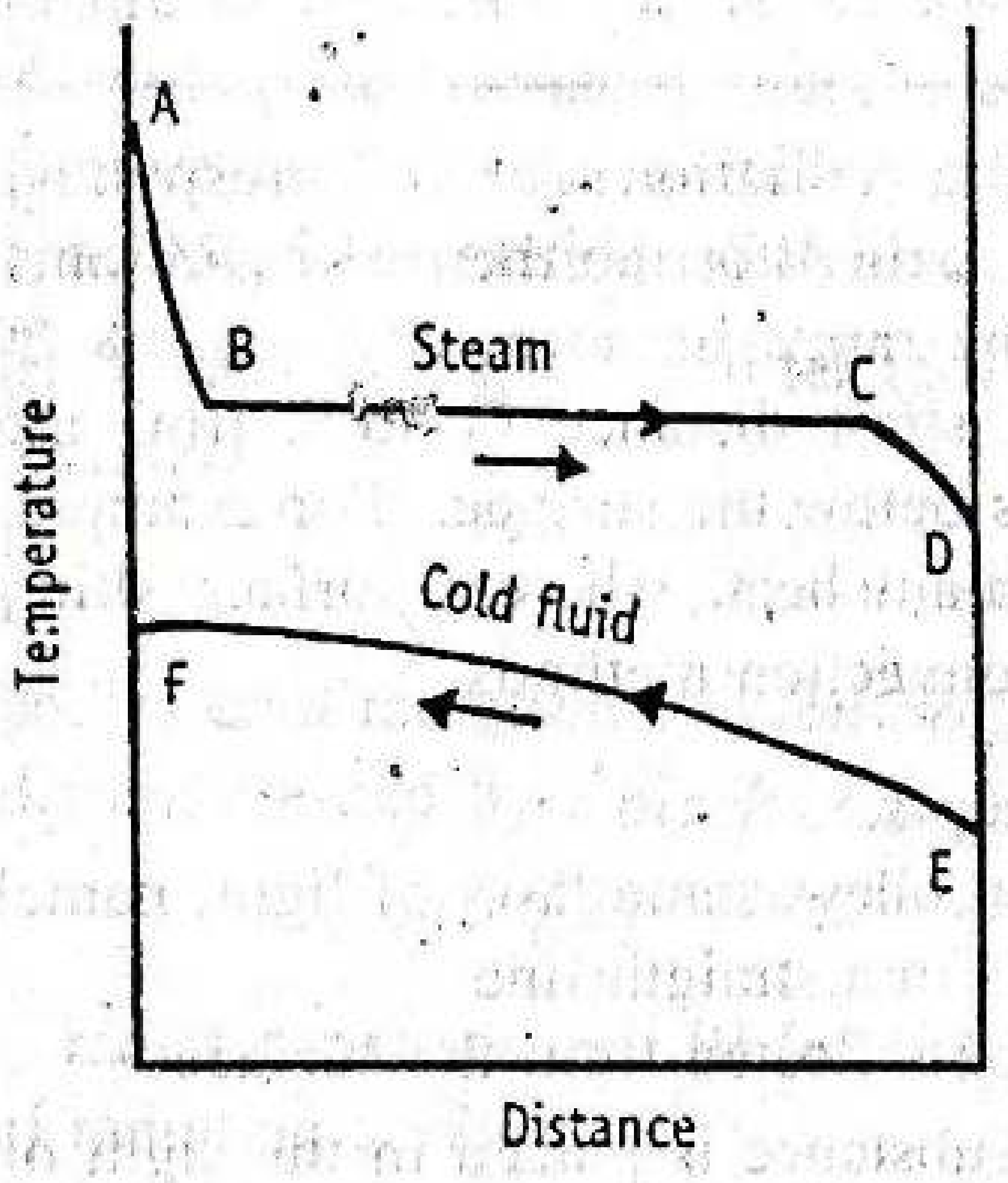


Figure 5-9. Temperature difference in counter-current heat flow in which steam is used as the heating medium.

RADIATION

Radiation is a process in which heat flows. Heat is transferred through space by means of electromagnetic waves.

Thermal Radiation

Heat transfer by radiation is known as *thermal radiation.*

Radiation is effective across perfect vacuum and also through layers of air.

All solid bodies radiate energy when their temperatures are above the absolute zero. A solid surface emits radiant energy continuously and distributes over all wavelengths (i.e.. from zero to infinity), although a major portion is concentrated within a relatively narrow range of wavelengths.

Heat transfer (thermal energy) is predominant as the temperature of the body increases. The amount and kind of thermal energy radiated increases rapidly with temperature. Thermal radiation usually occurs simultaneously with heat transfer by convection and conduction.

Various Forms of Emitters

Various forms of emitters used for the supply of radiant energy are given below:

Radiation source	*Wavelength*	*Applications*
IR lamp (1000°C)	1 μm	high intensity radiation.
Ceramic rods and panels heated by gas or electricity (500° to 300°C).	2 to 4 μm	Pharmaceutical purposes, thermolabile substances.

Advantages : The radiation source corresponding to wavelengths from 0.8 to 400 μm is used for the thermal radiation. For most cases of industrial interest, the range is narrowed from 0.8 to 25 μm. Radiant energy penetrates a short distance (1 to 2 μm) into materials. The heating effect occurs below the surface. For example, a film of solution can be dried by radiant heat, whereas surface skin retards the drying process in case of convection methods.

Fundamental Concepts

Thermal radiation obeys same laws of light, namely—

(a) it travels in a straight line

(b) it may be reflected from the surface

Suppose a cold substance is placed in the sight of a hot body inside an enclosed space. The cold body intercept the radiation emitted by the hot body. The fraction of radiations falling on the body may be reflected, which is known as *reflectivity*, ρ. The fraction that is absorbed is known as *absorptivity*, α. The fraction that is transmitted is known as *transmissivity*, τ. The sum of these fractions must be unity or:

$$\alpha + \rho + \tau = 1$$

In practice, reflected and transmitted radiations usually fall on other absorptive bodies. The absorbed radiation is transformed into heat. This fraction is not available for the emission of radiation.

Black Body

All solid bodies radiate energy at a temperature above the absolute zero, however, not at the same rate. For the purpose of heat transfer, a theoretic substance is proposed and designated as black body.

Black body is defined as a body that radiates maximum possible amount of energy at a given temperature.

No physical substance is a perfect black body. The black matte surface approaches a black body, when visible light (rays) alone is considered. Light coloured substances deviate widely from it. Black surfaces are better emitters of heat radiation than polished surfaces.

Further the term 'black' is nothing to do with the colour of the body. Similarly it has nothing to do with the amount of energy it radiates.

In theory, a black body is considered to be an enclosed space with a small (negligible) opening. The temperature in the enclosed space should be constant and uniform, because the amount of energy escaping through a small opening is negligible. In practice, a convenient black body is made from a tube of carbon. Both the ends are plugged, with a small hole at the centre of one end. When viewed through this small hole, the inside enclosed space (furnace) is considered as a black body, provided the temperature is uniform. Similarly all objects within the furnace (enclosed space) can be considered as black bodies.

A good absorber of heat is a good emitter too. Conversely a poor absorber is a poor emitter.

Rate of Radiation

Normally, hot bodies emit radiation. *Stefan-Boltzmann law* gives the total amount of radiation emitted by a *black body*.

$$q = bAT^4 \tag{37}$$

where q = energy radiated per second, W (or J/s)

A = area of radiating surface, m^2

T = absolute temperature of the radiating surface, K

b = constant, W/m^2·K^4

According to equation (37), the rate of heating depends upon the temperature and surface area of the emitter. At the same time, it also depends upon the absorption capacity of the material to be heated.

For a black body, the value of b is 5.67×10^{-8} W/m^2·K^4. Actual bodies do not radiate as much as the black body. Therefore, equation (37) is modified for the *actual bodies*

$$q = \varepsilon bAT^4 \tag{38}$$

where ε is equal to the emissivity of the actual body. Emissivity may be expressed at the same temperature as:

$$\textit{Emissivity},\ \varepsilon = \frac{\text{energy emitted by actual body}}{\text{energy emitted by black body}} \tag{39}$$

As per equation (39), emissivity is one for a black body. For actual bodies, ε is less than one, because a fraction of the radiation is absorbed, which appears as heat. The fraction of energy absorbed is denoted by absorptivity, α (other fractions are either reflected or transmitted).

A good absorber of heat is also a good emitter at a given temperature. If emissivity is equal to absorptivity ($\varepsilon = \alpha$), then a substance is considered as a black body. Since emissivity of a black body is 1, the absorptivity must be one. Therefore, the black body absorbs all the radiation falling on it.

Grey Body

Absorption of energy by a substance depends on its properties. Fairly high amount of energy will be absorbed by dark coloured, opaque and rough surface bodies. Least energy is absorbed by light coloured, transparent and smooth surfaced substances.

At a given temperature, the value of α varies somewhat with the wavelength of the radiation falling on it. This complicates the solving of problems in practice. Therefore, the concept of grey body has been introduced.

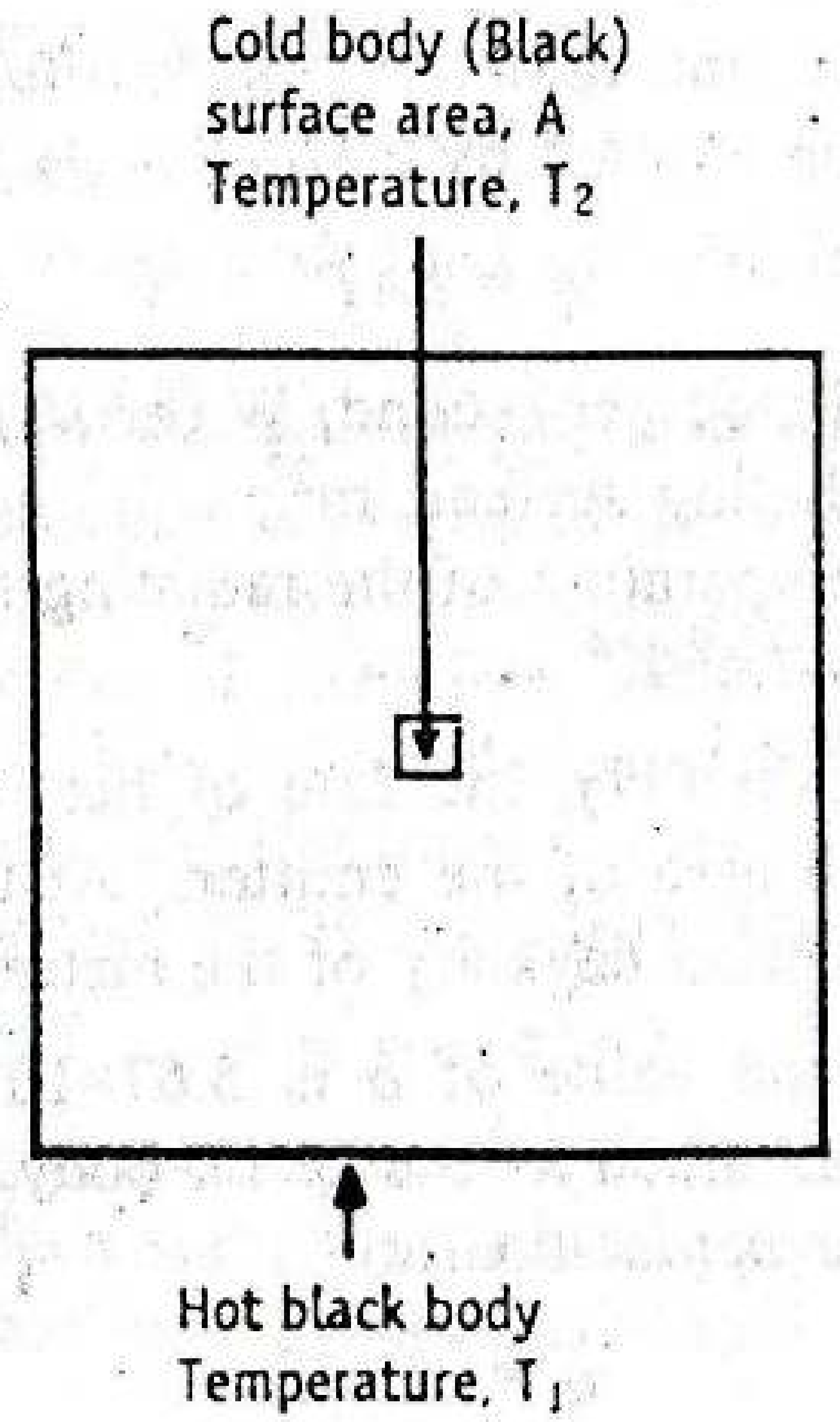


Figure 5-10. Heat transfer through radiation.

A *grey body* is defined as that body whose absorptivity is constant at all wavelengths of radiation, at a given temperature.

Consider a small cold body with a surface area of A and temperature of T_2 is completely surrounded by a hot black body at temperature T_1 (Figure 5-10). The amount of heat transferred in such a process is expressed by the Stefan law, which may be written as:

$$q = bA(T_1^4 - T_2^4) \tag{40}$$

Equation (40) assumes that all the heat radiated by a cooler body also falls on the hotter body.

EQUIPMENT

HEAT EXCHANGERS AND HEAT INTERCHANGERS

Most of the chemical and pharmaceutical industries employ a variety of heat transfer equipment. The materials to be heated may be liquids or gases and occasionally solids (which is a separate case by itself). The heating media may be a hot fluid or condensed steam. Some of the processes, which involve the heat transfer encountered in pharmacy are:

- Preparation of starch paste (steam jacketed kettles) for granulation
- Crystallization
- Evaporation
- Distillation

In industrial processes, heat energy is transferred by various methods. The principles, construction and working of equipment used for the transfer of heat energy are as follows:

Heat exchangers : *Heat exchangers* are the devices used for transferring heat from one fluid (hot gas or steam) to another fluid (liquid) through a metal wall.

Heat interchangers : *Heat interchangers* are the devices used for transferring heat from one liquid to another or from one gas to another gas through a metal wall.

The classification given above is vague and many times used interchangeably. Therefore, it is appropriate to call them as heat transfer equipment.

Some of them are discussed in the following sections.

Heaters or Heat Exchangers

Heat exchangers are the devices used for transferring heat from one fluid (hot gas or steam) to another fluid (liquid) through a metal wall.

Some heat transfer (or heaters) equipment are:

(1) tubular heater (shell-and-tube heater)
(2) multipass heater
(3) two pass floating head heater

In heat exchangers, the film coefficients on the steam side are usually much larger than the film coefficients on the cold liquid side. Therefore, the overall heat transfer coefficients will be nearer to the cold liquid side (because it is smaller of the two coefficients). Hence, heat transfer becomes less. The efficiency can be improved by passing the liquid at a high velocity. As a result, the thickness and resistance of the liquid film decrease. Normally, the space outside the tubes is large, but steam velocity is low. Still heat exchangers are useful, because of the high values of the steam film coefficients.

Tubular heater (Shell-and-tube heater) : Shell-and-tube heater is the simplest form of a tubular heater. It is a single-pass tubular heater.

Construction : The construction of a simple tubular heater is shown in Figure 5-11. Tubular heater consists of a bundle of parallel tubes, which are relatively thin walled. The ends of these tubes are expanded into two tube sheets, B_1 and B_2. The bundle of tubes is enclosed in a cylindrical shell or casing, C, to which the tube-sheets are fitted. Many heaters have a cast iron shell.

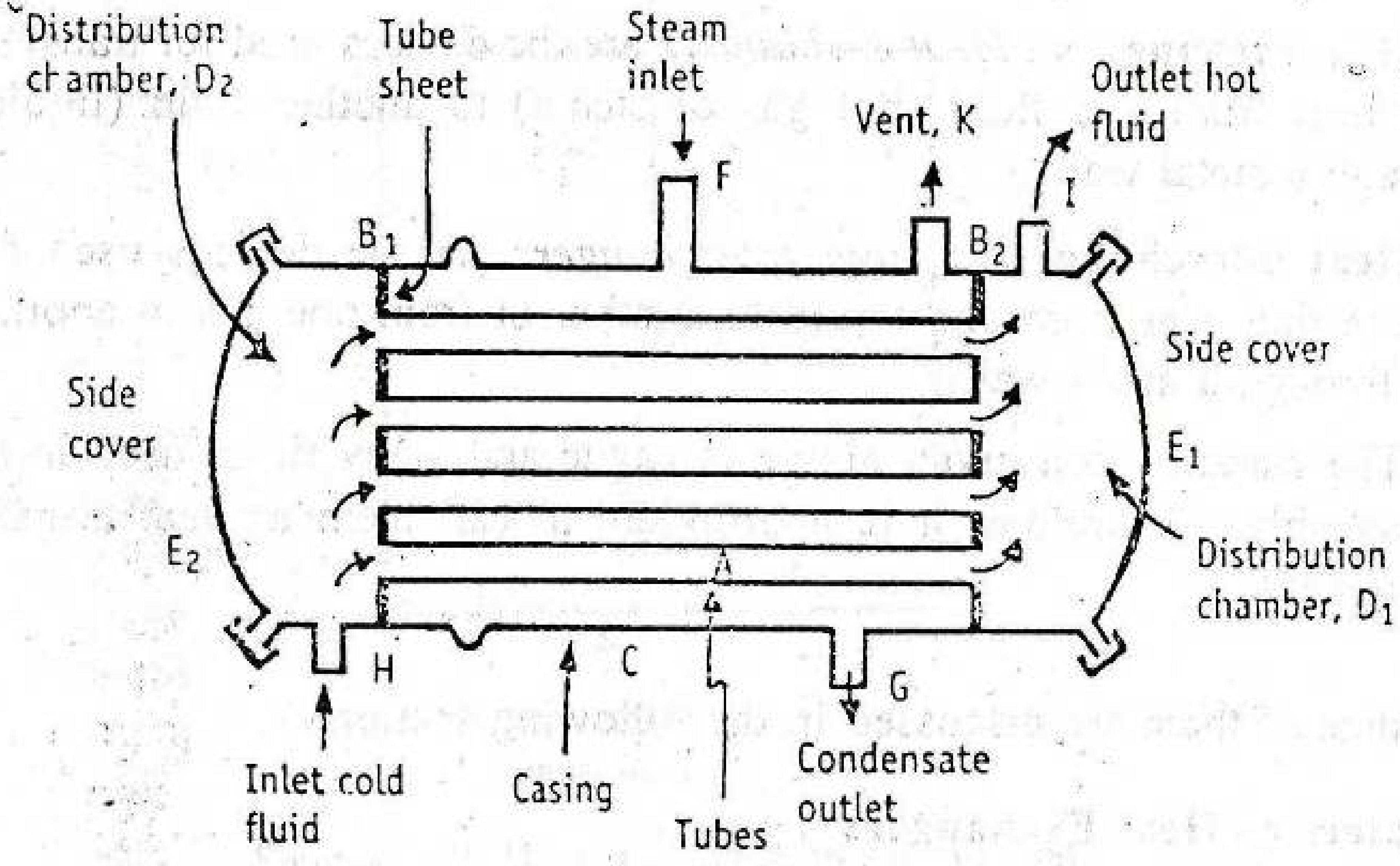


Figure 5-11. Construction of single-pass tubular heater.

Two distribution chambers, D_1 and D_2 are provided at each end of the casing C. Fluid inlet is provided to the distribution chamber D_2. The heated fluid outlet is provided to the distribution chamber D_1. Two covers, E_1 and E_2 are provided to close the distribution chambers from the sides. Steam or other vapour is introduced by a connection, F. Provisions are made for the escape of non-condensable vapour K and condensed vapour to drain at G.

Working : Steam or other vapour is introduced through a connection F into the space surrounding the tubes. The steam flows down the tubes. In this process, the tubes get heated. The condensed vapour is drained at G. Non-condensable gases, if any, escape through the vent K provided at the top of the casing.

The fluid to be heated is pumped through the connection H into distributing chamber D_2. The fluid flows through the tubes. The steam and fluid are physically separated, but are in thermal contact through the thin tube walls. The fluid in the tubes get heated due to heat transfer by conduction through the metal wall, followed by stagnant layer and finally by convection. The total heat transfer is effected by single pass of fluid. Thus, the heated fluid reaches the distributing chamber D_1 and leaves through the exit point, I

In the sheet-and-tube heater, the cross sectional area of the tubes is larger. Hence, the velocity of the fluid inside the tubes is low.

Advantage : In single-pass tubular heater, large heating surface can be packed into a small volume.

Disadvantages : (1) The velocity of fluid flowing in these tubes is low, because of large cross-sectional area or larger surface.

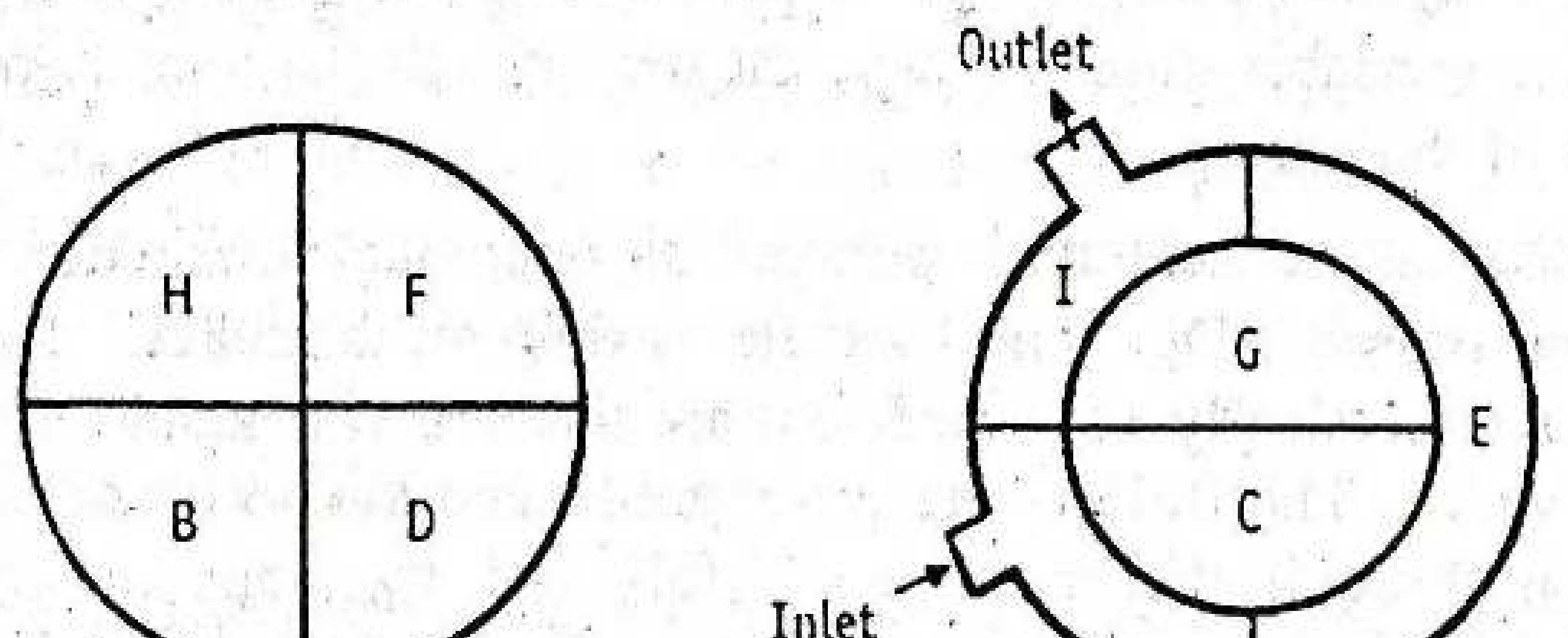
(2) The expansion of the tubes and shell takes place due to differences in temperatures. This may lead to the loosening of the tube sheets or buckle the tubes.

Multipass heater : In a multi-pass heater, the velocity of fluid can be increased. As a result, heat transfer coefficient also increases. As the name indicates, the liquid to be heated is passed through the tubes several times before leaving the equipment. This facilitates the heat transfer. Therefore, multipass tubular heaters are superior to the single-pass shell-and-tube heaters.

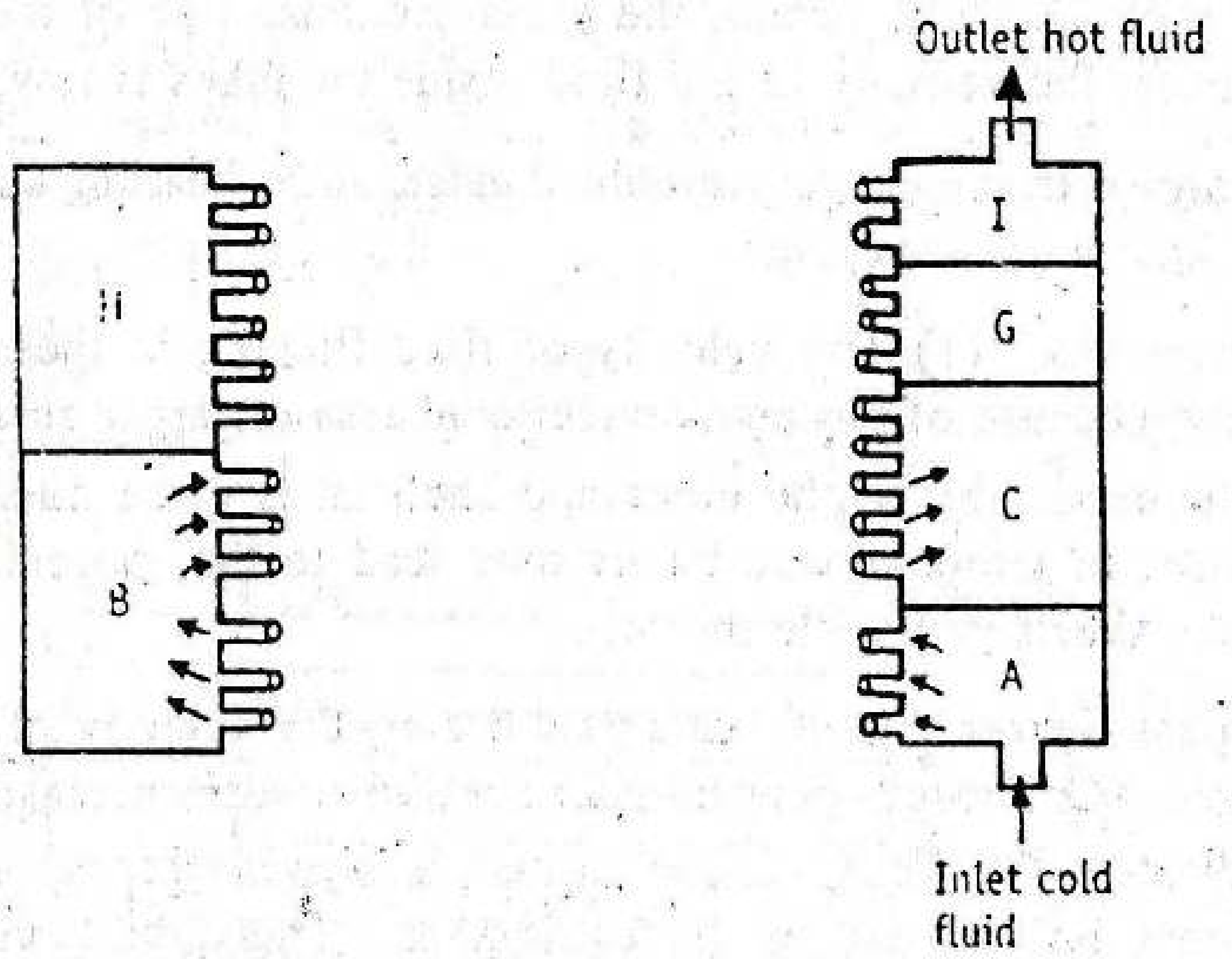
Construction : The construction of a multipass heater is same as tubular heater mentioned above, however, with some modifications (Figure 5-12).

Tubular multipass heater consists of a bundle of parallel tubes. The ends of these tubes are expanded into two tube sheets. The tubes bundle is wrapped in a cylindrical casing. Two distribution chambers are provided at each end of the casing. Since the heater is multipass, the same liquid has to flow through several tubes back and forth. In order to facilitate this process, distribution chambers are partitioned by means of baffles and their arrangements are different in the two chambers (Figure

5-12). The entrance and exit points of the fluid are arranged in the same distribution chamber (right side).



(a) When viewed from the side



Left-side distribution chamber (partitions F and D are below the page)

Right-side distribution chamber (Partition E is below the page)

(b) When viewed from the front

Figure 5-12. Construction of a multipass heater. In this figure, the modifications of distribution chambers and partitions are shown.

Working : Steam is introduced through the connection into the space surrounding the tubes. As the steam flows down, the tubes get heated. The condensed vapour is drained. Non-condensable gases, if any, escape through the vent provided at the top of the casing.

The fluid to be heated is pumped at high velocities into the right distribution chamber through the compartment, A. High velocity facilitates the effective heat transfer. In this construction, fluid is directed to enter only a fraction of the tubes by means of baffles placed in the distribution chamber.

The liquid enters compartment A and flows to the left into compartment B, back to the right to compartment, and so on in the same sequence of alphabetical order. During this process, fluid in the tubes get heated, due to heat transfer by conduction through the metal wall, followed by a stagnant layer and finally by convection. The net result is enhanced rate of heat transfer. Thus, the fluid passes back and forth through the several tubes and then leaves the equipment at I.

If the fluid is to be introduced at high velocities, pumping should be effective, which increases the cost of the power, though the cost of heater is low. Too low a velocity saves power for pumping, but needs a very large heater. Therefore, a balanced approach should be worked out based on economy.

Advantages : Multipass construction decreases the cross section of the fluid path, thereby increases the fluid velocity. Thus, multipass tubular heaters are superior to the single-pass shell-and-tube heaters.

Disadvantages : (1) The fabrication of a multipass heater is more complicated. (2) The pressure-drop through the apparatus is increased, because of enhanced velocity of fluid flow. (3) More number of exit and entrance points increase the friction losses. This increases the cost of pumping of fluid.

Floating-head two-pass heater : In floating-head two-pass heater, the ends of the tubes are structurally independent of the shell.

Construction : The construction of a two-pass floating head heater is shown in Figure 5-13. Its construction is the same as tubular heater with some modifications.

Two-pass floating head heater consists of a bundle of parallel tubes. These are enclosed in a shell (casing). The right-side of the distribution chamber is partitioned and fluid inlet and outlet are connected to the same chamber. The partition is such that both have equal number of tubes. On left-side, the distribution chamber is not connected to the casing. It is structurally independent, which is known as *floating head*. The other end of the tubes is embedded into the floating head. Steam or other vapour is introduced through inlet provided to the shell. Provisions are made for the escape of non-condensed vapour and an exit for the condensate.

Working : Steam is introduced through the inlet (Figure 5-13). As the steam flows down the tubes, they get heated. The condensed vapour escape through the bottom of the shell. Non-condensable gases, if any, escape through the vent at the top of the shell.

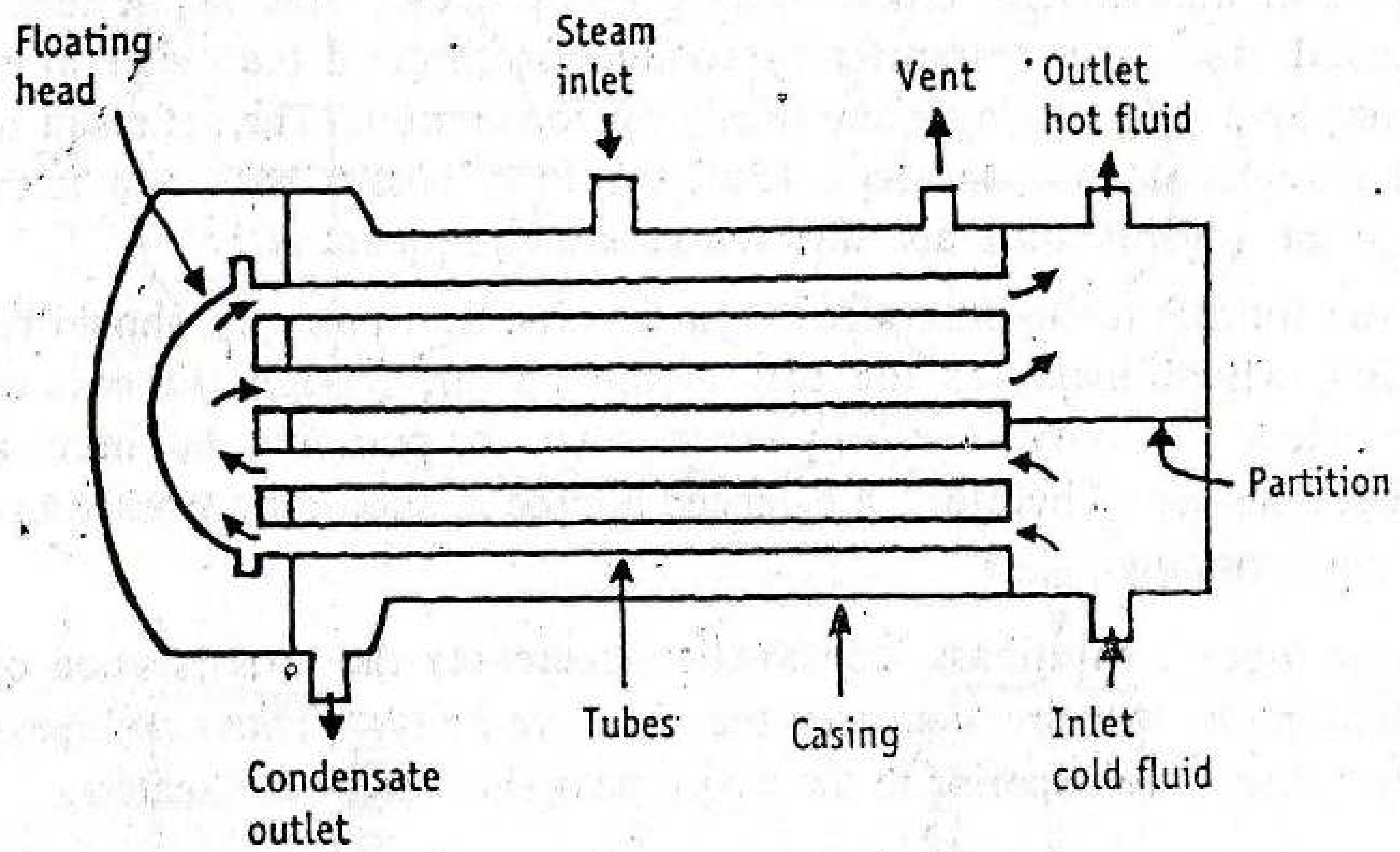


Figure 5-13. Construction of a two-pass floating head heater.

The fluid to be heated is introduced into the distribution chamber on right-side of the heater. The fluid flows through few tubes present in that part of the partition. The fluid reaches the floating head and changes direction. Now it passes back to the next part of the partition chamber on right-side. Therefore, the fluid flows twice through the tubes, i.e., two pass. During this process, fluid in the tubes get heated, due to heat transfer by conduction through the metal wall, followed by a stagnant layer and finally by convection. Then the fluid leaves the outlet provided in the shell.

Advantages : In a shell-and-tube heat exchanger, tubes and shell may get expanded due to differences in temperature. Similarly contractions are also possible when heater is switched off. It leads to loosening of tube sheets or buckles the tubes. Therefore, constructing the tubes independent of the shell can prevent these effects. Such an arrangement is *floating head.*

Heat Interchangers

Heat interchangers are the devices used for transferring heat from one liquid to another or from one gas to another gas through a metal wall.

In heat interchangers, the heating medium is a hot liquid. The liquid to be heated is the cold liquid. In this case, the film coefficients both outside and inside the tubes are nearly of same magnitude. The value of the overall heat transfer coefficient, U, will be near that of the smaller of the two film coefficients. Hence, heat transfer is not efficient.

The film coefficients can be enhanced by increasing the velocity of flow. From the point of construction, it is difficult to increase the velocity of the hot fluid outside the tubes. However, surface area of contact can be increased, by introducing baffles in the construction. The increased surface area of contact enhances the coefficient. Thus the rate of heat transfer is enhanced. These principles are illustrated using different heat interchangers.

Baffles : Baffles consist of circular discs of sheet metal with one side cut away. These are perforated to receive tubes. To minimize leakage, the clearance between the baffles, shell and tubes should be small. The baffles are supported by one or more guide rods, which are fastened between the tube sheets by set-screws.

Working : Baffles are placed outside the tubes. These increase the velocity of liquid outside the tubes. Baffles make the liquid flow more or less right angles to the tubes, which creates more turbulence. This helps in reducing the resistance to heat transfer outside the tubes. Therefore, baffles constitute an important part in the heat transfer.

The construction of a liquid-to-liquid heat interchanger illustrates the principle of introducing the baffles into the equipment.

Liquid–to–liquid interchanger : The basic construction and working of any heat transfer equipment more or less remains the same. Only a few modifications are included.

Construction : The construction of a liquid-to-liquid heat interchanger is shown in Figure 5-14. Normally, tube sheets, spacer rods and baffles are assembled first and then tubes are installed. The most important parts in the construction of the heat interchanger are the baffles.

Appropriate size of tube sheets is chosen for the fabrication. One or more guide rods are fixed to the tube sheets by means of set-screws. Baffles consist of circular discs of a metal sheet, with one side cut away. Baffles are placed at appropriate places using guide rods. The baffles are arranged with appropriate spacing using short sections of the same tubing as shown in Figure 5-14. Baffles have perforations through which tubes are inserted. The ends of tubes are expanded into the tube sheets. The above assembly is enclosed in a shell.

The shell has a provision for introducing the heating medium, hot fluid. The outlet for the fluid is at right-side top.

On each side of the tubes, two distribution chambers are provided. Left-side chamber contains an inlet for fluid to be heated. The outlet for the hot fluid (that is heated) is provided at the centre of the right-side distribution chamber.

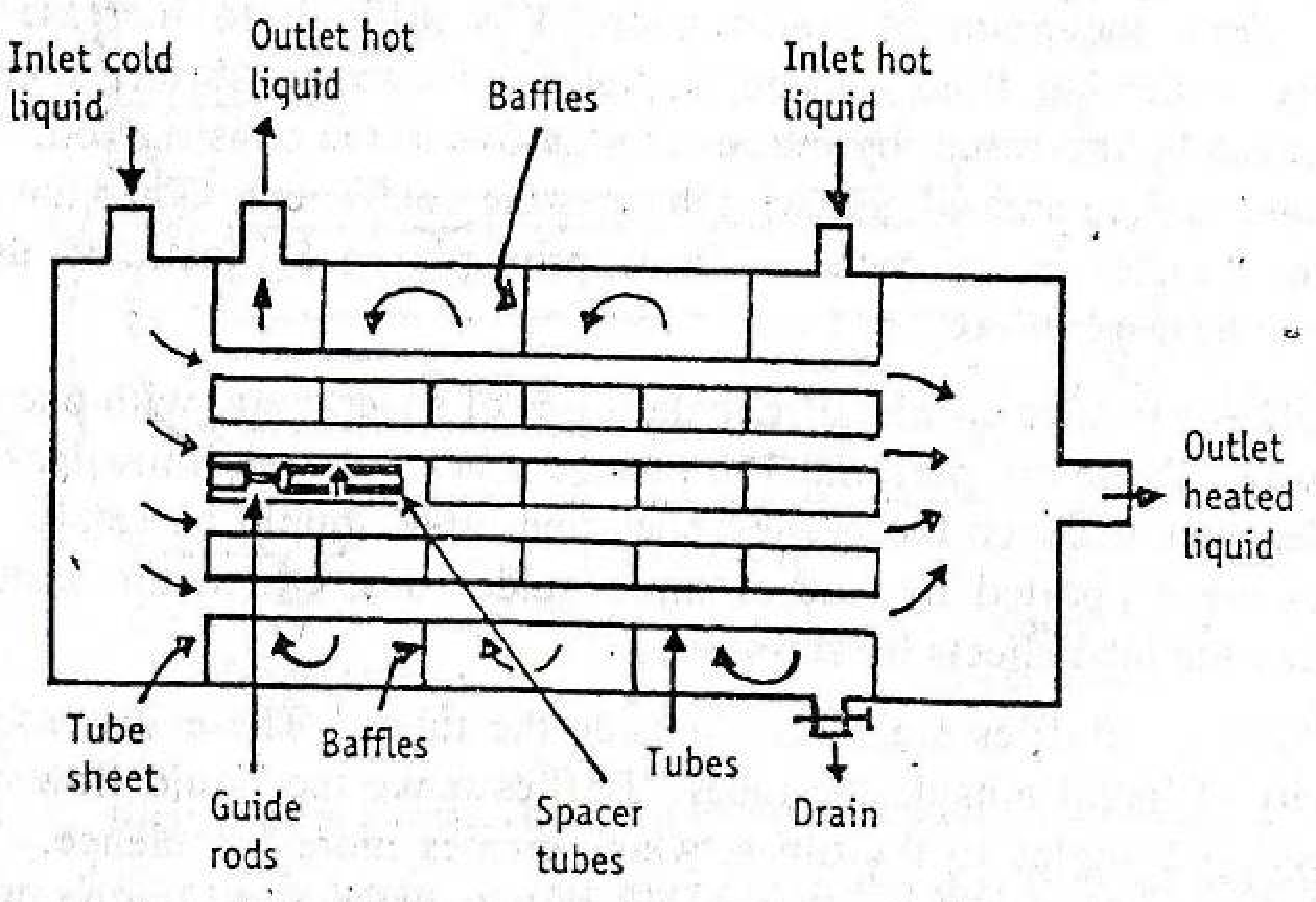


Figure 5-14. Construction of liquid-to-liquid heat interchanger.

Working : The hot fluid (heating medium) is pumped from the left-side top of the shell. The fluid flows outside the tubes and moves down directly to the bottom. Then, it changes the direction and rises again. This process is continued till it leaves the heater. Baffles increase the velocity of the liquid outside the tubes. Baffles also allow the fluid to flow more or less right angles to the tube, which creates more turbulence. These help in reducing the resistance to heat transfer outside the tubes. Baffles lengthen the path and decrease the cross-section of path of the cold fluid. The path of travel is as shown in Figure 5-14. The baffles get heated and provide greater surface area for heat transfer. Simultaneously, during the flow, the tubes also get heated. As a result, the film coefficient inside the tube also increases.

The liquid to be heated is pumped through the inlet provided on left-side distribution chamber. The liquid passes through the tubes and gets heated. The flow of liquid is single-pass. The heated liquid is collected from the right-hand side distribution chamber.

Advantages : In a liquid-to-liquid interchanger, heat transfer is rapid as the liquid

(1) passes at high velocity outside the tubes.

(2) flows more or less at right angles to the tubes.

Double-pipe heat interchanger : In a liquid-to-liquid heat interchanger, the fluid to be heated is passed only once through the tubes before it gets discharged, i.e. single pass. The heat transfer in this case is not efficient. When few tubes per pass is desirable, double pipe heat interchanger is employed.

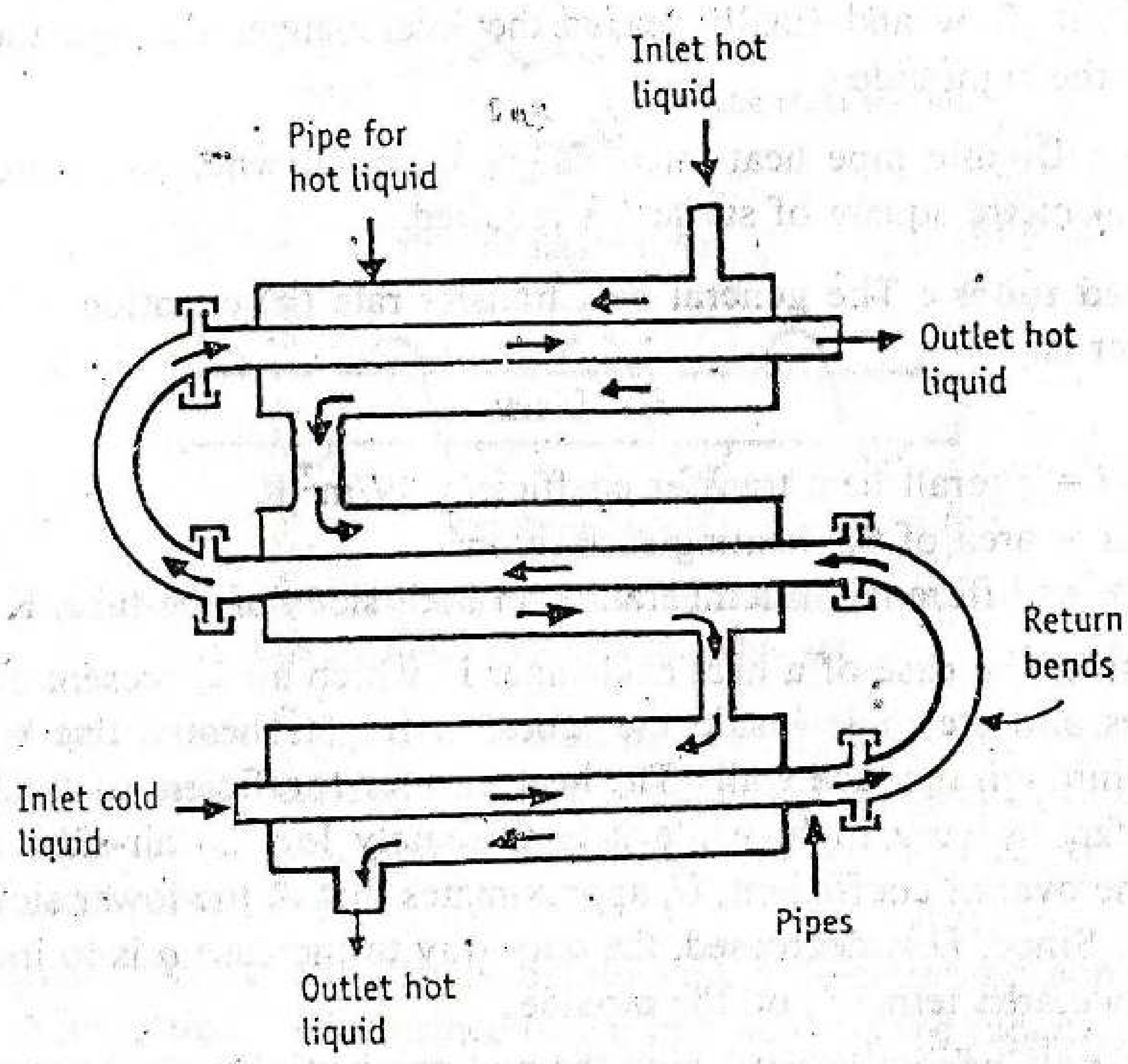


Figure 5-15. Construction of double-pipe heat interchanger.

Construction : The construction of a double-pipe heat interchanger is shown in Figure 5-15. In this, two pipes are used: one is inserted in the other. The inside pipe (or tube) is used for the pumping of cold liquid to be heated. The outer pipe acts as a jacket for the circulation of the hot liquid. All jacketed sections are inter-connected.

Normally, the number of pipe sections is few. The length of the pipe is also less. Glass tube, standard iron pipe and graphite constructions are available. Standard metal pipes are assembled with standard return bends. A proper number of such pipes are connected in parallel and stacked vertically. The pipes may have longitudinal fins on its outer surface.

Working : The hot liquid (heating medium) is pumped into the jacketed section. The hot fluid is circulated through the annular spaces between them and carried from one section to the next section. Finally it leaves the jacket. In this process the pipes get heated, while the hot fluid looses its temperature.

The liquid to be heated is pumped through the inlet provided at right side. The liquid gets heated up and flows through the bent tubes into the next section of the pipe. The liquid further gets heated. The same liquid continues to flow and finally leaves the interchanger through the exit point on the right side.

Uses : Double pipe heat interchanger is useful when not more than 0.9 to 1.4 metre square of surface is required.

Finned tubes : The general heat transfer rate (q) equation in a heat exchanger is:

$$q = UA\Delta t$$

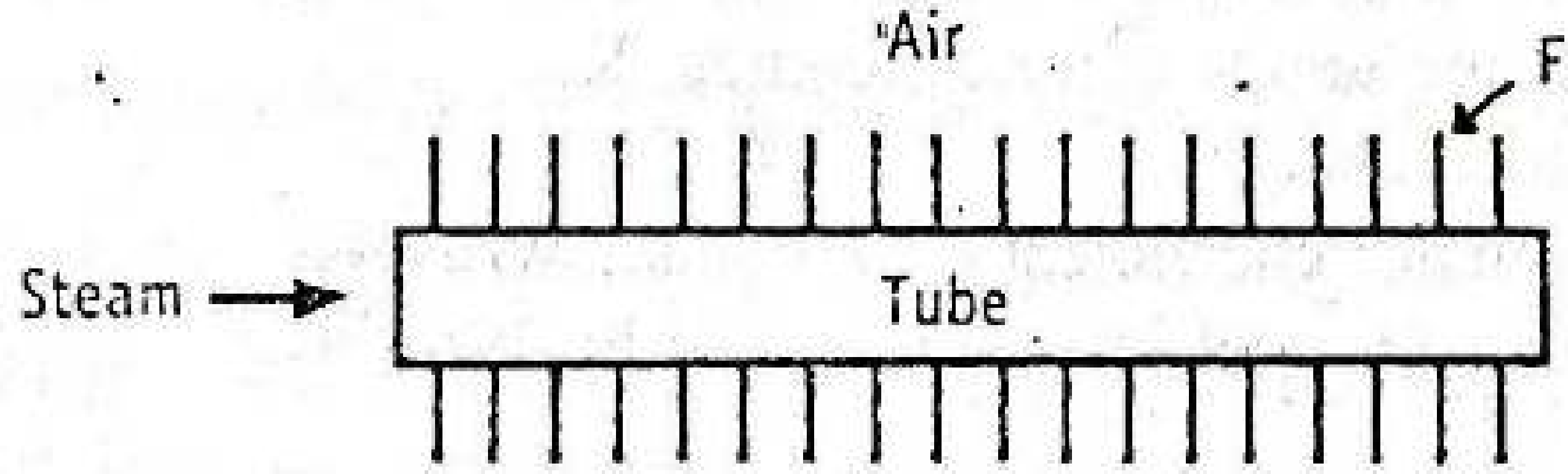
where U = overall heat transfer coefficient, W/m^2.K
A = area of the heating surface, m^2
Δt = difference in temperature on both sides of the tube, K

Consider the case of a heat exchanger in which air is present outside the tubes and steam is inside the tubes. Air gets heated due to heat transfer through the tube wall. The heat transfer coefficient on the steam side surface is very high, while it is extremely low on air-side. As a result, the overall coefficient, U, approximates that of the lower side, i.e., air-side. Since, U is decreased, the only way to increase q is to increase the surface area term, A, on the air-side.

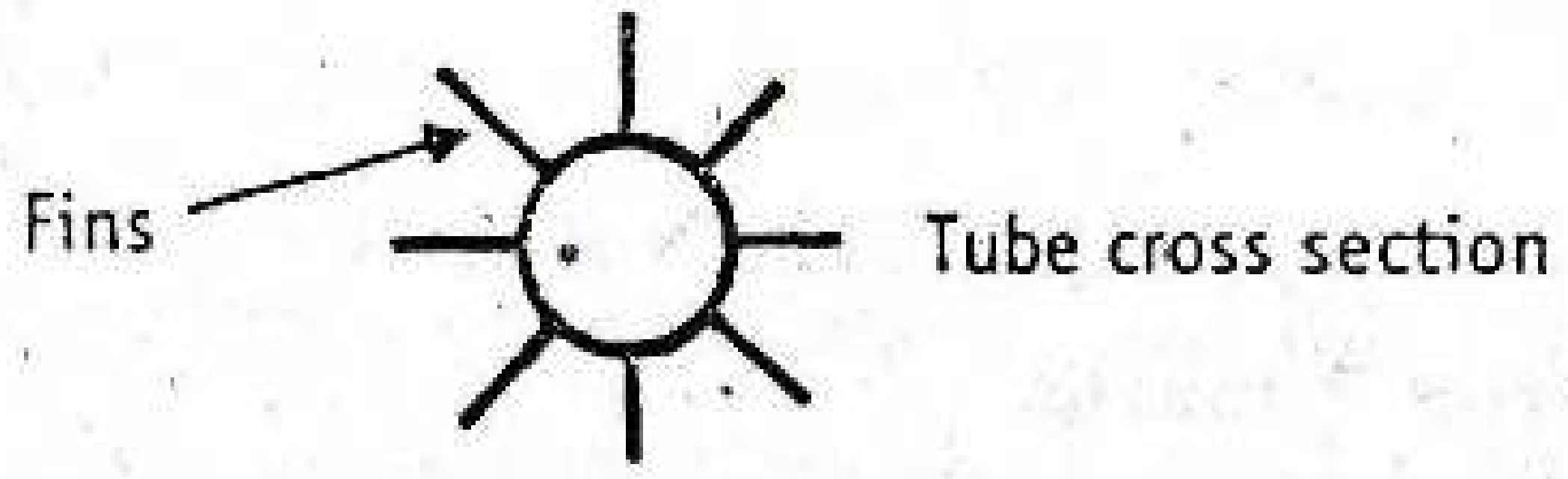
As metals generally have high thermal conductivity, the temperature of the metal surface approximates to that of steam. Surface area of contact is enhanced by fixing fins on outside of the tubes, without putting more number of tubes in the heater.

Construction : A variety of fins are used as shown in Figure 5-16. Fins may be placed on the inner wall as well as on the outside of the tubes. Rectangular discs of a metal may be placed at right angles to the tubes (Figure 5-16a). Longitudinal fins are also employed (Figure 5-16b). Spiral fins may be attached to the tubes (Figure 5-16c).

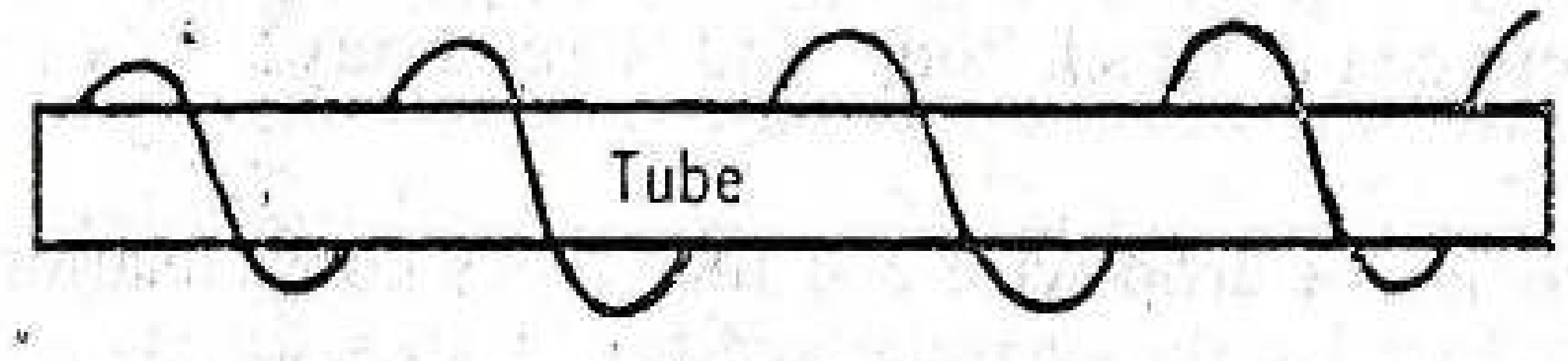
Uses : Fins greatly reduce the size of the apparatus. They also increase the surface area of contact. This in turn enhances the rate of heat transfer in a heat exchanger. In double-pipe heat interchanger, fins are employed.



(a) Rectangular fins



(b) Longitudinal fins



(c) Spiral fins

Figure 5-16. Variations in the arrangements of fins on tubes in a heat interchanger.

Heat insulation : The distribution of steam through the pipe can be reduced using heat insulators. The pipes should be lagged, i.e., covered with a layer of porous, poor conducting material such as kieselguhr, asbestos and glass wool.

Alternatively, several layers of aluminium foil can be applied for effective insulation. The surface of the foil prevents the radiation losses and air trapped between the layers minimizes convection losses.

Glossary of Symbols

A = Area of the heating surface, m^2.
A_m = Mean area of a cylinder, m^2.
b = Stefan Boltzmann's constant, W/$m^2 \cdot K^4$.
h_1 = Surface coefficient on the hot side, W/$m^2 \cdot$K.
h_2 = Surface coefficient on the cold side, W/$m^2 \cdot$K.
k_m = Mean proportionality constant, W/m·K.
L = Thickness of the heating surface, m.
N = Length of the hollow cylinder, m.
q = Rate of heat transfer, W (J/s).

r = Radius of the thin cylinder for heat transfer, m.
r_m = Logarithmic mean radius, m.
T = Absolute temperature, K.
t_1 = Temperature at the hot surface, K.
t_2 = Temperature at the cold surface, K.
Δt_m = Arithmetic average temperature difference, K.
Δt = Temperature difference, K.
U_1 = Overall heat transfer coefficient on hot side, $W/m^2 \cdot K$.
U_2 = Overall heat transfer coefficient on cold side, $W/m^2 \cdot K$.
α = Absorptivity
ρ = Reflectivity
τ = Transmissivity
ε = Emissivity

QUESTION BANK

Each question carries 2 marks

1. Describe the types of condensation for saturated vapour free from non-condensible gases.
2. Differentiate between a 'Black body' and 'Grey body'. Give characteristics of a black body.
3. Give characteristics of drop-wise and film types condensation.
4. Drop-wise or film type condensation gives superior value of overall heat transfer coefficient and why?
5. List the characteristics of heat transfer by radiation.
6. What are 'Grey bodies'? How do they radiate heat?
7. Give the final equation for heat transfer by conduction through resistances in series and explain the terms.
8. What are 'overall heat transfer coefficient' and 'individual film coefficient'?
9. Explain the terms 'Black body' and 'Grey body'.
10. Differentiate between film coefficient and overall heat transfer coefficient.
11. State the relationship between individual film coefficients and overall heat transfer coefficient.
12. Define conductivity with a suitable example
13. State and explain Stefen Boltzmann's law of heat radiation.
14. State and explain Fourier's law of heat transmission with equation.
15. Explain 'nucleate boiling' and 'film boiling'.
16. Define radiation. Explain Stefan Boltzmann's law.
17. Write the final equation for heat transfer by conduction through resistances in parallel and explain the terms.

18. Differentiate log mean radius and arithmetic mean radius in conduction of heat. What are its applications?
19. What is meant by overall heat transfer coefficient? What is its significance?
20. Differentiate between a heat interchanger and heat exchanger.

Each question carries 5 marks

1. Compare and contrast heat transmission following counter-current and parallel-current feed techniques with relevant equations.
2. Derive an equation for heat transfer by conduction through compound resistances in series.
3. Draw a neat and labelled diagram of a shell-and-tube heat exchanger and explain its construction.
4. Describe finned tube heat exchanger and its specific advantages.
5. Describe the conduction of heat through a circular pipe. Give suitable equations for rate of heat transfer and explain terms.
6. Describe the conduction of heat through compound resistances in series.
7. Derive an expression for the logarithmic mean temperature difference.
8. Describe liquid heat interchangers. What are its advantages?
9. Explain the working of a heat exchanger with a labelled diagram.

Each question carries 10 marks

1. With the help of a neat diagram, explain the concept of film and overall heat transfer coefficients in forced convection. Deduce relevant mathematical equations.
2. Derive an equation for heat transmission through a circular pipe from Fourier's law.
3. Describe the construction, operation, advantages and disadvantages of a multipass heater.

6

Size Reduction

Size reduction is a process of reducing large solid unit masses (vegetable or chemical substances) into small unit masses, coarse particles or fine particles.

Normally, pharmaceutical powders are *polydisperse*, i.e., consisting particles of different sizes. Polydisperse powders create considerable difficulties in the production of dosage forms. Particles of monosize (equal size) may be ideal for pharmaceutical purposes. In practice, powders with narrow range of size distribution can obviate the problems in processing them further. Size reduction alone is not sufficient to obtain mono-size or narrow size range powder. Therefore, size reduction and size separation should be combined to obtain powders of desired size. (The fundamental aspects on powder, their characteristics and methods of evaluation are given in the book, "*Textbook of Physical Pharmaceutics*" by C.V.S. Subrahmanyam, Vallabh Prakashan, Delhi).

Size reduction process is also termed as *comminution* or *diminution* or *pulverisation*. Normally, size reduction may be achieved by two methods, namely precipitation or mechanical process.

In the *precipitation method*, the substance is dissolved in an appropriate solvent. Subsequently, it is finely precipitated by the addition of another solvent, which is miscible with the first, but in the later the substance is insoluble. This method is suitable for the production of raw materials and bulk drugs. Inorganic chemicals, such as calcium carbonate, magnesium carbonate and yellow mercuric oxide, are prepared by precipitation method.

In the *mechanical process*, the substance is subjected to mechanical forces using grinding equipment (ball mill, roller mill, colloid mill etc.). In general, dry grinding or milling is used in the production of tablets and capsules, while wet grinding is used in the preparation of suspensions, emulsions and ointments. The method of milling is applied either in the production of raw materials or as a part of the production cycle in the manufacture of dosage forms.

Size reduction of substances offers several **advantages**. These are as follows.

Content uniformity : Mixing of different ingredients can be effective, if the particle size is uniform and small. Size reduction ensures this objective. Particles of optimum size are desirable for effective mixing.

As the size of particles is small, the number of particles per unit weight (dose) is large. The larger the number of particles, the better is the mixing. Thus, better content uniformity can be obtained for a given dose. This is particularly important in formulations containing potent and low dose drugs.

Uniform flow : Smaller particle size and controlled size distribution promote the flow of the powder into dies during compression of tablets. The same principles are used in the production of capsules.

Effective extraction of drugs : Smaller particles allow rapid penetration of menstruum or solvent into the tissue or cells of vegetable and animal origin (liver and pancreas). As a result, extraction or leaching of active constituents becomes effective and complete in preparation of galenicals. The time required for extraction can be shortened. For example, pancreas is subjected to grinding action for the extraction of insulin.

Normally, fine powders are preferred for compound powders, while moderately coarse powders are used for the preparation of tinctures. Coarse powder without fines is employed in percolation process.

Effective drying : Drying of a granular mass can be rapid and effective, if the size of granules is small and uniform. Such techniques are used in the production of tablets. Similarly drying of medicinal plant parts can be quick and fast after size reduction.

Improved physical stability : In case of suspensions and emulsions, the rate of sedimentation decreases to a large extent if particle size is small.

Improved dissolution rate : Size reduction increases surface area, which facilitates intimate contact of solid particles and gastric or intestinal juices. Thus, the rate of dissolution enhances. For example, size reduction of griseofulvin led to the development of oral dosage regimen with a dose half that of the originally marketed product. In case of insufflations (preparations inhaled directly into the lungs), the drug should be usually smaller than about 5 µm. Micronized powder of aspirin is used in the preparation of tablets, microfined aspro (analgesic and anti-inflammatory agent).

Improved rate of absorption : The smaller the particle size, the faster is the absorption, because of enhanced dissolution. Chloramphenicol has been shown to absorb faster when given with particle size of 50 µm compared to particle size of 400 µm. Keeping in view of the advantages, pharmacopoeia specifies particle size as a quality control tool. For example, griseofulvin (antifungal antibiotic) should have surface area of not less than 1300 to 1700 metre square per kilogram (as per IP). If it is less, the absorption of the drug decreases. Sulphonamides attain their antibacterial activity at powder sizes of about 1 µm or below. Increased antiseptic action has been demonstrated when the particle size of calomel has been reduced.

The **disadvantages** of size reduction process are as follows.

(1) *Drug degradation* : Drug decomposition is possible due to the heat produced during milling. Thermo-labile substances are the most affected. The increased surface area also facilitates drug decomposition owing to enhanced dissolution.

Cooling support systems are provided to decrease the heat in milling equipment. Drugs containing waxy materials become soft due to heat generated during milling. Therefore the feed is chilled before milling.

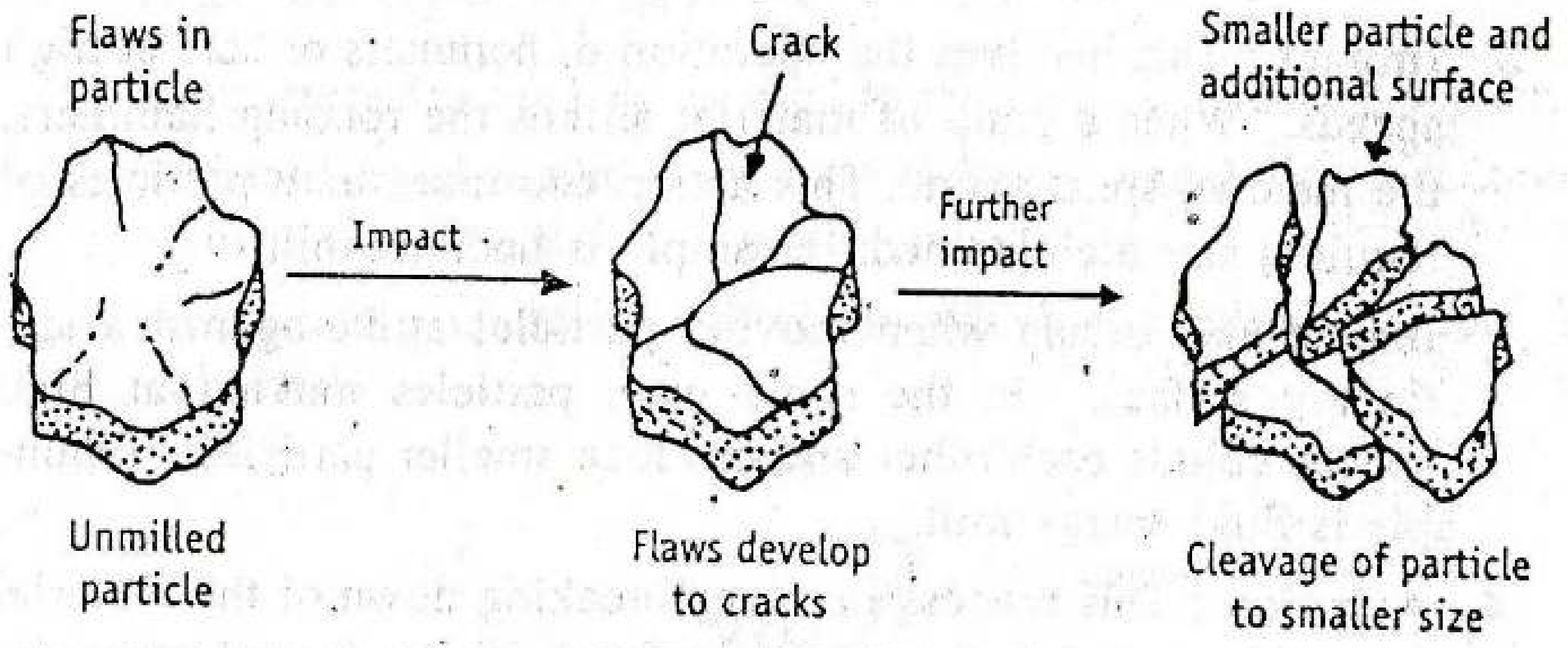
(2) *Poor mixing* : Normally, very small particles possess strong cohesive forces, hence, aggregation of particles is possible. Aggregation inhibits the effective blending of different additives. An increase in surface area may promote the adsorption of air, which may inhibit wettability of the drug during production. Therefore, optimum particle size is desirable to improve blending and to avoid poor mixing.

(3) *Contamination* : During milling and grinding, the grinding surfaces wear off (examples are ceramic or iron equipment), the particles of which are present as impurities in the powder. Such type of mills should be avoided, when drugs of high purity are required.

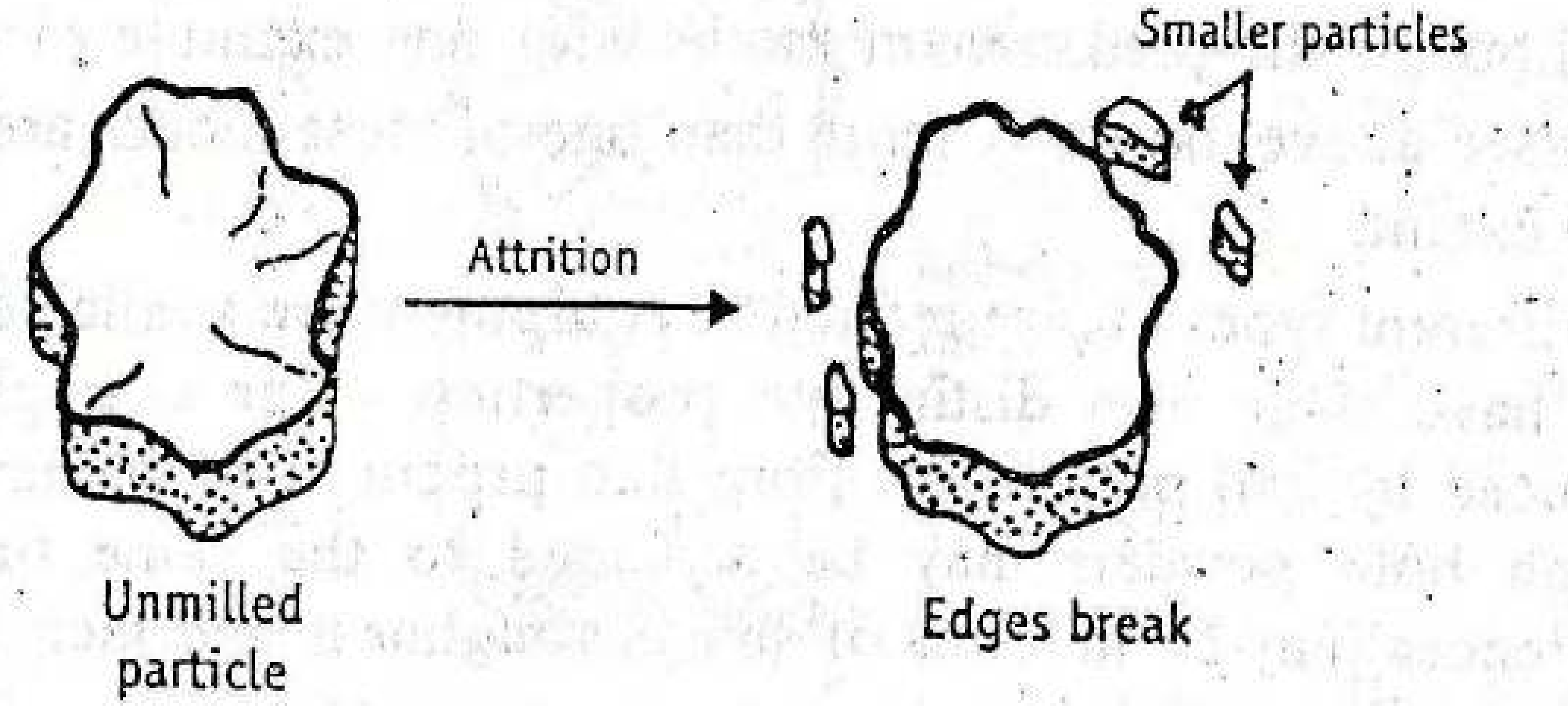
The importance of size reduction is so profound that it is used in the production of all dosage forms such as tablets, capsules, suspensions, emulsions, injections and galenicals. The principles of size reduction, construction and working of equipment are discussed in this chapter. The equipment, which are used in pharmaceutical industry, are given importance.

MECHANISMS OF SIZE REDUCTION

The mechanism of size reduction may vary with the nature of material. Therefore, each drug may require a separate treatment. However, the general mechanism may be described as follows.



(a) Mechanism of size reduction when impact type of stress is applied.



(b) Mechanism of size reduction when attrition type of stress is applied.

Figure 6-1. Mechanisms of size reduction.

Particles, be it amorphous or crystalline, will have flaws to a definite degree. These constitute weak parts in the particles. When sufficient stresses such as impact, shear and compression are applied, the weak flaws develop into cracks, which eventually lead to cleavage (Figure 6-1a). Thus, smaller particles are obtained with additional surface area.

When stress in the form of attrition is applied, the particle surfaces chip and produce small particles (Figure 6-1b).

MODES OF STRESS APPLIED IN SIZE REDUCTION

The mechanisms have demonstrated that stresses of varied nature are required to achieve size reduction. The common modes of size reduction are explained as follows.

1. **Cutting :** The material is cut by means of a sharp blade(s). Example is cutter mill.
2. **Compression :** In this mode, the material is crushed between rollers by the application of pressure. Example is roller mill.
3. **Impact :** This involves the operation of hammers or bars at high speeds. When a lump of material strikes the rotating hammers, the material splits apart. This action continues until particles of required size are obtained. Example is hammer mill.

   Impact also occurs when moving particles strike against a stationary surface. In the same way, particles moving at high speeds collide each other and produce smaller particles. Example is fluid energy mill.
4. **Attrition :** This process involves breaking down of the material by rubbing action between two surfaces, i.e., surface phenomena. Example is fluid energy mill.

Although the predominant mode with one example of equipment is discussed above, normally more than one of these modes are exhibited to some extent.

Different types of size reduction equipment are available, since materials have their own distinctive properties. For example, a powder produced by ball mill differs from that produced by hammer mill, even though both powders may be screened to the same fineness. The differences may be in terms of shape, roughness and their internal pore-structure of a particle.

CLASSIFICATION OF SIZE REDUCTION EQUIPMENT

A. Crushers, examples are edge runner mill, end runner mill.

B. Grinders: (1) Impact mill, example is hammer mill.
   (2) Rolling-compression, example is roller mill.

   (3) Attrition mills, example is attrition mill.
   (4) Tumbling mills, example is ball mill.

C. Ultrafine grinder, example is fluid energy mill.

D. Cutting machine, example is cutter mill.

Some of them are discussed individually in the following sections.

SIZE REDUCTION—EQUIPMENT

The equipment described in this chapter are used in small-scale plants. The basic principles and working remain same even in large-scale operations. Other variants are also included in brief.

General Parts of Size Reduction Equipment

The milling or grinding equipment consists of three basic components. These are shown in Figure 6-2.

(1) A structure for feeding material to the mill. It is called *hopper*.

(2) The milling chamber is the one in which actual size reduction takes place. It consists of a rotor and a stator.

(3) A discharge chute or receiver in which the milled product is collected.

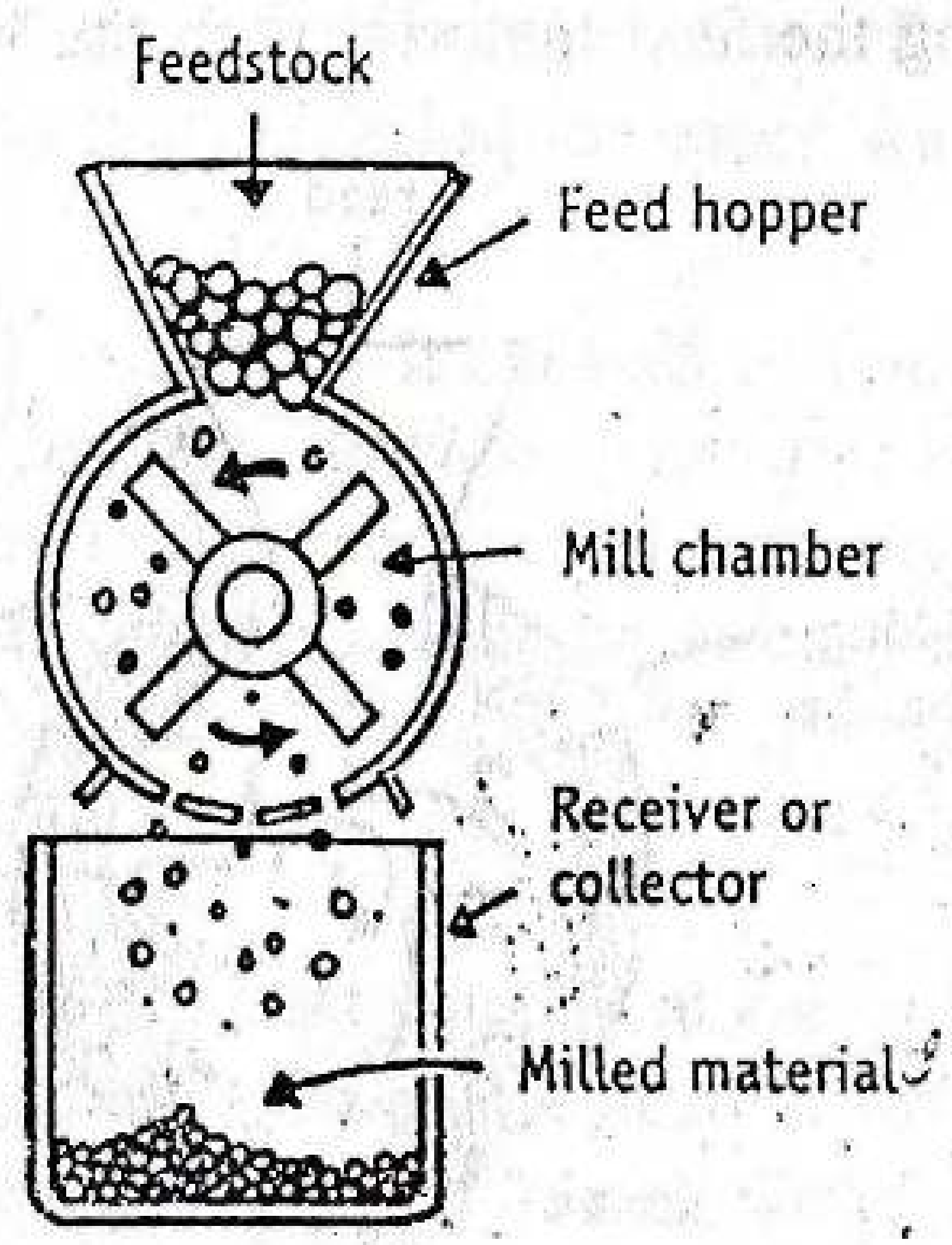


Figure 6-2. General parts of size reduction equipment. Three basic components.

Other Accessories

(1) Sieves or screens are enclosed in the milling chamber to classify the particles by size.

(2) Cyclone separator or centrifugation equipment is fitted to the mills for separation of particles by their sizes.

(3) Dust collectors are employed in order to collect the fine powder and dust that may arise during milling process.

Special Features

(1) Cooling devices are fitted to the chamber to reduce the heat produced during milling.

(2) A closed environment is desirable for milling hygroscopic substances. For this purpose, dehumidified air is necessary.

(3) Closed system with inert atmosphere (nitrogen or carbon dioxide) is desirable for milling of drugs, which are oxidisable or combustible. Similarly, material to be used in the production of parenterals should be milled under sterile environment.

Though general parts of the equipment are identical, several modifications have been incorporated in order to make the process easy to handle and to provide desired discharge.

ROTARY CUTTER MILL

Principle : In the cutter mill, size reduction involves successive cutting or shearing the feed material with the help of sharp knives.

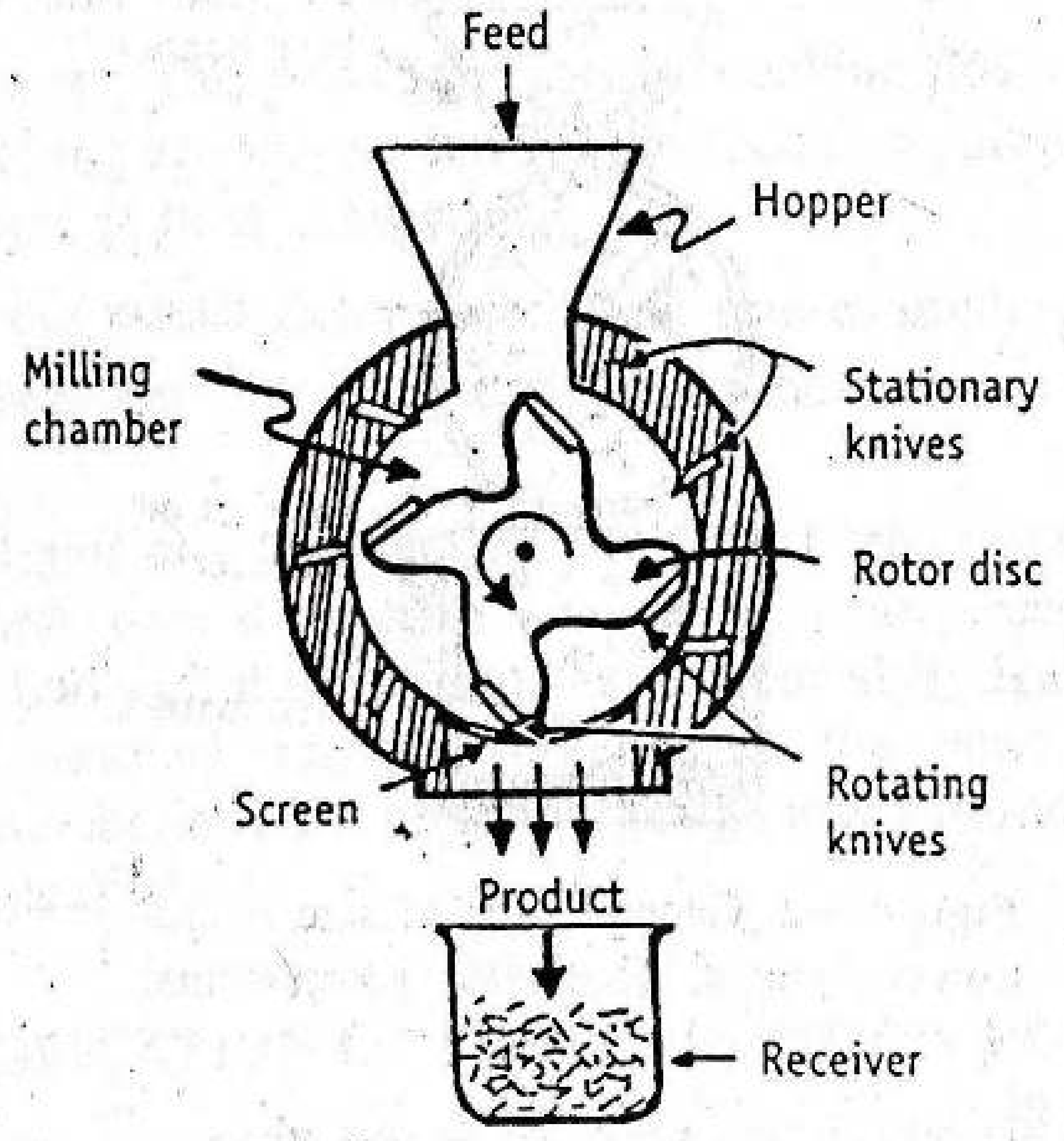


Figure 6-3. The construction of cutter mill.

Construction : The construction of a cutter mill is shown in Figure 6-3. The milling chamber consists of two types of knives, namely rotating knives and stationary knives. A horizontally mounted rotor disc consists of 2 to 12 knives spaced uniformly. The casing also has several stationary knives. The hopper is placed above it. The bottom of casing holds a screen that controls the size of the material. Discharge chute is attached at the bottom of the mill.

Working : The rotor disc is allowed to rotate at speeds from 200 to 900 revolutions per minute. The feed material is loaded into the hopper, which flows down by the force of gravity. During the rotation of disc, the material comes very close between the stationary and rotating knives, thereby the material is cut into small pieces. Smaller particles pass through the screen. The knives lift the coarser particles up while rotating and promote further size reduction. The product is collected into a receiver.

The particle size and shape are determined by the rotor size, gap between the rotating and stationary knives and opening of the sieve.

Uses : Cutter mills are used for the size reduction (finer than 80 to 100 mesh) of tough and fibrous materials. Medicinal plants, plant parts and animal tissue are normally converted into small parts. Soft materials such as roots, peels and wood are cut before extraction. It is also used in the manufacture of rubber, plastics, recycling of paper waste and plastic materials.

Variants : *Double-runner disc mill*—It consists of two-vertical discs, each rotating in opposite directions. *Single runner disc mill*—only one disc may rotate and the other is stationary. The disc may be provided with cutting faces, teeth or knives. Clearance between the discs may be adjusted to obtain the desirable particle size.

MORTAR AND PESTLE

This is the classical and the simplest equipment for grinding. In this method, the material is crushed by the application of attrition and pressure. The apothecaries used an array of metal, wooden and ceramic mortars and pestles for the production of pills. In this equipment, both mortar and pestle are rotating, whereas a scraper is static. Heavy pestles provide the force of compression, which is an efficient process for wet grinding. This equipment cannot be provided with a sieve for continuous removal of fines.

ROLLER MILL

Principle : The material is crushed (compressed) by the application of stress, though attrition also influences. Stress is applied by rotating heavy wheels, mullers or rollers.

Construction : The construction of a roller mill is shown in Figure 6-4. Roller mill consists of two cylindrical rollers made of stone or metal, which are mounted horizontally. Rollers can have a diameter ranging from a few millimetres up to a metre. Rollers are capable of rotating on their longitudinal axes. Generally, one of the rollers is driven directly using a motor, while the second one runs freely. The gap between the rollers can be controlled to obtain the desired particle size.

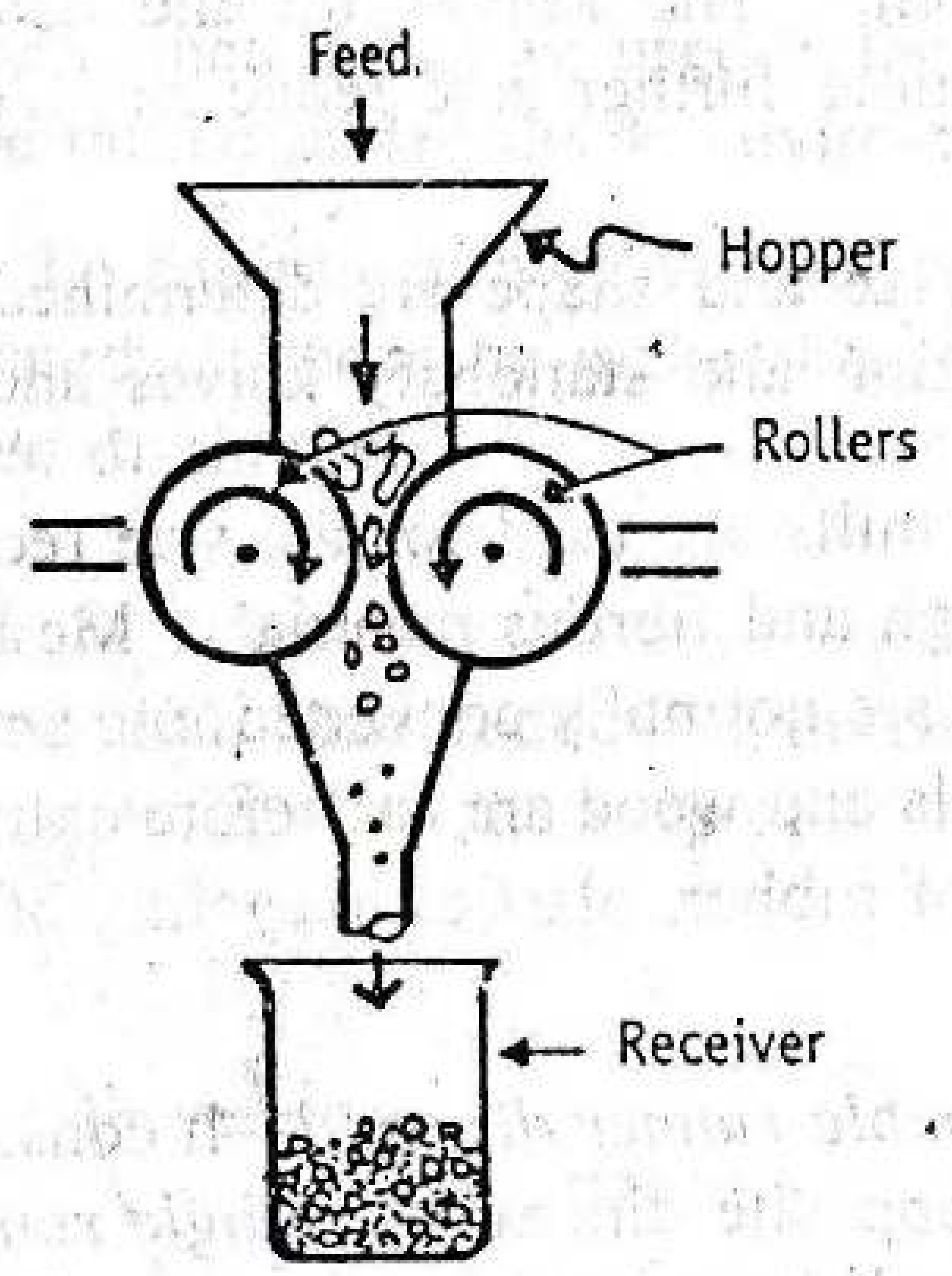


Figure 6-4. The construction of roller mill.

Working : The rollers are allowed to rotate. The material is fed from the hopper into the gap between the two rollers. The material is crushed while passing through the rollers under high pressure. The clearance (gap) between the rollers can be adjusted to control the degree of size reduction. The product is collected into a receiver.

Uses : Roller mill is used for crushing and cracking of seeds before extraction of fixed oils. It is also used to crush soft tissue to help in the penetration of solvent during extraction process.

Variants : Multiple smooth rollers or corrugated, ribbed, or saw-toothed rollers can provide cutting action also.

HAMMER MILL

Principle : The hammer mill operates on the principle of impact between rapidly moving hammers mounted on a rotor and the powder material.

Construction : The construction of a hammer mill is shown in Figure 6-5. The hammer mill can be either the horizontal or the vertical shaft type. Hammers are usually made of hardened steel, stainless steel with impact surface made of an extremely abrasive resistant material such as haystellite and carbaloy. Stainless steel hammers are sufficient for pharmaceutical purposes.

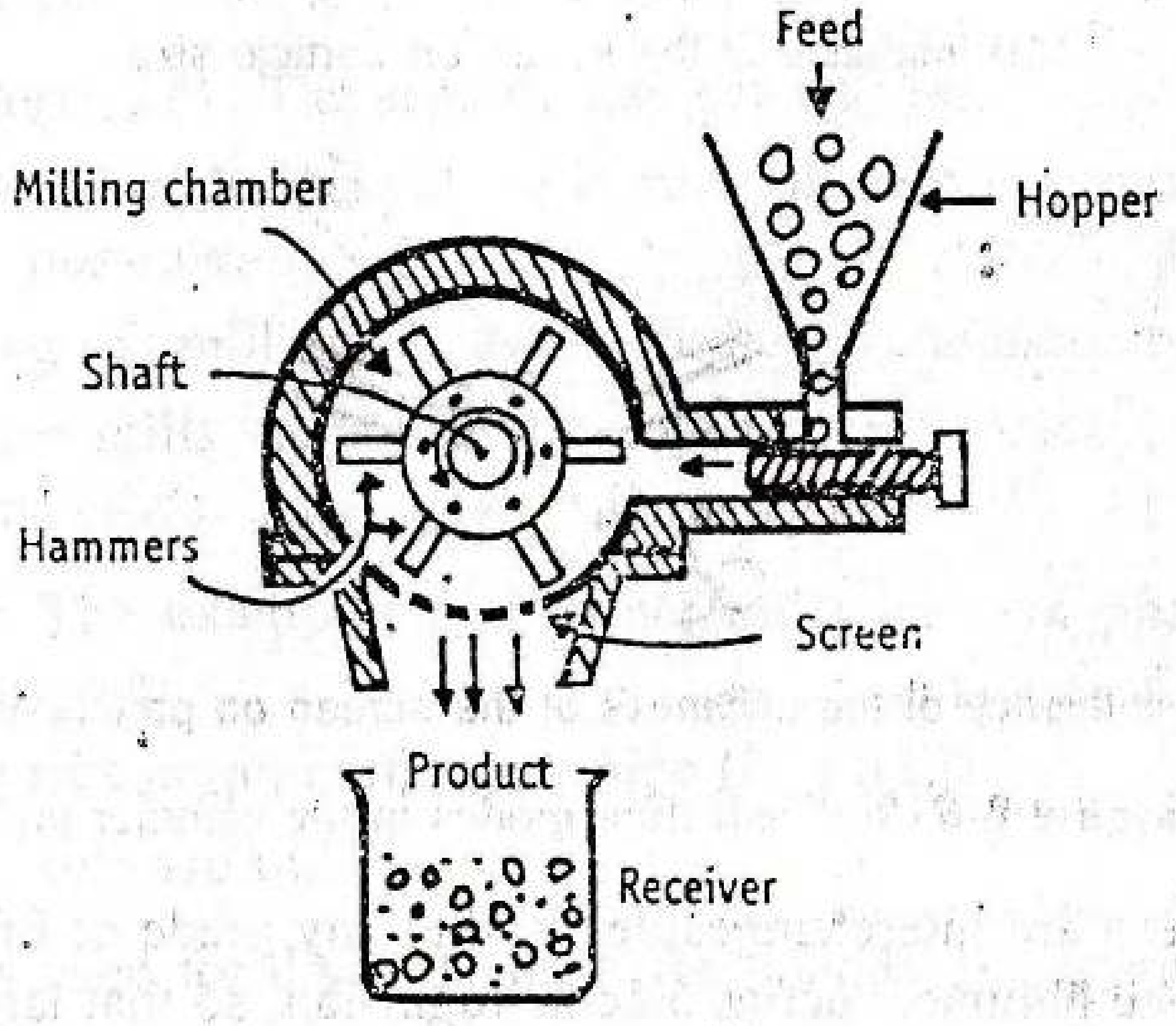
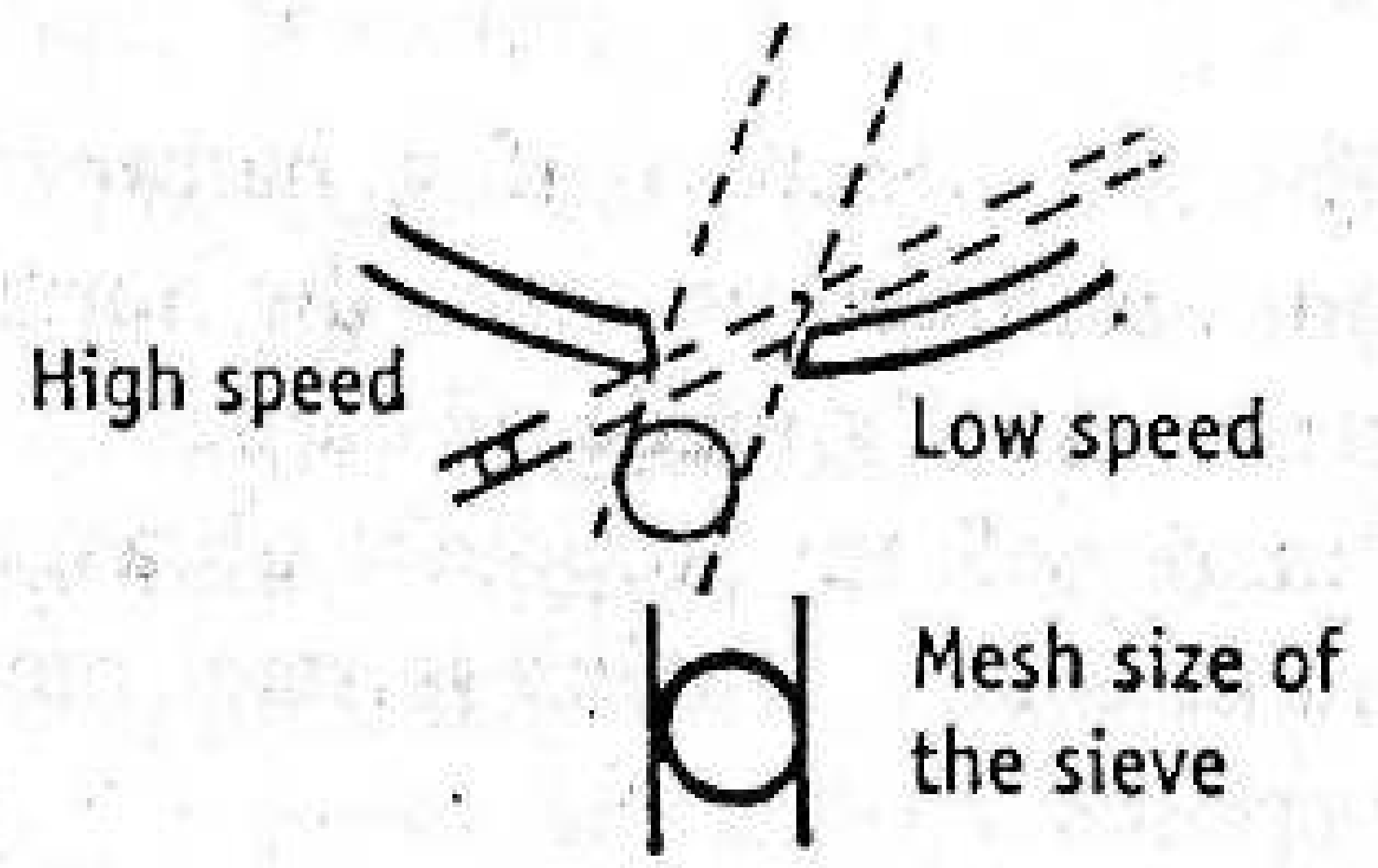


Figure 6-5. The construction of Hammer mill.

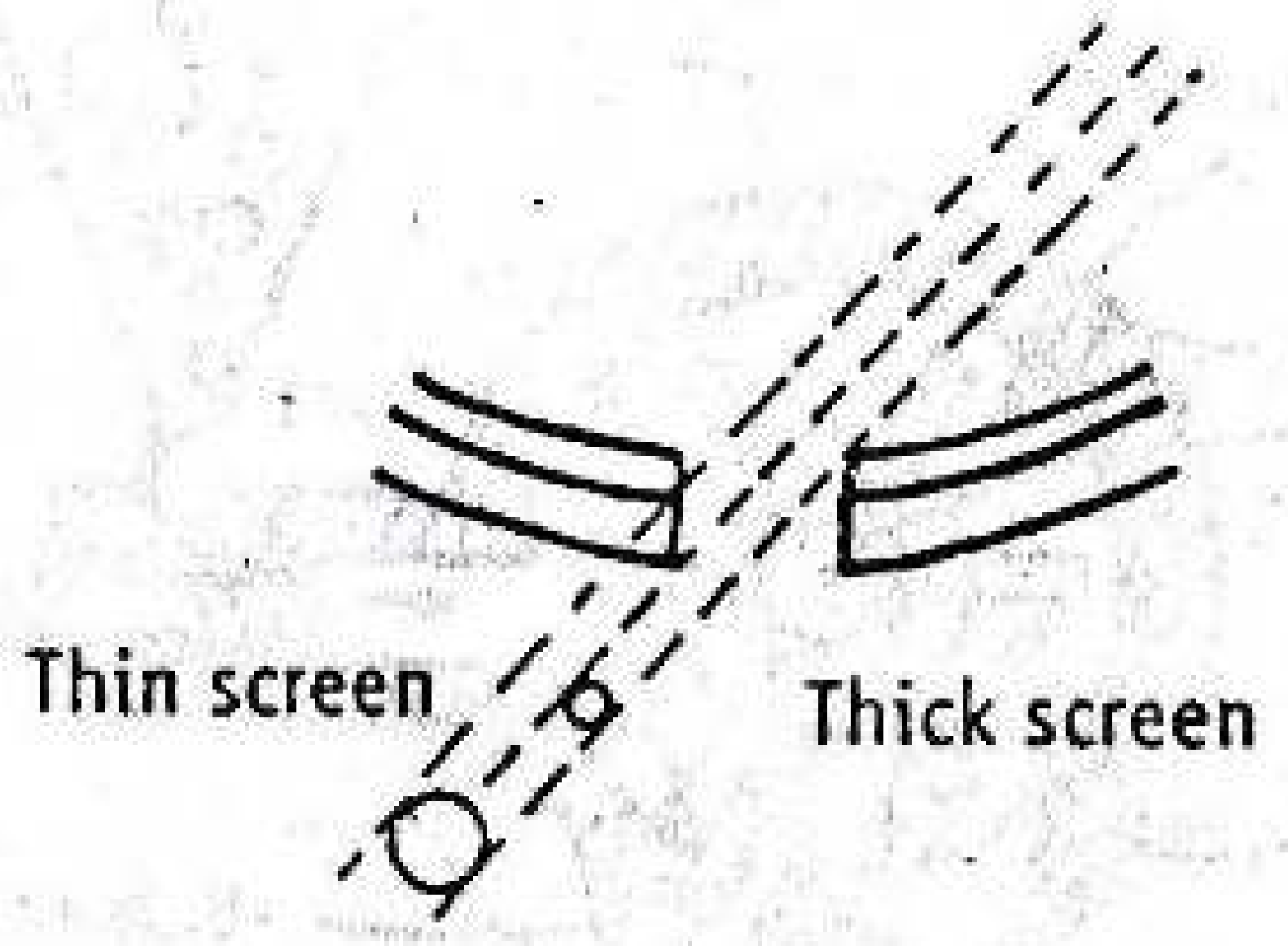
Hammers may take several shapes. Two basic shapes are the stirrup and the bar. Bar-shaped hammers are used extensively in tablet granulation. The hammer blades can be with flat edges or sharp edges or both on each side. Hammers may be either rigid or swing-type. Free swinging type has an advantage that there will be increasing clearance between hammers and screen, if excessive build occurs in the mill.

This unit is enclosed with a chamber containing a grid or removable screen through which the material must pass. These screens are not of woven type. Screens are prepared using metal sheet of varying thickness with perforated holes or slots.

Working : The hammers are allowed to be in continuous motion (8000 to 15000 revolutions per minute). The feed material is placed into the hopper, which flows vertically down and then horizontally, while hammers are in continuous motion. These rotating hammers beat the material to yield smaller particles. Then, these pass through the screen. Due to the tangential exit, the size of the product is considerably smaller than the aperture of the screen as seen in Figure 6-6a.



(a) Influence of the speed on particle size.



(b) Influence of the thickness of the screen on particle size.

Figure 6-6. Size reduction modes in the hammer mill.

The screens are interchangeable, so that any grade of fineness can be achieved. The hammers act as a centrifugal fan, so that large amount of air is drawn through the mill. In most cases, this is sufficient to counteract the heat generated during milling.

The fineness of the product can be regulated by altering:

- rotor speed,
- feed rate,
- clearance between hammers and grinding plates,
- number and type of hammers,
- size of the discharge opening (screen).

Uses : Fine to moderate grinding of powders may be obtained, depending on the speeds of the hammer. The expected particle size may vary from 10 to 400 mm. Non abrasive to moderately abrasive, brittle materials can be used as feed stock.

It is used to mill dry materials, wet filter press cakes, ointments, slurries etc. Brittle material is best fractured by impact from blunt hammers; fibrous material is best reduced in size by cutting edges.

Advantages : (1) Hammer mill is easy to setup (install), dismantle and clean up.

(2) Scale-up problems are minimal provided same type of mill is used.

(3) Various types of feed stock can be handled using screen of different sizes.

(4) Hammer mill occupies small space.

(5) It is versatile, i.e., speed and screen can be changed rapidly.

(6) As it is operated in a closed environment, dust can be reduced and explosion hazards can be prevented.

Disadvantages : (1) The screens may get clogged.

(2) Heat buildup during milling is more, therefore, product degradation is possible.

(3) Wearing of mill and screen is more with abrasive materials.

(4) Hammer mills cannot be employed to mill sticky, fibrous and hard materials.

Variants : The examples of hammer mills used in pharmaceutical industry are:

(a) Fitzpatrick comminuting machine (Fitz mill)

(b) Stokes tornado mill

Fitz mill is used for drugs, roots, herbs, glands, livers, soaps etc.

Micropulveriser : Micropulveriser has been used for sugar, chemicals, pharmaceuticals and cosmetics. The construction is almost same as shown in Figure 6-5. The liner of the mill housing is made of multiple serrations, which promote the breakage of particles thrown against the wall by the rotating hammers. An air injection feeder can be used to project the feed directly in front of the hammer tips, which are fitted with tungsten carbide inserts. This arrangement increases mill efficiency.

Hammer crusher and *vertical impact pulveriser* work on the principle of impact for size reduction.

BALL MILL OR PEBBLE MILL

These are also known as *tumbling mills.*

Principle : The ball mill works on the principle of impact between the rapidly moving balls and the powder material, both enclosed in a hollow cylinder. At low speeds, the balls roll over each other and attrition (rubbing action) will be the predominant mode of action. Thus, in the ball mill, impact or attrition or both are responsible for the size reduction.

Construction : The construction of a ball mill is shown in Figure 6-7. Ball mill consists of a hollow cylinder, which is mounted on a metallic frame in such a way that it can be rotated on its longitudinal axis. The length of the cylinder is slightly greater than its diameter. The cylinder is made of a metal and is usually lined with chrome. In pharmaceutical industry, sometimes the cylinder is lined with rubber or porcelain.

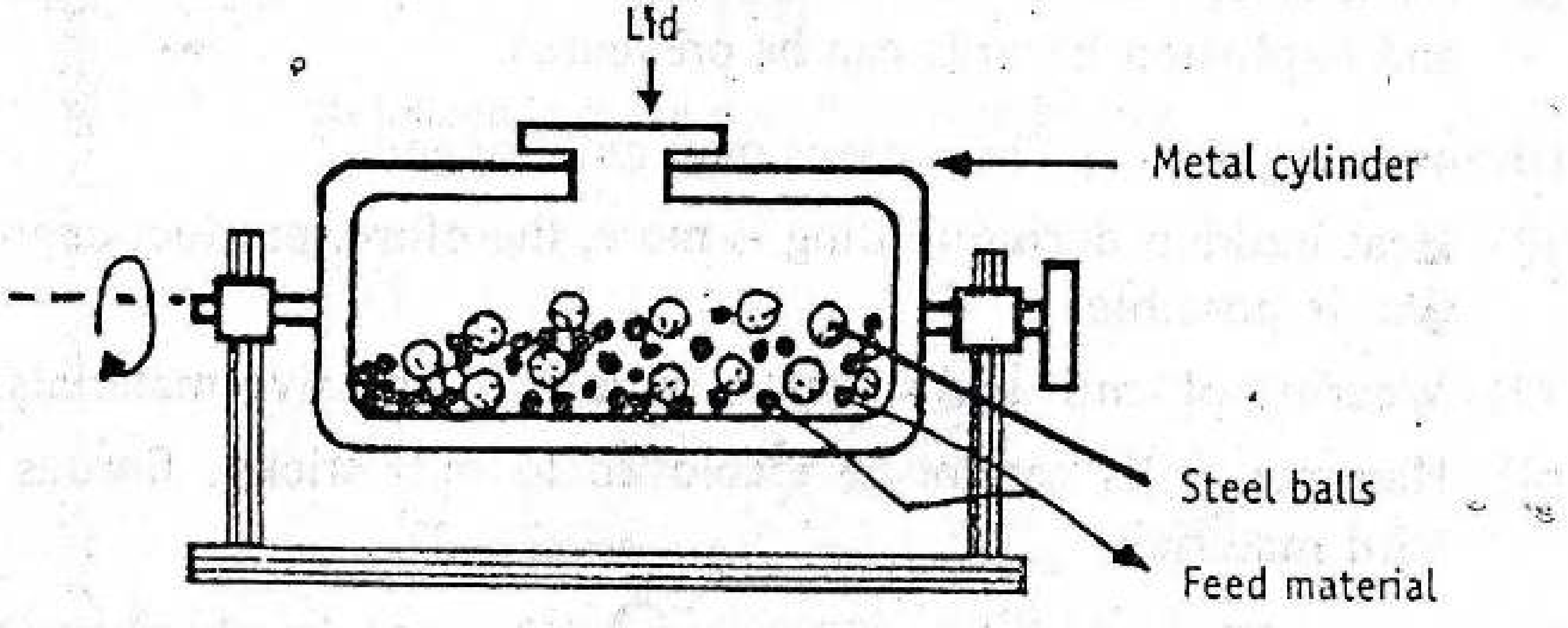


Figure 6-7. The construction of ball mill.

The cylinder contains balls that occupy 30 to 50 % of the mill volume. The weight of the balls is kept constant. The ball size depends on the size of the feed and the diameter of the mill. Balls are made of steel, iron or stoneware. These act as the grinding medium.

Working : The drug to be ground is put into the cylinder of the mill in such a quantity that it is filled to about 60% of the volume (material to void ratio). A fixed number of balls are introduced and the cylinder is closed. The mill is allowed to rotate on its longitudinal axis.

The speed of rotation is very important. At low speeds, the balls roll over each other and attrition will be a predominant mode of stress (Figure 6-8A). The use of small balls (or glass pebbles) is recommended so that the surface is the greatest. This mode of attrition is used for wet grinding. It may be useful to add surface active agents to prevent agglomeration.

At correct speed, the centrifugal force just occurs, as a result the balls are picked up by the mill wall and carried nearly to the top, where they break contact with the wall and fall to the bottom to be picked up (Figure 6-8C). In this manner, impact stress will also be induced and the size reduction is made effective.

At still higher speeds. the balls are thrown out to the wall by centrifugal force. Hence, grinding will not occur. The compression by the balls against the wall will not be sufficient for effective comminution of the substance. (Figure 6-8B)

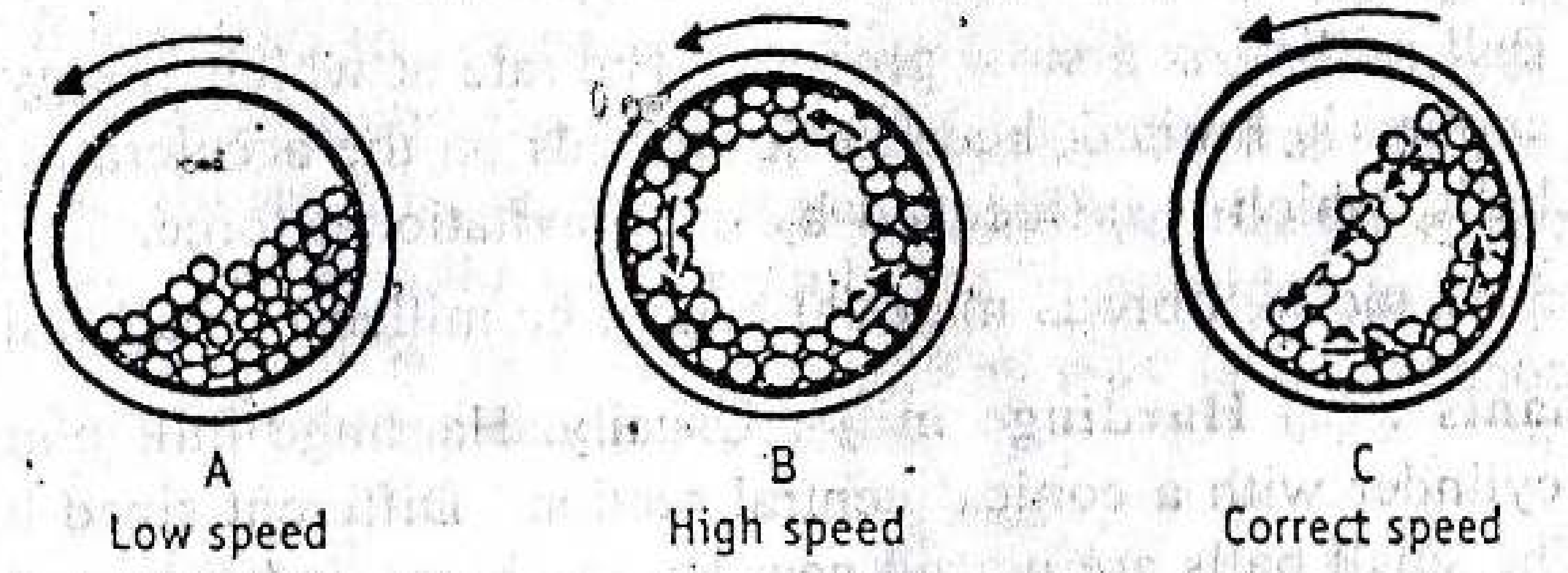


Figure 6-8. The modes of rolling of balls in the ball mill operations.

Uses : Fine grinding with a particle size of 100 to 5 mm or less can be obtained, particularly for hard and abrasive materials. Stainless steel balls are preferred in the production of ophthalmic and parenteral products, as there is a less chance of contamination due to wear. Ball mill at low speeds is used for milling dyes, pigments and insecticides.

Advantages : Ball mill offers several advantages and is widely used. These are:

(1) It can produce very fine powder.

(2) It is used for batch operation. It can be made continuous operation by including a chamber next to the cylinder. These are separated using a sieve.

(3) Ball mill is suitable for both wet and dry grinding processes.

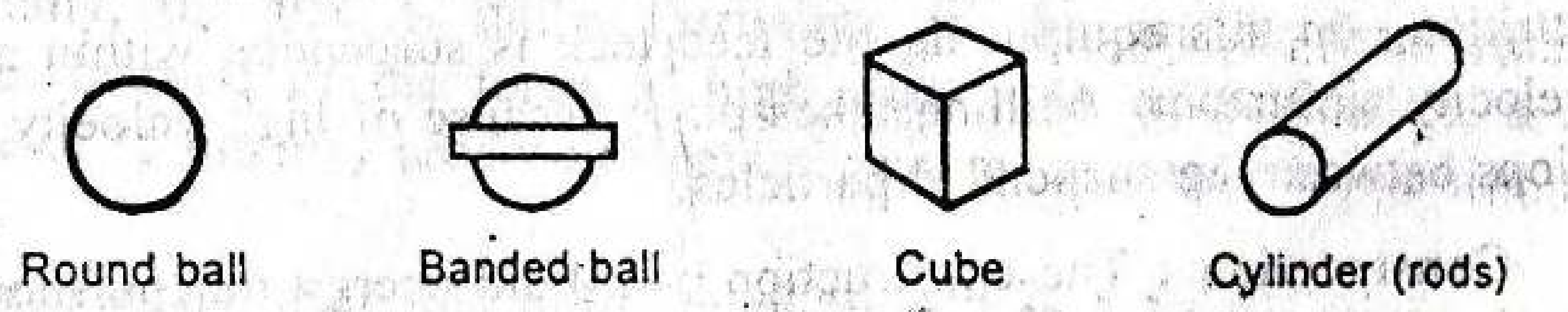
(4) Toxic substances can be ground, as the cylinder is a closed system.

(5) Since the mill is a closed system, sterility can be achieved.

(6) Milling operation can be accomplished in an inert atmosphere, if oxygen sensitive substances are to be milled.

(7) Balls can be of various shapes and sizes. Rods or bars may be used instead of balls. Rod mill is particularly useful for milling of sticky materials.

(9) In ball mill, installation, operation and labour costs are low.



Commonly used balls

Disadvantages : Some of the disadvantages are:

(1) The ball mill is a very noisy machine.

(2) Wear occurs from the balls as well as from the casing, which may result in contamination of the product.

(3) Ball milling is a slow process. The rate at which energy can be applied is limited, because it depends on the acceleration of the balls, which is influenced by the gravitational force.

(4) Soft, tacky, fibrous material cannot be milled by ball mill.

Variants : (a) Hardinge mill : Usually, Hardinge mill consists of hollow cylinder with a conical central section. Different sized balls are used. The small balls are placed near the discharge end, where they can perform the finest grinding. The largest balls remain in the cylindrical feed-end with gradual decrease in size of balls. As the charge rotates, differential centrifugal force causes the finer particles to move towards the discharge end. In this equipment, removal of discharge can be done from the side covers. So the mill operates simultaneously for size reduction as well as classification.

(b) **Continuous ball mills :** In the simple type of ball mill, it is not possible to remove fines without emptying the mill. Sieving of powder should be done separately. In continuously operating ball mills, a series of chambers are separated by sieves of successively finer mesh size. The equipment is positioned under a small slope so that the powder can pass to the next chamber.

(c) **Vibrating ball mills :** In vibrating ball mills, the metallic cylinder is supported on a spring base and subjected to forced vibrations induced by electromagnetic means. These have several advantages: (1) Mill is free from rotating parts, (2) It is easy to integrate the mills by classifiers and other ancillary system, (3) Vibrating mill grinds at rates often as high as 20 to 30 times that of the conventional mills, (4) Grinding efficiency is also high.

FLUID ENERGY MILL OR JET MILL OR MICRONIZERS OR ULTRAFINE GRINDERS

Principle : Fluid energy mill operates on the principle of impact and attrition. In this equipment, the feedstock is suspended within a high velocity air stream. Milling takes place because of high velocity collisions between the suspended particles.

Construction : The construction of a fluid energy mill is shown in Figure 6-9. Fluid energy mill consists of an elliptical pipe, which has a height of about 2 metres and diameter may be ranging from 20 to 200 millimetres. The mill surface may be made of either soft stainless steel or tough ceramics. Usually, mills are constructed such that the contact surfaces are merely linings, which can be removed or replaced, if excessively eroded after use.

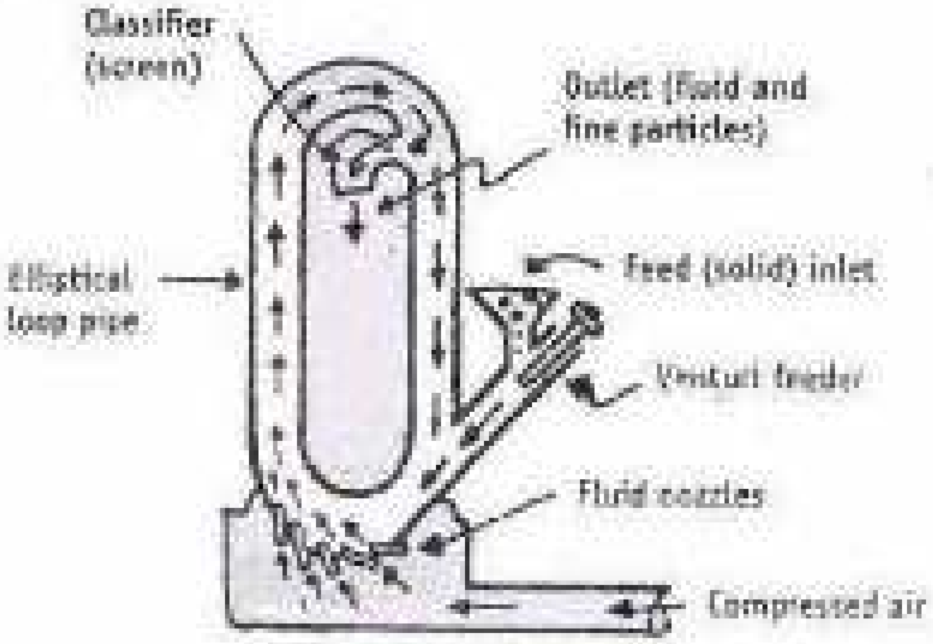


Figure 6-9. The construction of fluid energy mill.

Grinding nozzles (usually two to six) may be placed tangential ~~and/or opposed to the initial flow path of a powder~~. Normally, compressed air is used at 600 kilopascals to 1.0 megapascals. Inert gases can be used to minimize or eliminate the oxidation of susceptible compounds.

Venturi feeder is provided in the path of the airflow. An outlet with a classifier (cyclone separator or bag filter) is fitted to allow the escape of air.

Working : Powder is introduced through the inlet of venturi. The air entering through the grinding nozzles transport the powder in the elliptical or circular track of the mill. In the turbulent stream of air, the suspended particles collide with each other and break. Thus, impact and attrition forces operate in size reduction. The resultant small particles (by entrapment of air) are carried to outlet and removed by cyclone or filters.

The coarser particles undergo re-circulation in the chamber on account of its own weight. These re-circulated particles collide again with new in-coming feed stock particles. The powder remains in the mill, until its size is reduced sufficiently. Later it leaves via the sieve. Hence, fluid energy mill produces particles with narrow size distribution.

Some times the particles, which are entrapped by the drag of gas, leave the mill and carried out to a cyclone separator or bag collector for size separation.

Uses : Fluid energy mill is used to reduce the particle size of most of the drugs such as antibiotics and vitamins. When strict quality control is desirable for the purpose of better absorption (bioavailability), this mill is the preferred one. Ultrafine grinding can be achieved. Moderately hard materials can be processed for size reduction.

Advantages : (1) It has no moving parts, hence, heat is not produced during milling. Therefore, heat-labile substances can be milled. Examples are sulphonamides, vitamins and antibiotics. Due to the expansion of gases under pressure cooling effect is produced during milling.

(2) It is a rapid and an efficient method for reducing powders to 30 mm or less.

(3) Since there is no wear of the mill, contamination is not possible.

Disadvantages : (1) Fluid energy mill is not suitable for milling of soft, tacky and fibrous materials.

(2) The equipment is expensive, because it needs additional accessories particularly fluid energy source and dust collection equipment.

Variants : *Centrifugal-impact pulverizer*—In centrifugal impact pulverizers, a rotor is spinned to induce high centrifugal force on the feed particles. The particles move towards the impactors, which are set at the periphery of the rotor. On striking these impactors, the material is further hurled against the outer casing where final reduction is achieved. The material is removed from the conical discharge at the bottom.

Particle size reduction in the range of 10 to 325 meshes can be obtained with this type of mill with minimum fines. Centrifugal impact pulverizers have been used for the size reduction of a variety of materials ranging from soft organic molecules to hard abrasive materials. It is also well suited for the size reduction of heat sensitive materials.

COLLOID MILL

Principle : Colloid mill consists of two steel discs having very small clearance between them. One disc is rotating, while the other one is stationary. When the material is passed through these discs, they get sheared. Thus, coarse particles are broken down into small particles due to shear.

Construction : The construction of a colloid mill is shown in Figure 6-10. The colloid mill consists of high-speed rotor and stator with conical milling surface. The milling surfaces may be smooth surfaced or rough surfaced. Rough surfaced mills are used for fibrous material because fibres tend to interlock and clog smooth surfaced mills. The clearance between rotor and stator can be adjusted from 0.05 to 0.75 millimetres. During milling, the heat generated may rise the temperature up to 40°C. Hence, cold water circulation is provided to reduce the temperature as much as 20°C. The discharge pipe is also connected to hopper, so that discharge can be recycled.

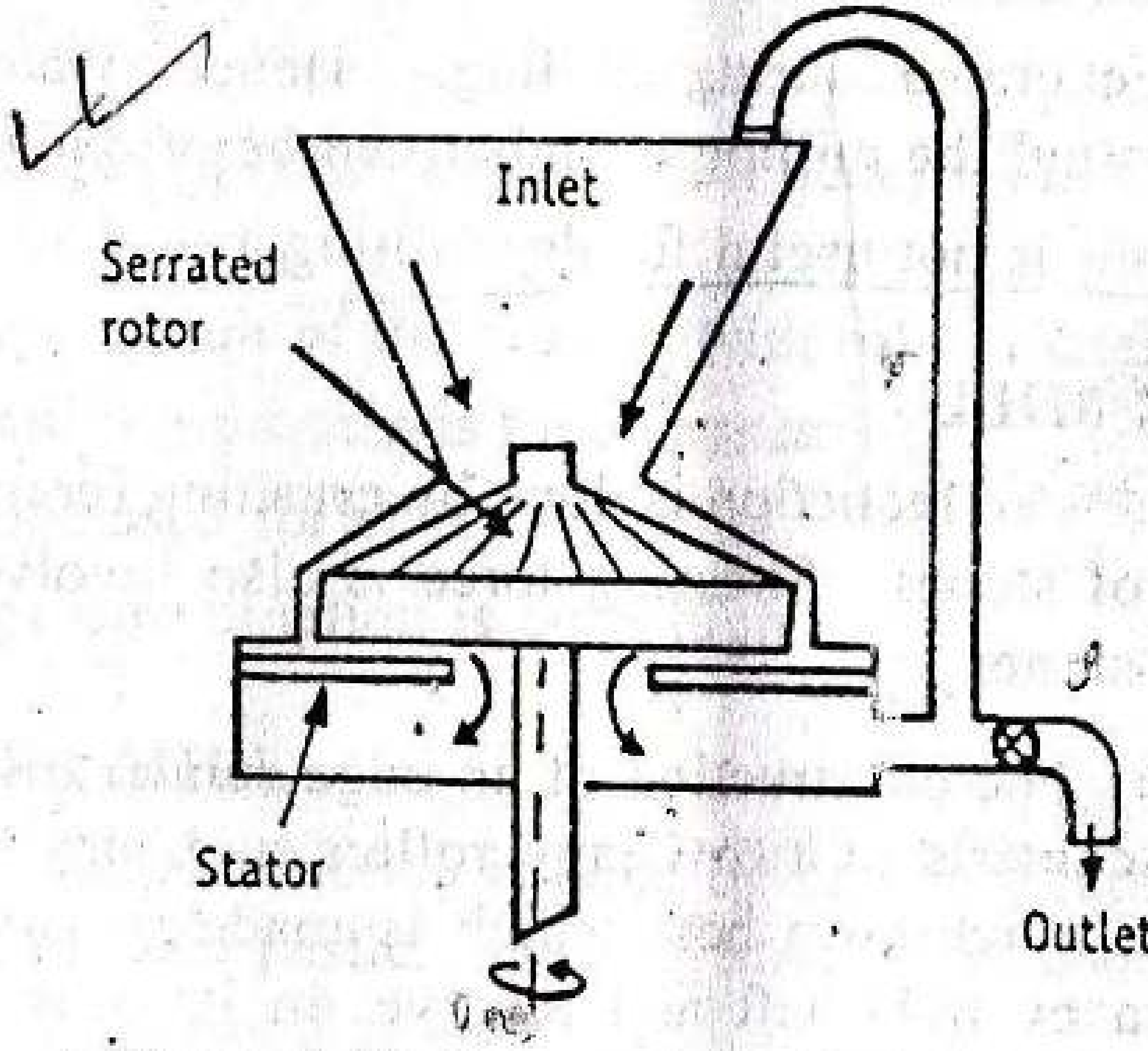


Figure 6-10. Construction of colloid mill.

Working : Materials such as suspensions and emulsions are placed in the hopper. Usually, the solids are pre-milled to prevent the damage of colloid mill. The solids are mixed with the liquid vehicle before being introduced into the colloid mill. The dispersion flows down and adheres to the rotor. During the movement of rotor (3000 to 20000 revolutions per minute), centrifugal force throws a part of the dispersion on to the stator. Depending on the clearance, the dispersion is sheared between rotor and stator. Thus, size reduction can be achieved. The milled liquid may be recycled. After achieving the desired size, the discharge is collected from the outlet in the periphery of the housing.

Normally, the size of milled particles may be smaller than the clearance, because of the force of high shear. In emulsification, a clearance of 75 µm may produce dispersion with an average particle size of 3 µm.

The capacities of colloid mills range from 2 to 3 L/min for small mills to 440 L/min for the larger mills.

Uses : Colloid mill is used for preparing colloidal dispersions, suspensions, emulsions and ointments. It is not used for dry milling. Particle size as small as 3 µm can be obtained. Fibrous material can be milled using rough surfaced rotor and stator.

Advantage : Colloid mill can be sterilised. So it can be used in the production of sterile products.

Disadvantages : (1) Colloid mill tends to incorporate air into the finished product. Therefore, the product should be allowed to rest for some time for deaeration.

(2) Heat is generated during milling. Hence, water circulation facility around the milling chamber can be provided.

(3) Colloid mill is not useful for dry milling.

EDGE RUNNER MILL

Principle : The size reduction is done by crushing (compression) due to heavy weight of stones. Shearing force is also involved during the movement of the stones.

Construction : The construction of an edge runner mill is shown in Figure 6-11. It consists of two heavy rollers and may weigh several tons. The rollers move on a bed, which is made of stone or granite. Each roller has a central shaft and revolve on its axis. Further, the rollers are mounted on a horizontal shaft and move around the bed.

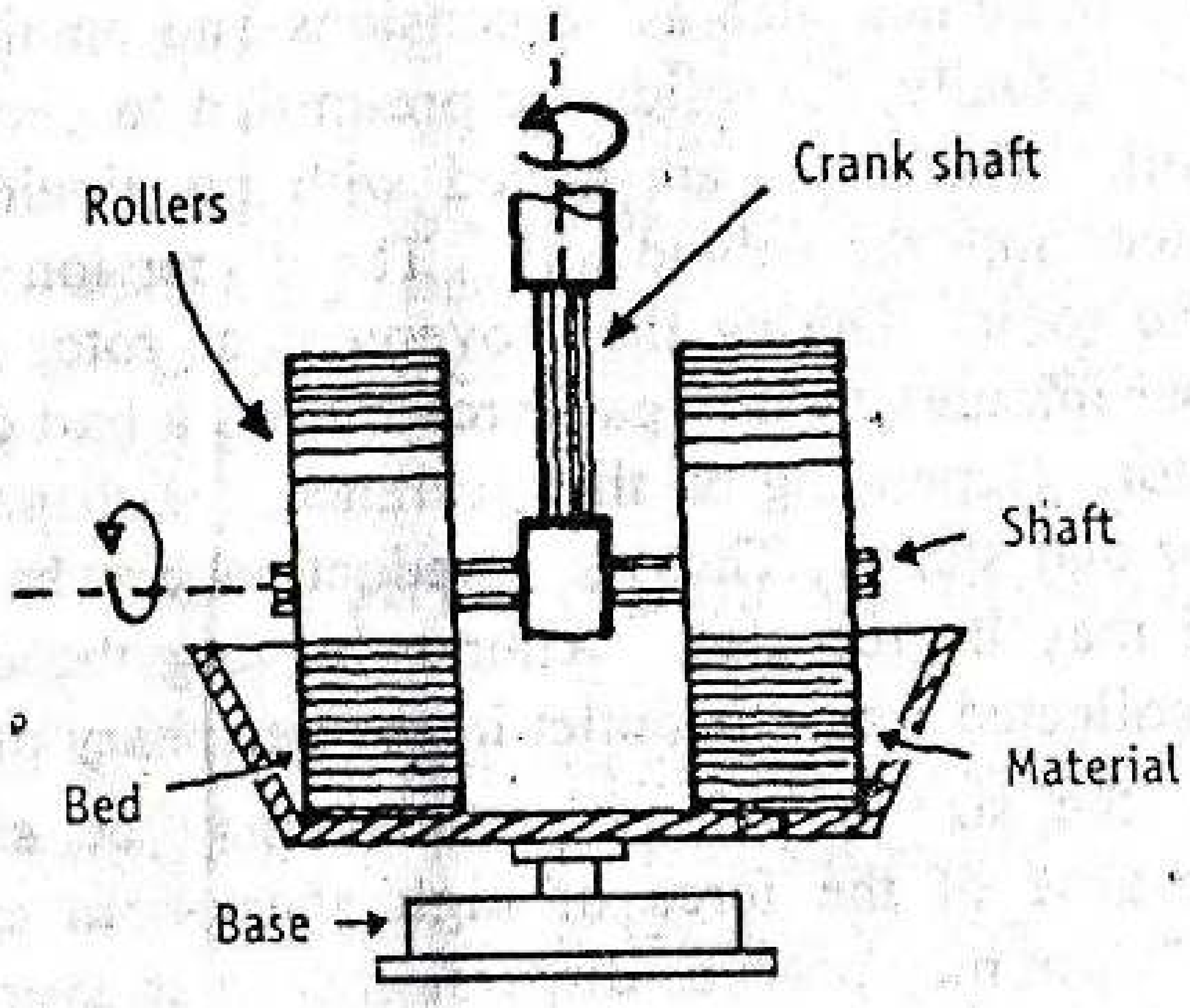


Figure 6-11. Construction of edge runner mill.

Working : The material to be ground is placed on the bed. With the help of a scrapper, it is kept in the path of the stone wheel. The stones revolve on its axis, and at the same time travel round the shallow stone bed. The outer part of the wheel has to travel a greater distance than the inner, so that size reduction is achieved by shearing as well as crushing. The material is ground for a definite period. The powder is collected and passed through a sieve to get powder of the required size. It is a batch process.

Uses : Edge runner mill is used for grinding tough materials to fine powder. It is still used for plant-based products, while more sophisticated mills are used for chemicals and drugs.

Advantages : Edge runner mill does not require attention during operation.

Disadvantages : (1) Edge runner mill occupies more space than other commonly used mills.

(2) Contamination of the product with roller material is possible.

(3) The milling process is time consuming.

(4) It is not used for sticky materials.

(5) Energy consumption is quite high.

END RUNNER MILL

Principle : Size reduction is done by crushing (compression) due to heavy weight of steel pestle. Shearing stress is also involved during the movement of mortar and pestle.

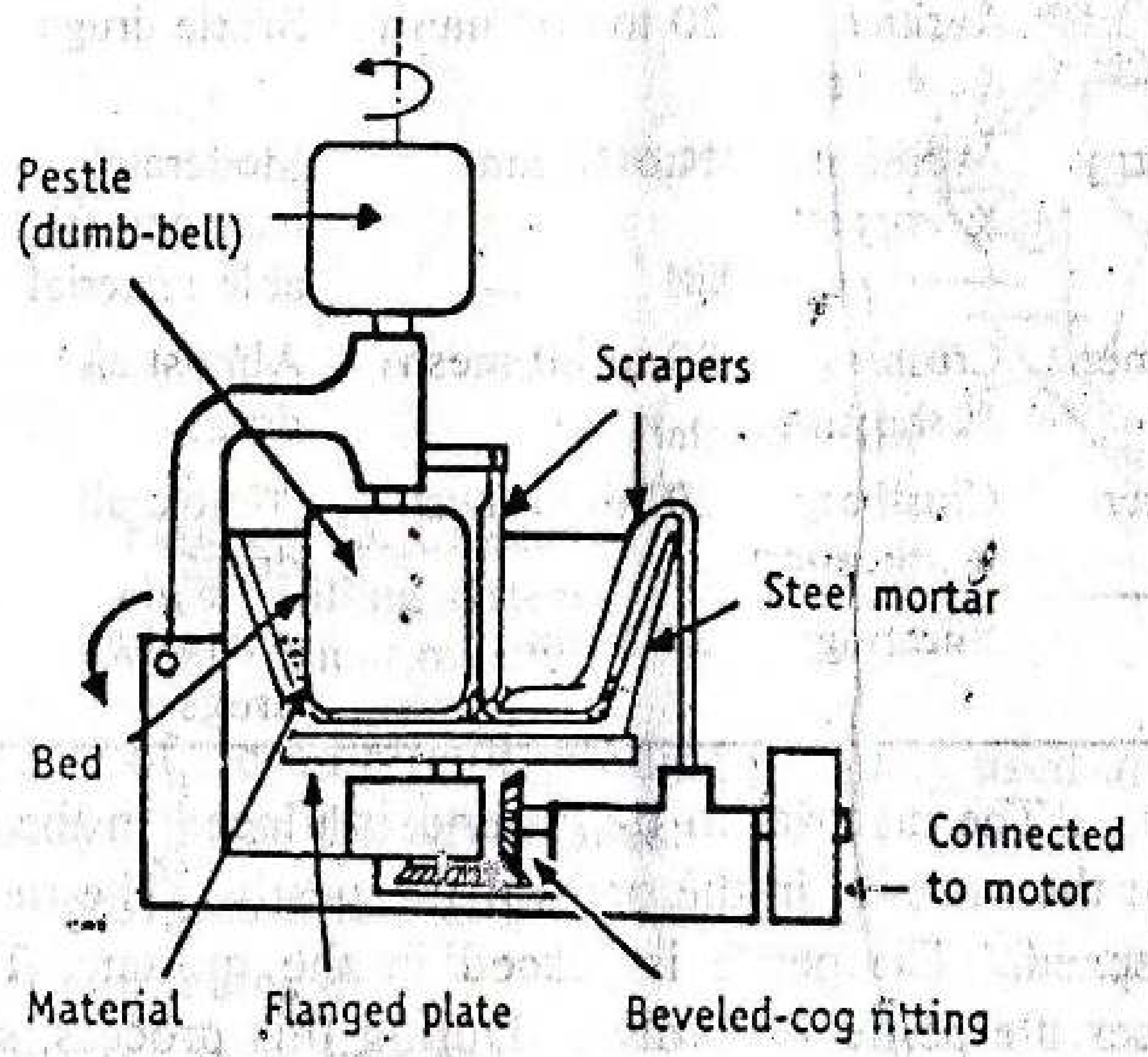


Figure 6-12. Construction of end runner mill.

Construction : The construction of an end runner mill is shown in Figure 6-12. It is considered as a mechanical mortar and pestle. It consists of a steel mortar, which is fixed to a flanged plate. Underneath the flanged plate, a bevelled cog fitting is attached to a horizontal shaft bearing a pulley. Hence, the plate with mortar can be rotated at a high speed.

The pestle is dumb-bell shaped so that balancing and efficient grinding by its weight can be achieved. The bottom of pestle is flat rather than round. The pestle carries an arm, which is hinged. By this arrangement, the pestle can be raised from the mortar to facilitate emptying and cleaning. The narrow central portion of the pestle is longer than the band of the arm around it. Hence, pestle can rise and fall over the material in the mortar.

TABLE 6-1

General Characteristics of Various Types of Mills

Sl. no.	*Name of the mill*	*Action*	*Product size*	*Uses*	*Not used for*
1.	Cutter mill	Cutting	20 to 80 mesh	Fibrous, crude (animal and vegetable drug)	Friable material
2.	Roller mill	Compression	20 to 200 mesh	Soft material	Abrasive material
3.	Hammer mill	Impact	4 to 325 mesh	All most all drugs	Abrasive material
4.	Ball mill	Attrition & impact	20 to 200 mesh	Brittle drugs	Soft material
5.	Fluid energy mill	Attrition & impact	1 to 30 mm	Moderately hard and friable material	Soft and sticky material
5.	Edge runner mill	Crushing & shearing	20 to 80 mesh	Almost all drugs	Sticky material
6.	End runner mill	Crushing & shearing	20 to 80 mesh	Almost all drugs	Sticky material
7.	Colloid mill	Shearing	3-75 μm	Almost all drugs	Dry milling

Working : The material to be ground is placed in the mortar. The scraper puts the material in the path of the pestle. The mortar revolves at a high speed. The pestle is placed in the mortar. The revolving mortar causes the pestle to revolve. During this process, size reduction is achieved by shearing as well as crushing. The material is collected and passed through a sieve to get the powder of desired size.

Uses : End runner mill is suitable for fine grinding. Now a days, this mill is replaced by more efficient and sophisticated milling equipment.

Disadvantage : End runner mill is not suitable for drugs, which are in unbroken or slightly broken conditions.

In summary, several size reduction equipment are described. Some general characteristics of various types of mills are given in Table 6-1.

OPEN CIRCUIT AND CLOSED CIRCUIT MILL

The size reduction process may be achieved in open circuit or closed circuit conditions.

An *open-circuit mill* is one in which milling operation is carried out in one attempt, i.e., by passing the feed material through the mill to obtain the desired size.

A *closed-circuit mill* is one in which the discharge from the milling process is passed through a size separation device or classifier, and the oversize particles are returned to the grinding chamber for further size reduction..

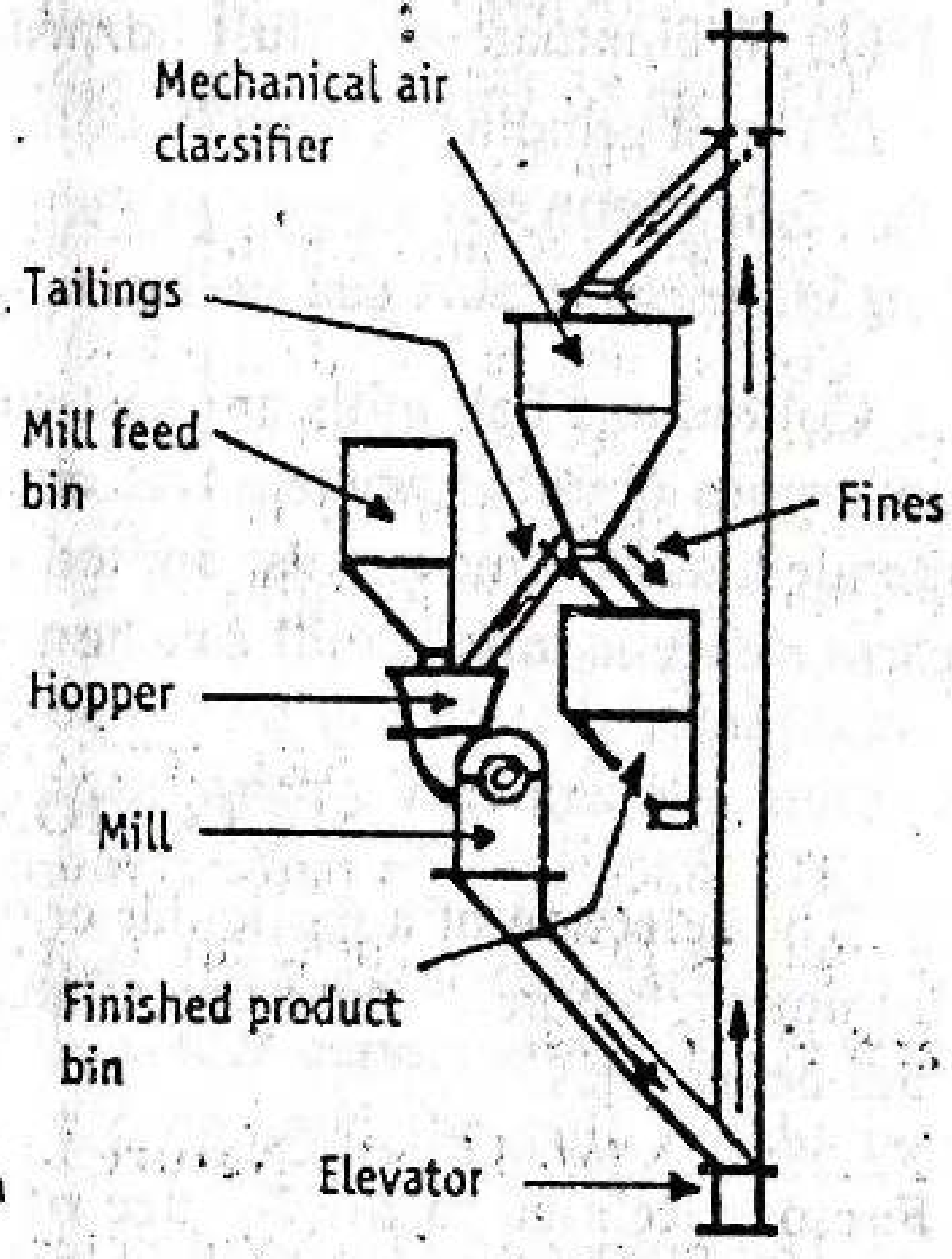


Figure 6-13. Closed circuit milling system with hammer mill.

The principle of closed circuit grinding is widely used in the pharmaceutical industry. It has the advantages:

(a) It provides fine and ultra-fine sizes.
(b) It eliminates dust.
(c) It eliminates overheating.
(d) It produces a product that is free from oversize or undersize.

A closed circuit with an air classifier is shown in Figure 6-13. In this type, size reduction is combined with size classification. The working of hammer mill is illustrated in Figure 6-13. The coarse material returning to the mill by a classifier is known as *circulating load.*

Dry and Wet Grinding

The use of a product and subsequent steps mainly decide the type of equipment used. In the preparation of colloidal dispersions, suspensions, emulsions and ointments, wet grinding offers advantages. In the production of suspensions and emulsions, wet grinding has become an integral part of the processing. For example, mill can be used as mixing equipment. Triple roller mill, colloid mill are used for such a purpose.

In practice, it is found that finer size can be achieved by wet grinding than by dry grinding. Wet grinding is used in the production of flocculated suspensions. In wet grinding, surfactants are added to attain particle size of 0.5 μm. The advantages of wet grinding are that:

(1) it eliminates the dust hazards.
(2) wet grinding is usually done at low speed, therefore, it consumes less power.
(3) grinding aids can be incorporated.

Colloid and ball mills are best suited for wet grinding. If the product undergoes physical or chemical changes in water, dry milling is recommended. The fineness is limited to 100 μm. All the mills reported earlier except colloid mill can be used for dry grinding.

SELECTION OF A MILL

The selection of a particular equipment for size reduction depends on a number factors. These are related to the feed, milled product, safety, and economics.

Factors Related to the Nature of Raw Materials

The properties of a solid determine its ability to resist size reduction and influence the choice of equipment used for milling. Some physical properties of the feed are as follows.

Hard materials : Iodine and pumice are hard and abrasive. In general, hard materials are most difficult to comminute. For iodine, hammer mill or fluid energy mill is used. Size reduction process of such materials can lead to abrasive wear of milling parts, which then cause contamination.

Fibrous materials : Glycyrrhiza, rauwolfia, ginger etc., are fibrous in nature and cannot be crushed by pressure or impact. Fibrous materials are tough in nature. They must be teared by a cutter. Nux vomica and ipecacuanha are processed in two stages to get fine powders.

Friable materials : Sucrose and dried filter-cake are friable and tend to fracture along well-defined planes. Brittle substances can be easily converted to smaller particles. Such materials are milled by the mechanisms such as attrition, impact or pressure. For example, sugar is milled using hammer and fluid energy mills.

Elastic materials : Synthetic gums, waxes and resins become soft and plastic during milling. These low-melting substances should be chilled before milling. Such materials are milled using hammer, colloid or fluid energy mill.

Hygroscopic materials : Substances such as potassium carbonate absorb moisture rapidly. This wet mass sticks and clogs the mill. They are prepared in a closed system such as porcelain ball mill.

Solvated materials : Sodium sulphate ($Na_2SO_4.10H_2O$) and other hydrates liberate water during milling and cause clogging of the mill.

Melting point : Solids with low melting points often become soft and melt owing to the heat generated during milling. Such materials are chilled before milling.

Thermolability : Certain substances undergo degradation reactions such as hydrolysis and oxidation due to the presence of moisture and atmospheric oxygen. Such reactions proceed faster owing to the heat produced during milling. They should be milled in a closed system with an inert atmosphere of carbon dioxide or nitrogen. Vitamins and antibiotics are milled using fluid energy and ball mills.

Flammability : Almost any fine dust, such as dextrin, starch and sulphur, is a potential explosive mixture under certain conditions. All electrical switches should be explosive proof and the mill should be properly grounded (earthed).

Particle size of the feed : For a mill to operate satisfactorily, the feed should be of proper size. For example, pretreatment of fibrous materials with high pressure rollers or cutters facilitates further comminution.

Moisture content : Presence of more than 5% water hinders the milling process and produces a sticky mass. The effect is more pronounced, when the concentration of water is more. In general, materials with moisture content below 5% are suitable for dry grinding and above 50% are suitable for wet grinding.

Pretreatment : For the mill to operate satisfactorily, the feed should be of a proper size and enter the equipment at a fairly uniform rate. Therefore, a pretreatment step should be included. For example, fibrous material should be treated with cutter or roller, which can facilitate further comminution.

Factors Related to the Nature of Finished Product

The nature of finished (milled) product also influences the selection of the equipment.

Particle size : If extreme size control is necessary, it may be essential to recycle the larger particles. This can be achieved by screening the discharge material and returning the over size particles for a second time milling. Moderately coarse or coarse powders with a minimum of fine powder are easily obtained by using a high-speed impact mill. For example, cascara, liquorice, belladonna leaves and roots are easily broken down by impact mill.

For example, particle size of griseofulvin is critical in the production. Similarly the particle size is also critical in the suspension of penicillin G procaine for intra-muscular injection due to its syringeability.

Ease of sterilisation : When preparations are intended for parenteral and ophthalmic uses, size reduction should be conducted in a sterile environment. The equipment should be sterilisable. Ball mills and fluid energy mills are suitable for this purpose.

Contamination of milled materials : In case of potent drugs and low dose products, contamination of the product should be avoided. Use of equipment that is free from wearing of mill parts is preferred. Fluid energy mill is suitable for this purpose.

In addition to the end use of a product, subsequent processing steps mainly determine the choice of wet or dry milling. In the preparation of colloidal dispersions, suspensions, emulsions and ointments, wet grinding offers advantages in terms of size reduction of materials, elimination of dust hazards. Thus, wet grinding has become an integral part of the processing of the above dosage forms. The same mill can also be used as mixing equipment. Examples are triple roller mill and colloid mill.

Factors Related to Safety

The factors related to safety are explosivity, irritability and toxicity. During milling, fine dust of drug arises which may become flammable under certain conditions. Explosion hazards of non-metallic materials, such as sulphur, starch and wood floor, are often appreciable. Metal powders pose a hazard because of their flammability. The useful precautions are:

(a) isolate the mill.
(b) use of non-sparking material of construction.

Stainless steel has less sparking tendency than ordinary steel or forging.

Factors Related to the Economy

Cost, power consumption, space occupied and labour costs are some of the economic factors that determine the selection of a mill.

Cost : Where the particle size control is not critical, the cost decides the type of equipment. In general, the cost of the size reduction increases, as the particle size decreases. Therefore, it is economically undesirable to reduce the particle size to a finer degree than necessary.

THEORIES OF COMMINUTION

Mechanical Behaviour of Solids

When various modes of stress are applied on a powder, the particles get strained. This stress-strain relationship is shown in Figure 6-14.

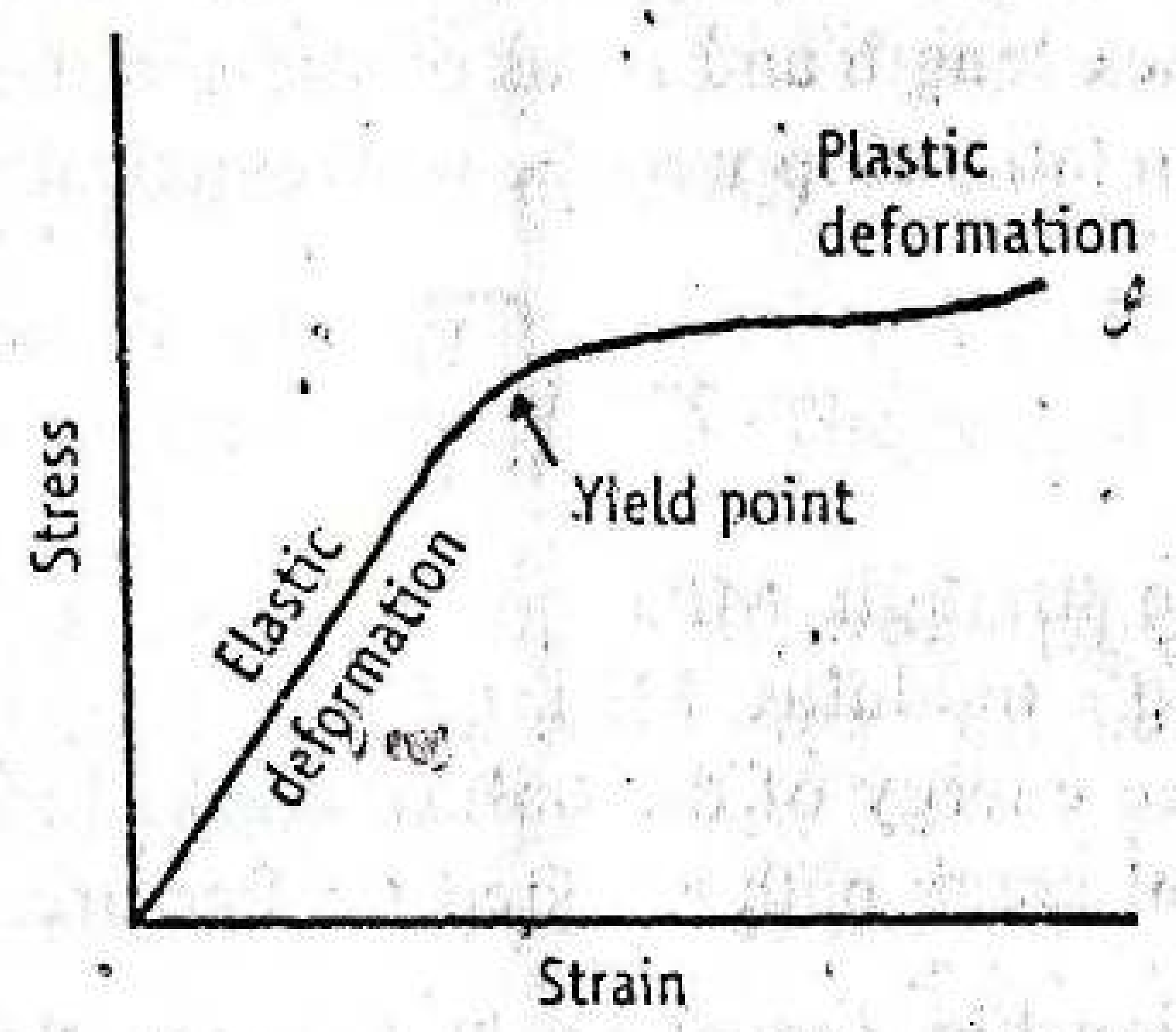


Figure 6-14. Stress-strain curve for a solid.

- In Figure 6-14, the initial linear portion is defined by Hooke's law. It states that stress is proportional to strain. The slope of linear portion represents *Young's modulus*. It expresses the stiffness or softness in megapascals.
- If the force of impact (stress) does not exceed the elastic limit (region of Hooke's law), the material is reversibly deformed.

When the force is removed, the particle returns to original condition. The elastic limit is known as *yield value*. The stress energy in the deformed particle appears as heat. Example is plastic material such as polymer.

- The stress-strain curve becomes nonlinear at the yield point. This is a measure of the resistance to permanent deformation.
- Beyond the yield point, the region represents irreversible plastic deformation.
- The area under the curve represents the fracture toughness (or modulus of toughness). This is an approximate measure of the impact strength of the material. Fracture of a particle can be obtained when the force exceeds the elastic limit.

Theories of Size Reduction

(1) According to Griffith theory, all solids contain flaws and microscopic cracks. A *flaw* is any structural weakness that may develop into a crack under strain. The weakest flaw in a particle determines its fracture strength. It controls the number of particles produced by fracture. The particles with the weakest flaw fractures most easily and produce largest possible pieces. In the next step, another weakest flaw fractures. This process continues until all flaws are fractured. The particle size produced in this process may not be the desirable one. However, Griffith theory is simple and explains the size reduction process reasonably.

According to Griffith theory, the amount of force to be applied depends on the crack length and focus of stress at the atomic bond of the crack apex. This relationship may be mathematically expressed as:

$$T = \sqrt{\frac{Y\varepsilon}{c}} \qquad (1)$$

where T = tensile strength, MPa
Y = Young's modulus, MPa
ε = surface energy of the wall of crack, J/m^2
c = critical crack path required for fracture, m

A linear relationship (equation 1) between the square of tensile strength of minerals and the critical height for drop weight impact suggests that the square of tensile strength is a useful criterion of impact fracture.

(2) If flaws are not present in a particle, the force of milling produces new flaws. The useful work in milling is proportional to the length of new crack formed. The mechanism of creating new flaws in a particle is as follows.

Usually, the surface of particles is irregular. The applied force is initially taken on the high portion of the surface. As a result, high stress and increased temperature may be set up locally in the particle. The bonds at this place become weak, which may be responsible for creating flaws. The particle further absorbs applied strain energy and is deformed. The strain energy required to extend the crack to fracture is proportional to the length of the crack formed. This energy is supplied by the flow of the residual strain energy to the crack.

3. Not all materials exhibit this type of brittle behaviour. They resist fracture even at much larger stresses, because these are tougher. They undergo plastic flow, which allows strain energy relaxation without crack propagation. When plastic flow occurs, atoms or molecules slip over one another and this process of deformation requires energy.

ENERGY FOR COMMINUTION

Size reduction begins with the opening of small flaws that were initially present. Based on the probability, larger particles may have numerous flaws and readily fracture when compared to smaller particles with fewer flaws. The supplied energy is used to:

- Increase new surface area from flaws.
- Initiate flaws or cracks in the particle.

This phenomenon is observed generally in fine grinding.

Most efficient mills utilise less than 1% of the energy input to fracture particles or create new surfaces. The rest of energy is dissipated in:

1. Elastic deformation of unfractured particles.
2. Transport of material within the milling chamber.
3. Friction between the particles.
4. Friction between the particles and mill.
5. Heat.
6. Vibration and noise.
7. Inefficiency of transmission and motor.

Energy input and utilisation are important factors to estimate the efficiency of a mill for a given material. A number of theories has been proposed to establish a relationship between energy input and the degree of size reduction produced.

The energy required to reduce the size of the particles is inversely proportional to the size raised to some power. This may be expressed mathematically as;

$$\frac{dE}{dD} = \frac{-C}{D^n} \qquad (2)$$

where E = amount of energy (work done) required to produce a change, kW·h
D = size of unit mass, μm
C = constant, W·h
n = constant

Equation (2) may be written (when n = 1) as:

$$E = C' \ln \left(\frac{d_i}{d_n}\right) \qquad (3)$$

where d_i = size of the feed, μm
d_n = size of the product, μm

In equation (3), (d_i/d_n) is known as *reduction ratio*. The usefulness of equation (3) is that it satisfies various laws proposed. These are:

For n = 1.0, equation (3) becomes Kick's law
For n = 1.5, equation (3) becomes Bond's law
For n = 2.0, equation (3) becomes Rittinger's law

Rittinger's Theory

According to the Rittinger's hypothesis, energy, E required for size reduction of unit mass is directly proportional to the new surface area produced. It is expressed as:

$$E = K_R (S_n - S_i) \qquad (4)$$

where S_i = initial specific surface area, $\mu m^2/\mu m^3$
S_n = new specific surface area, $\mu m^2/\mu m^3$
K_R = Rittinger's constant, energy per unit area, kW·h./μm^3
E = amount of energy (work done), kW·h

It is mostly applicable to brittle materials undergoing fine milling. Rittinger's theory ignores particle deformation before fracture.

Bond's Theory

According to the Bond's theory, the energy used in crack propagation is proportional to the new crack length produced. It states that the energy used for deforming or fracturing a set of particle of equivalent shape is proportional to the change in particle dimensions. According to Bond's theory, the equation can be written as:

$$E = 2K_B \left(\frac{1}{\sqrt{d_n}} - \frac{1}{\sqrt{d_i}}\right) \qquad (5)$$

where K_B = Bond's work index, energy per unit mass, kW·h·$\sqrt{\mu m}$
d_i = initial diameter of particles, μm
d_n = new diameter of particles, μm

Bond's work index is the work required to reduce a unit weight from a theoretical infinite size to 80% passing 100 μm. According to this theory, the energy used in crack propagation is proportional to the new crack length produced. This law is useful for rough mill sizing. The work index is useful for comparing the efficiency of milling operations.

Kick's Theory

According to the Kick's theory, the energy used in deforming or fracturing a set of particles of equivalent shape is proportional to the ratio of the change in size. It may be expressed as:

$$E = K_K \ln \frac{d_i}{d_n} \qquad (6)$$

where K_K = Kick's constant, energy per unit mass, kW·h
d_i = diameter of the particle in the initial stage, μm
d_n = diameter of the new particle, μm

The Kick's proposal was developed on a stress-strain diagram for cubes under compression. It assumes that the material has flaws distributed throughout its internal structure. For crushing (compression) of large particles, Kick's equation (equation 6) is more useful.

Equations (1 to 6) apply precisely only under the condition that all the energy is transferred into surface energy.

Size reduction of a material is alone not sufficient to obtain powder of desired size. It is followed by separation. Several equipment described earlier also include sieves or screens as integral parts. However, size separation is discussed separately in the following chapter.

Glossary of Symbols

C = Constant or coefficient.
c = Critical crack path required for fracture, m.

D = Size of unit mass, µm.
E = Amount of energy required to produce a change in unit mass. kW·h.
d_i = Size of the feed or initial diameter of particles, µm.
d_n = Size of the product or new diameter of the particles, µm.
ε = Surface energy of the wall of crack, J/m^2.
K_B = Bond's work index, energy per unit mass, kW·h·$\sqrt{\mu m}$.
K_K = Kick's constant, kW·h.
K_R = Rittinger's constant, kW·h/µm^2.
n = Constant.
S_i = Initial specific surface area, µm^2/µm^3.
S_n = New specific surface area, µm^2/µm^3.
T = Tensile strength, MPa.
Y = Young's modulus, MPa.

QUESTION BANK

Each question carries 2 marks

1. It is essential to include a sieve in the size reduction equipment. Why?
2. In a hammer mill, the particle size of the powders is far less than the mesh size of the screen. How is it possible?
3. Screen type of sieves gives more fine powder than the wire woven sieves. Why?
4. Size reduction of vegetable matter is essential for the extraction of crude drugs. Explain.
5. It is difficult to obtain uniform sized product during milling without the use of sieves. Why?
6. Fluid energy mill is better equipment for size reduction of thermo-labile substances compared to hammer mill. Substantiate.
7. Ball mill is not useful for size reduction of fibrous material. Explain
8. It is possible to prevent the heat generated during milling using colloid mill. How?
9. Size reduction of a material enhances the action of drugs. Explain.
10. When ball mill is used, size reduction is not obtained. Under what condition size reduction is not effective.
11. How do you prevent the problems of sticking and clogging of sieves in the size reduction?
12. List special precautions to be taken while thermolabile substances are subjected to size reduction process.
13. The powder must contain fewer amounts of fines when it is meant for percolation process of extraction. Why?
14. What are the advantages of swinging type of hammer compared to rigid hammers?

15. Powders of same particle size that are obtained by different equipment have same physicochemical characteristics. True or false. Justify.
16. List the areas in which size reduction equipment is used in tablet production.
17. A large number of size reduction equipment is available currently. Why do we require so many types of mills?
18. Size reduction of powders is not possible, if particles do not contain flaws or cracks. Explain.
19. The classical equipment mortar and pestle uses the mechanism of impact in size reduction. True or False. Explain.
20. Fluid energy mill is meant for wet grinding. True or false. Explain.
21. Reducing the size of the particles to fines leads to particle aggregation. True or false. Explain.
22. Size reduction mill can also be used as mixing or dispersion equipment. True or false. Explain.
23. How does stickiness affect the process of size reduction?
24. How does the presence of moisture interfere with the process of size reduction?
25. Differentiate the mechanisms, attrition and impact in size reduction.

Each question carries 5 marks

1. Describe five factors that influence the selection of milling equipment for size reduction.
2. Explain with the help of a diagram the construction and working of a ball mill.
3. Explain with the help of diagram the construction and working of a hammer mill.
4. Describe the mechanisms of size reduction with suitable examples of equipment.
5. What is ultra-fine grinder? Explain the concept of ultra-fine grinding.
6. Describe 'micronizer'. Describe aseptic grinding process of antibiotics.
7. List the laws governing size reduction. What is work index?
8. How is size reduction affected in ultra-fine grinders? Describe the mechanism.
9. How is energy utilised in size reduction accounted for?

Each question carries 10 marks

1. Explain the factors related to feed-material influencing size reduction.
2. Describe the construction, working, advantages and disadvantages of fluid energy mill.

3. Describe the milling equipment with the help of a neat diagram that uses the principle of shear and impac
4. Explain the theories related to the size reduction of a powder.
5. Explain the advantages and disadvantages of size reduction process.
6. State and explain the laws governing size reduction.
7. Describe the mechanisms and modes of size reduction of solid drugs.

7

Size Separation

Official Standards for Powders
Sieves
Modes of Motion in Size Separation
Sieve Analysis – Testing of Powder
Equipment for Size Separation

Size reduction of a solid material never gives particles of same size, but gives particles of varying sizes, i.e., distributes in different sizes. These materials must be subjected to a separation technique to obtain narrow size ranges. As far as possible size separation is included as an integral part of the size reduction process. When particle size distribution is to be controlled for the official specifications, size separation assumes greater importance and has to be handled independent of the size reduction.

Size separation is a unit operation that involves the separation of a mixture of various sizes of particles into two or more portions by means of screening surfaces.

Size separation is also known as *sieving, sifting, classifying* or *screening*. This technique is based on physical differences between the particles such as size, shape and density.

Screening is a method of separating particles according to size alone. Particles can be separated into individual sizes using sieves. The final portion consists of a more uniform size. The material that remains on the given screening surface is known as *oversize or plus material.* The material passing through the screening surface is known as *undersize or minus material.* Size separation process (or sieves) can be used:

1. As a method to determine particle size and size distribution, which are useful in the production of tablets and capsules.
2. As a quality control tool for the analysis of raw materials such as griseofulvin and aspirin.

3. To test the efficiency of a size reduction equipment or process.
4. To optimise the process conditions such as method of agitation, time of screening, feed rate etc.

The testing of a powder and equipment used for classifying has been discussed in the chapter. Mainly this chapter is purported to provide adequate support to the size reduction process discussed earlier.

OFFICIAL STANDARDS FOR POWDERS

In general, powders are vaguely described as coarse and fine powders. However, it is essential to identify with some guiding specifications.

Indian Pharmacopœia has prescribed standards for powders for pharmaceutical purposes. Accordingly, degree of coarseness or fineness is expressed with reference to the nominal aperture size of sieve through which powder is able to pass. The relevant grades of powders and sieve number along with nominal aperture size are shown in Table 7-1. The IP 1996 specifies five grades of powder.

TABLE 7-1
Grades of Powders and Sieve Number along with Nominal Aperture Size as per IP

Sl. No.	*Grade of powder*	*Sieve through which all particles must pass*	*Nominal mesh aperture size*	*Sieve through which 40% particles pass*	*Nominal mesh aperture size*
1.	Coarse powder	10	1.7 mm	44	355 μm
2.	Moderately coarse powder	22	710 μm	60	250 μm
3.	Moderately fine powder	44	355 μm	85	180 μm
4.	Fine powder	85	180 μm	—	—
5.	Very fine powder	120	125 μm	—	—

Coarse powder : A powder, all the particles of which pass through a sieve with nominal mesh aperture of 1.70 mm (No. 10 sieve) and not more than 40.0 per cent through a sieve with nominal mesh aperture of 355 μm (No. 44 sieve) is called coarse powder.

In a similar way, other definitions can be written for the contents of the Table 7-1. When fineness of a powder is described by means of a number, it is an indication that all the particles of the powder shall pass through the sieve of which the nominal mesh aperture in µm, is equal to that number.

Normally, for compound powders, fine powders are preferred, while moderately coarse powder is used for the preparation of tinctures. Coarse powder without fines is employed in percolation process.

The above mentioned terminology has applications in the production of galanicals. A few examples are given in the Table 7-2.

The pharmacopœia has prescribed upper and lower limits for the three coarse grades of powder. For two fine grades, the pharmacopœia has prescribed only the upper limit.

TABLE 7-2

Some Examples of Crude Drugs and Nature of Powder Required

Liquid extracts	*Useful parts*	*Grade of powder*
Ashoka	stem bark	coarse
Nux vomica	seeds	moderately coarse
Rauwolfia	roots	moderately coarse
Ergot	sclerotia	moderately fine
Ipecac	root	fine
Ephedra	stem	fine

SIEVES

Sieves are the simplest and sieving is the most frequently used method for size separation.

Construction

Sieves for pharmaceutical testing are constructed from wire cloth with square meshes, woven from wire of brass, bronze, stainless steel or any suitable materials. Sieves should not be coated or plated. There must be no reaction between the material of the sieve and the substance to be sieved.

Types of Sieves

The primary considerations for sieves are given to the size and shape of aperture opening. Square meshes are arranged as per the specifications. Sieves commonly used in pharmaceutical processing include:

- Woven wire sieves

- Bolting cloth sieves
- Closely spaced bars (screens)
- Punched plates

Woven wire sieves : Wire woven sieves are general-purpose sieves and widely used in the pharmacy practice. The types of woven wire sieves are:

- Plain weave
- Twilled weave

The nature of sieve surfaces is shown in Figure 7-1. For fine sieving, metal wire woven sieves are used. Common examples are hand sieves. These are included in roller mill, ball mill etc., during milling. In case of coarse sieves, the wire is generally given a double crimp to preserve the alignment of the wire.

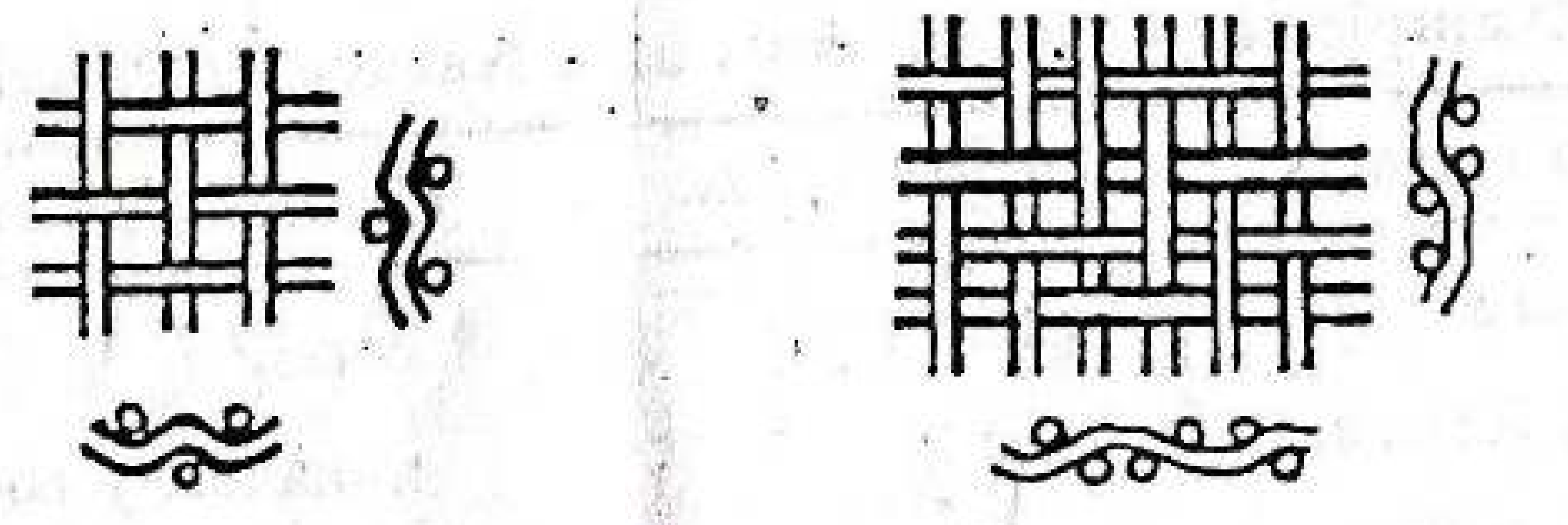

(a) Plain weave sieve
(b) Twilled weave sieve

Figure 7-1. The nature of sieve surfaces.

Bolting cloth sieves : Silk, nylon and cotton are generally woven from twisted multi-strand fibres. Nylon cloths are generally designated by their micrometer opening and available in different grades. These are used for the separation of fine powders. Hum-mer screen uses this type of screens.

Bar screens : Bar screens are generally used in handling large and heavy pieces of materials. The bars are fixed in parallel position and held by cross bars and spacers. Bars which taper in thickness from one end to the other are recommended, because they tend to avoid blinding. Grizzlies use this type of screens.

Punched plates (Perforated screens) : These are used for coarse sizing. The screens are prepared by using a sheet metal of varying thickness with perforated holes. The holes may be round, oval, square, or rectangular (Figure 7-2). These types of screens are used in a hammer mill.

A plate with a large number of holes and a small amount of residual metal will have a large capacity, but will wear rapidly and vice versa. In general, for openings much over 25 millimetres in diameter, a plate with round perforations is preferred over a wire screen. The applications of screen configurations are given in Table 7-3.

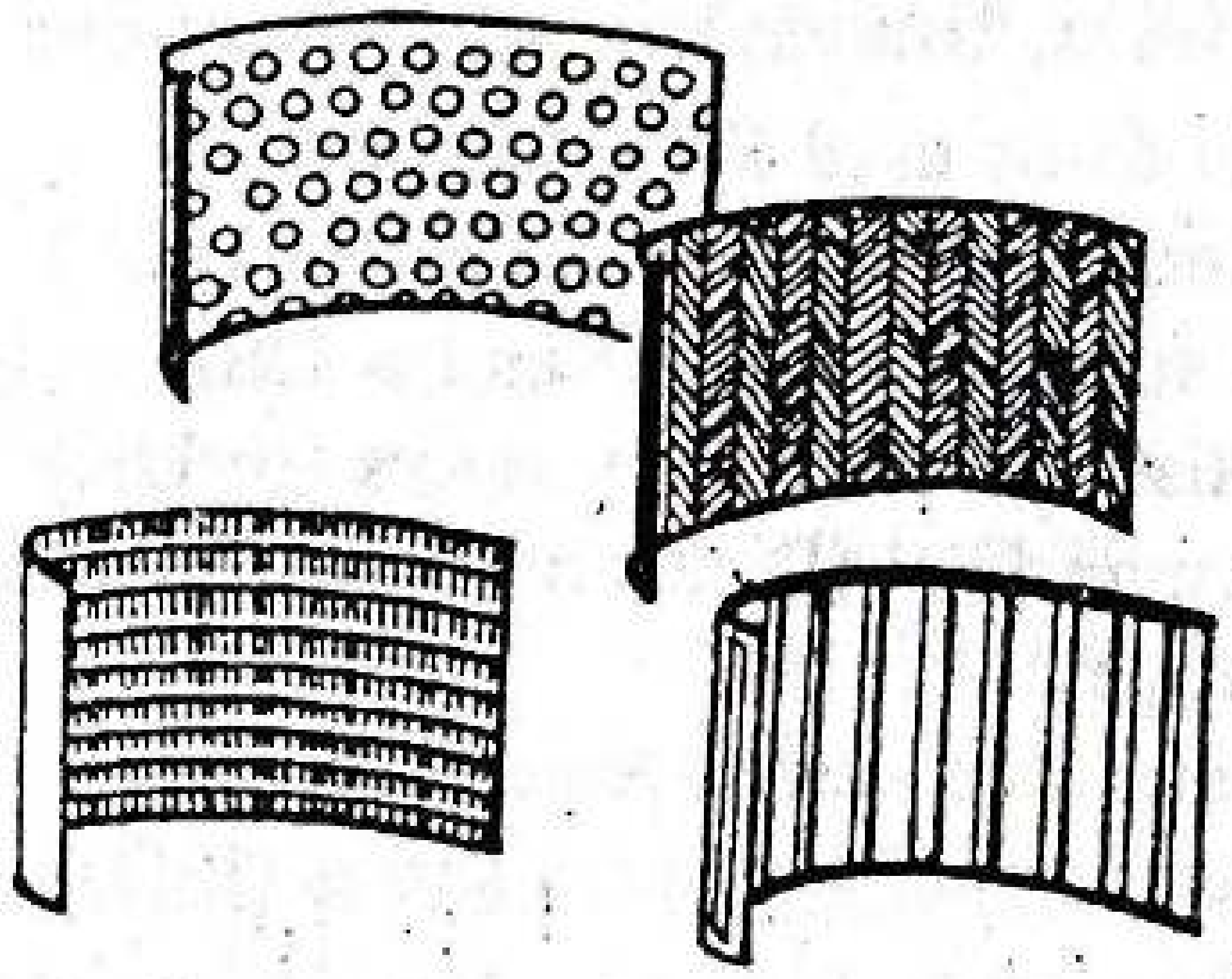


Figure 7-2. The configurations of punched plates or perforated screen.

TABLE 7-3

Applications of Various Mill Screen Configurations of Perforated Screens

Perforation shape	*Recommended use*	*Comments*
Round holes	Fibrous materials	Clogs more quickly; lower hole size is limited, because of structural strength.
Herringbone screen (slots)	Amorphous and crystalline materials	Slightly coarse powder than equal-diameter round perforations
Cross-slots	Amorphous materials and slurries with coarse particles	Same grind size as of equal sized round perforation; finer slot size attainable than round perforations.

Herringbone design : Herringbone design consists of a series of slotted holes repeated across the surface of the screen. These are made at an angle of 45 degrees to the length of the screen. It is preferred for grinding crystalline materials and for continuous operation. If the width of the slot is equal to the diameter of a round hole, it grinds the particles coarser than the round hole. This design should not be used for fibrous materials, as it is possible for fibres to align themselves along the slots and pass through with inadequate size reduction.

Cross-slot screens : In this type, openings are at right angles to the path travelled by milling mechanism. These are used for milling slurries, but not used for fine grinding in hammer mills as it clogs readily.

Standards of Sieves, Dimensions and Notations

Common standards used for sieves are:

- (a) Tyler standard sieve series (in USA)
- (b) US standard sieve series (in USA)
- (c) British standard sieve series (in UK)
- (d) German DIN (Deutsche Industrienormein) (in Germany and Europe)
- (e) IP standard sieve series (in India)
- (f) International test sieve series (ISO) (World wide)

Tyler and US standards can be interchangeable, since the difference between the two standards is less than the allowable tolerance in weaving of the screens. These are also known as *test sieves*. Sieves used for pharmacopœial testing must match with the following specifications:

1. **Number of sieve :** Sieve number indicates the number of meshes per linear length of 25.4 millimetres.
2. **Nominal size of aperture :** Nominal size of aperture indicates the distance between the two adjacent wires. It represents the side of a square aperture. IP 1996 gives the nominal mesh aperture size for majority of sieves in mm or in µm.
3. **Nominal diameter of the wire :** Wire mesh sieves are made from the wire having the specified diameter in order to give a suitable aperture size and sufficient strength to avoid distortion of the sieve.
4. **Approximate percentage sieving area :** This standard expresses the area of the mesh as a percentage of the total area of the sieve. It depends on the size of the wire used for any particular sieve. Generally, the sieving area is kept within the range of 35 to 40 per cent in order to give suitable strength to the sieve.
5. **Aperture tolerance average size :** Some variation in the aperture size is unavoidable. This variation is expressed as a percentage and is known as the *aperture tolerance average*. In fact, it is a limit given by pharmacopœia within which a particular dimension or average aperture size can be allowed to vary and still be acceptable for the purpose for which it is used. Fine meshes cannot be woven with the same accuracy as coarse meshes. Hence, the aperture tolerance average is lower for coarse sieves than the fine sieves.

According to IP 1996, a sieve must conform to the specifications given in Table 7-4.

TABLE 7-4
Standards for Sieves—Specifications

Sl no.	*Approximate sieve number*	*Approximate percentage sieving area*	*Nominal mesh aperture size (mm)*	*Tolerance average aperture size (± mm)*
1	4	55	4.0	0.13
2	6	51	2.8	0.09
3	8	48	2.0	0.07
4	10	46	1.7	0.06
5	12	41	1.4	0.05
6	16		1.0	0.03
7	—		µm	µm
8	22	37	710	25
9	25	36	600	21
10	30	38	500	18
11	36	36	425	15
12	44	38	355	13
13	60	37	250	13 (9.9)
14	85	35	180	11 (7.6)
15	100	36	150	9.4 (6.6)
16	120	34	125	8.1 (5.8)
17	150	36	106	7.4 (5.2)
18	170	35	90	6.6 (4.6)
19	200	36	75	6.1 (4.1)
20	240	34	63	5.3 (3.7)
21	300	35	53	4.8 (3.4)
22	350	34	45	4.8 (3.1)

Note : Figures in the brackets refer to close tolerance and those without brackets refer to full tolerance.

Comparison of Ideal and Actual Screens

An *ideal screen* would sharply separates the feed mixture in such a way that the smallest particle in the oversize would be just larger than the largest particle in the undersize.

Such an ideal separation defines a cut diameter, D_{pc} that makes the point of separation between the fractions. Usually, D_{pc} is chosen to be equal to the mesh opening of the screen.

An *actual screen* is the one, which does not give perfect separation about the cut diameter.

In an actual screen, the overlap between the smallest particle in oversize and the largest particle in undersize is more pronounced, when particles:

- are needle like, fibrous.
- tend to aggregate.
- tend to strike the screen surface endwise and pass through.
- tend to strike the screen sidewise and retained.

Commercial screens usually give poorer separations than testing screens of the same mesh opening when operated on the same mixture.

MODES OF MOTION IN SIZE SEPARATION

Screening is a method of separating particles according to size alone. The basic technique involved is passing the particles through a series of sieves of uniform size. In this, the particles drop through the openings due to gravity. Coarse particles can drop easily through large openings, but it is difficult to screen the fine powders. This process can be hastened by inducing some type (mode) of motion (movement) to the particles. Size separation is basically assisted by three methods.

1. **Agitation**
2. **Brushing**
3. **Centrifugal force**

These modes of shaking help to shake the material so that sieving will be quick and entire sieving area can be utilised.

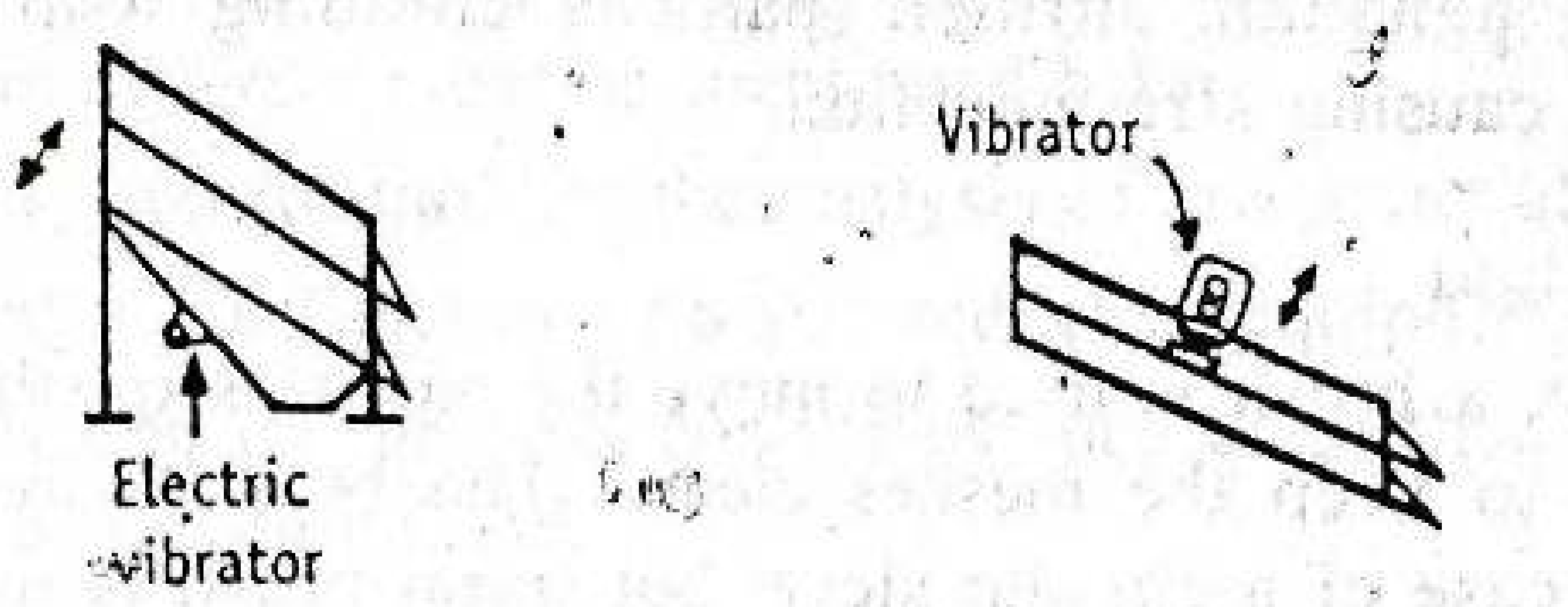
Agitation Method

Sieves are agitated in a number of ways. Some of them are discussed below.

Oscillation : The sieve is mounted in a frame that oscillates back and forth, i.e., reciprocal motion (Figure 7-3). It is a simple method, but the material may roll on the surface of the sieve. The motion is parallel to the plane of the sieve. The sieves can be slightly inclined. The reciprocating motion is induced by means of an ordinary eccentric on a rotating shaft.

Figure 7-3. Motion of screen, shaking (oscillations).

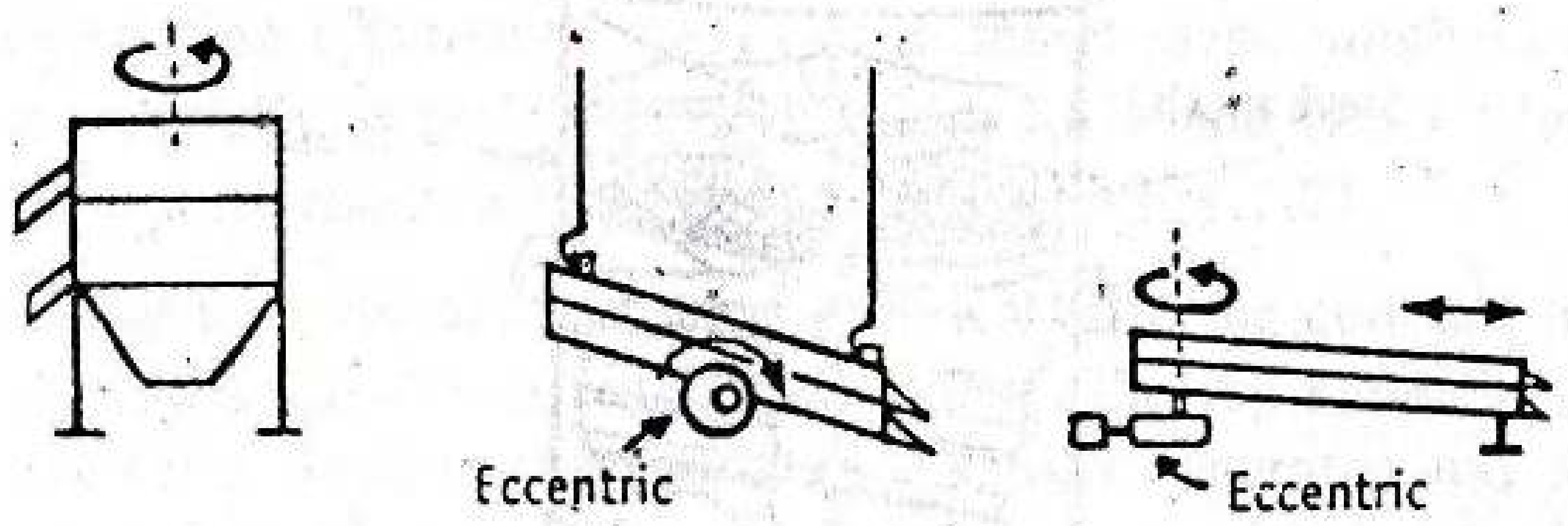
Vibration : The sieve is vibrated at high speed by means of an eccentric device (Figure 7-4) either electrically or mechanically. Rapid vibration is imparted to the particles that helps the powder to pass through the sieve. Electrically vibrated screens are particularly useful in the chemical industry. Example is hum-mer screen. They handle light, fine and dry materials successfully. Inducing vibrations also prevents blinding of meshes.



(a) Mechanically vibrated (b) Electrically vibrated

Figure 7-4. Motion of screens vibrating motion.

Gyration : In this method, a system is made so that sieve is on rubber mounting and connected to an eccentric flywheel (Figure 7-5). This gives a rotary movement of small amplitude to the sieve, which in turn gives spinning motion to the particles that helps to pass them through the sieve.



(a) Gyrations in horizontal plane (b) Gyrations in vertical plane (c) Gyration at one end, and shaking at other end

Figure 7-5. Gyratory motions of screens or sieves.

Gyratory screens are box like equipment, either round or square, with a series of screen cloths nested atop one another (Figure 7-5). Most gyratory screens have auxiliary vibrations caused by balls bouncing against the lower surface of the screen.

Agitation methods are not continuous methods. However, these can be made continuous by inclination of the sieves. Separate outlets are made for undersize and oversize particles. Normally, all the three modes of agitation are used simultaneously for an efficient size separation. Rotex screen works on this principle.

Advantages : (1) Agitation methods are inexpensive.

(2) Simple and rapid.

Disadvantages : (1) Agitation methods have lower limit of the particle size.

(2) If the powder is not dried, apertures become clogged with particles leading to improper sieving.

(3) During agitation, attrition (particles colliding with each other) occurs causing size reduction.

Brushing Method

In this case, a brush is used to move the particles on the surface of the sieve and to keep the meshes clear. The brush is rotated in the middle in the case of a circular sieve, but spiral brush is rotated on the longitudinal axis in case of horizontal cylindrical sieve. One example is brush sifter (Figure 7-6). This is used for size separation of greasy or sticky powders such as waxes and soaps.

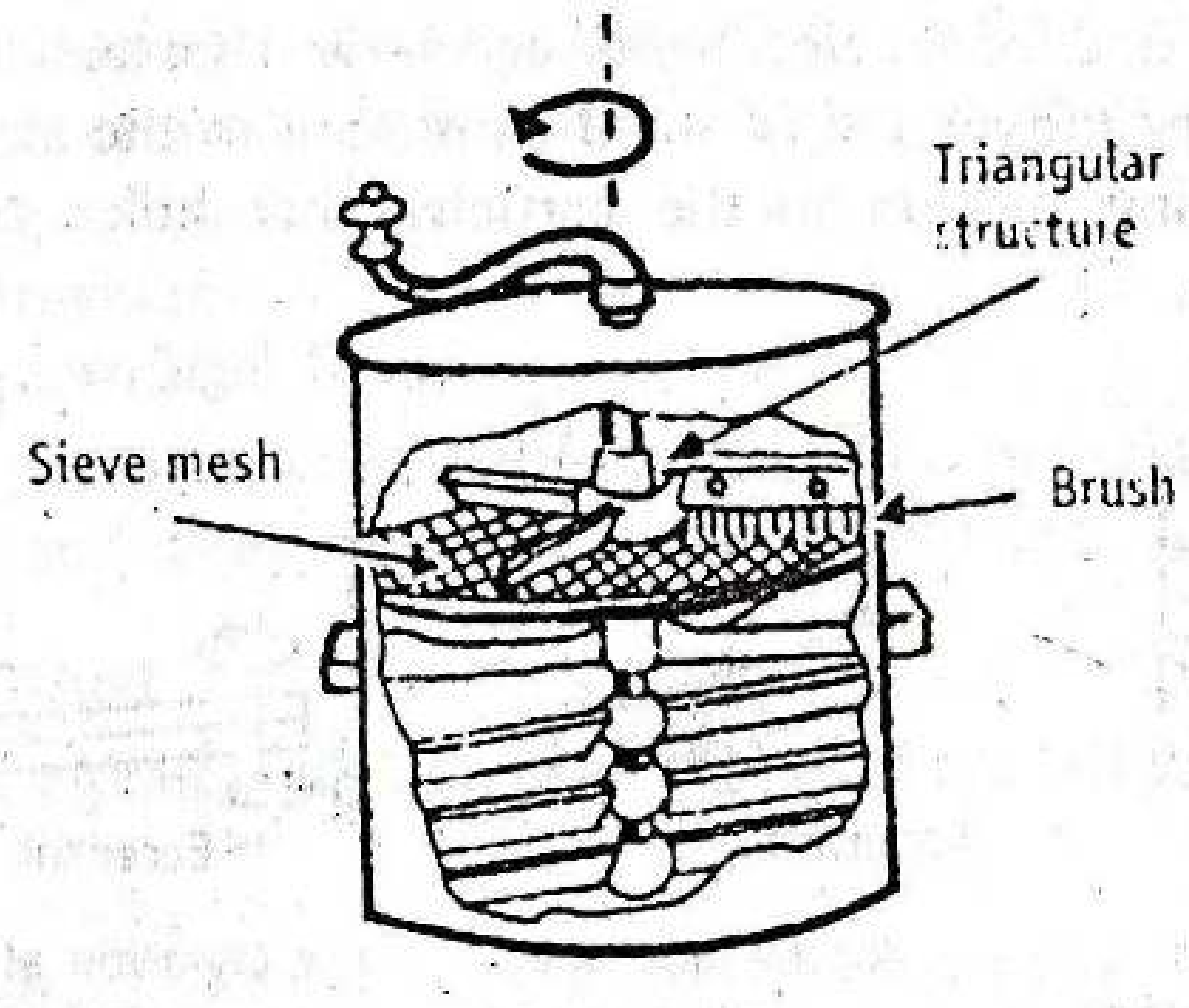


Figure 7-6. Brush sifter

Centrifugal Method

In this method, a high-speed rotor is fixed inside a vertical cylindrical sieve, so that on rotation the particles are thrown outwards by centrifugal force. The currents of air can be generated by means of a jet of air into the equipment, which helps in separating the particles. A few examples of equipment that work on this principle are cyclone separator and air separator.

Advantages : (1) Centrifugal methods are extremely useful in cases where conventional sieving tends to block the sieves.

(2) Extremely useful for fine powder, because sieves have the limitation of mesh size.

SIEVE ANALYSIS—TESTING OF POWDER

The milled material is subjected to size separation in order to obtain the powder of desired size or size distribution. Size distribution analysis is important in different areas as mentioned below.

- Quality control tool for the analysis of raw materials.
- Testing the efficiency of a size reduction equipment or process.
- Optimising the process conditions such as method of agitation, time of screening, etc.
- Selecting the sieve system for commercial equipment.

Errors can arise if the sieves are overloaded or if insufficient time is allowed for the particles to pass through.

Sieve Shaker Machine

Principle : The powdered drug is separated according to its particle size using a number of sieves in a nest. These are subjected to different types of agitation, so that size separation is rapid.

Construction : Standard sieves of different mesh numbers are available commercially as per the specifications of IP and USP. These sieves are fixed in a mechanical shaker apparatus (Figure 7-7).

Working : Sieves are arranged in a nest with the coarsest at the top. A sample (50 g) of the powder is placed on the top sieve (Figure 7-7). This sieve set is fixed to the mechanical shaker apparatus and shaken for a certain period of time (20 minutes). The powder retained on each sieve is weighed.

Practical considerations : Care should be taken in order to get reproducible results. The type of motion influences sieving; vibratory

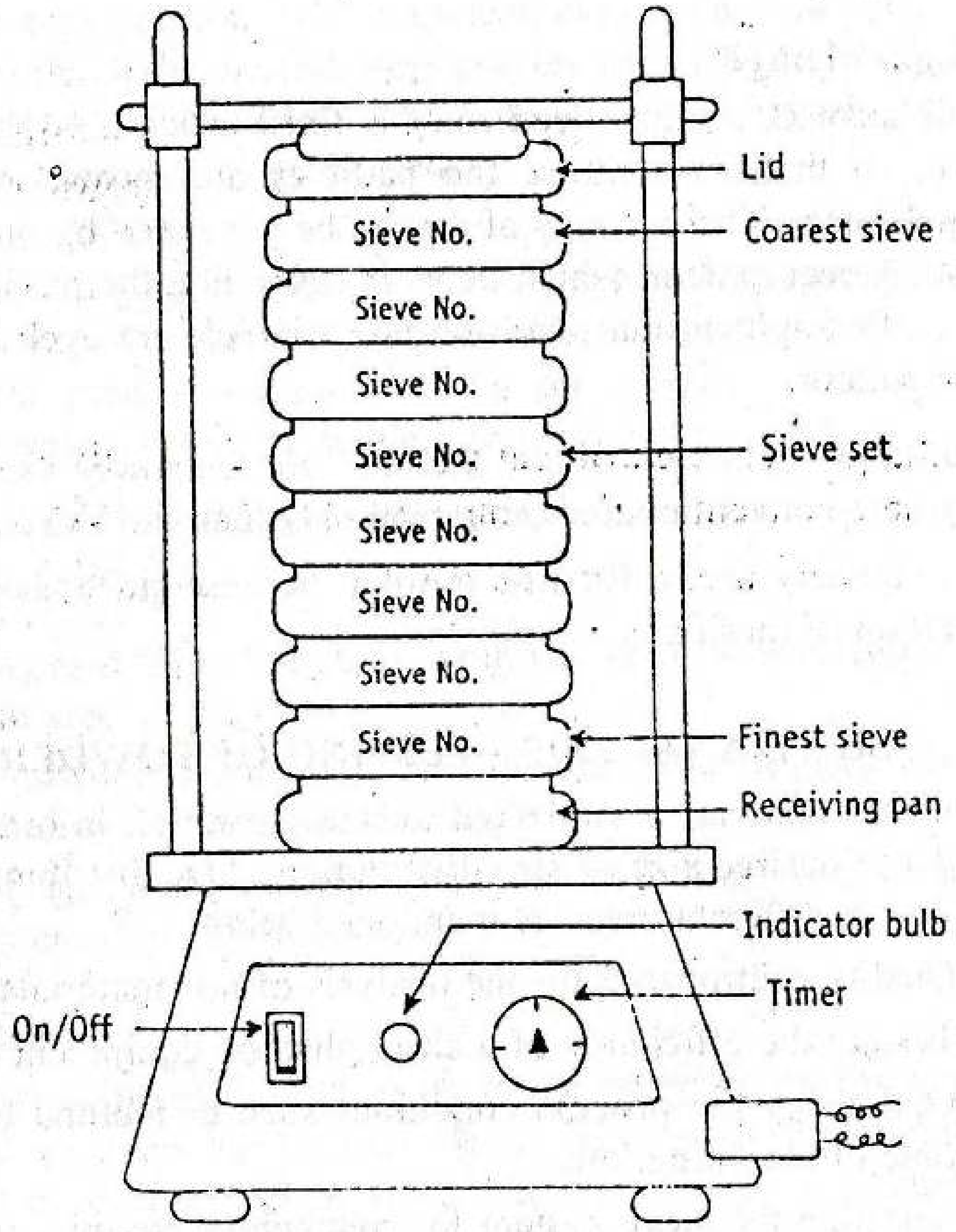


Figure 7-7. Laboratory sieve shaker machine.

motion is most efficient, followed by side-tap motion, bottom-pat motion, rotary motion with tap and finally rotary motion. The type of motion and intensity of the shaker are fixed and standardized. Shakers are commercially available.

Other factors are weight of the sample and duration of shaking. Sieves produced by photo-etching and electro-forming techniques are used to get a better estimate of the size distribution analysis with a lower limit of estimation of particle diameter 5 μm.

Advantages : It is inexpensive, simple and rapid with reproducible results.

Disadvantages : (1) Lower limit of particle size is 50 μm.

(2) If powder is not dry, apertures get clogged with particles, leading to improper sieving.

(3) During shaking, attrition (particles colliding with each other) occurs causing size reduction of particles. This leads to error in estimation.

Variants : *Electromagnetic sieve shaker*—It is useful for analysing powders under controlled conditions. *Sonic sifter* – This apparatus utilises sonic oscillations. A mechanical pulse action is used to reduce blinding and agglomeration in the sub-sieve sizes.

Alpine Airjet Sieve

Principle : In the Alpine airjet sieve, sieving action involves the application of a jet of air on one side of the sieve and suction on the other side. The material is maintained in a fluidised state on the screen by a stream of air. Vacuum is applied below the screen, so that the undersized powder is sucked through the sieve.

Construction : The construction of a Alpine airjet sieve is shown in Figure 7-8. It consists of a metal housing into which the sieve mesh is fitted. Sieve cover is placed in such a way that an air-tight seal is obtained. A slit is provided such that its upper edge is in level with the upper edge of the housing. Provision is made to pass airjet below the slit. Suction line is provided below the sieve, which can be controlled with the help of a manometer.

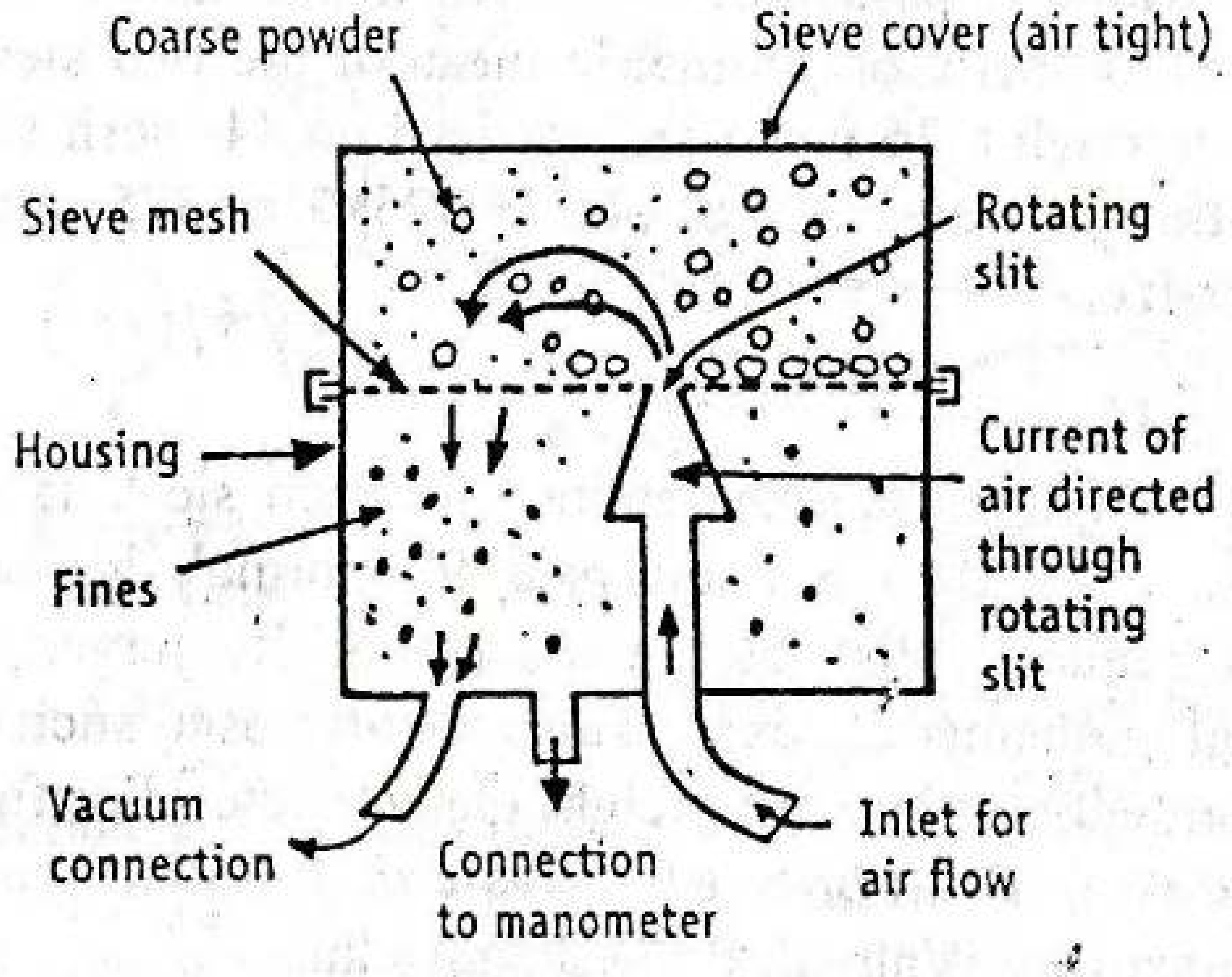


Figure 7-8. Construction of Alpine airjet sieve.

Working : A small amount of powder (about 10 g) is spread on the sieve. The cover is placed in position. The slit is set into rotation by sending a jet of air from below. The powder is fluidised in the upward jet of air. The suction is adjusted until the manometer reads about 27 kPa. The vacuum (in the interior of housing) sucks the undersized powder through the sieve. The material is recovered.

Sieving is continued for two minutes and the residual powder is weighed. This powder is transferred to the next sized mesh with a fine brush. This process is continued until all fractions are collected from the sample, by changing the sieve meshes as well as magnitude of the suction.

Uses : Alpine sieve method is used for the analysis of powder for its size distribution. This method is particularly useful in cases where conventional sieving tends to block the sieves below about 80 µm.

Advantages : (1) In Alpine airjet sieve, fluidisation of powder prevents blocking of the mesh.

(2) It is a rapid method and gives reproducible results.

(3) It is very useful for fine powders.

Disadvantages : (1) The capacity of Alpine airjet sieve is limited. Therefore, it is not useful for large-scale separations.

(2) This method is tedious, because each time only one particle size powder is obtained.

Data Presentation

Frequently a powder is assigned by a mesh number of the screen through which it passes or on which it is retained. It is expressed in terms of arithmetic or geometric mean of the two sieves, i.e., a powder passing through a 36 mesh and retained on 44 mesh sieve is assigned an arithmetic mean diameter of (425 + 325)/2 or 375 µm. This is reported as undersize.

Data Analysis

The weight of sample retained on each sieve is considered for the analysis. The data are analysed for normal, log-normal, cumulative percent frequency distribution and probability curves. Along with these, different mathematical expressions are also used such as average particle diameter, geometric mean weight diameter etc. For further analysis refer the book, "*Textbook of Physical Pharmaceutics*" by C.V.S. Subrahmanyam, Vallabh Prakashan, Delhi.

EQUIPMENT FOR SIZE SEPARATION

A wide variety of equipment have been developed differing in the scale of operation, ruggedness, method of movement of material and

material of construction. The modes of size separation are discussed earlier. Some factors to be considered are:

(a) wear of the sieves.

(b) blinding.

(c) machine noise.

General Classification of Screening Equipment

The screening or sieving machines may be divided into different classes.

1. *Grizzles* : For coarse materials above 50 mm — large lumps.
2. *Revolving screens* : Separations above 13 mm — trommels.
3. *Shaking screens* : Separation from 13 mm down wards to fines.
4. *Vibrating screens* : Coarse size (13 mm) to fines.
5. *Oscillating screens* : Fine mesh size.
6. *Fluidised systems* : For very fine powders.

Some important equipment are described below.

Shaking Screen

Principle : Particles of different sizes are separated by passing them through a sieve, which oscillates to and fro continuously.

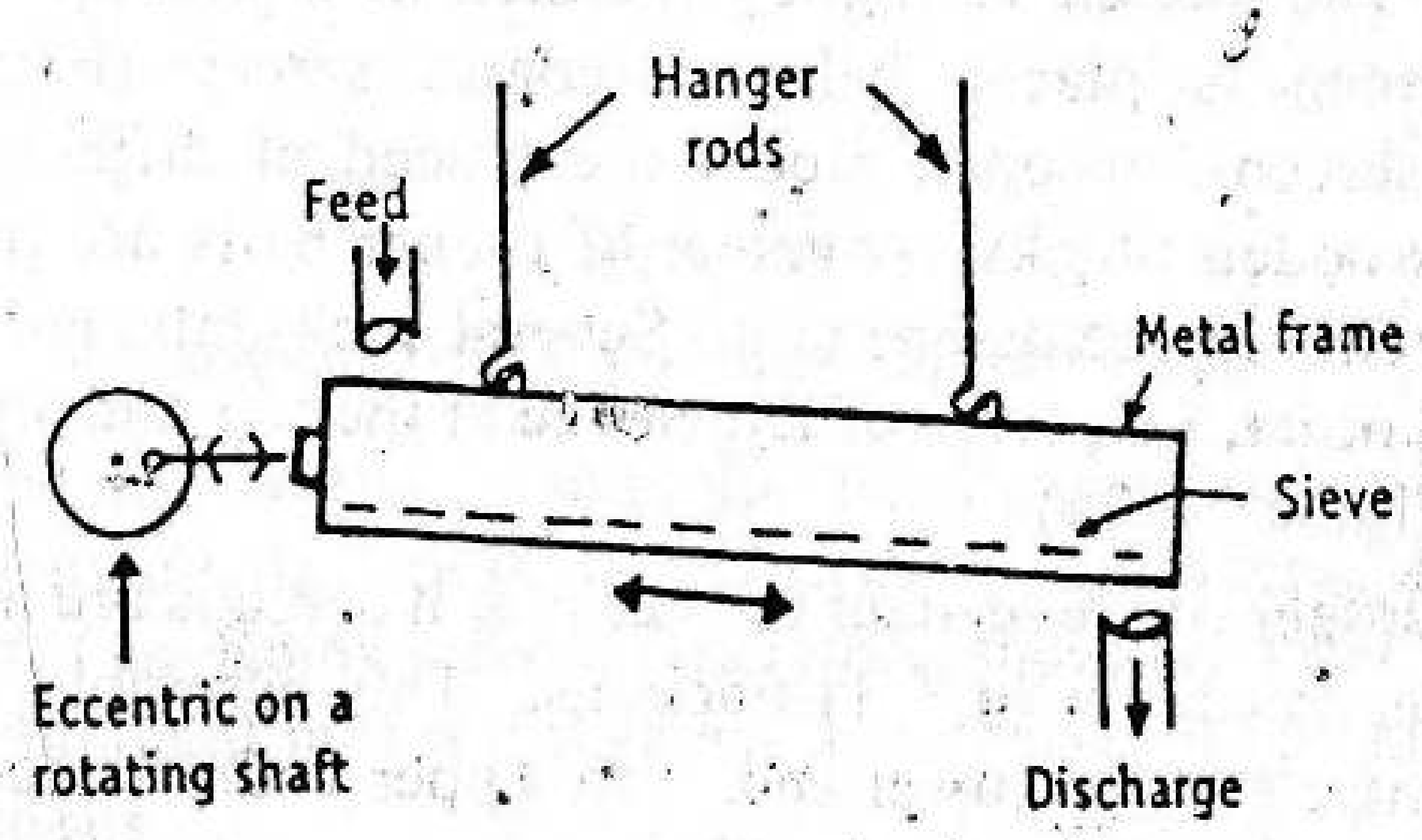


Figure 7-9. Construction of shaking screen in inclined position.

Construction : The construction of a shaking screen is shown in Figure 7-9. Shaking screen consists of metal frame to which a screen is fixed at the bottom. The screen cloth may be riveted directly or fitted using a removable bolted frame. The metal frame can be arranged horizontally or in inclined position. It is suspended by means of hanger rods, so that it can move freely. The side of the metal frame is connected to an ordinary eccentric on a rotating shaft. The entire frame can experience reciprocating motion.

Working : The screen is allowed to shake in a reciprocating motion. The feed (material to be screened) is introduced on to the screen from a side. Therefore, fine particles get screened off initially. The remaining material moves forward during the motion of the frame and gets separated. Thus, the desired size particles can be obtained from the material.

The **advantages** of shaker screen are that it requires low head-room and low power requirement.

The **disadvantages** are that shaker screen requires high cost of maintenance of screens and supporting structures. Its capacity is low.

Variants : The above screen system may be vibrated to keep the particles moving and to prevent blinding. It is used when large capacity and high efficiency is desired.

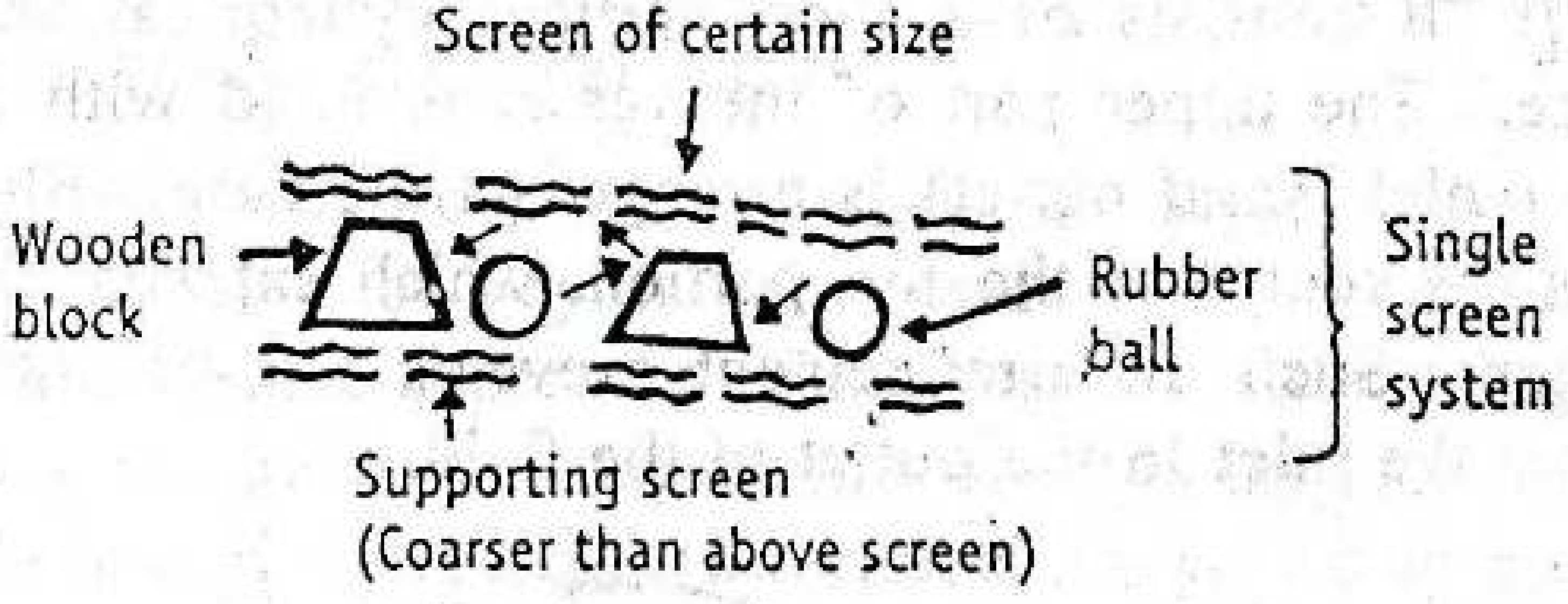
Rotex Screen

Principle : Rotex screen works on oscillating agitation (back and forth) by means of an eccentric mechanism. Further, vibrations are caused by balls bouncing against the lower surface of the screen cloth. This rapid motion helps the particles to roll on the surface of the screen and separate out.

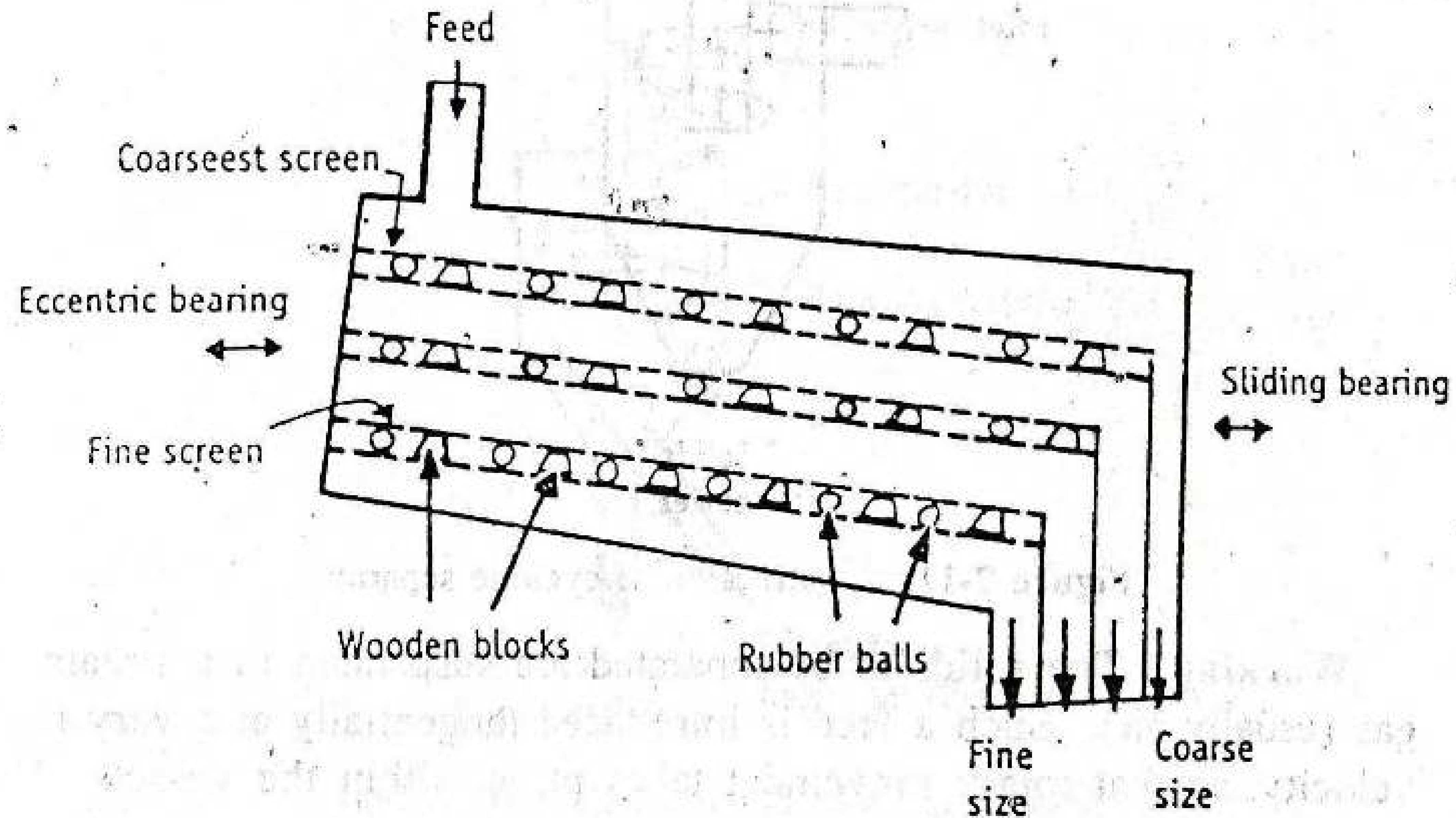
Construction : The construction of a Rotex screen is shown in Figure 7-10. The screen is slightly inclined at 5 degrees. A coarser supporting screen is placed below a coarse screen (Figure 7-10a). Between the screens, wooden blocks are placed at different intervals. Between the wooden blocks, a number of rubber balls are placed. This two-sieve system represents one unit. Several such units are arranged in the desending order, i.e., sieve of larger size at the top and smaller one at the bottom (Figure 7-10b).

If more number of sieve sizes are desired, n screens are arranged in a similar manner to obtain (n + 1) fractions. This assembly is supported on sliding contacts at the lower end. The upper end of screen system is connected to an eccentric pin on a flywheel.

Working : The screen system is allowed to agitate with the help of eccentric. The shaking motion of the screen causes balls to fly between the screens. As they strike the inclined sides of the wooden blocks, the balls deflect upward and strike the underside of the screening cloth and thus prevent the blocking of the mesh (Figure 7-10a). The feed is introduced at the elevated end of the screen. The material passes through the upper screen and reaches the next screen. This process continues until all the material is separated into fractions. The fractions are collected separately at the outlet point.



(a) Unit sieve system



(b) Assembly

Figure 7-10. Construction of Rotex screen.

Uses : Rotex screen is used for handling a variety of chemicals usually dry materials. Granular matrices and powdered foods are also size separated by Rotex screen. Therefore, these are used extensively as standard equipment in many chemical and processing plants for handling fine separations.

Cyclone Separator

Principle : In cyclone separator, centrifugal force is used to separate the solids from fluids. The separation process depends not only on the particle size, but also on the density of particles. Depending on the fluid velocity, the cyclone separator can be used to separate all types of particles. It is also possible to allow fine particles to be carried by the fluid.

Construction : The construction of a cyclone separator is shown in Figure 7-11. It consists of a short vertical, cylindrical vessel with a conical base. The upper part of the vessel is fitted with a tangential inlet. The outlet (solid outlet) is arranged at the base. Fluid outlet is provided at the centre of the top portion, which extends inwardly into the separator. Such an arrangement prevents the air short-circuiting directly from the inlet to the outlet of the fluid.

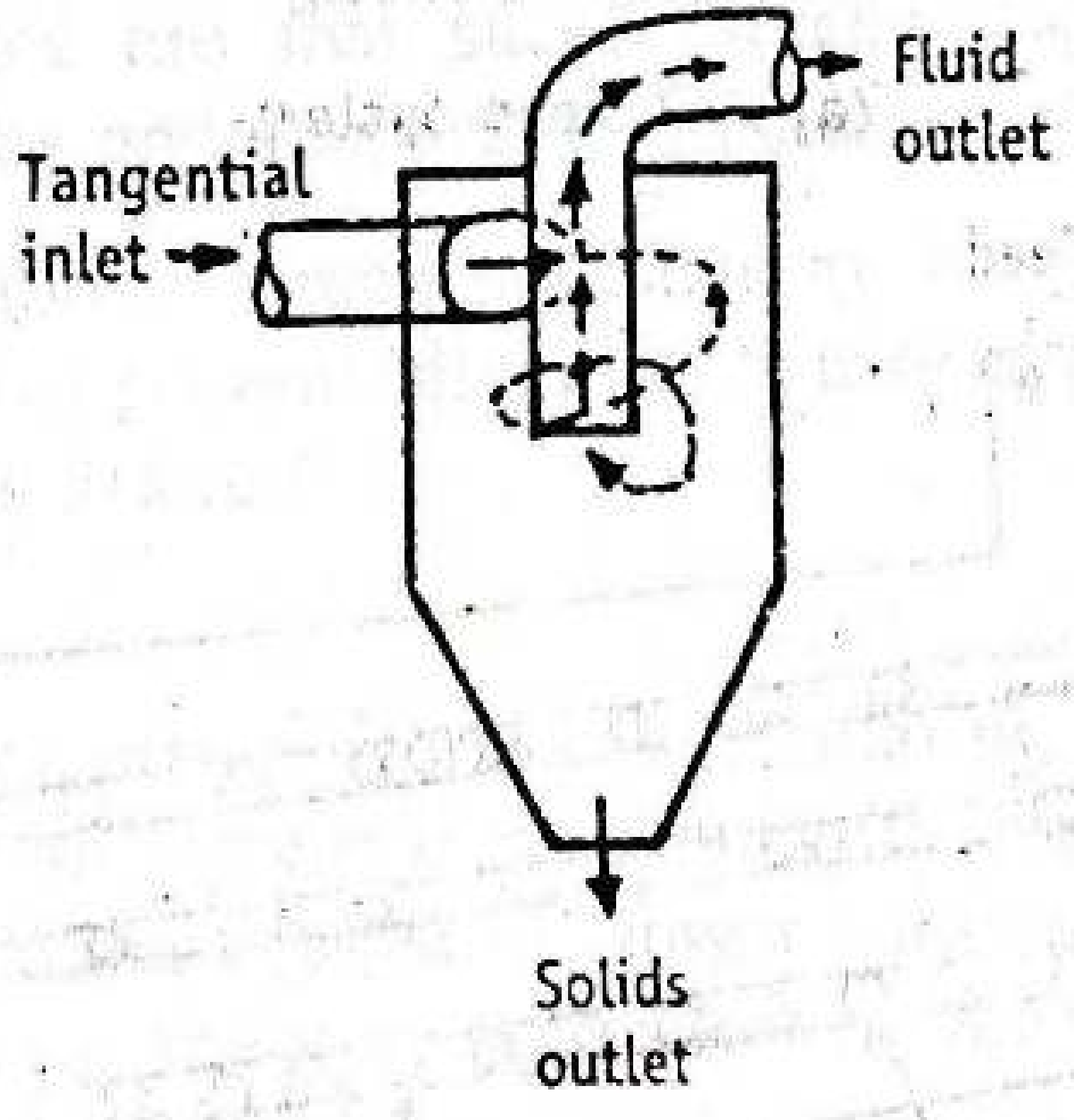


Figure 7-11. Construction of cyclone separator.

Working : The solids to be separated are suspended in a stream of gas (usually air). Such a feed is introduced tangentially at a very high velocity, so that rotary movement takes place within the vessel. The centrifugal force and vortexing throws the solids to the walls. As the speed of air diminishes, the particles fall to the conical base and are discharged through the solid outlet. The fluid (air) can escape from the central outlet at the top.

Uses : (1) Cyclone separator is used to separate the solids from gases.
(2) It is also used for size separation of solids in liquids.
(3) It is used for separating the heavy or coarse fraction from fine dust.

Variants : Cyclone separators are also used for size separation of solids suspended in a liquid such as water. Such separators are known as *wet or liquid cyclone*. One such apparatus used for this purpose is *Dorrclone*.

Air Separator

Principle : In air separator, centrifugal force is used to separate solids. The air environment is obtained by means of rotating disc and blades. To improve the separation, stationary blades are used. By controlling these blades and the speed of the rotation, it is possible to vary the size at which separation occurs.

Construction : The construction of an air separator is shown in Figure 7-12. It consists of a cylindrical vessel with a conical base. The feed inlet is fitted to the upper part of the vessel. The rotating disc and rotating blades are attached to the central shaft to produce air environment. At the base of the vessel, two outlets are provided; one for fine particles and the other for heavy particles.

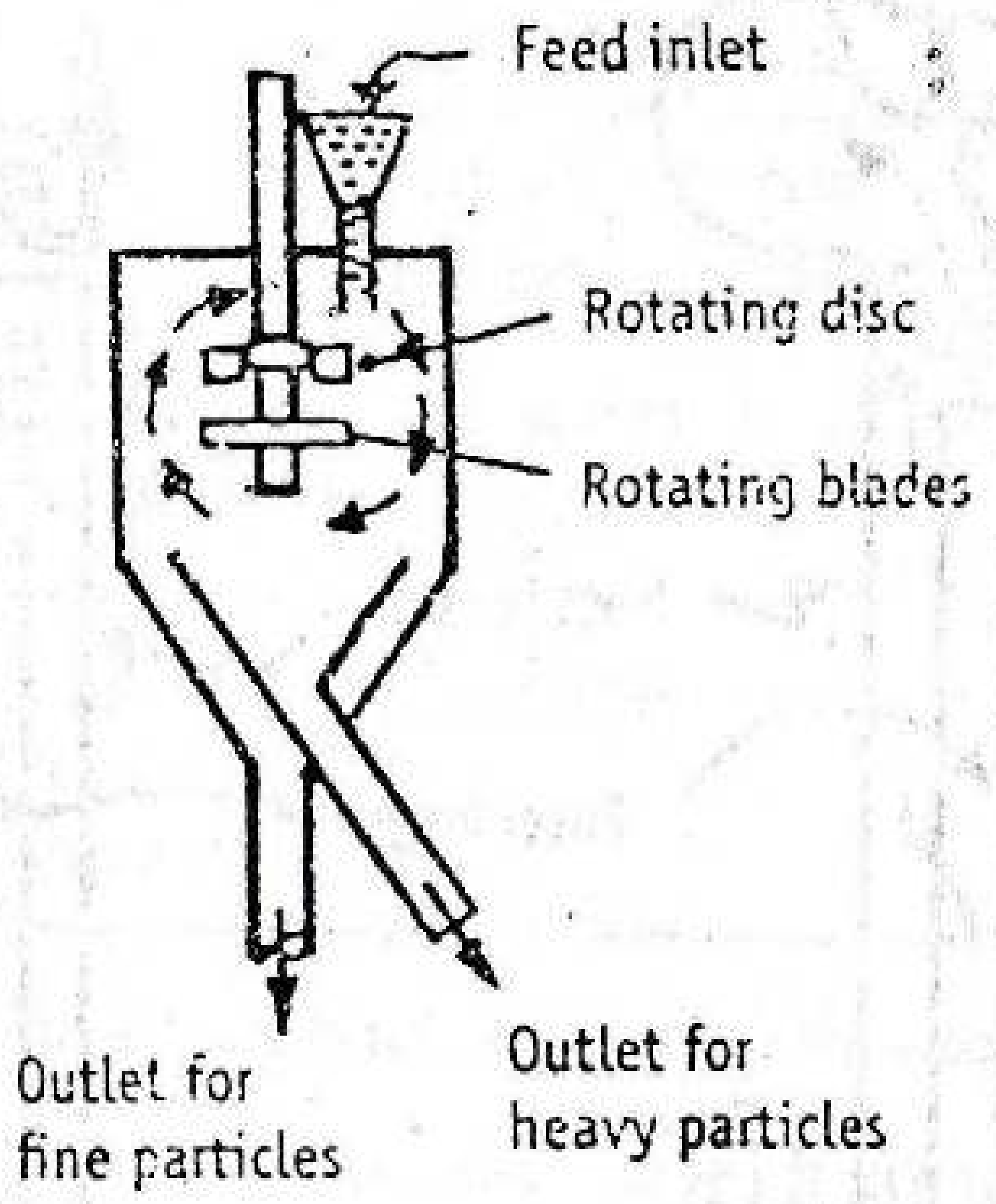


Figure 7-12. Construction of air separator.

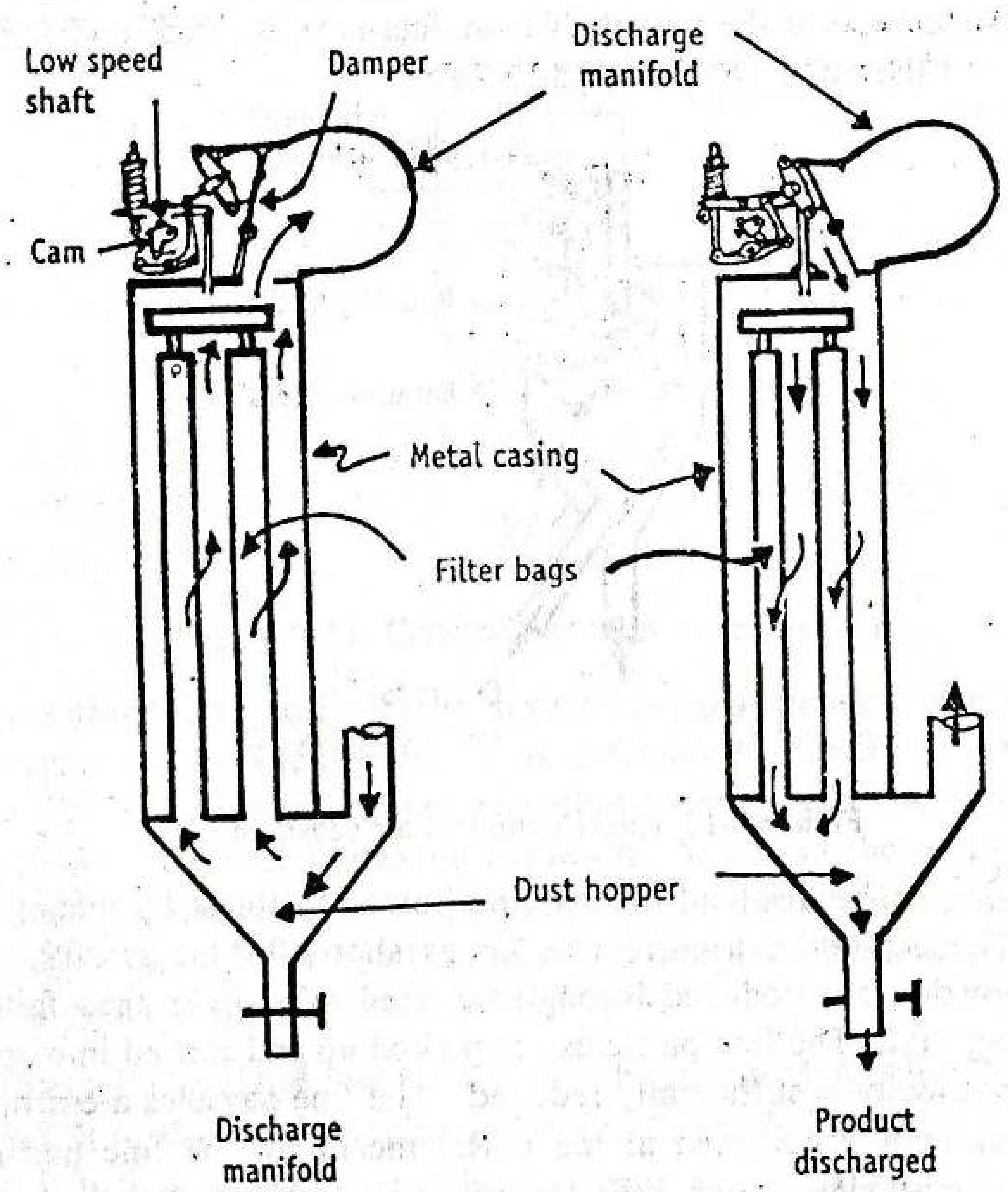
Working : The disc and blades are allowed to rotate by means of a motor. These produce a current of air as shown by the arrows. The sample powder is introduced through the feed inlet. The feed falls on the rotating disc. The fine particles are picked up and carried into space, where air velocity is sufficiently reduced. The fine particles are dropped and are ultimately collected at the outlet meant for the fine particles. The heavy particles, which fall downward, are removed at the outlet meant for heavy particles.

Uses : Air separators are often attached to the ball mill or hammer mill to separate and return over sized particles for further size reduction.

Bag Filter

Principle : In a bag filter, size separation of fines (or dust) from the milled powder is achieved in two steps. In the first step, the milled powder is passed through a bag filter (cloth) by applying the suction on the opposite side of the feed entry. This facilitates the separation. In the next step, pressure is applied in order to shake the bags so that powder adhering to the bag falls off, which is collected from the conical base.

Construction : The construction of a bag filter is shown in Figure 7-13. It consists of a number of bags made of cotton or wool fabric. These are suspended in a sheet metal container.



(a) Filtering period (b) Shaking period

Figure 7-13. Construction of bag filter.

A hopper is arranged at the bottom of the filter to receive the feed. At the top of the metal container, a provision is made for the exhaust. Adjacent to this, a bell crank lever arrangement is made to bring the filters to normal atmospheric conditions.

Working : The working of the bag filter consists of two steps. In the first step, the feed is separated from air by passing it through the cloth bags. In the subsequent step, the bags are shaken to collect the fines that are adhered to the bags. These two steps follow in succession and are controlled at different intervals with the help of a bell crank lever arrangement.

Bell crank lever arrangement : In this mechanism, a shaft with a cam is allowed to rotate at a low speed. During rotation, the cam can either press the bell crank lever or does not come into contact. Depending on this mechanism, the damper changes its position. The damper is a useful mechanism, which allows the two steps to occur as shown below.

		Movement of damper	
Step	*Mechanism*	*Contact between bags and suction*	*Contact between bags and atmosphere*
Filtering period	Cam does not press the bell crank lever (Figure 7-13a)	opens	closes
Shaking period	Cam presses the bell crank lever (Figure 7-13b)	closes	opens

These changes occur at intervals of a few minutes.

Filtering period : The exhaust fan positioned at the top keeps the bags under less pressure than atmospheric pressure. The gas containing fine particles (or dust) enters the hopper, as shown with arrows in Figure 7-13a, and passes up. The gas feed passes through the fabric of bag. During this process, the fines (or dust) are retained in the bags, while the gas reaches the top of the casing. Because of air, the bag remains taut during filtering operation.

Shaking period : Since vacuum is cut off in the chamber, air from outside enters the casing and passes through the bags. This results in violent shaking of the bags, so that the dust and fine particles are displaced from the bags and falls into the conical base. It is then removed at intervals.

Such devices are entirely automatic in their action and can be designed to affect very large filtering surface per unit floor space.

Uses : Bag filters are used along with other size separation equipment, for example, a cyclone separator. Bag filters are used to remove the fines from cyclone discharge. Bag filter is connected to the discharge end of the fluidized energy mill.

Advantages : (1) Bag filter is extremely useful for removing fines, which cannot be separated by other methods.

(2) These can be used even to remove dust. The ordinary household vacuum cleaner is a simple bag filter.

Disadvantage : Bag filter is not size separation equipment as such.

QUESTION BANK

Each question carries 2 marks

1. Name the standards of screens used in pharmaceutical practice.
2. What are standard sieves?
3. Differentiate ideal and actual screens.
4. List the specifications and standards for sieves.
5. Explain the term blinding of screen. How is it prevented?
6. What are various grades of coarse powders? Define them.
7. Give the classification of fine powders with definitions.
8. What are the advantages of expressing sieves by a sieve number over the nominal size of aperture?
9. Differentiate the terminology, nominal size of aperture and nominal diameter of the wire.
10. What are the uses of screen analysis? How is it expressed?
11. List the methods of sieve analysis used for testing the powders. Give their relative advantages.

Each question carries 5 marks

1. Explain the working of a cyclone separator and its usefulness.
2. Describe the method of size separation using a Rotex shaker screen.
3. Explain various grades of powders official in pharmacopœia.
4. Give details about the various standards fixed by the pharmacopœia for sieves.
5. Describe the specifications of standard sieves as per IP.

Each question carries 10 marks

1. Describe one industrial method for size separation of a powder and its applications.

8

Mixing

Section I—MIXING OF SOLIDS

Interparticle Interactions-Segregation
Mechanism of Mixing in Solids
Mixing Process-Steps
Degree of Mixing and Statistical Evaluation
Factors Influencing Mixing
Classification of Equipment for Solids Mixing Equipment

Mixing is defined as a process that tends to result in a randomization of dissimilar particles within a system.

The term *mix* means to put together in one mass or assemblage with more or less thorough diffusion of the constituent elements among one another. The term *blending* means to mix smoothly and inseparably together. During blending a minimum energy is imparted to the bed. These terms are commonly used interchangeably in the industry.

Some of the mixing operations in the dispensing practice are spatulation, trituration, tumbling, geometric dilution etc. However, industrial pharmaceutical mixing involves large-scale equipment. A major complication in the intimate mixing of particles is the segregation of particulate solids that results from gravitational effect on the agitated bed. Mixing can also be achieved by milling, kneading etc.

The diverse characteristics of particles, such as size, shape, volume, surface area, density, porosity, flow and charge, contribute to the solid mixing. It is difficult to predict the inter-particle interactions. Therefore, some empirical correlations are possible. In practice, optimum mixing is considered satisfactory.

Depending on their flow properties, solids are divided into two classes; cohesive and noncohesive. *Noncohesive materials* such as grain, dry sand and plastic chips readily flow out of a bin or silo.

8

Mixing

Section I—MIXING OF SOLIDS

Interparticle Interactions-Segregation
Mechanism of Mixing in Solids
Mixing Process-Steps
Degree of Mixing and Statistical Evaluation
Factors Influencing Mixing
Classification of Equipment for Solids Mixing
Equipment

Mixing is defined as a process that tends to result in a randomization of dissimilar particles within a system.

The term *mix* means to put together in one mass or assemblage with more or less thorough diffusion of the constituent elements among one another. The term *blending* means to mix smoothly and inseparably together. During blending a minimum energy is imparted to the bed. These terms are commonly used interchangeably in the industry.

Some of the mixing operations in the dispensing practice are spatulation, trituration, tumbling, geometric dilution etc. However, industrial pharmaceutical mixing involves large-scale equipment. A major complication in the intimate mixing of particles is the segregation of particulate solids that results from gravitational effect on the agitated bed. Mixing can also be achieved by milling, kneading etc.

The diverse characteristics of particles, such as size, shape, volume, surface area, density, porosity, flow and charge, contribute to the solid mixing. It is difficult to predict the inter-particle interactions. Therefore, some empirical correlations are possible. In practice, optimum mixing is considered satisfactory.

Depending on their flow properties, solids are divided into two classes; cohesive and noncohesive. *Noncohesive materials* such as grain, dry sand and plastic chips readily flow out of a bin or silo.

Cohesive materials such as wet clay are characterised by their resistance to flow through openings.

There are significant differences between solid mixing and liquid mixing. These are given below.

Liquid mixing	*Solid mixing*
Flow currents are responsible for transporting unmixed material to the mixing zone adjacent to impeller.	Flow currents are not possible.
Truly homogeneous liquid phase can be observed	Product often consists of two or more easily identifiable phases.
Small sample size is sufficient to study degree of mixing	Large sample size is required
Mixing requires low power	Mixing requires high power

Applications

Mixing is one of the most common pharmaceutical operations. It is involved in the preparation of many types of formulations. Mixing is also an intermediate stage in the production of several dosage forms.

- Wet mixing in the granulation step in the production of tablets and capsules.
- Dry mixing of several ingredients ready for direct compression as in tablets.
- Dry blending of powders in capsules, dry syrups and compound powders (insufflations).
- Production of pellets for capsules.

In the manufacture of tablets, normally a number of additives are added. Therefore mixing of powders becomes an essential part of the process. When the dose of the active substance is high (for example paracetamol tablets) mixing is not a problem. But in case of potent drugs and low dose drugs, high amounts of adjuvants (for example lactose) are added. Therefore, mixing is considered as a critical factor. Otherwise, content uniformity of tablets does not confirm to the pharmacopœial specifications. Similarly weight variation increases.

Mixing of cohesive materials is even more difficult due to formation of aggregates and lumps. Wet mixing is also encountered in pharmacy as an individual operation or as a subsequent step after dry blending. In several situations, these operations are carried out in a vessel and by some mixing element. Hence, this section describes some aspects of theoretical considerations and equipment for dry as well as wet mixing.

INTERPARTICLE INTERACTIONS—SEGREGATION

The particle characteristics such as size, size distribution, shape and surface influence the interparticle interactions in a powder bed.

Inertial Forces

Inertial forces tend to hold neighbouring particles in a fixed relative position. These are van der Waals, electrostatic and surface forces. A special mention of surface forces is relevant.

Surface (or interface) forces : The cohesive forces prevent intimate mixing owing to interaction of their surfaces (or interfaces). Frictional forces also resist the movement of particles so that they tend to form lumps. These depend on surface area, surface roughness, surface polarity, surface charge and adsorbed substances such as moisture. During mixing, the particles develop surface charges. Surface charges produce particle-particle repulsions, which make random mixing impossible. For effective mixing, surface to surface interactions should be minimal, which can be achieved by surface treatment.

Segregation occurs due to the following reasons.

(1) Poor flow properties of the powder bed inside a blender.

(2) Wide differences in particle sizes in a dry mixture.

(3) Differences in the mobilities of individual ingredients.

(4) Differences in particle density and shape to a lesser extent.

(5) Transporting stage, pouring the powder from one container to another (hopper or drums), or emptying the container.

(6) Dusting stage, fine particles become air borne and separate from the bulk of the powder.

Segregation may occur even after the mixing.

Gravitational Forces

Gravitational forces tend to improve the movement of two adjacent particles or groups of particles. Tumbling action promotes the interparticulate movement due to gravitational forces.

Motion of particles can result from direct contact with the mixer surface or/and from contact with one another. These processes accelerate the movement of translational and rotational modes of single particle or groups of particles. When particle-particle collisions occur, exchange (transfer) of momentum is achieved. Continuous exchange or distribution of momentum between translational and rotational modes is necessary for effective mixing. The efficiency of momentum transfer depends on:

(1) Elasticity of the collisions—If collisions are elastic, effective transfer of momentum does not take place. The loss due to inelasticity should be minimal.

(2) Coefficient of friction—Particles with high coefficient of friction will be likely to exchange rotational momentum more readily.

(3) Surface area of contact—The larger the surface area of contact, greater the exchange of momentum.

(4) Surface roughness—The surface 'roughness' of the particles involved in collisions determines the distribution of the transferred momentum between translational and rotational modes.

(5) Centrifugal forces—These act on rotating aggregates to break them into smaller units and aid in mixing process.

MECHANISMS OF MIXING IN SOLIDS

Segregation of particles occurs due to a number of reasons. Mixing can prevent it. The principal mechanisms in solid-solid mixing are:

Convective Mixing

It is achieved by the inversion of the powder bed using blades or paddles or screw element.

A large mass of material moves from one part to another. Convective mixing is referred to as *macromixing*.

Shear Mixing

In this type, the forces of attraction are broken down so that each particle moves on its own between regions of different composition and parallel to their surfaces.

In a particulate mass, the forces of attraction are predominating, which make the layers slip over one another. Such types of attraction forces are predominant among same type of particles. Shear forces reduce these attractions and reduce the scale of segregation.

Diffusive Mixing

It involves the random motion of particles within the powder bed, thereby particles change their positions relative to one another.

Diffusive mixing occurs at the interfaces of dissimilar regions. Diffusion is sometimes referred to as *micromixing*.

The motion of particles to achieve random distribution assumes that no other factor influences the distribution. This is rarely the case. Instead, a number of properties of the powders influence the approach to randomness. Flow characteristics of powders largely determine the ease with which the primary particles can be mixed.

MIXING PROCESS—STEPS

In the solid-solid mixing operation four steps are involved. These are:

1. Expansion of the bed of solids.
2. Application of three-dimensional shear forces to the powder bed.
3. Mix long enough to permit true randomization of particles.
4. Maintain randomization (no segregation after mixing).

When dry materials are loaded into a mixer, they form a static bed. This bed expands sufficiently when mixing is initiated. Therefore, there should be enough void space in the mixer after it is charged with the ingredients.

The shear force produces movement of particles. This is accompanied by expansion of powder bed. The stress induces the movement of particles in three directions. This turbulent movement of particles can achieve randomization. If the forces are inadequate, particle agglomerates move together leading to poor mixing.

Mixing is expected to produce random distribution of particles. It depends on the probability that an event happens in a given time. The law of mixing appears to follow a first order.

$$M = A\,(1 - e^{-kt}) \qquad (1)$$

where M = degree of mixing after time t
t = time, min
A and k = constants

The constants A and k depend on the mixer geometry, physical characteristics of the powders and proportion of the material being mixed.

Initially the rate of mixing is rapid. At a later stage the rate decreases. Since the rate process is first order (asymptotic), perfect mixing is not attainable, i.e., it takes infinite time. Empirically the best mixing time would be 30 to 35 minutes. Once the desired mixture has been achieved, the process should be stopped.

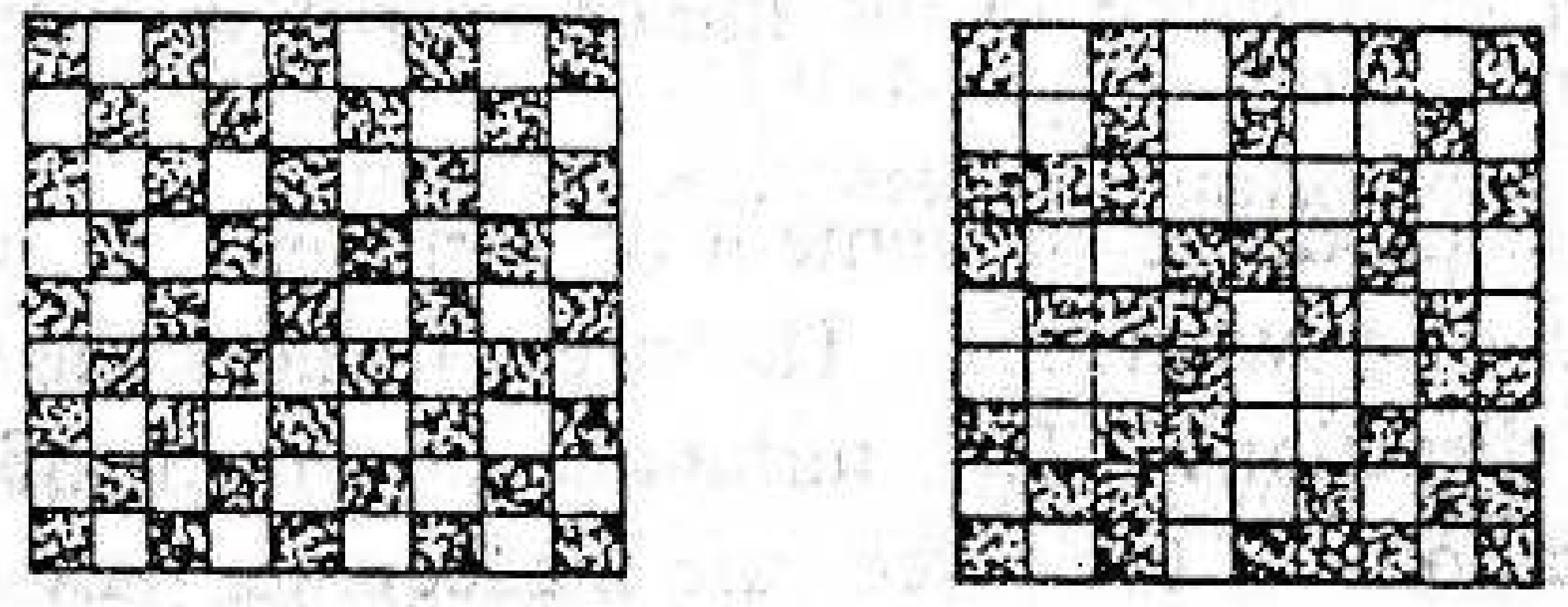
Once mixing is stopped, the blend should exist in static equilibrium. Subsequent handling of the mixture should be so as not to disturb the static equilibrium.

DEGREE OF MIXING AND STATISTICAL EVALUATION

Degree of mixing is also known as *degree of homogeneity*. After mixing, the best possible degree of mixing can be achieved provided each particle moves freely to every spot of the equipment. It requires the movement of particles in three directions. The degree of mixing must be considered for the purpose of economics. Time of mixing should be long enough to obtain an acceptable randomisation.

Ideal Mixing or Perfect Mixing

As illustrated by equation (1), the mixing process will never yield an *ideal* or *perfect* mixture. Ideal degree of mixing is represented schematically in Figure 8-1a by a chessboard with black and white squares representing two components (equal quantities). It indicates that each particle of one component is lying nearly adjacent to a particle of another component. In practice, degree of mixing is indicated by its standard deviation.



(a) Perfect mix (b) Randomized mix

Figure 8-1. Types of binary mixtures.

Acceptable Mixing

Since perfect mixing can not be achieved, other alternatives for obtaining an acceptable mix must be considered.

Random mixing : It is indicated by random distribution of particles as shown in Figure 8-1b. *Random mixing* means same ratio of components in the entire mixture. Artificial randomization in the Figure 8-1b is based on random numbers in statistical tables. However, it should be noted that the use of random motion to achieve random distribution assumes that no other factor influences the distribution. This is rarely the case. Instead a number of properties of the powders being mixed influence this approach to randomness.

Ordered mixing : Ordered mixing is described as the use of mechanical, adhesional and coating forces. Ordered units in the mix should be such that ordered unit will be the smallest possible sample to the mix. It will be nearly identical in composition to all other ordered units in the mix.

Ordered mixing probably yields the closest situation of the perfect mix. This can be achieved by a number of ways.

(1) Mechanical means of ordered mixing : The mass of each ingredient is divided and recombined a number of times in the powdered bed (Figure 8-2). The smaller the units, the more uniform the mix. Since no particulate adhesion is present, segregation of the mix easily takes place on further handling.

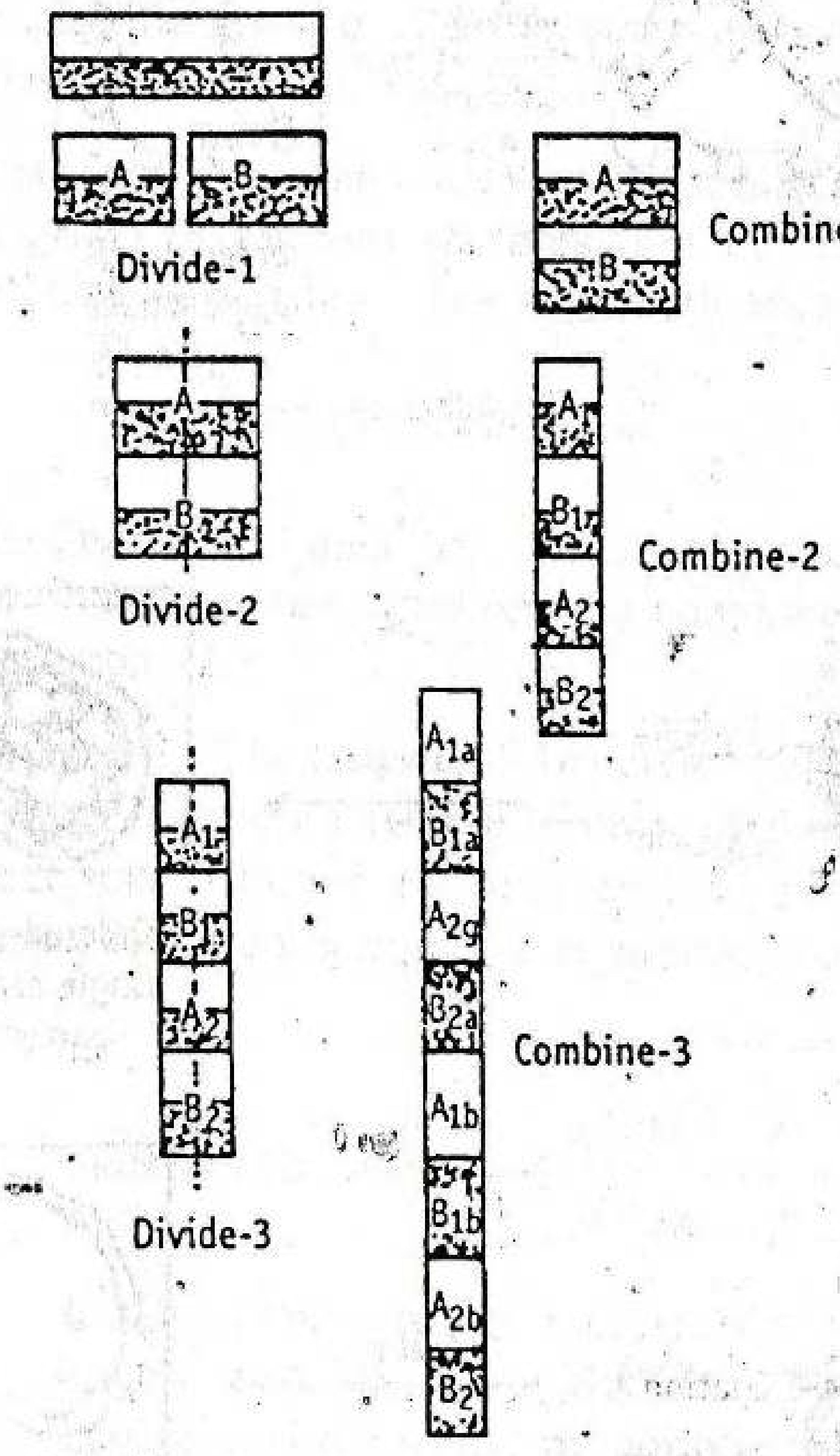
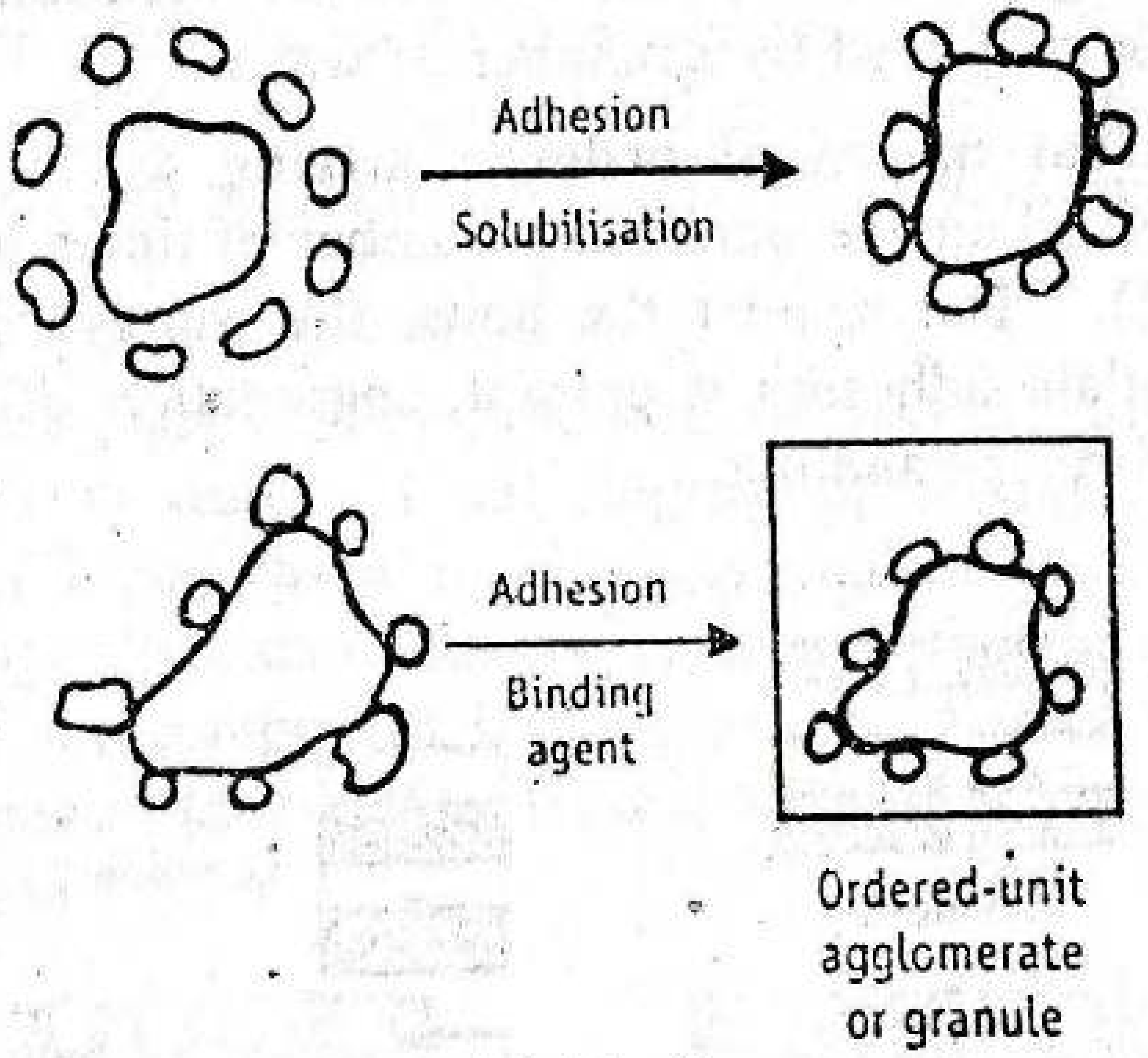


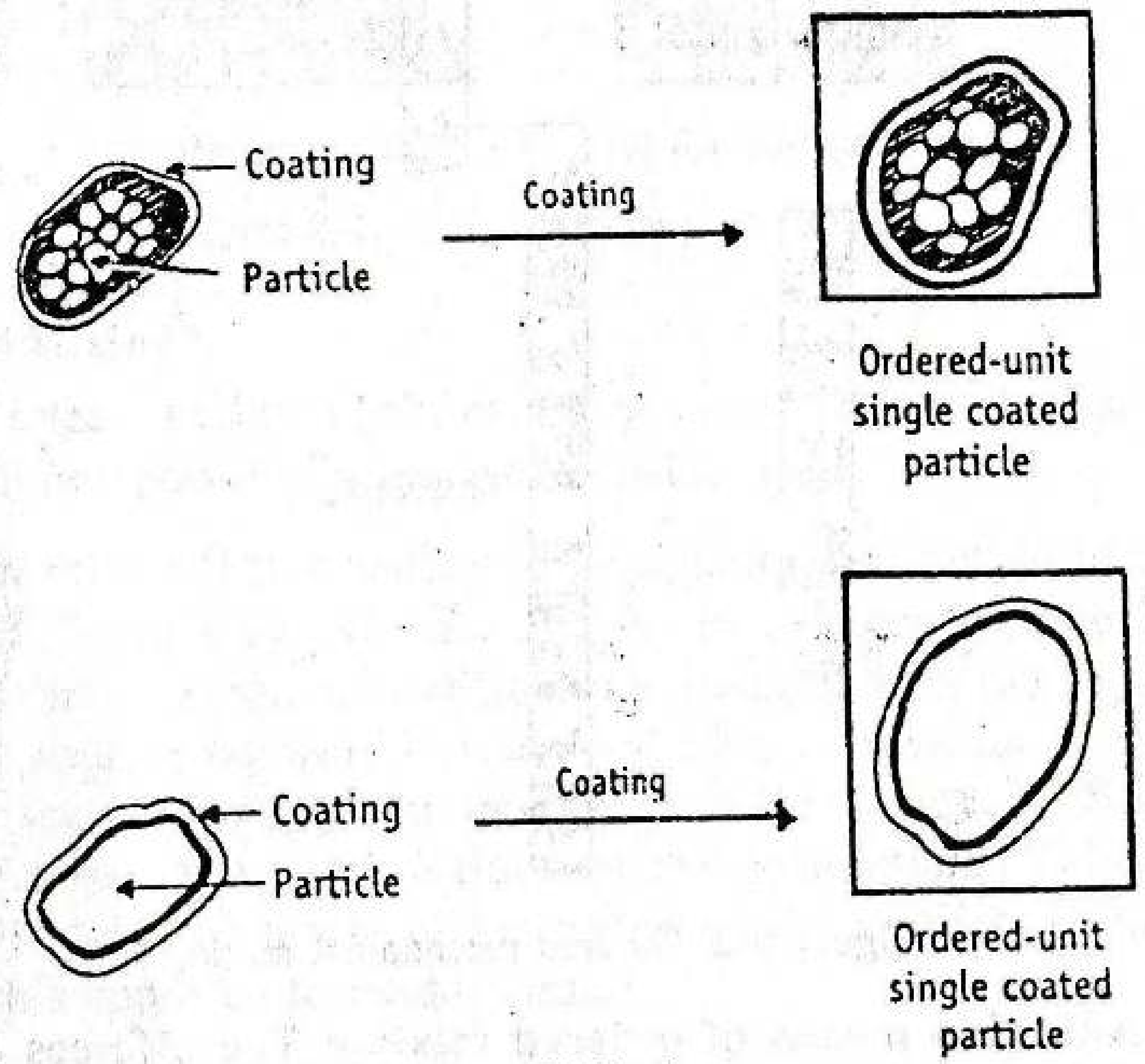
Figure 8-2. Ordered mechanical mixing.

(2) Adhesion means of ordered mixing: These forces of particles may create ordered units of nearly identical composition depending on the process (Figure 8-3a). Partial solubilisation or the use of a binding agent during wet granulation approximates the same effect as shown in Figure 8-3a.

(3) Coating means of ordered mixing: Particles in an assemblage may also be coated with other ingredients to give an ordered mix either as individual or coated particle agglomerates (Figure 8-3b).



(a) Adhesion



(b) Coating

Figure 8-3. Ordered mixing based on the principles of (a) adhesion and (b) coating.

Ideally, the degree of mixing begins rapidly up to a particular level and slows down gradually. Uniform degree of mixing can be resulted by continuing mixing for some more time. The practical definition of mixing uniformity is selected to relate as closely as possible to the desired properties of the mix. The sampling technique largely determines the validity and interpretation of the derived mix.

Statistical Parameters

The analysis of samples before and after mixing provides information about the degree of mixing. Solid mixing with some kind of tracer material is used for easy analysis. Some important methods of analysis are the particle size distribution and the assay procedures for different ingredients in the sample.

Arithmetic mean : The mean (assay value or size distribution analysis) value of a group of random samples is a measure of the central tendency of the batch population. The arithmetic mean is expressed as:

$$\text{Arithmetic mean, } \bar{y} = \sum_{i}^{n} \frac{y_i}{n} \qquad (2)$$

Taking a number of samples (n), the true mean, $\bar{y}$, is estimated. Mean may be attributed to concentration of a component or particle size of a particular component.

Standard deviation : The spread of dispersion of individual samples is important, because it is impracticable to obtain the same true mean for the same product mix obtained by another lot or by another mixer. Therefore, standard deviation is used. It is expressed as:

$$\text{Standard deviation, } \sigma = \sqrt{\frac{\sum_{i}^{n}(y_i - \bar{y})^2}{(n-1)}} \qquad (3)$$

Variance, which is a square term of standard deviation, can also be used for characterisation of powder mix. Standard deviation is applicable for a specific material and a specific mixer.

Mixing of pharmaceutical powders should be continued until the amount of the active drug that is required in a dose is within ± 3 SD units of that found by assay in a representative number of sample doses. To achieve this objective, n should be large. This is possible by milling the ingredients to fineness.

Relative standard deviation : One may follow the mixing operation in a given process by plotting the standard deviations as a function of time. The relative standard deviation (RSD) should replace the standard deviation as a measure of sample uniformity, which is expressed as:

$$\textit{Percent relative standard deviation (RSD)} = \frac{\text{standard deviation } (\sigma)}{\text{mean } (y)} \times 100 \qquad (4)$$

Equation (4) is useful for comparing the efficiency of two or more mixing operations or different sample sizes or different compositions.

Mixing Indices

The selection of a mixer depends on the mixing index or degree of mixing. The above mentioned statistical parameters are useful for evaluating the mixing indices.

Mixing index involves the comparison of standard deviation of sample of a mixture under study with the estimated standard deviation of a completely random mixture.

Mixing index is expressed by Lacey. Two of them are:

$$\textit{Mixing index, } M = \frac{\text{standard deviation of random blend}}{\text{standard deviation of the sample blend}} = \frac{\sigma_R}{\sigma} \qquad (5)$$

$$\textit{Mixing index, } M = \frac{\sigma_0 - \sigma}{\sigma_0 - \sigma_R} \qquad (6)$$

where σ_0 = standard deviation of unmixed powder.

The ratio will be less than 1. The higher the M value, the greater the homogeneity. Equations (5) and (6) are used to determine homogeneity in a mixture depending on the objectives at hand. The selection of a particular equation is essential when the mechanism of mixing is being Results of practical use can be achieved by using statistical analysis.

The differences may indicate poor or inadequate sampling, inappropriate mixing operation, improper handling of the powder sample, unsuitability of the mixer, operational conditions etc.

Before mixing has begun, the material in the mixer exists in two layers, one of which contains no tracer material and one of which is tracer only. Under these conditions, the standard deviation at zero time (σ_0) may be expressed as:

$$\sigma_0 = \sqrt{a(1-a)} \qquad (7)$$

where a = overall fraction of tracer in the mixture.

Statistical Evaluation

Mixer selection depends on the degree of mixing of the powder in the final product. The procedure involves sampling and analysis. The sequence of steps involved in the evaluation of the degree of mixing or degree of homogeneity is given in the Table 8-1.

The objectives have been specified in the Table 8-1. The sampling technique largely determines the validity and interpretation of the derived mix.

Criteria of sampling : While sampling a bed of powder, there should be assurance that the bed is sampled uniformly. It is assumed that the powder bed consists of a number of zones. Within each zone the composition is uniform, but among zones, the composition is different. Therefore, method of sampling is very important. For this purpose, two concepts are important.

Scale of segregation : It is a function of size of the zone. It assumes that zones are having uniform bed, but differing in composition. Good mixing should yield more number of zones with small size. Then the sample reflects the true character of the powder bed.

Intensity of segregation : It is a function of composition differences among zones. Generally the process of mixing tends to reduce the intensity of segregation.

Sample size guidelines : The number of samples required should be not less than 20, preferably 30 and more ideally 100. Analysis of these samples is time consuming and tedious. Therefore, economic considerations suggest 20 samples.

Random sampling is the method of choice for studies. Sample size, in most cases, should approximate the unit dose size of the final product.

Collection of samples : Some golden rules of sampling are:

1. A powder should be sampled when it is in motion.
2. The whole of the stream of powder should be taken for many short increments of time in preference to a part of the stream taken for the whole time.
3. Sampling after completion of the mixing.

TABLE 8-1

Statistical Evaluation Procedure for the Blending or Mixing of Powders

---

Objectives

1. To compare the efficiency of two or more mixing operations.
2. To compare the efficiency of two or more equipment.
3. To follow the mixing process with time.
4. To optimise processing parameters.
5. To investigate the mechanism of mixing in a given piece of equipment.

Sample size guidelines: (a) Random sampling
(b) Number of samples

Number of samples: Required — 30; Ideal — 100;
Economical sampling — 20 (preferred).

Sample size — approximately a unit dose of the final product.

Sample collection: (a) At different intervals when the blend is in motion.
(b) After blending is completed (preferred).

Sample utilization: (a) Scooping sampling
(b) Thief probing (preferred)

Sampling methods: (a) Returning the sample to the bulk, for example, after completion of particle size analysis (non-destructive evaluation).
(b) Not returning the sample to the bulk, for example, due to solubilisation for assay procedure (destructive method).

Statistical Analysis

- Determination of arithmetic mean and standard deviation of the randomly mixed sample (standard).
- Determination of arithmetic mean and standard deviation of the unmixed blend of sample (initial stage).
- Determination of arithmetic mean and standard deviation of the sample after blending (test sample).
- Comparing mean values (sample) with target value (true mean).
- If they are comparable, standard deviation should be calculated (indicates uniformity of the sample). High standard deviation indicates less uniformity.
- Determination of mixing indices.
- Scattering of sample about mean or standard deviation (plot of standard deviation vs. time).
- Accuracy and precision assessments of these estimates.

Some times, powder sample cannot be sampled from a moving stream, because:

(1) configuration of the mixer -- for example the shape of the bowl does not lend itself to dumping.

(2) size of the batch - large volumes are not conducive to routine transfer from the blender to drum or larger collectors.

(3) possibility of mixture segregation biasing the sample.

Therefore, it is always preferable to collect the sample once mixing is completed.

Method of collecting samples : Samples should be collected at selected points or serially as the powder is discharged from the mixer. Two types of sampling methods are adopted.

(1) Scoop sampling of the bulk mixture
(2) Thief probing of the bulk mixture

Scoop sample : This method has some drawbacks. (A) Surface layer sample may represent segregated mixture. (B) Samples can not be removed from the bottom and middle of the blender or container.

Thief probe : This method has some drawbacks. (i) During sampling, some compaction takes place around the thief. (ii) As the thief is inserted in the powder bed, it carries material from the surface of the mixture down into the mixture.

Thief probe is preferred over the scoop, because samples can be taken from deep within the powder bed and a fair degree of random sampling can be achieved.

Sample utilization : If the method of analysis is non-destructive, for example, particle size analysis, the sample can be returned to the mixture after analysis. If the method is destructive, for example assay, the sample can not be returned.

Analysis of data : Several statistical parameters and mixing indices are calculated. The comparison of the mean value of the sample under analysis and the target value. If the mean value of the sample under analysis is on or near the target value, calculation of the standard deviation (and or variance) will give an indication of the uniformity of the sample. Other details are given in the Table 8-1.

FACTORS INFLUENCING MIXING

Particle and powder characteristics influence the mixing process. Aggregation inhibits proper mixing. Therefore, higher shearing forces are applied. Hence, correct mixing of one component does not imply good mixing of other components. Therefore, adding dye to the mixture is often misleading. The dye may not aggregate, but active substance may aggregate.

A single factor can in no way be considered as a unique indication of mixing. However, flow properties of the components is the most important consideration which is again influenced by a number of factors.

Nature of the surface : Rough surface of one of the components does not induce satisfactory mixing. This can be due to the entry of active substance into the pores of the other ingredients.

Adding a substance, which will be adsorbed on its surface, can decrease aggregation. Example is the addition of aerosil (colloidal silicon dioxide) to zinc oxide. Thus, a strongly aggregating zinc oxide becomes a fine dusting powder, which can be mixed easily.

Density of the particles : It is of minor importance. Demixing is accelerated when the density of the smaller particles is higher or when the mixing process is stopped abruptly. This is due to the fact that dense material always moves downward and settles at the bottom.

Particle size : It is easy to mix two powders having approximately the same particle size. The variation of particle size can lead to separation, because the small particles move downward through the spaces between the bigger particles. As the particle size increases, flow properties also increase due to the influence of gravitational force on the size. Beyond a particular point, flow property decreases. The powders with a mean particle size of less than 100 µm are free flowing, which facilitates mixing.

Particle shape : The ideal particle is spherical in shape for the purpose of uniform mixing. The irregular shapes can become interlocked and there are less chances of separation of particles once these are mixed together.

Particle charge : Some particles exert attractive forces due to electrostatic charges on them. This can lead to separation or segregation.

Proportion of materials : The best results can be obtained if two powders are mixed in equal proportion by weight and by volume. If there is a large difference in the proportion of two powders, mixing is always done in the ascending order of their weights.

The fundamental aspects of the particles and powders are discussed in the *Textbook of Physical Pharmaceutics* by C.V.S. Subrahmanyam (Vallabh Prakashan, Delhi).

CLASSIFICATION OF EQUIPMENT FOR SOLIDS MIXING

Based on the flow properties of the powders, appropriate mixer should be selected.

(i) shape
Free flowing solids – V cone blender , (ii) Y shape blender
(iii) – Double cone blender
(iv) – cube blender (v) Ablige cone blen
Cohesive solids (vi) – Planetary mixer
(vii) – Sigma blender
(viii) – Nam mixer (ix) Conc. blender

Based on the scale of mixing, mixing equipment may be classified as given in Table 8-2.

TABLE 8-2
Classification of Mixing Equipment

S.No.	*Nature of mixer*	*Examples*	*Mechanism of mixing*
1.	**Batch type** Small scale	Mortar and pestle	Trituration
2.	Tumbling mixers or cylindrical mixers without mixing blade	Double cone blender, V cone mixers without baffles Cube blender	Tumbling action
3.	Tumbling mixer with a mixing blade	V cone blender with a mixing blade Double cone blender with a mixing blade	Tumbling action as well as shearing with blade
4.	Static mixers	Ribbon blender Sigma blender Planetary paddle	Stationary shell and rotating blade
5.	Air mixers or fluidized mixers	Fluidised mixer	Air supported blending
6.	**Continuous type** Large scale	Barrel type Zigzag type	Rotating shell with rotating blade

EQUIPMENT

A mixer that promotes the randomness in mixing should be selected. It should also prevent the conditions responsible for segregation. Therefore, optimization of operational conditions is critical.

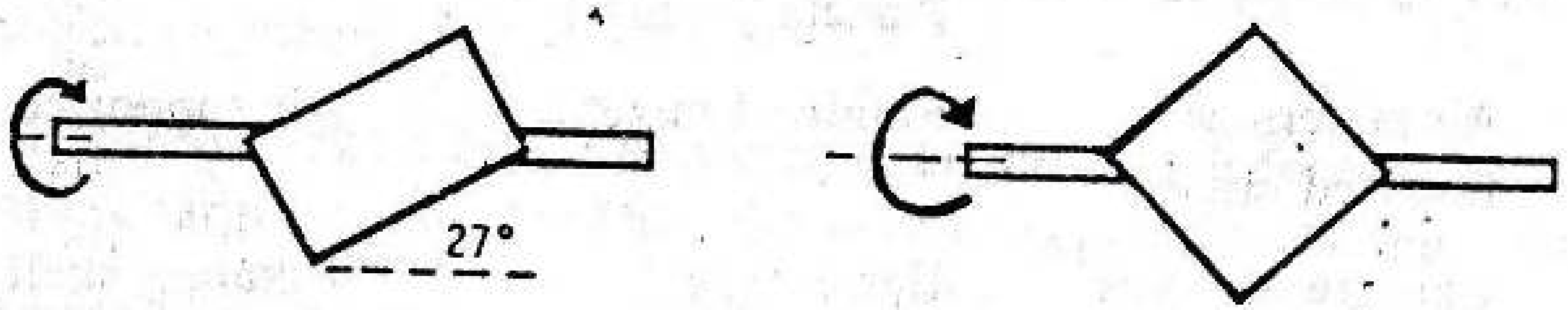
Mixing Equipment—Criteria

1. The powder bed may expand sufficiently, therefore, equipment should never be filled for more than about 60% so as to leave sufficient mixing volume.
2. The particles should be subjected to movement in three directions.
3. The shearing force should be sufficient to prevent aggregation. Appropriate mixing mechanism should be selected and allowed to continue for optimum time.
4. There should be no centrifugal effect, so that the powder does not get separated according to their weights.
5. The forces should not cause breakage of the particles, which may bring about demixing due to differences in particle size.
6. The mixing process should be stopped abruptly, because slow or diminishing forces in one direction might cause demixing. Therefore handling of powder blend after mixing is equally important.

Some mixing equipment are discussed below.

TUMBLERS OR CYLINDRICAL BLENDERS WITH NO MIXING BLADE

This is a general class of equipment meant for blending of dry powders. The equipment consists of a container of one of the several geometric form. These are mounted so that it can be rotated about an axis. These do not have packing glands (seals) round the shaft. Cubes or hexagonal cylinders may be rotated in any axis depending on the manufacture (Figure 8-4). Such a cylindrical vessel is not suitable for mixing since one-dimensional movement would be obtained.



(a) Cylindrical blender.

(b) Cube blender.

Figure 8-4. Tumbler blenders without agitator blade.

Edge of 27 degrees is good for mixing. Special rollers are available so that any vessel can be placed on it at the optimal condition. It is very handy since the vessel can be used every where in the process. When mixed, cohesive powders tend to ball up and aggregate. Therefore, tumbler type is not suitable.

The efficiency of a tumbling mixer highly depends on the speed of rotation. It should be critical.

(1) Slow rotation – No intense tumbling, no cascade motion. Not enough shear rates is applied.

(2) Rapid rotation – Sufficient centrifugal action to hold the powder to the sides of the mixer, more dusting and segregation of fines is possible.

Therefore, the rate of rotation should be optimal, which depends on the size, shape of the tumbler and the nature of material to be mixed. Common range is 30 to 100 rpm.

Neither cylindrical nor cube mixers are used to a great extent in the industry. For simple blending of dry mixers, V cone and double cone blenders without baffles are used. The tumbling motion is accentuated by means of baffles or simply by virtue of the shape of the container.

TWIN SHELL BLENDER OR V CONE BLENDER

The construction of a twin shell blender is shown in Figure 8-5. It is made of either stainless steel or transparent plastic. Smaller models take a charge of 20 kg and rotate at 35 revolutions per minute, while larger ones take a charge of about 1 tonne and rotate at 15 revolutions per minute. The material is loaded through either of the shell hatches. Emptying of the blend is normally done through an apex port.

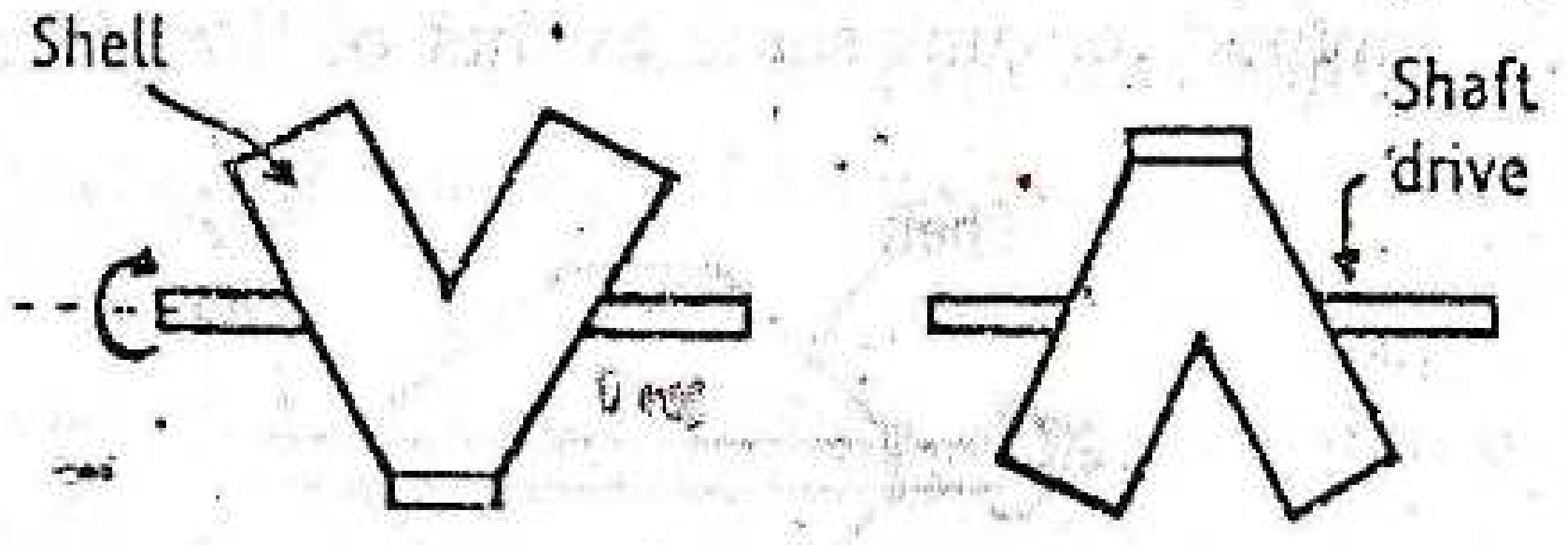


Figure 8-5. V cone blender. Rotating shell without baffles.

The material (to be blended) is loaded approximately 50 to 60 % of its total volume. As the blender rotates, the material undergoes tumbling motion. When the V is inverted, the material splits into two portions. This process of dividing and recombining continuously yields ordered mixing by mechanical means. The powder mass is converted shock-wise, so that no demixing due to density differences will occur. It is rotated so that the material alternatively is collected in the bottom of the V.

Blender speed is the key for mixing efficiency. At high speeds, more dusting or segregation of fines is possible, while at low speeds, not enough shear may be applied.

Advantages : (1) If fragile granules are to be blended, twin shell blender is suitable because of minimum attrition.

(2) They handle large capacities.

(3) Easy to clean, load and unload.

(4) This equipment requires minimum maintenance.

Disadvantages : (1) Twin shell blender needs high headspace for installation.

(2) It is not suitable for fine particulate system or ingredients of large differences in the particle size distribution, because not enough shear is applied.

(3) If powders are free flowing, serial dilution is required for the addition of low dose active ingredients.

DOUBLE CONE BLENDER

The construction of a double cone blender is shown in Figure 8-6. It is usually charged and discharged through the same port. It is an efficient design for mixing powders of different densities. These are used mostly for small amounts of powders. The rate of rotation should be optimum depending on the size and shape of the tumbler, nature of material to be mixed. Commonly the range is 30 to 100 revolutions per minute. The method remains same as that of the V-cone blender.

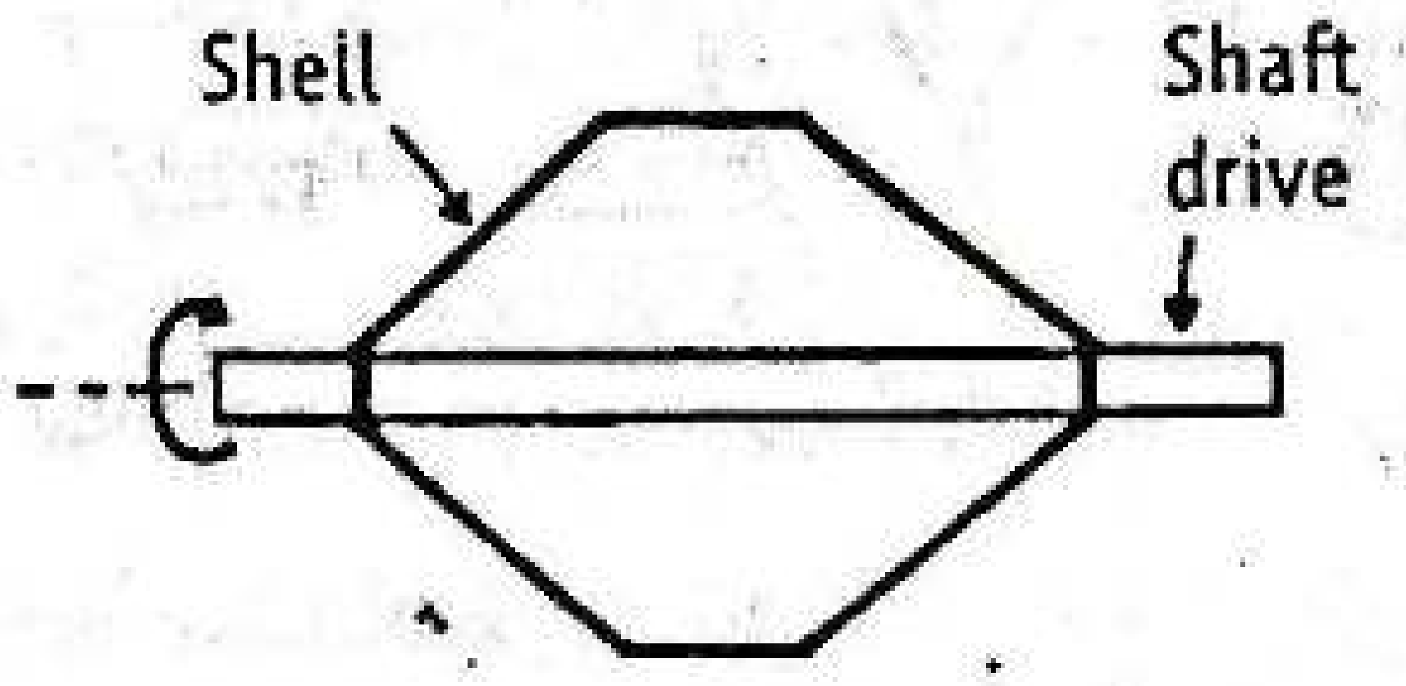


Figure 8-6. Double cone blender.
Rotating shell without baffles.

The advantages and disadvantages for double cone blender are same as given in Twin shell blender (or V cone blender).

TUMBLING BLENDERS WITH AGITATOR MIXING BLADE

The V-cone blender and double cone blender with agitator blade (baffles) are shown in Figures 8-7 and 8-8, respectively. The general construction and working is same as mentioned above. Agitator blades are added which have several advantages.

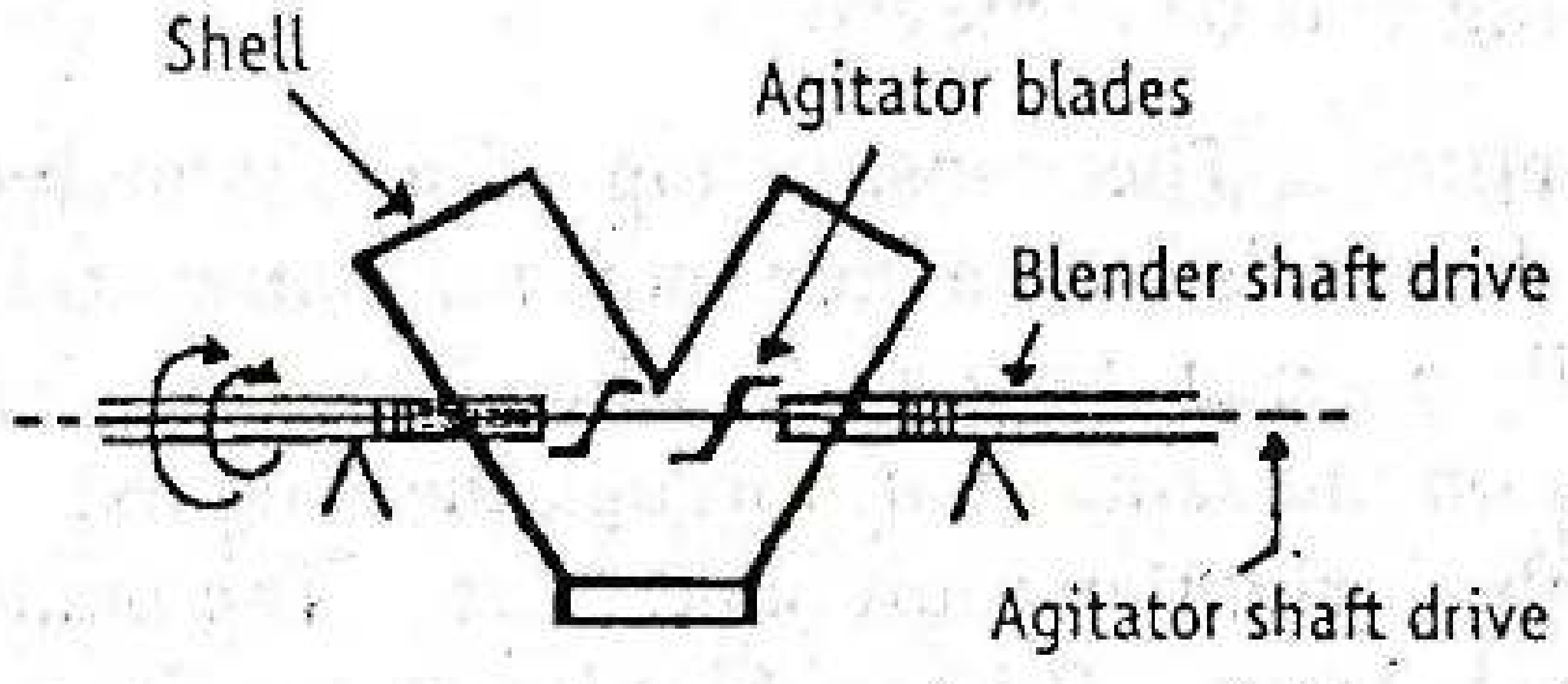


Figure 8-7. V cone blender.
Rotating shell with rotating baffles.

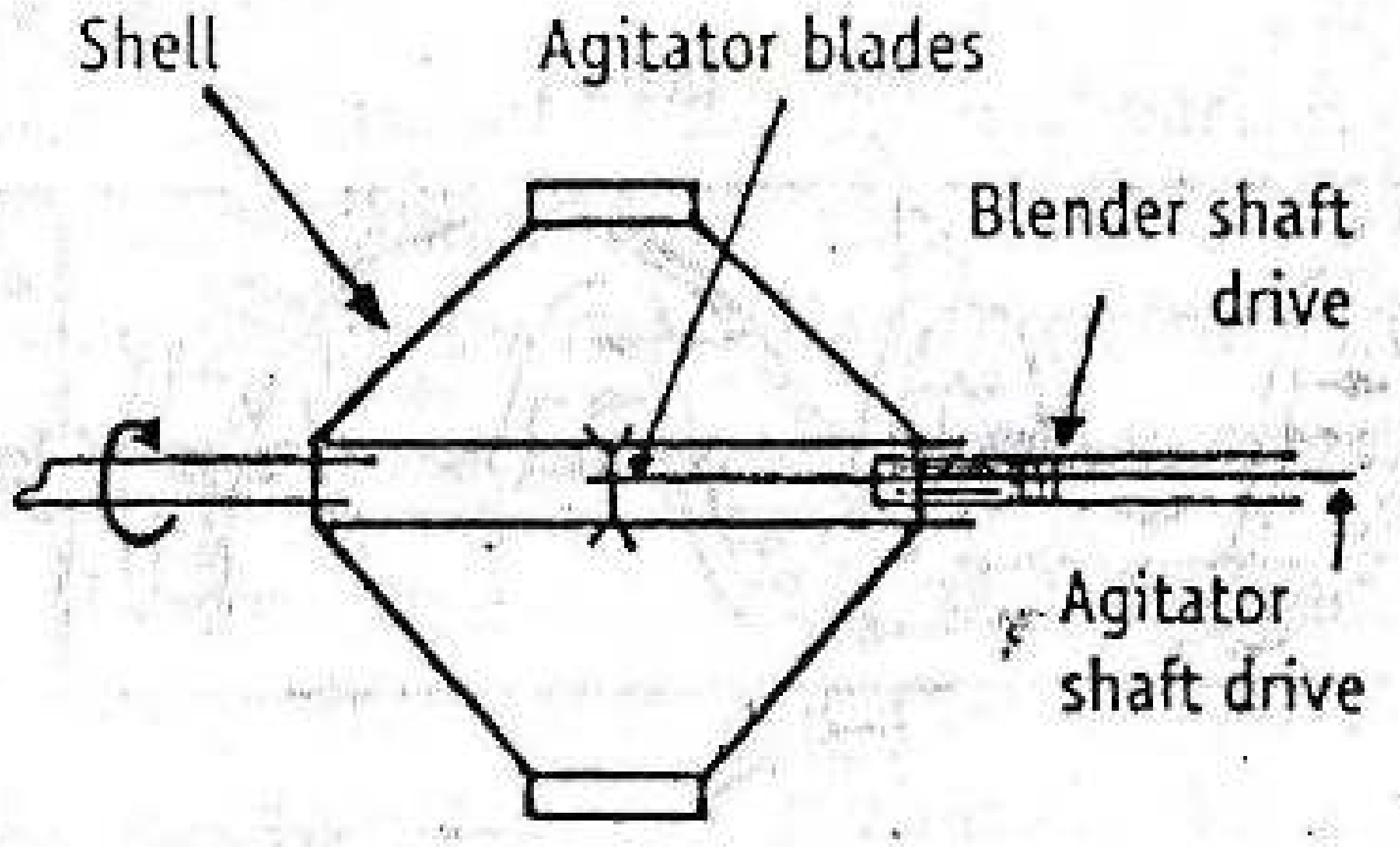


Figure 8-8. Double cone blender.
Rotating shell with rotating baffles.

Advantages : (1) Baffles are useful for both wet and dry mixing.

(2) Wide range of shearing force can be applied with agitator bars permitting the intimate mixing of very fine as well as coarse powders.

(3) Serial dilution is not needed when incorporating low-dose active ingredients.

Disadvantages : (1) Attrition is large, size reduction of friable particles results.

(2) Scale-up can prove a problem, because general principles of scale up do not work.

(3) Cleaning may be a problem, because the agitator assembly must be removed and the packing should be replaced for a product changeover.

(4) Potential packing (sealing) problems.

RIBBON BLENDER

Principle : The mechanism of mixing is shear. Shear is transferred to the powder bed by moving blades (ribbon shaped) in a fixed (non-movable) shell. High shear rates are effective in breaking lumps and aggregates. Convective mixing also occurs as the powder bed is lifted and allowed to cascade to the bottom of the container. An equilibrium state of mixing can be achieved.

Construction : The construction of a ribbon blender is shown in Figure 8-9. It consists of a non-movable horizontal cylindrical trough (shell) usually open at the top. It is fitted with two helical blades, which are mounted on the same shaft through the long axis of the trough. The blades have both right and left hand twists. The blades are connected to a fixed speed drive. Ribbon blender is top loading with a bottom discharge port. The trough can be closed with a lid.

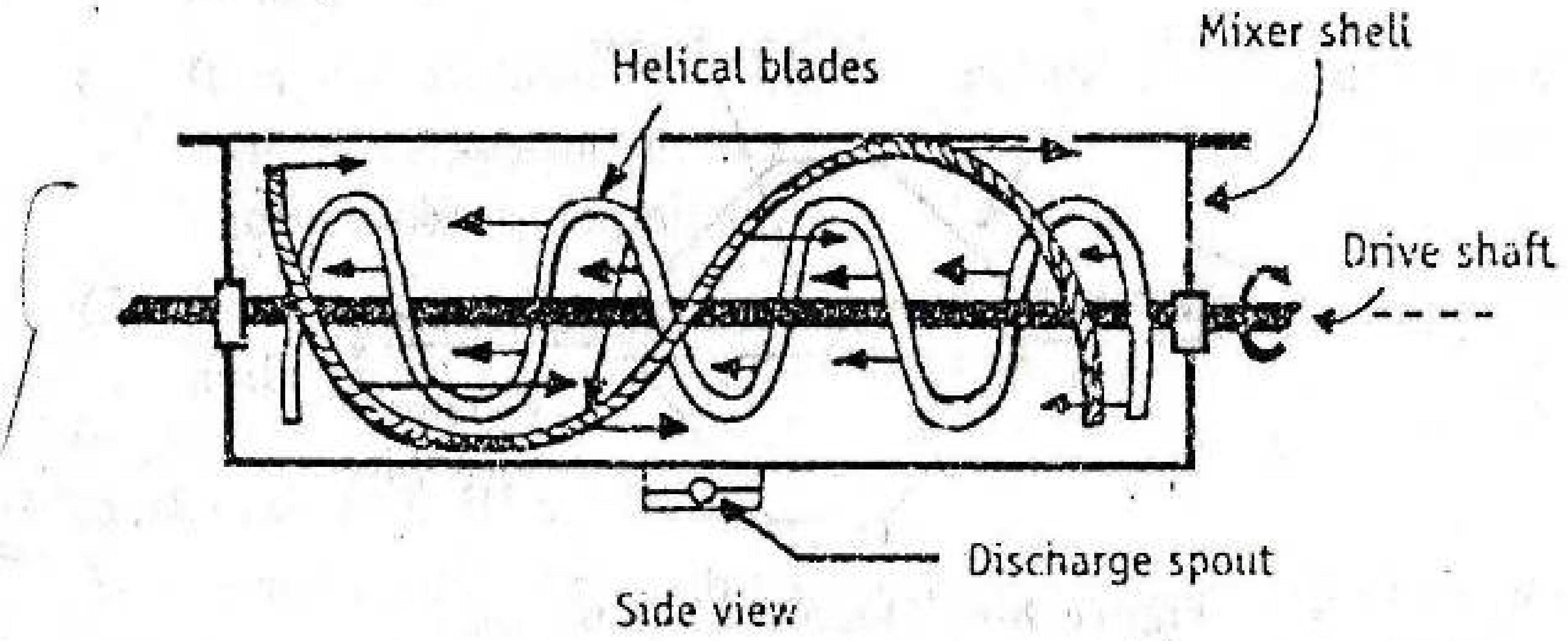


Figure 8-9. Ribbon mixer. Stationary shell and rotating blades.

Working : Through the fixed speed drive, ribbons are allowed to rotate. One blade moves the solids slowly in one direction and the other moves them quickly in opposite direction. Different powders are introduced from the top of the trough. The body is covered because considerable dust may be evolved during dry blending and granulating solution may evaporate during wet granulation.

The powders are lifted by a centrally located vertical screw and allowed to cascade to the bottom of the container (tumbling action). The counteracting blades set up high shear and are effective in breaking up lumps or aggregates. Helical blades move the powders from one end to another as shown in Figure 8-9. The final stage of mix represents an equilibrium state. The operating conditions of a given mixer can markedly effect the steady state and thus the quality of the mixing. The blend is discharged from the bottom opening.

Uses : Ribbon blender is used to mix finely divided solids, wet solid mass, sticky and plastic solids. Uniform size and density material can be easily mixed. It is used for liquid-solid and solid-solid mixing.

Advantages : High shear can be applied by using perforated baffles, which bring about a rubbing and break down aggregates. Headroom requirement is less.

Disadvantages : (1) It is a poor mixer, because movement of particles is two-dimensional.

(2) Shearing action is less than in planetary mixer.

(3) Dead spots (areas that remain unmixed) are observed in the mixer, though they are minimum.

(4) It is having fixed speed drive.

SIGMA BLADE MIXER

Principle : The mechanism of mixing is shearing. The inter-meshing of sigma shaped blades creates high shear and kneading actions. Convective mixing is achieved by cascading the material.

Construction : The construction of a sigma blade blender is shown in Figure 8-10. It consists of double trough shaped stationary bowl. Two sigma (indicating the shape of the *Greek* letter) shaped blades are fitted horizontally in each trough of the bowl. These are connected to a fixed speed drive. The mixer is loaded from the top and unloaded by tilting the entire bowl by means of a rack-and-pinion drive.

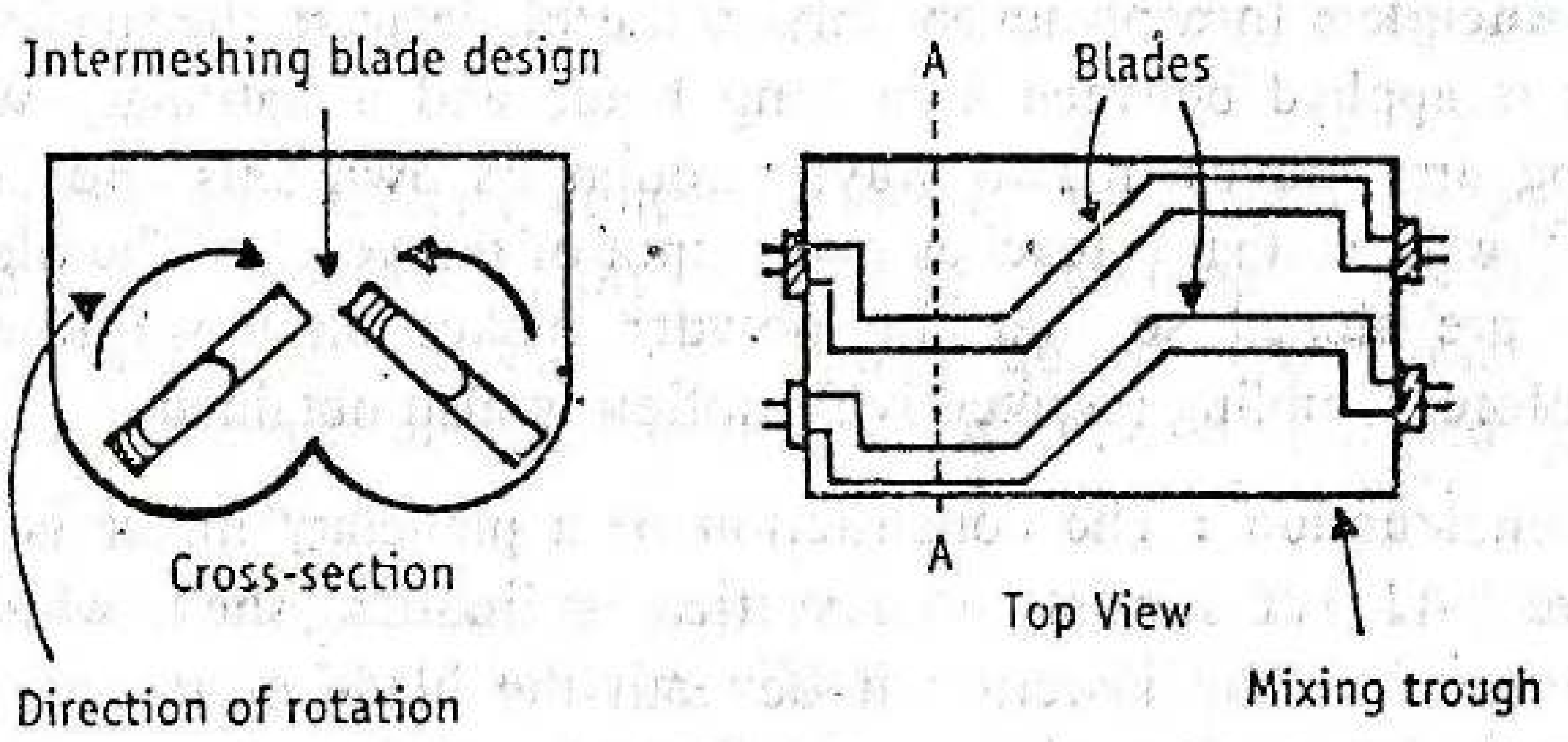


Figure 8-10. Sigma blade mixer. Stationary shell and rotating blades.

Working : Different powders are introduced from the top of the trough. The body is covered because considerable dust may be evolved during dry blending and granulating solution may evaporate during wet granulation.

Through the fixed speed drive, the sigma blades are allowed to rotate. The blades move at different speeds, one usually about twice the speed of other, resulting in lateral pulling of the material. They turn towards each other so that the powders move from the sides to the centre of the bowl. The material further moves from the top to downwards over the point and then sheared between the blades and the wall of the trough. Thus cascading action (convective) as well as shear action can be achieved. The perforated blades help in breaking lumps and aggregates. Thus high shear forces are set up. The final stage of mix represents an equilibrium state. The operating conditions of a given mixer can markedly effect the steady state and thus the quality of the mixing. By means of a rack-and-pinion drive the bowl is tilted to empty the blend.

Uses : Sigma blade mixer is commonly used for mixing of dough ingredients in the baking industry. It is used in wet granulation process in the manufacture of tablets, pill masses and ointments. It is primarily used for liquid-solid mixing, although it can be used for solid-solid mixing.

Advantages : (1) Sigma blade mixer creates a minimum dead space during mixing.

(2) It has close tolerances between the blades and the side-walls as well as bottom of the mixer shell.

Disadvantage : Sigma blade mixer works at a fixed speed.

PLANETARY MIXER

Principle : In a planetary mixer, the blade tears the mass apart and shear is applied between a moving blade and a stationary wall. The mixing arm moves in two ways, around its own axis and around the central axis, so that it reaches every spot of the vessel. The plates in the blade are sloped so that the powder makes an upward movement. Therefore, tumbling (convective) motion is also obtained.

Construction : The construction of a planetary mixer is shown in Figure 8-11. It consists of a vertical cylindrical shell, which can be removed either by lowering it beneath the blade or raising the blade above the bowl. The mixing blade is mounted from the top of the bowl. The mixing shaft is driven by a planetary gear train, as indicated in the Figure 8-11. It rotates around the ring gear, which further rotates round the mixer blade. It is normally built with a variable speed drive.

Working : In the planetary mixer, the agitator has a planetary motion. It rotates on its own and around the central axis so that it reaches all parts of the vessel. Beater is shaped to pass with close clearance over the side and bottom of the mixing bowl. Therefore, literally there are no dead spaces in the mixing bowl. The blade tears the mass apart and shear is applied between the moving blade and the stationary wall. The plates in the blade are sloped so that the powder makes an upward movement. Therefore, tumbling (convective) motion is also obtained. Since it is a variable speed driven, initially the blade moves slowly for premixing and finally at increased speed for active mixing. Thus high shear can be applied for mixing.

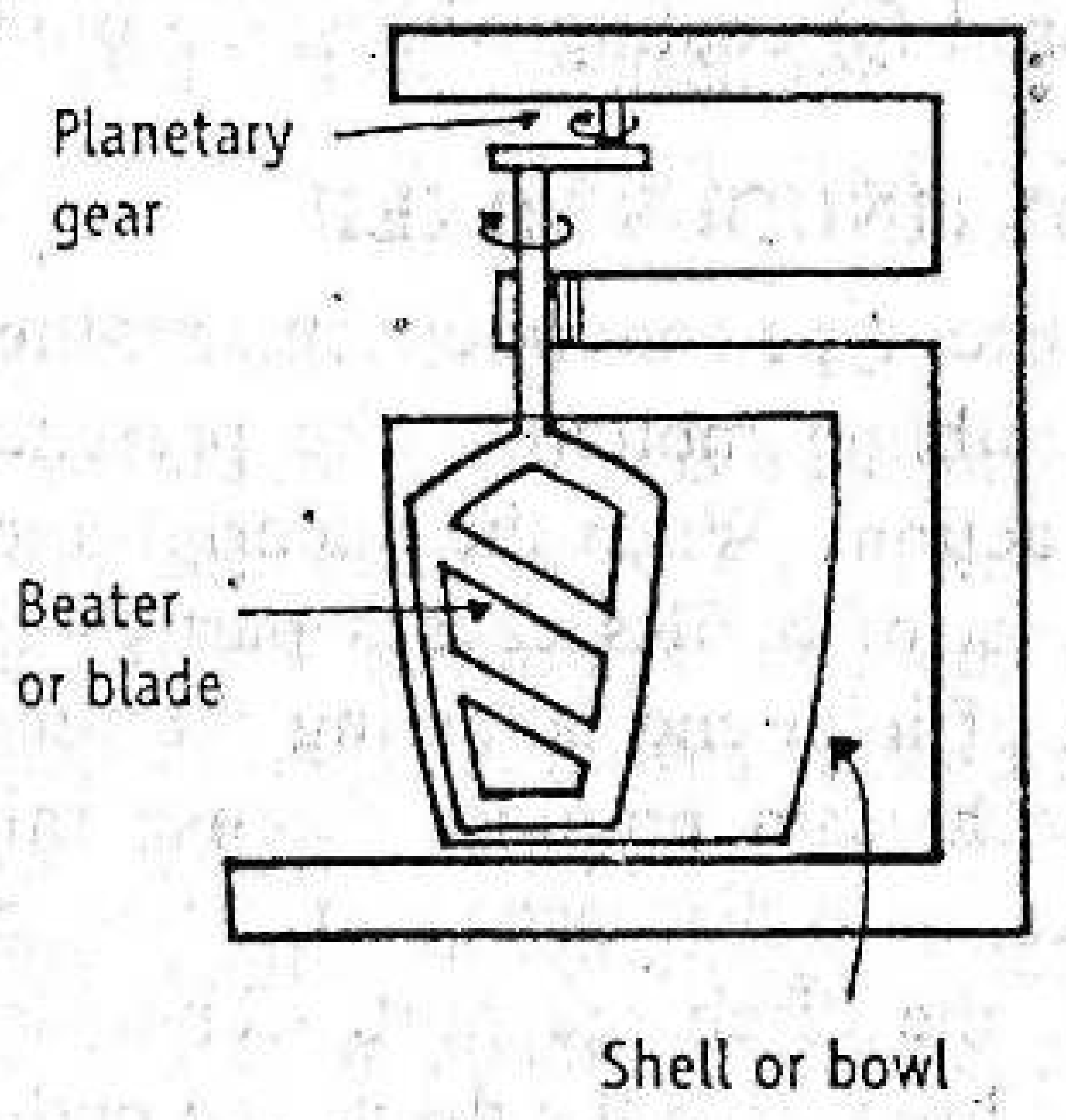


Figure 8-11. Planetary mixer.

Emptying the bowl may be done by hand (scooping) or by dumping mechanism.

Uses : Planetary mixer produces precise blends in addition to breaking down of agglomerates rapidly. Low speeds are used for dry blending and faster speeds for the kneading action required in wet granulation. Steam jacketed bowls are used in the manufacture of sustained release products and ointments.

Advantages : Speed of the rotation can be varied at will, so it is advantageous over sigma blade or ribbon type blenders. This is more useful for wet granulation process. There are no packing glands in contact with the product.

Disadvantages : (1) Mechanical heat is built up within the powder mix.

(2) It requires high power.

(3) It has limited size and is useful for batch work only.

AIR MIXER OR FLUIDIZED MIXER

Principle : The air movement is used for mixing powders. The powders are mixed in a stationary cylindrical vessel. Air is admitted at its base at an angle. This gives tumbling action and spiral movements to the powder. Thus mixing is achieved.

The construction and working of an air mixer or fluidised mixer remains same as shown in fluidised bed dryer in the Chapter Drying.

Advantages : Air mixer shortens the mixing time. It is useful as a through-output. Mixing is intimate and efficient. It is also used for wet granulation in tablets. With additional attachments, this equipment is useful for mixing, wet massing and drying in the wet granulation method. This method is also used for coating with some modifications.

BARREL TYPE CONTINUOUS MIXER

Principle : In a barrel type continuous mixer, the rotating shell keeps the material under tumbling motion. The presence of baffles further enhances the mixing action. When the material approach the mid-point of the shell, another set of baffles causes part of the material to move towards the direction of inlet end, allowing the remaining part to move forward. Such a mechanism provides intense mixing of ingredients. This process continues up to discharge end, where another set of baffles guide the material to the discharge port. The blended material at an equilibrium state overflows from the discharge end.

Construction : The construction of a barrel type mixer is shown in Figure 8-12. It resembles a large cement mixer. Baffles are fitted to the inner surface of the shell. The shell is fixed to a shaft, which is allowed to rotate using electric power. Side openings are provided on each side for charging and discharging of materials.

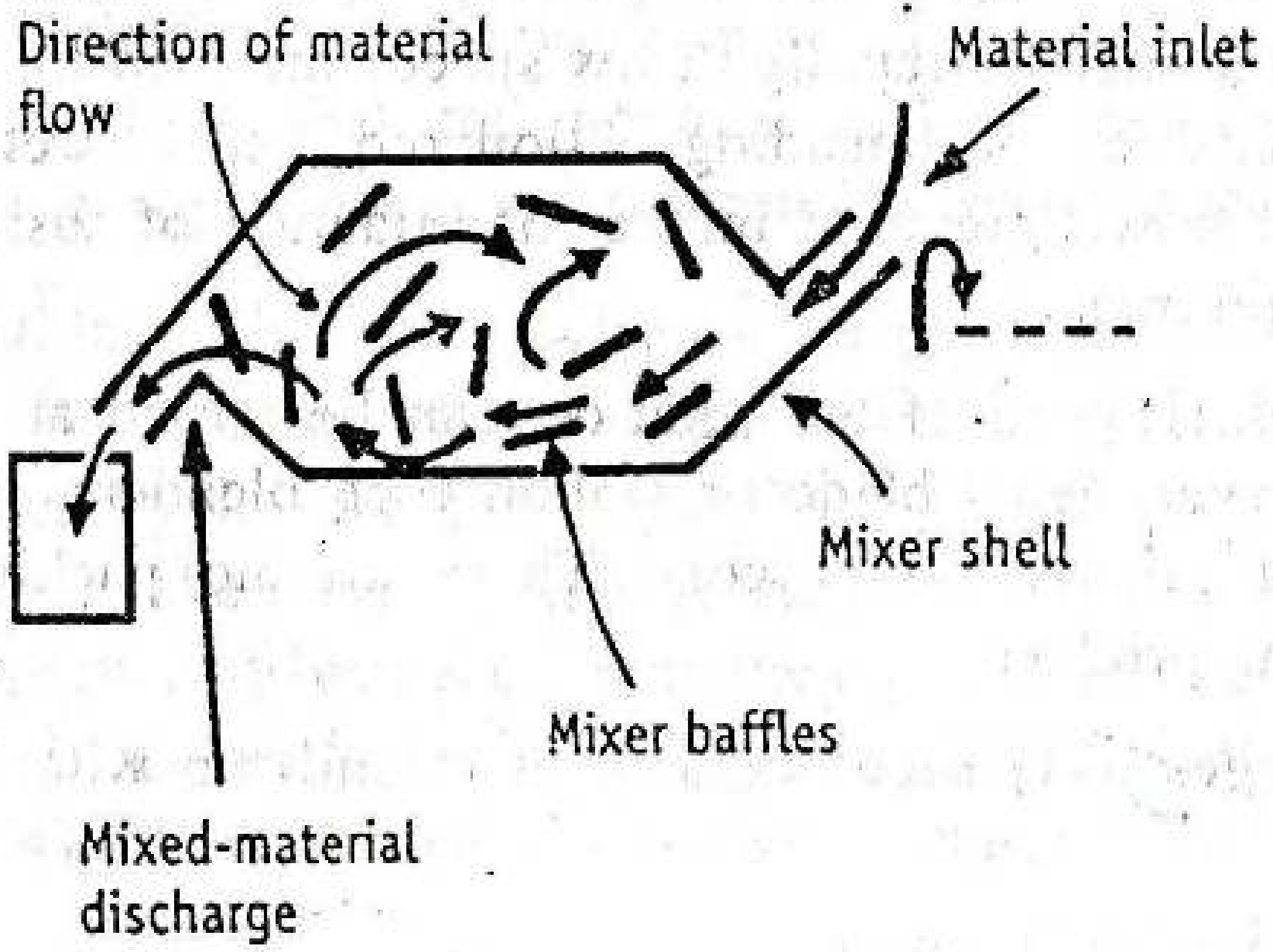


Figure 8-12. Construction of barrel type continuous mixer.

Working : The mixer is allowed to rotate. Along with it the baffles also rotate. The ingredients are introduced into the shell through the inlet. They begin moving towards the opposite end of the blender due to tumbling action. Baffles further enhance the mixing. As the material approaches the mid-point of the mixer shell, the baffles are so positioned to cause the feedback of part of the material in the direction of the inlet end. The movements are shown in Figure 8-12 using arrow markings. The feedback action continues up to the discharge end, where another set of baffles guides the material to the discharge port. The overflow of material causes the blended solids to discharge. Since charging and discharging are simultaneously done, the process becomes continuous.

ZIGZAG CONTINUOUS BLENDER

Principle : Zigzag continuous blender is a rotating shell type having several V shaped blenders connected in series. The material undergoes tumbling motion. When the V section is inverted, the material splits into two portions; one-half of material moves backward (into the preceding section), while another-half of material moves forward. Due to inclined axis of the shell towards the discharged end, the material gets discharged. As the first V section clears the charge, a fresh feed enters. Thus, it is used for continuous blending of solids.

Construction : The construction of a zigzag continuous blender is shown in Figure 8-13. The shell takes the shape of several V shaped

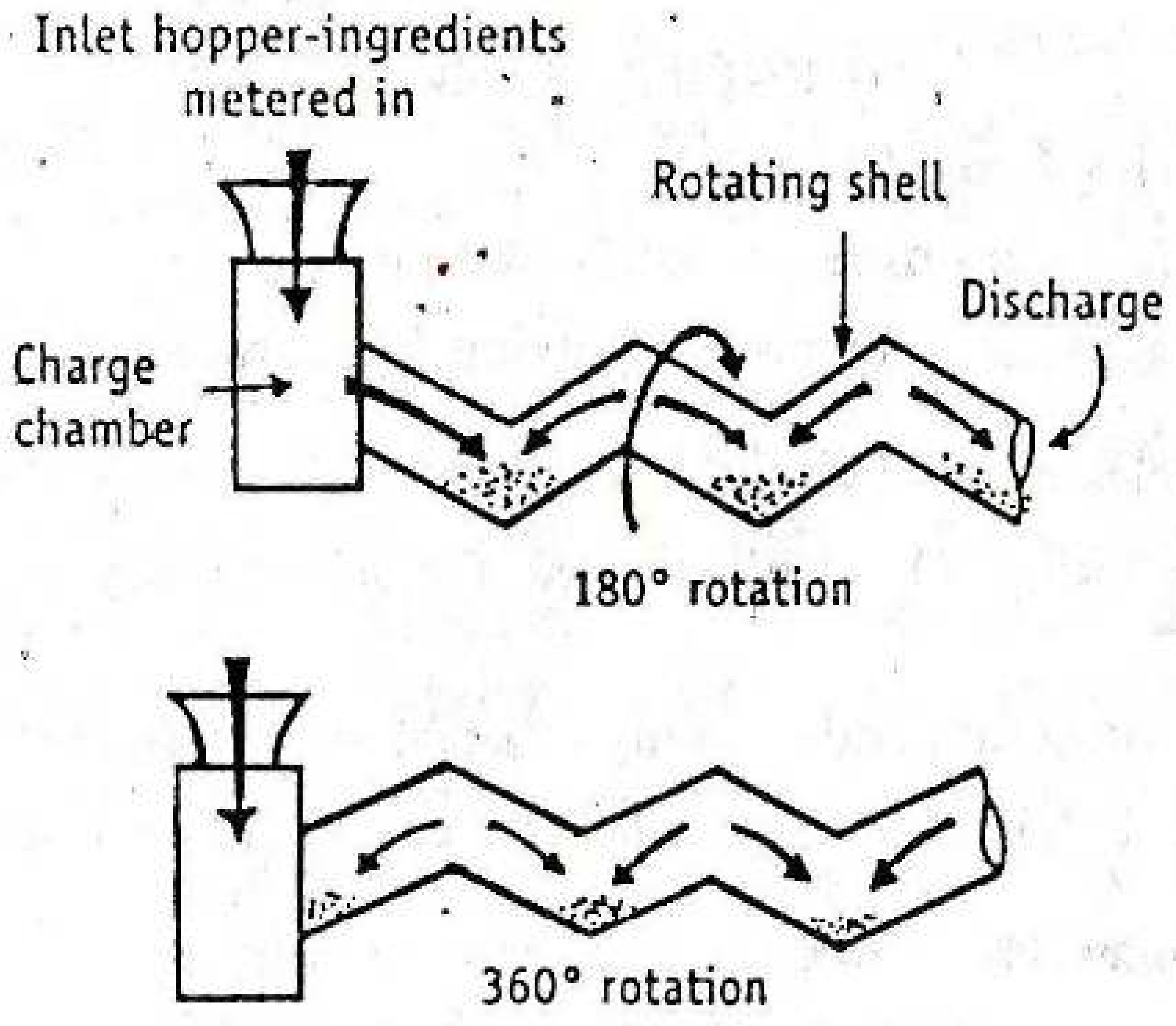


Figure 8-13. Construction of zigzag continuous blender.

blenders connected in series. A chamber for charging is attached to one end of the shell. The other end allows the discharge of material. The shell is inclined towards the discharge end.

Working : A single pre-weighed charge is introduced into the charge chamber. As the shell rotates, at one particular angle (Figure 8-13) a metered material enters the V-shaped section by gravity. With each rotation, one-half of the blend material moves downward back to the preceding leg and another-half of the material moves forward to the next leg of the blender. In each rotation, a part of the material moves towards the discharge end.

As the first charge clears the first V section, which may take only a few minutes, the next charge is added. The uniformity of blending depends on the flow properties of the ingredients.

Glossary of Symbols

A = Constant.
a = Overall fraction of tracer in the mixture.
t = Time, min.
k = Constant.
M = Degree of mixing or mixing index at time, t.
n = Number of samples.
RSD = Relative standard deviation.
σ = Standard deviation
σ_0 = Standard deviation of unmixed powder.
σ_R = Standard deviation of random blend.
y = Arithmetic mean (particle size or concentration).
$\bar{y}$ = True mean of the standard.
y_i = The value of a given sample.

QUESTION BANK

Each question carries 2 marks

1. Mention the equipment used for solid-solid mixing.
2. List the equipment used for powder mixing in pharmaceutical industry.

Each question carries 5 marks

1. Explain the working of a mixer used for mixing dry powders before granulation.
2. Explain the construction and working of a ribbon blender for mixing solids.
3. Draw the neat sketch of the sigma blade blender and give its working.

Each question carries 10 marks

1. Describe the equipment for solid-solid mixing of pharmaceutical materials.

Section II—MIXING OF LIQUIDS

Liquid-liquid mixing is considered as a simple operation compared to that of solid-liquid mixing. It involves the formation of a homogeneous system. Similar to solid-solid mixing, fluid (or liquid) mixing also involves the application of shear. Agitation and mixing are not synonymous.

Agitation refers to the induced motion of a material in a specified way, usually in a circulatory pattern inside a container.

Mixing refers to the random distribution into or through one another of two or more separate phases.

The nature of liquids mainly determines the ease of mixing. According to theories of solutions, liquid mixtures are classified as follows.

(1) Miscible liquids : These are miscible in all proportions. For example, ethyl alcohol and water are miscible in all proportions. These liquids can be mixed easily by employing the mechanisms of bulk transport and shear. Cosmetics (after-shave lotion), elixirs etc., belong to this class.

(2) Partially miscible liquids : These are miscible in one another at one particular proportion. Their miscibility depends on temperature and pressure. For example, p-cresol and water are miscible in a certain proportion. Mixing poses certain difficulties in the preparation of disinfectant solutions.

(3) Immiscible liquids : As the name indicates, these are not miscible. For example, vegetable oils and water are not miscible or their miscibility is very low. Normally, they form emulsions. Mixing of these liquids is very difficult. A homogeneous dispersion may be obtained by adding emulsifying agents. Mixing them requires high shear.

The mixing of immiscible liquids is discussed as a separate section. In pharmacy, one of the liquids normally used is water. A number of solid and liquid ingredients are added in the formulation of dosage forms. Based on the shear stress-shear rate relationship, fluids are classified as

Newtonian and non-Newtonian systems. The general flow characteristics of the fluids have been discussed in the *Textbook of Physical Pharmaceutics*, by C.V.S. Subrahmanyam (Vallabh Prakashan, Delhi).

Applications of Liquid Mixing

Liquid mixing promotes heat transfer between liquid and a heating source. This step is essential in the crystallization of drug substances. Uniform heat transfer in the solution yields crystals of same size. For example agitated batch crystallizer works on this principle.

Liquid mixing process is essential in the manufacture of a number of dosage forms. Some of them are listed below.

Preparations	*Phases mixing*	*Examples*
Suspensions	Solid-liquid	Calamine lotion
Emulsions	Liquid-liquid (immiscible)	Benzyl benzoate emulsion
Solutions	Soluble solid-liquid	B Complex elixir
Solutions	Soluble liquid-liquid	Alcohol-water (elixir) Chloroform-water (preservative)
Aerosols	Liquid-gas	Salbutamol inhaler

M+

MECHANISMS OF MIXING

The mechanisms of liquid mixing can be studied under four classes. They are:

- Bulk transport
- Turbulent mixing
- Laminar mixing
- Molecular diffusion

Bulk Transport

Bulk transport is defined as the movement of a large portion of a material from one location to another location in a given system.

For this purpose, mixing devices such as rotating blades and paddles are used, which moves the material in different directions.

Turbulent Mixing

Turbulent mixing is defined as mixing due to turbulent flow, which results in random fluctuation of the fluid velocity at any given point within the system.

In the turbulent flow, fluid velocity at a given point fluctuates continuously in three directions, x, y and z. However, the liquid moves in one direction depending on the dominant component. In general, the liquid has different velocities at different locations at the same time.

Turbulent flow is a highly effective mechanism for mixing. Turbulent flow can be seen as a composite of eddies of various sizes. An *eddy* is defined as a portion of fluid moving as a unit in a direction. Large eddies tend to break up forming eddies of smaller size, until they are no longer distinguishable. An additional characteristic of turbulent flow is its intensity, which is related to the velocities with which eddies move.

Laminar Mixing

Laminar mixing is the mixing of two dissimilar liquids through laminar flow, i.e., the applied shear stretches the interface between them.

In this mechanism, layers fold back upon themselves. Thus the number of layers increases. Hence, the interfacial area between them also increases exponentially with time. Mixing may also result in simple stretching of the fluid layers without any significant folding action. This is also suitable for liquids, which require moderate mixing.

Molecular Diffusion

Molecular diffusion is the mixing at molecular level in which molecules diffuse due to thermal motion.

Molecular diffusion is explained by the Fick's law, which depends on the concentration gradient at different regions. The concentration gradient decreases with time and it reaches zero when mixing is completed, i.e., equilibrium condition. When molecular diffusion and laminar flow occur simultaneously, molecular diffusion reduces the sharp discontinuities at the interface between the two layers.

Simultaneously more than one mechanism may operate during mixing.

MIXING VESSELS

The mixing apparatus consists of a container (tank) and a mixing device. These are assembled and used for a batch process. ~~The general construction of the mixing tank or container is shown in Figure 8-14 along with other accessories required for mixing.~~ A mixing device is called impeller, which is mounted with the help of a shaft. The shaft is driven by a motor.

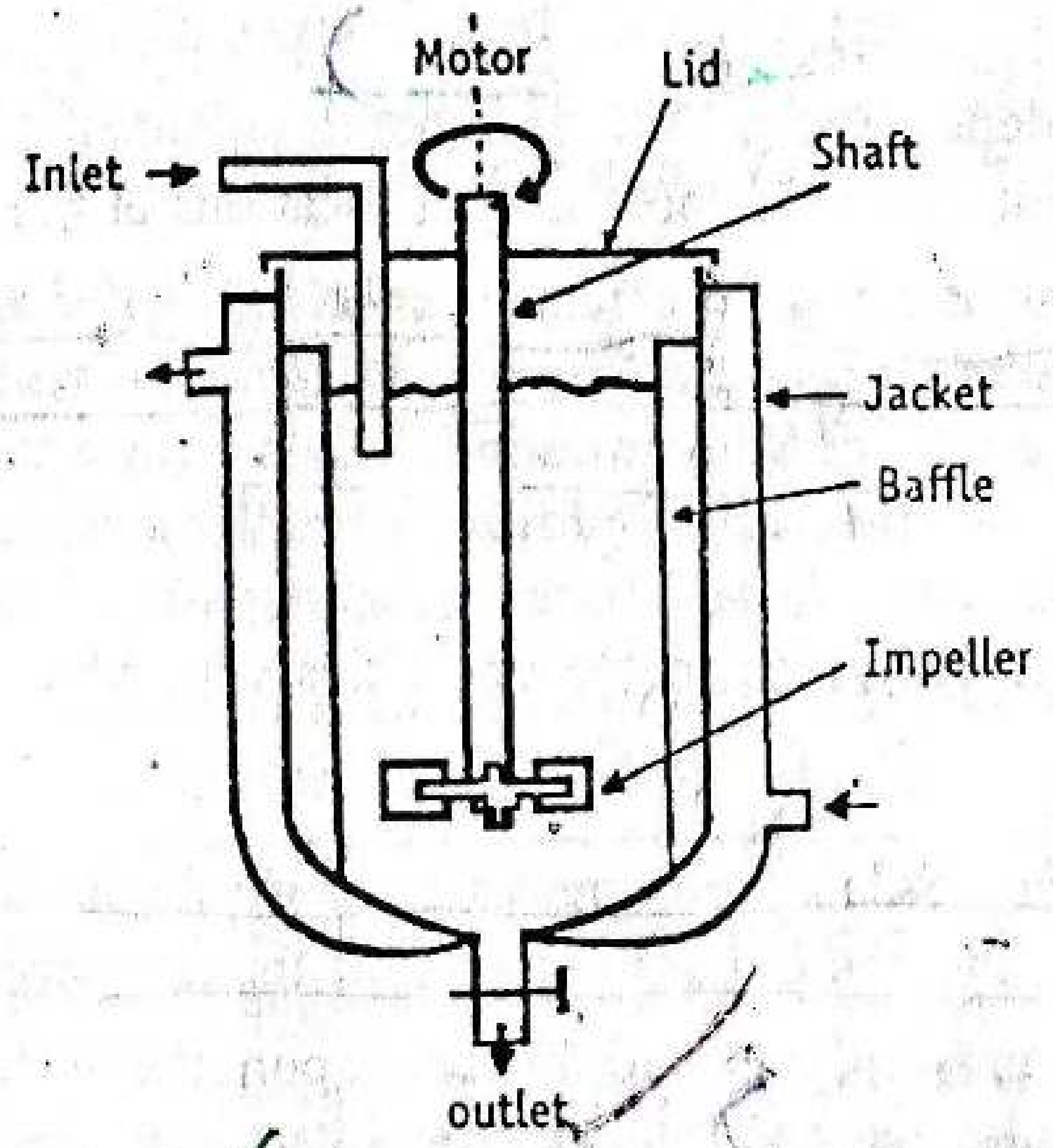


Figure 8-14. Mixing vessel or tank.

The tank is made up of stainless steel. The top of the tank may be open or closed. It is constructed with tank diameter to liquid height ratio of 1:1. The size of the tank depends on the nature of the agitation method. The tank bottom is rounded (not flat) to eliminate sharp corners or regions into which fluid would penetrate. It also carries an outlet, coils, jackets, temperature measuring device etc., wherever necessary.

Baffles : Containers can be either baffled or unbaffled. Baffled containers are those in which metal strips (baffles) are placed vertically to the internal surface. When bulk transport is important in mixing, baffles are used. These are particularly desirable in the initial stages of mixing when segregation is present on a large scale. Baffles facilitate intermingling of the liquids even from remote regions of the mixer.

In most of the cases four baffles are sufficient. Even one or two baffles provide a strong effect on mixing. The width of the baffle may be from 1/10th to 1/18th of the tank diameter. If solids are present in the liquid to be mixed, the baffles are fixed with a gap of about 25 millimetres between the baffle and the tank surface.

The above discussion includes containers in which the liquids move. In some cases, the container itself moves to mix the liquids. One example is *shaker mixer*. Oscillatory movement is applicable on a small scale whereas rotary movement is applicable on a large scale. Shaker mixers are rarely used in pharmacy.

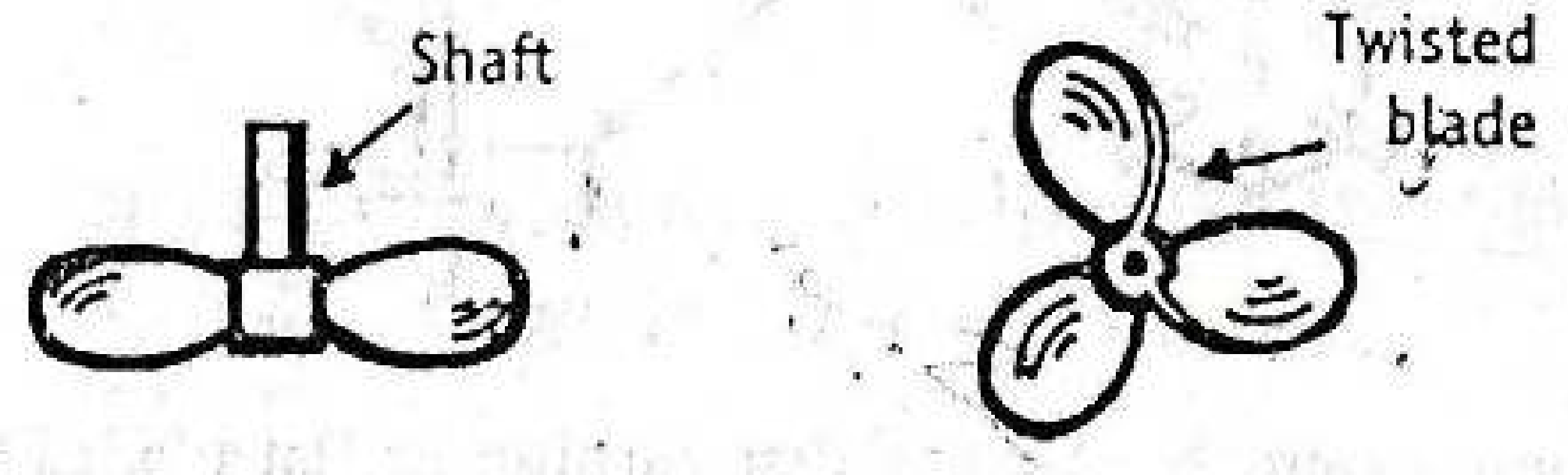
MIXING DEVICES—FLOW PATTERN

Mixing devices are used to supply energy to the system so long as to bring about reasonably rapid mixing. Flow currents are responsible for transporting unmixed materials to the mixing zone.

Mixing devices are technically called as *impellers*. Impellers are classified on the basis of the shape and pitch of the blades that are attached to the central shaft. Three main types of impellers are used namely, propellers, turbines and paddles. These are discussed below.

Propellers

A propeller normally contains a number of blades (Figure 8-15). A three bladed design is the most common for liquids. The marine type propeller is similar to the blades of a table fan or a ceiling fan.



(a) Side view (b) Top view

Figure 8-15. Propeller type of mixing devices. A three bladed design.

Propellers may be either right or left handed, depending on the direction of slant of their blades. Four bladed or toothed or similar design propellers are used for special purposes. In a deep tank, push-pull propeller is used in which two or more propellers may be attached to the same shaft. These work in opposite directions to create a zone of high turbulence. The size of the propeller is small, i.e., the ratio of diameters between propeller and container of 20 is sufficient for low viscous liquids. However, for large tanks the maximum size of 0.5 metres propeller is used. Small propellers turn at full motor speed up to 8000 revolutions per minute.

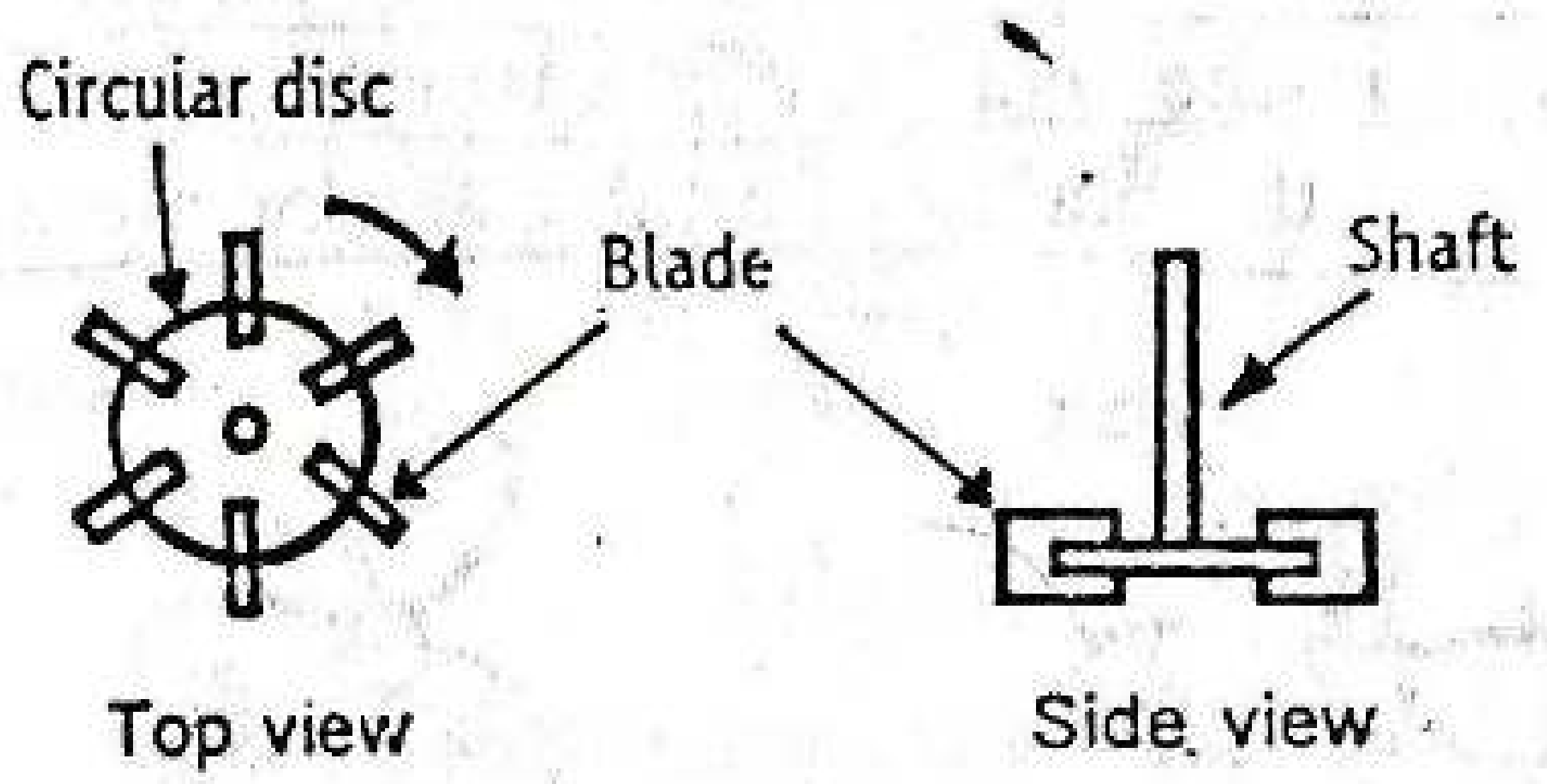
The propeller produces axial (longitudinal) movement of the liquid. The flow currents leaving the propeller continue through the liquid in a given direction until deflected by the floor or wall of the tank.

Uses : Propellers are used when high mixing capacity is needed. These are effective in handling liquids having a maximum viscosity of about 2.0 pascals·second and slurries up to 10% solids of fine mesh size. They can be used upto 3.5 metre cube (or 3500 litres). Effective gas-liquid dispersion is possible at the laboratory scale. Multivitamin elixir, disinfectant solutions are manufactured using propellers.

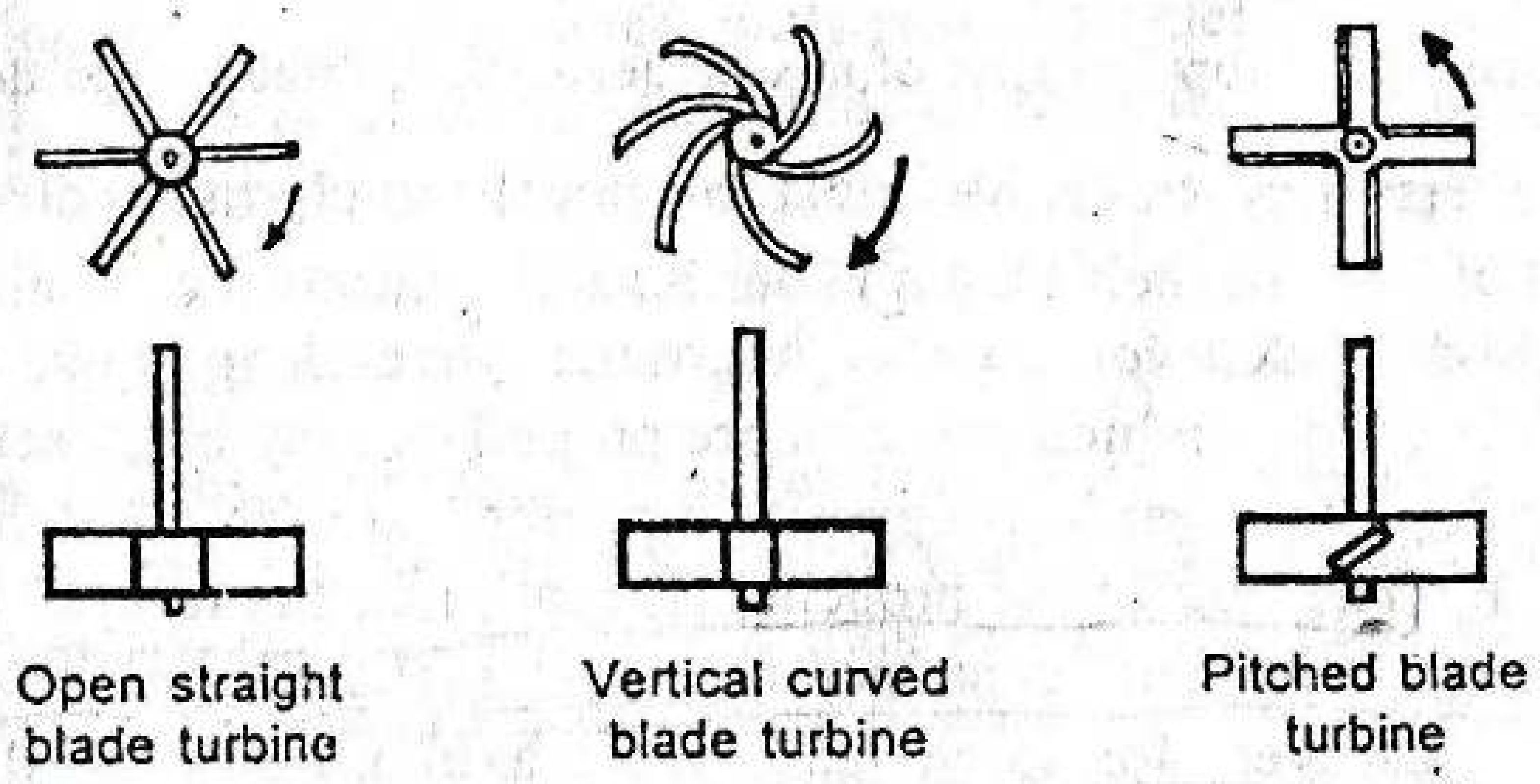
Disadvantage : Propellers are not normally effective with liquids of viscosity greater than 5 pascal-second, for example, glycerin, castor oil etc.

Turbines

A turbine consists of a circular disc to which a number of short blades are attached. (Figure 8-16a). The diameter of the turbine ranges from 30-50 percent of the diameter of the vessel. It rotates at a lower speed than propeller (50-200 revolutions per minute). Different forms of terbines are shown in Figure 8-16. The blades may be straight, curved, pitched or vertical.



(a) General assembly of blade disc turbine or flat bladed turbine.



Open straight blade turbine

Vertical curved blade turbine

Pitched blade turbine

(b) Various types of turbines

Figure 8-16. Turbine impeller (or mixing element).

A flat bladed turbine produces radial and tangential flow, but as speed increases, radial flow dominates. A pitched blade turbine produces axial flow.

Pitch is defined as the distance the impeller would move through the fluid per revolution, if slippage does not occur.

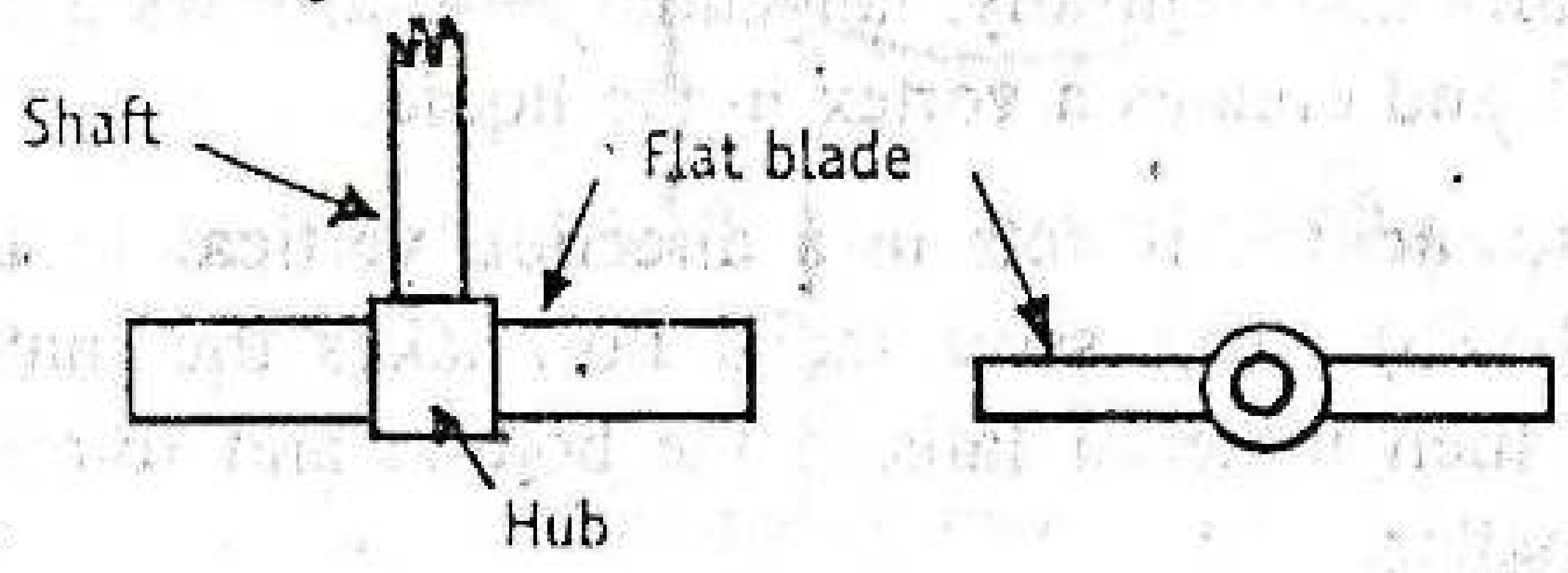
Near the impeller, the zone of rapid currents, high turbulence and intense shear is observed. The shear produced by turbines can be further enhanced using a diffuser ring. A *diffuser ring* is a stationary perforated or slotted ring, which surrounds the turbine. It increases shear forces. The liquid passes through the perforations reducing rotational swirling and vortexing.

Uses : Turbines are effective for high viscous solutions with a very wide range of viscosities upto 700 pascal-seconds. A few examples are syrups, liquid paraffin, glycerin etc. In low viscosity materials of large volumes, turbines generate strong currents (intense shear) which spread throughout the tank destroying stagnant pockets. They can handle slurries with 60% solids. Turbines are suitable for liquids of large volume and high viscosity, if the tank is baffled.

Advantages : Turbines give greater shearing forces than propellers, though the pumping rate is less. Therefore, turbines are suitable for emulsification.

Paddles

A paddle consists of a hub centrally with two long flat blades attached to it vertically (Figure 8-17).



(a) Side view (b) Top view

Figure 8-17. Paddle type of agitator or impeller.

Paddles with two blades or four blades are common. Sometimes, the blades are pitched. In some paddles, the blades are dished or hemispherical in shape and have a large surface area in relation to the tank in which they are used. Because of this shape, paddles pass close to the tank walls and effectively mix viscous liquids, avoiding dead spots and deposited solids.

A shaft carrying hub-blades rotates at a low speed of the order of 100 revolutions per minute. They push the liquid radially and tangentially with almost no axial motion unless the blades are pitched. In deep tanks several paddles are attached one above the other on the same shaft. At very low speeds it gives mild agitation in an unbaffled tank, where as for higher speeds baffles are necessary. Otherwise, the liquid is swirled around the vessel with little mixing.

Uses : Paddles are used in the manufacture of antacid suspensions (aluminium hydroxide gel and magnesium hydroxide), agar and pectin related purgatives, antidiarroheal mixtures such as bismuth-kaolin.

Advantage : Vortex formation is not possible with paddle impellers because of low speed mixing.

Disadvantage : Mixing of the suspension is poor, therefore, baffled tanks are required.

Flow Pattern During Mixing

Liquids are mixed usually by impellers, which produce shear forces, for inducing necessary flow pattern in the container. Mixing takes place due to the resultant effect of three components acting on the liquid. These are radial component, longitudinal component and tangential component (Figure 8-18).

Tangential component (or circular) : It acts in a direction tangent to the circle of rotation around the impeller shaft (Figure 8-18a). If shaft is placed vertically and centrally, tangential flow follows a circular path around the shaft and creates a vortex in the liquid.

Radial component : It acts in a direction vertical to the impeller shaft (Figure 8-18b). Excessive radial flow takes the material to the container wall, then material falls to the bottom and rotate as a mass beneath the impeller.

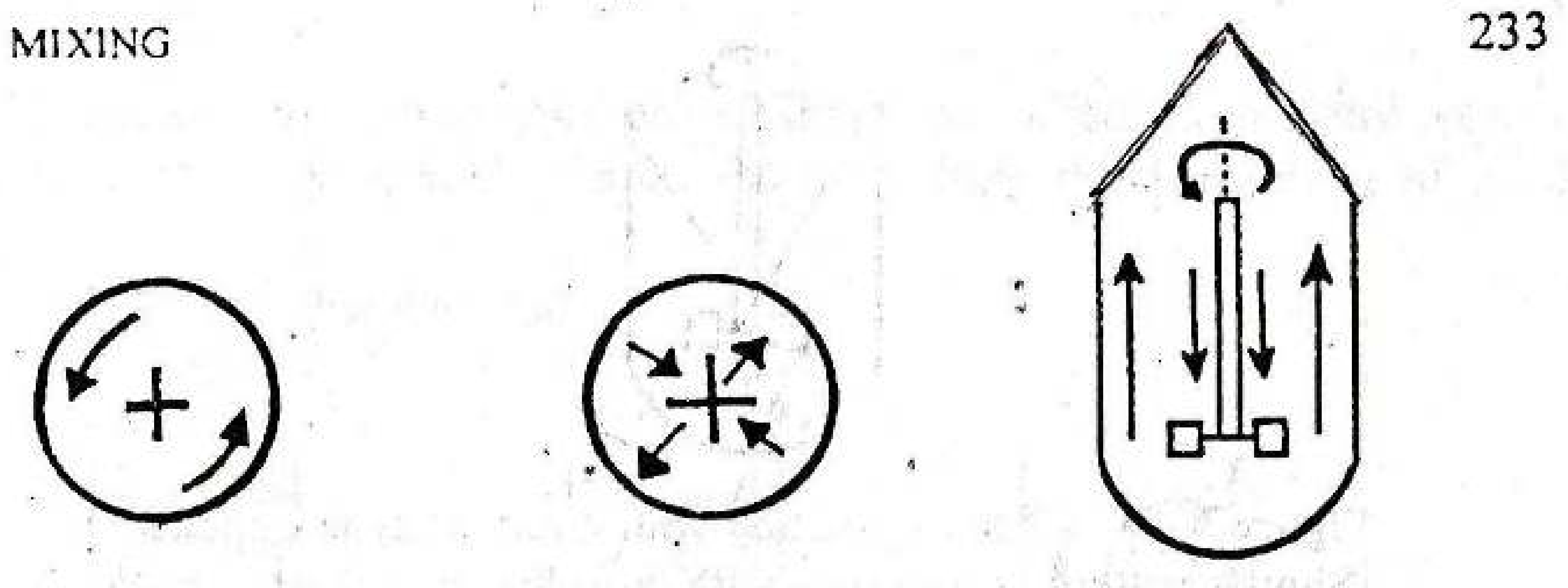
Axial component (or longitudinal or vertical) : It acts in a direction parallel to the impeller shaft (Figure 8-18c). Inadequate longitudinal component causes the liquid and solid to rotate in layers without mixing. Adequate longitudinal pattern is best used to generate strong vertical currents particularly when suspending solids are present in a liquid.

These may occur singly or in various combinations. A satisfactory flow pattern depends on the balance of the components. The flow patterns of different impellers are given in Table 8-3.

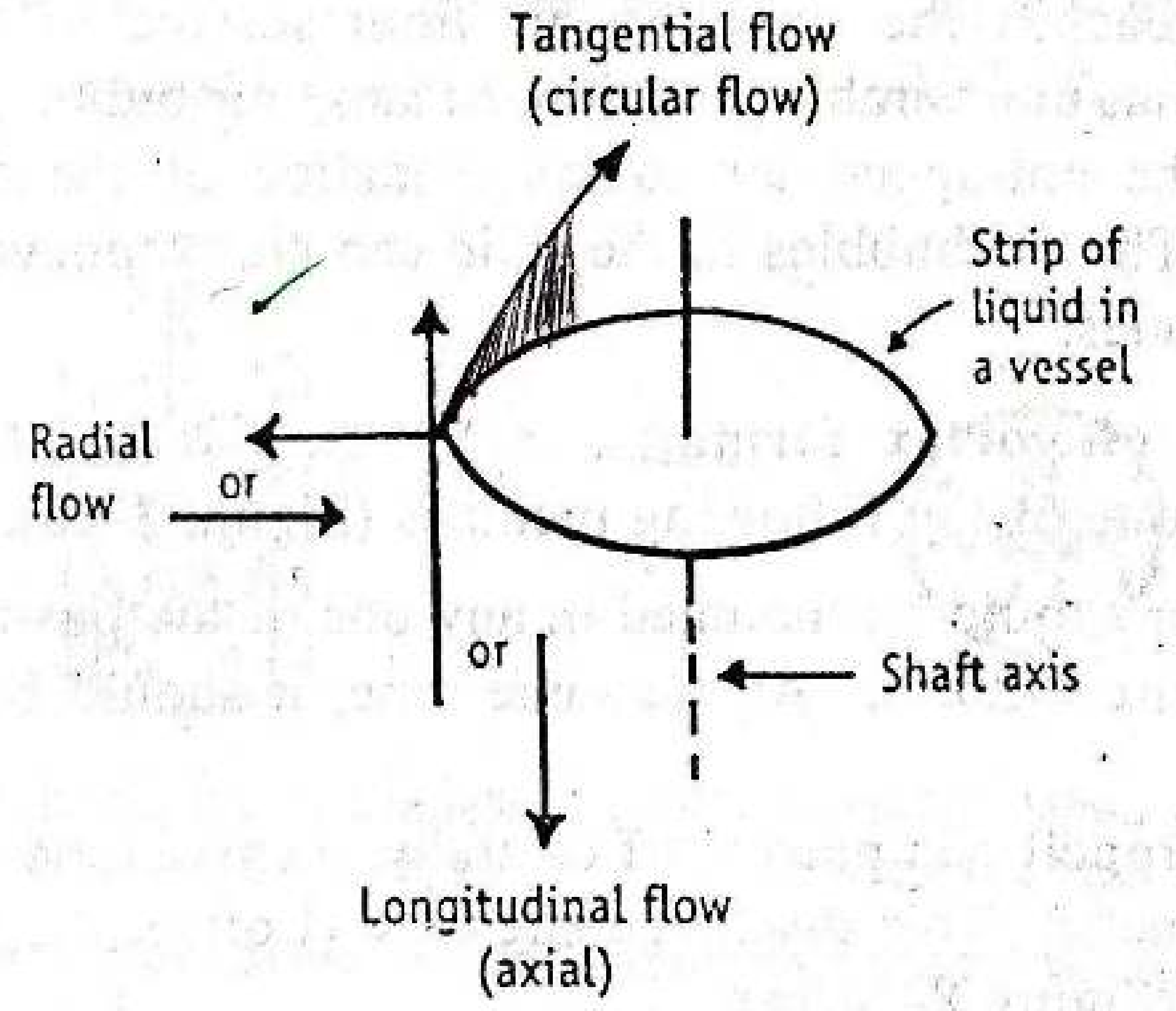
TABLE 8-3

Flow Patterns of Impellers

Impeller type	*Flow component*
Propellers	axial
Turbines	axial or tangential or both
Paddles	radial and tangential not axial
Paddles with pitch	radial, tangential and axial



(a) Tangential or circular flow (top view)　(b) Radial flow (top view)　(c) Axial or longitudinal flow (side view).



(d) Different components of flow at a horizontal strip of liquid section.

Figure 8-18. Diagrammatic representation of a cylindrical tank with tangential, radial and axial flow. Each diagram represents one type of flow (a, b, and c). In usual situations, one or more or a combination of these flow patterns occur simultaneously (d).

Vortex Formation

A strong circulatory flow pattern sometimes manifests into formation of a vortex near the impeller shaft (Figure 8-19).

Vortex can be formed when:

- The shaft is mounted vertically in the centre of the tank, i.e., symmetry. Such a mounting tend to induce tangential flow.
- Blades in the turbines are arranged perpendicular to the central shaft.
- At high impeller speeds.
- In unbaffled tanks.

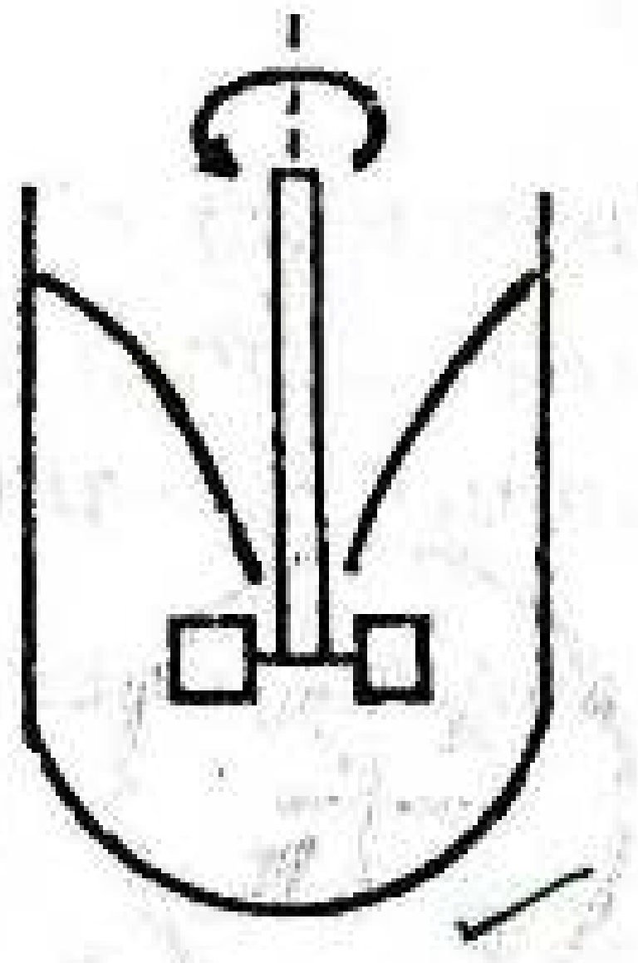


Figure 8-19. Vortex formation with a turbine type impeller (Similar pattern is observed with propeller type also).

drawbacs

Disadvantages : Vortex formation reduces the mixing intensity by reducing the velocity of the impeller relative to the surrounding fluid. When vortex reaches the impeller, air from surface of the liquid is drawn. This is an undesirable situation, because air bubbles are difficult to remove. The entrapped air causes oxidation of the substances in certain cases. The air bubbles in the fluid can create uneven loading of the impeller blades.

Prevention of vortex formation : Vortex formation can be prevented by any one of the following methods (Figure 8-20).

(1) Impeller should be mounted in any one of the positions to avoid symmetry (Figure 8-20.1). At the same time, it should be deep in the liquid.

When the propeller is placed off centrally, a small amount of tangential flow is induced. This discharge stream will offset the swirl induced by its rotation (Figure 8-20.1a).

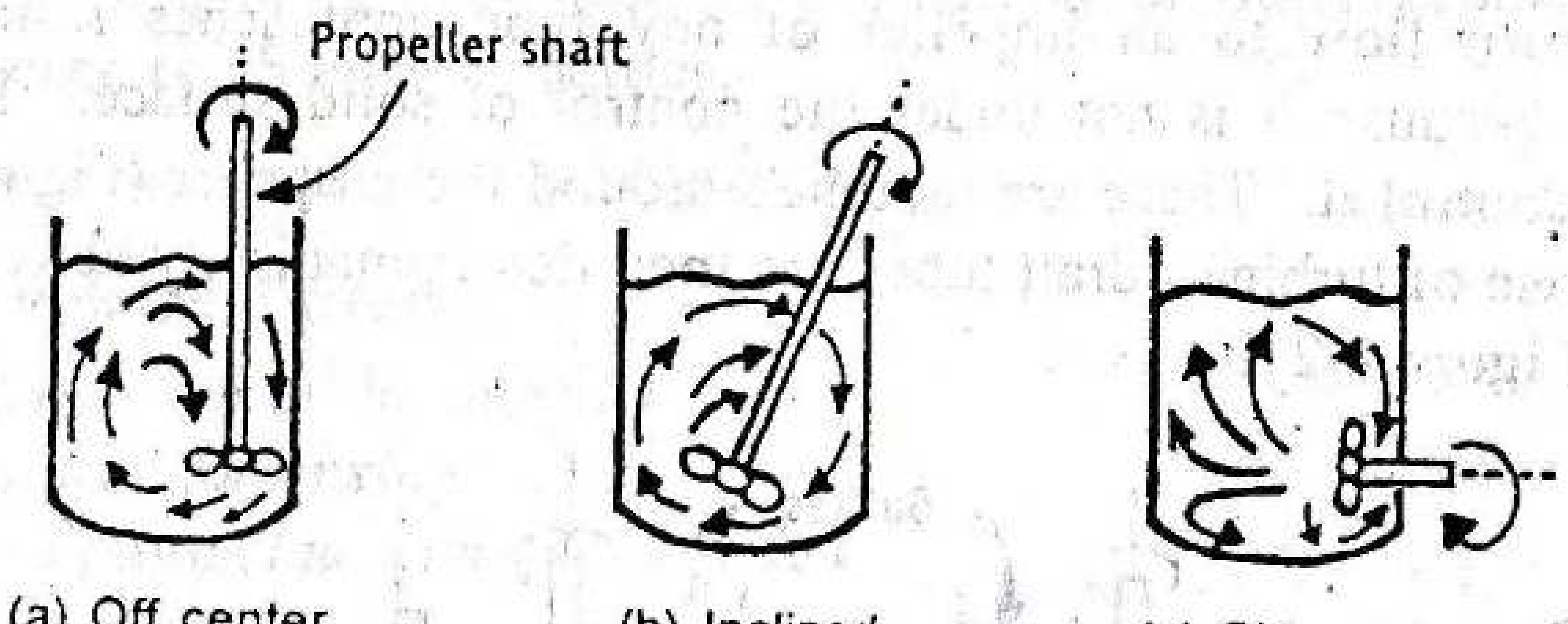
A similar effect can be observed by placing the impeller in an inclined position (Figure 8-20.1b).

In side entering propeller, swirl is seldom a problem. This geometry provides a baffling effect and results in circulation of material from the top to bottom in a vessel (Figure 8-20.1c). The disadvantage for this position is leakage, therefore, the packing round the shaft must be secured. Side entry is also a source of contamination, which is difficult to clean.

(2) Baffled containers should be used (Figure 8-20.2i). In such a case, impeller can be mounted vertically at the center.

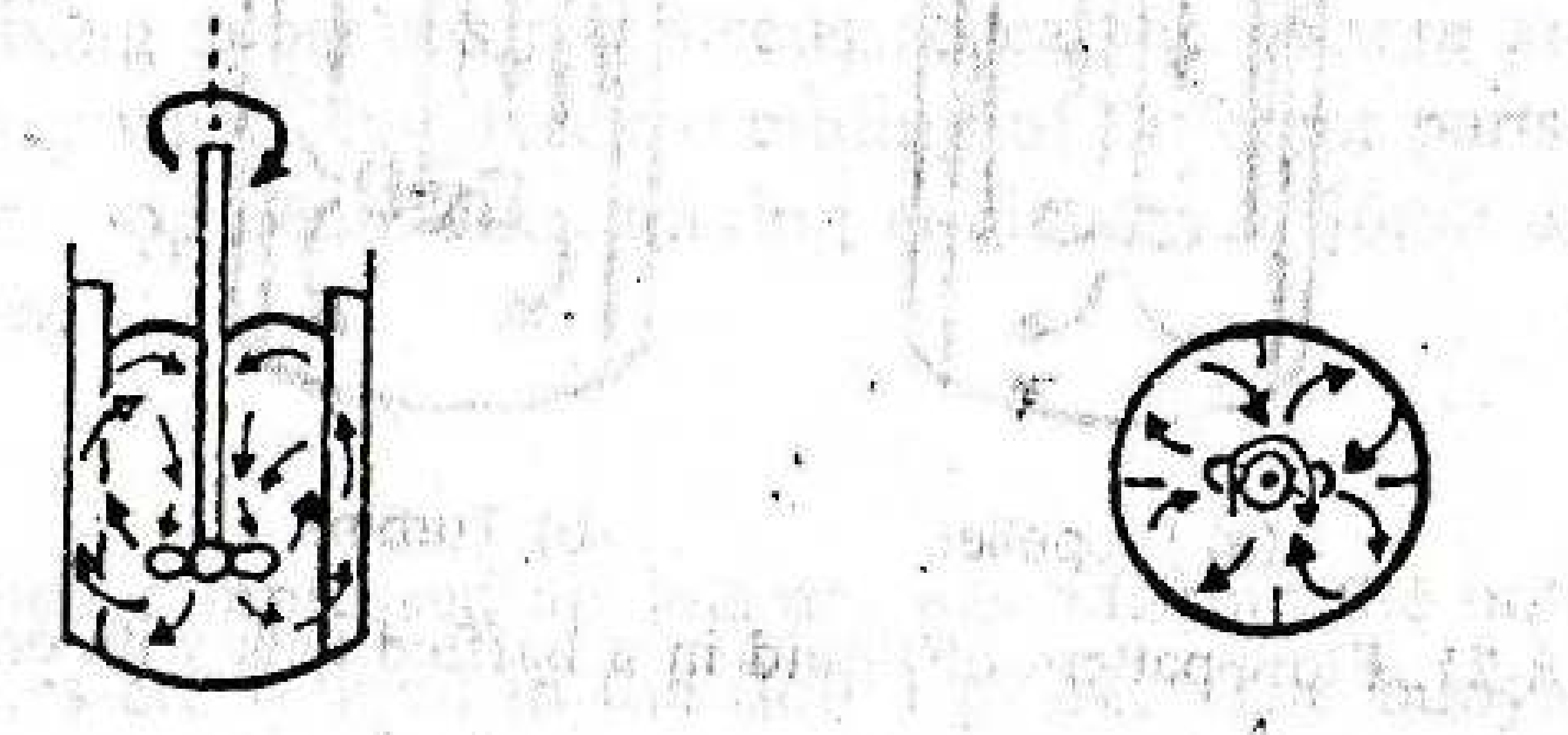
(3) Two or more impellers are mounted on same shaft in a tank where greater depth is desired. This system is known as *push-pull mechanism*. With such an arrangement each impeller acts as a separate mixer. Two types of flow are produced from impellers. The bottom impeller is placed about one impeller diameter above the bottom of the tank (Figure 8-20.3a and b). It creates a zone of high turbulence.

(4) Tanks other than cylindrical shape are used to prevent vortex formation. However, such shapes may facilitate the formation of dead spots.



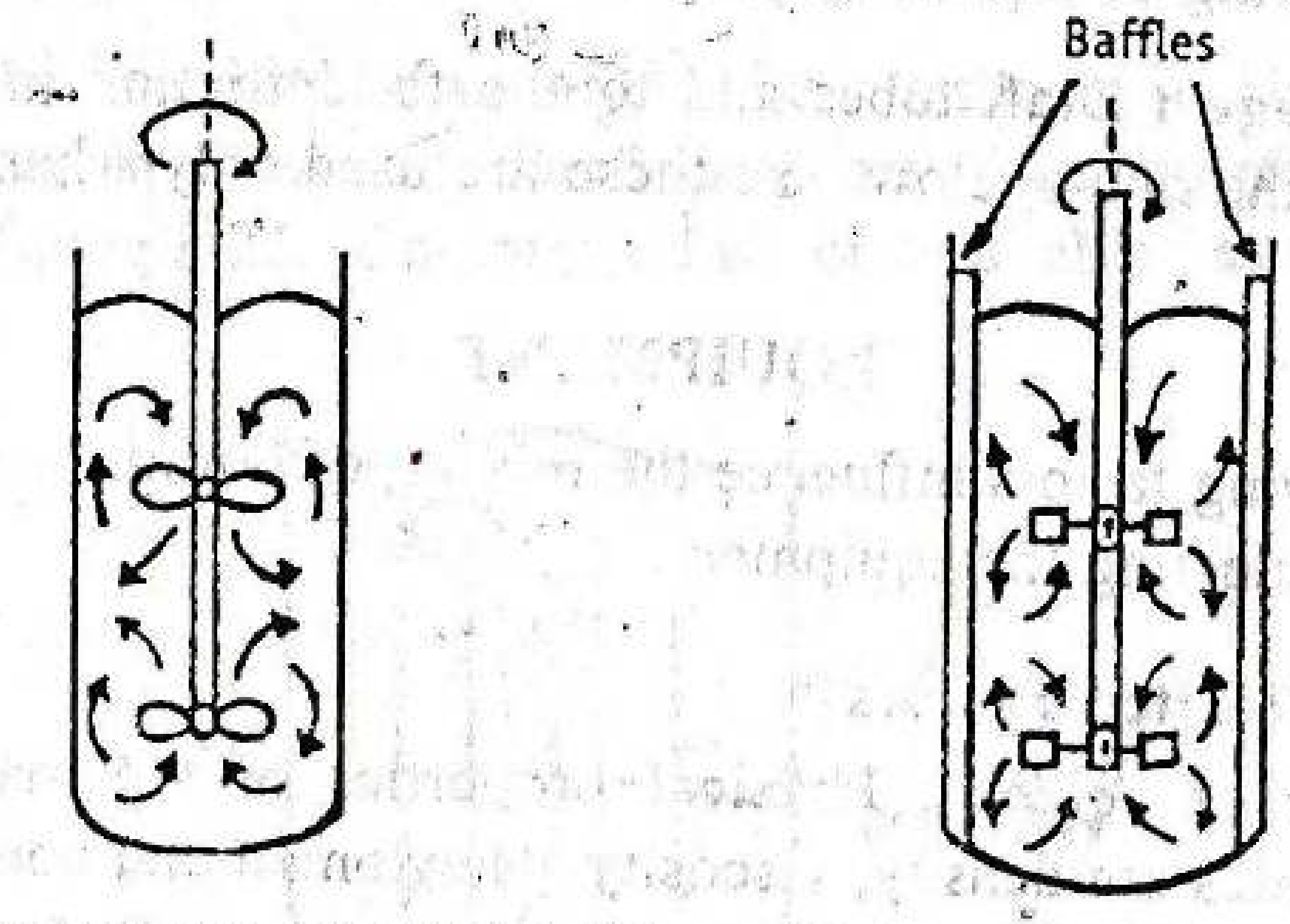
(a) Off center (b) Inclined (c) Side entry

1. Positions of propellers with flow pattern in a vessel to prevent vortex.



(i) Centrally placed propeller in a baffled tank, side view (ii) Centrally placed propeller in a baffled tank, top view

2. Arrangement of baffles and flow pattern in a vessel to prevent vortex.



(a) Propeller in an unbaffled tank (b) Turbine in a baffled tank

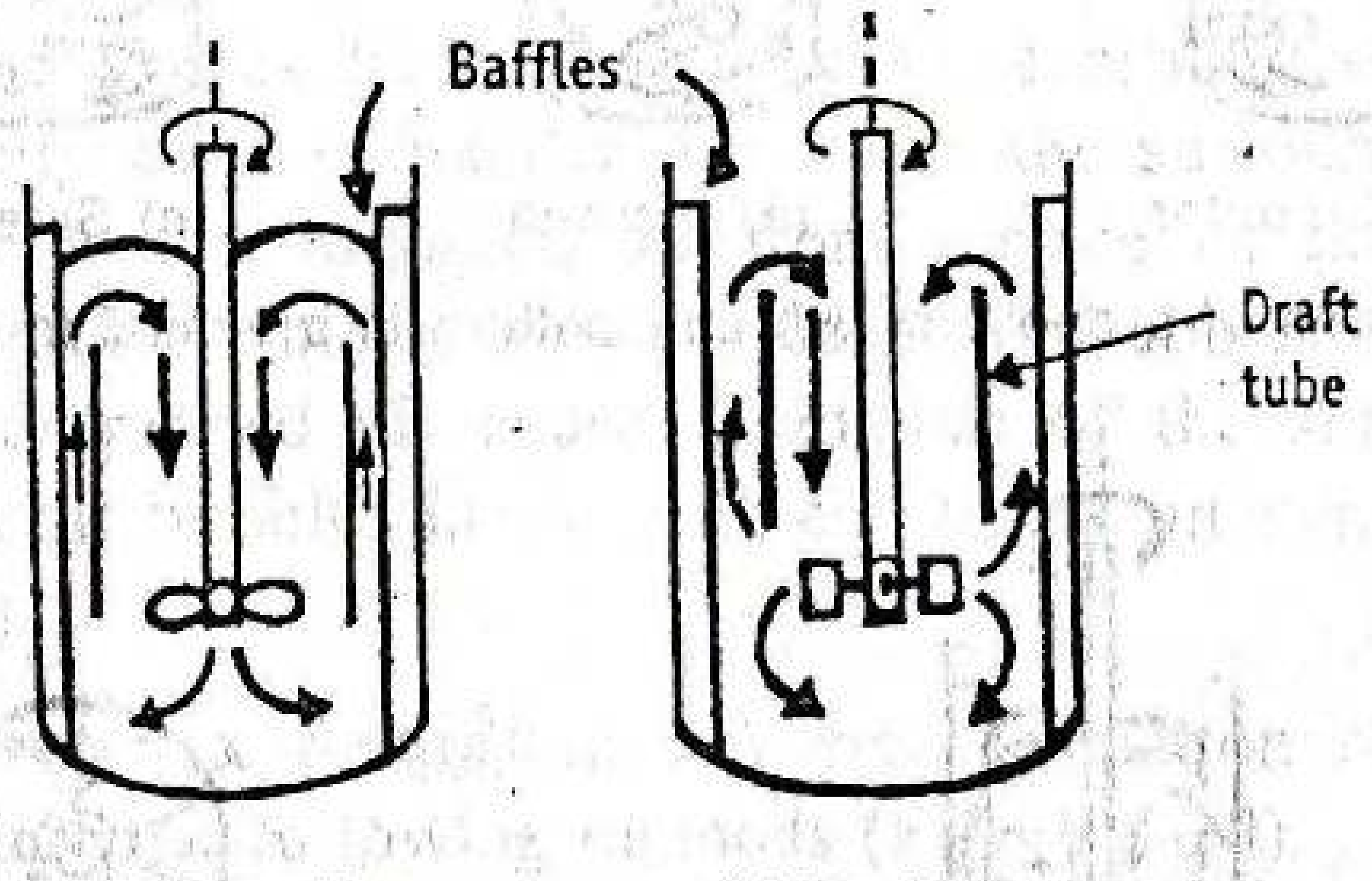
3. Arrangement of push-pull mechanism with flow patterns in a tank to prevent vortex.

Figure 8-20. Positions of impellers with flow pattern in a vessel to prevent vortex formation and gas entrapment.

Return Flow with Draft Tubes

Draft tubes are placed to control the direction and velocity of the flow to the impeller.

The return flow to an impeller of any type approaches from all directions, because it is not under the control of solid surface. Draft tubes can control it. These are mounted around the propeller (Figure 8-21a). In case of turbines, draft tubes are mounted immediately above the impeller (Figure 8-21b).



(a) Propeller (b) Turbine

Figure 8-21. Flow pattern of liquid in a baffled tank with draft tubes

Uses : Draft tubes are fitted to equipment used in the manufacture of certain emulsions. When solid particles tend to float on the surface of the liquid, they are dispersed using draft tubes. Airjet mixers for continuous mixing of liquids employ draft tubes.

Disadvantage : Draft tubes add to the fluid friction in the system. These reduce the rate of flow. So these are used only when required.

EQUIPMENT

The following factors influence the mixing of liquids in tanks. These also help in selecting the equipment.

A. Material Related Factors

Properties of liquids : Physical properties of the materials to be mixed. Examples are density, viscosity (Newtonian and non-Newtonian) and miscibility (intermolecular attractions).

B. Equipment Related Factors

Shape of the impeller : Propeller type, straight, vertical, curved or pitched.

Position of the impeller : Central, off-center, side entry, vertical or inclined etc.

Shape and size of the container : Cylindrical or other geometric forms. Presence or absence of baffles.

Cost of equipment and its maintenance.

C. Process Related Factors

Speed of rotation of the impeller
Time required for mixing
Amount of power that can be expended
Ease of operation
Batch size

The general mixing apparatus are discussed earlier. These are used for batch operations, which involve assembling of different parts. It is also possible to develop continuous mixing equipment. Some of them are discussed below.

AIRJET MIXER

Principle : When compressed air jets are passed from the bottom of a vessel, air bubbles are formed in the liquid phase. The buoyancy of the bubbles lifts the liquids, which are confined to the central portion due to the presence of draft tubes. The liquids flow down from the periphery of the vessel and enter from the bottom due to suction effect. Thus mixing is achieved.

Working : The assembly of an airjet mixer is shown in Figure 8-22. The liquid is placed in the vessel. Draft tubes are placed surrounding air jet as shown in Figure 8-22. Compressed air or a suitable gas is allowed

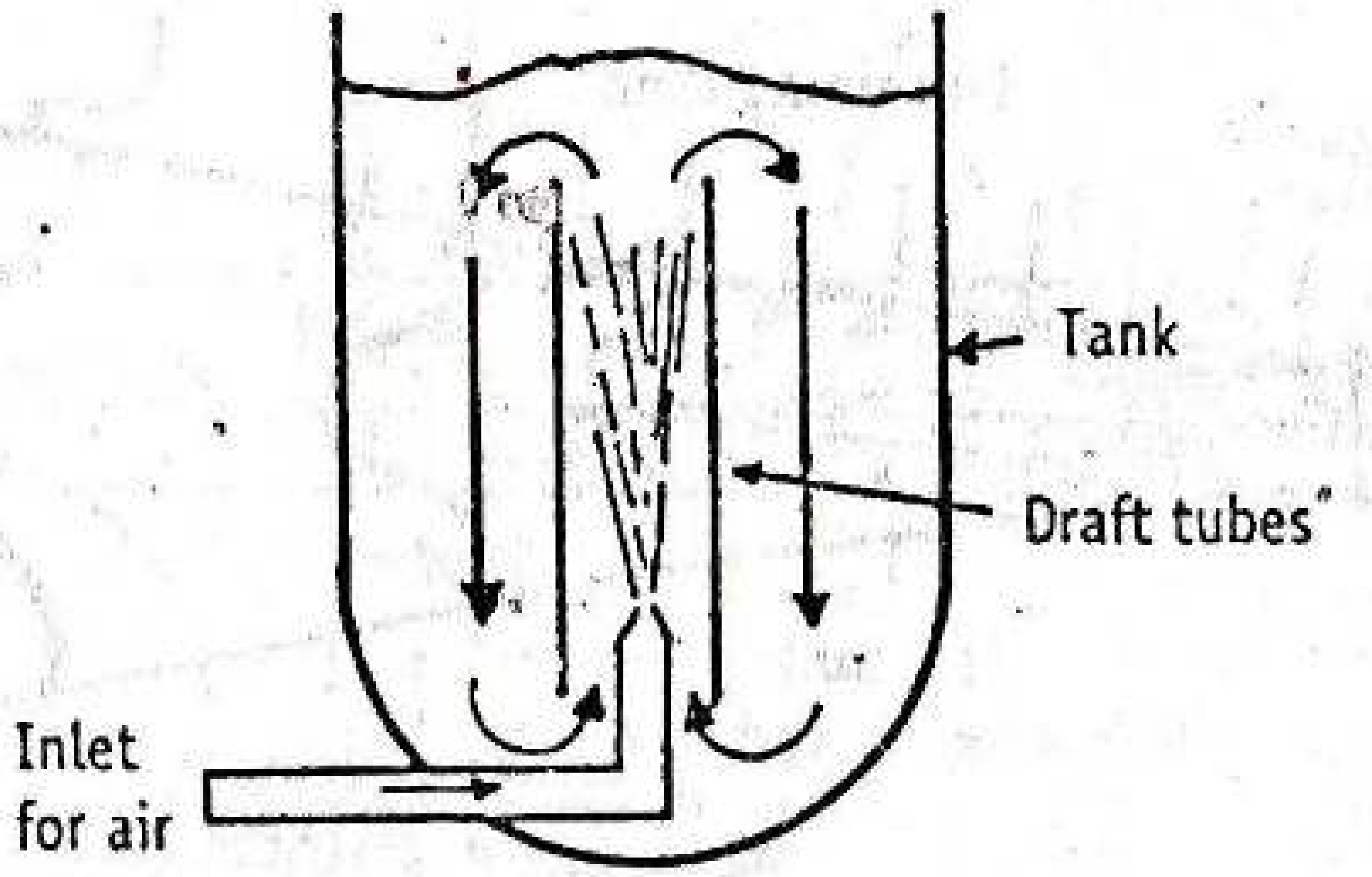


Figure 8-22. Vertical tank with centrally located airjet and draft tube. Mechanism of mixing.

to pass at high pressure from the inlet provided at the bottom of the tank. This causes buoyancy of the bubbles, which lifts the liquids from bottom to the top of the vessel.

Draft tubes serve to confine the expanding bubbles and entrained liquids to the central portion. This results in a more efficient lifting action by the bubbles. The liquid mixture flows down from the periphery of the vessel. The overall circulation brings liquids from all parts of the vessel to the region of the jet itself. Thus mixing is achieved.

Uses : Liquids of low viscosity, non-foaming, non-reactive with gas are mixed by using airjet mixer.

JET MIXER

Principle : The liquids to be mixed are pumped separately into a jet mixer at different velocities. The high velocity fluid has a lower static pressure than surrounding liquid (higher static pressure). During mixing, the slow moving liquid will be drawn into the high velocity jet. This increases the volume of the jet and decreases velocity, which causes the jet to expand. Thus shear is developed and aids in mixing.

Working : The construction of a jet mixer is shown in Figure 8-23. Two liquids are introduced into the mixing tank at different velocities. One liquid is pumped through a small nozzle at uniform high velocity. The second liquid enters the tank at a low velocity. The fast moving liquid impinges on the slow moving liquid at high velocity. As the jet moves away from the orifice, the area of its influence decreases. The core of the jet is surrounded by an expanding turbulent jet, in which the radial velocity decreases with distance from the center-line of the jet.

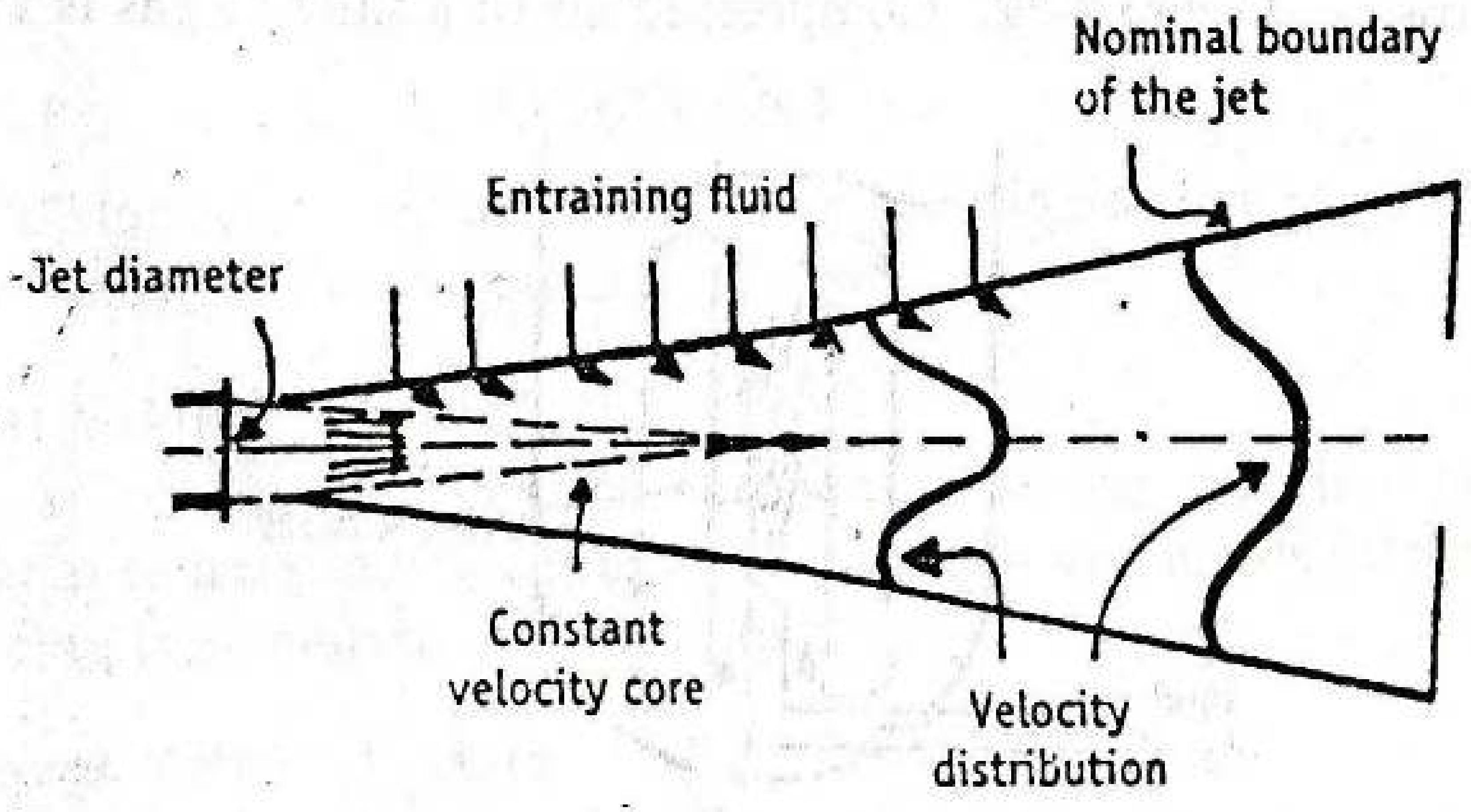


Figure 8-23. Mechanism of mixing in submerged circular jet mixer.

When a rapidly moving liquid comes in contact with slow moving (or almost stationary) liquid, high velocity gradient will be developed at the boundary. As a result, strong shear stresses exist at the boundary, which induce mixing in two ways.

(1) The stresses tear off portions of the fast moving stream and send it off into the slower moving areas as vortexes or eddies. The shear stresses tear off eddies and generates considerable turbulence, which contributes to the mixing action.

(2) When a slow moving liquid enters the jet, the volume of jet increases and velocity decreases. This decreasing velocity causes the jet to expand. Thus shear develops which aids in mixing.

Enough time and space must be provided for the stream to blend thoroughly into the mass of fluid by the mechanism of entrainment.

Advantage : The power required for pumping is often sufficient to accomplish the mixing operation.

FLOW MIXER OR LINE MIXER OR PIPE MIXER

The constructions of a baffled pipe mixer and a chamber mixer are shown in Figure 8-24a and b, respectively. Liquids to be mixed are passed through the pipe. Mixing takes place mainly through bulk transport in the direction of flow. Placing certain devices, such as vanes, baffles, screws, grids and a combination of them, enhances the mixing efficiency. Little additional power supplied to pump the liquid itself accomplishes mixing.

For an effective mixing, controlling the feed rate is essential. Suitable metering devices are employed. If input rate is difficult to control

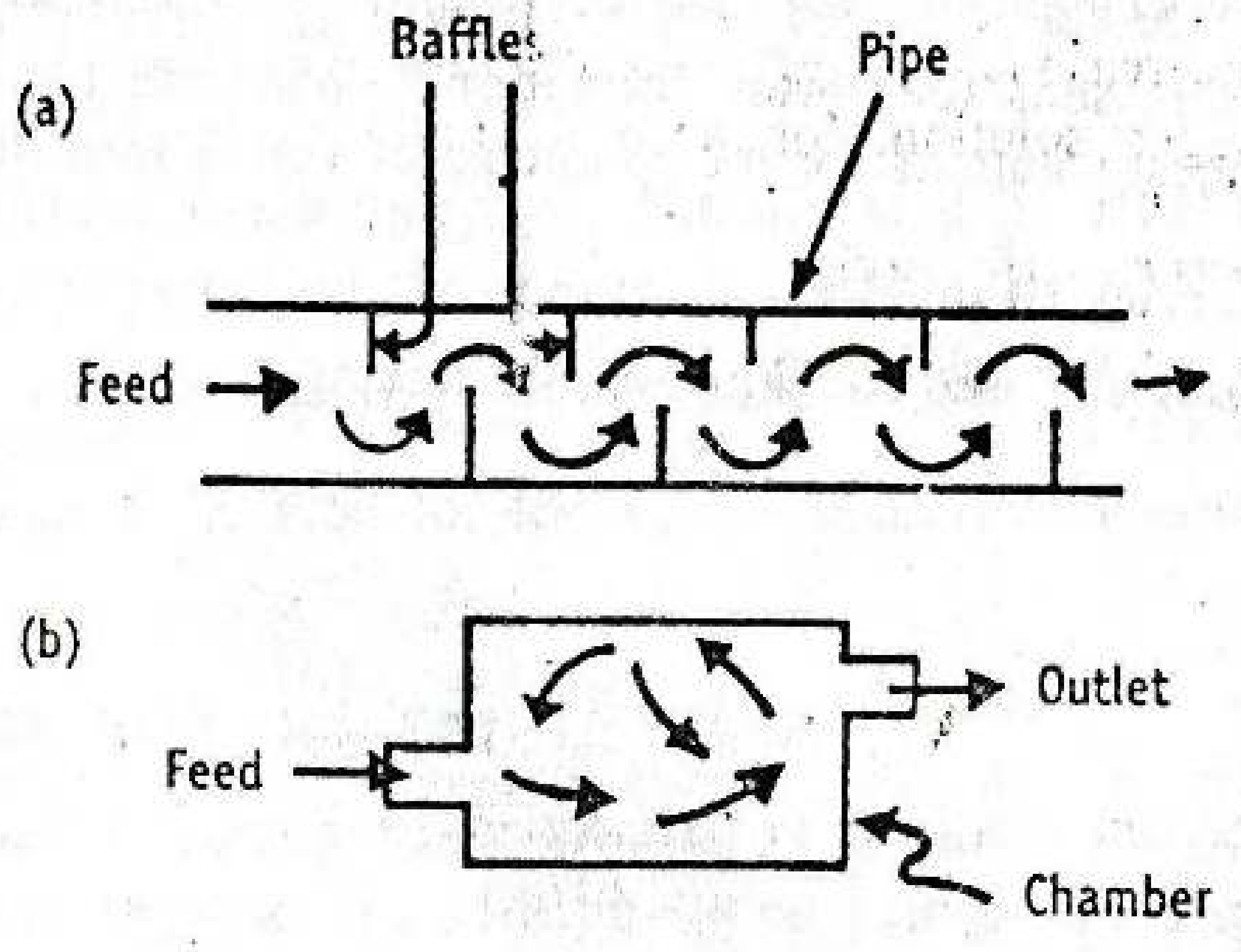


Figure 8-24. Flow pattern of continuous mixer or line mixer.

and fluctuations in the added proportions of the liquids are unavoidable, continuous mixing equipment of tank type is preferable, because hold-up of the liquids and back flow or recirculation is possible.

Uses : When large volume of liquids are to be mixed, flow mixers are used.

(a) Baffled pipe mixer with little back flow.
(b) Chamber mixer with flow induced recirculation and hold up.

QUESTION BANK

Each question carries 2 marks

1. Define and differentiate mixing and agitation.
2. Classify liquids based on their miscibility. Give one example in each case.
3. Enumerate the applications of liquid mixing.
4. Describe the mechanisms for liquid mixing.
5. What are the factors affecting selection of a mixer?
6. How are pipe mixers advantageous in liquid mixing?
7. What do you mean by vortex? How is it prevented?

Each question carries 5 marks

1. Give the characteristics of mixing impellers.
2. Describe the operation of agitator mixers.
3. Describe the turbine mixer with flow pattern.
4. Suggest a suitable mixer and its operation for mixing of viscous liquids.
5. Draw a neat-labeled diagram of mixing tank with accessories for efficient liquid mixing.
6. Describe the principle, working and advantages of jet mixer.
7. What are flow components for liquids? Explain their role during mixing.
8. What are the reasons for vortex formation? What are the drawbacks of vortex? Suggest solutions for the problems of vortex formation.

Each question carries 10 marks

1. Discuss the devices used for liquid-liquid mixing.

Section III—MIXING OF IMMISCIBLE LIQUIDS

Equipment

Mixing of immiscible liquids is carried in pharmacy mainly in the manufacturing of emulsions. The equipment used for the preparation of an emulsion is known as *emulsifier*. Generally a fine emulsion can be obtained and, therefore, equipment is also known as *homogenizer*.

Fine emulsion is prepared in two stages. In the first stage, coarse emulsion is prepared by using one of the following.

– wedge wood	– porcelain mortar and pestle
– mechanical blender	– milk-shake mixer
– hand homogenizer	– propeller in a baffled tank.

Sometimes, the above equipment directly gives fine emulsion. Otherwise, coarse emulsion is subjected to homogenization in the second stage to get fine emulsion by using one of the following.

- Silverson emulsifier
- Colloid mill
- Rapisonic homogenizer

Hence these equipment are also known as *homogenizers*.

EQUIPMENT

Factors Influencing the Selection of an Emulsifier

Quantity of emulsion to be prepared : Batch wise or continuous operation.

Flow properties of liquids : Newtonian, plastic, pseudoplastic or dilatant.

Temperature maintenance : Mixing will be effective at high temperatures provided the material is stable.

Desired rate of cooling : If elevated temperatures are applied.

Some equipment used for the preparation of emulsions are described below.

SILVERSON MIXER—EMULSIFIER

Principle : Silverson mixer-emulsifier produces intense shearing forces and turbulence by the use of high-speed rotors. This turbulence causes the liquids to pass through fine interstices formed by closely placed perforated metal sheets. Circulation of material takes place through the head by the suction produced in the inlet at the bottom of the head. Circulation of the material ensures rapid breakdown of the dispersed liquid into smaller globules.

Construction : The construction of a Silverson emulsifier is shown in the Figure 8-25. It consists of long supporting columns connected to a motor which give support to the head. The central portion contains a shaft, one end of which is connected to the motor and the other end is connected to the head. The head carries turbine blades. The blades are surrounded by a mesh, which is further enclosed by a cover having openings.

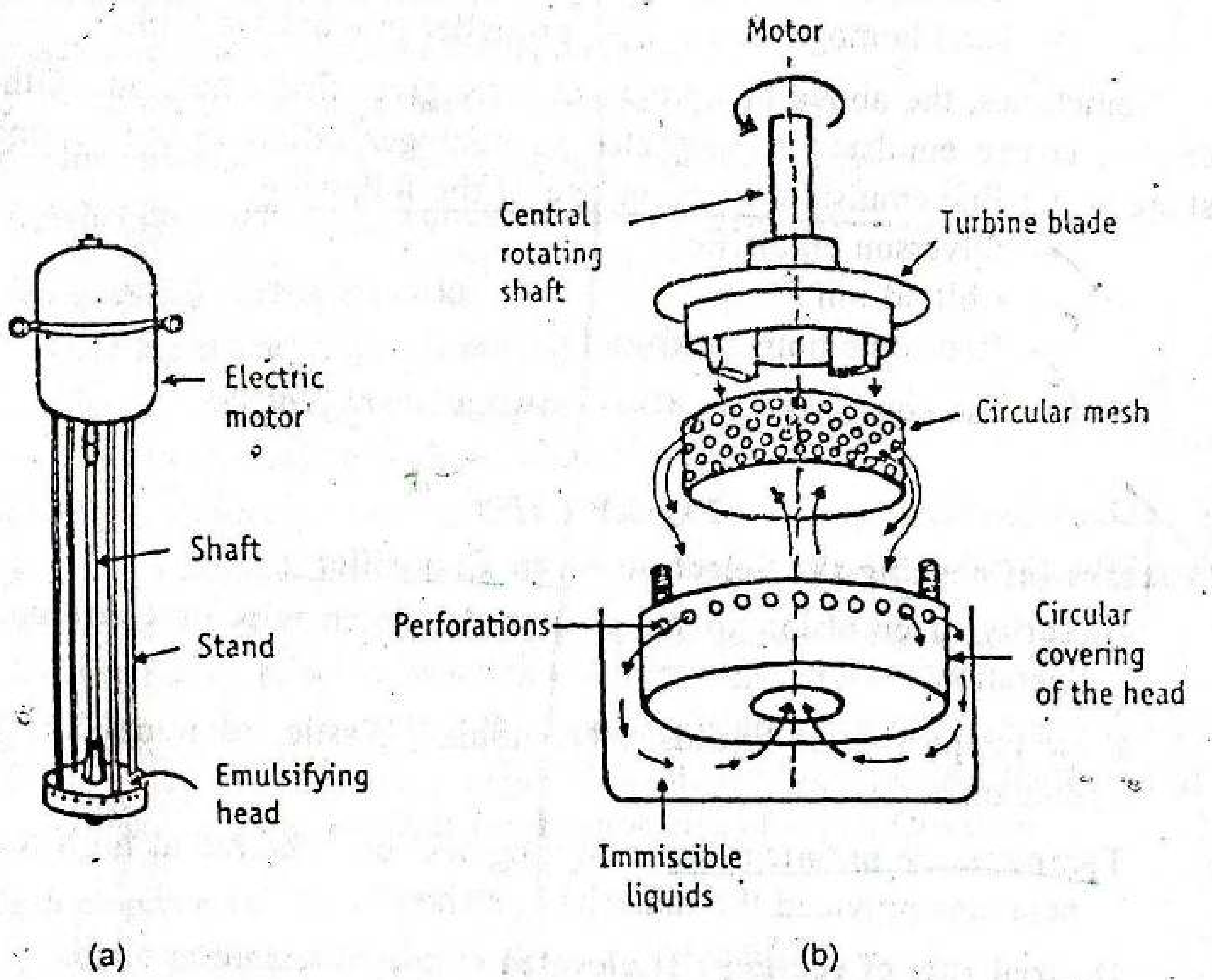


Figure 8-25. Construction of Silverson emulsifier.

Working : The emulsifier head is placed in the vessel containing immiscible liquids (or coarse emulsion) in such a way that it should get completely dipped in the liquid. When the motor is started, the central rotating shaft rotates the head, which in turn rotates turbine blades at a very high speed. This creates a pressure difference. As a result, liquids are sucked into the head from the center of the base and subjected to

intense mixing action. Centrifugal forces expel the contents of the head with great force through the mesh and onto the cover (Figure 8-25b). As a result a fine emulsion emerges through the openings of the outer cover. The intake and expulsion of the mixture set up a pattern of circulation to ensure rapid breakdown of the bigger globules into smaller globules.

Uses : Silverson mixer is used for the preparation of emulsions and creams of fine particle size.

Advantages : (1) Silverson mixer is available in different sizes to handle the liquids ranging from a few millilitres to several thousand litres.

(2) It can be used for batch operations. It is also used for continuous operation by incorporating into a pipeline, through which the immiscible liquids flow.

Disadvantage : Occasionally, there is a chance of clogging of pores of the mesh.

COLLOID MILL

Principle : Colloid mill is based on the principle that the coarse emulsion is intensely sheared in a narrow space between the fast moving rotor and stator for a short period to get a very fine emulsion.

Colloid mill is a mixer as well as milling equipment because size reduction is also simultaneously involved. The construction, working, advantages and disadvantages are discussed in the Chapter 6, Size Reduction.

ULTRASONIC EMULSIFIERS—RAPISONIC HOMOGENIZER

Principle : When a liquid is subjected to ultrasonic vibrations, alternate regions of compression and rarefaction are produced in the liquid. Cavities are formed in the regions of rarefaction, which subsequently collapse in the regions of compression. This results in the generation of great forces for emulsification.

Construction : The construction of a Rapisonic homogenizer is shown in Figure 8-26. It consists of a pump driven by a motor. It is connected with an inlet tube and outlet tube for the discharge of a fine emulsion. The homogenizer head consists of a flat jet for liquid inlet. Facing the jet, a thin blade is present with edges facing each other. This blade vibrates at its natural frequency of about 30 kilohertz.

Working : Coarse emulsion is pumped into Rapisonic homogenizer through one end of a tube. A powerful stream of liquid is forced through the jet. Liquid impinges on the blade causing it to vibrate. The streaming liquid deflects on either side alternatively with the result that oscillations above the sonic range are produced in the liquid. During this process, the emulsion experiences alternate regions of compression and rarefaction. In the regions of rarefaction, cavities are formed. Because of external pressure, the cavities collapse violently afterwards. Thus sufficient turbulence is created which is capable of causing dispersion of phases. Thus a coarse emulsion is converted into a fine emulsion.

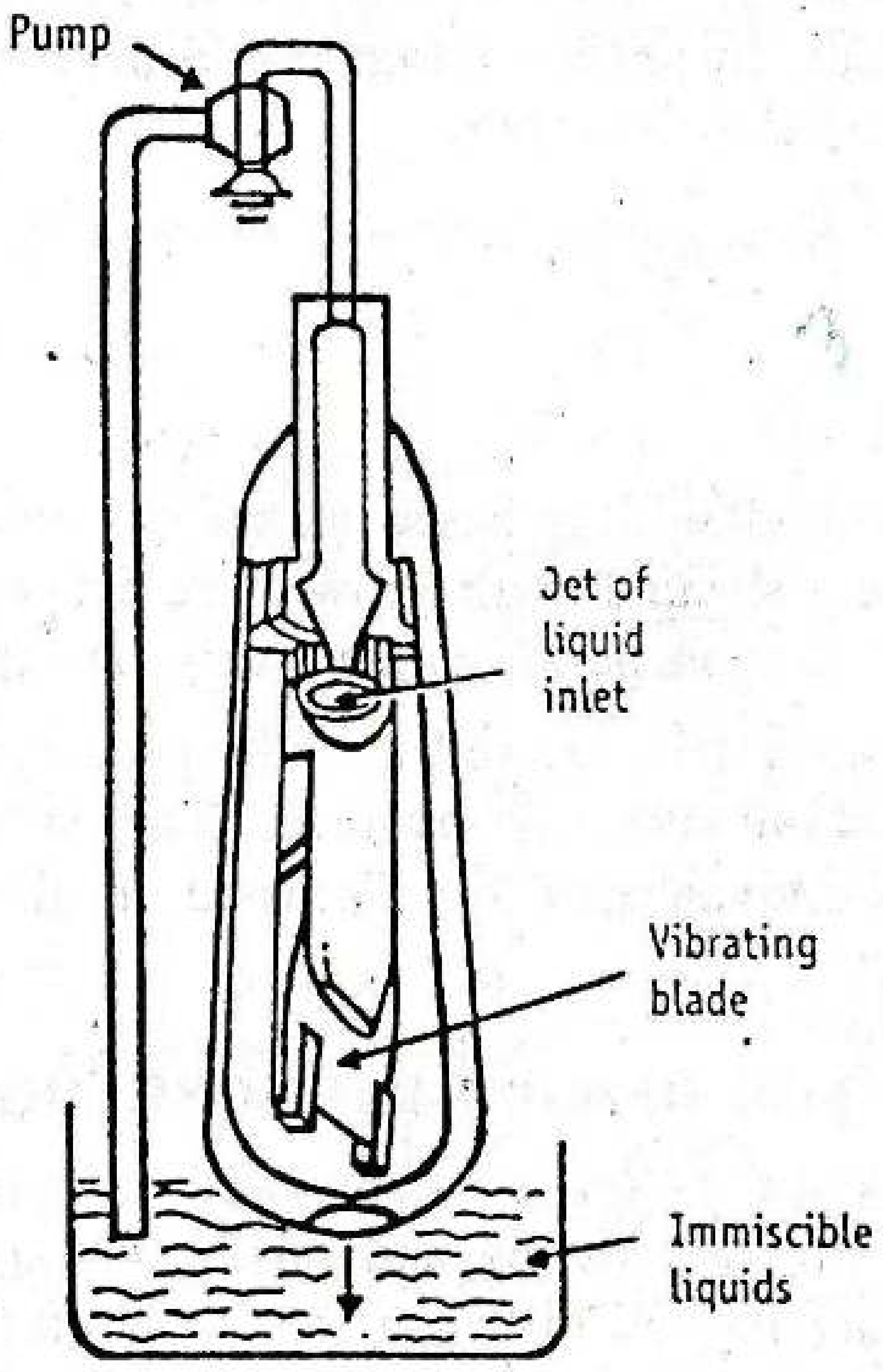


Figure 8-26. Construction of Rapisonic homogenizer.

Advantages : (1) Rapisonic homogenizer can be used either for batch process by placing it in a tank or for continuous process by keeping in a pipeline. In a pipeline, the time of exposure is less for a given sample of liquid in one pass. So, mixing may be incomplete. To ensure complete mixing, liquids must be recirculated.

(2) It has the capacity to produce dispersed globules of one micron size.

(3) As this method is highly efficient to decrease globule size. reduced concentration of emulgents is sufficient.

(4) Its capacity of mixing liquids ranges from 20 to 500 litres per minute.

(5) In Rapisonic homogenizer, heat is not generated during mixing unlike colloid mill. Hence this is suitable for thermolabile substances.

Disadvantage : Rapisonic homogenizer is useful only with liquids of low viscosity.

Section IV—MIXING OF SEMISOLIDS

Equipment

Semisolid dosage forms include ointments, pastes, creams, jellies etc. While mixing such dosage forms, the material must be brought to the agitator or the agitator must move the material throughout the mixer. The mixing action includes combination of low speed shear, smearing, wiping, folding, stretching and compressing. A large amount of mechanical energy is applied to the material by moving parts. Sometimes, a part of the supplied energy appears as heat. The forces required for efficient mixing are high and consumption of power is also high. Hence, the equipment must be ruggedly constructed to tolerate these forces. Mixing equipment are also used for preparing tooth-pastes, pill masses and wet mass for granulation.

Some semisolids exhibit dilatant property, i.e., viscosity increases with increase in shear rates. Therefore, mixing must be done at lower speeds. The speed must be changed accordingly to thixotropic, plastic and pseudoplastic materials.

EQUIPMENT

Classification of Equipment

Agitator mixers : Examples are sigma mixer and planetary mixer.

Shear mixers : Examples are triple roller mill and colloidal mill.

Sigma blade mixer and planetary mixer are discussed in the solid-solid mixing. Colloidal mill is discussed in the Chapter 'Size Reduction'. Triple roller mill is discussed here.

Selection of Mixing Equipment for Semisolids

(1) Physical properties of the materials - density, viscosity and miscibility.

(2) Economic considerations regarding processing - time required for mixing and power consumption.

(3) The cost of equipment and its maintenance.

TRIPLE ROLLER MILL

Principle : The differential speed and the narrow space between the rollers develop high shear over the material. This shear causes crushing of aggregates, particles and also distributes the drug uniformly throughout the semisolid base.

Construction : The construction of a triple roller mill is shown in Figure 8-27. It consists of three parallel rollers of equal diameters. These are made up of hard abrasion resistant material, normally stainless steel. The rollers are mounted in a rigid framework horizontally. The pressure and gap between the rollers are independently adjustable. A hopper is arranged between the first two rollers. A scrapper is attached to the last roller.

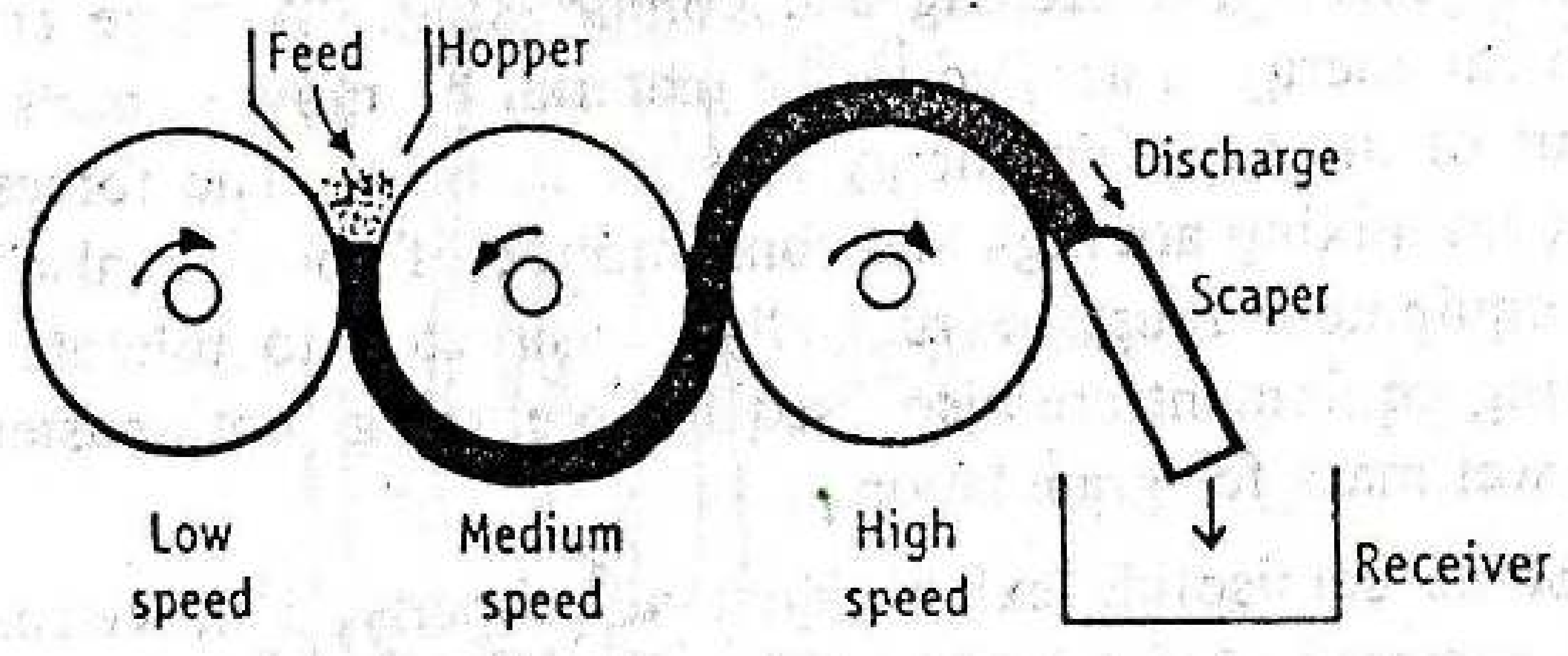


Figure 8-27. Construction of triple roller mill.

Working : The gap between the last two rollers is adjusted to be less than the gap between the first two rollers. The rollers are rotated at different speeds. In practice, the first roller (receiving-roller) rotates at a slower speed compared to the second roller. Similarly second roller speed is less than that of third roller (discharge roller).

The feed is passed through the gap between the first and second rollers. The aggregates and particles are crushed and then abraded by the rubbing action of the rollers, which is developed due to different speeds of rotation. A film of appreciable thickness of the feed is produced. The material passes from slow rotating to fast rotating roller. Between second and third roller, the gap is small and produces a thinner film of feed. The speed of the third roller is increased to compensate the reduction of cross sectional area. In the thinning film, more crushing and more abrasion are developed.

Finally the scrapper removes the material completely from the last roller which can be collected immediately into the receiver or transported through a suitable conveyor.

Advantage : Triple roller mill is suitable for continuous processes. Extremely uniform dispersion is obtained.

QUESTION BANK

Each question carries 2 marks

1. Suggest suitable mixing equipment for semisolids.
2. Describe the different factors influencing the selection of an emulsifier.

Each question carries 5 marks

1. Describe the construction and working of a Silverson mixer-emulsifier with the help of a neat diagram.

Each question carries 10 marks

1. With a neat sketch, describe the construction and working of equipment for mixing pastes and plastic masses. What are their pharmaceutical applications?

9

Filtration

- Mechanisms of Filtration
- Theories of Filtration
- Factors Influencing Filtration
- Filter Media and Filter Aids
- Classification of Filtration Equipment
- Equipment

Filtration may be defined as a process of separation of solids from a fluid by passing the same through a porous medium that retains the solids, but allows the fluid to pass through.

The suspension to be filtered is known as *slurry.* The porous medium used to retain the solids is known as *filter medium.* The accumulated solids on the filter are referred to as *filter cake,* while the clear liquid passing through the filter is *filtrate.*

When solids are present in a very low concentration, i.e., not exceeding 1.0% w/v, the process of its separation from liquid is called *clarification.*

Clarification is generally employed when contaminating material is finely subdivided, amorphous or colloidal in nature. These solids tend to plug the filter medium. Several other processes having similar mechanisms are decolouration, decantation, colation, expression etc.

Process of Filtration

A typical filtration operation is shown in Figure 9-1. The pores of the filter medium are smaller than the size of particles to be separated. Filter medium (for example filter paper or muslin cloth) is placed on a support (a sieve). When slurry (feed) is passed over the filter medium, the fluid flows through the filter medium by virtue of a pressure differential across the filter. Gravity is acting on the liquid column. Therefore, solids are trapped on the surface of the filter medium.

Once the preliminary layer of particles is deposited, further filtration is brought about wherein the filter medium serves only as a support. The filter will work efficiently only after an initial deposit. In an industrial scale, large quantities of suspensions are mechanically handled. After a particular point of time, the resistance offered by the filter cake is high that virtually filtration is stopped. For this reason, a positive pressure is applied on the filter cake (upstream) or negative pressure (suction) is applied below the filter medium (downstream).

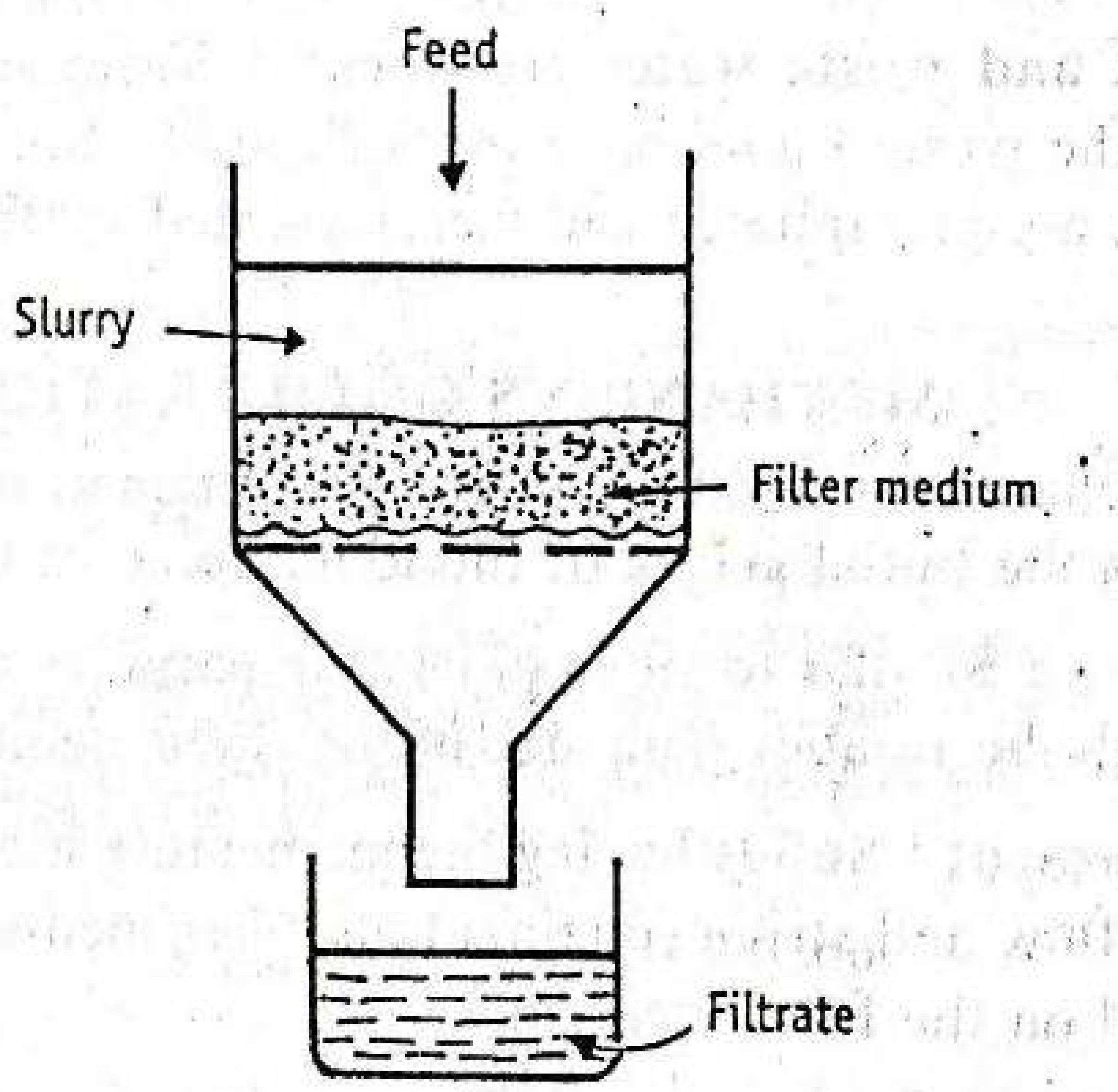


Figure 9-1. Principle of filtration.

Applications

Production of sterile products : Air is filtered through HEPA filters (high efficiency particulate air filters) or laminar air bench to obtain sterile air, which maintains good environment prior to and during manufacture of sterile products.

A solution is passed through a bacteria proof filter in order to obtain sterile solution, particularly when heat sterilisation is not suitable on account of thermolabile nature of the contents. In case of sterile products, particles as small as 0.2 μm should be removed, which includes the bio-burden of fungi, bacteria etc.

Similar facilities are required for the production of antibiotics by fermentation, recombinant technologies of biological products and vaccines.

Production of bulk drugs : Solids of intermediates and finished products are separated from the reaction mixture by filtration techniques. By this method, impurities can be removed.

Production of liquid oral formulations : Filtration is an essential step in the production of liquid orals for obtaining clear solutions (clarification).

(a) Dewaxing of oils.
(b) Removing suspended oils from aqueous solutions. Examples are aromatic waters, syrups, elixirs, eye drops etc.
(c) Removing of undesirable solids, which interfere with the transparency of the liquids. Examples are honey and fruit juices.
(d) Clarifying the potable water.

Affluent and waste water treatment : Waste solids must be separated from the waste liquid prior to its disposal. Sometimes, the soluble components are precipitated and then separated by filtration.

MECHANISMS OF FILTRATION

The mechanism whereby particles are retained by a filter is significant only in the initial stages of filtration. Some of the mechanisms are:

Straining : Similar to sieving, i.e., the particles of larger size cannot pass through the smaller pore size of the filter medium.

Impingement : Solids having the momentum move along the path of streamline flow and strike (impinge) the filter medium. Thus, the solids are retained on the filter medium.

Entanglement : Particles become entwined (entangled) in the mass of fibres (of cloth with a fine hairy surface or porous felt) due to smaller size of particles than the pore size. Thus the solids are retained on the filter medium.

Attractive forces : Solids are retained on the filter medium as a result of attractive forces between particles and filter medium, as in case of electrostatic precipitation.

In practice, filtration may combine various mechanisms.

Types of Filtration

Based on the mechanism, two types of filtration are broadly identified.

Surface filtration (Screen filtration) : It is a screening action by which pores or holes of the medium prevent the passage of solids.

The mechanisms, straining and impingement are responsible for surface filtration. For this purpose, plates with holes or woven sieves are used (Figure 9-2). Its efficiency is defined in terms of mean or maximum pore size.

Depth filtration : In this process, slurry penetrates to a point where the diameter of solid particles is greater than that of the tortuous void or channel.

Depth filtration is aided by the mechanism entanglement. The solids are retained with a gradient density structure by physical restriction or by adsorption properties of the medium (Figure 9-2). It is extensively used for the removal of small amounts of contaminants from relatively large volumes of liquids (clarification). These are also used for roughing or prefiltering pharmaceutical solutions. Examples are ceramic filters, sintered (bed) filters.

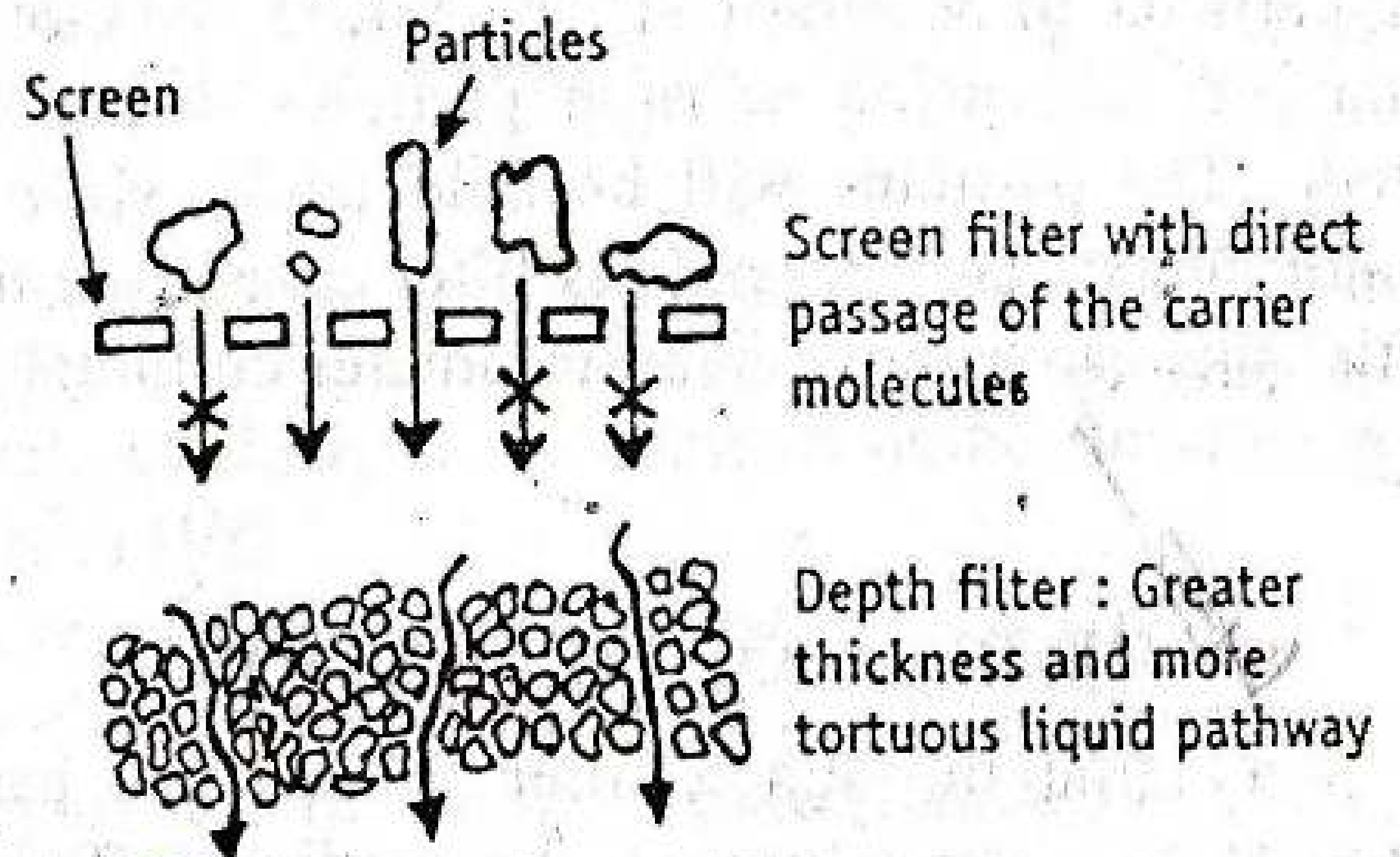


Figure 9-2. Types of filtration.

②

TABLE 9-1

Differences Between Surface and Depth Filtration

Surface filtration	*Depth filtration*
The size of the particles retained is slightly higher than the mean pore size of the medium.	The size of the particles retained is much smaller than the pores through which fluid passes.
Mechanical strength of the filter medium is less, unless it is made of stainless steel.	Mechanical strength is high.
It has low capacity	It has high capacity
The size of the particles retained is more predictable.	The size of the particles retained is less predictable.
Equipment is expensive because it should require ancillary equipment such as edge clamps, which should be much finer tolerances.	Cheaper because ancillary equipment is not required.
Example is cellulose membrane filter.	Examples are ceramic filters, and sintered (bed) filters.

A special case of depth filtration is the *sheet filtration*, in which the slurry is passed through a series of pads mounted endwise to the flow of fluids. The pads commonly consist of a mixture of asbestos fibres embedded in cellulose.

The differences between surface and depth filtration are given in Table 9-1.

Cake filtration : A filter consists of a coarse woven cloth through which a concentrated suspension of rigid particles is passed so that they bridge the holes and form a bed.

The cloth may be ineffective when the holes are likely to be much larger than the particles to be removed. Therefore, the cloth is presented with a concentrated suspension of rigid particles that bridge the holes and form a bed. The particles will be held back, while liquid passes through the small interstices. Example is filter cake made from diatomite (100 µm). This cake can remove submicrometer colloidal particles with high efficiency.

THEORIES OF FILTRATION

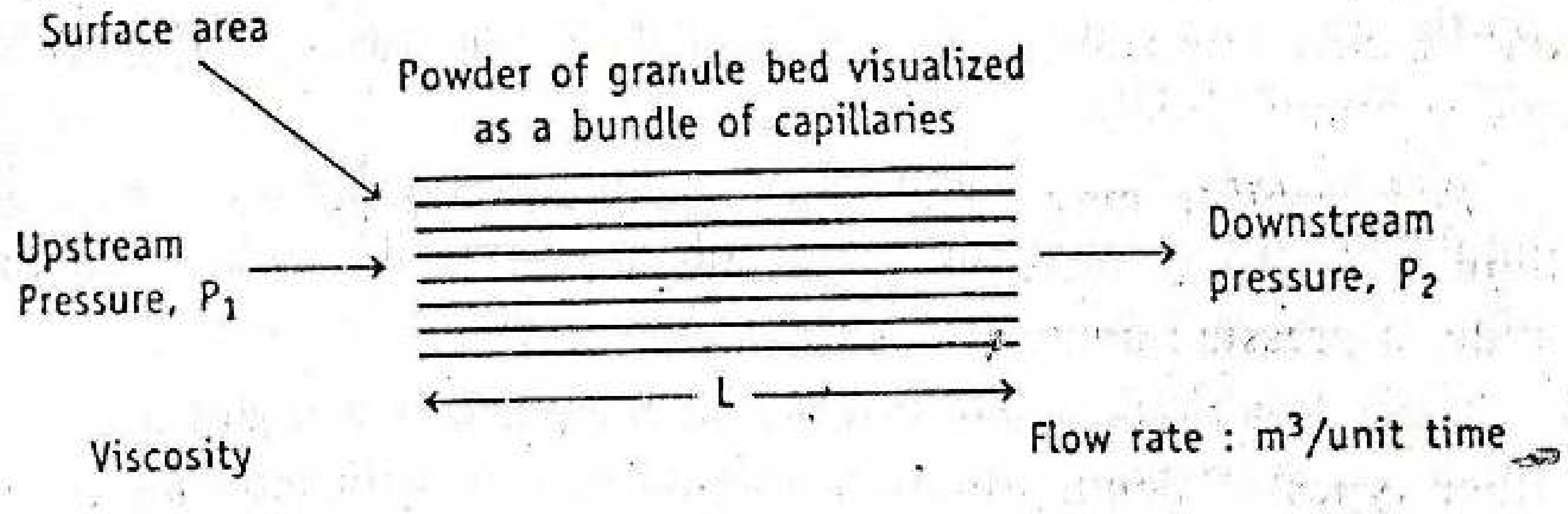
The flow of a liquid through a filter follows the basic rules that govern the flow of any liquid through the medium offering resistance. The rate of flow may be expressed as:

$$Rate = \frac{\text{driving force}}{\text{resistance}} \qquad (1)$$

The rate of filtration may be expressed as volume (litres) per unit time (dv/dt). The driving force is the pressure differential between the upstream and downstream of the filter. The resistance is not constant. It increases with an increase in the deposition of solids on the filter medium. Therefore filtration is not a steady state.

The rate of flow will be greatest at the beginning of the filtration process, since the resistance is minimum. Once the filter cake is formed, its surface acts as filter medium and solids continuously deposit adding to the thickness of the cake. The resistance to flow is related to several factors as mentioned below.

$$\text{Resistance to movement} = \frac{\text{pressure upstream} - \text{pressure downstream}}{\text{length of capillaries}} \qquad (2)$$



Poiseuille's Equation

Poiseuille considered that filtration is similar to the streamline flow of a liquid under pressure through capillaries. Poiseuille's equation is:

$$V = \frac{\pi \Delta P r^4}{8L\eta} \qquad (3)$$

where V = rate of flow, i.e., volume of liquid flowing in unit time, m^3/s (l/s)

ΔP = pressure difference across the filter, Pa

r = radius of the capillary in the filter bed, m

L = thickness of the filter cake (capillary length). m

η = viscosity of the filtrate, Pa·s

If the cake is composed of a bulky mass of particles and the liquid flows through the interstices (correspond to a multiplicity of capillary tubes), then the flow of liquids through these may be expressed by Poiseuille's equation.

Darcy's Equation

Poiseuille's law assumes that the capillaries found in the filter are highly irregular and nonuniform. Therefore, if the length of a capillary is taken as the thickness of the bed, a correction factor for radius is applied so that the rate equation is closely approximated and simplified. The factors influencing the rate of filtration has been incorporated into an equation by Darcy, which is:

$$V = \frac{KA\Delta P}{\eta L} \qquad (4)$$

where K = permeability coefficient of the cake, m^2

A = surface area of the porous bed (filter medium), m^2

Other terms are same as shown in equation (3). The term K depends on the characteristics of the cake, such as porosity, specific surface area and compressibility.

Permeability may be defined quantitatively as the flow rate of a liquid of unit viscosity across a unit area of cake having unit thickness under a pressure gradient of unity.

This model relates not only to filter beds or cakes but also applies to other types of depth filter. Equation (4) is valid for liquids flowing through sand, glass beads and various porous media. Darcy's equation is further modified by including characteristics of K by Kozeny-Carman.

Kozeny-Carman Equation

Poiseuille's equation is made applicable to porous bed, based on a capillary type structure by including additional parameters. Thus the resultant equation, which is widely used for filtration is Kozeny-Carman equation.

$$V = \frac{A}{\eta S^2} \cdot \frac{\Delta P}{KL} \cdot \frac{\varepsilon^3}{(1-\varepsilon)^2} \qquad (5)$$

where ε = porosity of the cake (bed)

S = specific surface area of the particles comprising the cake, m^2/m^3

K = Kozeny constant

Other terms are same as shown in equations (3) and (4). The Kozeny constant is usually taken as 5. The effect of compressibility of the cake on flow rate can be appreciated from equation (1), since the flow rate is proportional to $\varepsilon^3/(1-\varepsilon)^2$. A 10 per cent change in porosity can produce almost 3-fold change in V.

Limitations of Kozeny Carman equation : Kozeny Carman equation does not take into account of the fact that the depth of the granular bed is lesser than the actual path traversed by the fluid. The actual path is not straight throughout the bed, but it is sinuous or tortuous.

FACTORS INFLUENCING FILTRATION

A simple straining process does not provide a complete description of how particles are removed from a suspension. The particles are exposed to a number of forces including gravity or electrical fields. Some of the factors influencing the filtration are:

(1) Properties of the liquids—density, viscosity and corrosiveness.

(2) Properties of the solids—particle shape, particle size, particle charge, density, particle size distribution, rigidity or compressibility of the solid under pressure and tendency of particle to flocculate or adhere together.

(3) Proportion of solids in the slurry—rate at which the filter cake is formed, especially in the early stages of the filtration.

(4) Objectives—whether the solids or the liquid or both are to be collected.

(5) Temperature of the suspension.

Surface Area of the Filter Medium

According to equation (5), rate of flow of filtrate flowing through the filter is inversely proportional to the specific surface of the filter bed. On the other hand, if the surface area of the filter medium is considered, the rate of filtration is directly proportional to the surface area of the filter medium (equation 4). Hence, the rate can be increased either using a larger filter or connecting a number of small units in parallel. For example, filter press works on the principle of connecting the units in parallel. Pleating the filter paper or using a pleated funnel increases the effective surface area for filtration.

Pressure Drop Across the Filter Medium

According to equation (5), rate of filtration is directly proportional to the overall pressure drop across filter medium and filter cake. The pressure drop can be achieved in a number of ways:

Gravity : A simple method of obtaining a pressure difference is maintaining a head of slurry above the filter medium. The pressure developed depends on the density of the slurry. As a rough guide, a head of 10 metres of water creates a pressure difference of 100 kilopascals.

Applying pressure : The most common method of obtaining a pressure difference is applying pressure on the surface of the slurry, i.e., pumping the slurry onto the filter.

The pressure difference obtained by this method is greater than that is achieved by reduced pressure. Industrial plant may be operated at pressure up to 1500 kilopascals. However, in the early stages of filtration, pressure difference should be less. This is to prevent the pores of the filter medium from clogging or plugging, which subsequently increases resistance to the flow.

Reducing pressure : The pressure underneath the filter medium may be reduced below atmospheric pressure by connecting the filtrate receiver to a vacuum pump. This creates a pressure differential across the filter. This factor has limited applications, because the pressure difference of about 100 kilopascals may be achieved. Reduction of pressure lowers the boiling point of liquids so that it is possible for the filtrate to boil in the receiver. Apart from the loss of liquid, the vapour may damage the vacuum pump.

Advantage of this method is that it is safe. If a part of the equipment fails, it will collapse and not explode. Therefore, this method is commonly applied in a laboratory, where the apparatus is usually made of glass. However, in the industrial scale, the plant is usually constructed with a metal that is able to withstand high pressure.

Centrifugal force : Centrifugal force could replace the gravitational force and is used to increase the rate of filtration. The principle behind centrifugation is discussed separately in the chapter 10.

Viscosity of Filtrate

According to equation (5), rate of filtration is inversely proportional to the viscosity of the fluid. The viscosity of the liquid, not the slurry is important, since the resistance to flow occurs as the filtrate flows through the filter cake.

Raising the temperature of the liquid, which lowers the viscosity, may increase the rate of filtration. This is not practicable, if thermolabile materials are involved or if filtrate is volatile. Another alternative to decrease the viscosity is to dilute the filtrate. In this case, it is important to ensure that by doubling the volumes, the rate must be more than double, which should indicate the advantage.

In brief, surface area and pressure differences are the two factors, which are applied, in industrial practice. According to equation (5), other factors such as porosity also influences the rate of filtration. These are discussed below with filter-aids.

FILTER MEDIA AND FILTER AIDS

Filter Media

The *filter medium* acts as a mechanical support for the filter cake and is also responsible for the collection of solids.

Characteristics : Filter medium should have the following characteristics.

(1) It should have sufficient mechanical strength.

(2) It must be inert, for example, it should not show chemical or physical interaction.

(3) It should not absorb the dissolved material.

(4) It should allow the maximum passage of liquid, while retaining the solids. It means that it must offer low resistance to flow. The resistance offered by the filter medium is not significant in large scale operations and can be neglected.

The magnitude of the resistance of the filter medium will change due to the layers of solids deposited earlier, which may block the pores or may form bridges over the entrances of the channels. Therefore, the pressure should be kept low at the beginning to avoid the plugging of the pores. The usual procedure is to filter at constant rate by increasing the pressure as necessary. When normal working pressure is reached, it is maintained. On continued filtration, the thickness of the cake further builds up and hence the rate of filtration decreases. When the rate is uneconomical, filtration is stopped. The filter cake is removed and filtration is restarted.

Materials : The following materials are used as filter media.

(1) *Woven materials such as felt or cloth.* Woven material is made of wool, cotton, silk, glass, metal or synthetic fibres (rayon, nylon etc.). Synthetic fibres have greater chemical resistance than wool or cotton, which are affected by alkali and acid, respectively. The choice of the fibre depends on the chemical reactivity with the slurry.

(2) *Perforated sheet metal.* For example stainless steel plates have pores which act as channels as in case of metafilter (edge filter).

(3) *Bed of granular solid built up on a supporting medium.* In some processes, a bed of graded solids may be formed to reduce the resistance to the flow.. Typical examples of granular solids are gravel, sand, asbestos, paper, pulp and keiselguhr. The choice of solids depends on the size of the solids in the process.

(4) *Prefabricated porous solid unit.* Porous solids prefabricated into a single unit are being increasingly used for its convenience and effectiveness. Sintered glass, sintered metal, earthenware and porous plastics are some of the materials used for the fabrication.

(5) *Membrane filter media.* Cartridge units are economical and available in pore size of 100 μm to even less than 0.2 μm. These can be used either as surface cartridges or depth type cartridges.

(a) *Surface type cartridges* : These are corrugated and resin treated papers. These are used in hydraulic lines. Ceramic cartridges are advantageous in cleaning for reuse by back flushing or firing. Porcelain filter candles are used for sterile filtration.

(b) *Depth type cartridges* : These are made of cotton, asbestos or cellulose. These are disposable items, since cleaning is not feasible.

Filter Aids

Filter aid forms a surface deposit which screens out the solids and also prevents the plugging of the supporting filter medium.

Justification : The object of the filter aid is to prevent the medium from becoming blocked and to form an open, porous cake, hence, reducing the resistance to flow of the filtrate.

(a) Usually, low resistance is offered by the filter medium itself, but as the layers of solid built up the resistance will be increased. The cake may become impervious by blocking of the pore in the medium. Flow rate is inversely proportional to the resistance of the solid cake.

(b) Slimy or gelatinous material and highly compressible substances form impermeable cakes. The filter medium gets plugged and the flow of filtrate stops.

Characteristics : The important characteristics of the filter aids are:

(a) Chemically inert to the liquid being filtered and free from impurities.

(b) Low specific gravity, so that filter aids remain suspended in liquid.

(c) Porous rather than dense, so that pervious cake can be formed.

(d) Recoverable

Disadvantages : The filter aids remove the coloured substances by absorbing them. Sometimes active principles such as alkaloids are adsorbed on the filter aid. Rarely, filter aids are a source of contaminants such as soluble iron salts, which can provoke degradation of sensitive ingredients. Liquid retained in the pores of the filter cake is lost in the manufacturing process.

Examples of filter aids are:

Keiselguhr
Paper pulp
Talc
Bentonite
Charcoal
Fullers earth
Asbestos

Activated charcoal is used for removal of organic and inorganic impurities. Kieselguhr is a successful filter aid and as little as 0.1 percent can be added to the slurry. The rate of filtration is increased by 5 times or more, at the above concentration, though the slurry contains 20% solids.

Handling of filter aids : Filter aids are mostly used for clarification processes, i.e., where solids are discarded. Different flow rates can be achieved depending on the grade of the aids.

Low flow rate (fine solids)—Fine grade filter aids—mainly intended for clarity.

Fast flow rate (coarse solids)—coarse grade filter aids—acceptable filtrate.

The filter aid can be employed in either one or both ways.

(1) Firstly, a pre-coat is formed over the medium. For this purpose, a suspension of the filter aid is filtered to give a coating up to 0.5 kg per metre square.

(2) Secondly, a small proportion of filter aid (0.1 to 0.5% of total batch weight) is purposely added to the slurry. So the filter cake has a porous structure and filtration can be efficient. The filter aid of 1 to 2 parts per each part of contaminant is mixed in the feed tank. This slurry is recirculated through the filter until a clear filtrate is obtained. Filtration then proceeds to completion. The body mix method minimizes equipment requirements and cross contamination potentials.

CLASSIFICATION OF FILTRATION EQUIPMENT

Equipment are classified based on the application of external force.

(1) *Pressure filters*—Plate and frame filter press and metafilter.

(2) *Vacuum filters*—Filter leaf.

(3) *Centrifugal filters*—These are discussed in the centrifugation chapter

Classification based on the operation of the filtration.

(a) *Continuous filtration*—Discharge and filtrate are separated steadily and uninterrupted.

(b) *Discontinuous filtration*—Discharge of filtered solids is intermittent. Filtrate is removed continuously. The operation should be stopped to collect the solids.

Classification based on the nature of filtration.

(a) *Cake filters*—Remove large amounts of solids (sludge or crystals).

(b) *Clarifying filters*—Remove small amounts of solids.

(c) *Cross-flow filters*—Feed of suspension flows under pressure at a fairly high velocity across the filter medium.

EQUIPMENT

In the bulk drug industry, solid is the desired product. Its size, physical properties and purity are important. These factors should be considered, while selecting the equipment and operating conditions. Some of them are:

Materials related:

(a) Properties of the fluid—viscosity.

(b) Nature of the solids—particle size, shape, size distribution and packing characteristics.

(c) Concentration of solids in suspension.

(d) Quantity of material to be handled.

(e) Whether it is necessary to wash the filtered solids

(f) Whether any form of pretreatment will be helpful

Equipment and process related:

(a) Flow rate.

(b) It should be absolute in the sense, the limit to size of particles passing through the filter should be known.

(c) It should be sterilisable by heat, radiation or gas (examples are ethylene oxide, formaldehyde etc.).

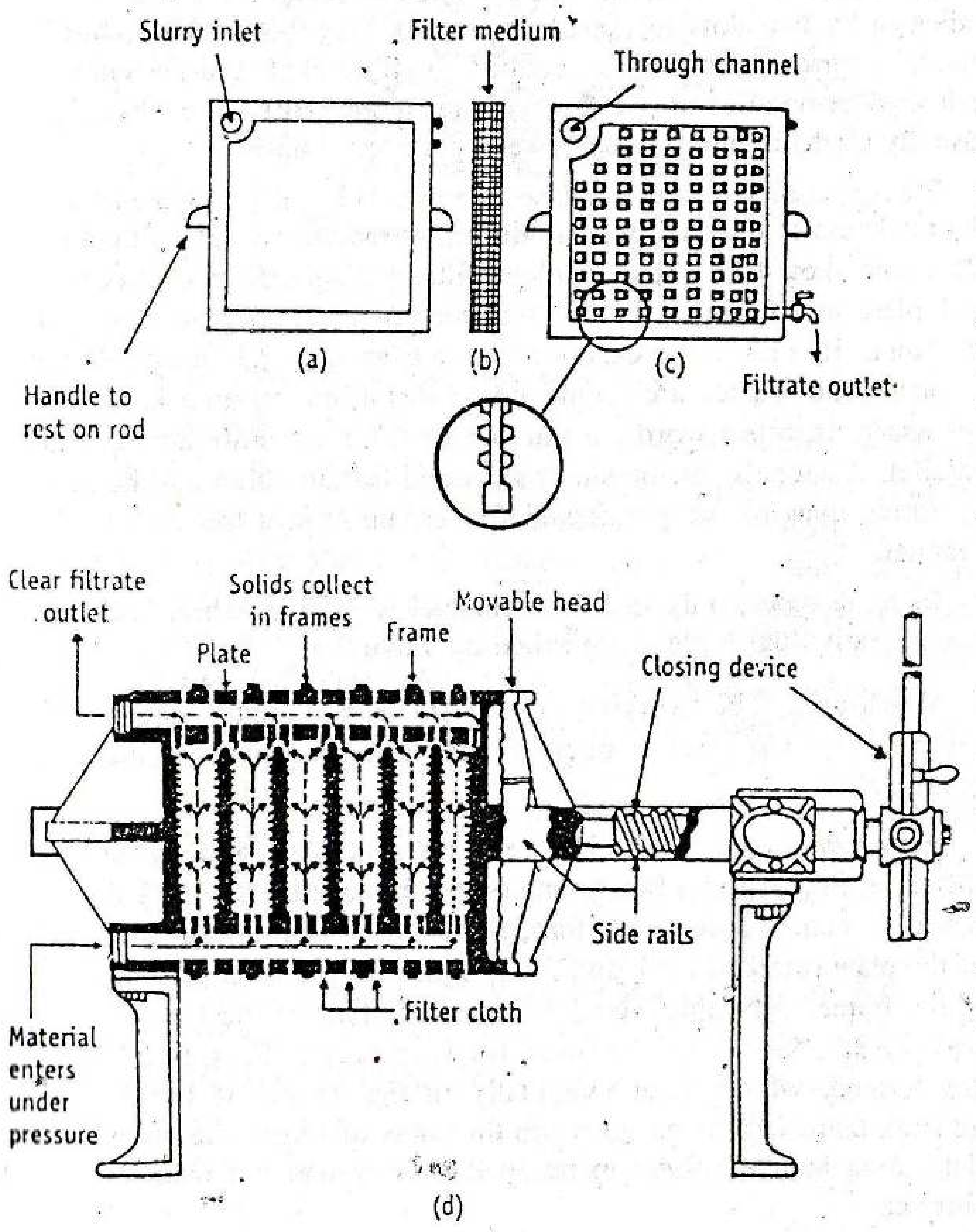
(d) Independently checking the efficiency of filter. It should be economical.

Different forms of equipment are employed for filtration. Some of them are discussed below.

PLATE AND FRAME FILTER PRESS

Principle : The mechanism is surface filtration. The slurry enters the frame by pressure and flows through the filter medium. The filtrate is collected on the plates and sent to the outlet. A number of frames and plates are used so that surface area increases and consequently large volumes of slurry can be processed simultaneously with or without washing.

Construction : The construction of a plate and frame filter press is shown in Figure 9-3. The filter press is made of two types of units,



(a) Frame—Maintains the slurry reservoir, inlet (eye) for slurry.
(b) Filter medium.
(c) Plate along with section—supports the filter medium, receiving the filtrate and outlet (eye).
(d) Assembly of plate and frame filter press.

Figure 9-3. Plate and frame filter press.

plates and frames. These are usually made of aluminium alloy. Sometimes, these are also lacquered for protection against corrosive chemicals and made suitable for steam sterilisation.

Frame contains an open space inside wherein the slurry reservoir is maintained for filtration and an inlet to receive the slurry. It is indicated by two dots in the description (Figure 9-3a). The plate has a studded or grooved surface to support the filter cloth and an outlet. It is indicated by one dot in the description (Figure 9-3c). The filter medium (usually cloth) is interposed between plate and frame.

Frames of different thicknesses are available. It is selected based on the thickness of the cake formed during filtration. Optimum thickness of the frame should be chosen. Plate, filter medium, frame, filter medium and plate are arranged in the sequence and clamped to a supporting structure. It is normally described by dots as 1.2.1.2.1 so on. A number of plates and frames are employed so that filtration area is as large as necessary. In other words, a number of filtration units are operated in parallel. Channels for the slurry inlet and filtrate outlet can be arranged by fitting eyes to the plates and frames, these join together to form a channel.

In some types, only one inlet channel is formed, while each plate is having individual outlets controlled by valves.

Working : The working of the frame and plate process can be described in two steps, namely filtration and washing of the cake (if desirable).

Filtration operation : The working of a plate and frame press is shown in Figure 9-4. Slurry enters the frame (marked by 2 dots) from the feed channel and passes through the filter medium on to the surface of the plate (marked by 1 dot). The solids form a filter cake and remain in the frame. The thickness of the cake is half of the frame thickness, because on each side of the frame filtration occur. Thus, two filter cakes are formed, which meet eventually in the centre of the frame. In general, there will be an optimum thickness of filter cake for any slurry, depending on the solid content in the slurry and the resistance of the filter cake.

The filtrate drains between the projections on the surface of the plate and escapes from the outlet. As filtration proceeds, the resistance of the cake increases and the filtration rate decreases. At a certain point, it is preferable to stop the process rather than continuing at very low flow rates. The press is emptied and the cycle is restarted.

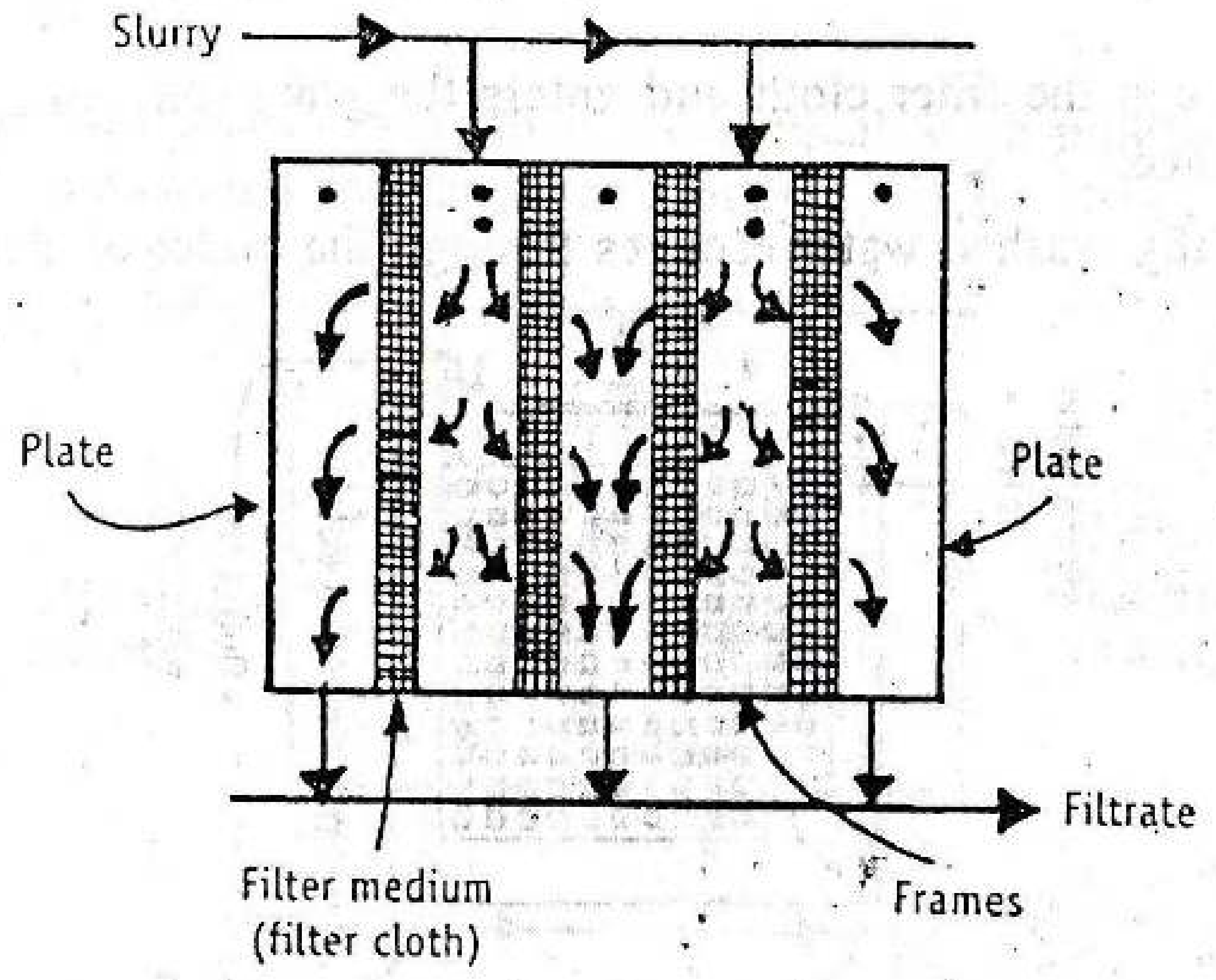


Figure 9-4. Plate and frame filter press, principle of operation (filtering).

Washing operation : If it is necessary to wash the filter cake, the ordinary plate and frame press is unsatisfactory. Two cakes are built up in the frame meeting eventually in the middle. This means that flow is brought virtually to a stand still. Hence, water wash using the same channels of the filtrate is very inefficient, if not impossible. A modification of the plate and frame press is used. For this purpose, an additional channel is included (Figure 9-5). These wash plates are identified by three dots. In half the wash plate, there is a connection from the wash water channel to the surface of the plate.

The sequence of arrangement of plates and frames can be represented by dots as 1.2.3.2.1.2.3.2.1.2.3.2.1 so on (between 1 and 1, 2.3.2 must be arranged). Such an arrangement is shown in Figure 9-6 (a) and (b) for the operations of filtration and water washing, respectively.

The procedure for washing the press is shown in Figure 9-6. The steps are as follows.

(1) Filtration proceeds in the ordinary way until the frames are filled with cake.

(2) To wash the filter cake, the outlets of the washing plates (three dots) are closed.

(3) Wash water is pumped into the washing channel. The water enters through the inlets on to the surface of the washing (three dots) plates.

(4) Water passes through the filter cloth and enters frame (two dots) which contains the cake. Then water washes the cake, passes

through the filter cloth and enters the plate (one dot) down the surface.

(5) Finally washed water escapes through the outlet of that plate.

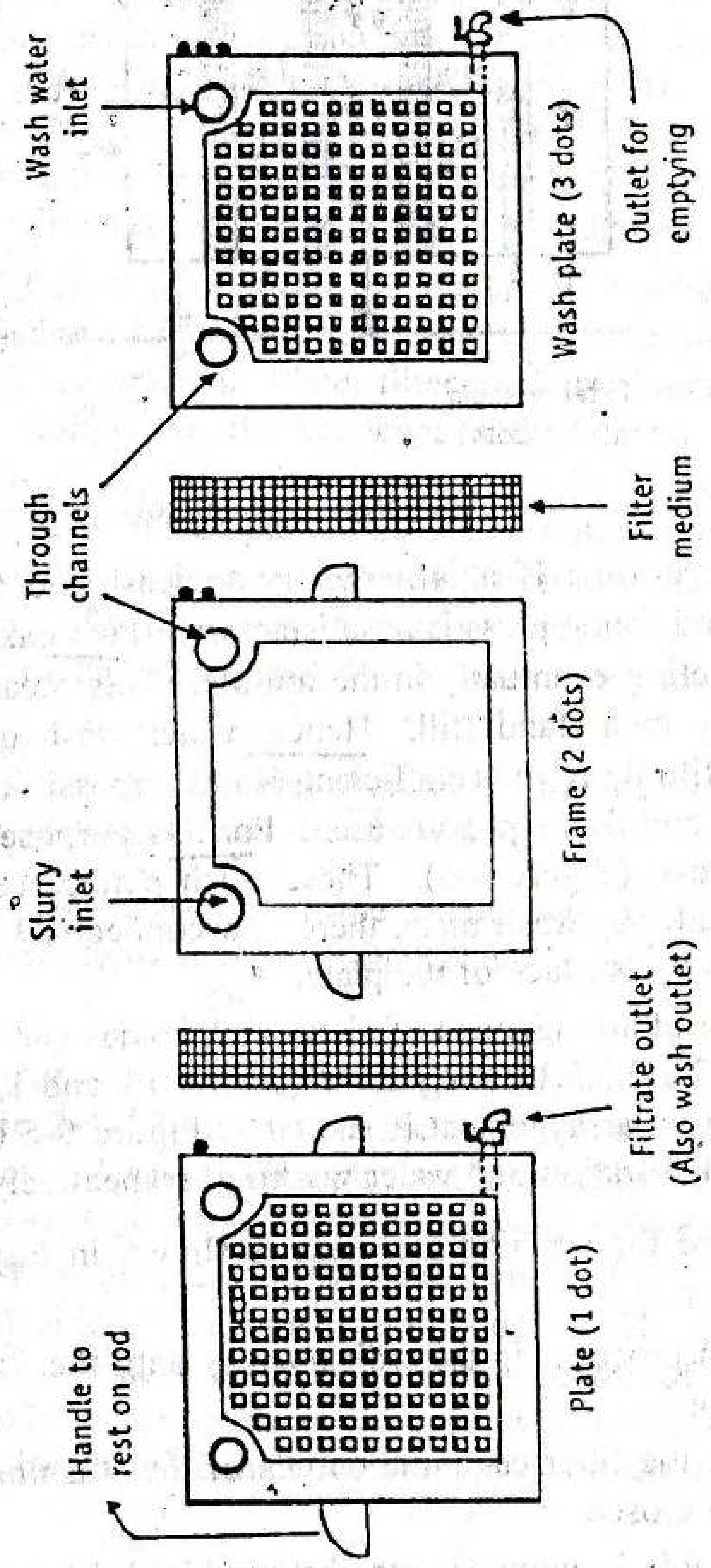
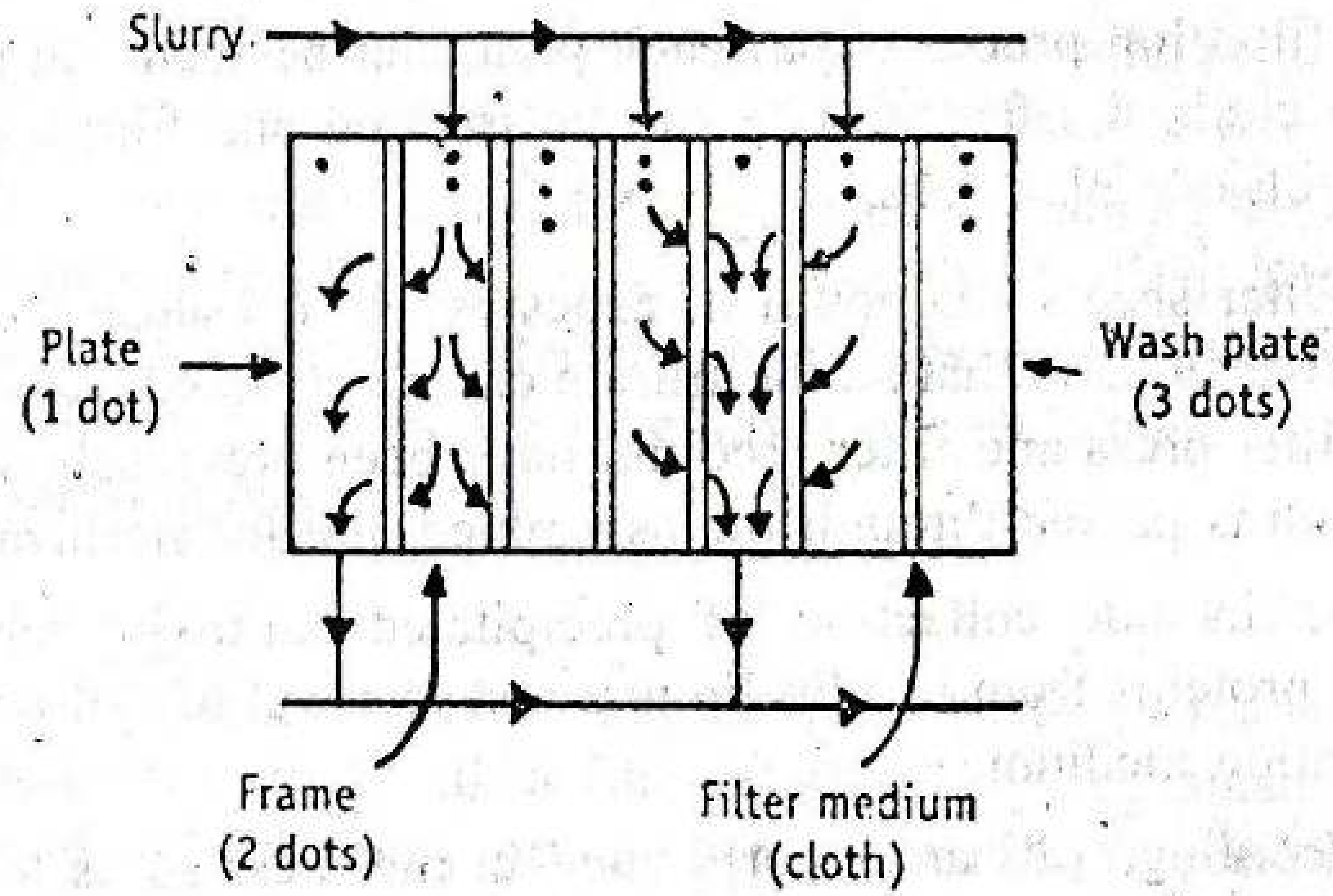
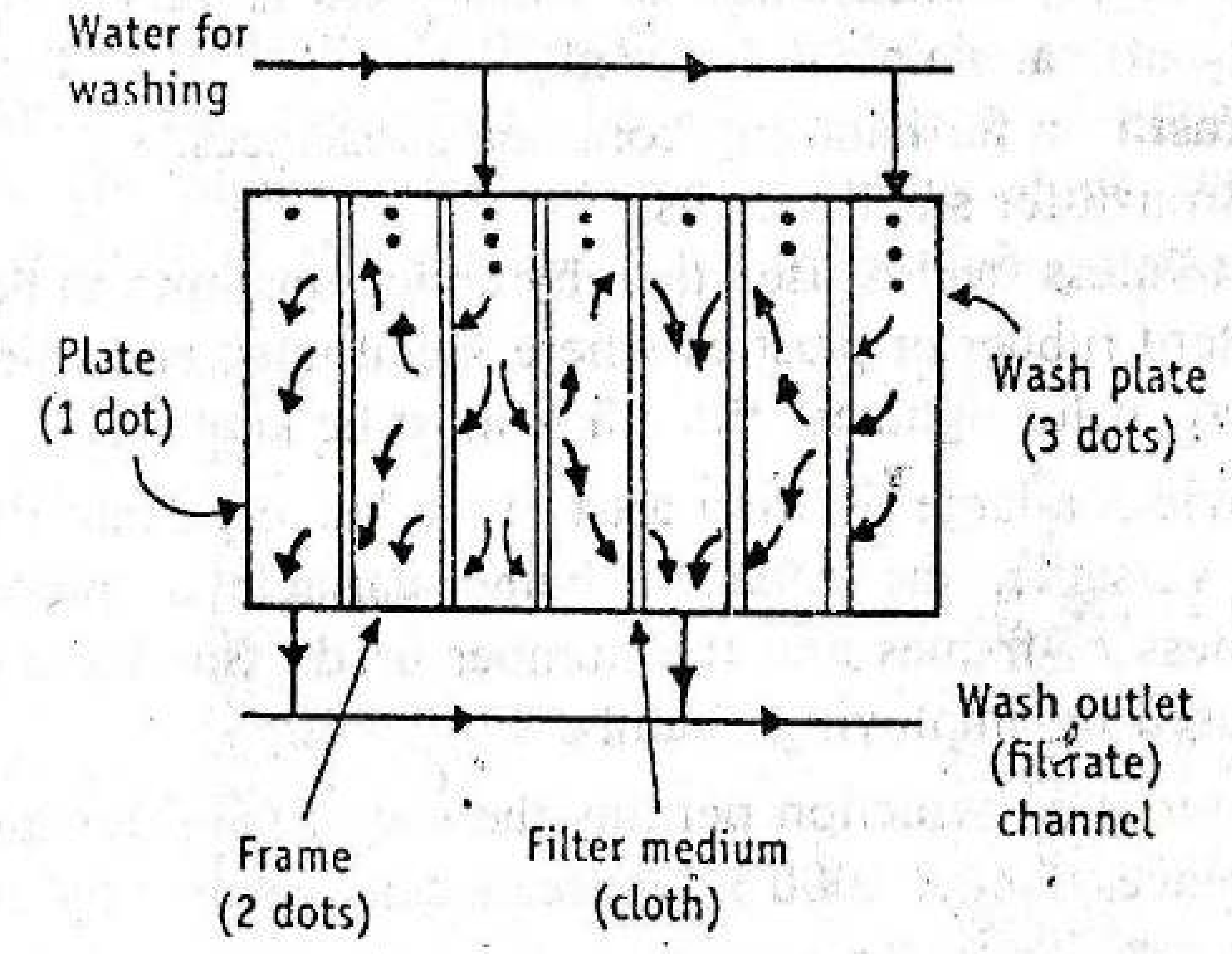


Figure 9-5. Plate and frame filter press with water wash facility.

Thus with the help of special washing plates, it is possible for the wash-water to flow over the entire surface of washing (three dots) plate, so that the flow resistance of the cake is equal to all points. Hence, the entire cake is washed with equal efficiency.



(a) Principles of filtration operation using the three types of plate and frame.



(b) Principles of cake washing using three types of plate and frame.

Figure 9-6. Plate and frame filter press. Principles of filtration and washing.

It should be noted that water-wash is efficient only if the frames are full with filter cake. If the solids do not fill the frame completely, the wash water causes the cake to break (on the washing plate side of the frame), then washing will be less effective. Hence, it is essential to allow the frames become completely filled with the cake. This helps not only in emptying the frames but also helps in washing the cake correctly.

Special provisions : (1) Any possible contamination can be observed by passing the filtrate through a glass tube or sight glass from the outlet on each plate. This permits the inspection of quality of the filtrate. The filtrate goes through the control valve to an outlet channel.

(2) The filtration process from each plate can be seen. In the event of a broken cloth, the faulty plate can be isolated and filtration can be continued with one plate less.

Uses : Filter sheets composed of asbestos and cellulose are capable of retaining bacteria, so that sterile filtrate can be obtained, provided that the whole filter press and filter medium have been previously sterilized. Usually steam is passed through the assembled unit for sterilization.

Examples include collection of precipitated antitoxin, removal of precipitated proteins from insulin liquors and removal of cell broth from the fermentation medium.

Heating/cooling coils are incorporated in the press so as to make it suitable for the filtration of viscous liquids.

Advantages : (1) Construction of filter press is very simple and a variety of materials can be used.

- Cast iron for handling common substances.
- Bronze for smaller units.
- Stainless steel is used thereby contamination can be avoided.
- Hard rubber or plastics where metal must be avoided.
- Wood for lightness though it must be kept wet.

(2) It provides a large filtering area in a relatively small floor space. It is versatile, the capacity being variable according to the thickness of frames and the number used. Surface area can be increased by employing chambers up to 60.

(3) The sturdy construction permits the use of considerable pressure difference. About 2000 kilopascals can be normally used.

(4) Efficient washing of the cake is possible.

(5) Operation and maintenance is straight forward, because there are no moving parts, filter cloths are easily renewable. Since all joints are external, a plate can be disconnected if any leaks are visible. Thus contamination of the filtrate can be avoided.

(6) It produces dry cake in the form of slab.

Disadvantages : (1) It is a batch filter, so there is a good deal of 'down-time', which is non-productive.

(2) The filter press is an expensive filter. The emptying time, the labour involved and the wear and tear of the cloth resulting in high costs.

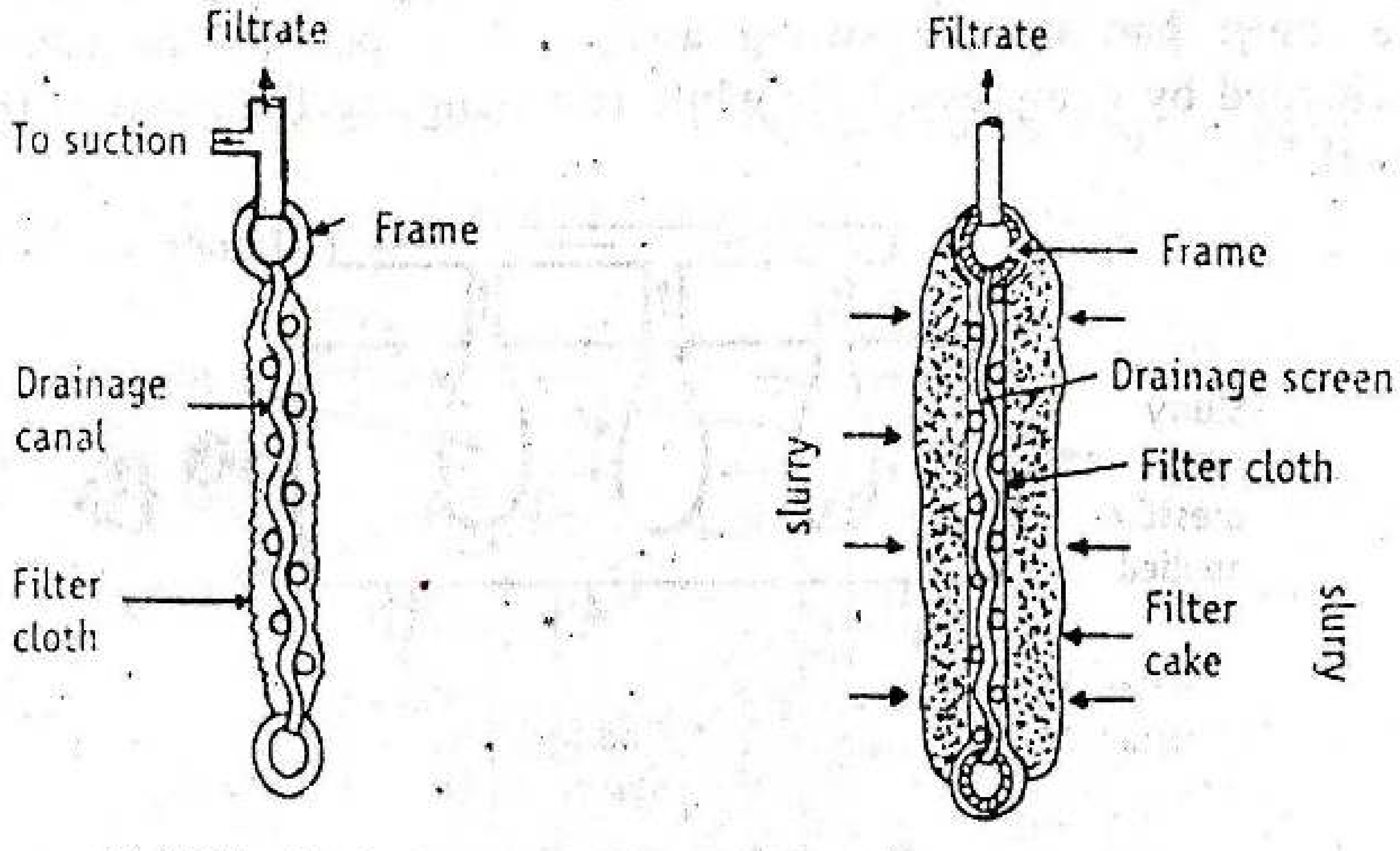
(3) Operation is critical, as the frames should be full, otherwise washing is inefficient and the cake is difficult to remove.

(4) The filter press is used for slurries containing less than 5% solids. So high costs make it imperative that this filter press is used for expensive materials. Examples include the collection of precipitated antitoxin and removal of precipitated proteins from insulin liquors.

FILTER LEAF

Principle : Filter leaf is an apparatus consisting of a longitudinal drainage screen covered with a filter cloth. The mechanism is surface filtration and acts as sieve or strainer. Vacuum or pressure can be applied to increase the rate of filtration.

Construction : The general arrangement of a filter leaf is shown in Figure 9-7. It consists of a narrow frame enclosing a drainage screen or grooved plate. The frame may be of any shape, circular, square or rectangular. The whole unit is covered with filter cloth. The outlet for the filtrate connects to the interior of the frame through suction.



(a) Filter leaf (b) Filter leaf during filtration.

Figure 9-7. Assembly of filter leaf.

Working : The filter leaf is immersed in the slurry. Vacuum system is connected to the filtrate outlet. The slurry passes through the filter cloth. Finally filtrate enters the drainage canal and goes through the outlet into the receiver. Air is passed to flow in reverse direction which facilitates removal of cake.

Uses : The filter leaf is satisfactory, if the solid content of the slurry is not too high, about 5%, i.e., dilute suspensions.

Advantages : (1) Filter leaf is a versatile piece of equipment. Filter leaf is probably the simplest form of filter used for batch processes.

(2) A number of units can be connected in parallel to increase the surface area for filtration.

(3) Pressure difference can be obtained either with vacuum or using pressure up to the order of 800 kilopascals.

(4) Labour costs for operating the filter leaf are fairly moderate.

(5) The efficiency of washing is high.

(6) Slurry can be filtered from any vessel. Simply immersing the filter in a vessel of water can wash the cake.

Variants : *Sweetland filter* : A variation is to enclose the filter leaf in a special vessel into which the slurry is pumped under pressure. In this form, a number of leaves are connected to a common outlet to provide a large area for filtration. A typical example of this kind is the Sweetland filter shown in Figure 10-8. The vessel is cylindrical and filter leaves are arranged so that they are supported by the upper part. The lower part can be swung away. This permits the cake to be discharged by compressed air while removing the filter leaves from the vessel.

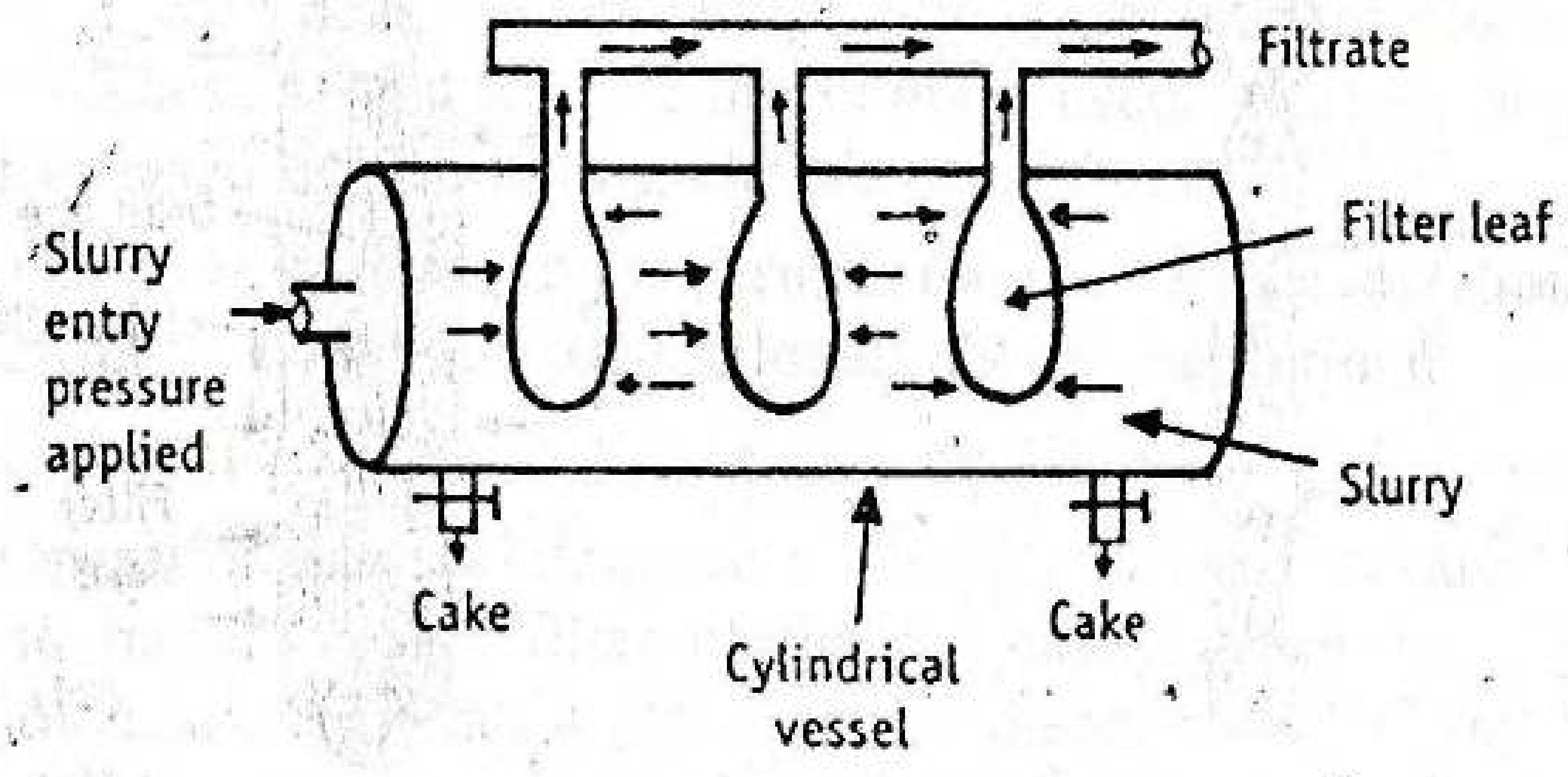


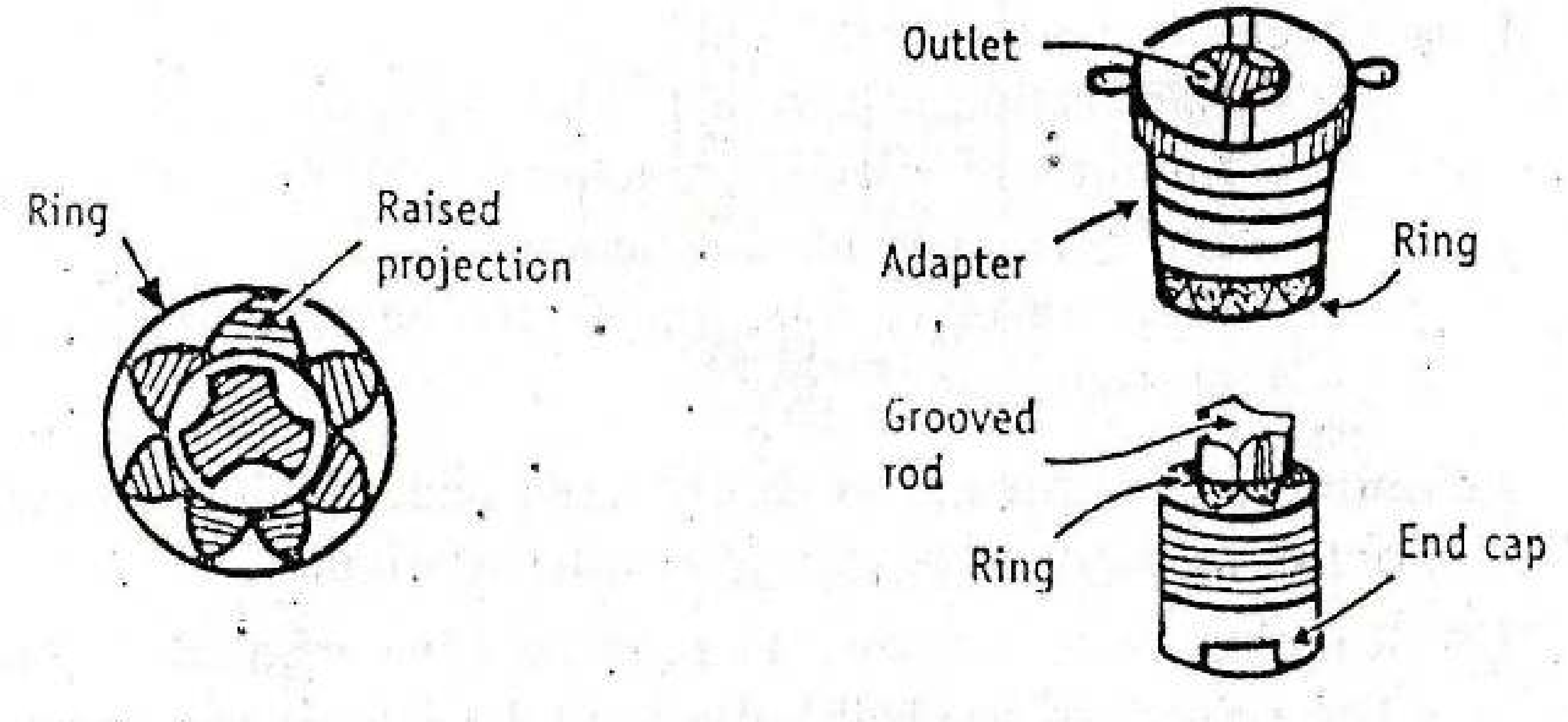
Figure 9-8. Sweetland filter

METAFILTER

Principle : Metafilter functions as a strainer (surface filtration) for the separation of particles. In this method, metal rings contain semicircular projections, which are arranged as a nest to form channels on the edges. This channel offers resistance (strainer) to the flow of solids (coarse particles). The clear liquid is collected into a receiver from the top.

Construction : The construction and assembly of a metafilter is shown in Figure 9-9. The metafilter consists of a series of metal rings. These are threaded so that a channel is formed on the edges. It contains a grooved drainage column on which a series of metal rings are packed. These rings are usually made of stainless steel and have dimensions of about 15.0 millimetres internal diameter and 22.0 millimetres external diameter.

Each metal ring has a number of semicircular projections (0.8 millimetres in thickness) on one side of the surface as shown in Figure 9-9a. The projections are arranged the same way up. These rings are tightened



(a) Surface view of a ring. (b) Assembly of rings on column.

Figure 9-9. Metafilter.

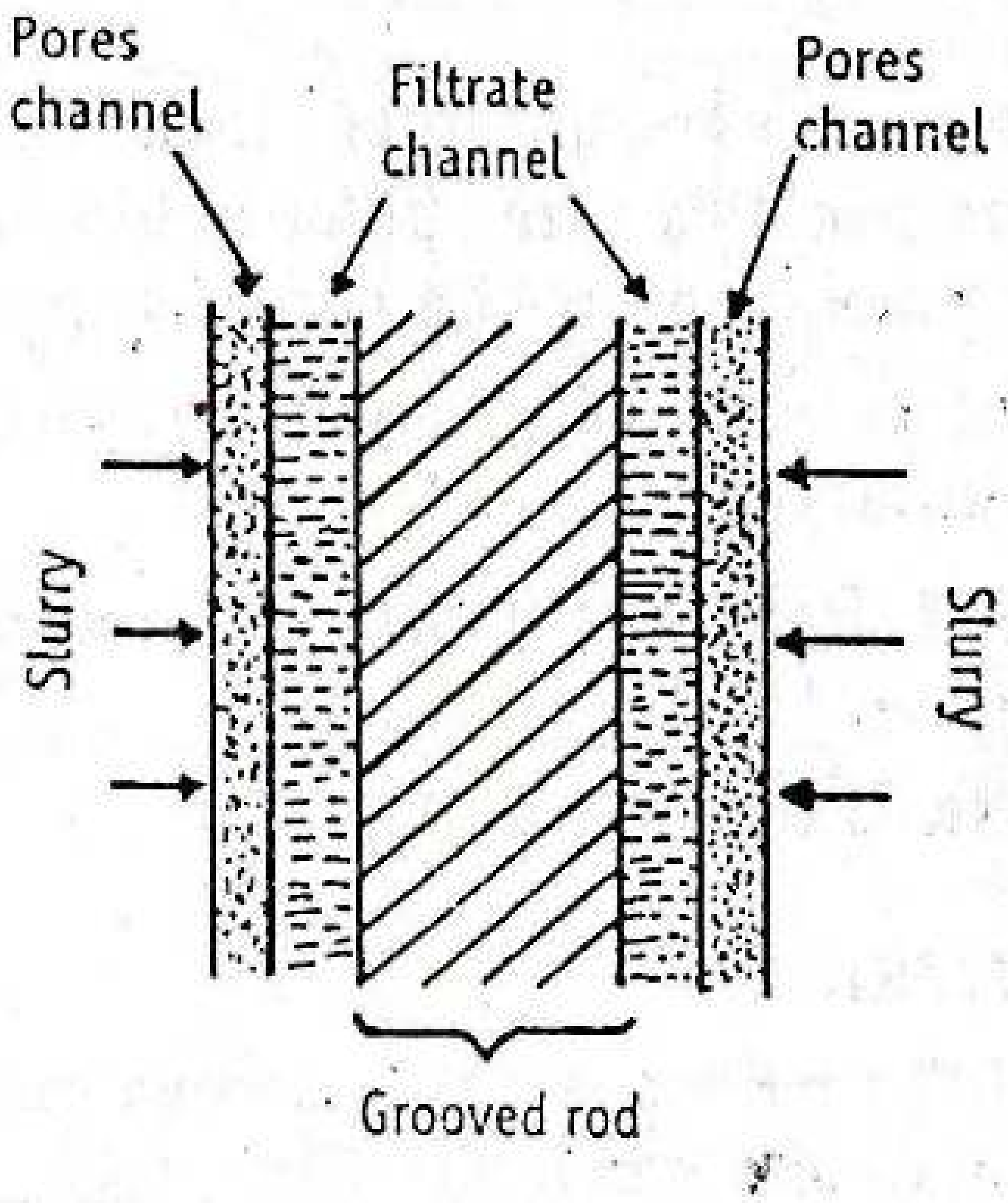


Figure 9-10. Mechanism of filtration through metafilter.

on the drainage column with a nut. Therefore, metafilter is also known as *edge filters*.

Working : The working principle of a metafilter is shown in Figure 9-10. These filters are placed in a vessel and may be operated by pumping the slurry under pressure or occasionally by the application of reduced pressure to the outlet side. The slurry passes through the channels formed on the edges between the rings. The clear liquid rises up and collected from the outlet into the receiver. Metafilter functions as a strainer (surface filtration).

For the separation of fine particles, a bed of suitable material such as kieselguhr is first built up. The pack of rings serves essentially as a base on which the true filter medium is supported.

Uses : Metafilter can be used for:
- clarification of syrups
- filtration of injection solutions
- clarification of insulin liquors
- filtration of viscous liquids can be achieved by applying pressure.

Advantages : (1) Metafilter can be used under high pressures, without any danger of bursting the filter medium.

(2) Running costs are low, as separate filter medium is not used. The volume of residual hold-up in the filter is less.

(3) It can be constructed from a material that can provide excellent resistance to corrosion and avoid contamination of sensitive products.

(4) It is an extremely versatile filter. It can be used for the filtration of very fine particles using filter aids. Large particles can be separated by building up of a bed of same particles.

(5) Removal of cake is carried out effectively, by simply back-flushing with water.

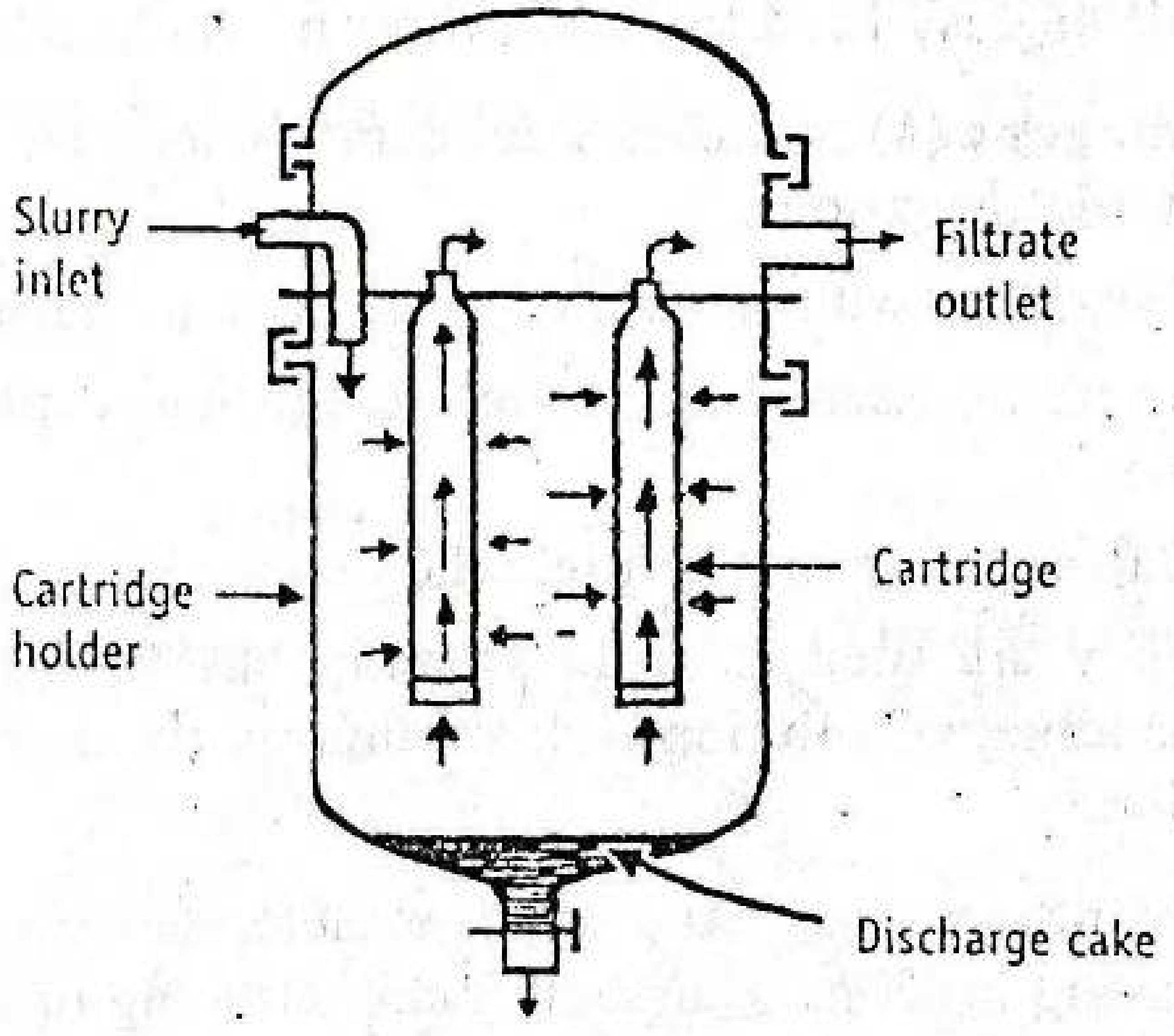
(6) Change over from one batch to another or one product to another is easy.

(7) Sterile products can be handled.

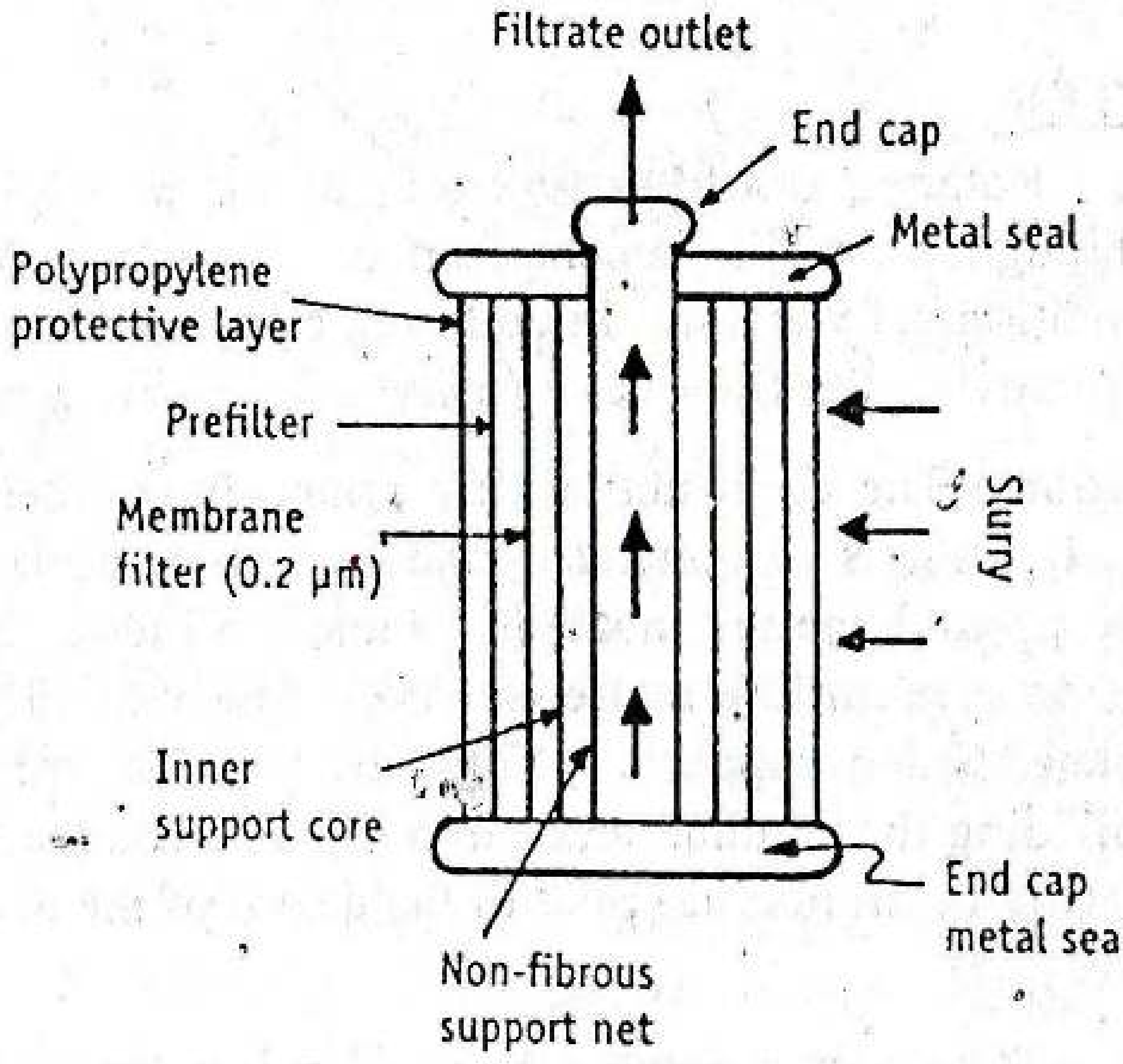
CARTRIDGE FILTER

Principle : Cartridge filter is a thin porous membrane in which prefilter and membrane filter are combined into a single unit. The filtration action is mainly sieve-like and the particles are retained on the surface.

Construction : The construction of a cartridge filter is shown in Figure 9-11a. Cartridge filter has a cylindrical configuration made with disposable or changeable filter media. These are made of either plastic or metal. It consists two membrane filters (sieve-like) made of polypropylene: a prefilter and an actual filter for filtration. A protective layer surrounds them. The cartridges are housed in a holder. A number of cartridges



(a) Filter assembly.



(b) Cartridge filter unit.

Figure 9-11. Cartridge filter.

can be placed in the same housing. The housing is closed with a lid. The housing has provisions for slurry inlet and filtrate outlet.

Working : The slurry is pumped into the cartridge holder. It passes through cartridge filter unit by the mechanism of straining. The clear liquid passes to the centre and moves up to collect through the outlet.

Uses : Cartridge filter is particularly useful for the preparation of particulate free solutions for parenteral and ophthalmic uses. This filter holder will process 1000 to 15000 litres of sterile solution per hour.

Advantages : (1) Stainless steel construction permits autoclaving for sterile operations.

(2) Cartridges with self-cleaning devices are advantageous.

(3) Rapid disassembling as well as reusing of filter media is possible.

(4) Cartridges are not brittle, when they are dry.

(5) They are used as in-line continuous filtration, which reduces handling of solutions. It minimizes the chances of contamination.

Disadvantages : (1) Cost of disposable elements offsets the labour saving in terms of assembly and cleaning of cartridge clarifier.

(2) A number of manufacturers provide the components, which are generally not interchangeable between suppliers.

DRUM FILTER

Principle : Rotary drum filter functions on the principle of filtering the slurry through sieve-like mechanism on a rotating drum surface, under the conditions of vacuum. In addition, compression, drying (using hot air) and removing the filter cake (using a knife) are possible.

Construction : The construction of a rotary drum filter is shown in Figure 9-12. It consists of a metal cylinder mounted horizontally. The drum may be up to 3 metres in diameter and 3.5 metres in length and gives a surface area of 20 metre square. The curved surface is a perforated plate, which supports a filter cloth. The drum is radially partitioned dividing the annular space into separate compartments. Each of it is connected by an internal pipe to the centre of the drum through a rotating valve.

Working : The drum is rotated at a speed less than one revolution per minute. The drum just enters the slurry in the trough (Figure 9-12). As it dips, vacuum is applied in this segment so that the solid is build up on the surface. The liquid passes through the filter cloth into an internal pipe and valve. Finally the filtrate reaches the collecting tank.

As the drum leaves the slurry section, it enters the drainage zone. Here excess of the liquid is drawn inside. Special cake compression rollers may be included at this stage, so that the cake is consolidated by the compression of the cake. This improves the efficiency of washing and drying process.

- Vacuum is applied to carry the slurry along with the drum
- Drainage zone
- Water washing arrangement
- Drying zone - dry air supply
- Cake removal zone

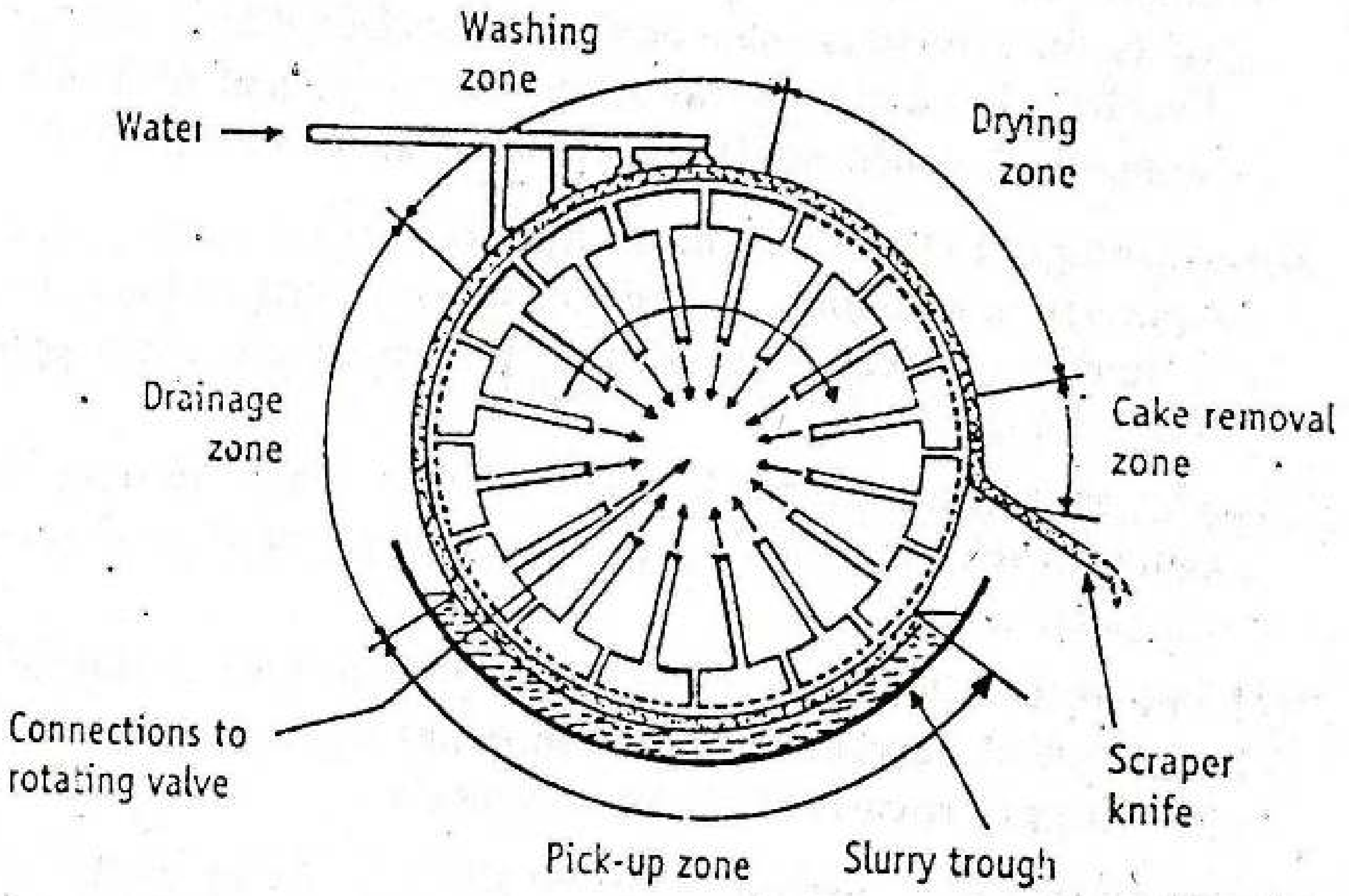


Figure 9-12. Drum filter.

As the drum leaves the drainage zone, it enters the water wash section. Water is sprayed on the cake. A separate system of vacuum is applied on the panel in order to suck the wash liquid and air through the cake of solids. Wash liquid is drawn through the filter into a separate collecting tank.

Then the cake enters the drying zone, where hot air is blown on the cake. The cake may have the moisture content less than one percent. Finally the cake is removed using a doctor knife and discharged.

All these steps are completed in one rotation of the drum. Now the drum is ready to receive a fresh lot of slurry.

Uses : Drum filter is used for continuous operation and is utilised to filter slurries containing high proportion of solids up to 15 to 30 percent. In the production of penicillins, the extract is separated from mycelium (cell mass) by drum filters. These are used for collecting calcium carbonate, starch and magnesium carbonate.

Advantages : (1) Cake is removed simultaneously during operation. Therefore, suitable for use with concentrated slurries.

(2) The labour costs are very low on account of automatic and continuous operation of the rotary filter.

(3) The filter has large surface area.

(4) The speed of rotation can be varied and the cake thickness can be controlled. For example; if the solids form an impenetrable cake, the thickness may be limited to less than 5 millimetres. On the other hand, if the solids are coarse and form a porous cake, the thickness of 100 millimetres or more, can be obtained.

Disadvantages : (1) Rotary drum filter is expensive equipment with complex functioning. It contains moving parts and also requires a number of accessories such as vacuum pumps, vacuum receivers, traps etc.

(2) The cake tends to crack due to the air drawn through by the vacuum system. This makes washing and drying processes inefficient.

(3) The rotary filter is suitable only for straightforward slurries. It is less satisfactory, if the solids form an impermeable cake or it is difficult to remove the cake adequately.

Variants : *String discharge rotary filter*: It is especially used for filtering the fermentation liquor in the manufacture of antibiotics, where the mould is difficult to filter by ordinary methods, because it forms a felt-like cake. A number of loops of string are kept on the drum surface, which pass round the drum. The cake is formed on the strings. These strings lift filter cake off the filter medium and is thus removed.

Glossary of Symbols

A = Surface area of the porous bed (filter medium), m^2.
ε = Porosity of the cake.
η = Viscosity of the filtrate, Pa·s.
K = Constant in Kozeny-Carman equation.
K = Permeability coefficient in Darcy's equation, m^2.
L = Thickness of the cake (capillary length), m.

ΔP = Pressure difference across the filter, Pa.
r = Radius of the capillary, m.
S = Specific area of the particles comprising the cake in Kozeny-Carman equation, m^2/m^3.
V = Rate of filtration, i.e., volume of liquid flowing in unit time, m^3/s.

QUESTION BANK

Each question carries 2 marks

1. List the factors influencing the rate of filtration.
2. Write Kozeny-Carman equation and give its significance.
3. List the functions of filter aids.
4. Give the principle of filtration process.
5. * Differentiate between pressure filtration and vacuum filtration.
6. List the properties of filter aids.
7. * Distinguish filtration and clarification.
8. What are filter aids? Give two examples.

Each question carries 5 marks

1. * Explain the mechanisms of filtration.
2. What are filter aids? Name the filter aids commonly used in pharmacy practice.
3. * Describe the construction and working of a rotary continuous filter.
4. * Describe the construction and working of leaf filters.

Each question carries 10 marks

1. Explain the construction, working, advantages and disadvantages of filter press.
2. Explain the theories of filtration giving the principle, mechanism and factors affecting the process.
3. With a neat diagram, describe the construction and working of a suitable industrial filter for handling of high solid containing slurries.
4. With a neat diagram, describe the construction and working of an industrial filter suitable for clarification of syrups.

10

Centrifugation

chapter

- Theory of Centrifugation
- Classification of Centrifuges
- Equipment

Centrifugation is a unit operation employed for separating the constituents present in a dispersion with the aid of centrifugal force.

Centrifugal force is used to provide the driving force for the separation. It replaces gravitation forces in the sedimentation. Centrifugation is particularly useful when separation by ordinary filtration is difficult, for example, separating highly viscous mixtures and colloidal dispersions (particle size less than 5 mm), in which difference in the densities is less. In short, centrifugation provides a convenient method of separating either two immiscible liquids or a solid from a liquid. The equipment used for the separation are known as *centrifuges*.

Process of Centrifugation

The centrifuge consists of essentially a container in which a mixture of solid and liquid or two liquids is placed and rotated at high speeds. The mixture is separated into its constituent parts by the action of centrifugal force on their densities. A solid or liquid of higher specific gravity is thrown outward with greater force. Therefore, it is retained at the bottom of the container leaving a clear supernatant layer of pure liquid.

Biological
Biological Product

The speed of a centrifuge is commonly expressed in terms of the number of revolutions per minute of the rotor.

Applications

Production of bulk drugs : Centrifugation technique is used to separate crystalline drugs such as aspirin from the mother liquor. Free flowing product results due to the removal of traces of mother liquor and avoidance of effervescence.

Production of biological products : Most of the proteinaceous drugs and macromolecules are present as colloidal dispersion in water. By normal methods, it is difficult to produce them in large scale. Centrifugal methods are used for the separation of these constituents from water. Insulin can be obtained in pure form by selectively precipitating other fractions of proteins and subsequently separating them by ultracentrifugation. Centrifugation is employed for separating the blood cells from blood.

Biopharmaceutical analysis of drugs : Drugs present in the blood, tissue fluids and urine are normally present in the form of colloidal dispersions. Centrifugation is used for separating the drugs. This method is essential for the evaluation of pharmacokinetic parameters and bioequivalence studies.

Evaluation of suspensions and emulsions : Centrifugation method is used as a rapid empirical test parameter for the evaluation of suspensions and emulsions. Normally, creaming is slow process in emulsions. This process can be hastened by inducing stress condition (using a centrifuge). A stable emulsion should not show any signs of separation even after centrifuging at 2000-3000 revolutions per minute at room temperature.

Determination of molecular weight of colloids : Determination of molecular weight of a polymer is not possible by ~~usual method~~. Ultracentrifugation methods are used for determination of molecular weight of serum albumin, insulin, methylcellulose. Centrifugation (ultra-centrifugation) is also used for ascertaining the degree of homogeneity of the sample. For example, insulin is a monodisperse protein composed of two polypeptide chains, whereas gelatin is found to be polydisperse protein with fractions of molecular weight 10,000 to 1,00,000.

This chapter deals with the principles of centrifugation, equipment used and examples of the use of the methods in pharmacy practice on commercial scale.

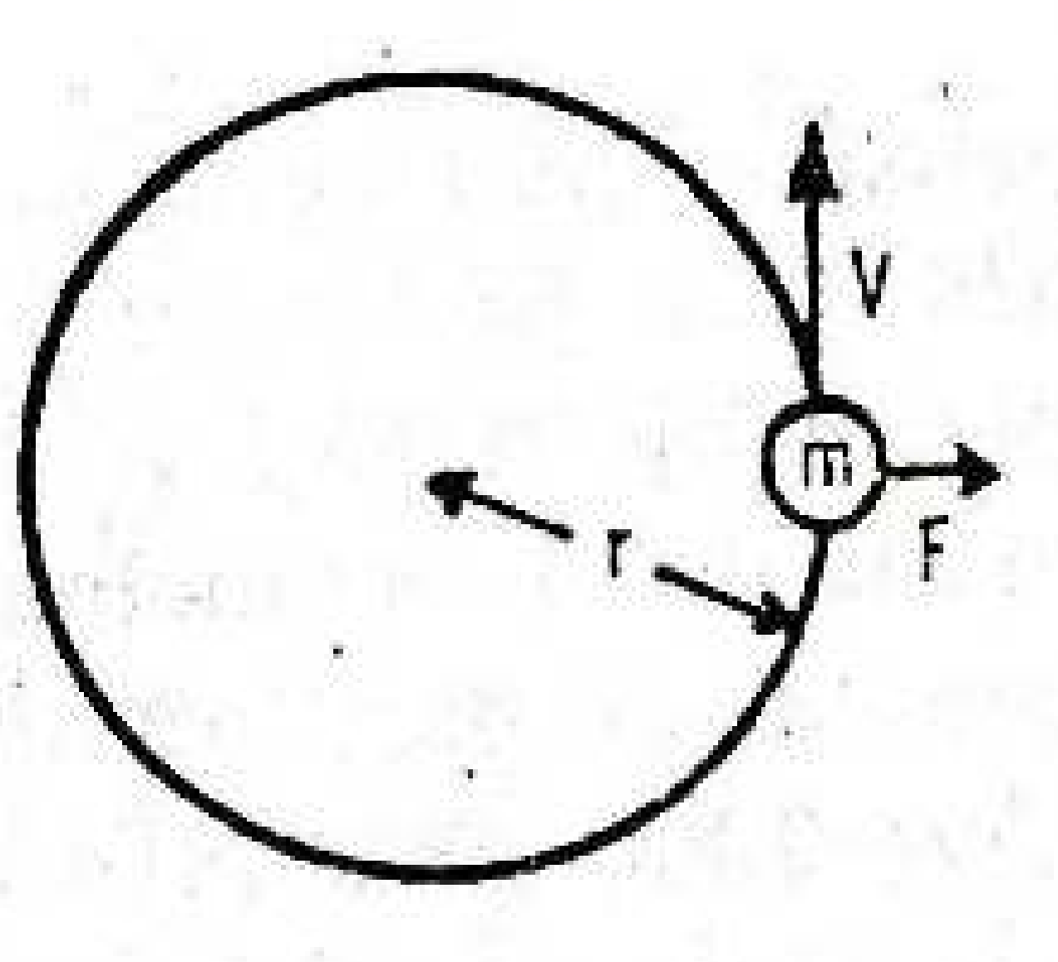
THEORY OF CENTRIFUGATION

In a colloidal dispersion, the dispersed phase may be either a solid or a liquid. Particles having a size above 5 μm sediment at the bottom due to gravitation force. In such cases, separation of solids is possible by simple filtration. If particles are of the order of 5 μm or less, they undergo Brownian motion. Hence, they do not sediment under gravity. Therefore, a stronger force, centrifugal force is applied in order to separate them. The sedimentation also depends on the densities of the dispersed phase and dispersion medium. If the difference in the densities of these phases is less, again separation is difficult. By applying centrifugal force, it is possible to facilitate (increase the rate of sedimentation) the separation process.

Centrifugal Effect or Relative Centrifugal Force (RCF)

The centrifugal operation is described by equations including the gravitational constant. The derivation is as follows.

Consider a body of mass m kg rotating in a circular path of radius r metres at a velocity of v metres per minute (Figure 10-1). The force acting on the body in a radial direction is given by:



Gmg = (mg)
G = mg

Figure 10-1. Principle of centrifugation.

$$\text{Force acting in radial direction, } F = \frac{mv^2}{r} \qquad (1)$$

where F = centrifugal force, N

G/mg

The same body is experiencing gravitational force (newton). It can be expressed as:

$$\text{Gravitation force, } G = mg \qquad (2)$$

where g = acceleration due to gravity, m/s^2

The *centrifugal effect* is expressed as a ratio of centrifugal force to gravitational force. In other words, centrifugal effect is a force, which is a number of times greater than the gravitation force.

Separating power of a centrifuge is expressed as a ratio of the centrifugal force to the gravitation acceleration. This ratio may have a value as high as 10^4.

The centrifugal effect can be expressed as:

$$\text{Centrifugal effect, } C = \frac{\text{force acting in radial direction}}{\text{gravitational force}} = \frac{F}{G}$$

$$= \frac{mv^2}{mgr} = \frac{v^2}{gr} \qquad (3)$$

But $v = 2\pi rn$, where n = speed of rotation (revolutions per second of centrifuge). Substituting this in equation (3) yields

$$C = \frac{(2\pi rn)^2}{gr} = \frac{4\pi^2 r^2 n^2}{gr} = \frac{4\pi^2 r\, n^2}{g} \qquad (4)$$

Since $2r = d$, where d = diameter of the rotation. Substituting the value in equation (4) gives:

$$C = \frac{2\pi^2 d\, n^2}{g} \qquad (5)$$

The gravitational constant has a value of 9.807 m/s^2, so that equation (5) can be simplified as:

$$\textit{Centrifugal effect} = 2.013\, n^2 d \qquad (6)$$

In equation (6), n is expressed in s^{-1} and d is in metres.

Whether the measurement of d is made from the free surface of liquid or from the tip of the tube to the centre of a centrifuge should be mentioned while reporting the centrifugal effect.

From equations (5) and (6), it can be inferred that

- Centrifugal effect $\propto$ diameter.
- Centrifugal effect $\propto$ (speed of rotation)^2.

Equation (5) helps in the selection of the type of centrifuge and other experimental conditions.

- If it is required to increase the centrifugal effect, it is of greater advantage to use a centrifuge of the same size at a higher speed rather than using a larger centrifuge at the same speed of rotation.
- It is always better to use the smallest size of centrifuge that has the appropriate capacity, since the centrifuge (equipment) is subjected to considerable stress in operation, largely due to the pressure of the fluid on the walls. It can be shown that the pressure is directly proportional to the square of the speed and the diameter. This principle is useful for the separation of two liquids as in emulsions.
- The centrifuge is designed to suit the required purpose. If a large amount of material is to be processed and a low centrifugal effect is sufficient to separate, then it is economical to use a large centrifuge operating at a low speed.

The centrifugal sedimentation of very small particles requires high centrifugal effect. For this purpose, equipment of a small diameter is used, but operated at very high speed. For example, tubular bowl centrifuge functions on this principle.

The centrifuge is comparable to a pressure vessel. Therefore, it must be handled with the same care as that of a high-pressure autoclave.

CLASSIFICATION OF CENTRIFUGES

Centrifuges are classified based on their mechanisms of separation.

Sedimentation Centrifuge

Sedimentation centrifuge is a centrifuge that produces sedimentation of solids based on the difference in the densities of two or more phases of the mixture.

The efficiency depends on the velocity of rotation to which the mixture is subjected. Examples are horizontal continuous centrifuge, supercentrifuge and conical disc centrifuge.

Ultracentrifugation : When extremely fine solid matter is to be separated from a liquid for example in colloidal research, ultracentrifuge is used. In this instrument, a relatively small rotor is operated at speeds exceeding 1,00,000 revolutions per minute and with forces up to one million times gravity.

Centrifuges have replaced the gravity separators to a considerable extent in production operations because of their effectiveness in separation.

Uses : (1) Suspensions containing low concentration of solids can be separated quickly.

(2) Lanolin is recovered from the wool by scouring process.

(3) Olive and fish liver oils are purified by removing dirt and water.

(4) The liquid/liquid phases are separated in the extraction of drugs, for example, manufacture of antibiotics.

(5) Bacterial enzymes are prepared by removing bacteria.

(6) Blood plasma is separated from whole blood.

(7) Starch is collected after washing and purification stages.

(8) In the manufacture of insulin, liquor is clarified so as to remove the precipitated proteins.

Advantages : (1) Centrifuges are compact and occupy a very small space.

(2) The separating efficiency is very high, so that the particles are deposited very rapidly. It is suitable, if the sediment is a fluid deposit or sludge.

(3) Two immiscible liquids are easily separated on a continuous process.

(4) By controlling the speed of rotation and rate of flow, coarse particles are separated, while finer particles remain in the suspension.

Disadvantages : (1) The construction of sedimentation centrifuges is complicated.

(2) Its capacity is limited.

Filtration Centrifuge

Filtration centrifuge is a centrifuge in which solids pass through the porous medium based on the difference in the densities of the solid and liquid phases.

In this type the container contains a porous wall through which the liquid phase may pass and on which the solid phase is retained. Examples are perforated basket centrifuge and semi-continuous centrifuge. The solids that form a porous cake can be separated in the filtration centrifuge. Normally perforated wall is covered with a filter medium such as canvas or metal cloth.

Uses : (1) When solid recovery is the primary goal, centrifugation must be considered as an alternative to simple filtration.

(2) It is also used for removing unwanted solids from a liquid. For example, precipitated proteins are removed from insulin.

Advantages : (1) It can handle slurries with a high proportion of solids and even those having paste like consistency.

(2) The final product has very low moisture content.

(3) In this method, the dissolved solids are separated from the cake.

Disadvantages : (1) The entire cycle is complicated resulting in considerable labour costs.

(2) It is a batch process or semi-continuous type.

(3) The solids may form a hard cake, due to the centrifugal force, which is difficult to remove.

Classification Based on Scale of Usage

Laboratory scale : Horizontal spinning arm type
Angle centrifuge (45 to 50 angle)
High speed centrifuge (10,000 revolutions per minute)
Ultracentrifuge (85,000 revolutions per minute)

Commercial scale
Batch type : Perforated basket centrifuge
Semi-continuous scale : Short-cycle batch centrifuge
Continuous centrifuge : Supercentrifuge

EQUIPMENT

Centrifuges of different types are available to meet the specific requirements of the slurry and the end product. In addition, experimental conditions are established by considering the factors affecting the process. Some of them are:

- Nature of slurry
- Flow of feed or slurry
- Centrifuge dimensions
- Densities of the materials to be separated
- Bottle (centrifuge) size
- Centrifugation time

Some pharmaceutically important centrifuges are discussed below.

PERFORATED BASKET CENTRIFUGE

In this centrifuge, a basket is mounted above a driving shaft. Such an arrangement is described as *under-driven*. Conversely, if the basket is suspended from a shaft, it is described as *over-driven*. These are used for batch processes. An under-driven bowl centrifuge is described below.

Principle : Perforated basket (bowl) centrifuge is a filtration centrifuge. The separation is through a perforated wall based on the difference in the densities of solid and liquid phases. The bowl contains a perforated side-wall. During centrifugation, the liquid phase passes through the perforated wall, while solid phase is retained in the bowl. The solid is removed after cutting the sediment by a blade after stopping the centrifuge.

Construction : The construction of a under-driven perforated basket centrifuge is shown in Figure 10-2. It consists of a basket, made of steel (sometimes covered with vulcanite or lead) or copper or monel or any other suitable metal. The basket material of construction should be such that it offers the greatest resistance to corrosion. The basket may have a diameter of 0.90 metres and a capacity of 0.085 metre cube. The diameter of the perforations should be selected based on the size of crystals to be separated. In case, the size of perforations is bigger than that of the particles, a filter cloth is employed.

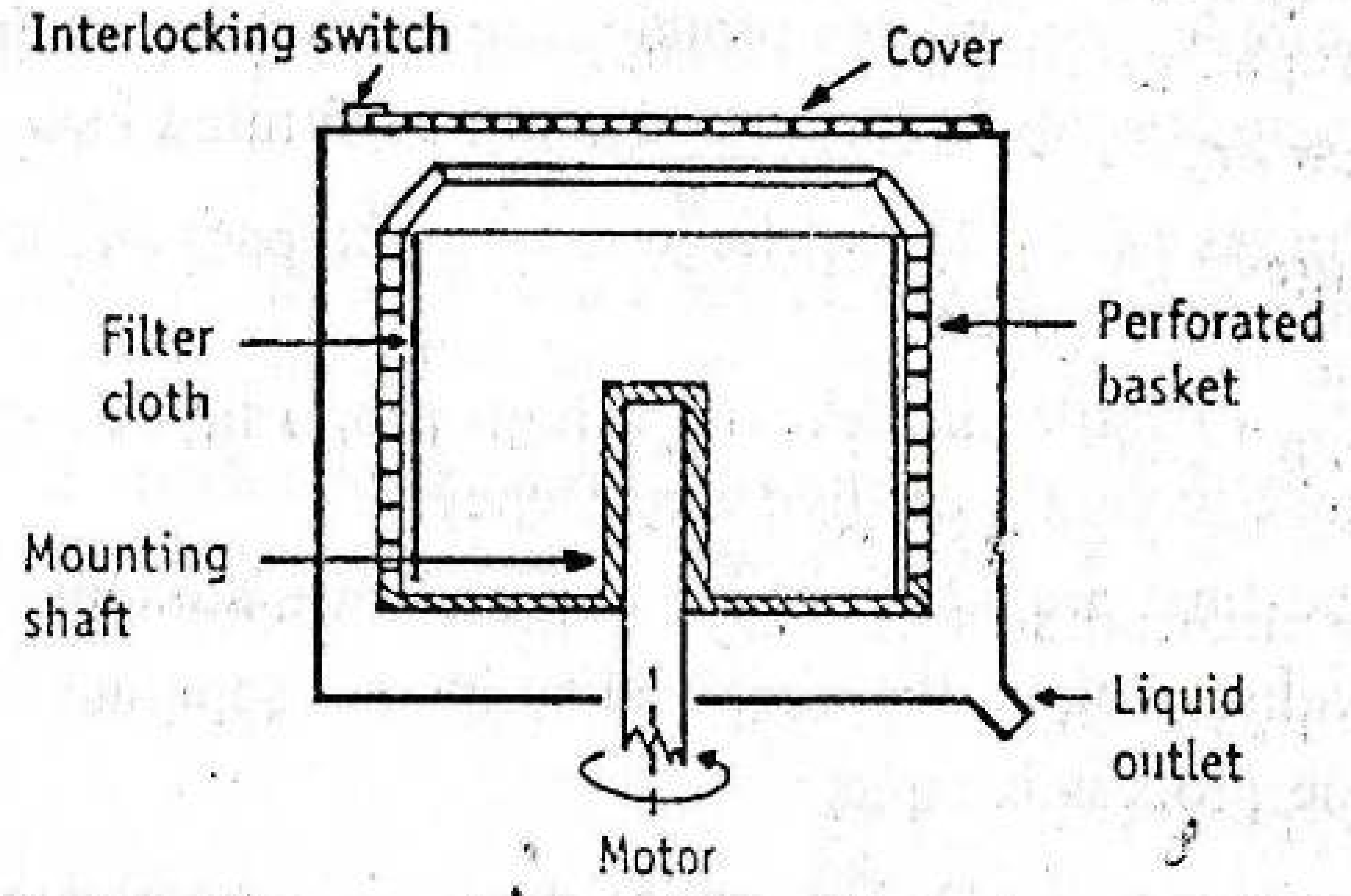


Figure 10-2. Construction of perforated basket centrifuge.

The basket is suspended on vertical shaft and is driven by a motor using suitable power systems such as belt pulleys, water turbines and electric motors. The basket may require about 5 kilowatt power for starting and 2 kilowatt power for running. Sometimes, steel hoops are used externally to strengthen the basket. Surrounding the basket, a casing (stationary) is provided which collects the filtrate and discharges it at the outlet.

Working : The material is kept in the basket when the basket is stationary. The amount of material should be optimum, otherwise, during centrifugation it puts a great strain on the basket. The loading of material must be done to give even distribution. Power is applied to rotate the basket and maximum speed must be attained quickly. The basket runs at 1000 revolutions per minute. The power required for running is small compared to the power required for starting and bringing it to the full speed.

During centrifugation, the liquid passes through the perforated wall, while the solid phase retains in the basket. The liquid leaves the basket and is collected at the outlet. The cake is then spun to dry as much as possible. Sometimes higher speeds are used so that the cake will be completely dried. After a definite period of time, the power is turned off. By applying a brake the centrifuge is stopped. The basket is brought to rest. The solid cake is cut using a blade and then unloaded manually.

Uses : (1) Perforated basket centrifuge is extensively used for separating crystalline drugs (such as aspirin) from the mother liquor. Free flowing product can be obtained because mother liquor is removed completely.

(2) It is also used for removing unwanted solids from a liquid. For example, precipitated proteins are removed from insulin.

(3) Sugar crystals are separated using perforated basket centrifuge.

Advantages : (1) The centrifuge is very compact and it occupies very little floor space.

(2) It can handle slurries with a high proportion of solids and even those having paste like consistency.

(3) The final product has very low moisture content.

(4) In this method, the dissolved solids are separated from the cake.

(5) The process is rapid.

Disadvantages : (1) The entire cycle is complicated resulting in considerable labour costs.

(2) It is a batch process.

(3) If the machine is adapted for prolonged operation, there is considerable wear and tear of the equipment. On prolonged operation, the solids may form hard cake, due to the centrifugal force, which is difficult to remove simultaneously.

Variants : For the separation of fine crystals, the perforations of 3 millimetres in diameter are sufficient. But for finely ground materials, the basket is lined with fine meshed gauze or with a cloth supported on a coarser gauge. When a mixture of liquids is to be separated, the denser liquid is collected near the walls and the lighter liquid forms an inner layer. Overflow weirs are arranged so that the two constituents are continuously removed.

NON-PERFORATED BASKET CENTRIFUGE

Principle : This is a sedimentation centrifuge. The separation is based on the difference in the densities of solid and liquid phases without a porous barrier. The bowl contains a non-perforated side-wall. During centrifugation, solid phase is retained on the sides of the basket, while the liquid remains at the top, which is removed by a skimming tube.

Construction : The construction of a under-driven non-perforated basket centrifuge is shown in Figure 10-3. It consists of a basket, which may be made of steel or any other suitable metal. The basket is suspended on vertical shaft and is driven by a motor using a suitable power system.

Working : The suspension is fed continuously into the basket. During centrifugation, solid phase is retained on the sides of the basket, while liquid remains on the top. The liquid is removed over a weir or through a skimming tube (Figure 10-3). When a suitable depth of solids has been deposited on the walls of the basket, the operation is stopped. The solids are then scraped off by hand or using a scraper blade.

Uses : Non-perforated basket centrifuge is useful when the deposited solids offer high resistance to the flow of liquid.

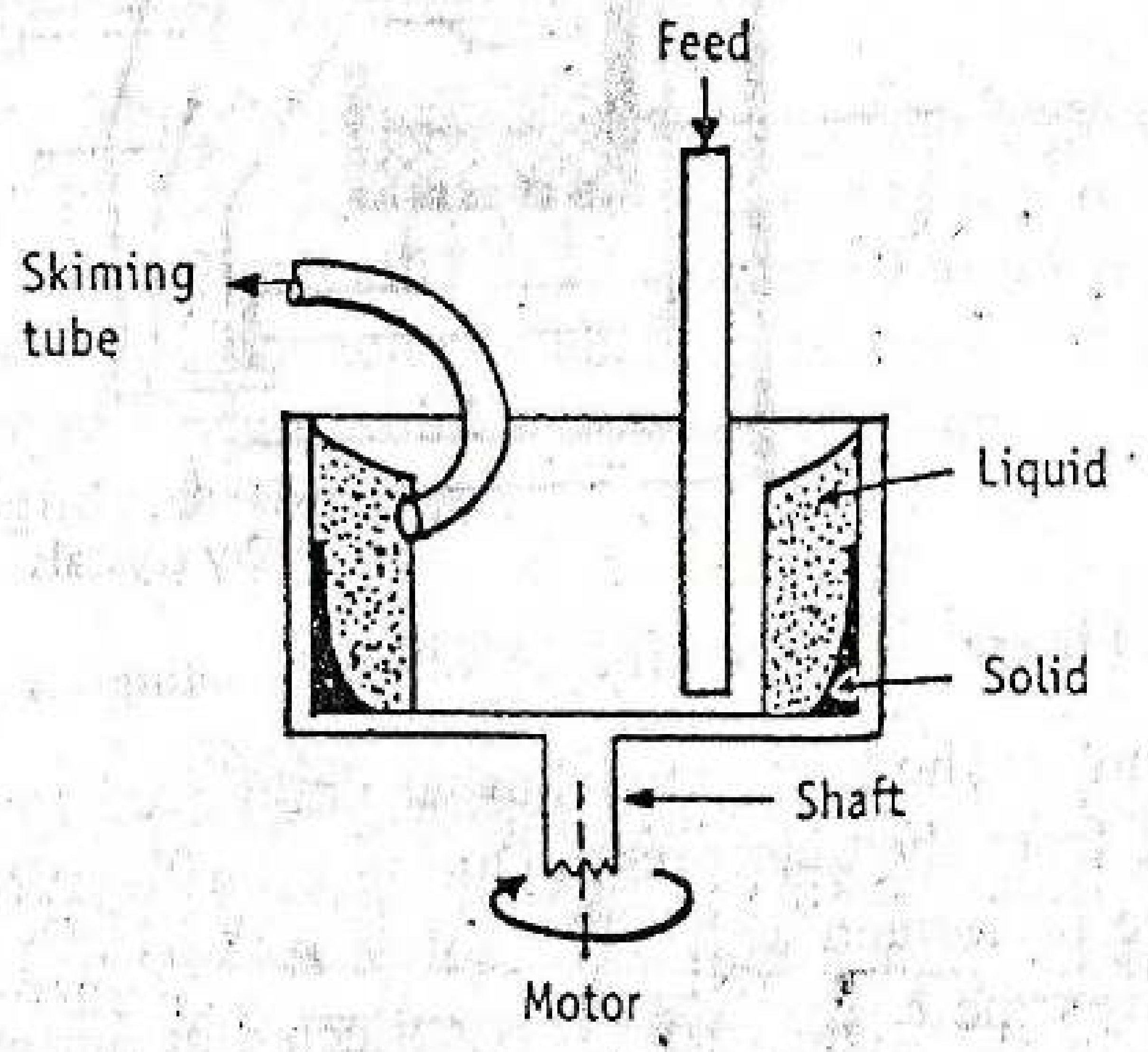


Figure 10-3. Construction of non-perforated basket centrifuge.

SEMI-CONTINUOUS CENTRIFUGE OR SHORT CYCLE AUTOMATIC BATCH CENTRIFUGE

Principle : Semi-continuous centrifuge is a filtration centrifuge. The separation is through a perforated wall based on the difference in the densities of solid and liquid phases. The bowl contains a perforated side-wall. During centrifugation, the liquid phase passes through the perforated wall, while solid phase retains in the bowl. The solid is washed and removed by cutting the sediment using a blade. It is a short cycle automatic batch centrifuge.

Construction : The construction of a semi-continuous centrifuge is shown in Figure 10-4. It consists of a vertical perforated basket, which is supported from a horizontal shaft driven by a motor. From the open side of the basket, provisions are made at the centre to introduce feed and wash pipe through horizontal tubes. A feeler (not shown) rides over the feed, which is connected to diaphragm valve through air supply. The feeler controls the thickness of the feed. Hydraulic cylinder attachment is made in such a manner that the discharge chute enters from the sides of basket, when discharge of crystals is desirable.

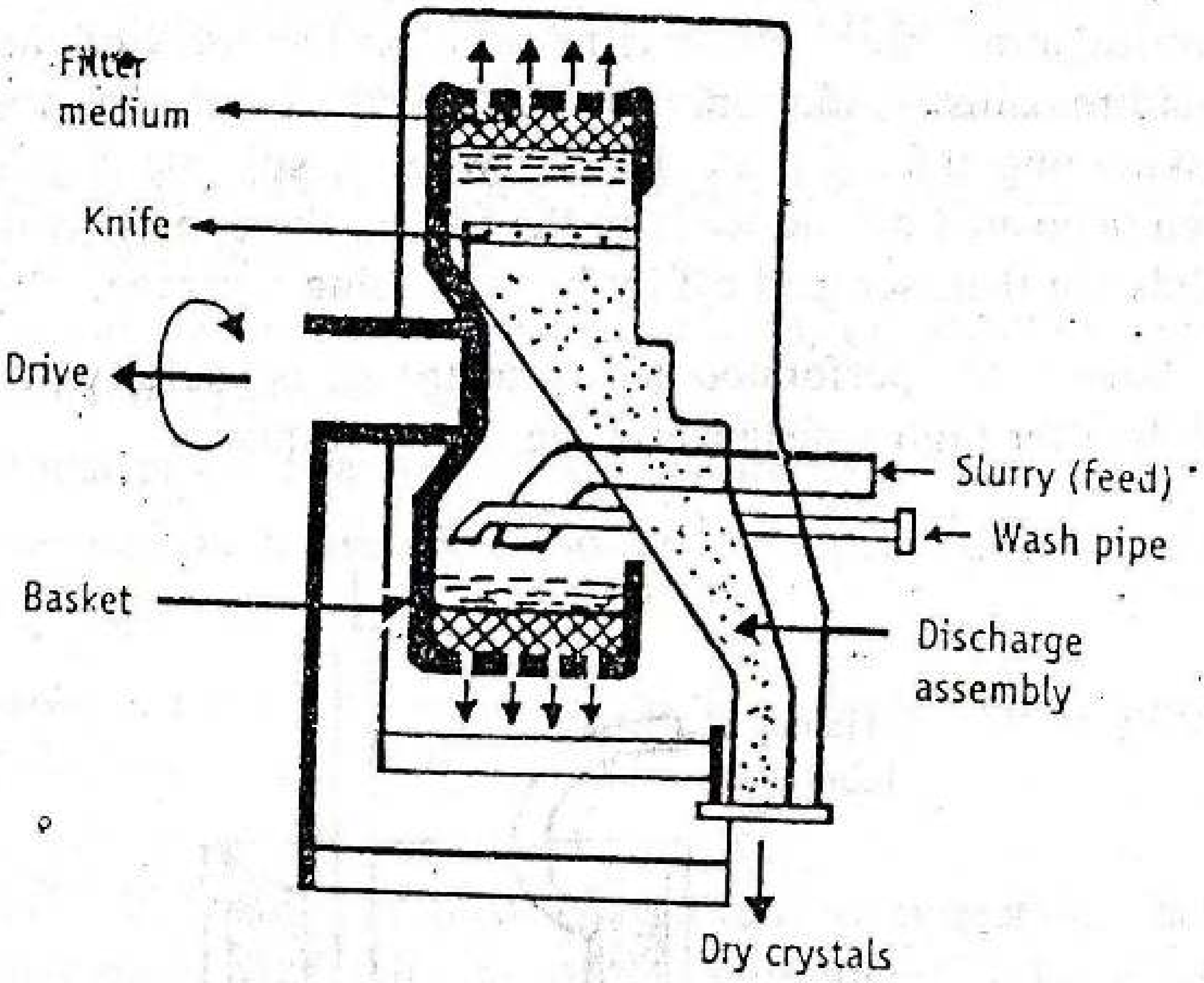


Figure 10-4. Construction of semi-continuous centrifuge.

Working : The perforated basket is allowed to rotate and slurry is introduced from the side pipe. During centrifugation, the slurry passes through the perforated wall. The solids are retained in the basket, while filtrate leaves the basket, which is collected at outlet. Further, the cake is washed with water. The wash escapes from the basket through the filtrate outlet.

After achieving the desired thickness (50 to 70 millimetres), the feeler cuts off the air supply to a diaphragm valve that automatically shuts off the entry of slurry. The hydraulic cylinder is actuated, which lifts the knife along with the discharge chute. The knife does not cut the cake completely down to the screen, but leaves a layer of crystals that acts as a filter medium for further separation in the next cycle. The residual crystals may be given a brief wash before starting the next cycle.

Through a timer and air supply mechanisms, diaphragm valve controls all steps. Therefore, the entire cycle is semiautomatic. The discharged crystals may contain 2 to 4% of moisture.

Advantages : Short-cycle automatic batch centrifuge is used when solids can be drained fast from the bowl.

Disadvantage : During discharge, considerable breakage of crystals is possible. Many moving parts are involved making the construction and functioning complicated.

CONTINUOUS HORIZONTAL CENTRIFUGE

Principle : This is a sedimentation centrifuge. The separation is based on the difference in the densities of solid and liquid phases without a porous barrier. When slurry is introduced through the shaft of the screw element into conical bowl, sedimentation of solids takes place due to centrifugal action. The solids are lifted up by the screw element, while the liquid phase is continuously drained.

Construction : The construction of a horizontal continuous centrifuge is shown in Figure 10-5. It consists of a cylindrical or conical bowl mounted horizontally and capable of rotating at 50 to 65 revolutions per second. The bowl has a diameter of about 0.5 metres. Within the bowl, a screw conveyor is placed which rotates in the same direction as the bowl, but at a slightly slower speed.

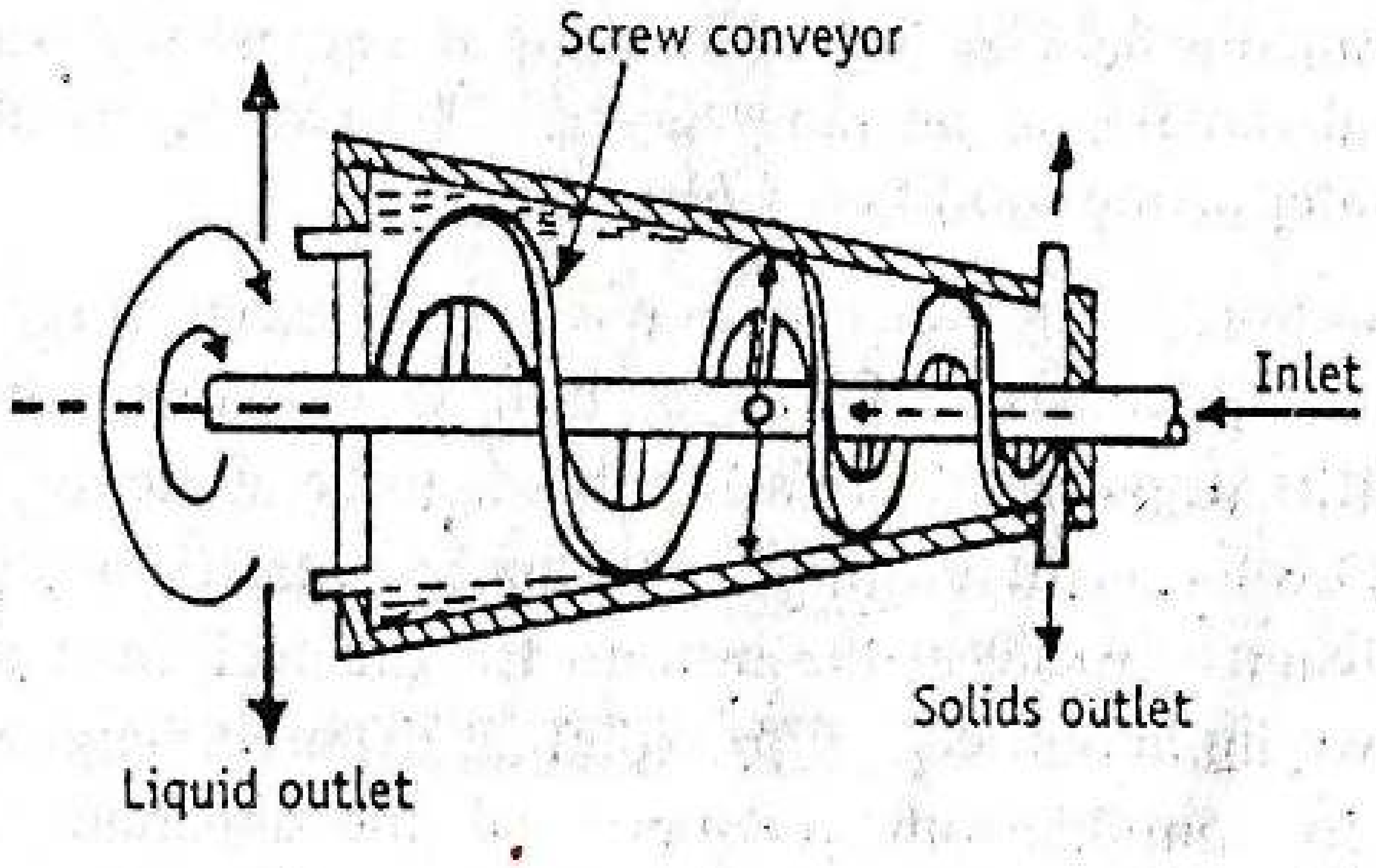


Figure 10-5. Construction of the horizontal continuous centrifuge.

Working : The bowl and the screw conveyor are allowed to rotate using suitable power supply. The slurry is introduced through the shaft as shown in Figure 10-5. The liquid moves into the wider portion of the bowl. Sedimentation of solids takes place due to centrifugal action. The solids are lifted by the screw element, while the liquid phase is continuously drained. The solid material is carried towards outlet by the conveyor and is discharged continuously. The solids are conveyed to a dry 'beach' where they get dried.

Uses : Horizontal continuous centrifuge is used when a high proportion of solids is present in the slurry.

Advantages : (1) Continuous centrifuge is very flexible in operation.

(2) It is capable of handling solids as large as 10 to 15 millimetres or as small as a few microns.

(3) It can be used for slurries with concentrations ranging from 0.5 to 50%.

Variants : The conical form as shown in Figure 10-5 is in common use, but some materials are difficult to convey when dry. for example, if the material is soft and compressible. In such cases, a cylindrical bowl is used with a short conical section near the outlet. As a result, the solid is submerged in the liquid for most of the time and is separated only when it is near the discharge point.

SUPERCENTRIFUGE

Supercentrifuge is a continuous centrifuge used for separating two immiscible liquid phases.

Principle : Supercentrifuge is a sedimentation centrifuge. The separation is based on the difference in the densities between two immiscible liquids. Centrifugation is done in the bowl of small centrifuge. During centrifugation, the heavier liquid is thrown against the wall, while the lighter liquid remains as an inner layer. The two layers are simultaneously separated using modified weirs.

Construction : The construction of a supercentrifuge is shown in Figure 10-6. It consists of a long hollow cylindrical bowl of small diameter. It is suspended from a flexible spindle at the top and guided at the bottom by loose-fit bushing. It can be rotated on its longitudinal axis. Provision is made at the bottom for the feed inlet using pressure system. Two liquid outlets are provided at different heights at the top of the bowl, for simultaneous recovery of the separated liquids using modified weirs.

Working : The centrifuge is allowed to rotate on its longitudinal axis at a high frequency usually about 2000 revolutions per minute with the help of drive-assembly. The feed is introduced from the bottom of the centrifuge using a pressure system. During centrifugation, two liquid phases separate based on the difference in their densities. The heavier liquid is thrown against the wall, while the lighter liquid forms an inner layer. Both liquids rise to the top of the vertical bowl.

The liquid-liquid interface (the so-called neutral zone) is maintained by an hydraulic balance. These two layers are simultaneously separately removed from different heights through modified weirs (as shown in Figure 10-6). Thus the supercentrifuge can work for continuous separation of immiscible liquid phases.

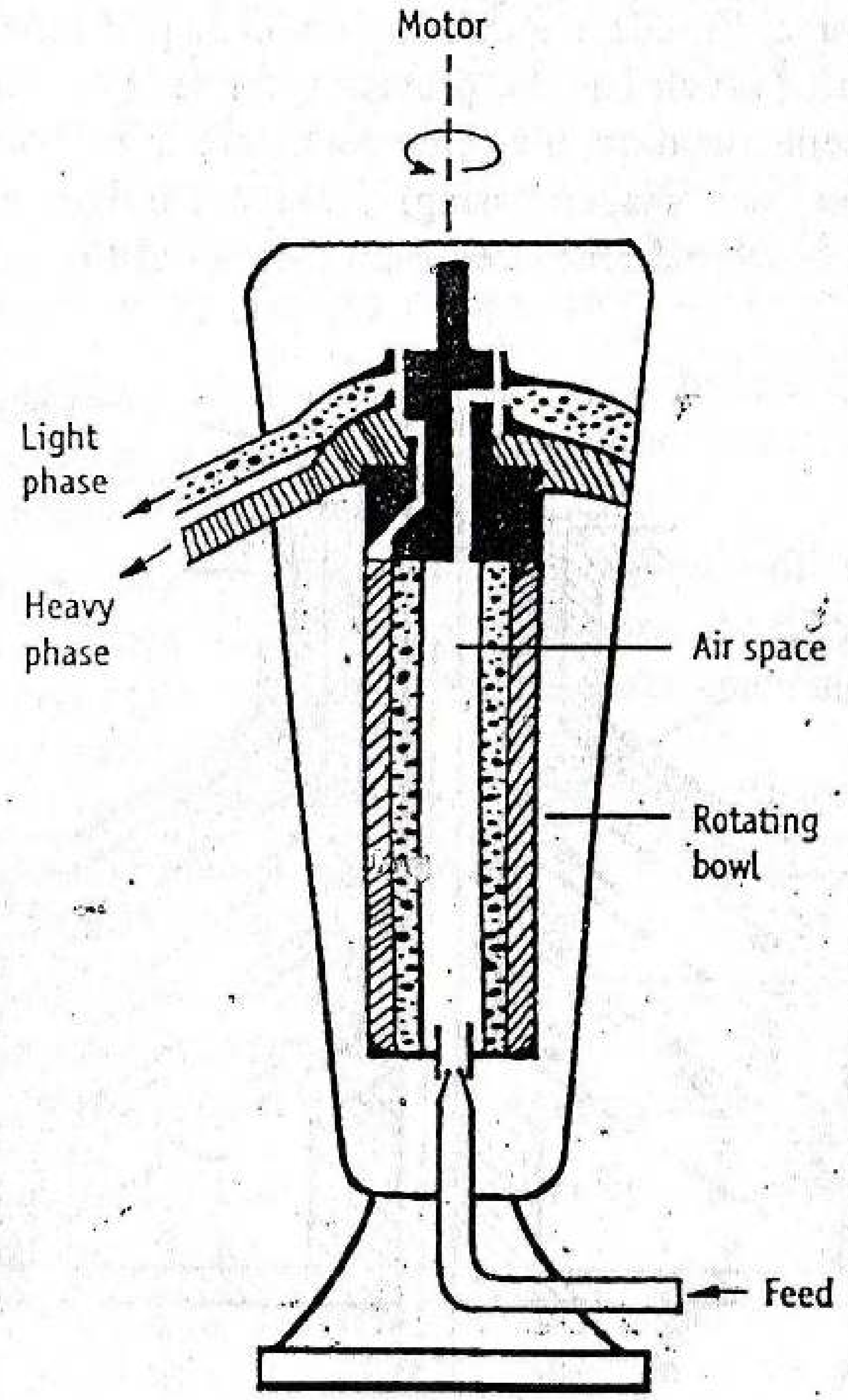


Figure 10-6. Construction of supercentrifuge.

Use : Supercentrifuge is used for separating liquid phases of emulsions in foods and pharmaceuticals.

Variants : *Tubular bowl centrifuge* : It is used to separate solids and liquids, when the solid content is low. It is a cylindrical bowl and other facilities remain the same. During centrifugation, clear liquid overflows from the weir at the top, solids are deposited on the wall and are removed at intervals, if necessary. Capacity of this centrifuge is limited.

CONICAL DISC CENTRIFUGE OR DE LAVAL CLARIFIER

As it is a clarifier, solids or immiscible liquids are present in low concentration in the feed. Complete clarification of the feed is possible by centrifugal means.

Principle : It is a sedimentation centrifuge. The separation is based on the difference in the densities between the phases under the influence of centrifugal force. In this, a number of cone-shaped plates are attached to a central shaft (which has the provision for feed) at different elevations. During centrifugation, the dense solids are thrown outwards to the underside of the cone shaped casing, while the lighter clarified liquid passes over the bowl and recovered from the top of the cone.

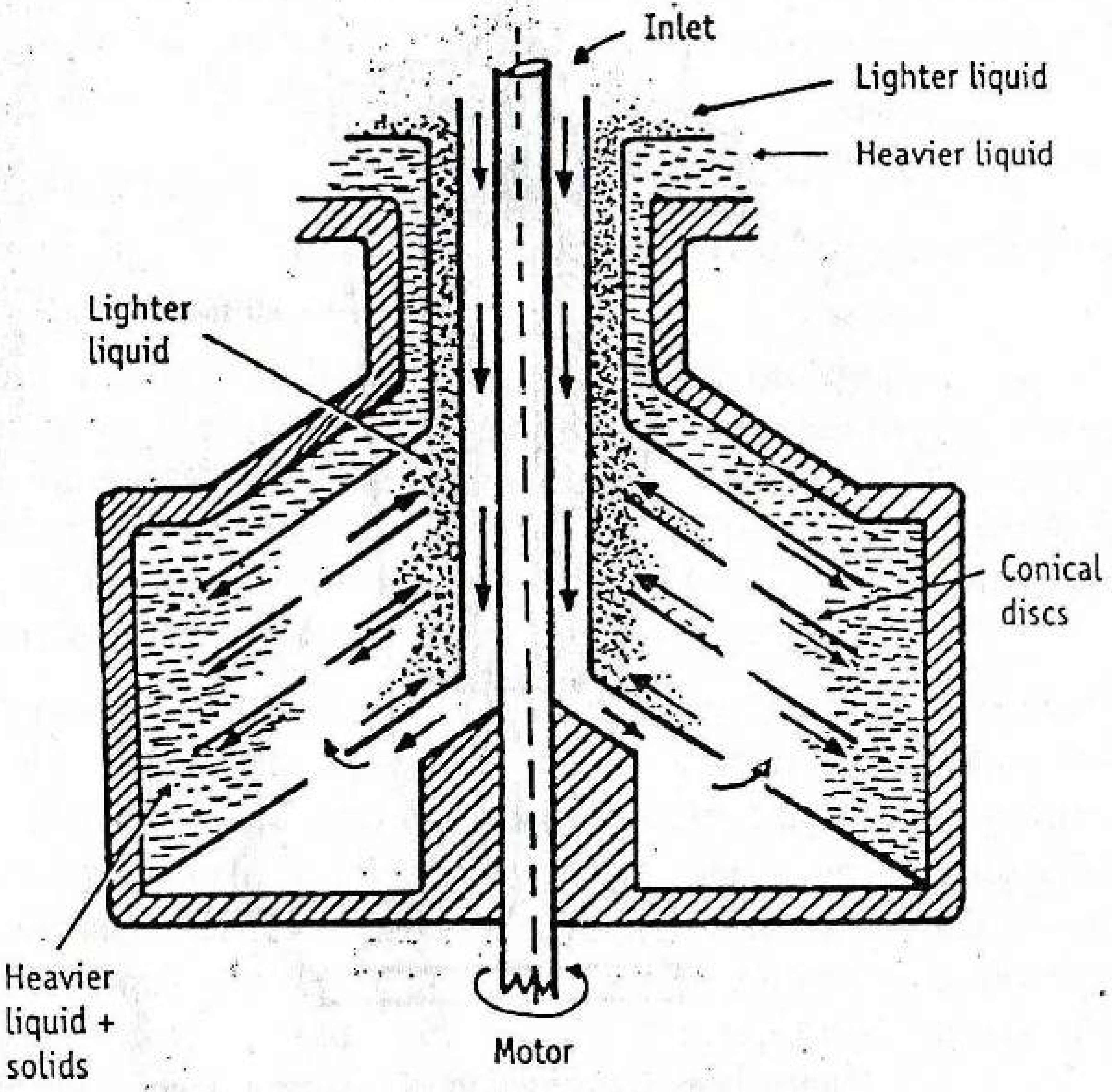


Figure 10-7. Construction of the conical disc centrifuge.

Construction : The construction of a conical disc centrifuge is shown in Figure 10-7. It consists of a shallow form of bowl containing a series of conical discs attached to the centre shaft at different elevations. The discs are made up of a thin sheet of metal or plastic separated by narrow spaces. Matching holes in the discs about half way between the axis and the wall of the bowl form channel through which the liquid passes. A concentric tube is placed surrounding the central drive shaft.

Working : Centrifuge is allowed to rotate. Low speed and short time of centrifugation is sufficient to give high degree of clarification. The feed is introduced through the concentric tube surrounding the shaft. The feed flows down and enters into the spaces between the discs (shown by the arrows). During centrifugation, the liquid flows into the channels (holes at the centre of the disc) and upward past the discs. These substances move along the surfaces of the discs to the limits of the inner and outer layers. The solids and heavy liquids are thrown outward and move underside of the discs.

Then the solids deposit at the bottom of the cone, which is removed intermittently. The lighter liquid moves to the upper side of the discs. The liquid raises to the top and escapes from the outlet.

Uses : (1) Two immiscible liquids can be easily separated by a continuous process after liquid/liquid extraction as in case of manufacture of antibiotics.

(2) Suspensions containing low concentration of solids can be separated quickly. Solids that are gelatinous or slimy can be separated by disc cone centrifuge. Such substances may plug the filter in other methods.

(3) Starch is collected after washing and purification stages.

(4) In the manufacture of insulin, the liquor is clarified to remove the precipitated proteins.

(5) Concentration of one fluid phase as in the separation of cream from milk, concentration of rubber latex, removing solids from lubricating oils, inks and beverages are possible.

Advantages : (1) Conical disc centrifuges are compact occupying a very small space.

(2) The separating efficiency is very high, so that the particles are deposited very rapidly. It is suitable, if the sediment is a fluid deposit or sludge.

(3) By controlling the speed of rotation and rate of flow, particles are separated into two size fractions.

Disadvantages : (1) The construction of a conical disc centrifuge is complicated.

(2) Its capacity is limited.

(3) It is not suitable if the sediment of solids forms a hard cake.

Glossary of Symbols

C = Centrifugal effect, m/s^2.
d = Diameter of the rotation, m.
F = Centrifugal force, N.
G = Gravitation force, N.
g = Acceleration due to gravity, m/s^2.
m = Mass of the body, kg.
r = Speed of the rotation, revolutions per second.
r = Radius from the centre to the moving body in a circular path, m.
v = Velocity of the moving body, m/s

QUESTION BANK

Each question carries 2 marks

1. Write two pharmaceutical applications of centrifugal sedimentation.
2. What are basket centrifuges? Describe their applications.
3. Write the applications of perforated basket centrifuges.
4. Explain the principle behind centrifugal separation.

Each question carries 5 marks

1. Classify industrial centrifuges. Write construction and working of a perforated basket centrifuge.
2. Give five pharmaceutical applications of industrial centrifuges.
3. Describe continuous centrifuges, giving their advantages.
4. Describe the construction and working of a Sharples supercentrifuge.
5. Describe the theory of centrifugation.

Each question carries 10 marks

1. Discuss construction and working of a discontinuous centrifuge for solid separation.
2. Describe the construction and working of a centrifuge used for the separation of slurry containing high percentage of solids.
3. Describe the construction and working of a centrifuge used for the separation of two liquid phases as in case of emulsions.

11

Distillation

Theory
General Equipment for Distillation
Classification of Distillation Methods
Simple Distillation
Flash Distillation
Fractional Distillation
Azeotropic and Extractive Distillation
Distillation under Reduced Pressure
Steam Distillation
Molecular Distillation
Destructive Distillation
Compression Distillation

Distillation is defined as the separation of the components of a liquid mixture by a process involving vaporization and subsequent condensation at another place.

The distillation process involves two steps; (a) converting a liquid into vapour phase and (b) transferring the vapour to another place and recovering the liquid by condensation. The feed liquid is known as *distilland*. The condensed liquid is known as *distillate* or *condensate*.

If one component is volatile and others are non-volatile, it is possible to separate volatile components from non-volatile components by distillation. In such cases, distillation is considered as a separation or purification method. When heat is supplied to a mixture, a more volatile liquid evaporates readily than the less volatile liquid. As a result, the condensed liquid consists of a high proportion of highly volatile liquid and less amount of less-volatile liquid. Therefore, distillation is said to be *partial separation method*. The extent of separation is governed by the properties of the components involved and the physical arrangements used for distillation.

In practice, it is difficult to distinguish three processes, namely evaporation, distillation and drying. Only working definitions help in differentiating them.

1. *Distillation* operation is used when condensed vapour is required as a product.
2. *Evaporation* operation is used when the concentrated liquid residue is needed as a product. The temperature of the liquid is maintained below its boiling point. Further vapour is not condensed, unless recovery is essential.
3. *Drying* operation is used when dried solid residue is required as a product.

Applications

Separation of volatile oils : Volatile oils are separated from cloves, anise seeds and eucalyptus leaves by the method of steam distillation.

Purification of organic solvents : Normally, simple distillation method is used for the purification of liquids having single component as a major fraction. Simple distillation method is also used for determining the boiling range of a liquid as per IP, 1996, as a method to decide the purity. Absolute alcohol (100% ethanol) can be obtained by azeotropic distillation.

Manufacture of official preparations : Spirit of nitrous ether and aromatic spirit of ammonia are prepared by simple distillation. Distilled water and water for injection are prepared as per the specifications of pharmacopoeia by simple and compression distillation methods.

Refining of petroleum products : In the petroleum industry, the crude oil is refined into different fractions using flash distillation. Each fraction is a multicomponent system. Examples are petroleum ether 60, 80 etc.

Recovery of solvents : Solvents are used for extraction of drugs from plant parts and synthetic reaction mixtures. These solvents must be recovered, in order to prevent environmental contamination. The recovered solvent may be recycled for further use.

Quality control methods : Distillation method is used for determining alcohol content in liquid dosage forms such as elixirs, as per IP, 1996. Azeotropic distillation method is used for the determination of water content in a substance using toluene according to IP, 1996.

Separation of drugs obtained from plant and animal sources : Drugs of natural origin (such as plants) are normally extracted using maceration or percolation methods. The menstruum (solvent) used for extraction is distilled off and the active constituents are separated. For example, vitamin A is separated from fish liver oil using the method of molecular distillation.

Purification of drugs obtained from chemical process : Many chemical processes involve the conversion of raw materials into products. The products are separated from the reaction mixture and purified using the methods of distillation.

In order to handle distillation effectively and economically, it is necessary to understand the theory behind this process. Several variables are involved in the process, which are often interrelated. Theory includes the understanding of different factors influencing the distillation process. The laws of conservation of matter and conservation of energy have to be applied. This chapter deals with the theory, methods and types of equipment involved in the distillation process.

THEORY

Distillation is a process of separating and purifying the components in a liquid mixture. The primary data required to solve any distillation problem are vapour-liquid equilibrium relationship. Distillation method depends on the relative volatilities of the components present in the mixture. Some of these aspects are discussed below.

When two liquids are mixed together, they may be miscible with each other in all proportions. Such miscible liquids are known as *binary mixtures* of liquids.

Examples of binary mixtures are ethyl alcohol and water, water and acetone, benzene and carbon tetrachloride. It is essential to understand theories of ideal and real solutions (non-ideal).

Ideal Solutions

Ideal solution is defined as the one in which there is no change in the properties of the components other than dilution, when they are mixed to form a solution.

Heat is neither absorbed nor evolved during mixing. The final volume of the solution represents the additive property of the individual constituents. Example is methanol and water, which have similar properties. Ideal solution theory provides a model system to which real or non-ideal solutions can be compared. Ideal solutions are characterised by one of the important physicochemical properties of liquids namely vapour pressure.

Raoult's Law

Raoult's law expresses a quantitative relationship between the concentration and vapour pressure.

Raoult's law states that the partial vapour pressure of each volatile constituent is equal to the vapour pressure of the pure constituent multiplied by its mole fraction in the solution at a given temperature.

Since the solution is homogeneous by definition, the relative numbers of components on the surface reflect the numbers of these components in the whole of solution. These numbers can be expressed on mole fraction scale. Thus Raoult's law is appropriately suited to describe an ideal solution.

Consider a mixture of miscible liquids A and B. In this mixture:

Let partial vapour pressure exerted by A = p_A kPa.
Let partial vapour pressure exerted by B = p_B kPa.
Let vapour pressure exerted by the pure component of A = $p^o{}_A$ kPa.
Let vapour pressure exerted by the pure component of B = $p^o{}_B$ kPa.
Let mole fraction concentration of liquid A = X_A
Let mole fraction concentration of liquid B = X_B

Raoult's law may be mathematically expressed as:

Partial vapour pressure of a liquid = vapour pressure of pure liquid × mole fraction of the liquid

$$p_A = p^o{}_A X_A \qquad (1)$$

$$p_B = p^o{}_B X_B \qquad (2)$$

A mixture of ethylene chloride and benzene obeys Raoult's law. When two liquids are mixed, the vapour pressure of each one is reduced by the presence of other to the extent of dilution of each phase.

Ideal solution is defined as the one that obeys Raoult's law. Raoult's law is obeyed by only a few solutions of liquid in liquids. These solutions are also known as *'perfect' solutions.* The components of these solutions have a similar structure. Examples are benzene and toluene, n-hexane and n-heptane, ethyl bromide and ethyl iodide. The individual components do not have interaction of any kind or complete uniformity of attractive forces is observed.

Dalton's Law

Dalton's law of partial vapour pressures states that the total pressure exerted by a mixture of ideal gases may be considered as sum of the partial vapour pressure exerted by each gas, if alone were present and occupied the total volume.

Dalton's law is mathematically expressed as:

Total vapour pressure = partial pressure of A + partial pressure of B

$$P = p_A + p_B \qquad (3)$$

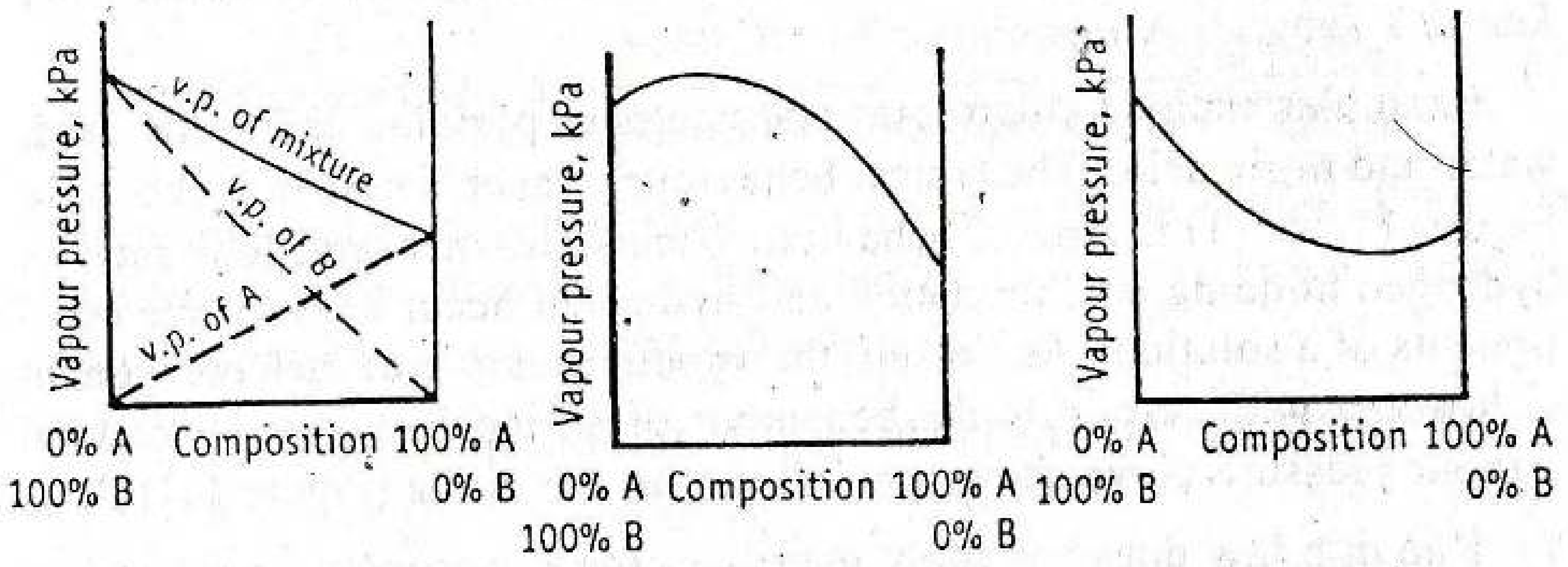
Substituting equations (1) and (2) in equation (3) gives

$$P = p^o{}_A X_A + p^o{}_B X_B \qquad (4)$$

Their properties are additive, i.e., the total vapour pressure of the mixture is the weighted average of the vapour pressures of pure individual constituents. This behaviour is shown in Figure 11-1a. The following conclusions can be drawn from Figure 11-1a.

- The partial pressure of the component varies linearly from zero to full vapour pressure as the mole fraction varies from zero to one.
- The total pressure exerted by the system at a particular composition is equal to the sum of the partial pressures of its components.

Applications : According to an ideal solution, the component having relatively greater vapour pressure will be distilled first. This principle is used in simple distillation.



(a) Ideal curve- Raoult's law (b) Positive deviation from Raoult's law (c) Negative deviation from Raoult's law

Figure 11-1. Vapour-composition diagrams for different liquid-liquid systems.

Real Solutions

Most systems show varying degree of deviation from Raoult's law, depending on the nature of the liquids and the temperature. These solutions are known as *real solutions.*

Deviations are observed because solute-solute, solvent-solute and solvent-solvent interactions are unequal. Examples include carbon tetrachloride and cyclohexane, and chloroform and acetone. Mutual interactions lead to either lowering or enhancing of the vapour pressure of the mixture with respect to ideal behaviour.

These are described as follows.

Positive deviation : In some liquid systems, the vapour pressure is greater than the sum of the partial pressures of the individual components. Such systems are said to exhibit *positive deviation from Raoult's law.*

Examples include carbon tetrachloride and cyclohexane, benzene and ethanol. The typical behaviour of such a system is shown in Figure 11-1b. This type of behaviour occurs when the components differ in their polarity, length of hydrocarbon chain and degree of association. The degree of deviation from Raoult's law decreases as the temperature increases, since the differences in the nature of components are reduced at higher temperatures. Conversely a decrease in temperature may lead to a decrease in miscibility of two components and phase separation.

Negative deviation : In some liquid systems, the vapour pressure is lower than that of the sum of the partial pressures of the individual components. Such systems are said to exhibit *negative deviation from Raoult's law.*

Examples include chloroform and acetone, pyridine and acetic acid, water and nitric acid. The typical behaviour of such a system is shown in Figure 11-1c. This type of behaviour occurs, when interactions such as hydrogen bonding, salt formation and hydration occur between the components of a solution. As a result, the vapour pressure of each component is lowered with respect to the behaviour of an ideal solution. The total vapour pressure curve shows a minimum in the curve (Figure 11-1c).

Raoult's law does not apply over the entire concentration range in a non-ideal solution. If one liquid is present in high concentrations, it is considered as a solvent. The other liquid is very dilute. Hence, Raoult's law is valid for that composition, though the liquid pair behaves non-ideal manner.

Applications : The differences in the behaviour of a mixture influence the method of distillation. The areas include fractional distillation of intermediates and drugs, purification of alcohol and other organic solvents. Complete separation of the components of a mixture by fractional distillation may not be achieved if large positive or negative deviations from Raoult's law are observed. Such solutions form so-called azeotropic mixtures. Therefore, the principles of real solutions are important in distillation.

Volatility

The *volatility* of any substance in a solution may be defined as the equilibrium partial pressure of the substance in the vapour phase divided by the mole fraction of the substance in the solution.

For example, a substance A in a liquid mixture has partial pressure p_A and its concentration in the mixture is X_A on mole fraction scale. Then volatility of A (v_A) may be mathematically expressed as:

$$\textit{Volatility of component } A,\ v_A = \frac{\text{partial vapour pressure of A}}{\text{mole fraction of A in solution}} = \frac{p_A}{X_A} \qquad (5)$$

The volatility of a material in the pure state is equal to the vapour pressure of the material.

Relative Volatility

Consider a liquid mixture containing two components A and B. In such a case, the volatility of one component is expressed in terms of the second. *Relative volatility* may be defined as:

$$\textit{Relative volatility, } \alpha = \frac{\text{volatility of component A}}{\text{volatility of component B}} = \frac{v_A}{v_B} \qquad (6)$$

Relative volatility is commonly expressed with the higher of the two volatilities in the numerator. This means that the relative volatility should never have a numerical value less than 1.0.

Since, $v = p/X$ (equation 5), it may be substituted in equation (6)

$$\alpha = \frac{p_A/X_A}{p_B/X_B} = \frac{p_A X_B}{p_B X_A} \qquad (7)$$

According to Dalton's law, the partial vapour pressures of A and B may be expressed as:

$$p_A = Y_A.P \qquad (8)$$

$$p_B = Y_B.P \qquad (9)$$

where Y_A = mole fraction A in the vapour state
Y_B = mole fraction B in the vapour state
P = total pressure of the vapour, kPa

Relative volatility may also be expressed by substituting equations (8) and (9) in Equation (7) gives:

$$\alpha_{AB} = \frac{Y_A P.X_B}{Y_B P.X_A} = \frac{Y_A X_B}{Y_B X_A} \qquad (10)$$

Equation (10) is often gives as the definition of relative volatility.

Using equation (10), the value of relative volatility can be calculated directly from the vapour-liquid equilibrium data. For example, a mixture of methyl alcohol and water is having a total vapour pressure of 101.31 kPa (760 mmHg). This liquid contains 0.40 mole fraction of methyl alcohol and the equilibrium vapour contains 0.729 mole fraction. The data may be written as:

$$X_A = 0.4;\ \ Y_A = 0.729;\ \ X_B = 0.6;\ \ Y_B = 0.271$$

$$\text{Relative volatility} = \frac{0.729 \times 0.60}{0.271 \times 0.40} = 4.035$$

Sometimes, relative volatility may change with concentration especially if the binary solution do not obey Raoult's law. However, mixtures that obey Raoult's law show only a slight change in relative volatility with concentration variation.

GENERAL EQUIPMENT FOR DISTILLATION

The construction of equipment for the distillation has been described using several figures in subsequent sections. The general equipment, either for laboratory use or for industrial scale, consists of three parts.

STILL

It is a vaporizing chamber and used to place the material to be distilled. The size of the still should be such that only one-half to two-thirds full of liquid is filled. If the still is too large, superheating and some times decomposition of liquid may occur. The still is heated by a suitable means (example, steam) for the vaporisation of the volatile constituents. The temperature at which the liquid boils is of considerable importance. Therefore, provision is made to place the thermometer in the still. A condenser is attached to the still using appropriate joints.

On laboratory scale, round bottom flasks made of glass are used so that the progress of the distillation can be noticed. At the same time, the feed can be added as and when required. Stills are made of stainless steel, copper or suitable material to provide efficient heat transfer. In these stills, an observation window is provided.

Some liquids have a tendency to bump or froth, which promotes the carrying of liquid with vapour. To prevent this, a trap is inserted between distillation flask and condenser.

CONDENSER

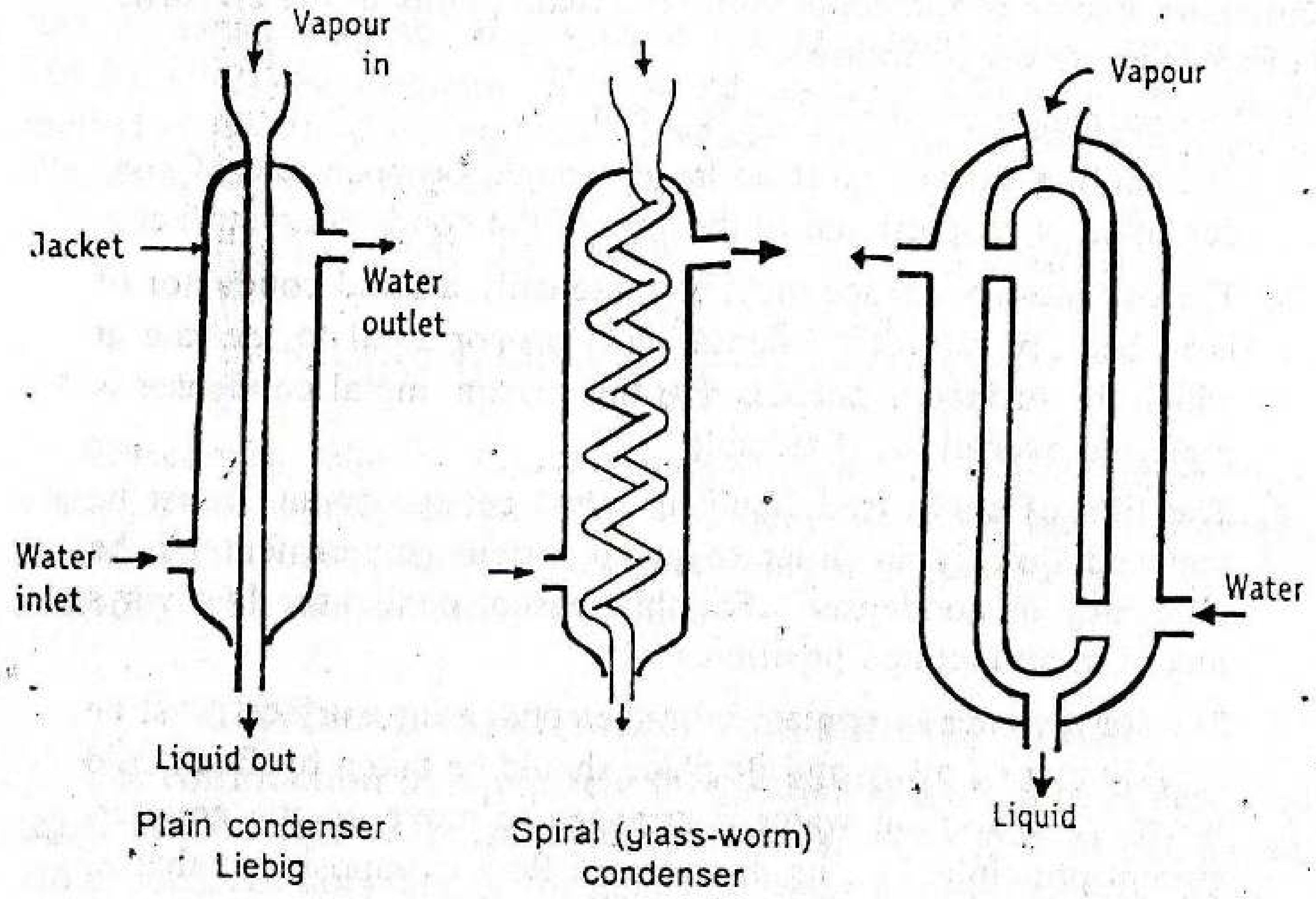
Condenser helps in condensing the vapour. Condenser is a heat exchanger. It is kept cold by circulating water through water jacket. The boiling point and volatility of a substance are the main factors governing the choice of the condenser. The main points in the construction of a condenser are as follows.

1. The condenser must be easy to clean.
2. The cooling surface must be large enough, because rate of condensation is proportional to the area of the condensing surface.
3. The condensing surface must be reasonably a good conductor of heat, because rate of condensation is proportional to the rate at which the surface is cooled. For this reason, metal condenser is preferred over glass, if suitable.
4. The film of condensed liquid is a bad conductor and must be removed quickly in order to avoid serious impairment of the efficiency of condenser. For this reason, condenser is always placed in an inclined position.
5. The warm water in contact with the condensing surface must be quickly carried away and its place should be taken by fresh cold water. The cooling water is arranged to move on the counter-current principle, i.e., its direction of flow is opposite to that of the flow of vapour to be condensed.

The condenser is connected to the receiver through a suitable adapter. *Adapter* may be employed where the receiver cannot be conveniently supported at the end of the condenser. Some times, the adapter has a provision to connect to the vacuum pump as in case of vacuum distillation. Condenser is placed in an upright or oblique position. Different types of condensers are used (Figure 11-2). Three classes of condensers are described below.

1. *Single-surface condensers* : Examples are Liebig condenser (Figure 11-2a), spiral (glass-worm condenser) (Figure 11-2b).
2. *Double-surface condensers* : The efficiency of the condensation increases. (Figure 11-2c).
3. *Multi-tubular condensers* : These are usually made of metal and used for large scale work. In the preparation of distilled water and water for injection, multi-tubular condensers are used.

The basic differences in the construction show variations in the efficiency of the condensation. Water-cooled condensers are not suitable for liquids, which boil above 130°C. In such cases, *air condenser* may be used in place of water condenser. Air condenser is a straight tube with sufficient length (1-2 metres long), which is passed through the bung of the flask. The vapour rises in the air-cooled tube and gets condensed.



(a) Single surface condensers (b) Double surface condenser

Figure 11-2. Different types of condensers.

RECEIVER

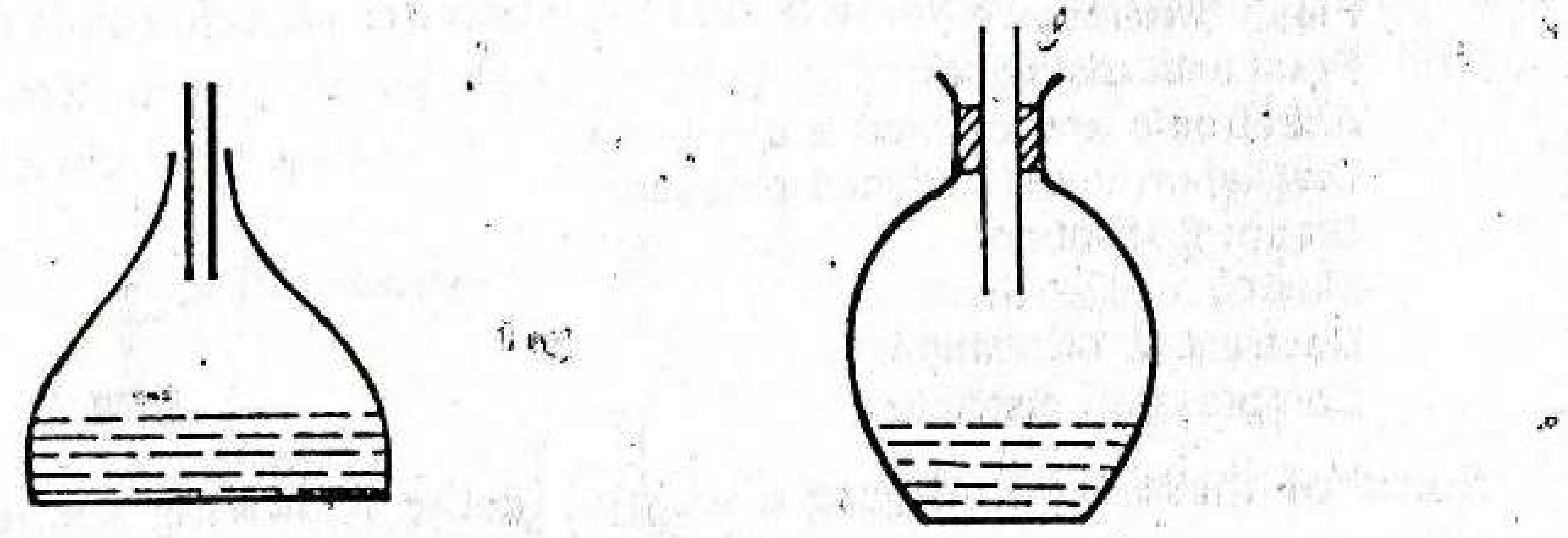
It is used to collect the distillate. It may be a simple flask (Figure 11-3a & b) or modified flasks such as Florentine receivers (Figure 11-3c & d). Some times, the receiver is immersed in an ice-bath or any other freezing mixture. This minimizes loss of volatilization. Florentine receivers are used for the separation of oil and water. These are two types.

Type I : These are used for the separation of oil heavier than water.
Type II : These are used for the separation of oil lighter than water.

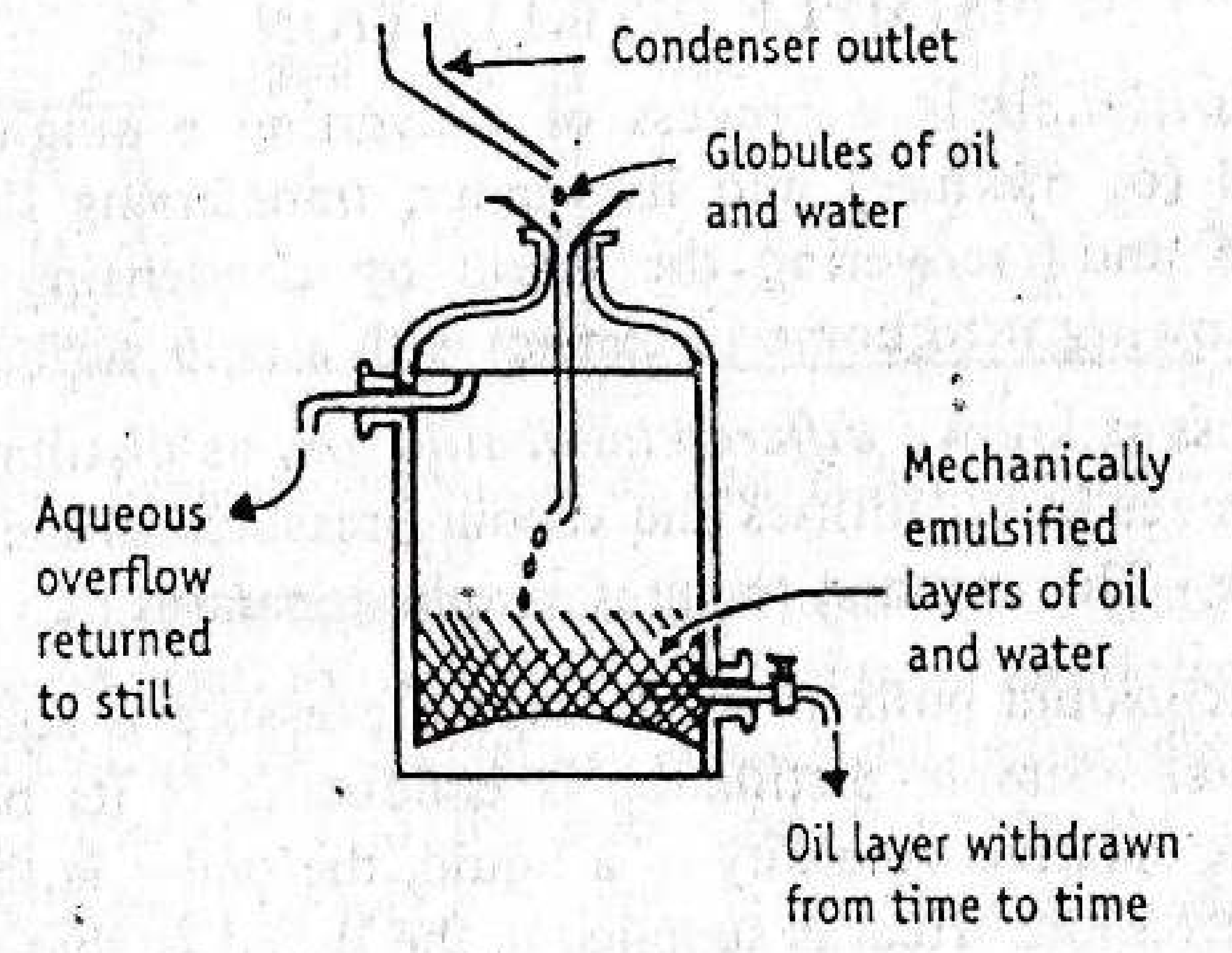
The receiver used for oil heavier than water has two taps (Figure 11-3c). The tap fitted near the bottom of vessel is used for collecting oil, while the tap fitted near the top of the vessel for water to overflow.

The receiver used for oil lighter than water is fitted with siphon at the bottom, which works when it gets filled with water (Figure 11-3d), while the tap fitted near the top is an outlet for the flow of oil.

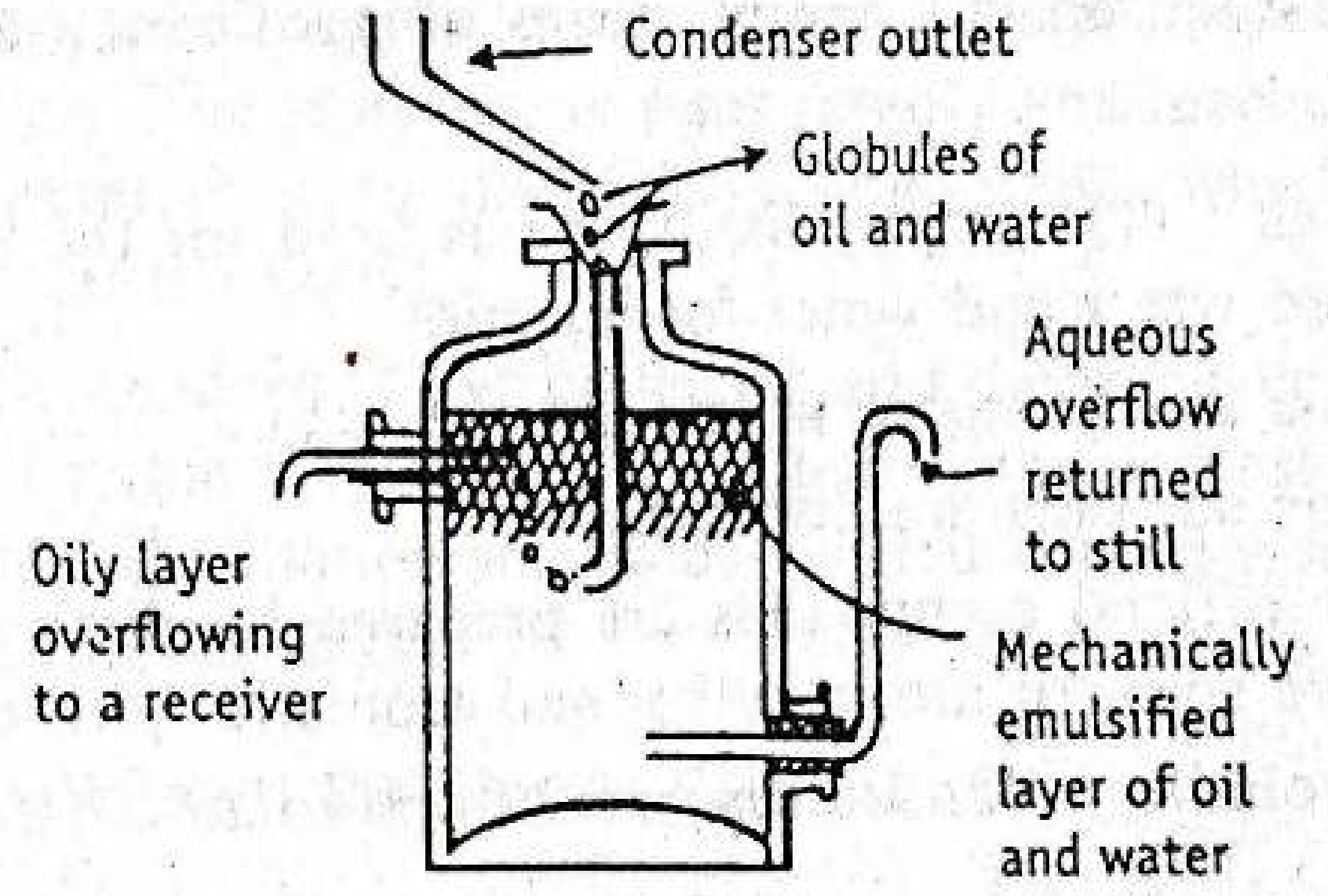
Some times, the receiver is immersed in an ice-bath or any other freezing mixture. This minimizes loss due to volatilization.



(a) Conical flask as receiver (b) Flat bottom round flask as receiver



(c) Florentine receiver for oils heavier than waters



(d) Florentine receiver for oils lighter than water

Figure 11-3. Different types of receivers.

CLASSIFICATION OF DISTILLATION METHODS

Simple distillation
Flash distillation
Fractional distillation
Azeotropic and extractive distillation
Distillation under reduced pressure
Steam distillation
Molecular distillation
Destructive distillation
Compression distillation

Some of these methods are discussed in the following sections both on laboratory scale and industrial scale along with the specific theories.

SIMPLE DISTILLATION

Simple distillation is a process of converting a single constituent from a liquid (or mixture) into its vapour, transferring the vapour to another place and recovering the liquid by condensing the vapour, usually by allowing it to come in contact with a cold surface.

This process is known *differential distillation,* as distillation is based on the differences in volatilities and vapour pressures of the components in the mixture. This method requires simple apparatus.

Principle : Liquid boils when its vapour pressure is equal to atmospheric pressure. Simple distillation is conducted at its boiling point. The higher the relative volatility of a liquid, the better is the separation by simple distillation. Heat is supplied to the liquid so that it boils. The resulting vapour is transferred to a different place and condensed. If the liquid of interest is volatile and remaining components are nonvolatile, then simple distillation is a useful means of purification and separation of liquids.

Applications : (1) Simple distillation is used for the preparation of distilled water and water for injection.

(2) Volatile and aromatic waters are prepared.

(3) Organic solvents are purified.

(4) A few official compounds are prepared by distillation. Examples are spirit of nitrous ether and aromatic spirit of ammonia.

(5) Non-volatile solids are separated from volatile liquids.

Laboratory Scale Apparatus for Distillation

Assembling of apparatus : The construction of a simple distillation apparatus is shown in Figure 11-4. It consists of a distillation flask with a side arm sloping downwards. Condenser is fitted into the side arm by means of a cork. The condenser is usually water condenser, i.e., jacketed for circulation of water. The condenser is connected to a receiver flask using an adapter. On a laboratory scale, the whole apparatus is made of glass.

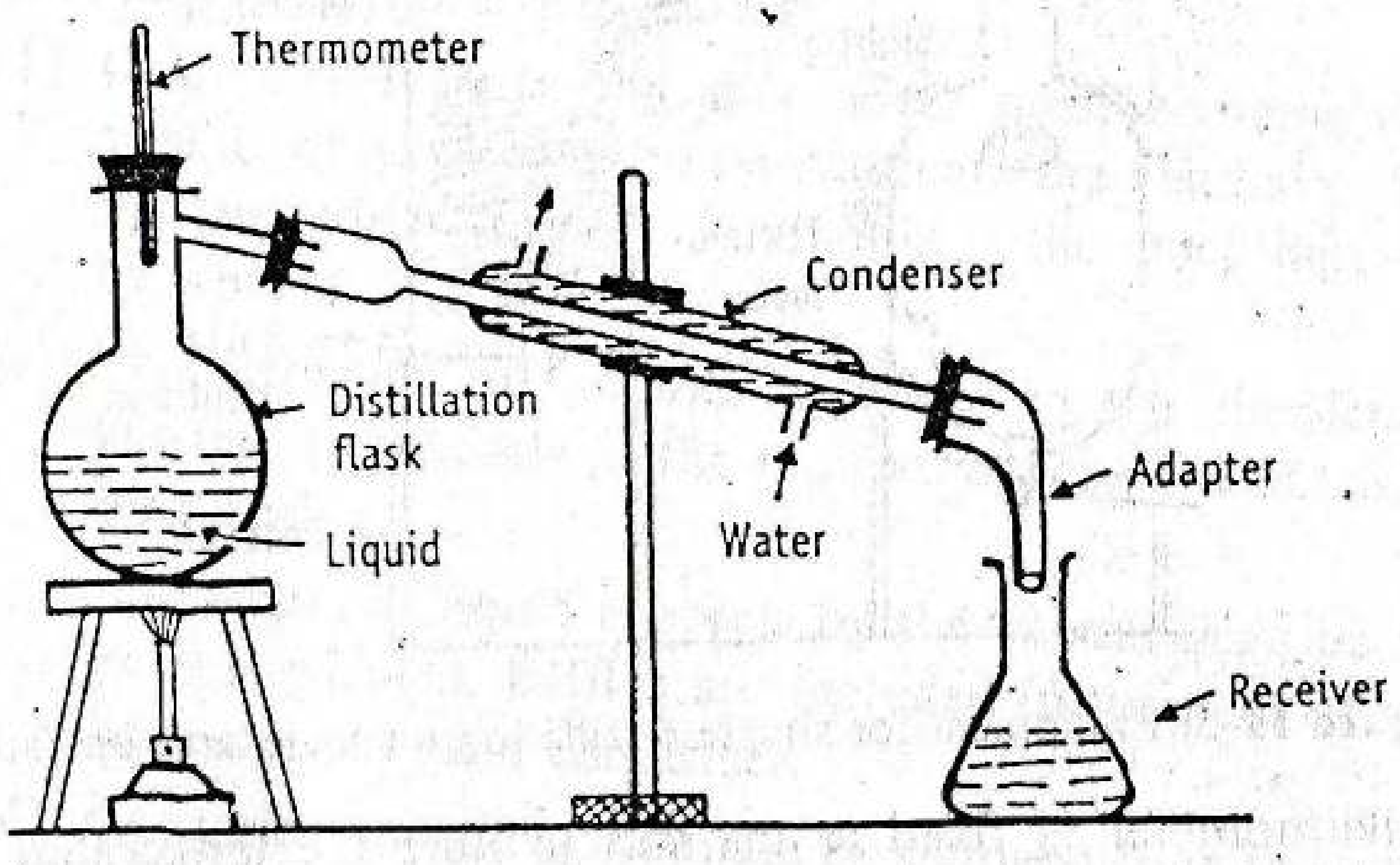


Figure 11-4. Apparatus for simple distillation (on laboratory scale).

Procedure : In the laboratory scale, the liquid to be distilled is filled into the flask to one-half to two-third of its volume. Bumping is avoided by adding small pieces of porcelain or porous pot before distillation. A thermometer is inserted into the cork and fixed to the flask. The thermometer bulb must be just below the level of the side arm. Water is circulated through the jacket of the condenser as shown in Figure 11-4.

The contents are heated gradually. The liquid begins to boil after some time. The vapour begins to rise up and passes down the side arm into the condenser. The temperature rises rapidly and reaches a constant value. The temperature of the distillate is noted down, which is equal to the boiling point of the liquid.

The vapour is condensed and collected into the receiver. The flame is adjusted so that the distillate is collected at the rate of one to two drops per second. Distillation should be continued until a small volume of liquid remains in the flask.

Large Scale Equipment for Simple Distillation

Construction : A simple still as shown in Figure 11-5 is used for large-scale distillation. It is made up of stainless steel, copper or any other suitable material. A still of this kind has a limited heating surface and functions perfectly with volatile solvents, but is not useful for concentrating dilute solutions. Specially designed stills suited to one product or a group of products are used for frequent and continuous use.

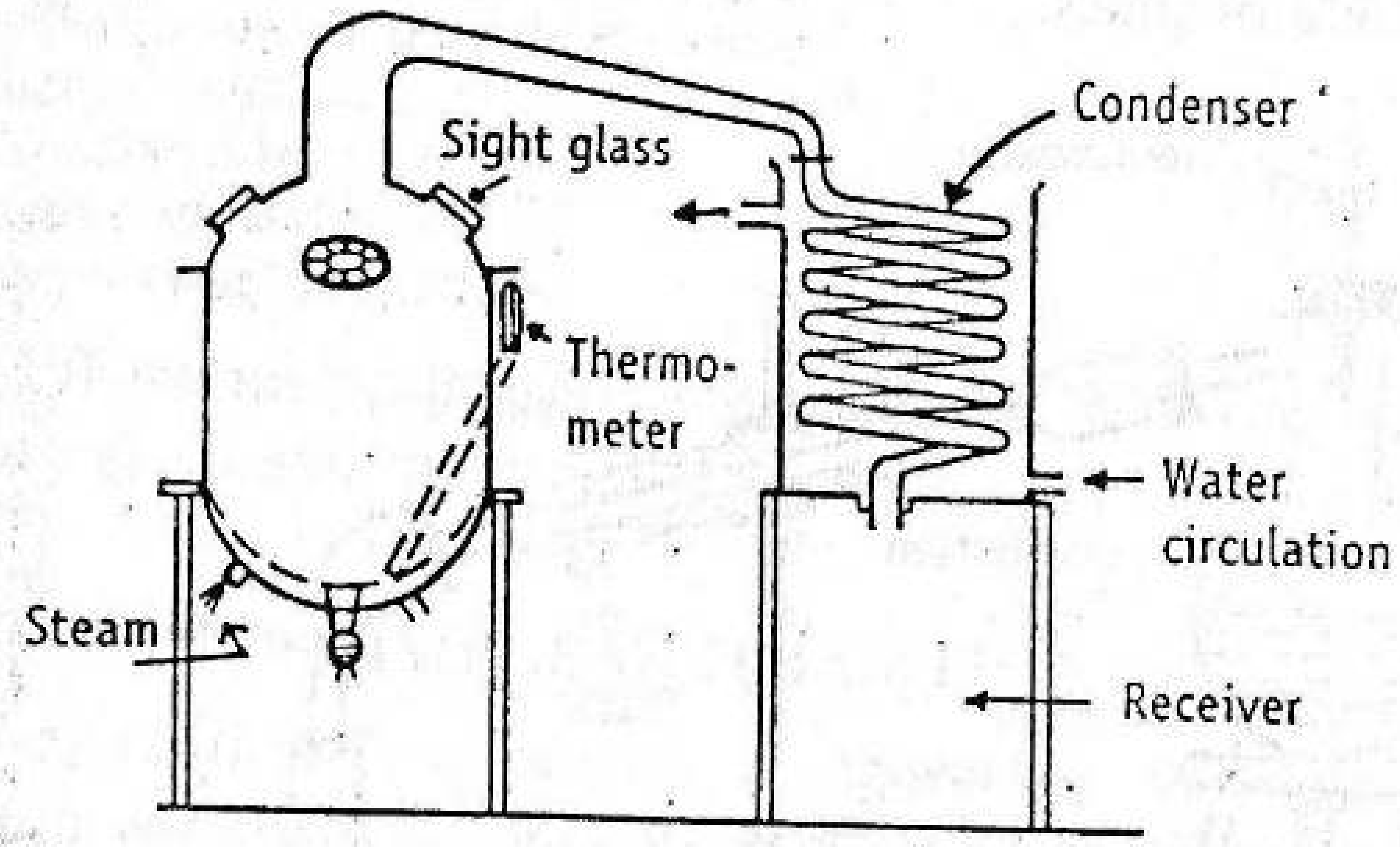


Figure 11-5. Equipment for simple distillation on large scale operation.

A thermometer is fixed to the still to note the temperature of the boiling liquid. An observation window in the hood is helpful to the operator to see the progress of the distillation and the level of the contents to be distilled. The still is connected to a condenser and then to a receiver. The still is heated using steam. Therefore, a steam inlet at the bottom of the still and an outlet for removing the condensed steam are provided.

Working : A liquid to be distilled is filled into the still to one-half to two-third of its volume. Bumping is avoided by adding small pieces of porcelain or porous pot before distillation. A thermometer is inserted into the still. Water is circulated through the jacket of the condenser as shown in Figure 11-5.

Steam is passed through the inlet. The contents are heated gradually. The liquid begins to boil after some time. The vapour begins to rise up and passes into the condenser. The temperature rises rapidly and reaches a constant value. The temperature is noted down, which is equal to the boiling point of the liquid.

The vapour is condensed and collected into the receiver. The passage of steam is regulated so that the distillate is collected at a slower rate (a few drops per second). Distillation should be continued until a small volume of liquid remains in the still.

Water stills are used for producing distilled water including water for injection on a continuous basis.

Preparation of Purified Water (BP) and Water for Injection (BP) By Distillation

The principle involved in the preparation of water for injection by distillation is same as that of the simple distillation. However, it is a special case for the following reasons.

(1) Gases dissolved in the raw water must be removed. These should not be allowed to contaminate the distillate. Such gases include carbon dioxide. Ammonia is the most important gas to be avoided.

(2) The carryover of soluble materials in the droplets must be avoided, particularly if the product is required for use as water for injection.

(3) Entrapment of liquid droplets by the vapour must be prevented. For this purpose, baffles are included in the path of the vapour between boiler and condenser.

(4) Contamination of the distillate by pyrogen from feed water must be avoided.

(5) The residue of solids must not be concentrated to a point where hydrolysis occurs. Otherwise, the distillate may be contaminated by volatile material produced during hydrolysis. For example, hydrolysis of chlorides produces hydrochloric acid.

Construction : The arrangement of an apparatus for the continuous production of distilled water or water for injection is shown in Figure 11-6. The distillation apparatus consists of a boiler, which may be made of cast iron. Baffles and condenser tubes are made up of stainless steel or monel metal. The top of the condenser jacket is open, so that gases from water can escape into atmosphere. The condenser tubes are vertical and open at both ends, as shown in Figure 11-6.

Working : Water (feed) enters at the base of the still and rises in the jacket, which contains a number of tubes. In the condenser tubes, the condensed liquid descends. The rising feed water gets heated on account of condensate in the tubes. The rate of flow is adjusted in such a way that the water gets heated to 90–95 °C, before it enters the boiler. The dissolved gases in water escape to the atmosphere. The heated water then enters the boiler, in which steam is circulated under pressure through a copper coil. The steam that is obtained by feed water cannot escape except through the condenser tubes, whose upper ends are protruded into the boiler head. The descending steam is condensed into distilled water, which flows from the lower ends of the tubes.

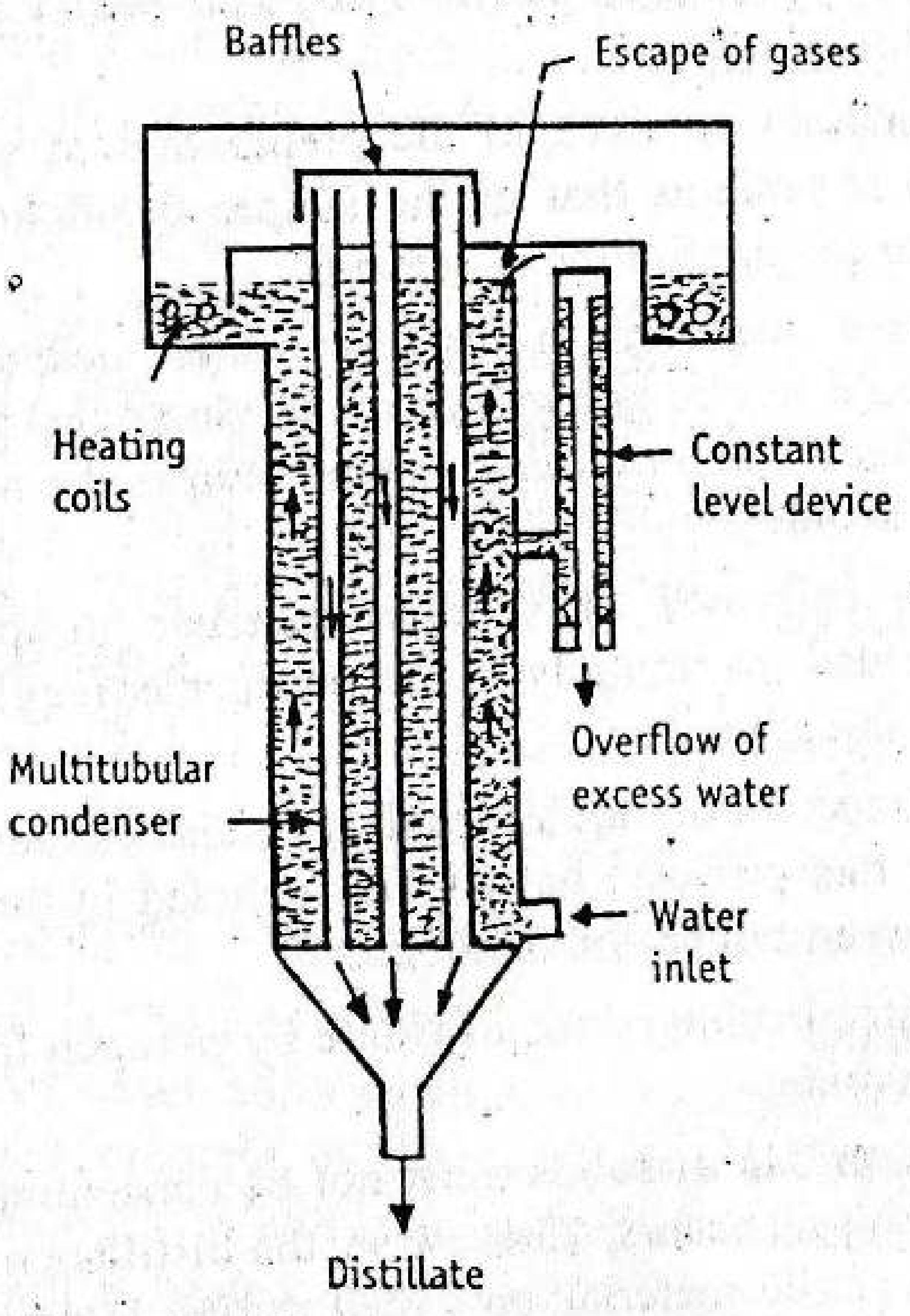


Figure 11-6. Construction of a distillation unit for the preparation of water for injection.

Advantages : This process is economical as the amount of steam used in coils is reduced on account of preheating of feed water by counter-current flow of the condensate. This also facilitates the escape of dissolved gases without any additional effort.

FLASH DISTILLATION

Flash distillation is defined as a process in which the entire liquid mixture is suddenly vaporized (flash) by passing the feed from a high pressure zone to a low pressure zone.

Flash distillation is also known as *equilibrium distillation,* i.e., separation is attempted when the liquid and vapour phases are in equilibrium. This method is frequently carried out as a continuous process and does not involve rectification.

Principle : When a hot liquid mixture is allowed to enter from a high-pressure zone into a low-pressure zone, the entire liquid mixture is suddenly vaporised. This process is known as *flash vaporisation.* During this process the chamber gets cooled. The individual vapour phase

molecules of high boiling fraction get condensed, while low boiling fraction remains as vapour. This process requires certain amount of time. Therefore, the liquid and vapour is kept in intimate contact until equilibrium is achieved. The liquid fraction is collected separately. The vapour is separated from the liquid and further allowed to condense.

Uses : Flash distillation is used for separating components, which boil at widely different temperatures. It is widely used in petroleum industry for refining crude oil.

Advantages : Flash distillation is a continuous process. It is used for obtaining a multi-component systems of narrow boiling range, especially in oil refinery. Examples are petroleum ether 60, 80 etc.

Disadvantages : Flash distillation is not effective in separating components of comparable volatility. It is not suitable for two component systems. It is not an efficient distillation when nearly pure components are required, because the condensed vapour and residual liquid are far from pure.

Equipment

Construction : The construction of a flash distillation apparatus is shown in Figure 11- 7. It consists of a pump, which is connected to a feed reservoir. Pump helps in pumping the feed into the heating chamber which contains a suitable heating mechanism. The other end of the pipe is directly introduced into the vapour-liquid separator through a reducing valve. The vapour outlet is provided at the top of the separator and liquid outlet is provided at the bottom.

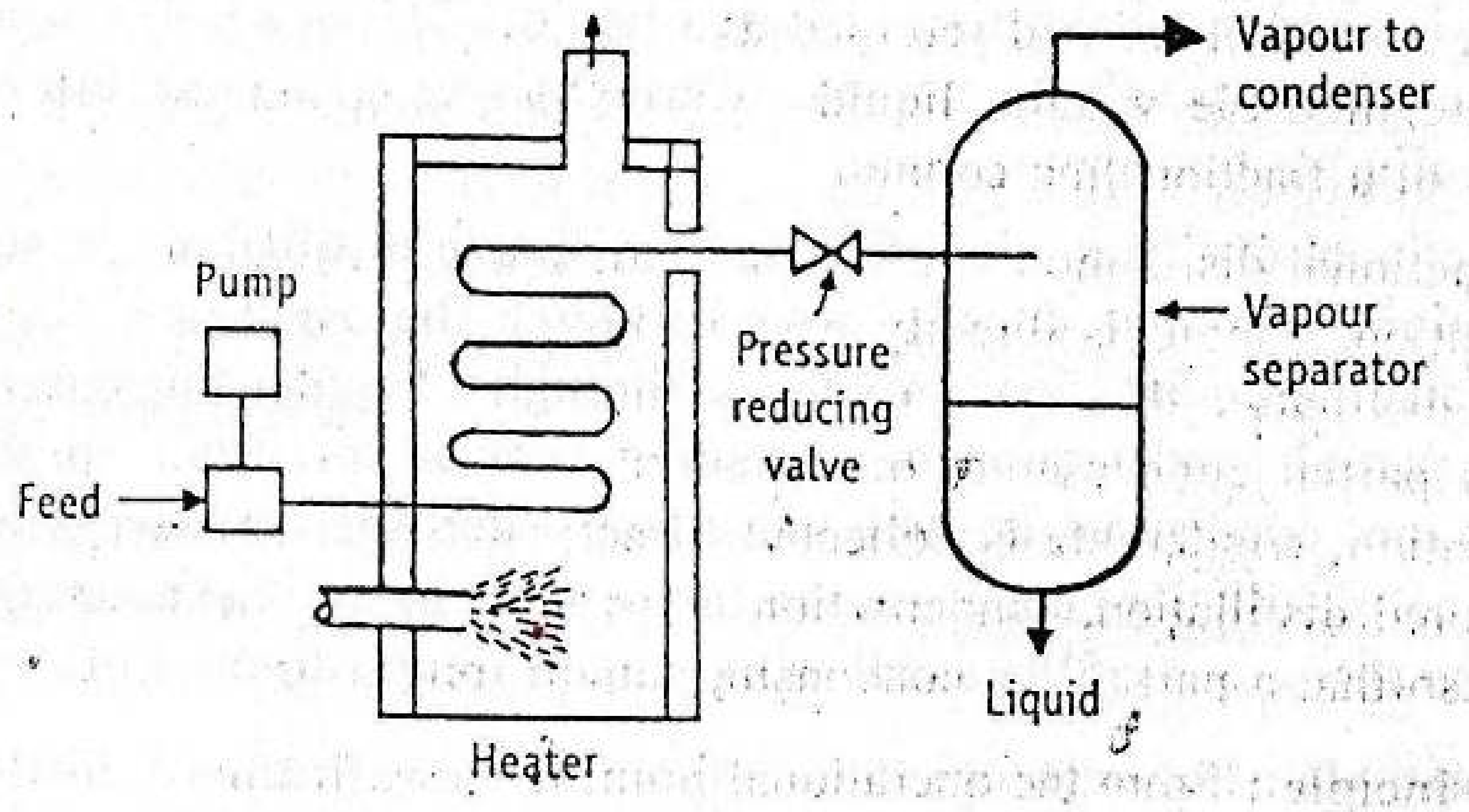


Figure 11-7. Apparatus for flash distillation.

Working : The feed is pumped through a heater at a certain pressure. The liquid gets heated, which enters the vapour-liquid separator through a pressure-reducing valve. Due to the drop in pressure, the hot liquid flashes, which further enhances the vaporisation process. The sudden vaporisation induces cooling. The individual vapour phase molecules of high boiling fraction get condensed, while low boiling fraction remains as vapour. The mixture is allowed for a sufficient time, so that vapour and liquid portions separate and achieve equilibrium. The vapour is separated through a pipe from above and liquid is collected from the bottom of the separator.

By continuously feeding into the still, it is possible to obtain continuous flash distillation. The operating conditions can be adjusted in such a way that the amount of feed exactly equals the amount of material removed. Therefore, vapour and liquid concentrations at any point remain constant in the unit.

FRACTIONAL DISTILLATION

Fractional distillation is a process in which vaporisation of liquid mixture gives rise to a mixture of constituents from which the desired one is separated in pure form.

This method is also known as *rectification*, because a part of the vapour is condensed and returned as a liquid. This method is used to separate miscible volatile liquids, whose boiling points are close, by means of a fractionating column.

Fractional distillation is different from simple distillation. In simple distillation, vapour is directly passed through the condenser. In fractional distillation the vapour must pass through a fractionating column in which partial condensation of vapour is allowed to occur. In simple distillation, condensate is collected directly into the receiver, while in fractional distillation, condensation takes place in the fractionating column, so that a part of the condensing vapour returns to the still.

Principle : From the operational point of view, fractional distillation is a mass transfer process involving counter-current diffusion of the components at each equilibrium stage.

When a liquid mixture is distilled, the partial condensation of the vapour is allowed to occur in a fractionating column. In the column, ascending vapour from the still is allowed to come in contact with the condensing vapour returning to the still. This results in enrichment of the vapour with the more volatile component. By condensing the vapour and reheating the liquid repeatedly, equilibrium between liquid and vapour is set up at each stage, which ultimately results in the separation of a more volatile component.

Applications : Fractional distillation is used for the separation of miscible liquids such as acetone and water, chloroform and benzene.

Disadvantage : Fractional distillation cannot be used to separate miscible liquids, which form azeotropic mixtures.

Theory : According to the principles of colligative properties, when a substance is dissolved in a liquid, the vapour pressure of solvent is lowered. When two miscible liquids are mixed, each may be considered as a solution of one in the other. The vapour pressure of each component is lowered. The pressure exerted by each one is known as *partial pressure.*

According to *Dalton's law*, the total pressure exerted by a gaseous mixture is the sum of the individual partial pressures of the component gases. If A and B are two miscible liquids and, p_A and p_B represent their partial pressures, respectively, then Dalton's law may be mathematically expressed as:

$$\text{Total pressure} = p_A + p_B$$

Like other gas laws, Dalton's law holds strictly good only when the partial pressures are not too high. Dalton's law is important because it permits the estimation of total vapour pressure, which should be equal to atmospheric pressure so as to reach the boiling point. At boiling point, the vaporization is maximum.

Based on the boiling point behaviour, the binary mixtures are classified into three classes.

Boiling Point—Composition Curves of Mixtures

Since repeated vaporisation and condensation processes are involved simultaneously, the composition of liquid and vapour phases change continuously. Hence, boiling point-composition curves are helpful in predicting whether the separation is possible or not, if possible, whether it is easy or difficult. These are helpful in designing the equipment for fractional distillation.

Boiling point–composition curves are constructed as follows:

(1) Mixtures of liquid A and liquid B are prepared in different proportions.

(2) Boiling point of each mixture is determined.

(3) Liquid composition of each component is analysed at its boiling point.

(4) Vapour composition of each component is analysed at its boiling point.

(5) The boiling points are plotted on y-axis against composition of the mixture (x-axis). The resulting plot is shown in Figure 11-8.

(6) The upper curve represents the vapour phase composition.

(7) The lower curve represents the liquid phase composition.

(8) The different areas correspond to the existence of liquid, vapour and liquid plus vapour phases.

The curves represent the equilibrium condition. Therefore, they are helpful in drawing conclusions regarding the composition of components at any given temperature.

Fractional Distillation–Type I Miscible Liquids (for Ideal Solutions)

Fractional distillation is suitable for a system when the boiling point of the mixture is always intermediate between those of pure components. There is neither a maximum nor a minimum in the composition curves as shown in Figure 11-8. These systems are known as *zeotropic mixtures*. Examples include benzene and toluene, carbon tetrachloride and cyclohexane, and water and methanol.

The usefulness of Figure 11-8 in the design of fractional distillation is illustrated in Figure 11-10.

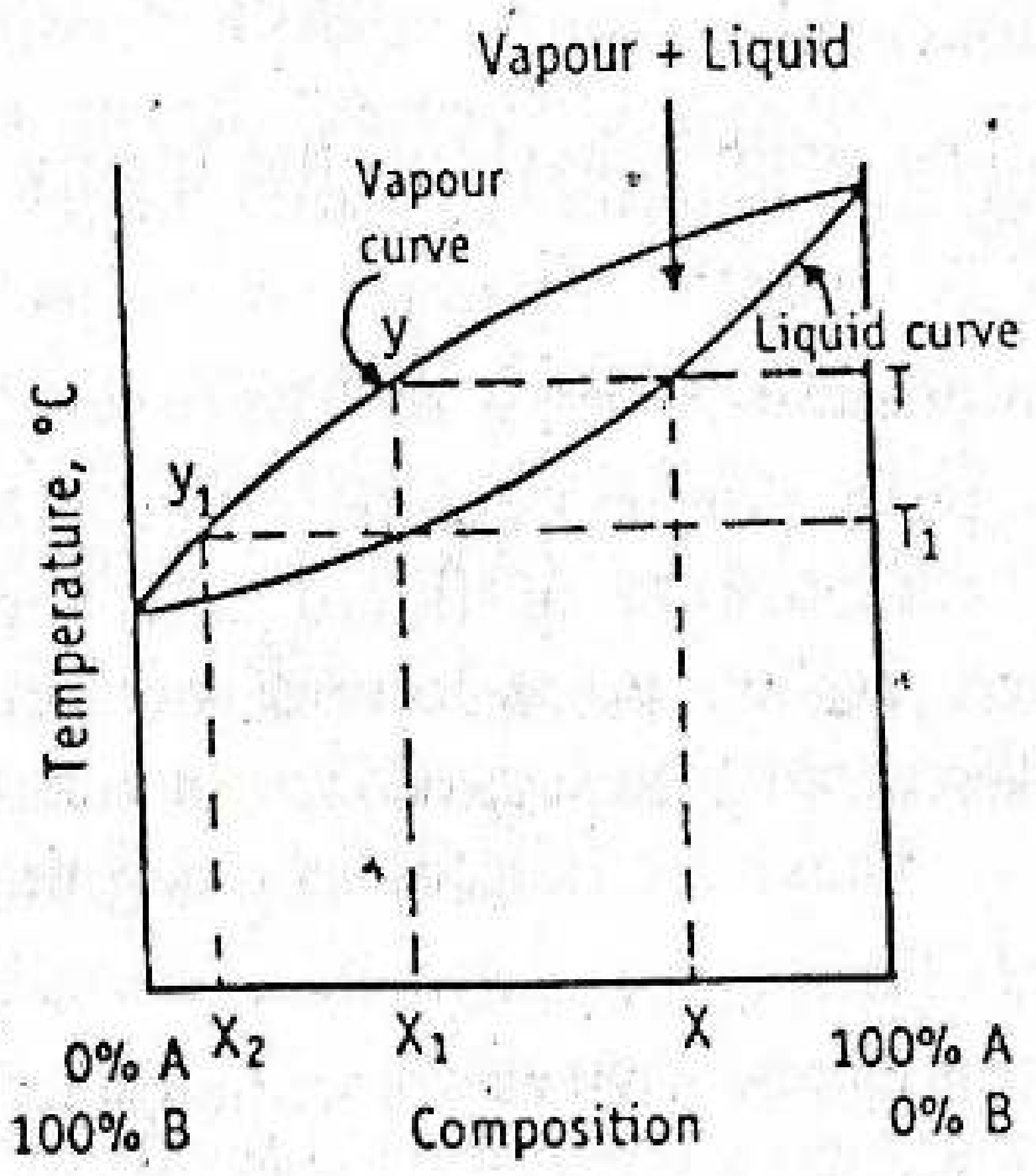


Figure 11-8. Boiling point–composition diagram of miscible liquids.

Fractional Distillation—Azeotropic Mixtures

Many liquid mixtures cannot be separated completely into pure components by simple distillation, because the volatilities of the components are equal. Such a mixture is known as an azeotrope (*Greek*: boil unchanged)

. *Azeotropic solution* is a solution which distils unchanged at a constant temperature.

Such solutions are also known as *constant boiling mixtures*. An example of this type is 89.43 mol % mixture of ethanol and water at atmospheric pressure. This mixture has a relative volatility of 1.0, further purification cannot be obtained by conventional distillation. These solutions deviate from the Raoult's law to a large extent.

Minimum boiling point azeotropic solutions–Type II solutions (non-ideal solutions) : System that exhibits a minimum value in the boiling point-composition curve is shown in Figure 11-9. Such a system is known as *azeotropic mixture* with a maximum vapour pressure or minimum boiling point. Examples include chloroform and acetone, pyridine and acetic acid, and water and nitric acid.

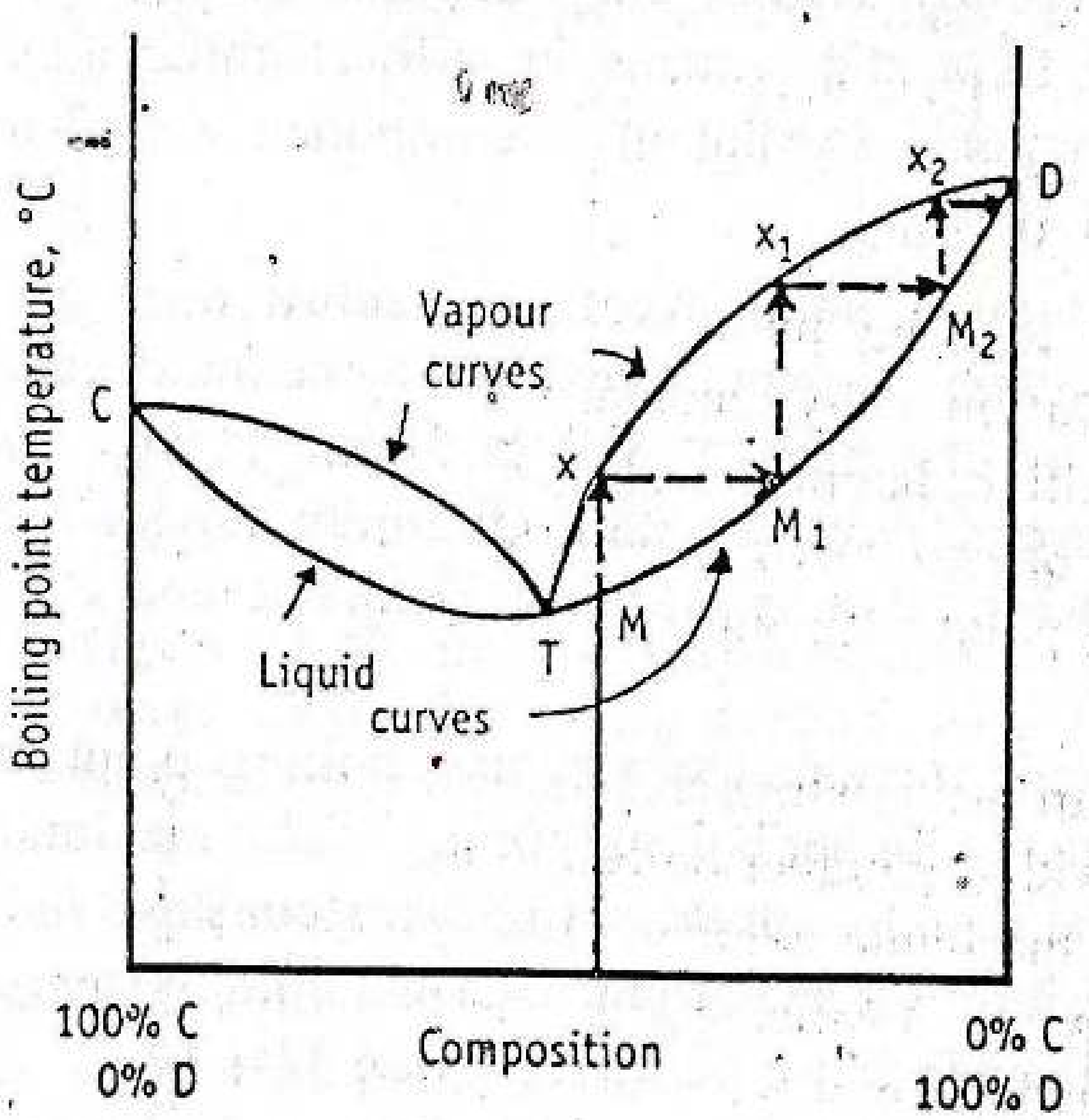


Figure 11-9. Boiling point-composition curves of a constant boiling azeotropic mixture having minimum boiling point.

The azeotropic mixture has a lower boiling point than that of the component with the least boiling point. At the minimum boiling point temperature, the liquid composition remains constant and is equal to the vapour composition (arising from such a liquid system). This is indicated by coincidence at the trough (Figure 11-9).

All mixtures of compositions lying between C and T (trough) can be separated by continuous fractional distillation. In this process, pure liquid C is recovered from the still and a mixture with constant composition (as of T) is obtained as a distillate from the condenser. In a similar way, all mixtures of compositions lying between T and D can be separated by continuous fractional distillation. In this process, pure liquid D is recovered from the still and mixture with constant composition (as of T) as condensate.

Since vapour gives constant composition of mixture, liquid curve (i.e., liquid present in the still) should be considered for the analysis (Figure 11-9).

Consider a hypothetical case (Figure 11-9) in which the mixture contains more of D than C, which is represented by M. If the mixture is distilled, the vapour has a composition of x. When this vapour is condensed, the liquid composition is represented by M_1, which is richer in D than C. When this liquid is redistilled, the vapour has composition of x_1. When this vapour is condensed, the liquid has the composition of M_2. Thus on repeated distillation (fractional distillation), the liquid D will be in pure form and remains in still. Similar arguments can be proposed for fractional distillation of component C by considering left-side curves to T (trough).

Maximum boiling point azeotropic solutions–Type III solutions (non-ideal solutions) : System that exhibits a maximum value in the boiling point-composition diagram is shown in Figure 11-10. Such a system is known as *azeotropic mixture* with a minimum vapour pressure or maximum boiling point. Examples include benzene and ethanol, water and ethanol.

The azeotropic mixture has a higher boiling point than that of the component with the higher boiling point. At the maximum boiling point temperature, the liquid composition remains constant and is equal to the vapour composition (arising from such a liquid system). This is indicated by coincidence at the peak, P (Figure 11-10).

All mixtures of compositions lying between P (peak) and A give pure liquid A as distillate and a mixture of A and B with constant composition in the still. In a similar way, all mixtures of compositions lying between B and P give pure B as distillate and a mixture of A and B with constant composition in the still.

Consider a hypothetical case (Figure 11-10) in which the mixture contains more of A than B, which is represented by L. If this mixture is distilled, the composition of vapour v is richer in A and poorer in B. At this state, the liquid residue in the distillation flask will be richer in B and poorer in A. The vapour at v is condensed, the liquid composition is represented by L_1. If this liquid is distilled, the composition of vapour v_1 is further richer in A and poorer in B. Thus on repeated distillations (i.e., fractional distillation), the liquid A in pure form can be obtained as a distillate. But the residue remained in the still is always the mixture of A and B of constant composition. Similar arguments can be proposed for fractional distillation of component B by considering left-side curves to P.

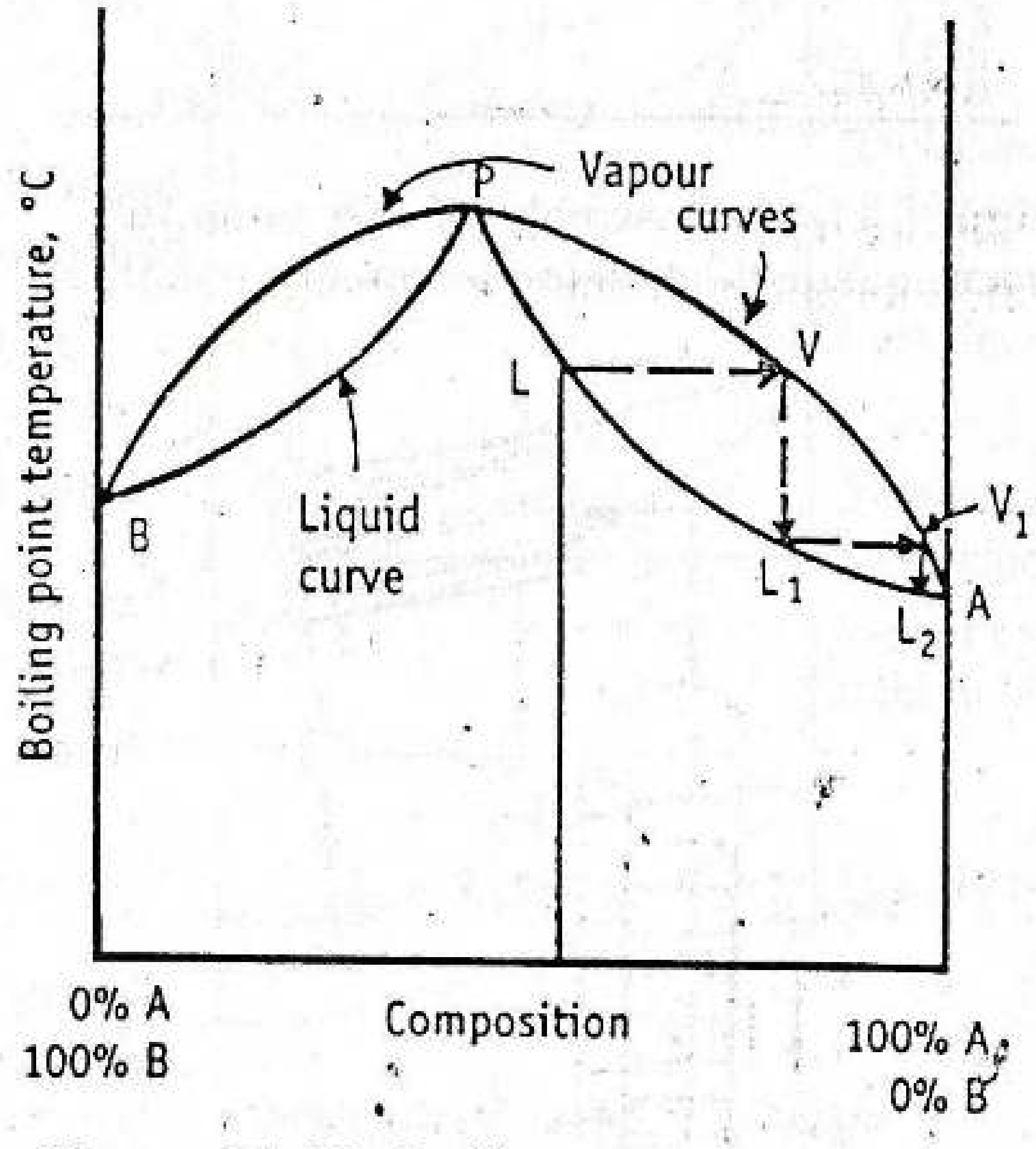


Figure 11-10. Boiling point-composition curves of a constant boiling azeotropic mixture having maximum boiling point.

General Method for Fractional Distillation

Construction : The assembly of apparatus for fractional distillation on a laboratory scale is shown in Figure 11-11. On a large scale, the construction of equipment for fractional distillation is shown in Figure 11-12. The fractionating column is inserted between the still and the condenser. A provision is made for the supply of heat (usually a steam coil) at the bottom of the column. At the top of column, a condenser is provided. The column has a large area for providing sufficient flow conditions. The broken lines across the column represent the contacting devices.

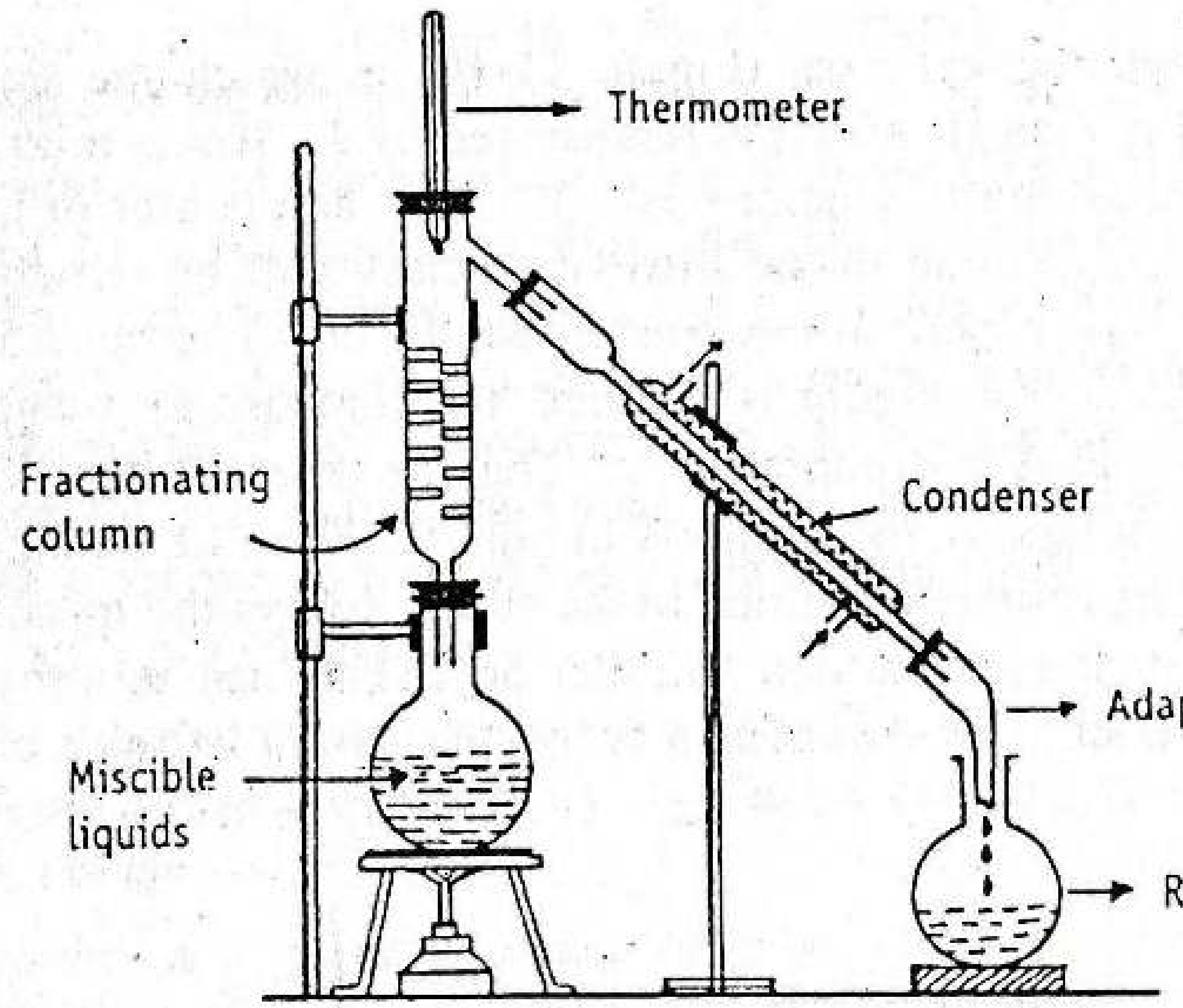


Figure 11-11. Assembly of apparatus for fractional distillation (on laboratory scale).

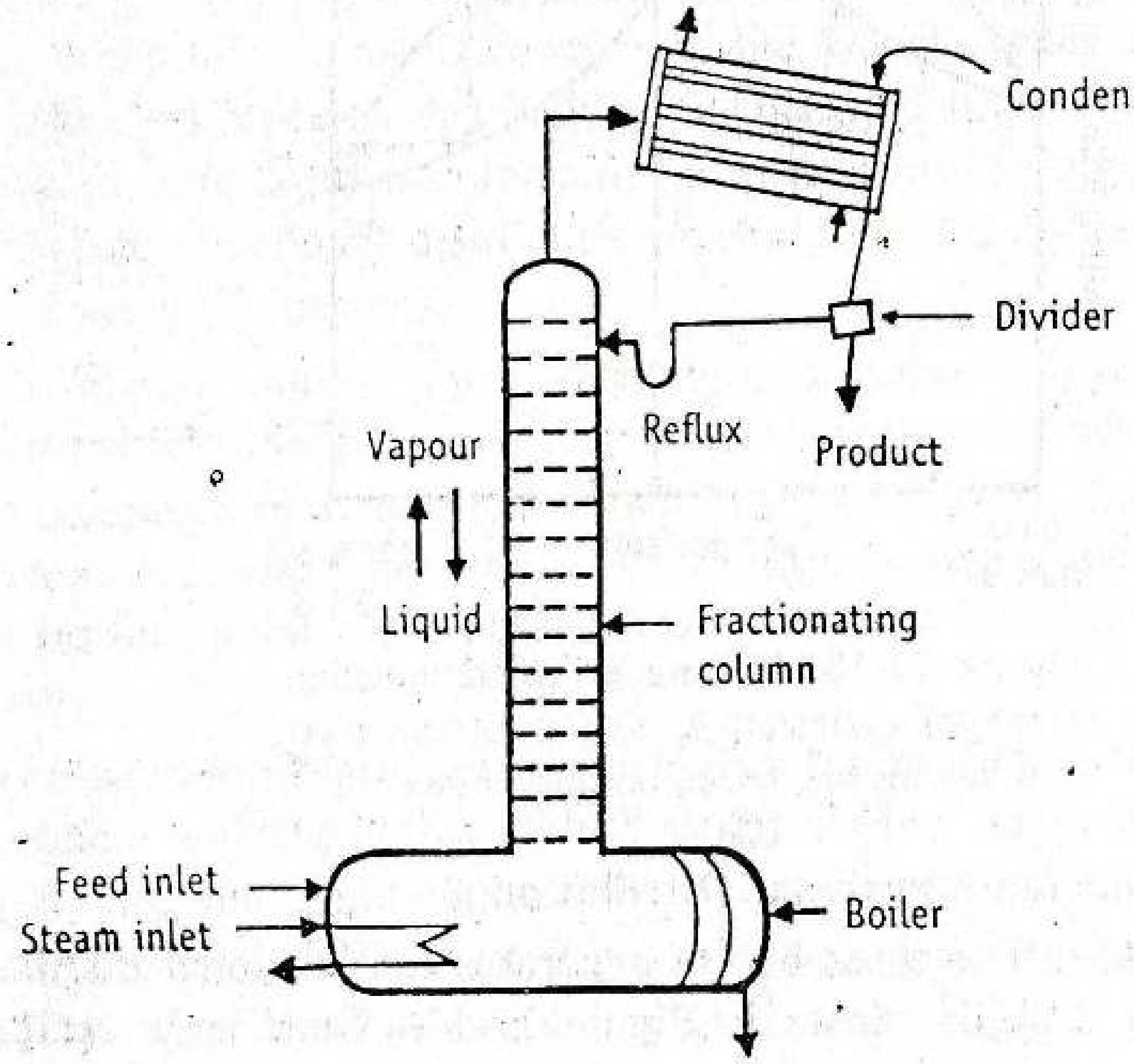


Figure 11-12. Fractional distillation apparatus for large scale operation.

Working : The mixture to be distilled is fed to the boiler and heated usually by steam. The sequence of events occurring in the fractionating column can be illustrated using the following general example (Figure 11-13).

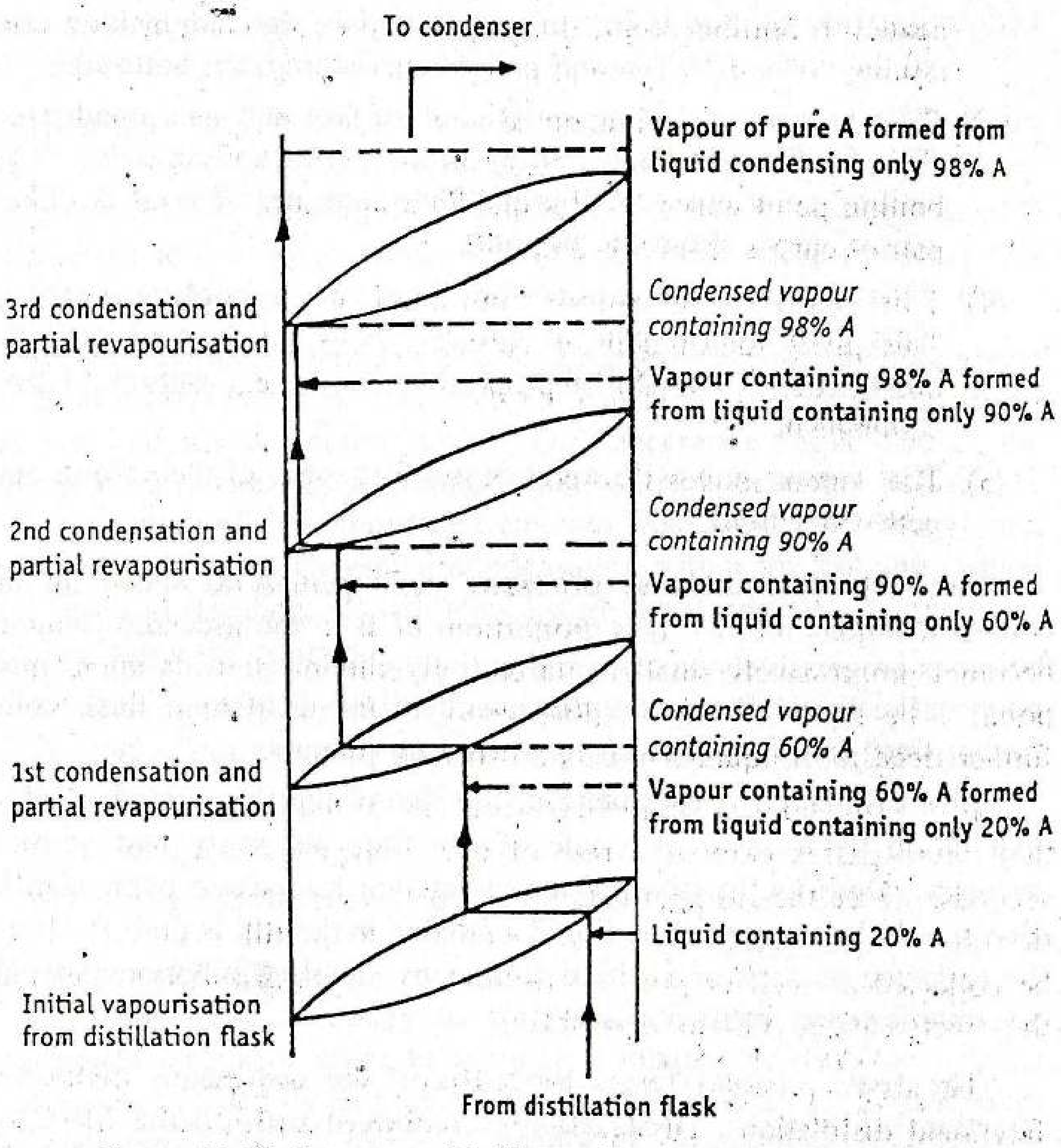


Figure 11-13. Sequence of boiling point–composition diagrams to illustrate the fractional distillation of a mixture of components.

Consider a mixture of two miscible liquids A and B containing 20% of A and 80% B. Liquid A (More Volatile Component, MVC) is having a lower boiling point than B (Less Volatile Component, LVC). These liquids do not produce constant boiling point mixture. The boiling point composition curves of this mixture are shown in Figure 11-13, which is similar to Figure 11-8, but written several times so as to represent the steps (i.e., in fractions) in fractional distillation.

(1) When the boiling point of the mixture is reached, the vapour-composition curves are drawn as shown by lowest pair of curves

(Figure 11-13). These curves indicate that the vapour contains 60% of A.

(2) When this vapour is condensed, the resulting liquid is again heated to boiling point, this vapour gives the composition containing 90% of A (second pair of curves from the bottom).

(3) This vapour impinging on a cool surface and gets condensed. This fraction is revaporised by heating to its boiling point. This boiling point curve of this distillate indicates 98% of A (Third pair of curves from the bottom).

(4) This fraction of vapour impinges on a cooling surface. This gives fourth pair of curves. Now this vapour contains higher (more than 98%) proportion of A, i.e., vapour of pure component.

(5) The vapour moves to a condenser at the top of the column and gets condensed.

Thus, repetition of these processes yield pure A as shown in the curves in Figure 11-13. The proportion of B in the ascending vapour becomes progressively smaller and entirely eliminated at its upper most point. The liquid B trickles downward to the distillation flask being further freed from liquid A on its downward journey.

Once distillation is commenced, the size of the flame is adjusted so that liquid passes over at a rate of one drop per every two or three seconds. Once the low boiling point fraction has passed over, distillation should be stopped. The liquid available in the still is pure B. It can be collected as such or purified further by simple distillation (keeping the fractionating column assembly).

The above process forms the basis of the continuous method of fractional distillation. Distillation is continued until all the MVC has been distilled off from the top as the product and the LVC is left in the still as a separate product.

Efficiency of the Fractional Distillation

The efficiency of separation of a mixture may be expressed in several ways.

Length of the fractionating column : A state of dynamic equilibrium is required for the separation. A maximum degree of separation of the components is obtained along the length of the column.

Reflux ratio : *Reflux ratio* is the quotient of the amount of liquid returning through the column to the amount collected into the receiver during the same interval of time. A column operating under total reflux will not yield distillate. The reflux ratio should be high. It is controlled by means of a suitable still.

Heat input : Heat input to the still should be controlled. If it is too little, the packing is insufficiently wetted. If it is too high, velocity may be too great for equilibrium to be attained. The size of the flame should be adjusted so that liquid passes over at a rate of one drop for every two or three seconds.

Column temperature : For a column operating at a temperature above 60°C, heat loss should be prevented by insulation. Examples are asbestos cord and silver vacuum jacket. For temperature above 100°C, the column is surrounded by a heating jacket, which is generally adjusted to the temperature of the vapour that emerges from the top of the column. Heat loss will cause excessive condensation within the column, which may result in flooding. It will also disturb the steady state temperature gradient along the column.

Other experimental conditions necessary for good separation are:

(1) There should be a comparatively large amount of liquid continuously returning through the column.

(2) Thorough mixing of liquid and vapour.

(3) A large active surface of contact between liquid and vapour.

Fractionating Columns

Generally, it is necessary to conduct distillation several times by appropriate means in order to separate a mixture of miscible liquids. This can be avoided by employing fractionating column for a reasonably complete separation. In fractional distillation, special type of still-heads are required so that condensation and revaporisation are affected continuously. These are known as *fractionating columns.*

A fractionating column is essentially a long vertical tube in which the vapour passes upward and gets partially condensed. The condensate flows down the column and is returned eventually to the flask. The columns are constructed so as to offer the following advantages simultaneously.

(1) It offers a large cooling surface for the vapour to condense.

(2) An obstruction to the ascending vapour allows easy condensation. The obstruction also retards the downward flow of liquid, which is a high boiling component.

Fractionating columns can be divided into two groups.

Packed columns : In this type, some form of packing is used in the column to affect the necessary liquid/vapour contact. The packing may consist of single turn helices (spirals) of wire or glass, glass rings, cylindrical glass beads, stainless steel rings etc. The height of packing is equivalent to *one theoretical plate.* Some types of fractionating columns are shown in Figure 11-14.

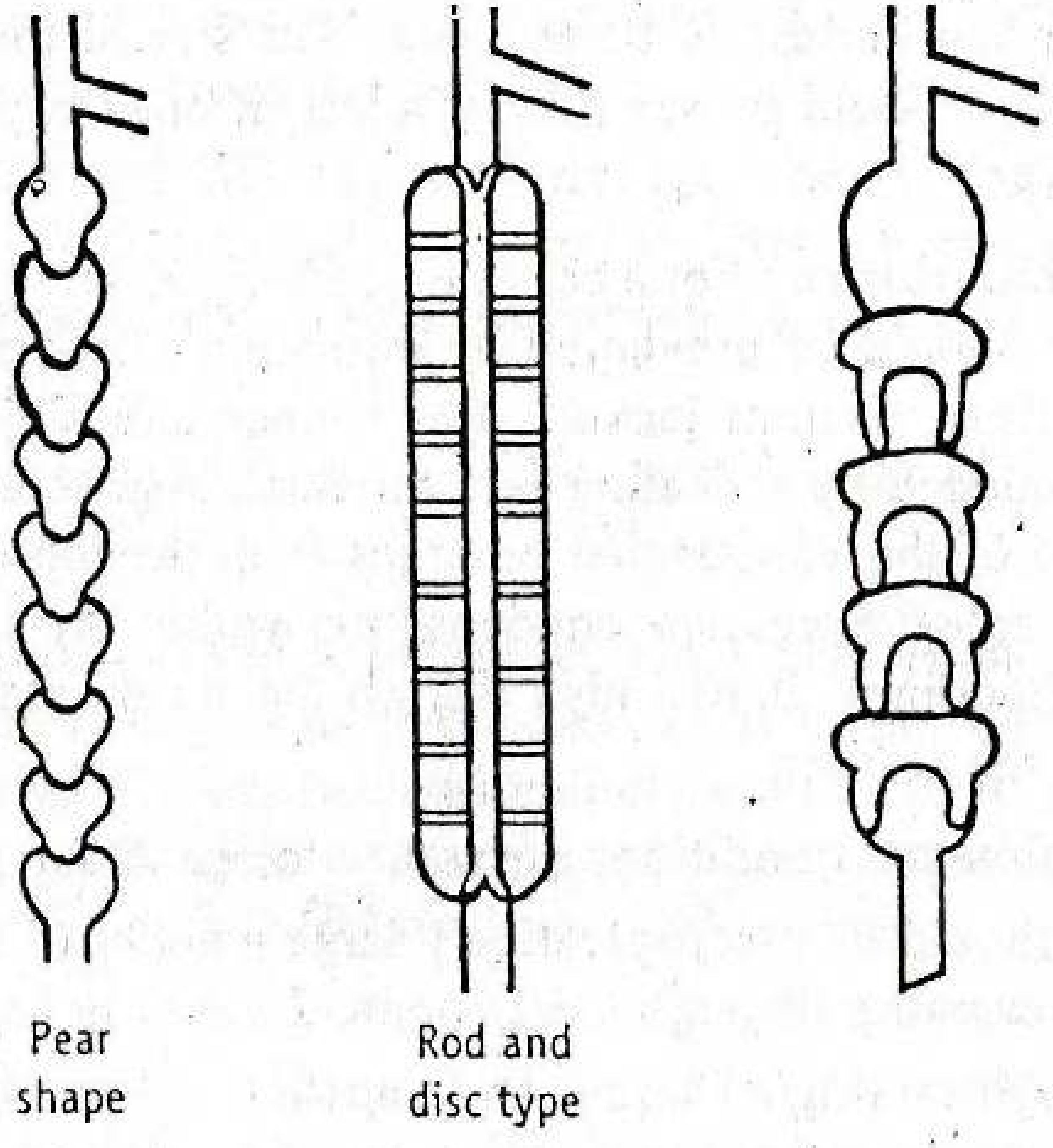


Figure 11-14. Different types of fractionating columns.

Construction : Packed column consists of a tower containing a packing that becomes wetted with a film of liquid, which is brought into contact with the vapour in the intervening spaces.

The same type of fractionating columns can be obtained in various lengths.

(a) A long fractionating column is necessary when the boiling points of the constituents are lying fairly close together.

(b) A short fractionating column is necessary when the boiling points of the constituents differ considerably.

Applications : Packing must be uniform so as to obtain proper channels. If packing is irregular, mass transfer becomes less effective. Packed columns are mainly used in laboratories. Example is Widmer column. (Figure 11-15).

Plate columns : Many forms of plates are used in the fractionating columns. These can be divided into two types, which are commonly used in pharmacy.

(a) Bubble cap plates

(b) Turbo grid plates

Bubble cap column is used in large distillation plants and is described below.

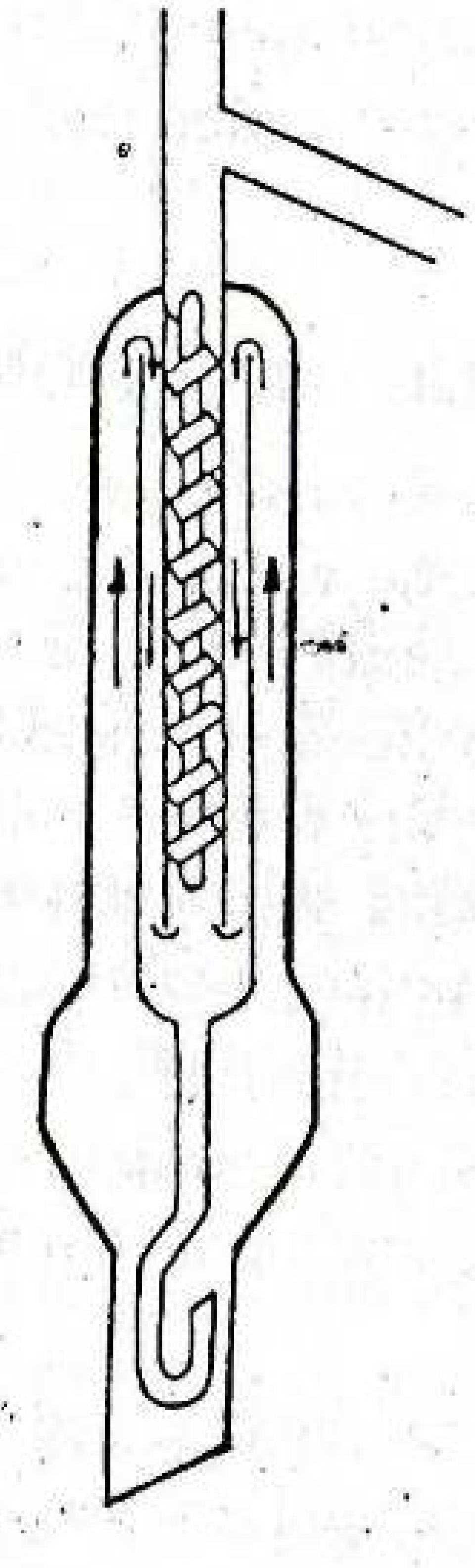


Figure 11-15. Widmer column.

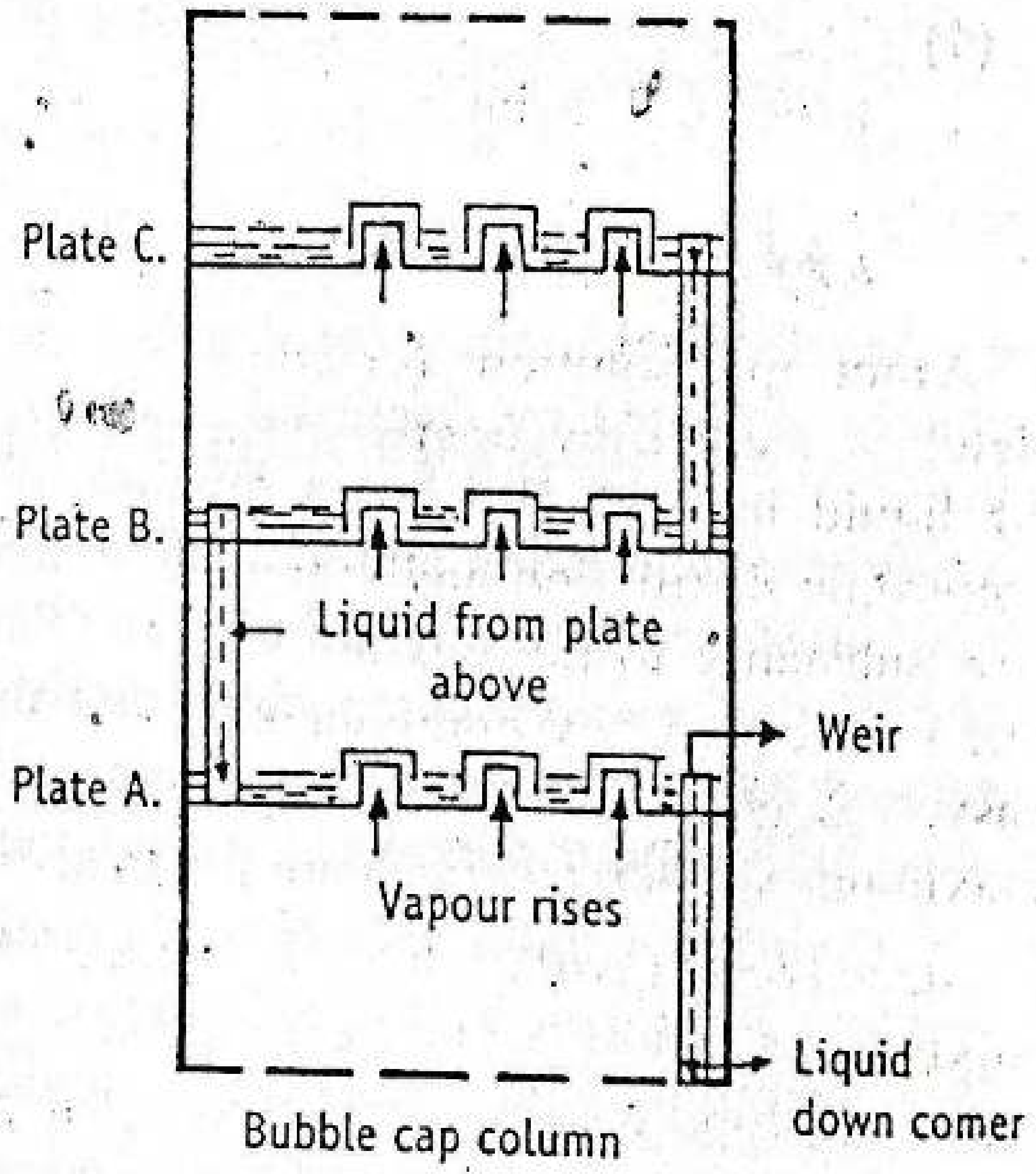


Figure 11-16. Construction of bubble cap column for fractional distillation.

Construction : The column consists of a number of plates mounted one above the other (Figure 11-16). The plates have a weir leading to a downcomer. Caps are present on each plate, which allow the vapour to escape by bubbling through the liquid.

Working : Ascending vapour from the still passes through the bubble-caps on plate A and the rising vapour will be richer in the more volatile component. This vapour passes through the liquid on plate B and partially condensed. The heat of condensation partially vaporizes the liquid. The process of condensation and vaporisation will be repeated at plate C and so on all the way up the column. Each bubble-cap plate has the same effect as a separate still.

Advantages : The bubble cap plate is effective over a wide range of vapour-liquid proportions and velocities. There is an excellent contact as the vapour bubbles through the liquid.

Disadvantages : (1) A layer of liquid on each plate results in considerable hold-up of liquid over the entire column.

(2) The need to force the vapour out of the caps through the liquid led to a large pressure drop through the column.

(3) The column does not drain even after completion of distillation.

(4) The structure is complicated making construction and maintenance expensive.

AZEOTROPIC AND EXTRACTIVE DISTILLATION

Azeotropic solutions (or constant-boiling solutions) cannot be completely separated by fractional distillation, because either the vapour or the liquid in the still has a mixture of components. The principle of azeotropic distillation and extractive distillation lies in the addition of a new substance to the mixture so as to increase the relative volatility of one of the two key components and thus making separation relatively easy. Azeotropic ternary mixtures with minimum boiling point (or maximum vapour pressure) are pharmaceutically important.

Azeotropic distillation is a distillation method in which azeotropic mixture is broken by the addition of a third substance, which forms a new azeotrope with one of the components.

The relative volatility of the liquid mixture can be changed by adding a third substance. For example, benzene is added to the azeotropic mixture of water and ethyl alcohol. Benzene breaks the mixture water-ethyl alcohol and forms a new azeotrope between benzene and ethyl ethyl alcohol. The volatility of the water (more polar liquid) is enhanced. On distillation, water distills at 65.85°C leaving alcohol and benzene behind. The boiling point of this binary mixture is 68.2°C and benzene gets distilled leaving pure alcohol behind. It can be distilled off at 78.3°C. The benzene can be recycled. Thus, using fractional distillation method, absolute alcohol can be prepared.

When glycerin is added to the above mixture, the vapour pressure of water is lowered. Practically pure ethanol can be obtained from the fractionating tower.

In *extractive distillation*, the third substance added to the azeotropic mixture is relatively nonvolatile liquid compared to the components to be separated.

The third component is withdrawn at the base of the fractionating column.

Example is separation of toluene from paraffin hydrocarbons of approximately same molecular weights. The separation of toluene and *iso*-octane (example for hydrocarbon) is difficult. In the presence of phenol, the relative volatility of *iso*-octane increases, therefore, separation of toluene is relatively easy. In another example, furfural is added for the separation of butadiene from its mixture containing butane and butene.

Applications : The liquor from fermentation process is a common source of ethanol and contains approximately 8 to 10%. Absolute alcohol can be prepared by azeotropic distillation. Petroleum refineries and distilleries use these types of distillation.

DISTILLATION UNDER REDUCED PRESSURE

Distillation under reduced pressure may be stated as a distillation process in which the liquid is distilled at a temperature lower than its boiling point by the application of vacuum.

Vacuum pumps, suction pumps, etc. are used to reduce the pressure on the liquid surface. Distillation under reduced pressure is based on the principle of simple distillation with some modifications.

Principle : Liquid boils when vapour pressure is equal to the atmospheric pressure, i.e., pressure on its surface. If the external pressure is reduced by applying vacuum, the boiling point of liquid decreases. Therefore, the liquid boils at a lower temperature. This principle is illustrated using an example of water. Water boils at 100°C at an atmospheric pressure of 101.31 kPa (760 mm Hg). At 40°C, the vapour pressure of water is approximately 9.33 kPa (70 mm Hg). Hence, the external pressure is reduced to 9.33 kPa (70 mm Hg) where water boils at 40°C. The net result is an increase in the rate of mass transfer into vapour.

The important factor in evaporation is:

$$\text{Mass of vapour formed} \propto \frac{\text{vapour pressure of evaporating liquid}}{\text{external pressure}}$$

According to this formula, water is allowed to evaporate at 40°C and 9.33 kPa (70 mm Hg) pressure, the mass of vapour formed in unit time is approximately 11 times, i.e. 760/70 for water.

Applications : Distillation under reduced pressure is essential and finds a number of applications.

Preventing degradation of active constituents : During extraction, concentration or processing at higher temperatures, the active constituents may undergo decomposition (inactivation). A few examples are given below. Hence extraction and concentration should be done at a lower temperature (≈55°C) under reduced pressure.

Category	*Reaction*	*Examples*
Enzymes	Inactivation	malt extract, pancreatin
Vitamins	Oxidation	thiamine, ascorbic acid
Glycosides	Hydrolysis	anthraquinones
Alkaloids	Racemization	hyocyamine to atropine
Tannins	Precipitation	phlobatanins to phlobaphenes

Changing physical form : In the preparation of *Cascara sagrada* tablets, granular extract is suitable. Drying at the atmospheric pressure yields a dense, compact residue, which is not desirable. In the initial stage, the liquid extract is concentrated under atmospheric pressure or under partially reduced pressure, until the residue has the consistency of treacle. The pressure is then quickly reduced, where upon the treacly semi-solid swells up due to sudden evolution of water vapour. This produces a light porous mass, which can readily be passed through a sieve to form a granular powder.

Disadvantages : In vacuum distillation, persistent foaming occurs. This may be overcome by adding capryl alcohol to the liquid or by inserting a fine air capillary tube in the second neck of the Claisen flask. The stream of air is drawn in and breaks the rising foam. The above method is not suitable for the preparation of semisolid or solid extracts.

Distillation Under Reduced Pressure

Assembling of apparatus : It consists of a double-neck distillation flask known as *Claisen flask* (Figure 11-17). Thick walled glass apparatus with interchangeable standard glass joints are used for vacuum distillation. In one of the necks of the Claisen flask, a thermometer is fitted. The second neck prevents splashing of the violently agitated liquid. Bumping occurs readily during vacuum distillation. Placing a fine capillary tube in the second neck of the flask can prevent bumping. The capillary tube is dipped in the boiling liquid, so that a stream of air bubbles is drawn out. Water bath or oil bath is used for heating.

The Claisen flask is connected to a receiver through a condenser. Vacuum pump is attached through an adapter to the receiver. A small vacuum gauge (manometer) should be inserted between the pump and the receiver.

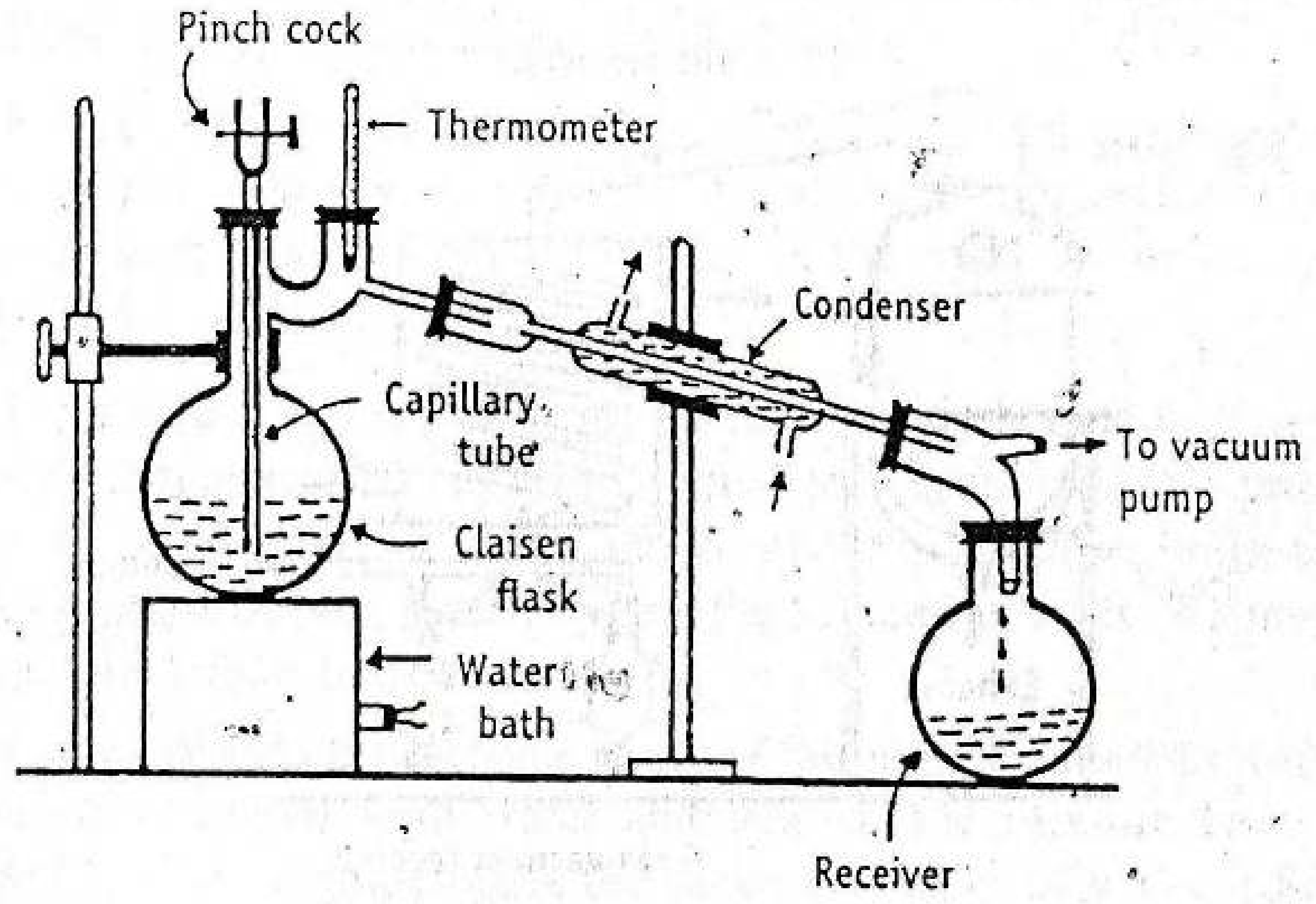


Figure 11-17. Assembly of apparatus for distillation under reduced pressure (on laboratory scale).

Procedure : The liquid to be distilled is filled one-half to two-third volume of the flask. Small pieces of porcelain are added to the liquid for facilitating distillation and prevent bumping. The capillary tube and thermometer are kept in place in the flask (Figure 11-17). The required vacuum is applied. The contents are heated gradually. The temperature rises and liquid gets vaporised rapidly due to vacuum. The vapour passes through the condenser. The condensate is collected in the receiver. The temperature is noted down, which would be less than the boiling point of the liquid.

When a large volume of a liquid is to be distilled under reduced pressure, it is more convenient to distil comparatively small volumes at a time.

Large Scale Apparatus Using Vacuum Stills for Distillation Under Reduced Pressure

Construction : The general construction of a large scale equipment for distillation under reduced pressure is shown in Figure 11-18. The vacuum jacketed still is generally made of stainless steel, copper or any other material, which can withstand a high vacuum. An observation window in the hood is helpful to see the progress of the distillation and also the level of the liquid contents. The still is fitted with a drainpipe at the bottom and an air vent. The still is connected to a condenser. A thermometer is incorporated in the still. Vacuum pump through vacuum gauge is connected as shown in Figure 11-18.

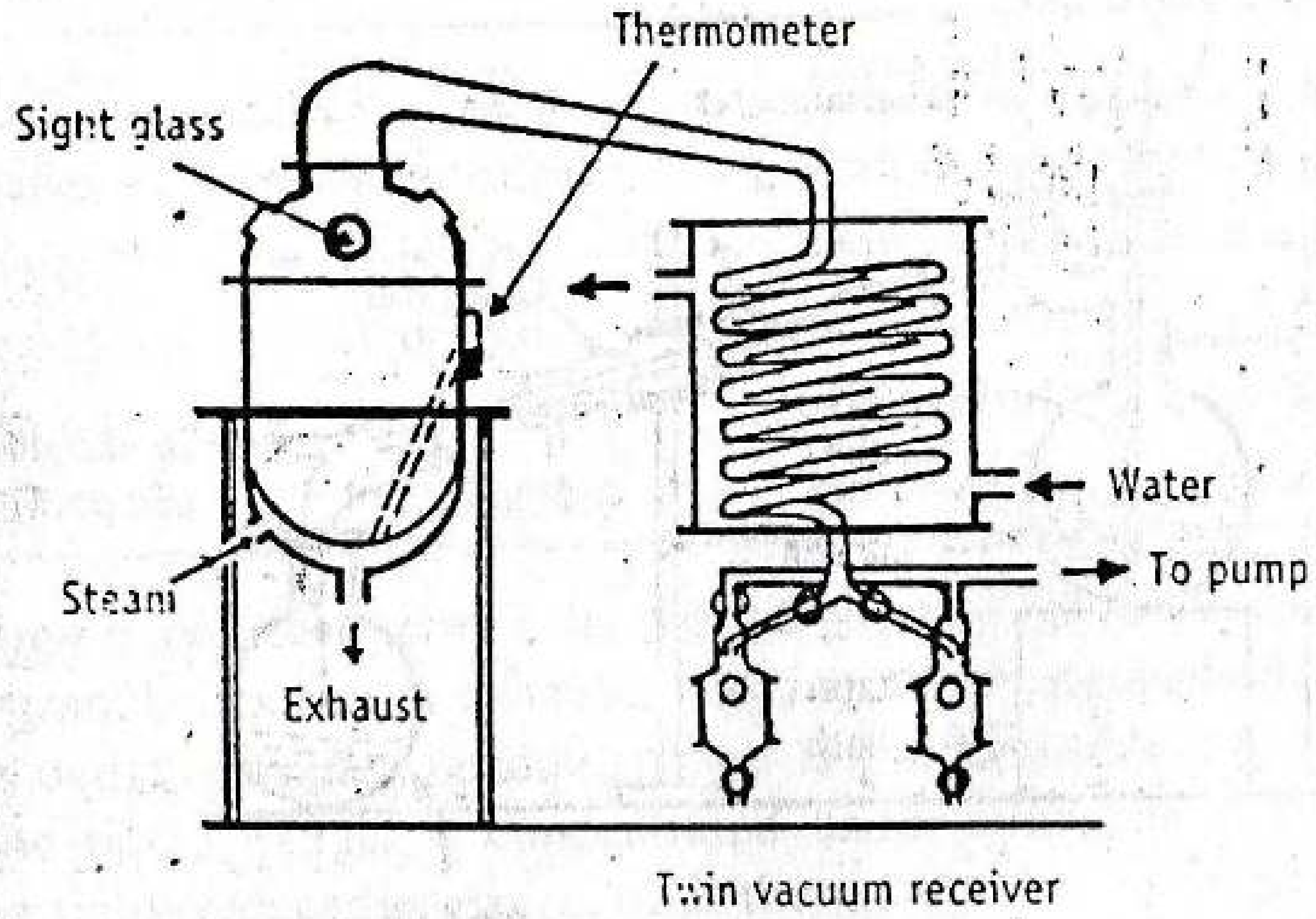


Figure 11-18. Assembly of apparatus for distillation under reduced pressure (on industrial scale).

Working : The still is filled with the liquid to be distilled through an attachment of a pipe with a tap. The other end of the pipe is connected to a reservoir of liquid, so that it can be filled at a controlled flow rate. Vacuum is created by means of a vacuum pump. Using the steam, the liquid is gradually heated. The temperature rises and the liquid gets vaporised rapidly due to vacuum. The vapour passes through the condenser and the condensate is collected into a receiver.

Normally two receivers are fitted with suitable arrangement of cocks, so that they can be used alternatively, the distillate being collected from one, while the other is connected to the still under vacuum. Therefore distillation need not be stopped.

Distillation is stopped while the contents of the flask are sufficiently fluid to run off through the drain pipe at the bottom. When spongy powdery mass is desired, the still can be provided with a stirring arrangement, which also hastens vaporization. According to the requirements, the capacity may be a few litres to thousands of litres.

STEAM DISTILLATION

Steam distillation is a method of distillation carried with the aid of steam and is used for the separation of high-boiling substances from non-volatile impurities.

High-boiling liquids cannot be purified by simple distillation, since the constituents in the mixture tend to decompose at higher temperatures. In such cases, steam distillation is employed. Steam distillation is used for the separation of immiscible liquids.

For substances, which are insoluble in water and not decomposed by heat, steam distillation provides an alternative to distillation under reduced pressure. Steam distillation is the most common example of *differential distillation.*

Principle : A mixture of immiscible liquids begins to boil when the sum of their vapour pressures is equal to the atmospheric pressure. In case of a mixture of water and turpentine, mixture boils below the boiling point of pure water, though the turpentine boils at a much higher temperature than that of water.

For example, the boiling point of turpentine is about 160°C. But when it is mixed with water and heated, the mixture boils at about 95.6°C. At this temperature, the vapour pressure of water is 86.245 kPa (647 mm Hg) and that of turpentine is 15.06 kPa (113 mm Hg). The sum of the vapour pressures is 101.31 kPa (760 mm Hg) which is normal atmospheric pressure. Thus, high boiling substances may be distilled at a temperature much below its boiling point, when water (steam) is used.

For volatile substances, which are miscible with water, steam distillation involves the same principle as fractional distillation.

Applications : (1) Steam distillation is used for the separation of immiscible liquids. Example is toluene and water.

(2) This method is used for extracting most of the volatile oils such as clove, anise and eucalyptus.

(3) It is useful in purification of liquid with high boiling point, for example essential oil of almond.

(4) Camphor is distilled by this method.

(5) Aromatic waters are prepared by this method.

Advantages : Volatile oils can be separated at a lower temperature in steam distillation, without any decomposition and loss of aroma. If a substance has low volatility, it can be satisfactorily distilled, provided its molecular weight is considerably higher than water.

Disadvantages : Steam distillation is not suitable when immiscible liquid and water react with each other

Apparatus Used for Laboratory Scale

Assembly of apparatus : The assembly of apparatus for steam distillation on laboratory scale is shown in Figure 11-19. It consists of a metallic '*steam can*' fitted with a cork having two holes. Through one of the holes, a long tube is passed so as to reach almost the bottom of the steam generator. This tube acts as a safety tube, so that in case the pressure inside the steam generator becomes too much, water will be forced out of it and the pressure will be relieved. Moreover, when steam starts coming out from the safety tube, it indicates that the steam can is almost empty. Through another hole, a bent tube is passed. The other end of the bent tube is connected to the flask containing non-aqueous liquid (for example, crude containing volatile oil) through a rubber bung. This tube should reach almost the bottom of the flask.

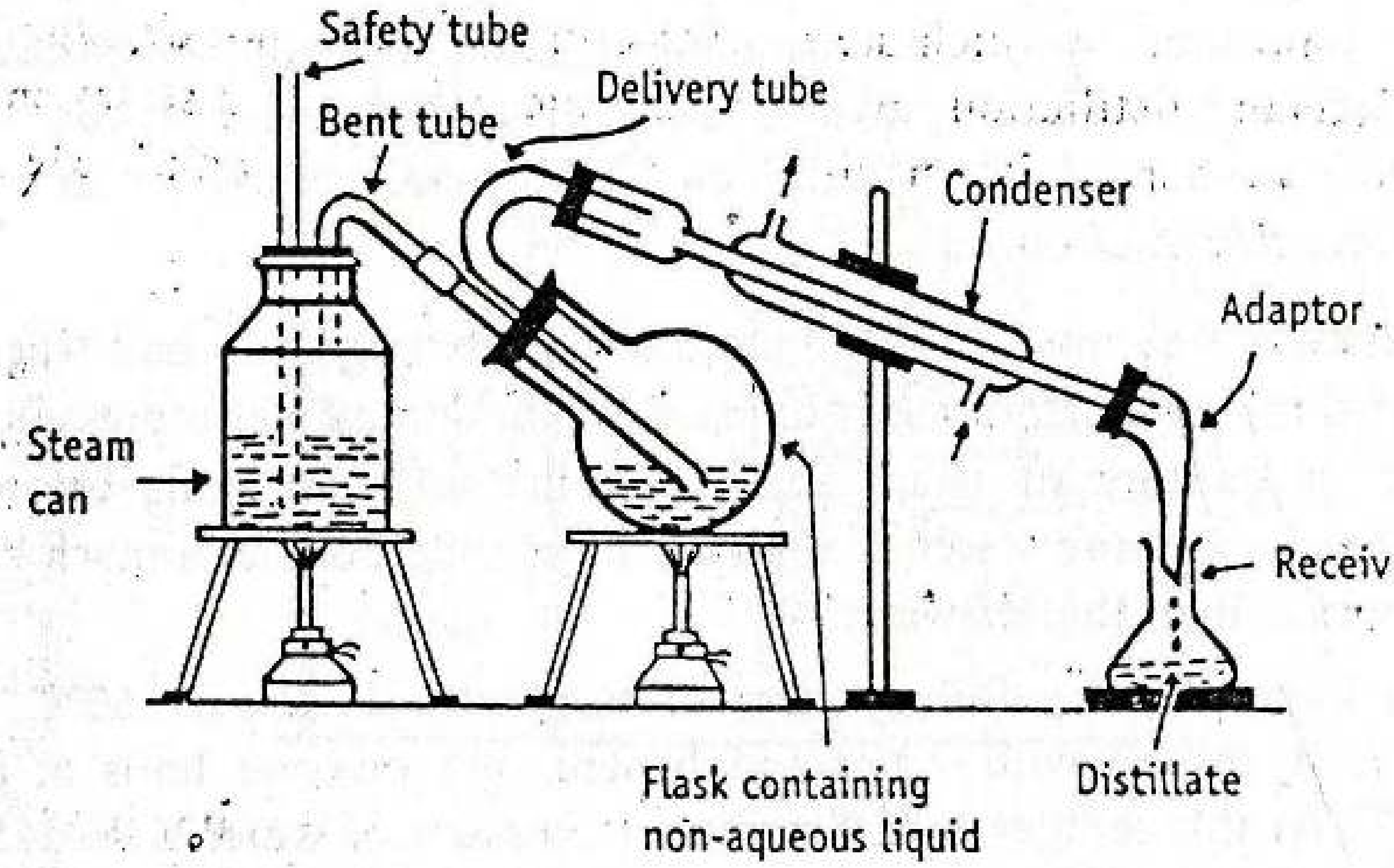


Figure 11-19. Assembly of apparatus for steam distillation (on laboratory scale).

Through the other hole of the rubber bung, a delivery tube is inserted which connects the flask and the condenser. The condenser is connected to a receiver flask using an adaptor. Provisions are made to heat the *steam can* and flask.

Procedure : The non-aqueous liquid is placed in the flask. A small quantity of water is added to it. *Steam can* is filled with water. The steam generator and the flask are heated simultaneously, so that a uniform flow of steam passes through the boiling mixture. The mixture gets heated. The steam carries the volatile oil and passes into the condenser, which is cooled by cold water. The condensed immiscible liquid is collected into the receiver.

Distillation is continued until all the non-aqueous liquid has been distilled. In the receiver, water and organic liquid form two separate layers, which can be easily separated using a separating flask.

For volatile substances, which are miscible with water, distillation with steam would involve the same principle of fractional distillation.

Equipment Used on Industrial Scale

Construction : Steam distillation unit is diagrammatically shown in Figure 11-20. It consists of a jacketed still with a perforated plate which forms a false bottom. Manholes are provided at the top and side for charging and discharging. A Florentine receiver is placed between the still and condenser. The condenser is cooled by circulating cold water.

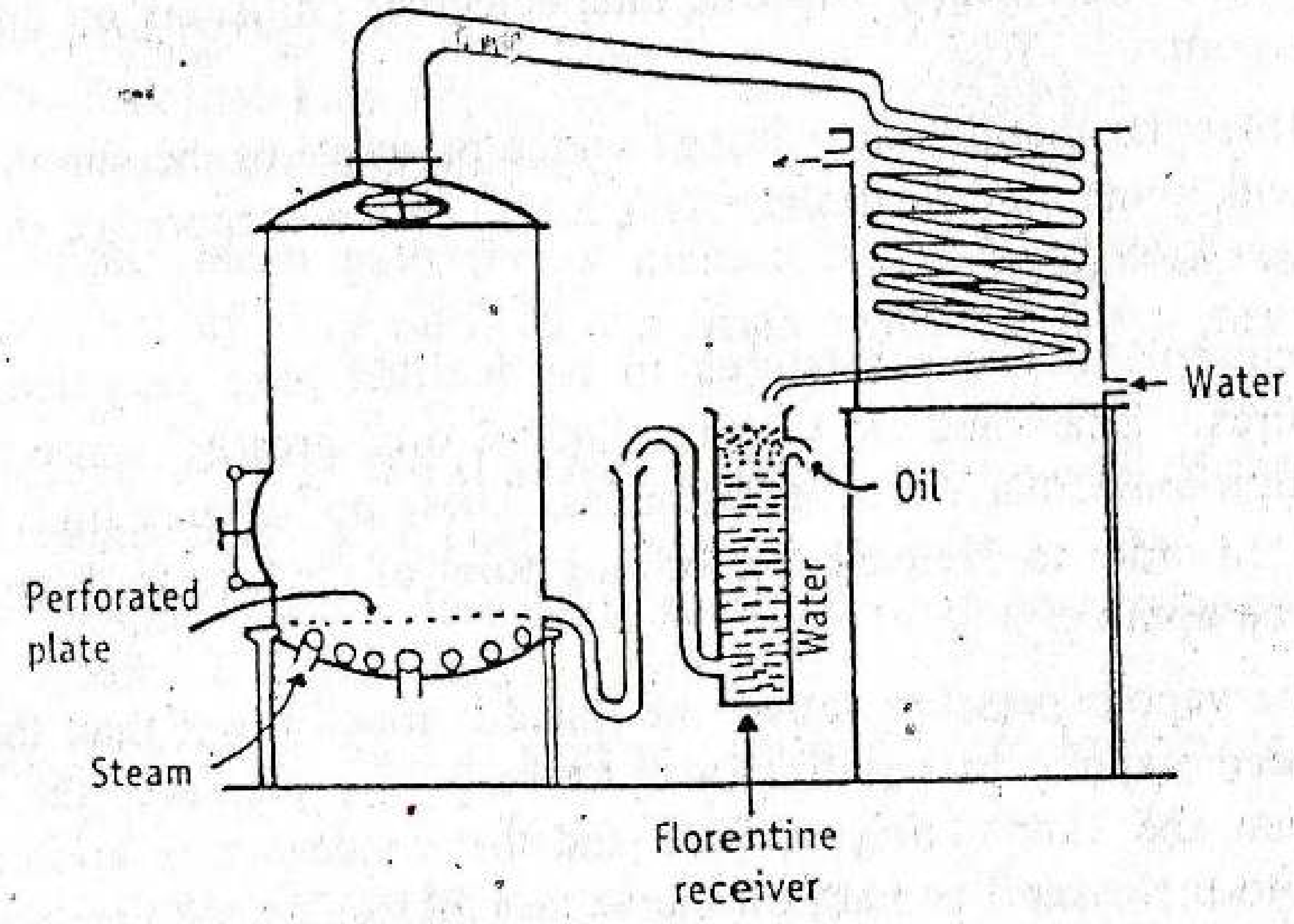


Figure 11-20. Assembly of apparatus for steam distillation (on industrial scale).

Working. : The material from which the volatile oil has to be extracted is placed in the still above the perforated plate. Steam is admitted to the jacket of the still. The water and material present in the still are heated to boiling. Simultaneously steam is also injected below the materials through a steam pipe from the jacket. The steam carries the volatile oil and gets condensed in the condenser, which is cooled by cold water. The condensate is collected into the Florentine receiver. Most volatile oils are lighter than water and well separated from the distillate as an upper layer and removed from the upper spout. The water can run off from the spout on the left and returns to the still.

Some volatile oils are heavier than water in which case the separation is reversed. Oil is collected from the lower spout.

Variants : (1) For volatile substances, which are miscible with water, distillation method combines the principles of the steam and fractional distillations.

(2) If the specific gravity of the oil is near 1.0, then separation does not take place. In such cases, it may be necessary to collect the whole of the distillate. Further it is extracted with an (volatile) organic solvent. The solvent should be distilled off to get the volatile oil.

MOLECULAR DISTILLATION

Molecular distillation is defined as a distillation process in which each molecule in the vapour phase travels mean free path and gets condensed individually without intermolecular collisions on application of vacuum.

Molecular distillation is based on the principle of the simple distillation with some modifications. This is also called evaporative *distillation* or *short path distillation.*

Principle : The substances to be distilled have very low vapour pressures. Examples are viscous liquids, oils, greases, waxy materials and high molecular weight substances. These boil at very high temperatures. In order to decrease the boiling point of the liquids, high vacuum must be applied.

The vapour pressure above the liquid is much lower than that of the saturated vapour in equilibrium. At very low pressure, the distance between the evaporating surface and the condenser is approximately equal to the mean free path of the vapour molecules. Molecules leaving the surface of the liquid are more likely hit the condenser surface than to collide with other molecules. Little or no re-condensation takes place at the surface of the liquid.

Applications : Molecular distillation is used for the purification and separation of chemicals of low vapour pressure.

(1) Purification of chemicals such as tricresyl phosphate, dibutyl phthalate and dimethyl phthalate.

(2) More frequently used in the refining of fixed oils.

(3) Vitamin A is separated from fish liver oil. Vitamin E is concentrated by this method from fish liver oils and other vegetable oils.

(4) Free fatty acids are distilled at 100°C. Steroids can be obtained between 100°C and 200°C, while triglycerides can be obtained from 200°C onwards. Proteins and gums will remain as non-volatile residues. Thus, the above mixture can be separated by molecular distillation.

Theory : The *mean free path of a molecule* is defined as the average distance through which a molecule can move without coming into collision with another.

The mean path (λ) can be expressed mathematically as:

$$\lambda = \eta\sqrt{\frac{3}{p\rho}} \qquad (11)$$

where p = vapour pressure, kPa
ρ = density, kg/m^3
η = viscosity, Pa·s
λ = mean path length, m

For example, mean path (heavy molecules) of butyl phthalate is about 30 mm and of olive oil is 20 mm when measured at a pressure of 0.1 pascal.

The characteristics of the substance influence the method of distillation. According to equation (11):

(a) Liquids having low viscosity and density posses long mean path. Distillation is simple.

(b) Substances having high pressures possess low mean free path.

The mean free path can be increased by decreasing the viscosity (η), which can be obtained at high temperature and low pressure. Thus, nonvolatile substances may become volatile and distillation is possible.

It is necessary to design the equipment based on the requirement of the molecular distillation. Some of them are as follows.

(1) The evaporating surface must be close to the condensing surface. This ensures the molecules to come in contact with the con-

denser as soon as they leave the evaporating surface. For this reason, this process is also known as *short path distillation*.

(2) The molecular collisions should be minimized because they change the direction of the path of molecules. In other words, intermolecular distances should be fairly high. It can be achieved under very high vacuum, usually of the order of 0.1 to 1.0 pascals.

(3) The liquid surface area must be as large as possible so that the vapour is evolved from the surface only, but not by boiling. Thus this process is also called *evaporation distillation*.

Based on the method of formation of the liquid film, apparatus may be divided into two types.

Falling Film Molecular Still or Wiped Film Molecular Still

Principle : In this method, vaporisation occurs from a film of liquid flowing down a heated surface under high vacuum. The vapour (molecules) travels a short distance and strikes the condenser nearby. Each molecule is condensed individually. The distillate is subsequently collected.

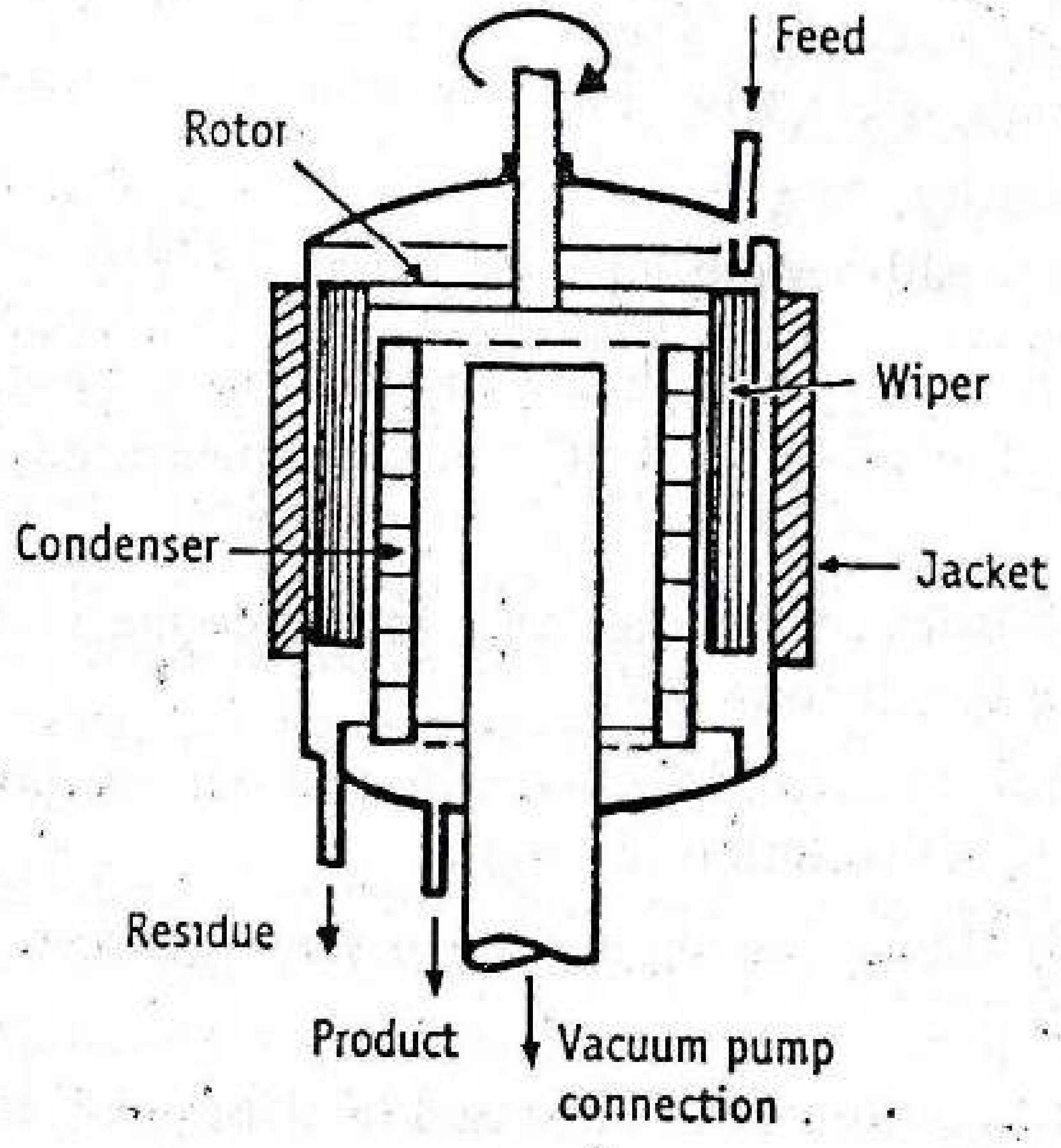


Figure 11-21. Wiped film molecular still.

Construction : The construction of a wiped film molecular still is shown in Figure 11-21. The vessel has a diameter of one metre. The walls of the vessel are provided with suitable means of heating (jacket). Wipers are provided adjacent to the vessel wall. Wipers are connected to a rotating head through a rotor. The condensers are arranged very close to the wall (evaporating surface) as shown in Figure 11-21. Vacuum pump is connected to a large diameter pipe at the centre of the vessel. Provisions are made for collecting the distillate and the undistilled liquid residue at the bottom.

Working : The vessel is heated by suitable means. Vacuum is applied at the centre of the vessel and wipers are allowed to rotate. The feed is entered through the inlet of the vessel. As the liquid flows down the walls, it is spread to form a film by PTFE (polytetrafluoroethylene) wipers, which are moving at a rate of 3 metre per second. The velocity of the film is 1.5 metres per second. Since the surface is already heated, the liquid film evaporates directly. The vapour (molecules) travels its mean free path and strikes the condenser. The condensate is collected into a vessel. The residue (undistilled or mean free path not travelled) is collected from the bottom of the vessel and re-circulated through the feed port for further distillation. Capacity is about 1000 litre per hour.

Centrifugal Molecular Still

Principle : In this method, liquid feed is introduced into a vessel, which is rotated at very high speed (centrifugal action). On account of heating, vaporisation occurs from a film of liquid on the sides of the vessel. The vapour (molecules) travels a short distance and gets condensed on the adjacent condenser. Each molecule is condensed individually. The distillate is subsequently collected.

Construction : The construction of a centrifugal molecular still is shown in Figure 11-22. It consists of a bucket-shaped vessel having a diameter of about 1 to 1.5 metre. It is rotated at high speed using a motor. Radiant heaters are provided externally to heat the fluid in the bucket. Condensers are arranged very close to the evaporating surface. Vacuum pump is connected to the entire vessel at the top. Provisions are made for introducing the feed into the centre of the bucket, for receiving the product and residue for re-circulation.

Working : Vacuum is applied at the centre of the vessel. The bucket shaped vessel is allowed to rotate at high speed. The feed is introduced from the centre of the vessel. Due to centrifugal action of the rotating bucket, liquid moves outward over the surface of the vessel and forms a film. Since, the radiant heaters heat the surface, the liquid evaporates directly from the film. The vapour (molecules) travels its mean free path and strikes the condenser. The condensate is collected into another vessel. The residue is collected from the bottom of the vessel and is re-circulated through the feed port for further distillation.

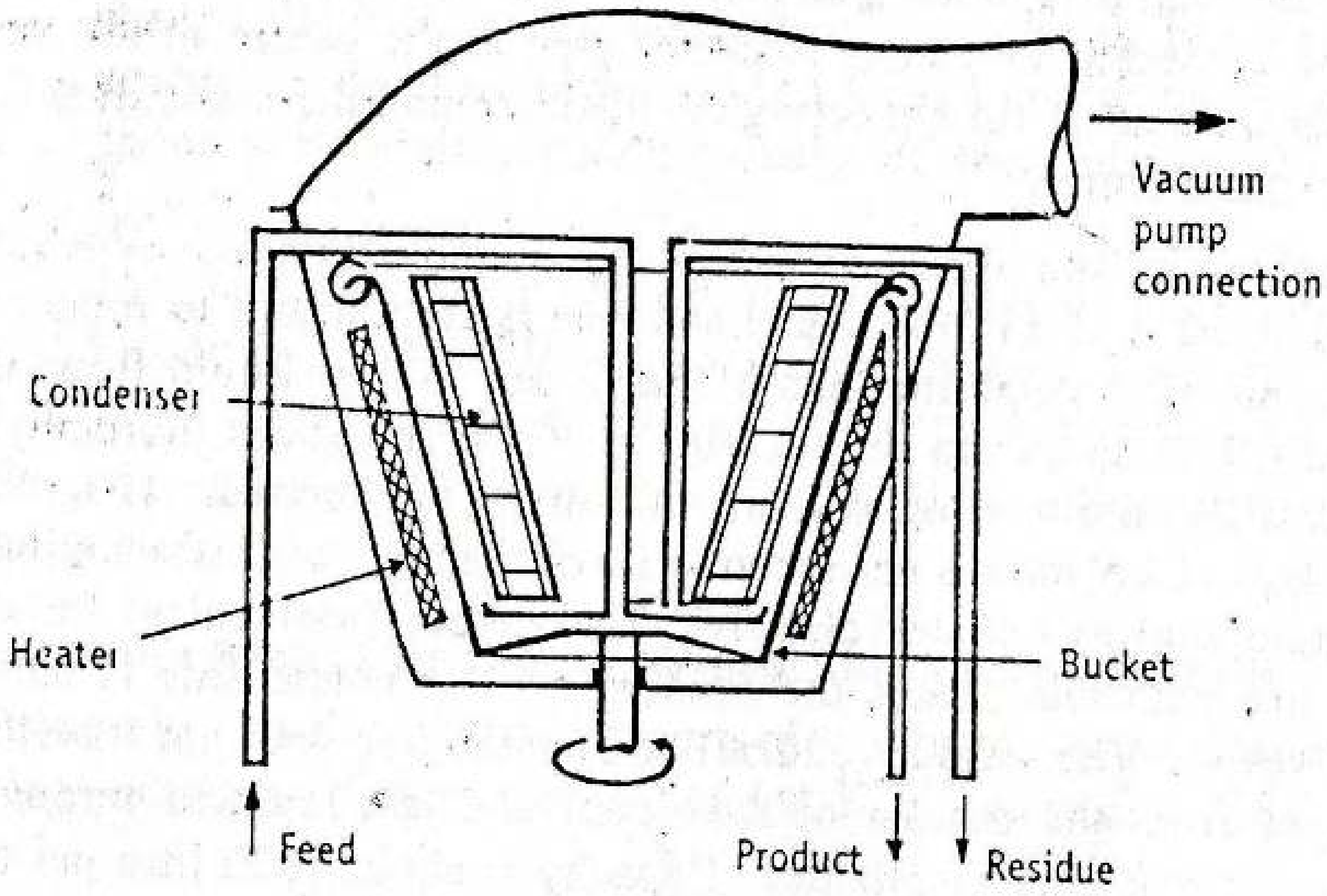


Figure 11-22. Centrifugal molecular still.

Disadvantages : Construction and operation are more complicated compared to falling film molecular still.

DESTRUCTIVE DISTILLATION

Destructive distillation is a distillation method in which the distillate is decomposition products of the constituents of the organic matter burnt in the absence of air.

This process is also known as *dry distillation*. It is not useful in laboratory practice, but one of the most important industrial processes for obtaining many valuable products from wood, coal, and animal matter. It involves the heating of dry organic matter in a suitable vessel in the absence of air, until all volatile substances are driven off. The distillate is the decomposition products. Wood distillation industry and coal carbonisation industry provide many useful materials.

COMPRESSION DISTILLATION

Compression distillation method was developed to meet the needs of Navy and Army for fresh water, which is obtained from sea-water. The product obtained is quite pure and pyrogen-free. Therefore, it meets the requirements of the pharmaceutical industry. It is economical from the standpoint of consumption of fuel and water.

The feed water is heated in an evaporator for boiling. The vapour produced in the tubes is separated from entrained distilland in a separator. The vapour is then conveyed to a compressor, which compresses it and raises its temperature to about 118°C. It then flows to the steam chest where it is condensed on the outer surface of the tube. During condensation, heat is released which is allowed for heating of the fresh feed in the tubes to the boiling point. The vapour is condensed and drained off as distillate.

Glossary of Symbols

P = Total vapour pressure of the mixture, kPa.
p = Partial vapour pressure of a liquid, kPa.
p^o = Vapour pressure exerted by pure solvent, kPa.
v = Volatility of the component, kPa.
X = Mole fraction of component in liquid state.
Y = Mole fraction of component in gaseous state.
α = Relative volatility.
ρ = Density, kg/m^3.
η = Viscosity, Pa·s.

QUESTION BANK

Each question carries 2 marks

1. Describe Raoult's law. What is its significance?
2. What are constant boiling mixtures? How are they separated?
3. What is meant by constant boiling mixtures? Give two examples.
4. Name the materials commonly used in packing of fractionating columns.
5. List the requisite characteristics that a packing material should possess.
6. Differentiate between plate towers and packed towers.
7. Describe the construction of any one fractionating column.
8. Distinguish between drying and distillation. Explain differential distillation.
9. Distinguish between 'stripping section' and 'rectifying section' of a rectifying column.
10. Name the characteristics of a packing material for use in fractionating columns.
11. Name different types of rectifying columns.
12. Define distillation. Mention two applications of it as per IP.
13. Differentiate between differential distillation and rectification.
14. Define 'ideal plate' and 'relative volatility'.
15. Define 'flash distillation'. List applications.

Each question carries 5 marks

1. Explain with relevant procedure the separation of an azeotropic mixture.
2. What is meant by steam distillation? What are its special advantages?
3. Describe the principles and applications of steam distillation.
4. What are constant boiling mixtures? Draw typical boiling diagrams for constant boiling mixtures.
5. Describe the construction of bubble cap column. What are its advantages?
6. Describe a bubble cap rectifying column. What are the specific drawbacks of bubble cap columns.
7. Describe one fractionating column of your choice. List its advantages and disadvantages.
8. Describe the construction and working of a distillation apparatus for the preparation of distilled water.

Each question carries 10 marks.

1. Explain the principle and procedure of molecular distillation. What are its applications?
2. Distinguish between plate columns and packed towers. Describe the types of packing for rectifying columns. How is absolute alcohol made?

12

Evaporation

Evaporation is a process of vaporising large quantities of volatile liquid to get a concentrated product.

Equipment used for the evaporation are known as *evaporators*. Heat is supplied to the evaporator, which transmits it to the evaporating liquid so as to provide latent heat of vaporisation. Steam is normally used as a source of heat. Evaporation is a surface phenomenon, i.e., mass transfer takes place from the surface. Thus no boiling occurs. In practice, surface evaporation is slow. Therefore, *the practical definition of evaporation* is the removal of solvent from the solution by boiling the liquor in a suitable vessel and withdrawing the vapour, leaving a concentrated liquid residue in the vessel.

Either solutions or suspensions can be subjected to evaporation. The only condition is that the liquid must be volatile, while the solute must be nonvolatile. Since heat is supplied, the constituents should be thermostable. In most of the operations, the liquid is water with a low solid content. The liquid to be evaporated may be less viscous than water or it may be so viscous that it will hardly flow. At the end of the process, the concentrate will be so viscous that further evaporation will be drastically reduced.

Evaporation some times overlap with other heat processes, though some distinctions can be drawn. These are given in Table 12-1.

Although the purpose of evaporation is to obtain a concentrated product, the solvent vapour is sometimes valuable, so recovery is essential. This prevents the environmental pollution, fire hazards and at the same time makes the process economical.

TABLE 12-1

Distinguishing Features of Evaporation with other Heat Processes

S.No.	*Evaporation*	*Other heat process*
1	The residue is a concentrated liquid.	*Drying*: the residue is solid.
2	Evaporating liquid is only one component in most of the cases.	*Distillation*: Evaporating liquid is a combination of two or more components.
3	No attempt is made to separate the mixture of vapour, even if any.	*Distillation*: It is compulsory to separate each component.
4	The purpose of evaporation is to get a concentrated liquid only, but not to get crystals as it happens in some situations.	*Crystallization*: The purpose of concentrating the solution is to get crystals.

Applications

Manufacture of bulk drugs : Evaporation process is used in pharmacy practice, pharmaceutical industries, chemical industries etc.

Manufacture of biological products : Evaporation is used in the manufacture of biological products such as insulin, biochemical products (example is penicillin) and plant products. Preparation of blood products such as blood plasma and serum involves evaporation. Enzymes, hormones and antibiotics are prepared.

Miscellaneous : Water containing minerals is subjected to evaporation to get demineralised water after condensation. The water so obtained is used for human consumption and for special processes. This is some sort of evaporation though the process is generally called distillation.

FACTORS INFLUENCING EVAPORATION

The rate of evaporation depends on several factors. The relationship may be expressed mathematically as:

$$M = \frac{KS}{p}(b - b') \qquad (1)$$

where M = mass of vapour formed per unit time (Rate), m^3/s

S = surface area of the liquid exposed, m^2

p = atmospheric pressure, kPa

b = maximum vapour pressure at the temperature of air, kPa

b' = pressure due to the vapour of the liquid, actually present in the air, kPa

K = constant, m/s

In general mass transfer also depends on the temperature.

Temperature

The higher the temperature, the greater the value of b and hence greater will be the evaporation.

At a given temperature, some molecules possess higher kinetic energy than average, while others have lower than average kinetic energy. Fast moving molecules escape from the surface of the liquid into vapour, while slow moving ones remain behind. When temperature of the liquid is raised, more molecules acquire sufficient kinetic energy and escape from the surface to vapour state. This is the situation below the boiling point of the liquid.

Below boiling point, vapour is formed from the surface only. At boiling point, vapour is formed throughout the body of the liquid as well as from surface. The vapour pressure of a liquid is lowered when a substance is dissolved in it and consequently the boiling point of the liquid increases.

Normally, glycosides and alkaloids decompose at high temperature. Hormones, enzymes and antibiotics are even more heat-sensitive. These products require special techniques to prevent decomposition during evaporation. For example, malt extract is prepared by evaporation under reduced pressure to avoid loss of enzymes. Antibiotics are concentrated by freeze-drying.

Vapour Pressure

Rate of evaporation is directly proportional to the vapour pressure of the liquid. The lower the p value in equation (1), the greater the evaporation. Lower the external pressure, the lower the boiling point of the liquid and hence greater will be the rate of evaporation. This condition is achieved by applying vacuum.

The nature of liquid is also important for rate of evaporation. Liquids with low boiling points evaporate quickly because of high vapour pressures at lower temperatures.

If the outer atmosphere is dry, the value of b' will be low and hence greater the evaporation. If the vapour of the liquid is removed as soon as it is formed (under reduced pressure or vacuum), the space above the liquid does not become saturated with the vapour. Hence, evaporation proceeds faster.

Surface Area

From equation (1), it is clear that the greater the surface area of the liquid, the greater will be the evaporation. For this reason, evaporation is conducted in evaporators with larger heating surface area.

Moisture Content of the Feed

Some drug constituents undergo hydrolysis readily in presence of moisture at high temperatures. To prevent decomposition, the material is exposed to lower temperature initially, then exposed to higher temperature for final concentration. For example, dry extract of belladonna is prepared in this manner.

Type of Product Required

Type of product required some times decides the apparatus for evaporation. Open pan produces liquid or dry concentrate. Film evaporator yields liquid concentrate. Spray dryer produces dry products with good solubility. Vacuum evaporator gives porous product suitable for conversion to granules, for example, preparation of granular extract of cascara for tablet making.

Time of Evaporation

If the time of exposure is longer, greater will be the evaporation, provided the constituents are thermostable. Exposure of a drug to a relatively high temperature for a short period of time may be less destructive of active principles than a lower temperature with long exposure period. For this reason, film evaporators are used.

Film and Deposits

When vegetable extracts are concentrated in steam pan, a film may be formed on the surface and/or precipitated matter may deposit on the heating surface. Film reduces the evaporating surface and precipitated matter hinders the transfer of heat. To avoid these problems, efficient stirring is necessary.

Economic Factors

Economies of labour, fuel, floor space and materials are of primary considerations. The recovery of solvents and the utilization of *waste heat* are also important as they involve considerable reduction of costs.

For evaporation, heat is necessary to provide the latent heat of vaporisation. Hence, rate of evaporation is controlled by rate of heat transfer. Therefore, evaporator is designed to give maximum heat transfer to the liquid.

CLASSIFICATION OF EVAPORATORS

I. Evaporators with heating medium in jacket
    Example: Steam jacketed kettle (evaporating pan)

II. Vapour heated evaporators with tubular heating surfaces

- (A) Evaporators with tubes placed horizontally
  - Examples: Horizontal tube evaporator
- (B) Evaporators with tubes placed vertically
  - i. Evaporators with short tubes
    - (a) Single effect evaporators
      - Examples: Short tube vertical evaporator (Standard vertical tube evaporator)
      - Short tube vertical evaporator with propeller
      - Basket type evaporator
    - (b) Multiple effect evaporator
      - Example: Triple effect evaporator
  - ii. Evaporators with long tubes
    - (a) Evaporators with natural circulation
      - Examples: Climbing film evaporator (Rising-film evaporator)
      - Falling film evaporator
    - (b) Evaporators with forced circulation
      - Example: Forced circulation evaporator

EQUIPMENT

STEAM JACKETED KETTLE OR EVAPORATING PAN

Principle : Steam is supplied to a jacketed kettle (evaporating pan) in which aqueous extract is placed. Steam gives out heat to the kettle. The heat is transferred to the aqueous extract by conduction and convection. The temperature raises and the escaping tendency of the solvent molecules into vapour increases. Stirring further enhances the vaporisation of solvent molecules.

Construction : The construction of a steam jacketed kettle is shown in Figure 12-1. It is a hemispherical structure consisting of an inner pan called *kettle*. It is enveloped with an outer pan called *jacket*. The two pans are joined to enclose a space through which steam is passed.

For smaller quantities, kettle is made up of a single sheet of metal. For larger capacities, several sheets are welded. Though several metals are used as a material of construction, for practical purposes the following are used. Copper is an excellent material for the kettle, because of its good conductivity. If acidic materials are evaporated, some quantity of copper would dissolve. For such preparations, tinned copper is used. Iron is used for the construction of the jacket, because it has minimum conductivity. To prevent rusting of the jacket, the iron is either tinned or enamelled on inner surface.

An inlet for the steam and an outlet (vent) for noncondensed gases are provided near the top of the jacket. Condensate leaves the jacket through the outlet provided at the bottom. The kettle is provided with one outlet for product discharge at its bottom.

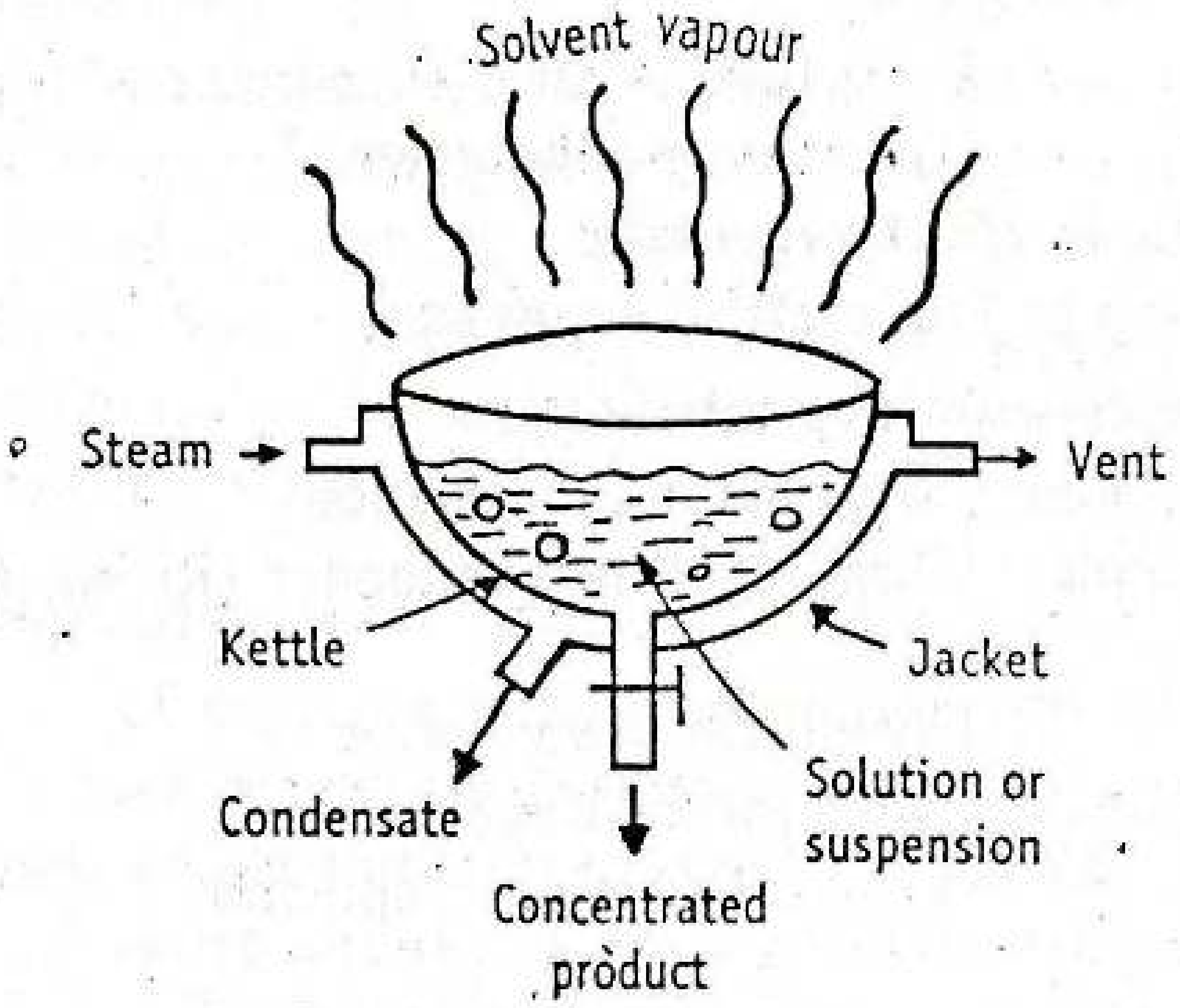


Figure 12-1. Steam jacketed kettle.

Working : Aqueous extract to be evaporated is placed in the kettle. Steam is supplied through the inlet. Steam gives out its heat to the contents and the condensate leaves through the outlet. The contents must be stirred manually for smaller volumes and mechanically for larger volumes. Mechanical stirrer is not shown in Figure 12-1. The rate of evaporation is fast in the initial stages and decreases gradually as the liquid gets concentrated.

Any room where evaporation is carried by this apparatus must have good ventilation to remove the vapour. Otherwise, the room is quickly filled with a dense fog of condensed vapour and water falls from the roof and runs down the walls. Fans fitted over the pan not only remove the vapour and prevent condensation in the room, but also accelerate the rate of evaporation by quickly removing saturated air from the surface of the liquid.

The kettle may be fixed or made to tilt. A kettle of capacity upto about 90 litres may be made to tilt. But above this capacity, the weight of the pan along with its contents becomes too great to tilt. Hence, the bottom outlet is used to collect the concentrated product.

Uses : Evaporating pan is suitable for concentrating aqueous and thermostable liquors, for example, liquorice extract.

Advantages : (1) Evaporating pan is constructed both for small scale and large scale operations.

(2) It is simple in construction and easy to operate, clean and maintain.

(3) Its cost of installation and maintenance is low.

(4) Wide variety of materials can be used for construction such as copper, stainless steel and aluminium.

(5) Stirring of the contents and removal of the product is easy.

Disadvantages : (1) In evaporating pans, heat economy is less. Hence, cost per unit material production is more.

(2) It is not suitable for heat sensitive materials due to long time of exposure.

(3) The heating area decreases as the product gets more concentrated.

(4) As it is open type, vapour passes into the atmosphere, which can lead to saturation of the atmosphere, slowing evaporation as well as causing discomfort.

(5) Boiling point of water cannot be reduced, since reduced pressure can not be created in open type evaporator.

HORIZONTAL TUBE EVAPORATOR

Principle : In horizontal tube evaporator, steam is passed through the horizontal tubes, which are immersed in a pool of liquid to be evaporated. Heat transfer takes place through the tubes and the liquid outside the tubes gets heated. The solvent evaporates and escapes from the top of the evaporator. The concentrated liquid is collected from the bottom.

Construction : The construction of a horizontal tube evaporator is shown in Figure 12-2. It consists of a large cylindrical body with conical or dome-shaped top and bottom. It is made up of cast iron or plate steel. An average size of the body ranges from 1.8 to 2.4 metres diameter and from 2.4 to 3.6 metres height.

The lower part of the body consists of a steam compartment with an inlet for steam at one end and a vent for noncondensed gases on the other end. A condensate outlet is provided at the bottom of the steam compartment. In the steam compartment, 6-8 stainless steel horizontal tubes are placed. The tubes are cut long enough so that they project about 25.0 millimetres beyond the tube sheet on both ends. The width of steam compartment is usually half the diameter of the body.

At one convenient point, an inlet for feed is provided (Figure 12-2). One outlet for vapour is placed at the top of the dome. Another outlet for thick liquid is placed at the centre of the conical bottom of the body.

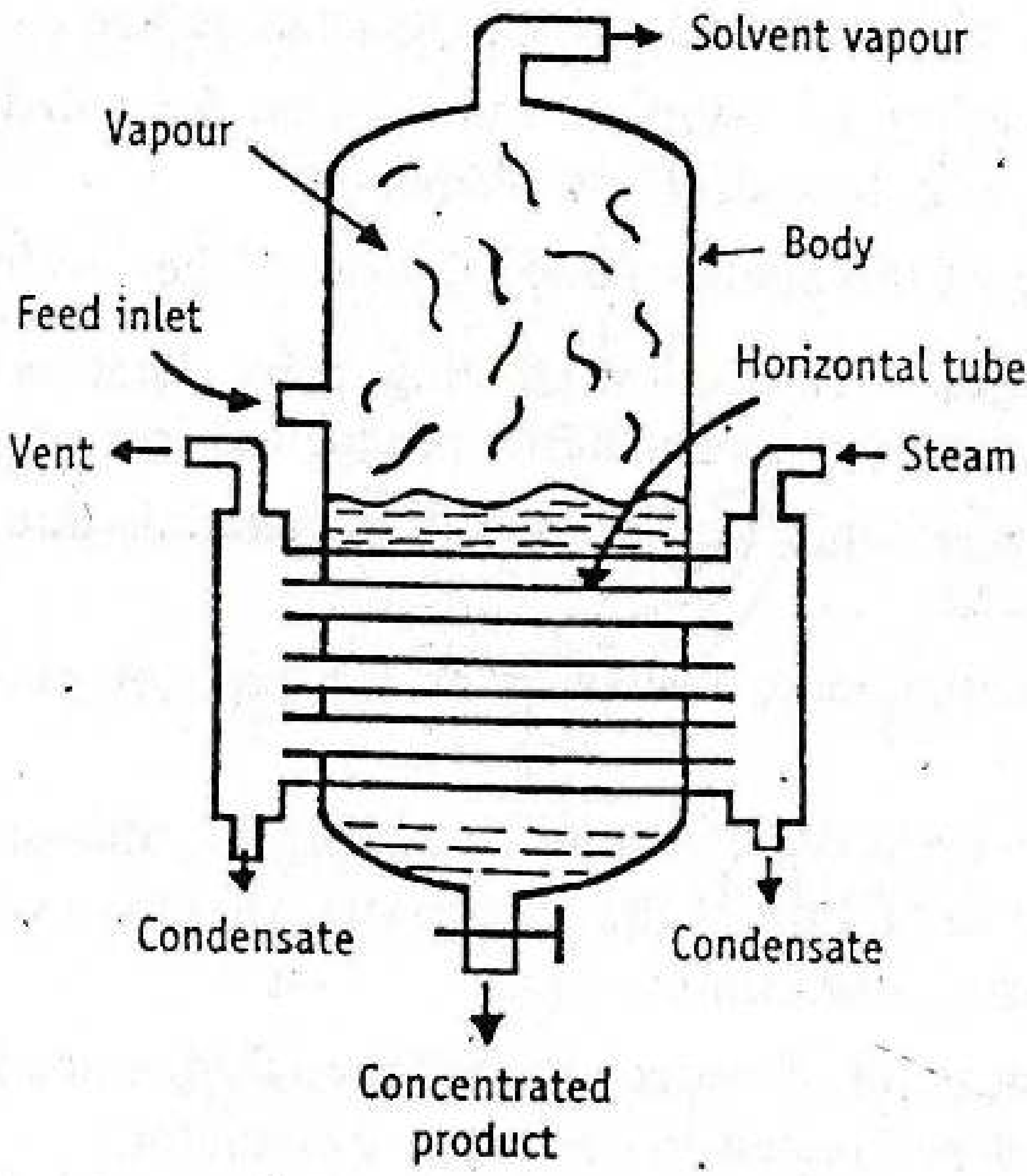


Figure 12-2. Construction of a horizontal tube evaporator.

Working : The feed is introduced into the evaporator until the steam compartment is satisfactorily immersed. Steam is introduced into the steam compartment. The horizontal tubes receive heat from the steam and conduct it to the liquid due to temperature gradient. Steam condensate passes through the corresponding outlet. The feed absorbs heat and solvent gets evaporated. The vapour then escapes through the outlet placed at the top. This process is continued until a thick liquid is formed, which can be collected from the bottom outlet.

Uses : Horizontal tube evaporator is the best suited for non-viscous solutions that do not deposit scales or crystals on evaporation, for example cascara extract.

Advantage : The cost per square metre of heating surface is usually less in horizontal tube evaporator.

VERTICAL TUBE EVAPORATOR
(Short Tube Evaporator)

Principle : In standard vertical tube evaporator, liquid is passed through the vertical tubes and the steam is supplied from outside the tubes. Heat transfer takes place through the tubes and the liquid inside the tubes gets heated. The solvent evaporates and the vapour escapes from the top. The concentrated liquid is collected from the bottom.

Construction : The construction of a standard vertical tube evaporator is shown in Figure 12-3. It consists of a large cylindrical body made up of cast iron with dome shaped top and bottom (Figure 12-3). In side the body, calandria is fitted at the bottom. Calandria consists of a number of vertical tubes, whose diameter ranges from 0.05 to 0.075 metres and length of 1-2 metres. About 100 such tubes are fitted in a body measuring 2.5 metres or more diameter. Inlets are provided for steam and feed. Outlets are provided for vapour, concentrated product, non-condensed gases and condensate.

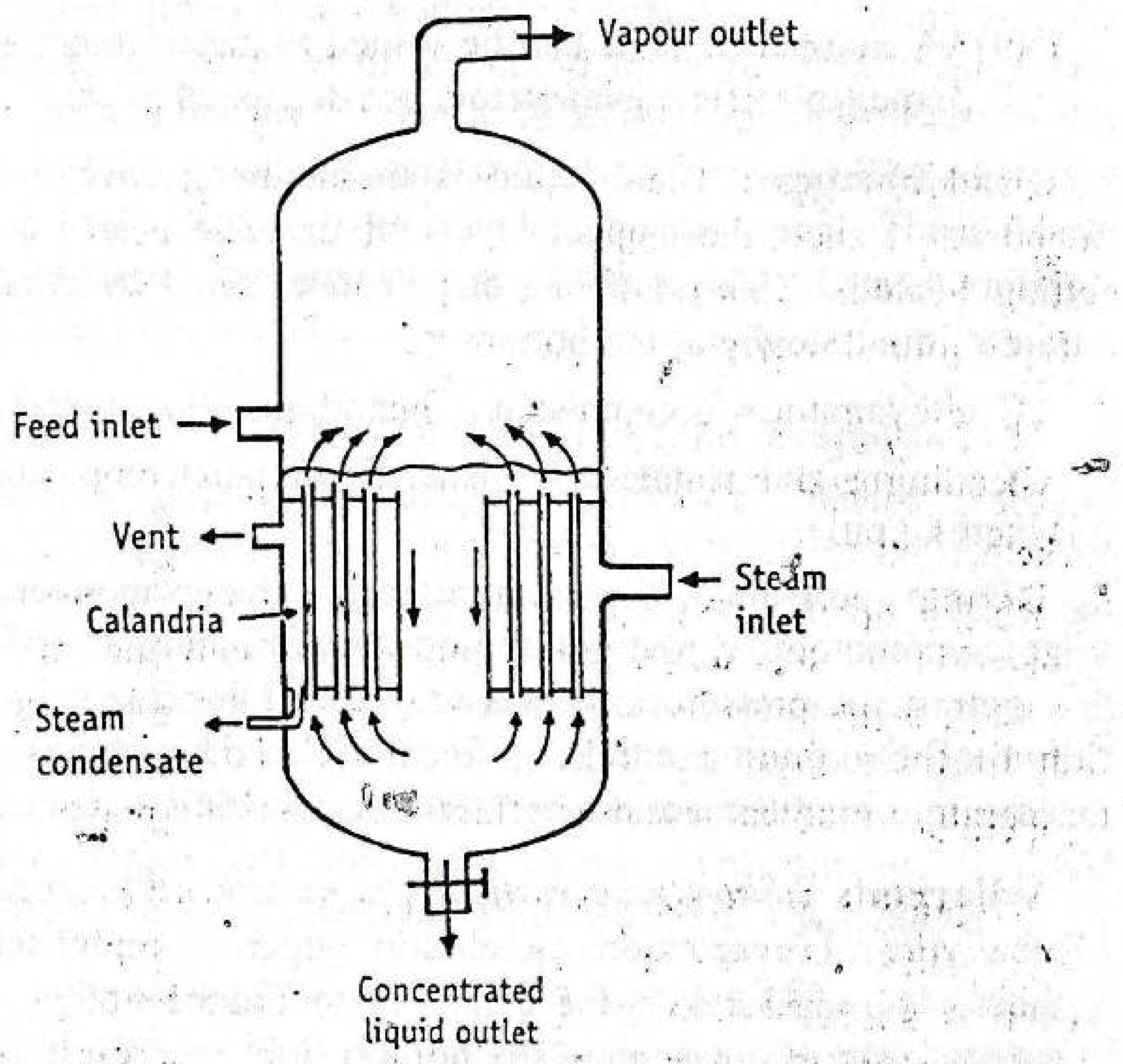


Figure 12-3. Construction of a short tube evaporator.

Working : Steam is introduced outside the tubes. The condensate is passed through the corresponding outlet and non-condensed gases escape through the vent. The feed is introduced in such a way as to maintain the liquid level slightly above the top of the tubes. The liquid inside the tubes is heated by the steam and begins to boil. As the liquid boils, it spouts up through the tubes and returns through the central down-take. It sets up a circulation of hot liquid, which enhances the rate of heat transfer. The vapour escapes through the top outlet. Steam is supplied until required concentration of the product is obtained. Finally, the product can be withdrawn from the bottom outlet.

Uses : Vertical tube evaporator is used in the manufacture of cascara extract, sugar, salt, caustic soda.

Advantages : (1) In vertical tube evaporator, tubes increase the heating surface nearly 10 to 15 times when compared with steam jacketed kettle.

(2) Vigorous circulation enhances the rate of heat transfer.

(3) It can be connected to a condenser and receiver, which further increases rate of evaporation. Such attachment is also suitable for volatile solvents.

(4) A number of units can be joined to obtain more efficient effect (multiple effect evaporators are discussed later).

Disadvantages : The liquid is maintained above the level of the calandria. Hence, the upper layers of the liquid need a long time for getting heated. This problem can be minimised by removing concentrated liquid slowly at the bottom.

The evaporator is complicated, hence, installation cost increases.

Cleaning and maintenance is difficult when compared with steam jacketed kettle.

During operation, the pressure inside the evaporator increases. In large evaporators, where the liquid depth may be of the order of 2.0 metres, the pressure increases to 25.0 kilopascals, leading to elevation of the boiling point by 5 or 6°C. This reduces the effective temperature gradient and may affect heat sensitive materials.

Variants : *Short tube vertical evaporator with propeller* : In short tube vertical evaporator, circulation depends completely on boiling. Steam is supplied into the calandria to induce boiling. When steam supply is stopped, automatically boiling stops. As a result the particles (if any) settle down. These particles act as nuclei which grow as crystals.

Therefore, this evaporator is sometimes used as a *crystallizing evaporator*. If such crystallization is undesirable, the problem can be avoided by installing a propeller in the central portion close to the bottom. By increasing the revolutions per minute of the propeller, the capacity of the evaporator can be doubled.

Uses : Since mild steel or cast iron is used, the evaporator suits well for clear liquids and crystallizing solutions. Non corrosive liquids and mild scaling solutions can also be handled.

Advantages : Heat transfer coefficients are high due to high temperature gradient values. It requires low head-room. Cleaning and maintenance is easy. It is relatively inexpensive.

Disadvantages : Heat transfer coefficients are low due to low temperature gradient. It requires high floor space and is more in weight. Relatively more liquid is retained. Rate of heat transfer further decreases due to high viscosity liquids. Since body is large, mild steel or cast iron are used for its construction to make it less expensive.

Basket type evaporator : The basket type of evaporator has a conical bottom and some times a flat bottom. In this type, boiling is quite violent. Hence, the spouting of the liquid leads to entrainment. This problem can be avoided by placing a deflector over the tubes. In this case, the down-take is annular instead of being central. The advantage of this type is that entire heating element is a single unit. The complete unit can be removed for repairs. In addition, the deflector prevents entrainment losses completely.

CLIMBING FILM EVAPORATOR (Rising Film Evaporator)

Principle : In climbing film evaporator, tubes are heated externally by steam. The preheated feed enters from the bottom and flows up through the heated tubes. The liquid gets heated rapidly due to enhanced overall coefficient of the preheated feed. The liquid near the wall becomes vapour and forms small bubbles. These tend to fuse to larger bubbles, which travel up in the tubes along with entrapped slug. The liquid films are blown up from the top of the tubes and strikes entrainment separator (deflector) kept above. This throws the liquid concentrate down into the lower part from where it is withdrawn.

Construction : The construction of a climbing film evaporator is shown in Figure 12-4. In this evaporator, the heating unit consists of steam jacketed tubes. Here, the tubes (long and narrow) are held between two plates. An entrainment separator is placed at the top to the vapour head. The evaporator carries steam inlet, vent outlet and condensate outlet. The feed inlet is from the bottom of the steam compartment.

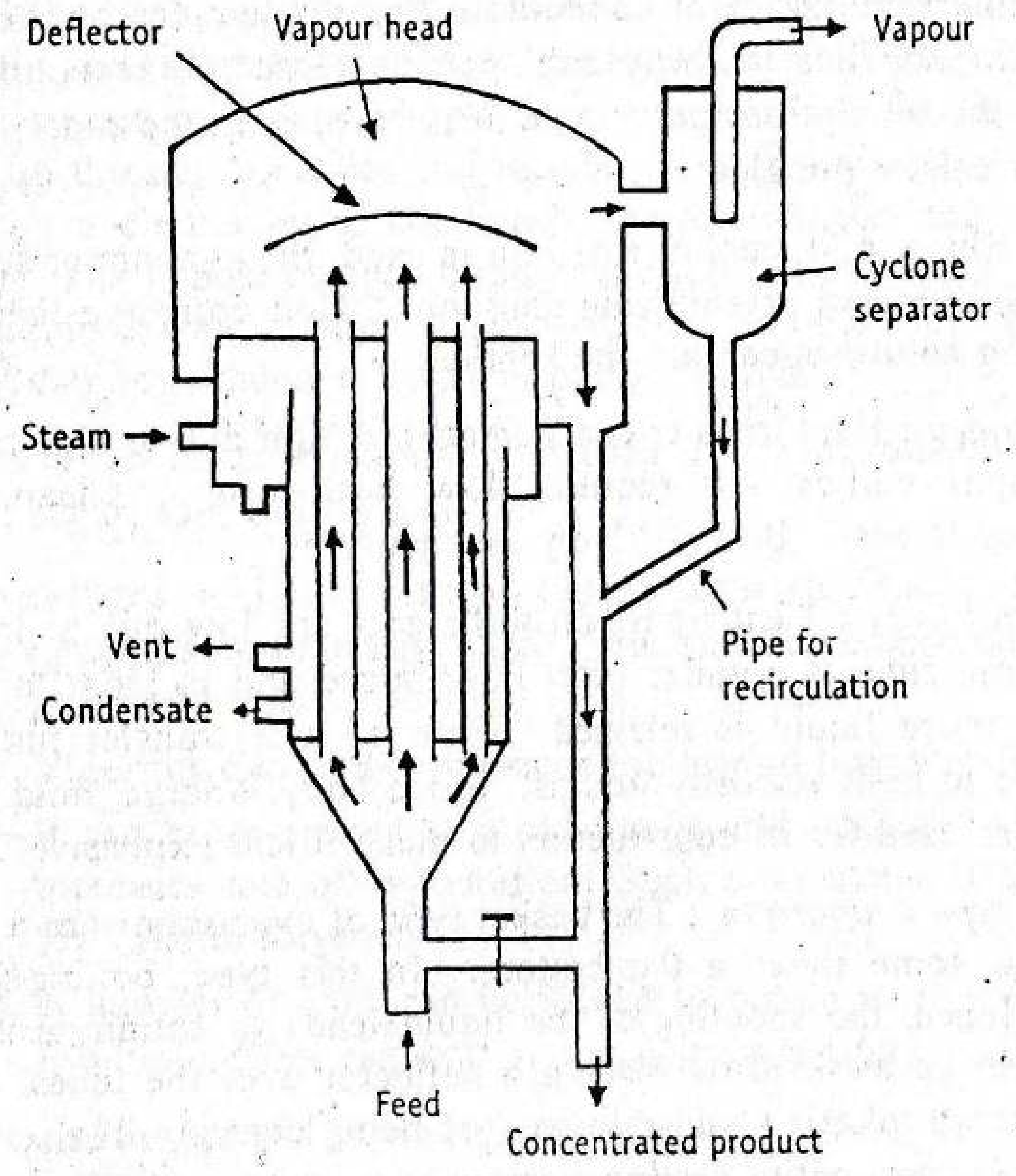


Figure 12-4. Construction of a climbing film evaporator.

Working : The preheated liquid feed (to be evaporated) is introduced from the bottom of the unit. The height of the liquid column is maintained low, i.e., 0.6 or 1.2 metres above the bottom tube sheet. Steam enters into the spaces outside the tubes through the inlet. Heat is transferred to the liquor through the walls of the tubes. The liquid becomes vapour and forms smaller bubbles, which tend to fuse to larger bubbles. These are of the width of the tubes, thereby the bubbles trap a part of the liquid (slug) on its way up in the tubes. As more vapour is formed, the slug of liquid is blown up in the tubes facilitating the liquid to spread as a film over the walls. This film of liquid continues to vaporise rapidly. Finally, the mixture of liquid concentrate and vapour eject at a high velocity from the top of the tubes.

The entrainment separator not only prevents entrainment, but also acts as a foam breaker. The vapour leaves from the top, while concentrate is collected from the bottom.

Uses : Using climbing film evaporator, thermolabile substances such as insulin, liver extracts and vitamins can be concentrated. Clear liquids, foaming liquids and corrosive solutions in large quantities can be operated. Deposit of scales can be removed quickly by increasing the feed rate or reducing the steam rate so that the product is unsaturated for a short time.

Advantages : (1) In a climbing film evaporator, large area for heat transfer is provided employing long and narrow tubes.

(2) Since liquid flows at a high velocity, the resistance for heat transfer at the boundary layers is reduced. As a result, the heat transfer is enhanced.

(3) The time of contact between the liquor and the heating surface is very short. The liquid is in the heater for one second, while its residence time is 20 seconds in the evaporator. Hence it is suitable for heat sensitive materials.

(4) Unlike short tube evaporator, the tubes are not submerged. So there is no elevation of boiling point due to hydrostatic head.

(5) It is suitable for foam-forming liquids, because foam can be broken by an entrainment separator.

(6) It requires low hold up and small floor space.

Disadvantages : (1) Climbing film evaporator is expensive, construction is quite complicated.

(2) It is difficult to clean and maintain.

(3) Large head space is required.

(4) It is not advisable for very viscous liquids, salting liquids and scaling liquids.

(5) If feed rate is high, the liquor may be concentrated insufficiently. If feed rate is low, film cannot be maintained. Dry patches may form on the tube walls.

FALLING FILM EVAPORATOR

Principle : In a falling film evaporator, feed enters from the top and flows down the walls of the tubes. The liquid gets heated rapidly due to heat transfer from steam. The liquid boils and becomes vapour, which forms small bubbles. They tend to fuse to form layers of bubbles, which travel down the tubes. Concentration takes place during this downward journey. Vapour and liquid are separated at the bottom.

Construction : The construction of a falling film evaporator is shown in Figure 12-5. It resembles climbing film evaporator, but is inverted. In this evaporator, the heating unit consists of steam jacketed tubes. The feed inlet is from the top of the steam compartment. The other provisions are steam inlet, vent and condensate outlet remain same. The outlet for the product is provided at the bottom and is connected to a cyclone separator.

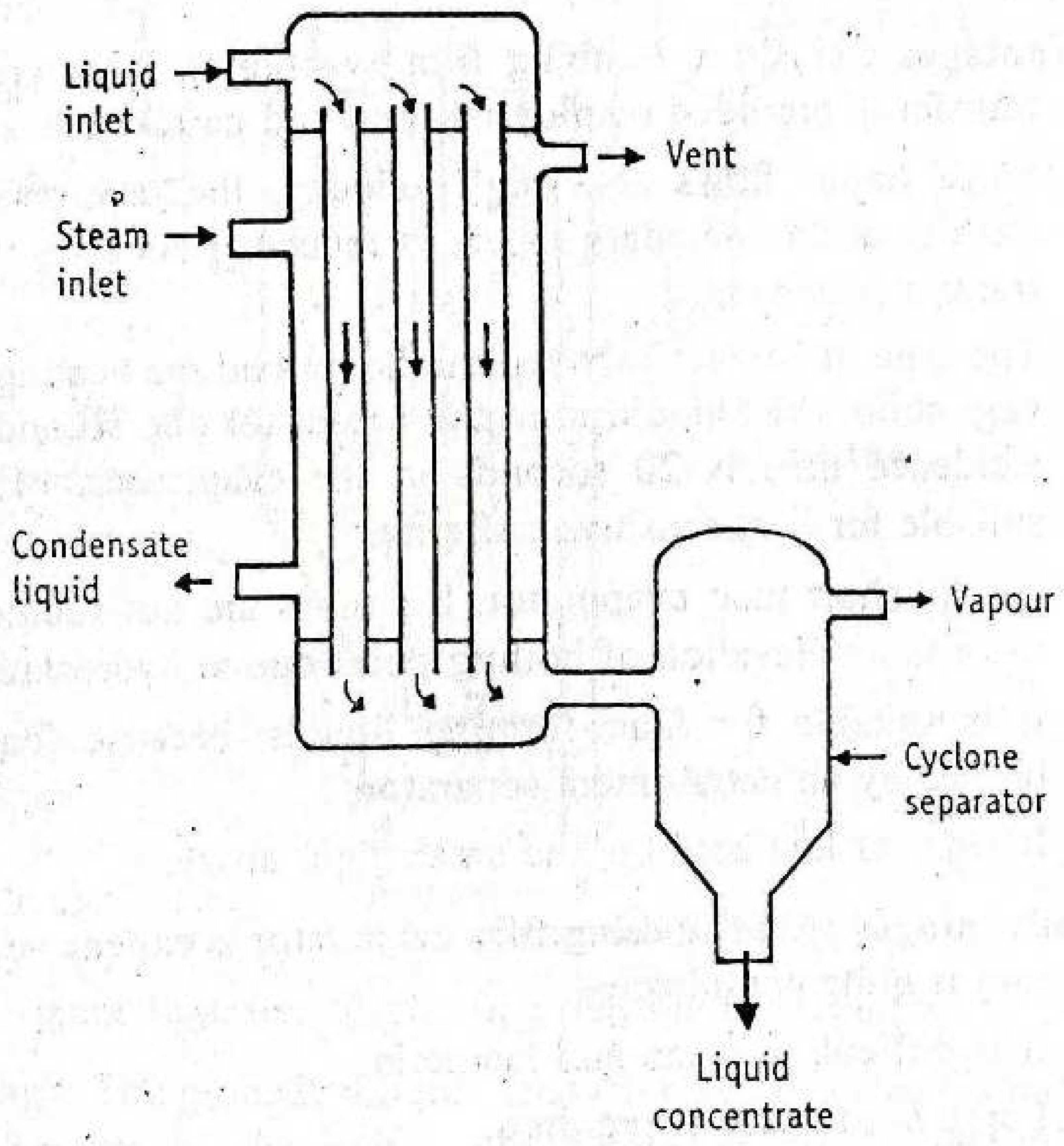


Figure 12-5. Falling film evaporator.

Working : Steam is supplied into the steam compartment. Feed enters from the top of the tubes. The temperature of the boiling liquid is same as that of the vapour head. The feed flows down the walls of the tubes. The liquid gets heated rapidly. The liquid boils and becomes vapour, which forms smaller bubbles. These tend to fuse to form layers of bubbles, which travel down the tubes. Concentration takes place during this downward journey. Vapour and liquid are separated in the cyclone separator.

Uses : Falling film evaporator is used to separate volatile and non-volatile materials, when the feed is of low viscosity. It is used for the concentration of yeast extract, manufacture of gelatin, extracts of tea and coffee. It is also useful for concentrating the heat sensitive materials such as fruit juices.

Advantages : (1) Falling film evaporator is suitable for high viscous liquids, because the flow of vapour film is assisted by gravity.

(2) The liquid hold-up is less and hold-up time is very small.

(3) The liquid is not overheated during passage and heat transfer coefficients are high even at low boiling temperature.

(4) Highly acidic and corrosive feeds can be concentrated using impervious graphite tubes and rubber lined vapour heads.

Disadvantages : Easy distribution of feed to the individual tubes may be accomplished using a perforated plate above the tubes or using spray nozzles. Hence, it is not suitable for suspensions, as the solids clog the perforated plate. It is not suitable for salting or scaling liquids. The feed distribution in the tubes is poor. For continuous supply, the liquid may be recirculated or the ratio of feed to evaporation is kept high.

FORCED CIRCULATION EVAPORATOR

Principle : In forced circulation evaporator, liquid is circulated through the tubes at high pressures by means of a pump. Hence, boiling does not takes place because boiling point is elevated. Forced circulation of the liquid also creates some form of agitation. When the liquid leaves the tubes and enters the vapour head, pressure falls suddenly. This leads to the flashing of super heated liquor. Thus evaporation is effected.

Construction : The construction of a forced circulation evaporator is shown in Figure 12-6. The steam jacketed tubes are held between two tube sheets. The tube measures 0.1 metres inside diameter and 2.5 metres long. The part of the tubes projects into the vapour head (flash chamber), which consists of a deflector. The vapour head is connected to a return pipe, which runs downwards and enters into the inlet of a pump.

Working : Steam is introduced into calendria. Pump sends the liquid to the tubes with a positive velocity. As the liquid moves up through the tubes, it gets heated and begins to boil. As a result, the vapour and liquid mixture rushes out of the tubes at a high velocity. This mixture strikes the deflector, which throws the liquid downward. This results in an effective separation of liquid and vapour. The vapour enters the cyclone separator and leaves the equipment. The concentrated liquid returns to the pump for further evaporation. Finally the concentrated product is collected.

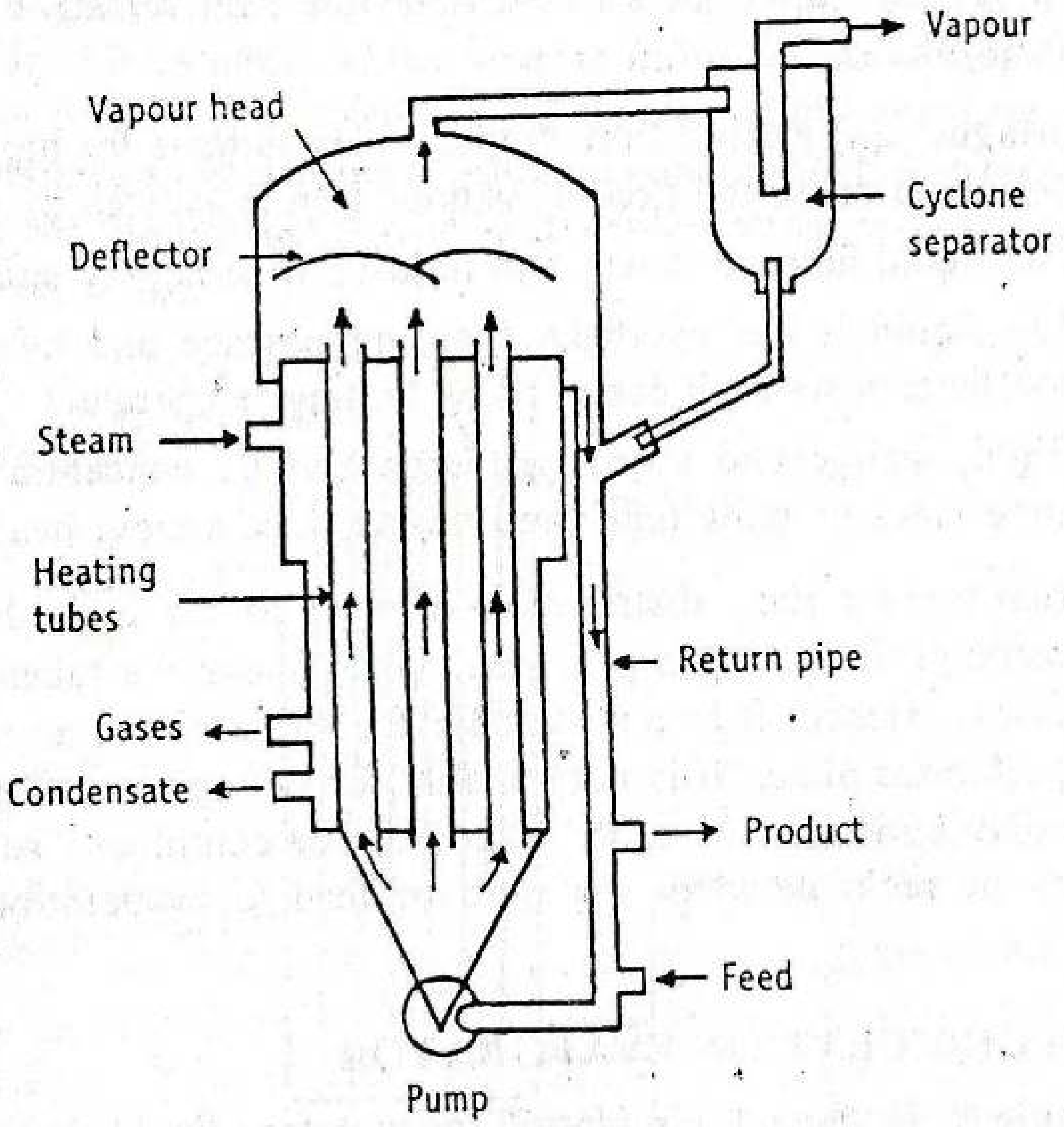


Figure 12-6. Forced circulation evaporator.

Uses : If evaporation is conducted under reduced pressure, forced circulation evaporator is suitable for thermolabile substances. This method is used for the concentration of insulin and liver extracts. It is well suited for crystallizing operations where crystals are to be suspended at all times.

Advantages : (1) In forced circulation evaporator, the heat transfer coefficient is high due to rapid liquid movement.

(2) Salting, scaling and fouling are not possible due to forced circulation.

(3) This evaporator is suitable for thermolabile substances because of rapid evaporation.

(4) It is suitable for high viscous preparations because pumping mechanism is used.

Disadvantages : In forced circulation evaporator, the hold-up of liquid is high. The equipment is expensive, because power (pump) is required for circulating the liquid.

THEORY

In an evaporator, heat is transferred to the evaporating liquid so as to provide latent heat of vaporisation. Generally, steam is used as a source of heat. Several heat exchangers have been discussed in Chapter 'Heat Flow'. Normally, tube and shell heat exchangers are used for heat transfer.

The amount of heat, which must be transferred through the walls of a calandria, varies with the nature of the liquid to be evaporated. The liquids used in pharmacy practice are water and hydroalcoholic solutions with low solid content. In case of bulk drugs, organic solvents are also used.

Evaporator Capacity

The total amount of heat required can be obtained by considering a simple diagram of an evaporator as shown in Figure 12-7.

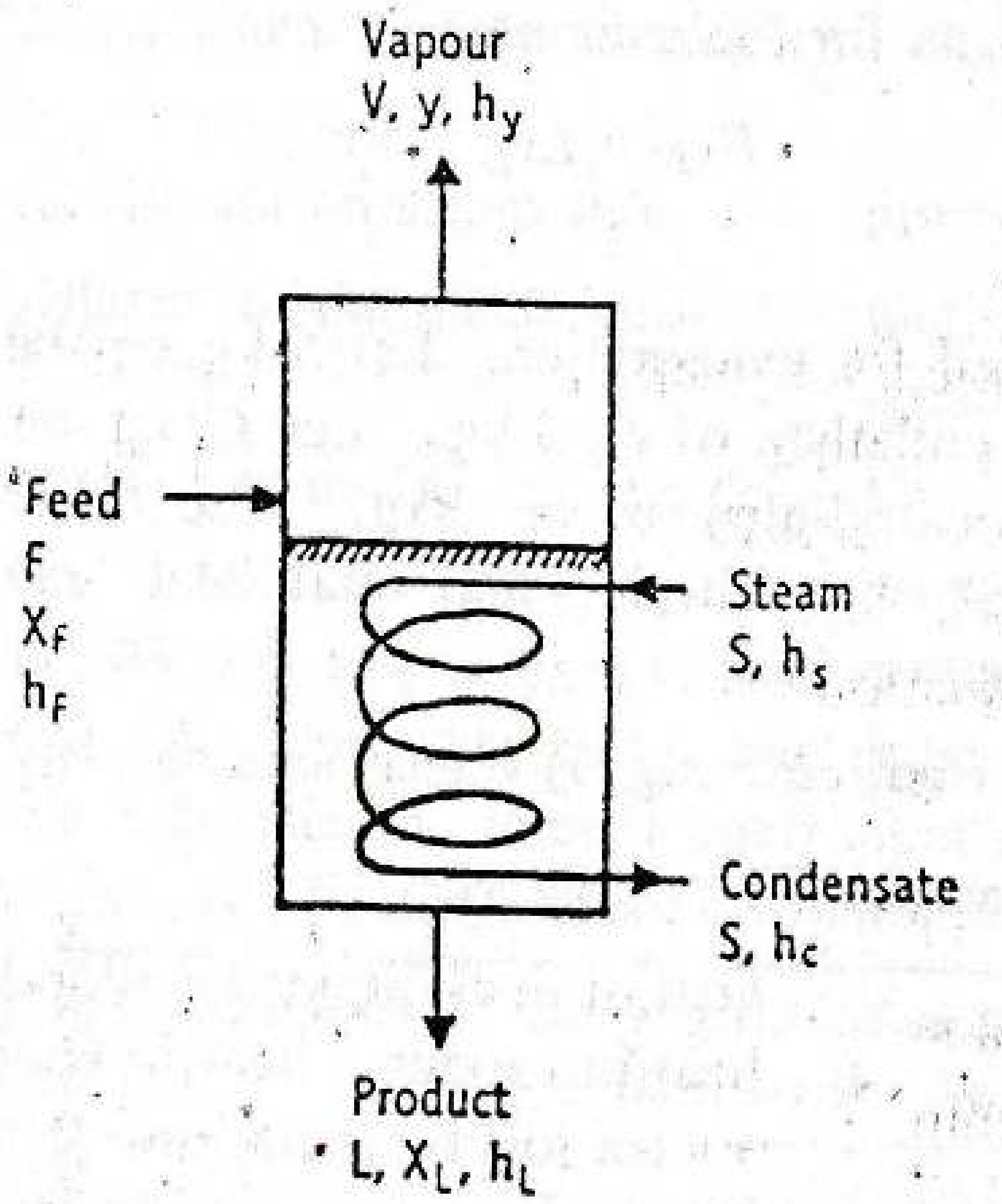


Figure 12-7. Evaporator system with its parameters.

Feed and steam are admitted into the evaporator. By consuming heat, the feed undergoes evaporation to form vapour, which will be allowed to escape. The concentrated product will be collected at its bottom. Simultaneously steam looses its heat energy and undergoes condensation, the condensate of which will be removed.

- Let F kg be the feed per hour to the evaporator, whose solid content is x_F (weight fraction) and enthalpy is h_F J/kg.

- Let L kg be the product collected per hour from an evaporator, whose solute composition is x_L (weight fraction) and enthalpy is h_L J/kg.
- Let V kg be the vapour liberated per hour from an evaporator, whose solute composition is y (weight fraction) and enthalpy is h_V J/kg. In most evaporators, the vapour is pure water as there is no entrainment and therefore y is zero.

Material Balancing

The material balance can be obtained from total material entering and total material leaving. It can be represented by an equation for the evaporation process.

Feed (kg) = product collected (kg) + vapour liberated (kg)

$$F = L + V \tag{1}$$

Equation (1) can also be written for material balancing in terms of mass x weight fraction for the solute as:

$$Fx_F = Lx_L + Vy \tag{2}$$

Energy Balancing

Steam is supplied for evaporation. Let S kg be the steam supplied per hour with an enthalpy of h_S J/kg. Let C kg be the condensate removed having an enthalpy of h_C J/kg. The heat balance can be obtained from total heat entering and total heat leaving. It can be represented by equation (3).

$$\text{Heat entering (J)} = \text{heat leaving (J)} \tag{3}$$

Equation (3) can also be written as:

$$\begin{array}{lcl} \text{Heat in feed +} & & \text{heat in thick liquor (product) +} \\ \text{heat in steam} & = & \text{heat in vapour + heat in condensate} \\ & & \text{+ heat lost by radiation.} \end{array} \tag{4}$$

Loss of heat by radiation is less and can be neglected. The equation (4) can also be written in terms of mass x enthalpy as:

$$Fh_F + Sh_S = Lh_L + Vh_V + Sh_C \tag{5}$$

Temperature difference is the difference between the saturation temperature of the steam and the boiling point of the liquid. Generally, a temperature difference of 20 to 30°C is sufficient for rapid evaporation of solution. But in practice, the feed may have the temperature less than boiling point of the liquid. The steam may be superheated and the condensate may get cooled. All these factors influence evaporator calculation with respect to mass balance.

Improving Heat Transfer Coefficients

Evaporator is considered as a heat exchanger. Like any heat exchanger, heat is transferred from steam to the product. The general equation for heat transfer can be expressed by equation (6)

$$Q = UA\Delta t \tag{6}$$

where Q = rate of heat transfer, W
U = overall heat transfer coefficient, W/m^{2}K
A = heating surface area, m^2
Δt = temperature difference, K

Equation (6) can be used to determine the Q.

Heating surface (A in equation 6) must be large. For this purpose more number of tubes are mounted in parallel to form a unit known as *calandria*. The overall heat transfer coefficient, U, can be regarded as follows.

– Fluid film coefficient on steam side	– always relatively higher.
– Thermal resistance of the metal wall.	– neglected because it is small.
– Fluid film coefficient on the liquid side	– low, major determinant in heat transfer.

The overall coefficient (U) is approximately nearer to the lowest surface coefficient of the film. Any factor that improves the coefficient on the boiling side increases the overall coefficient almost proportionally. Some of the factors affecting these coefficients are:

Steam side – film coefficients can be increased	*Boiling liquid side–surface coefficient can be increased*
Temperature drop should be large	increasing the velocity by pumping the liquid
High temperature at which condensation takes place	decreasing the viscosity by feeding hot liquid
Amount of non-condensed gas in steam should be minimum.	cleaning of the heating surface

Pumping liquids at high velocities (forced circulation) through the tubes has beneficial effect. Such high velocities tend to decrease the thickness of the viscous film and the buffer layer.

Overall coefficients may be seriously lowered because of—

- corrosion of the surfaces.
- deposition of solid material from the evaporating liquid.
- The presence of noncondensable gases in the heating steam (air).

Efforts should be made to prevent the above effects. Forced circulation is an important measure, i.e., increase the velocity of liquid flow to increase the capacity of the evaporator.

MULTIPLE EFFECT EVAPORATOR

Vertical tube evaporator discussed earlier is a single effect evaporator (Figure 12-3). Such evaporators are connected in several ways so as to achieve large scale evaporation as well as greater economy. Although multiple effect evaporators are not used in the pharmaceutical industry, the principles are of interest and should be understood. This is illustrated using an example of triple effect evaporator with a parallel feed mechanism.

Advantages : (1) It is suitable for large scale and for continuous operation.

(2) It is highly economical when compared with single effect.

(3) About 5 evaporators can be attached.

Construction : The construction of a multiple effect evaporator is shown in Figure 12-8 using 3 evaporators, i.e., triple effect evaporator. The other aspects of construction of vertical tube evaporator remain same as mentioned earlier. A perusal to Figure 12-8 indicates that the vapour from first evaporator serves as a heating medium for the 2nd evaporator. Similarly, vapour from 2nd evaporator serves as a heating medium for the 3rd evaporator. Last evaporator is connected to a vacuum pump.

Working : Parallel feed arrangement is used in this example.

Parallel feed : In this method, a hot saturated solution of the feed is directly fed to each of the three effects (evaporation) in parallel without transferring the material from one effect to the other. The parallel feed arrangement is commonly used in the concentration of salt solutions, where the solute crystallizes on concentration without increasing the viscosity.

Operations : In the beginning, the equipment is at room temperature and atmospheric pressure. The liquid feed is introduced to all the three evaporators up to the level of the upper tube sheets. The following operations are attempted to achieve the effects as specified below.

1. The vent valves V_1, V_2 and V_3 are kept open and all other valves are closed (not shown in Figure 12-8).
2. Now a high vacuum is created in the liquid chambers of evaporators.
3. The steam valve S_1 and condensate valve C_1 are opened. Steam is supplied. Steam first replaces cold air in the steam space of 1st evaporator. When all the cold air is removed, the valve, V_1 is closed.
4. The supply of steam is continued until the desired pressure P_0 is created in the steam space of 1st evaporator. At this pressure, the temperature of the steam is t_0.

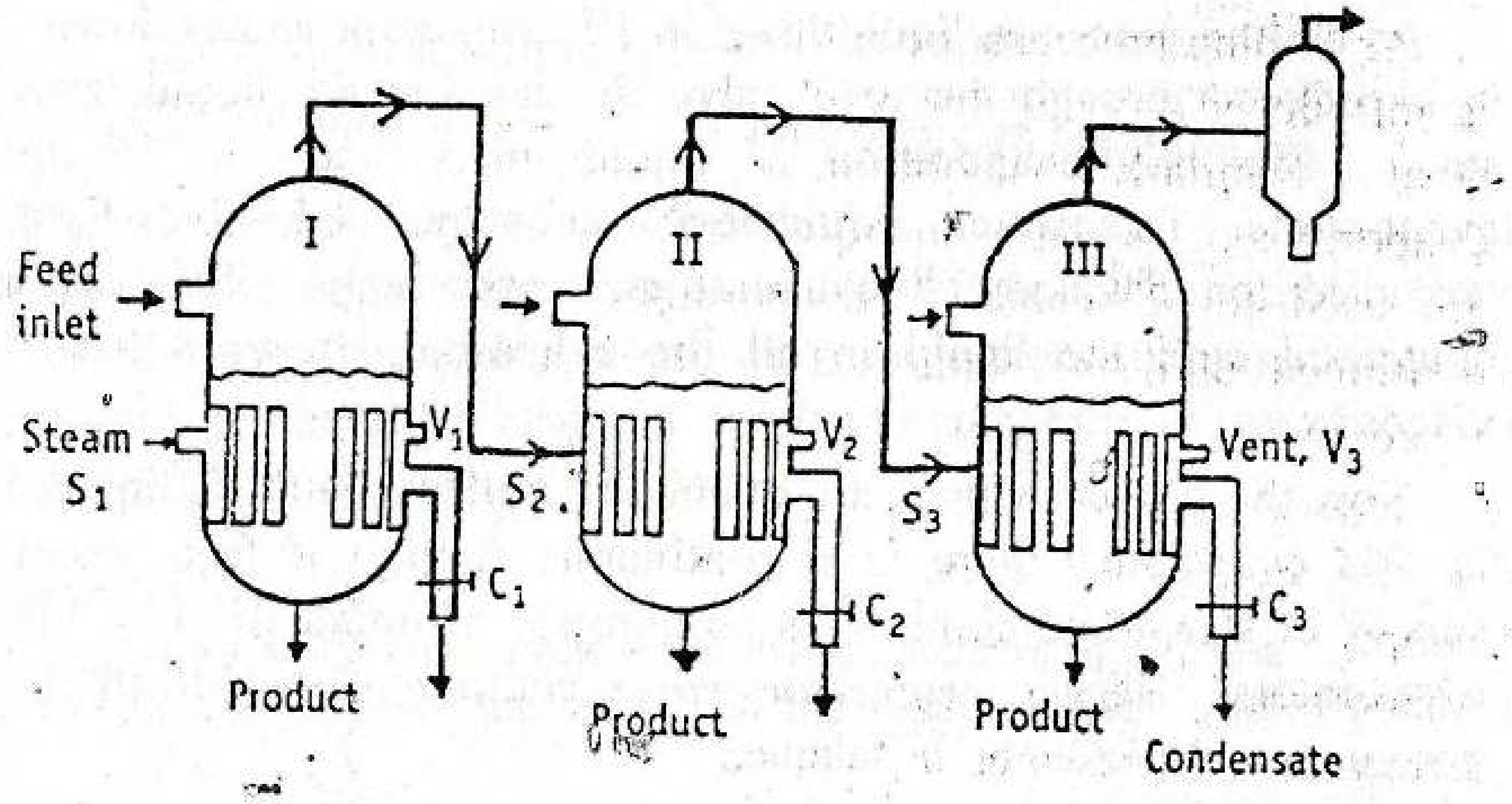


Figure 12-8. Triple effect evaporator with parallel feed arrangements.

5. Steam gives its temperature to the liquid feed in the 1st evaporator and gets condensed. Condensate is removed through the valve C_1.
6. Due to heat transfer, the liquid temperature increases and reaches the boiling point. During this process, vapour will be generated from the liquid feed.
7. So formed vapour displaces air in the upper part of 1st evaporator. Moreover, the vapour also displaces the air in the steam space of the 2nd evaporator.
8. After complete displacement of air by vapour in the steam compartment of 2nd evaporator, the valve V_2 is closed.

9. The vapour of 1st evaporator transmits its heat to the liquid of 2nd evaporator and gets condensed. Condensate is removed through the valve C_2. These steps continue in the 3rd evaporator also.

As the liquid in the 1st evaporator gains temperature, the difference in temperatures between the liquid and steam decreases, hence, the rate of condensation decreases. As a result, the pressure in the vapour space of 1st evaporator gradually increases to P_1 by increasing temperature to t_1, which is the boiling point of the liquid in 1st evaporator, and decreasing the temperature difference $(t_0 - t_1)$.

A similar change takes place in the 2nd evaporator and the liquid reaches the boiling point. Similarly, the process will be repeated in 3rd evaporator. Finally three evaporators (or effects as they are called) come to a steady state with the liquid boiling in all the three bodies.

As boiling proceeds, liquid level in 1st evaporator comes down. Feed is introduced through the feed valve to maintain the liquid level constant. Similarly evaporation of liquid takes place in 2nd and 3rd evaporators. To maintain liquid levels constant, feed valves F_2 and F_3 are used for 2nd and 3rd evaporators, respectively. This process is continued until the liquid in all the evaporators reaches the desired viscosity.

Now the product valves are opened to collect the thick liquid. Thus in this evaporator, there is a continuous supply of feed, continuous supply of steam and continuous withdrawal of liquid from all the three evaporators. Hence, evaporator works continuously with all the temperatures and pressures in balance.

The evaporator can also be fed by forward feed method, backward feed method and mixed feed method. In the forward feed method, the mother liquor is introduced into 1st then transferred to 2nd and then to 3rd. In the backward feed method, the mother liquor is introduced into the 3rd evaporator, then transferred to 2nd and then transferred to 1st. In mixed feed method, the mother liquor is introduced into 2nd evaporator then transferred to 3rd evaporator and then transferred to 1st evaporator.

Economy of Multiple Effect Evaporator

The economy of an evaporator is the quantity of vapour produced per unit steam admitted. It is calculated by considering the following assumptions.

Feed is admitted at its boiling point. Therefore, it does not require any more heat to raise its temperature. Hence, the supplied steam gets condensed to give heat of condensation. This heat will then be transferred completely to the liquid. The heat transferred now serves as latent heat of vaporisation, i.e., liquid undergoes vaporisation by receiving heat. Loss of heat by any means is negligible.

The economy of an evaporator may be expressed as:

$$\text{Economy of an evaporator} = \frac{\text{total mass of vapour produced}}{\text{total mass of steam supplied}}$$

In single effect evaporator, steam produces vapour only once. Hence

$$\text{Economy of a single effect evaporator} = \frac{\text{N units of vapour produced}}{\text{N units of steam supplied}} = 1$$

In multiple effect evaporator, one unit of steam produces vapour many times, depending on the number of evaporators connected. Hence,

$$\text{Economy of multiple effect evaporator} = \frac{\text{N units of vapour produced}}{\text{1 unit of steam supplied}} = \text{N}$$

Therefore, economy of multiple effect evaporator is N times the economy of the single effect evaporator. However, such a great economy is approximately true as it depends on many factors such as temperature of the feed, temperature range in the evaporator, ratio of weight of feed to the product and pressure difference.

Glossary of Symbols

b = Maximum vapour pressure at the temperature of air, kPa.
b' = Pressure due to the vapour of the liquid actually present in the air, kPa.
C = Amount of condensate removed, kg.
F = Amount of feed, kg.
h_C = Enthalpy of the condensate, J/kg.
h_F = Enthalpy of the feed, J/kg.
h_L = Enthalpy of the product concentrate, J/kg.
h_S = Enthalpy of the steam, J/kg.
h_V = Enthalpy of the vapour, J/kg.
K = Constant, m/s.
L = Mass of product collected from evaporator, kg.
M = Mass of vapour formed per unit time, m^3/s.
p = Atmospheric pressure, kPa.
Q = Rate of heat transfer, W.
S = Amount of steam introduced, kg.
S = Surface area of the liquid exposed, m^2.
Δt = Temperature difference, °K.

X_F = Solid content in the feed (weight fraction).
X_L = Solute composition in the product (weight fraction).
U = Overall heat transfer coefficient, W/m^2. K.
V = Amount of vapour liberated, kg.
y = Solute composition in vapour. (weight fraction)

QUESTION BANK

Each question carries 2 marks

1. Explain the term Evaporator capacity.
2. Define evaporation in terms of capacity and economy as applied to evaporation practice.
3. Explain the construction of calandria. Give its uses.

Each question carries 5 marks

1. Elaborate the concept of multiple effect evaporation. What specific advantages does it offer?
2. Describe the construction and working of film evaporator of any one type.
3. Explain the construction and working of a forced circulation evaporator.

Each question carries 10 marks

1. How do film evaporator function? Elaborate the answer with a neat sketch of one such evaporator. List the merits and demerits of film evaporator system.
2. Classify evaporators. Describe construction and working of a film evaporator.
3. Explain the terms 'multiple effect evaporation' and 'evaporator capacity'. How many effects generally go into a multiple effect evaporator?
4. What do you understand by 'multiple effect evaporator'? Describe one such evaporator. How do you feed such evaporator?

13

Crystallization

Characteristics of Crystals
Pharmaceutical Solids – Terminology
Theory of Crystallization
Equipment
Caking of Crystals

Crystallization is the spontaneous arrangement of the particles into a repetitive orderly array, i.e., regular geometric patterns.

In matter, particles are present randomly due to thermal agitation. In gases the disorderliness is highest and in liquids it is moderate. The liquids can solidify into crystalline forms, whenever attraction forces between particles are strong enough to overcome the disorderliness. Crystallization can take place directly from vapour of a substance. Examples are solid camphor from camphor vapour, solid iodine from iodine vapour. Such a process is known as *sublimation*. Crystals are commonly obtained from liquid state. Example is salt from brine. This chapter of crystallization deals with the later type, i.e., from solution to solid state.

Crystallization differs from precipitation in that the product is deposited from a supersaturated solution. Precipitation occurs when solutions of materials react chemically to form a product, which is sparingly soluble in the liquid and therefore deposits out.

Drugs are most commonly used in the solid state (powder forms) in the following dosage forms.

1. Bulk powders for internal use, examples are fine powders and granules.
2. Bulk powders for external use, examples are snuffs, dusting powders and tooth powders.
3. Simple and compound powders for internal use.
4. Powders in the form of compressed tablets and tablet triturates.
5. Powders enclosed in cachets and capsules.

In many occasions, drugs are supplied in the solid state even in the injection dosage forms from the point of chemical stability.

Applications

The use of drugs in the solid state has several advantages.

Purification of drugs : Crystallization is used as a purification process. It is used for removing impurities from pharmaceutical products, i.e., recrystallization technique.

Better processing characteristics : Crystallization technique is used to change the micromeritics of drugs such as compressibility and wettability.

Ease of handling : Crystallization facilitates various operations such as transportation and storage.

Better chemical stability : Crystallization increases the stability of drugs. For example, amorphous penicillin G is less stable than crystalline salt. Amitryptyline is more stable in crystalline form than in amorphous form.

Improved physical stability : Crystalline forms play an important role in product properties such as suspension stability and hardness of a tablet. Using dehydrating materials such as dehydrated alcohol and glycerol, the stability of hygroscopic substances can be enhanced.

Improved bioavailability : Some drugs are more effective in their crystalline form. For example, penicillin G does not dissolve immediately in the gastric fluids. Therefore, its degradation decreases. Hence, bioavailability of penicillin G enhances.

Sustained release : Drug substances with different sizes of crystals can be used in the production of sustained release dosage forms. For example, protamine zinc insulin in crystalline form slowly and continuously releases insulin from the site of injection for prolonged periods.

Miscellaneous : Certain crystals are used in the production of semiconductor devices, laser beams and artificial gems.

CHARACTERISTICS OF CRYSTALS

Crystal Lattice

A *crystal* can be defined as a solid particle, which is formed by the solidification (crystallization) process (under suitable environment) in which structural units are arranged by a fixed geometric pattern or lattice.

Crystal lattice is defined as an orderly internal arrangement of particles in three-dimensional space.

The geometric form in which structural units are arranged in a crystal is determined by means of X-ray diffraction pattern. The three dimensional arrangement of particles in a crystal is also known as *space lattice*.

The units that constitute the crystal structure are ions, atoms or molecules.

- Ions with opposite charges are bonded together by electrostatic attractions as in the crystals of sodium chloride.
- Atoms are bonded together by covalent bond as in diamond and graphite.
- In most organic compounds, molecules are held together by van der Waals forces and hydrogen bonding. Examples are naphthalene and *p*-hydroxy benzoic acid.

The smallest geometric portion, which repeats to build up the whole crystal, is called a *unit cell*.

A crystal is bounded by plane surfaces called *faces*.

In the crystal, the angle between the two perpendiculars to the intersecting faces is termed as the *axial angle*.

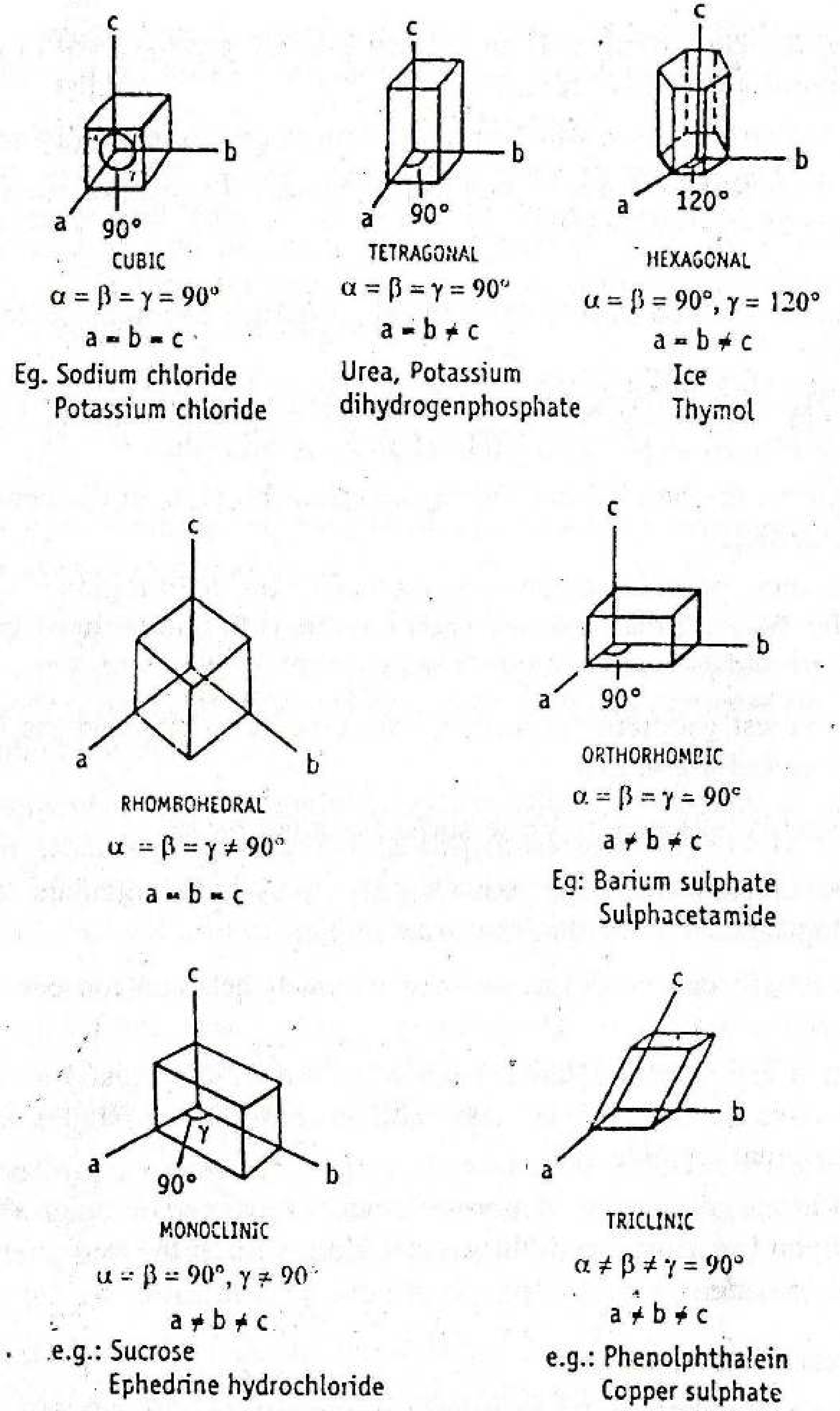
Axial length can be defined as the distance between the centres of two atoms.

- If a crystal is fractured, each fragment of the crystal also possesses plane surfaces with characteristic axial angles of the original crystal.
- Certain properties of crystals such as refractive index depend upon the direction in the crystal along which the determinations are made.

Crystal Systems or Forms

A finite number of symmetrical arrangements are possible for a crystal lattice and these may be termed as *crystal forms or crystal systems*.

Depending upon the axial length and axial angle, crystal forms are designated as cubic, hexagonal, tetragonal, orthorhombic, monoclinic and triclinic. They are shown in Figure 13-1. A chemical substance may exist in more than one form, i.e., polymorphism.



CUBIC
$\alpha = \beta = \gamma = 90°$
$a = b = c$
Eg. Sodium chloride
Potassium chloride

TETRAGONAL
$\alpha = \beta = \gamma = 90°$
$a = b \neq c$
Urea, Potassium dihydrogenphosphate

HEXAGONAL
$\alpha = \beta = 90°, \gamma = 120°$
$a = b \neq c$
Ice
Thymol

RHOMBOHEDRAL
$\alpha = \beta = \gamma \neq 90°$
$a = b = c$

ORTHORHOMBIC
$\alpha = \beta = \gamma = 90°$
$a \neq b \neq c$
Eg: Barium sulphate
Sulphacetamide

MONOCLINIC
$\alpha = \beta = 90°, \gamma \neq 90°$
$a \neq b \neq c$
e.g.: Sucrose
Ephedrine hydrochloride

TRICLINIC
$\alpha \neq \beta \neq \gamma = 90°$
$a \neq b \neq c$
e.g.: Phenolphthalein
Copper sulphate

Figure 13-1. Different types of crystal systems with characteristics and examples.

Crystal Habit

Crystal is a polyhedral solid with number of planar surfaces. A substance crystallizes in such a way that the angle between a given pair

of faces is same in all specimens. It is the characteristic of a particular substance irrespective of the relative sizes of the faces.

The shape and size of the crystals formed are markedly dependent on the conditions under which crystallization is carried out. For example, griseofulvin crystallized from acetone has a different form from the same drug crystallized from benzene or chloroform.

Depending on the arrangement of faces, crystal habits are described in different ways. These are shown in Figure 13-2.

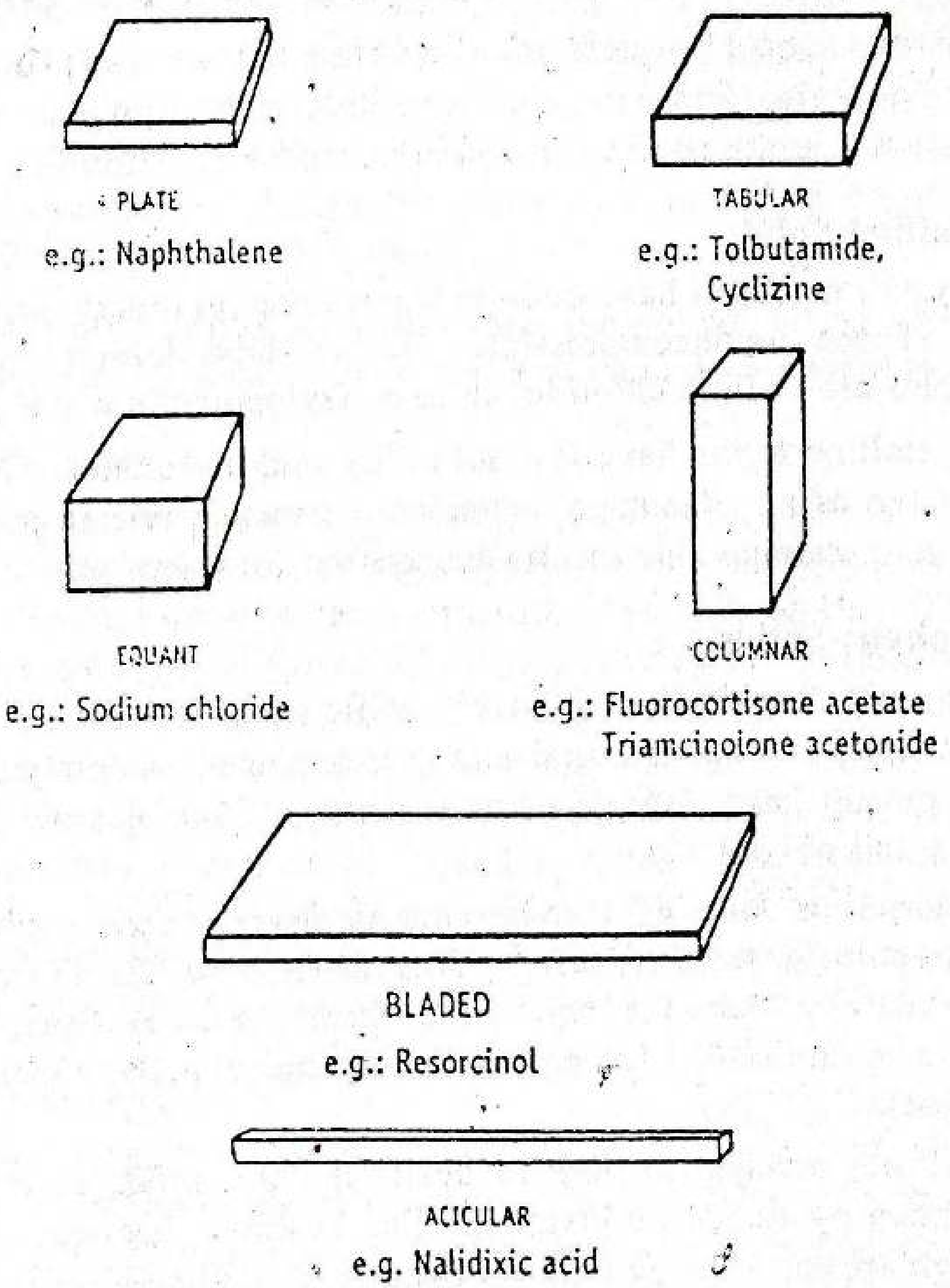


PLATE
e.g.: Naphthalene

TABULAR
e.g.: Tolbutamide, Cyclizine

EQUANT
e.g.: Sodium chloride

COLUMNAR
e.g.: Fluorocortisone acetate
Triamcinolone acetonide

BLADED
e.g.: Resorcinol

ACICULAR
e.g. Nalidixic acid

Figure 13-2. Different types of crystal habits with examples.

Columnar : Rod like particles having a width and thickness exceeding that of needle type particles. The term prismatic may also be used.

Blade : Long, thin and flat particles, which can also be referred to as being lath shaped.

Plate : Flat particles of similar length and width. They are also denoted as being lamellar or micaceous.

Tabular : Flat particles of similar length and width, but possessing greater thickness and flakes.

Equant : Particles of similar length, width and thickness.

Acicular: Needle like prisms.

PHARMACEUTICAL SOLIDS—TERMINOLOGY

Pharmaceutical powders are available either in amorphous form or in crystalline form. Further crystalline solids such as polymorphs, hydrates and solvates are used in the manufacture of dosage forms.

Crystalline Solids

Crystalline solids have definite shapes and an orderly arrangement of units. These are incompressible. These show definite melting point. Examples are sodium chloride, urea, benzylpenicillin and aspirin.

Crystalline forms have low solubility and dissolution. This fact has been taken as an advantage to produce sustained release products. Example is protamine zinc insulin suspension for injection.

Amorphous Solids

Amorphous solids do not have specific shape (Greek: *amorphe* meant without form). The structural units are arranged randomly in the solid. These do not have definite melting points. Examples are glass, pitch, plastics and novobiocin.

Amorphous form of a compound is always more soluble than the corresponding crystalline form. Therefore, it may exhibit better therapeutic activity than the crystalline form. For example, amorphous novobiocin (antibiotic) has significant biological activity than crystalline novobiocin.

It is not always possible to determine the solids as crystalline or amorphous by casual observation. For example, beeswax and paraffin although appear to be amorphous assume crystalline arrangements when heated and allowed to cool slowly.

Polymorphs

Certain drugs can exist in more than one crystalline form. Such a phenomenon is known as *polymorphism*. About 63% of barbiturates, 67% of steroids and 40% of sulphonamides exhibit polymorphism. Although the drug is chemically indistinguishable in each form, polymorphs differ significantly with respect to a number of properties such as density, melting point, solubility and dissolution rate.

Metastable polymorphs : These polymorphs slowly convert into stable polymorphs. If the rate of conversion is so slow as to be negligible during the expected life of a drug product, metastable polymorphs are preferred because of their unique physicochemical properties.

The metastable polymorphs have lower melting points, higher solubility and higher dissolution than their stable polymorphs. Therefore, these are preferred in the production of dosage forms. For example, riboflavin can exist in three different crystalline forms, which vary in water solubility at 25°C from 60 mg per litre to 1.2 g per litre. The increased solubility of metastable polymorph ordinarily results in increased dissolution and absorption.

Stable polymorphs : These are employed when metastable polymorphs are not suitable on account of rapid decomposition.

Crystal Hydrates

Some drugs have greater tendency to associate with water. The resulting substance is referred to as *drug hydrate*. Examples are caffeine hydrate, theophylline hydrate, ampicillin monohydrate etc. The anhydrous form dissolves more readily and gives better bioavailability than hydrous form. Therefore, anhydrous forms are the preferred ones. Water can combine with positive ions and neutral molecules. Sodium carbonate decahydrate, $Na_2CO_3.10H_2O$ is official in IP and BP. Some substances form a number of crystal hydrates. For example, sodium carbonate is available as $Na_2CO_3.10H_2O$, $Na_2CO_3.8H_2O$, $Na_2CO_3.6H_2O$, $Na_2CO_3.5H_2O$ and $Na_2CO_3.H_2O$. Similarly, ampicillin monohydrate and ampicillin trihydrate are available.

Crystal Solvates

Certain drugs have greater tendency to associate with solvents to produce crystalline forms of *solvates*. These solvates are also known as *pseudomorphs*. Examples are fluorocortisone with n-pentanol or ethyl acetate. Succinylsulphathiazole with n-pentanol dissolve much more rapidly than non-solvated form of succinylsulphathiazole. Therefore, for better bioavailability, solvate forms of drugs are preferred.

Isomorphs

When two or more substances possess the same crystalline form, the crystals of one such substance can be grown in the saturated solution of the other. This phenomenon is known as *isomorphism*. Such substances are said to be isomorphs (having the same shape). For example, chrome alum $K_2SO_4.Cr_2(SO_4)_3.24H_2O$ is isomorphic with potash alum $K_2SO_4.Al_2(SO_4)_3.24H_2O$. The chromium in chrome alum has the same valency as aluminium in potash alum.

THEORY OF CRYSTALLIZATION

Mechanism of Crystallization

The mechanism of the crystallization of substances from the solution is explained using Figure 13-3.

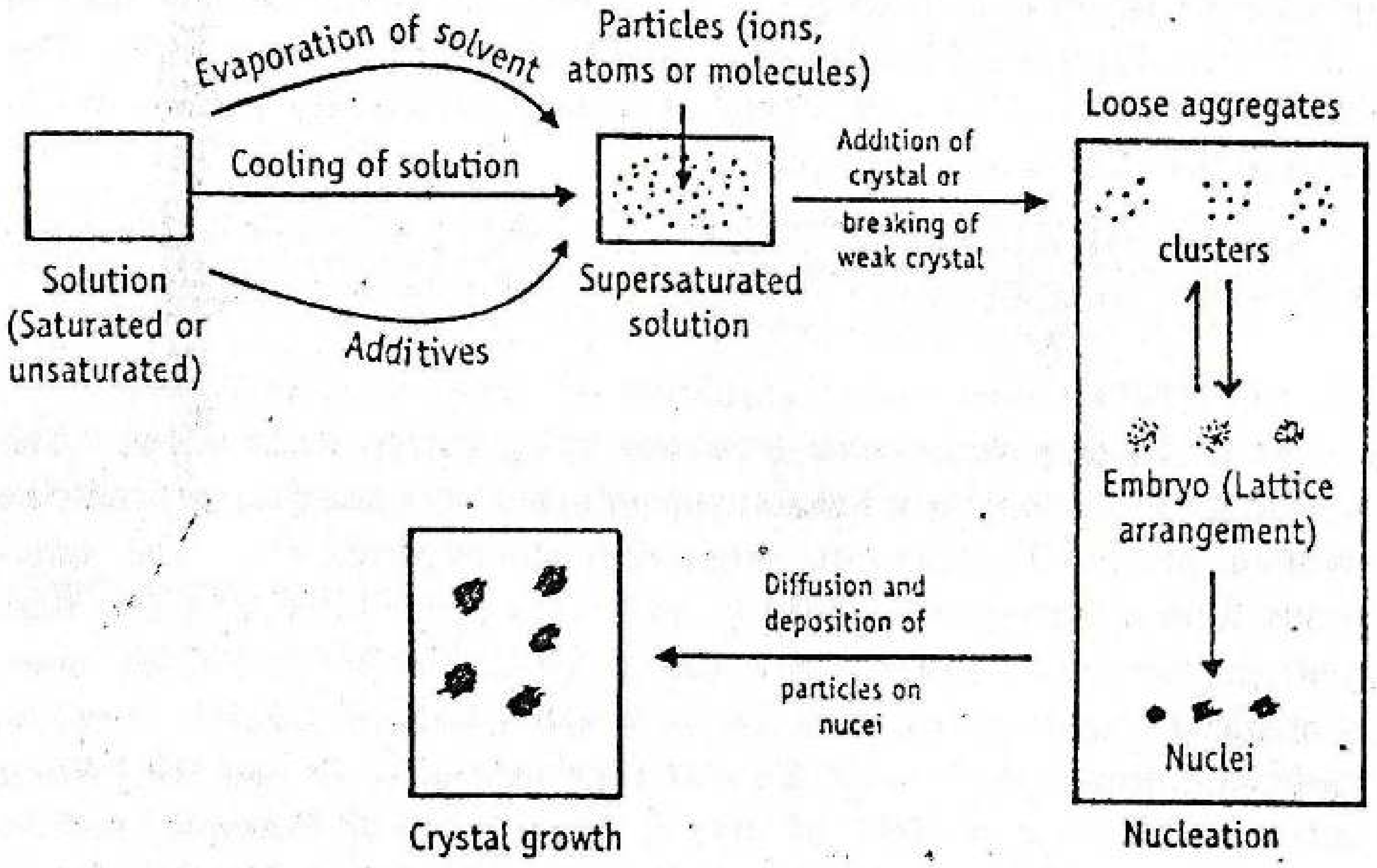


Figure 13-3. Mechanism of crystallization of solutes from a solution and the steps involved.

The formation of crystals from solution involves three steps.

(A) Supersaturation
(B) Nucleus formation
(C) Crystal growth

(A) Supersaturation : When the solubility of a compound in a solvent exceeds the saturation solubility, the solution becomes supersaturated and the compound may precipitate or crystallize. Supersaturation can be achieved through:

(1) Evaporation of solvent from the solution.
(2) Cooling of the solution, if the solute has a positive heat of solution.

(3) Formation of a new solute as a result of chemical reaction.
(4) Addition of a substance, which is more soluble in solvent than the solid to be crystallised.

In the absence of seed crystals, significant supersaturation is necessary to initiate the crystallization through formation of nuclei. The rate of separation, particle size, uniformity and distribution depend on two successive largely independent processes, namely, nucleation and growth of nuclei.

(B) Nucleation : *Nucleation* refers to the birth of very small bodies of a new phase within a homogenous supersaturated liquid phase.

Nucleation is a consequence of rapid local fluctuations at the molecular level when molecules or ions or atoms are in random motion in any small volume.

Initially several molecules or ions or atoms associate to form clusters. These are loose aggregates, which usually disappear quickly.

However, when enough particles associate to form an embryo, there is a beginning of the lattice arrangement and the formation of a new solid phase. In most of the cases, embryos have short lives and dissolve as soon as they form. An embryo may grow to such a size that it is in thermodynamic equilibrium with the solution.

The initially formed crystals are of molecular size, which are termed as *nuclei*.

On certain occasions, the nuclei grow in dimensions that are limited by the amount of material available and thus form crystals.

Several methods are available for nucleation. These are:

(1) Soft or weak crystals on impact with moving parts in a crystallizer can break into fragments which act as nuclei.
(2) Small crystals which are formed in the previous process are added to act as nuclei.
(3) In a supersaturated solution or under poor mixing, needle like structures are observed on the ends of crystals. These structures grow faster than the sides of the crystals and come out to give crystals of poor quality.

(C) Crystal growth : Crystal growth is a diffusion process and surface phenomenon. From solution, solute molecules or ions reach the faces of a crystal by diffusion. On reaching the surface, the molecules or ions must be accepted by the crystal and organized into the space lattice.

This phenomenon continues at the surface at a finite rate. Neither the diffusion nor the interfacial step will proceed unless the solution is supersaturated.

Mier's Supersaturation Theory

Mier's theory of supersaturation postulates a definite relationship between concentration and temperature at which crystals will spontaneously form in an initially unseeded solution.

According to it, the supersolubility curve represents the limit at which nucleus formation begins spontaneously and consequently the point where crystallization can start in the absence of any solid particle.

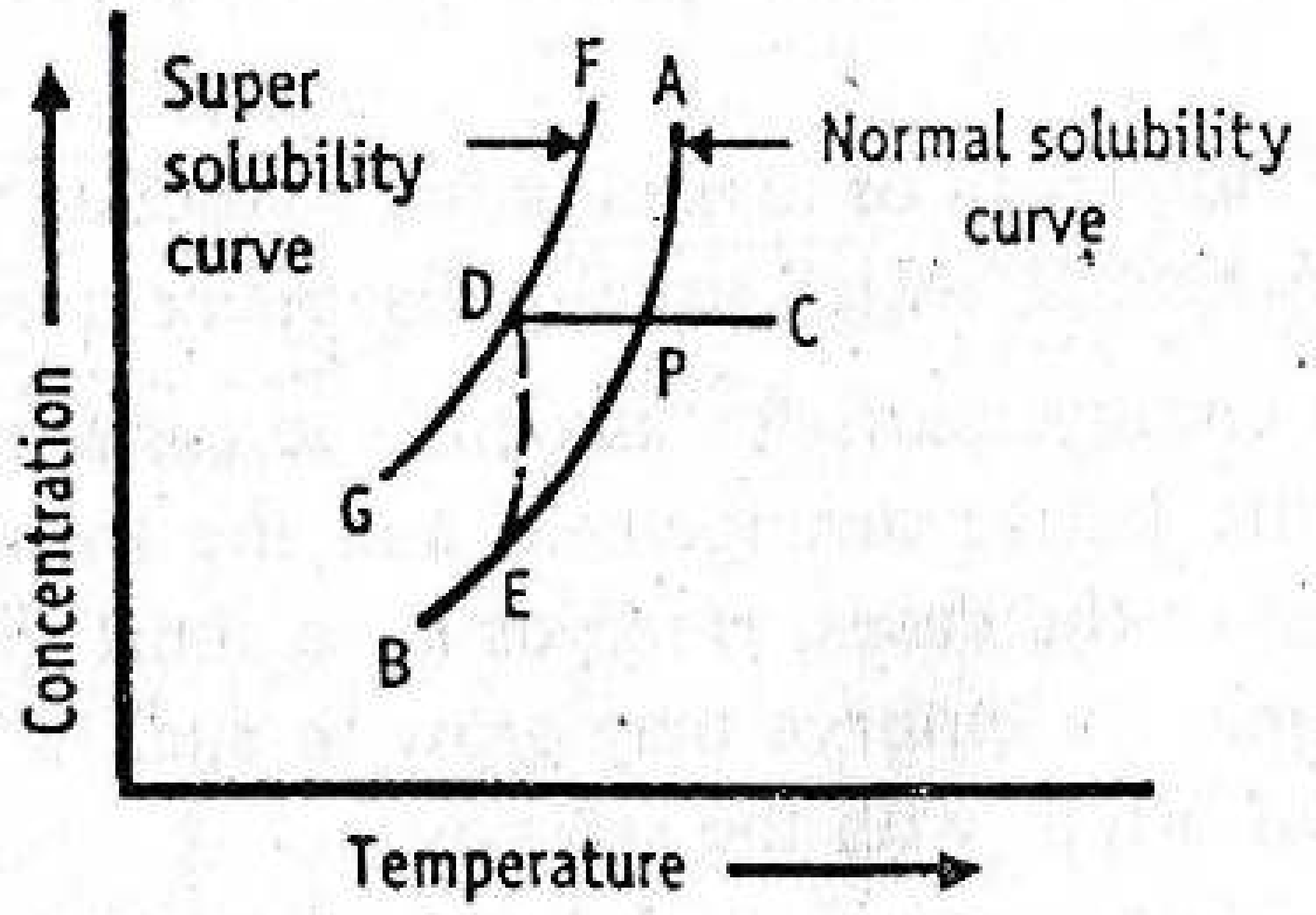


Figure 13-4. Mier's supersaturation theory, CPDE represent the path of cooling.

A plot of temperature vs. concentration of solute is shown in Figure 13-4. The curve AB represents the normal solubility. Any point on the curve represents the solute in equilibrium with the solvent. This is the maximum limit for the solubility of a substance. The curve FG represents the supersolubility, which is roughly parallel to the normal solubility curve. It represents the limit at which nucleus formation begins spontaneously. The region enclosed between these two curves AB and FG is referred to as *metastable state*, indicating that the system is unstable and undergoes changes.

The liquid may often be cooled a few degrees below its freezing point without crystallization taking place. Crystallization starts if this limit is exceeded. Consider a point C with a definite composition and temperature. On cooling this solution, crystallization is expected to start from point P, however, it does not happen.

According to Mier's theory, crystallization do not start at P but it takes place somewhere in the neighbourhood of the point D, when certain conditions are specified.

Mier states that under ideal conditions of crystallization nucleus formation starts at FG and crystal growth begins.

Then concentration of substance roughly follows the curve DE.

Conditions for obeying Mier's theory:

(1) The solute and the solvent must be pure.

(2) The solution must be free from solid solute particles.

(3) The solution must be free from foreign solid matter.

(4) The solution must be protected from entry of any particle.

(5) Soft or weak crystals must not form during the process.

(6) There should not be any fluctuations in maintaining the temperature.

Limitations:

(1) According to Mier's theory, crystallization starts at supersolubility curve. But general tendency is that crystallization takes place in an area rather than a line.

(2) If the solution is kept for longer periods, nucleation starts well below the supersolubility curve.

(3) If the solution is available in large volume, nucleation starts well below the supersolubility curve. This is because formation of nuclei depends on accidental collisions of molecules of solute. These collisions are more in large volumes than in small volumes.

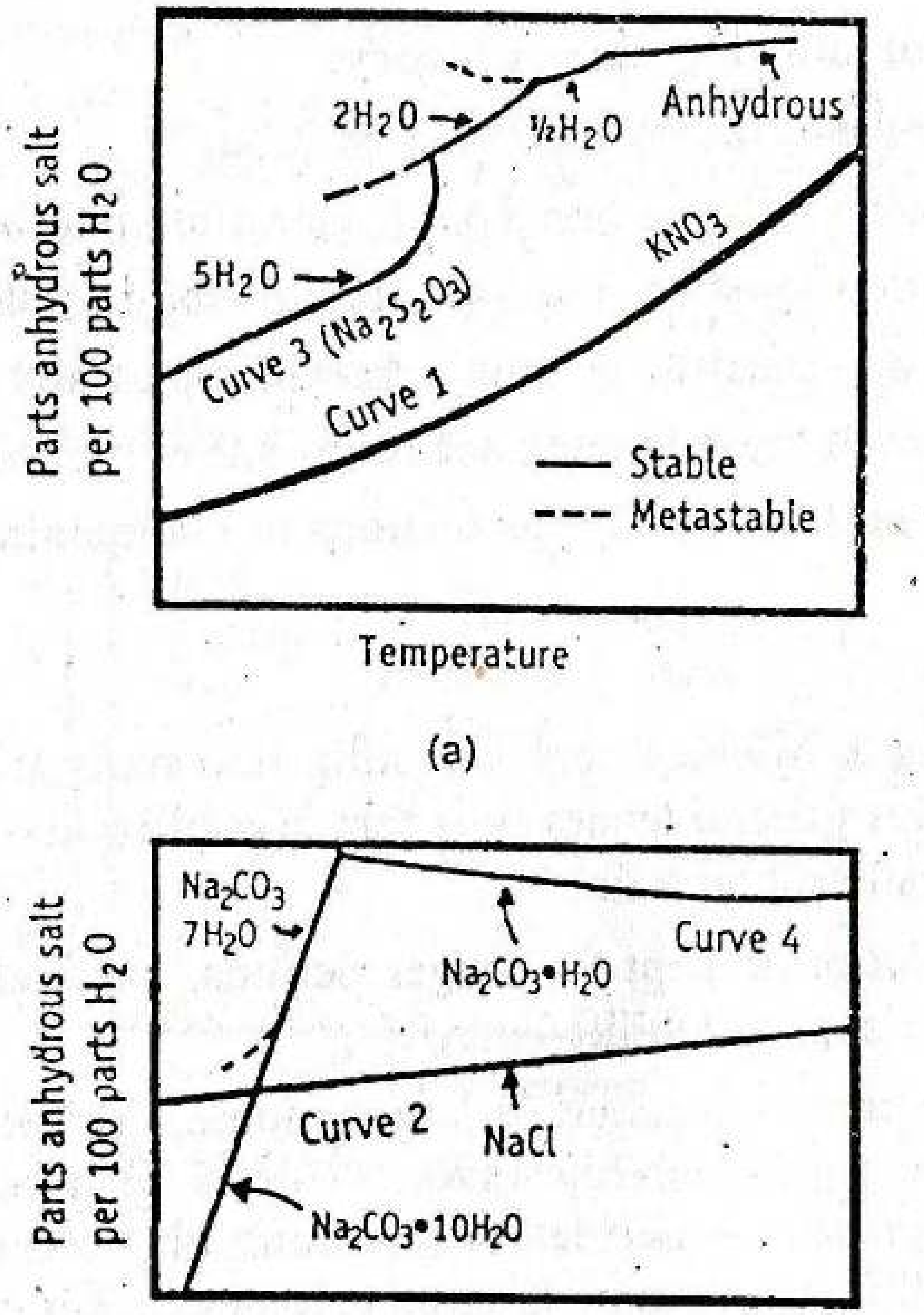
(4) Mier's theory is applicable when pure solute and pure solvent are used. In practice, it is impossible to get them in pure state.

(5) For crystallization, the solution must be stored for longer periods. During storage, millions of dust particles can enter. Nucleation can be initiated not only by solute molecules, but also by dust particles.

Solubility Curves

Solubility curves are useful in predicting the experimental conditions desired for crystallizing a substance. Since supersaturation is achieved by reducing the temperature, the influence of temperature on the solubility of a substance is important.

A substance dissolves and goes into solution, if the solution is not saturated. If the solution is supersaturated, crystallization takes place. Equilibrium is attained when the solution is saturated. The graph drawn by taking temperature on *x*-axis and solubility on *y*-axis gives the solubility curve, which represents stable equilibrium conditions. The metastable condition of the substance is also represented in dotted line. The solubility patterns of some substances are shown in Figures 13-5(a) and (b).



(a)

(b)

Figure 13-5. Typical solubility curves of certain substances.

The following conclusions can be drawn regarding the effect of temperature on the solubility.

(1) Curve 1 represents potassium nitrate. This is the most common type in which the solubility of a substance increases with temperature.

(2) Curve 2 represents sodium chloride. The solubility increases with increase in temperature, but to a marginal extent.

(3) Curve 3 represents sodium thiosulphate. Here solubility increases rapidly with temperature. But inflections are observed in the curve to represent different hydrates.

(4) Curve 4 represents sodium carbonate. This curve is unusual. Here solubility of sodium carbonate increases with temperature, if it is in hydrated form. Once the compound turns into monohydrate form, its solubility decreases.

EQUIPMENT

In commercial practice, it is highly desirable to have the product not only of uniform size, but also of a particular size distribution. It is necessary to control the formation of nuclei, since the number of nuclei controls the size of crystals. Once the nuclei are formed, they start growing.

Depending on the conditions of crystallization, it is possible to control or modify the nature of the crystals obtained.

(1) If the solution is cooled slowly, just above saturation point, crystals of larger size are formed since the number of nuclei is less.

(2) If the solution is chilled rapidly, a crop of small crystals is formed, since rapid cooling increases the degree of supersaturation resulting in a large number of nuclei.

(3) When polymorphs exist, careful temperature control and seeding with the desired crystal form are necessary.

(4) The habit or shape of a given form is often highly dependent on:
   (a) impurities in solution,
   (b) pH,
   (c) rate of stirring,
   (d) rate of cooling,
   (e) solvents.

Very rapid rate of crystallization can result in the entrapment of impurities in the crystals.

Crystallization equipment is classified according to the method employed for producing the supersaturated solution. Some large-scale crystallization equipment are discussed below.

Agitated Batch Crystallizer

Principle : In agitated batch crystallizer, saturated solution is made supersaturated by reducing the temperature. The crystals are formed from the supersaturated solution. Agitation of the solution facilitates the production of uniform size crystals.

Construction : The construction of an agitated batch crystallizer is shown in Figure 13-6. It consists of a cylindrical container with a conical bottom. A propeller is fixed centrally, which rotates on its own axis with the help of a motor. Pipes made up of good material for conducting heat are run from right bottom to left top of the crystallizer.

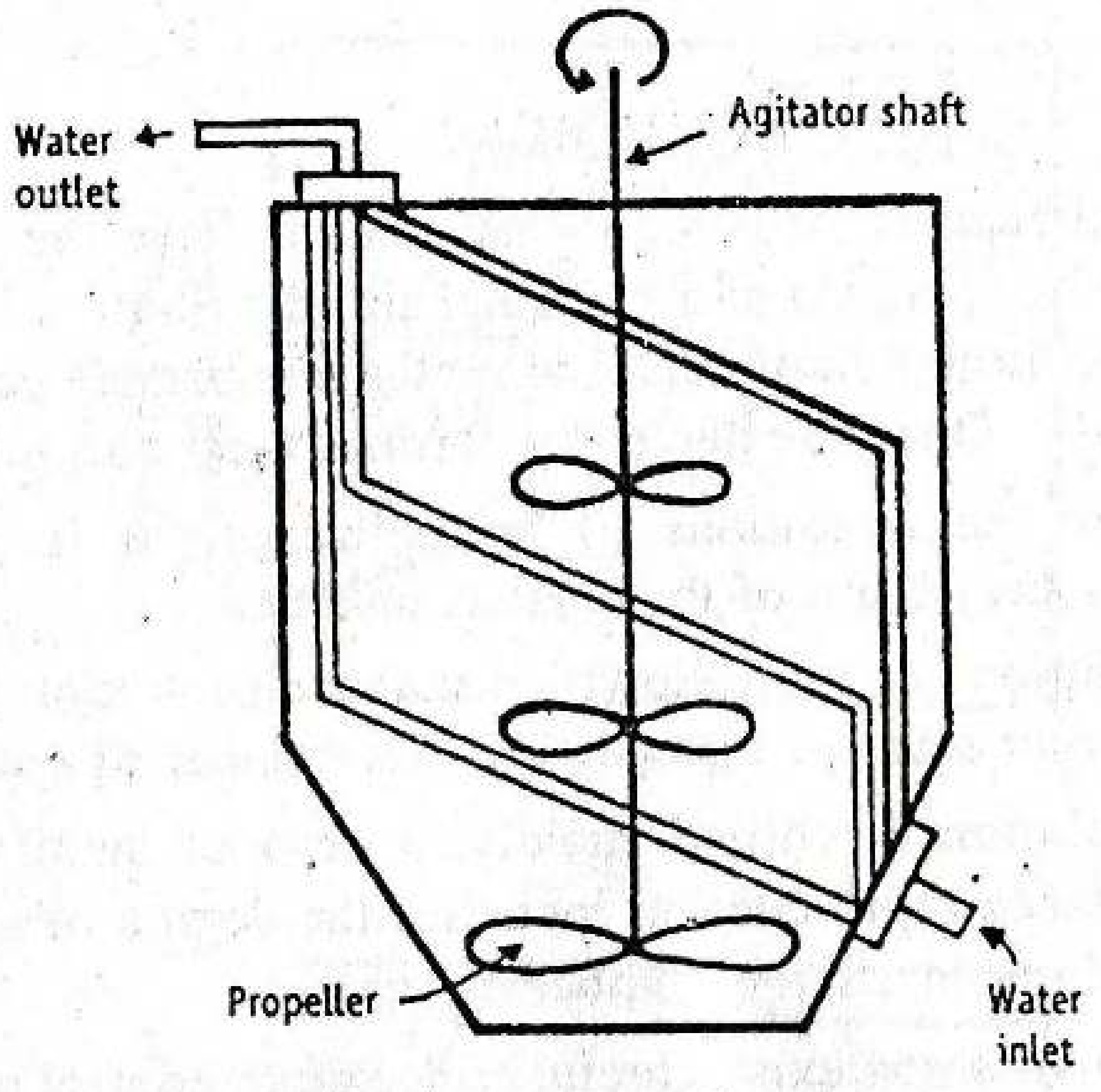


Figure 13-6. Construction of agitated batch crystallizer.

Working : Solution to be subjected for crystallization is placed in the crystallizer. Cold water is passed through the pipes continuously. Due to cooling. the solution becomes supersaturated and crystals are formed. The propeller is allowed to rotate, which serves two purposes. Firstly, it increases the rate of heat transfer thereby helps in maintaining the temperature of the solution almost uniform. Secondly, it keeps fine crystals in suspension, which facilitates them to grow uniformly. Otherwise, large crystals or aggregates may form. The crystals are collected from the bottom by a suitable mechanism for the separation of mother liquor.

Advantages : In agitated crystallizer, crystals formed are more uniform and also more fine compared to older crystallizer such as tank crystallizer.

Disadvantages : It is a batch or discontinuous equipment. Solubility is least at the surface of the cooling coils. Hence crystal growth is most rapid at this point and the coils rapidly build up with a mass of crystals that decreases the rate of heat transfer.

Swenson Walker Crystallizer

Principle : Crystallization is induced by passing the cold water in a direction opposite to the flow of hot concentrated solution. This results in supersaturation and subsequently crystals are deposited. Agitation prevents the accumulation of crystals on the cooling surface. The crystals are simultaneously separated from the mother liquor and therefore it can be used as a continuous process.

Construction : The construction of a Swenson Walker crystallizer is shown in Figure 13-7. It is a linear type and consists of a long open trough about 0.6 metres wide and 3 metres long with a semi-cylindrical bottom (side view of Figure 13-7). The trough is welded with a water jacket externally. Long pitch spiral scrapper is fixed as close to the bottom of the trough as possible (top view of Figure 13-7). Spiral scrapper rotates on its own-axis with the help of a motor. For higher capacity, maximum of four such units are joined together. For still higher capacities, several such sets are placed one above the other. In this arrangement, the solution flows from one set to its below set.

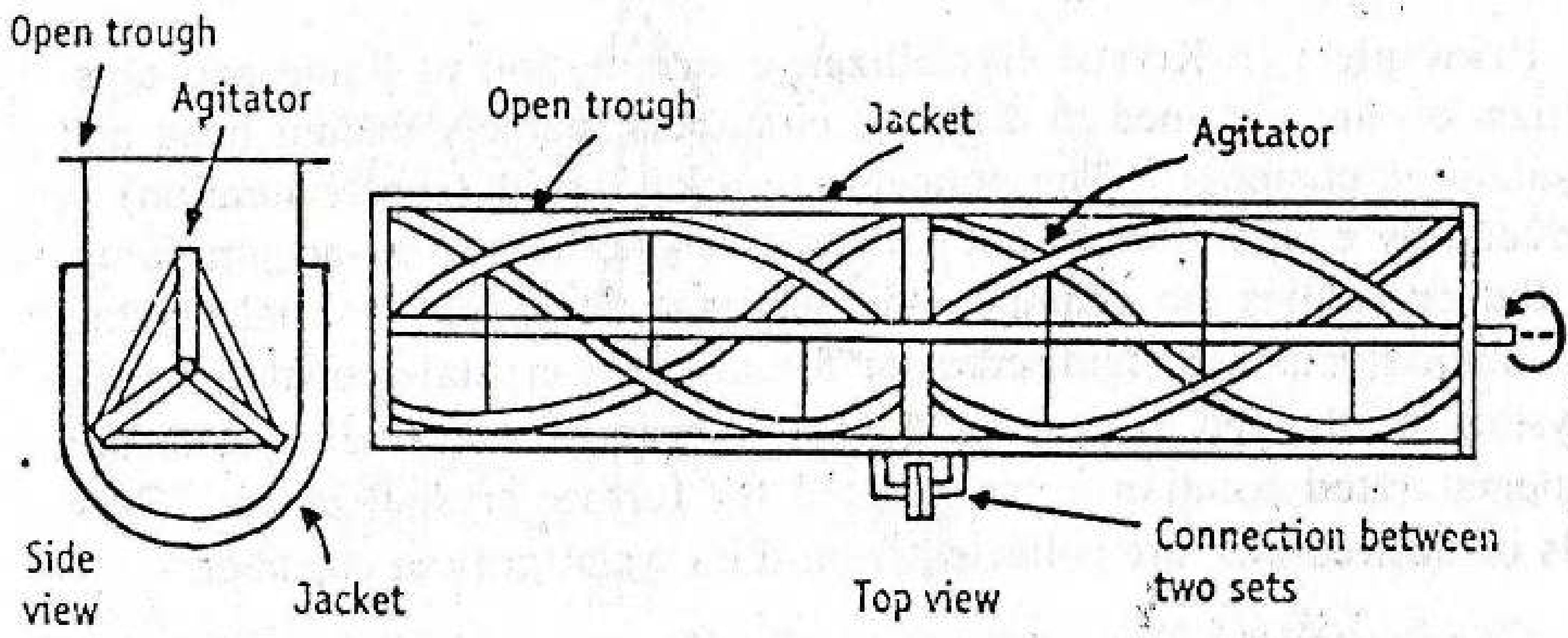


Figure 13-7. The construction of Swenson Walker crystallizer.

Working : The hot concentrated solution to be crystallized is fed at left side of the trough. Cooling water enters through (other end) right side in the jacket. Due to cooling of the hot solution, supersaturation is achieved and crystals begin to form. If necessary, the size of crystals can be controlled by injecting an extra amount of cooling water into the selected sections. Spiral scrapper rotates on its own-axis at a speed of 7 revolutions per minute. It helps in agitating the mixture and conveying of the crystals. It also prevents the accumulation of crystals on the cooling surfaces by lifting them. This results in a suspension, which allows the crystals to grow individually. Thus aggregation is prevented.

Draining table is attached to one end of the crystallizer. Mother liquor and crystals together over flows into the draining table. While crystals are retained, the mother liquor is sent back to crystallizer. The wet crystals are conveyed to a centrifuge.

A screw conveyor can also be used in place of the draining table. Screw conveyor with a slight inclination lifts the crystals from solution and delivers to a centrifuge. Mother liquor overflows at a convenient point.

Advantages : (1) Large saving in floor space, material and labour costs can be achieved in Swenson Walker crystallizer.

(2) It is a continuous process.

(3) Crystals of uniform size and free from inclusions or aggregations can be obtained.

Disadvantage : The scrapper may break the crystals to a little extent, while agitating the suspension.

Krystal Crystallizer

Principle : In Krystal crystallizer, concentration of liquid and crystallization are obtained in different chambers, namely vapour head and crystalling chamber. The concentration of liquid (supersaturation) is induced by evaporation of hot solvent with the help of a vacuum pump. In the crystallization chamber, the supersaturated solution and crystals are maintained in a fluidised state for uniform crystal growth. As the crystals of desired size settle down by gravity, the fine crystals and supersaturated solution is recirculated for further crystallization. Crystals of desired size are collected from the crystal growth chamber.

Construction : The construction of a Krystal crystallizer is shown in Figure 13-8. It consists of a vapour head and crystallizing chamber. Vapour head consists of a long tube, which extends almost to the bottom of crystallizing chamber. Other end of vapour head is connected to condenser and vacuum pump. A pump is provided which allows the feed to enter vapour head. On its way to vapour head, a heater is provided.

Working : Solution is pumped, which passes through the heater. The hot solution enters the vapour head. Because of reduced pressure, the hot solution undergoes flashing, which results in the formation of solvent vapour and supersaturated solution. Vapour is removed by suction pump. Supersaturated solution passes through long tube below. The operation is controlled in such a way that crystals do not form in the vapour head but should form in the crystallizing chamber.

The crystallizing chamber consists of a bed of crystals suspended in an upward flowing stream of liquid. Supersaturated liquid flows through the bed of crystals, which are maintained in a fluidized state. A uniform temperature is thereby attained. There is a continuous gradation of crystals in the chamber. Coarse crystals settle at the bottom, while fine crystals remain above coarser ones. Very fine crystals overflow through the liquid and enter into the re-circulating system, which then combine with fresh feed. From time to time, coarse crystals are taken out through the opening at the bottom of the chamber.

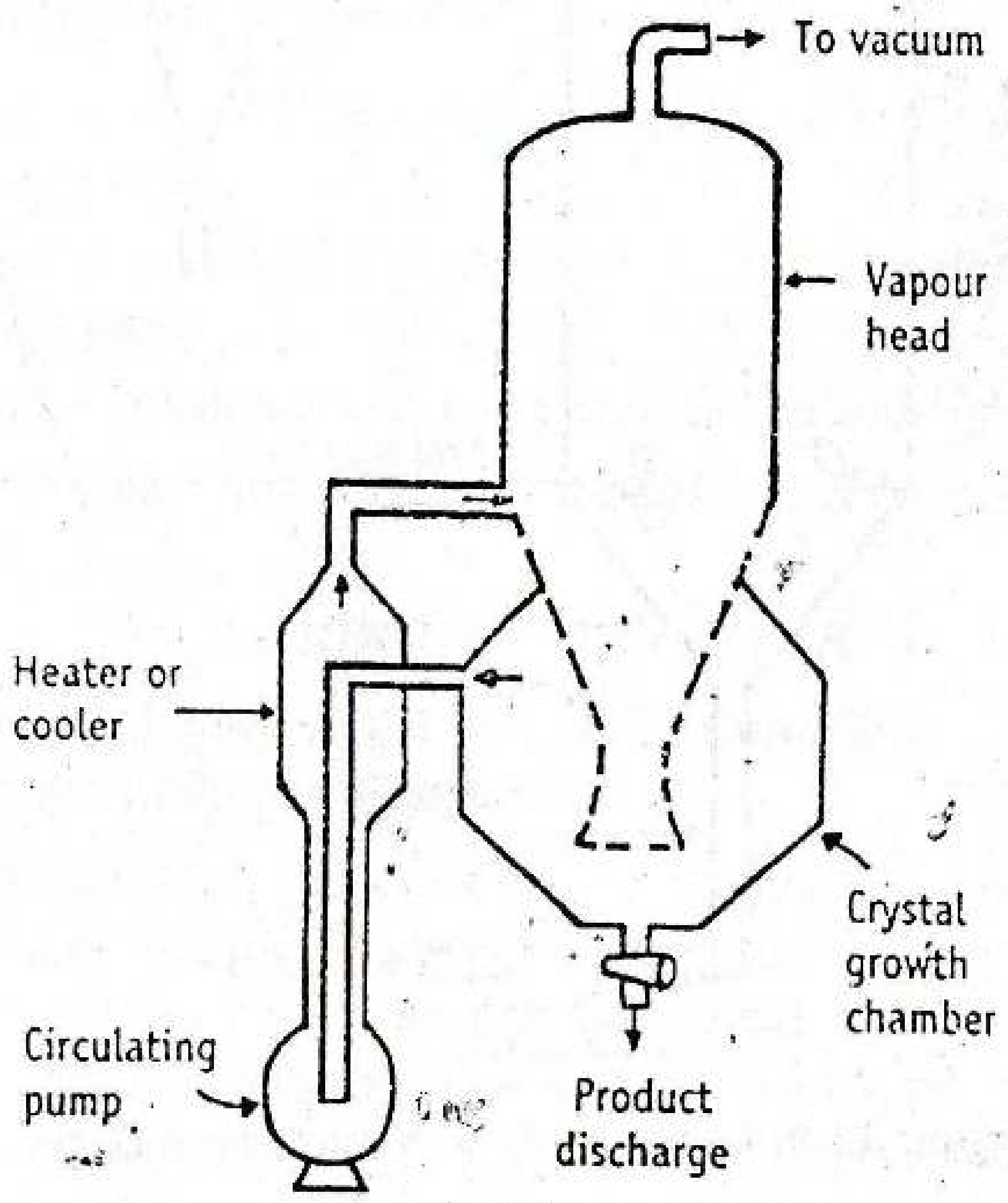


Figure 13-8. Krystal crystallizer.

Uses : Krystal crystallizer is used for crystallisation of sodium chloride and magnesium sulphate.

Advantages : (1) Krystal crystallizer is preferred when large quantities of crystals of controlled sizes are required.

(2) This crystallizer is available in very large sizes with a body up to 4.5 metres diameter and 6.0 metres height.

Vacuum Crystallizer

Principle : In vacuum crystallizer, supersaturation is obtained by adiabatic evaporative cooling. When warm saturated solution is introduced into the crystallizer, due to high vacuum the solution undergoes flashing. A part of the solvent gets evaporated, thereby causing cooling of the solution. From the resulting supersaturation, crystals are produced.

Construction : The construction of a vacuum crystallizer is shown in Figure 13-9. Vacuum crystallizer is a cylindrical body with a conical bottom. A condenser is attached to the crystallizer with a vacuum pump in between. The bottom of the crystallizer is attached to a discharge pipe. Internally, the body of the crystallizer can be lined with acid resistant material such as lead or rubber. Two propellers are placed above discharge pipe to prevent short circuit of the feed (to the discharge pipe).

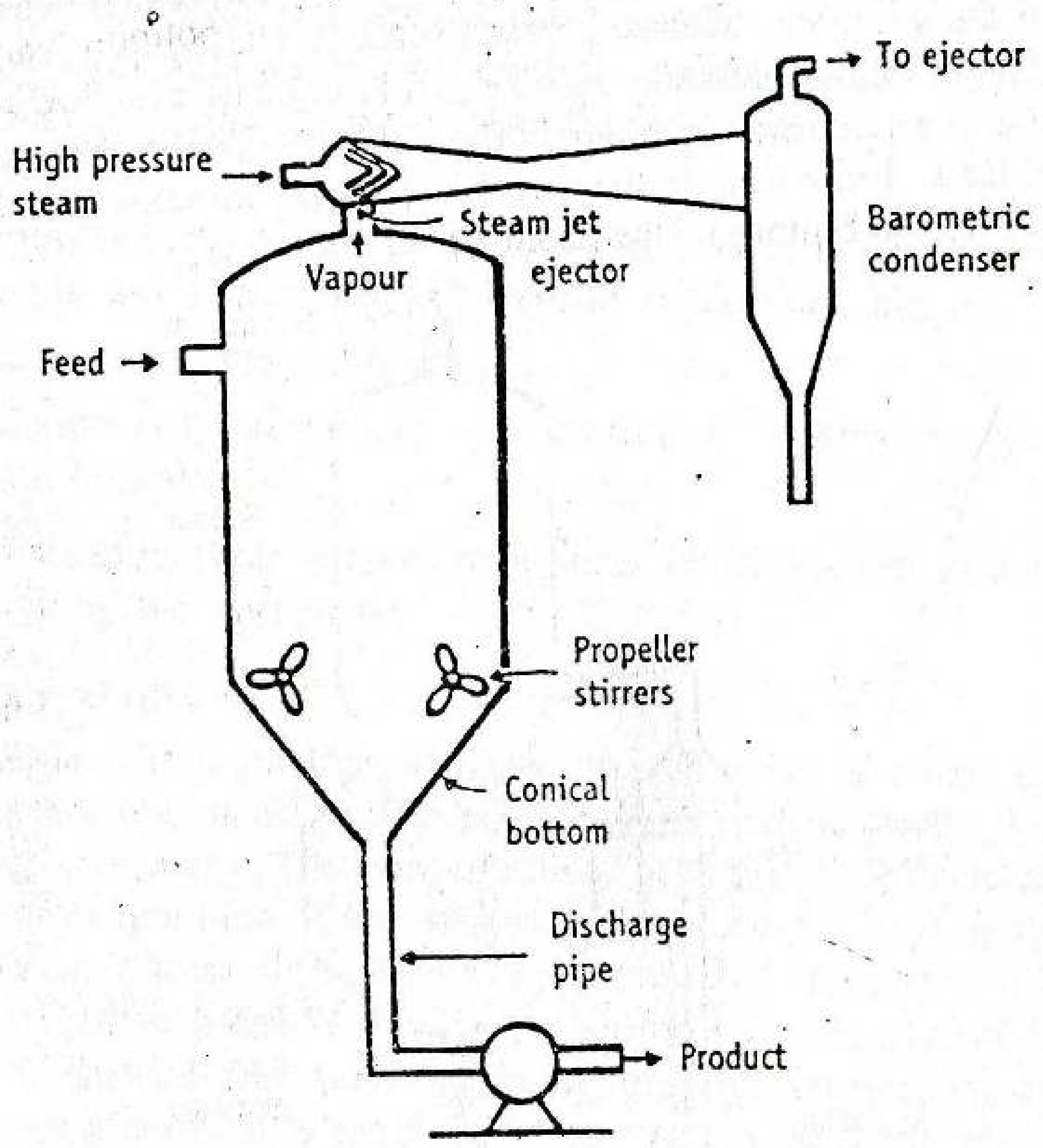


Figure 13-9. Construction of vacuum crystallizer.

Working : High vacuum is created using a vacuum pump. The vacuum so created must correspond to a boiling point of the solution, but lower than the feed temperature. Hot saturated solution is fed into the crystallizer at a convenient point. Solution undergoes flashing, which results in evaporation of solvent. This process is allowed adiabatically so that the crystallizer body is cooled. The resultant cooling causes supersaturation and crystallization. The evaporation of the solvent enhances the yield. Flashing of the solution in the crystallizer leads to ebullition, which keeps the crystals in suspension, until they become large enough to fall into the discharge pipe. The propellers mix the contents thoroughly and prevent the contents reaching the discharge pipe without flashing. With the help of pump, the product is collected and subjected to filtration or centrifugation to obtain crystals. The filtrate returns to the feed.

Uses : Vacuum crystallizer is suitable for thermolabile substances, due to low temperature conditions.

Advantages : (1) Vacuum crystallizer is very simple without any moving parts.

(2) Corrosive materials can be used, as inner surface can be made acid resistant.

(3) It can be constructed as large size as desired.

(4) It can be operated either batch wise or continuously.

CAKING OF CRYSTALS

Caking can be defined as the process of formation of clumps or cakes when crystals are improperly stored.

After crystallization, the crystals are required to be stored in bulk either for further use or for transportation or for the formulation of dosage forms. The crystals must retain good flow properties during storage. For example, they can pass freely from hopper to die in case of tablet punching. During storage, crystals may tend to form a cake. This problem is serious in case of small packages than in bulk packages. In some cases, the pressure of a thumb can easily break the lumps, but considerable pressure is required to break the cake in some other cases.

Critical humidity is the humidity above which crystals absorb moisture and below which they do not absorb moisture.

When a crystal is placed in contact of air, whose humidity is below the critical humidity, the crystal remains dry. On the other hand, if the air contains more moisture than critical humidity, the crystal absorbs moisture.

The crystals get a saturated film on the surface by adsorbing moisture. So formed saturated solution concentrates at the points of contact by capillary forces. When water evaporates or when the temperature decreases, crystallization of solute takes place to form a solid bridge.

Factors Affecting Caking

Size of the crystals : Crystals of larger size contain more void spaces. On the other hand, crystals of smaller size contain less void space and possess more points of contact. The more the points of contact, the higher will be the rate of caking. Hence, smaller sized particles tend to cake more than the larger particles.

Shape of the crystals : Spherical particles possess the least possible points of contact. The points of contact increase as the crystal shape deviates from spherical shape. Hence, distorted crystals tend to cake more than the spherical crystals.

Humidity : The higher the humidity of atmosphere to which crystals are exposed, more will be the rate of caking.

Time of exposure : The higher the time of exposure, the more will be the caking, provided the exposed atmosphere has humidity more than critical humidity.

Impurities in crystals : The crystals can be coated with the impurities derived from mother liquor. This may increase or decrease critical humidity. Once the critical humidity changes, the property of caking also changes. For example calcium chloride and magnesium chloride are the impurities for sodium chloride crystals to alter it's critical humidity.

Melting point of crystals : Melting point of certain crystals is near room temperature, crystals may melt. Then solidification by fusion of the melt leads to caking.

Temperature fluctuations : When temperature is increased, melting of the crystals takes place. Subsequent decrease in temperature leads to solidification. Therefore, temperature fluctuations cause variations in the solubility, which may lead to caking.

Prevention of Caking

(1) Crystals must be more spherical in shape, with the least points of contact.

(2) Crystals must be larger in size with more voids and must be of a narrow size distribution.

(3) Crystals must have highest possible critical humidity.

(4) Crystals must be coated with powdery inert material to prevent absorption of moisture. For example, table salt is coated with magnesia or tricalcium phosphate. Similarly, flake calcium chloride is coated with anhydrous calcium chloride.

QUESTION BANK

Each question carries 2 marks

1. Define crystal lattice and crystal habit.
2. Enumerate the characteristics of crystals.
3. Define crystal and critical humidity.
4. Enumerate different types of crystals.
5. Name a suitable crystallizer for the following.
   (a) to get large sized crystals.
   (b) to crystallize large quantity of substance.

Each question carries 5 marks

1. Describe the working of agitated batch crystallizer.
2. What is caking of crystals? List the factors affecting and preventive measures for caking.
3. Describe the salient features of vacuum crystallizer.
4. Describe different methods by which super-saturation can be brought about.
5. Draw the solubility curves and explain its relevance in crystallization.
6. Describe the operation of a suitable crystallizer to produce large crystals.
7. What are the different forms of crystals?
8. What are the conditions to be taken during crystallization to obtain large sized crystals?
9. Describe how nucleation and crystal growth take place during crystallization.
10. What are the pharmaceutical applications of crystallization?

Each question carries 10 marks

1. Discuss the Mier's super-saturation theory of crystallization. What are the limitations of the Mier's theory?
2. Explain the principle, construction, working and advantages of vacuum crystallizer.
3. Giving neat diagram, describe the construction and working of Krystal crystallizer. Write its advantages and applications.
4. Draw a neat labelled diagram of Swenson Walker crystallizer. Discuss the construction, working, advantages and disadvantages.

14

Drying

Theory of Drying
Classification of Drying Equipment
Equipment

Drying is defined as the removal of small amounts of water or other liquid from a material by the application of heat.

The liquid medium may be removed from the solids mechanically by a filter press or centrifuge or thermally by vaporisation. It is cheaper to remove liquid by mechanically than thermally. Therefore, it is advisable to reduce the liquid as much as possible before subjecting to the drying process.

Drying and evaporation are distinguishable by the relative quantities of liquid removed from the solid. In evaporation, the product obtained is either concentrated solution or suspension or wet slurry. In drying, dry solid is the product.

The liquid to be vaporised may remain:

- on the surface of the solid, as in drying of salt crystals,
- entirely inside the solid, as in solvent removal from a sheet of polymer,
- partly outside and partly inside, as in case of solvent removal from pharmaceutical powders.

Drying is possible when the environment is unsaturated with the water vapour. Hence, humidity in the environment is an important determinant for drying of the solids. Though several methods are available, thermal methods and freeze drying technique (nonthermal method) are included here. This chapter deals with the theoretical principles and equipment employed for drying.

Applications

Preparation of bulk drugs : In the preparation of bulk drugs, drying is the final stage of processing. A few examples are:

- dried aluminium hydroxide
- spray dried lactose
- powdered extracts

Drying step is essential after certain operations such as crystallization and filtration.

Preservation of drug products : Drying is necessary in order to avoid deterioration. A few examples are:

Crude drugs of animal and vegetable origin	- chemical decomposition
Blood products, skin, tissue	- microbial growth
Synthetic and semisynthetic drugs	- chemical decomposition
Effervescent tablets (aspirin, penicillins)	- chemical decomposition

Improved characteristics : Drying produces materials of spherical shape, uniform size, free flowing and enhanced solubility. Some specific areas of importance are:

(1) Granules are dried to improve the fluidity and compression characteristics. These are essential for the production of tablets and capsules.

(2) Viscous and sticky materials are not free flowing. Drying modifies these characteristics. Examples are male fern extract, malt extract and oleoresin.

Improved handling : Removal of moisture makes the material light in weight and reduces the bulk. Thus cost of transportation will be less and storage will be efficient. If moisture is present, size reduction of drugs is difficult. Drying reduces the moisture content.

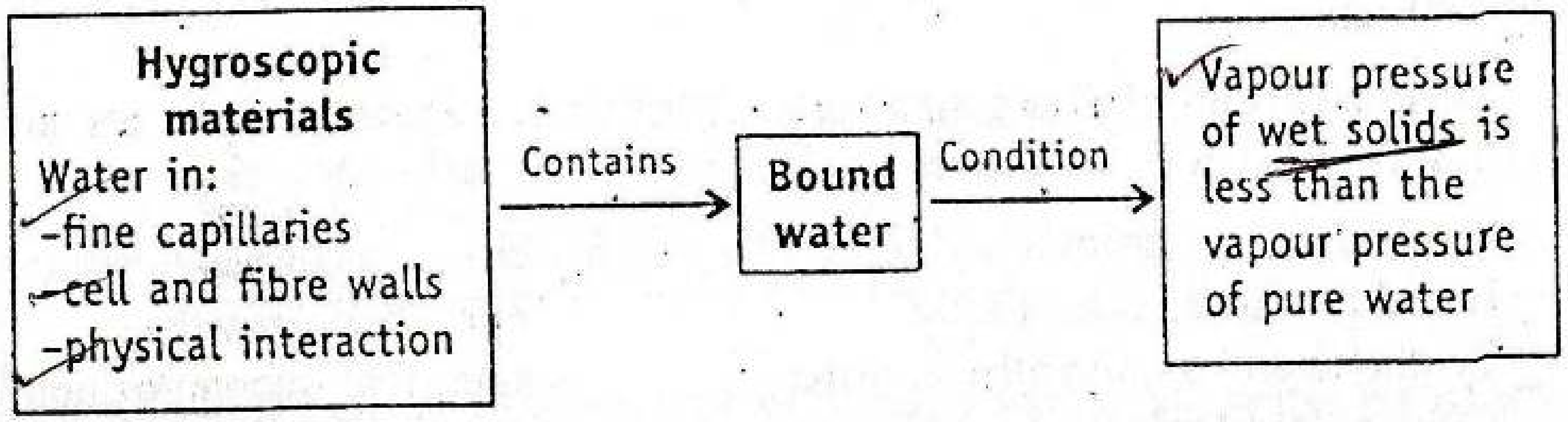
THEORY OF DRYING

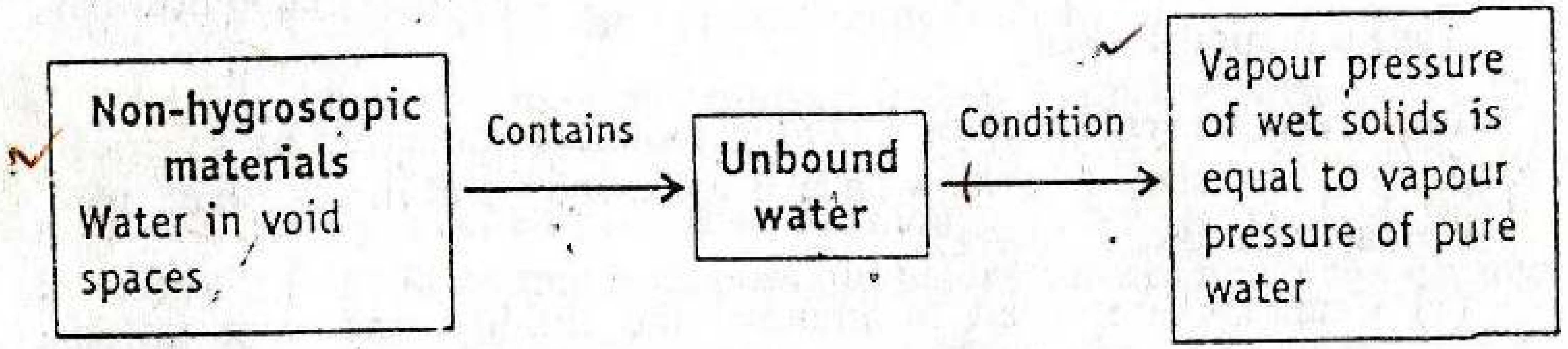
In a wet solid mass, water may be present as bound water and unbound water.

Bound water (moisture) is the minimum water (moisture) held by the material that exerts an equilibrium vapour pressure less than the pure water at the same temperature.

Unbound water (moisture) is the amount of water (moisture) held by the material that exerts an equilibrium vapour pressure equal to that of pure water at the same temperature.

Unbound water exists largely in the voids of the solid. Thus, in a non-hygroscopic material, all the liquid is unbound water. In a hygroscopic material, the unbound moisture is the liquid in excess of the equilibrium moisture content, corresponding to saturation humidity. Substances containing bound water are often called *hygroscopic substances.* The distinction between bound and unbound water depends on the material itself. These are described below.





Heat must be transferred to the material to be dried in order to supply the latent heat required for vaporisation of the moisture. Water diffuses through the material to the surface and subsequently evaporates into the air stream. Thus drying involves both heat transfer and mass transfer operations simultaneously.

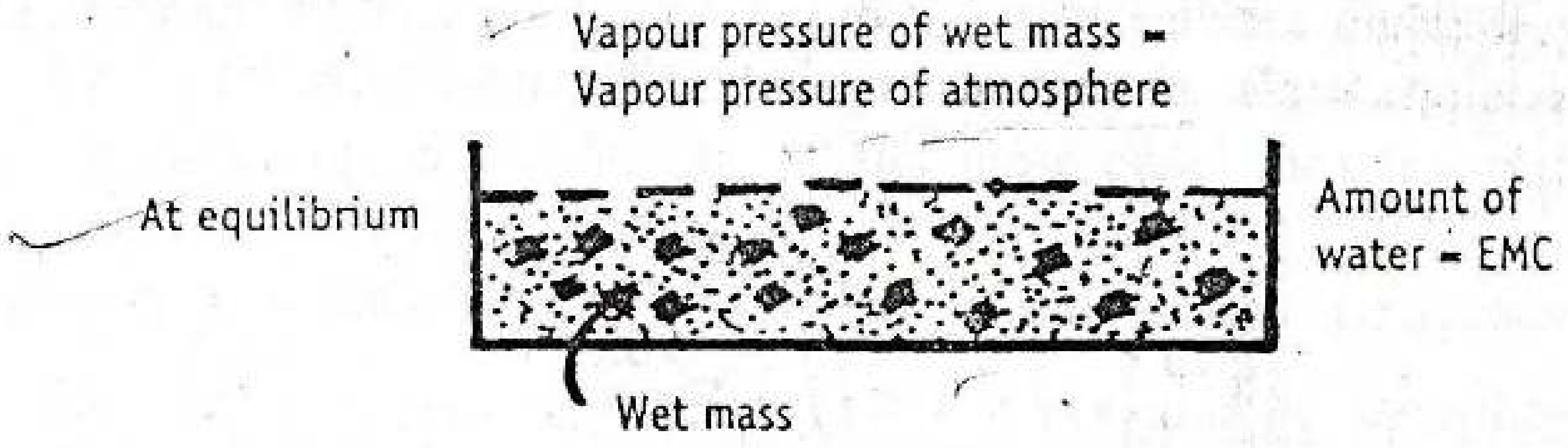
Theory can be discussed in two heads namely equilibrium relationships and rate relationships.

Equilibrium Relationships

Air ~~of constant temperature and humidity is~~ passed over the wet solid. After a long exposure, equilibrium is reached. On attaining equilibrium, further exposure will not alter moisture content in the solid. At this stage, vapour pressure of the wet solids is equal to that of the surrounding atmosphere. Hence there is no driving force for mass transfer.

Equilibrium moisture content (EMC) : It is the amount of water present in the solid which exerts ~~a vapour~~ pressure equal to the vapour pressure of the atmosphere surrounding it.

Equilibrium moisture content in a wet mass is shown below.

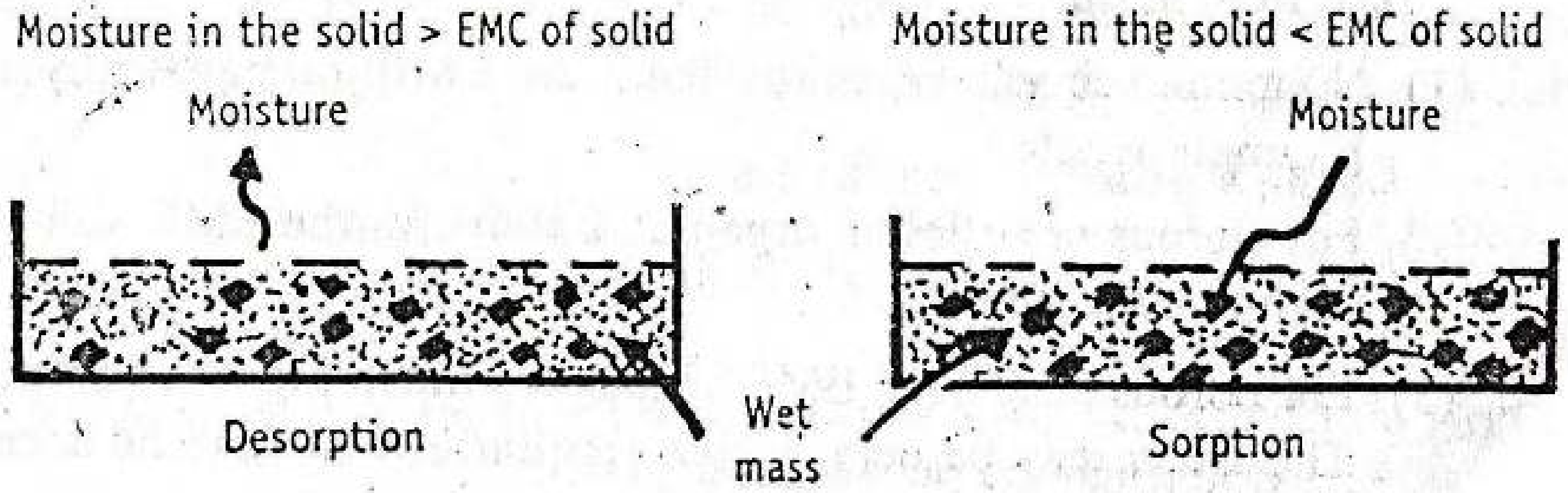


The characteristics of air such as temperature and humidity are maintained constant. Depending on these conditions, the solids may absorb or lose moisture.

(a) When air (of constant temperature and humidity) is continuously passed over the solid containing moisture more than EMC, then solid loses water continuously till EMC is reached. This phenomenon is known as *desorption.*

(b) When air (of constant temperature and humidity) is continuously passed over the solid containing moisture less than EMC, then solid adsorbs water continuously till EMC is reached. This phenomenon is known as *sorption.*

The behaviour of desorption and sorption is shown below. From the above observations it is clear that, material can be dried up to EMC but not below it.



At a given temperature and humidity of air

Measurement of EMC : The EMC of a material can be determined as follows. The solid samples are placed in a series of closed chambers such as desiccators. Each chamber consists of solution (desiccant), which maintains a fixed relative humidity in the enclosed air spaces. In other words, the solid samples are exposed to several humidity conditions. The exposure is continued until the material attains a constant weight (equilibrium conditions). The difference in the final and initial weights gives the moisture content.

Equilibrium moisture curve is drawn by taking relative humidity (%) on x-axis and moisture content on y-axis (Figure 14-1).

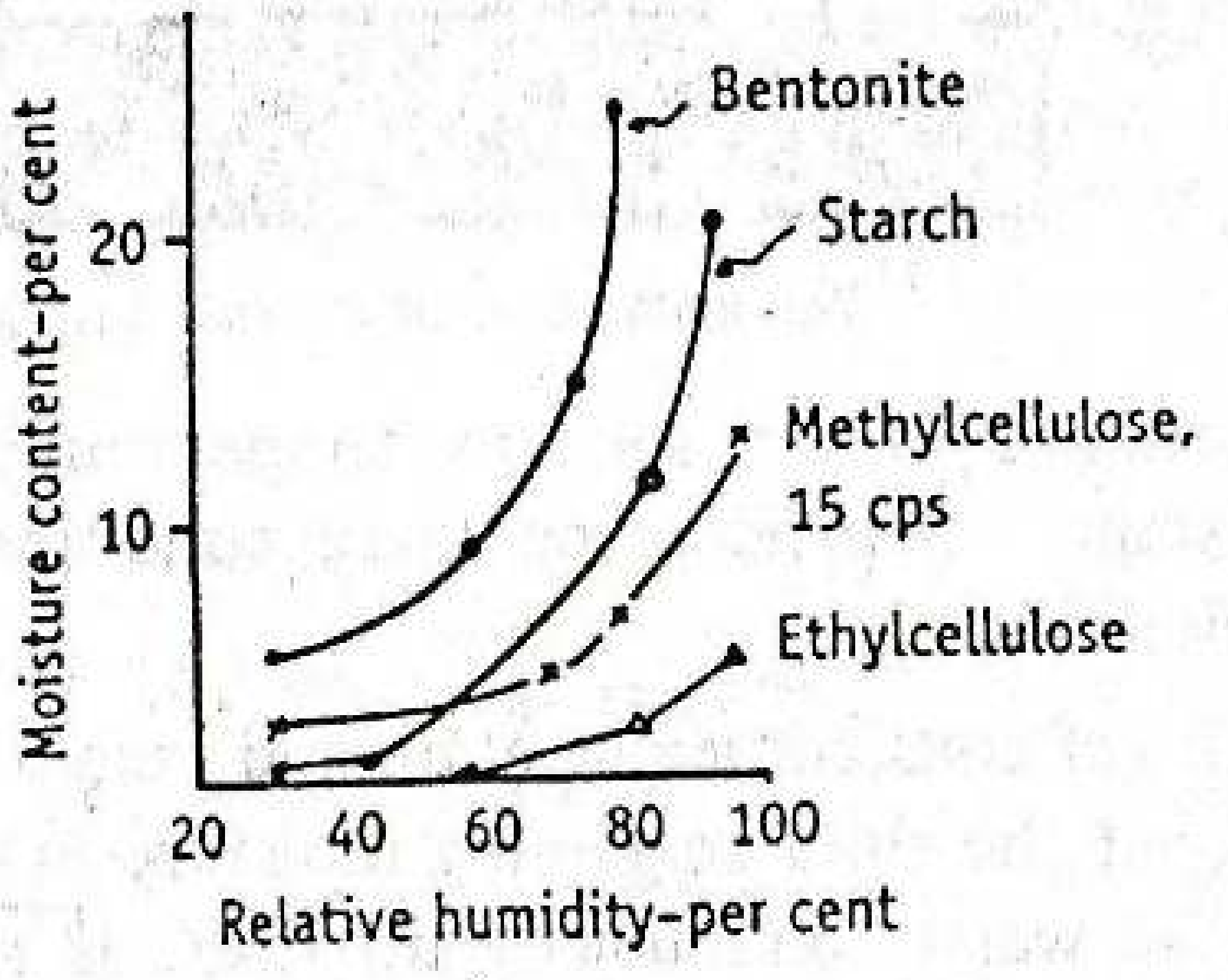


Figure 14-1. EMC curves for tabletting material.

Application of EMC : The EMC curve permits the selection of the experimental conditions to be used for drying of the product. Drying should be stopped when the moisture content reaches the level of the EMC under the exposed conditions. Over drying can be avoided.

Factors affecting EMC : EMC values vary depending on a number of factors.

Nature of material:

(1) Nonporous insoluble solids have an EMC of practically zero. Example is talc.

(2) For fibrous or colloidal organic substances, the EMC values are high and variable.

(3) For porous solids, the EMC values are much higher and variable. The water may be held in fine capillaries that have no access to the surface. The dissolved solid may reduce the vapour pressure and water may be molecularly bound.

Nature of air:

(1) For air of zero humidity, EMC of all materials is zero.

(2) As the temperature of air increases, the EMC of solid decreases.

EMC of solids is a constant for a given temperature and humidity of air. If the equilibrium curves (Figure 14-1) are continued up to 100% RH, the moisture content so obtained (EMC with saturated air) is the least moisture at which the material can exert a vapour pressure as high as that exerted by liquid water at the same temperature.

Free moisture content (FMC) : *Free moisture content* (FMC) is the amount of water that is free (easy) to evaporate from the solid surface.

Under the conditions of saturation humidity (100% RH), the EMC is the minimum moisture content. Under these conditions the water must be bound water which is minimum at that temperature. The remaining is unbound for which the FMC for a given condition can be written as:

Free moisture content (FMC) = total water content − equilibrium moisture content (EMC)

The distinction between free and equilibrium moisture depends on the drying conditions.

Rate Relationships

Rate relationships can be studied by considering a simple model, which mimic the conditions of a dryer. In this model, wet slab of material of sufficiently high moisture content to be dried is placed in a tray whose bottom and sides are insulated. The air is blown over the solid under constant drying conditions (air velocity, temperature, humidity and pressure are maintained constant). The superficial water diffuses through the surrounding stationary air film and is carried away rapidly by the moving air stream.

Periodically the slab is weighed. The difference in the weights of two successive periods gives the loss of moisture content, i.e., amount dried. The moisture present in the solid can be expressed on a wet weight or dry weight basis. Then the following calculations are made:

$$\%\ \textit{Loss on drying (LOD)} = \frac{\text{mass of water in sample (kg)}}{\text{total mass of wet sample (kg)}} \times 100$$

$$\%\ \textit{Moisture content (MC)} = \frac{\text{mass of water in sample (kg)}}{\text{mass of the dry sample (kg)}} \times 100$$

$$\textit{Drying rate} = \frac{\text{weight of water in sample (kg)}}{\text{time (h)} \times \text{weight of the dry solid (kg)}}$$

Drying rate is plotted against the midpoints of the time period. Similarly midpoints of the moisture content values can be plotted.

From the data obtained by the above experiment, a graph is plotted by taking FMC on x-axis and drying rate on y-axis. The curve so obtained (Figure 14-2) is called *drying rate curve*. It represents different changes during drying as explained below.

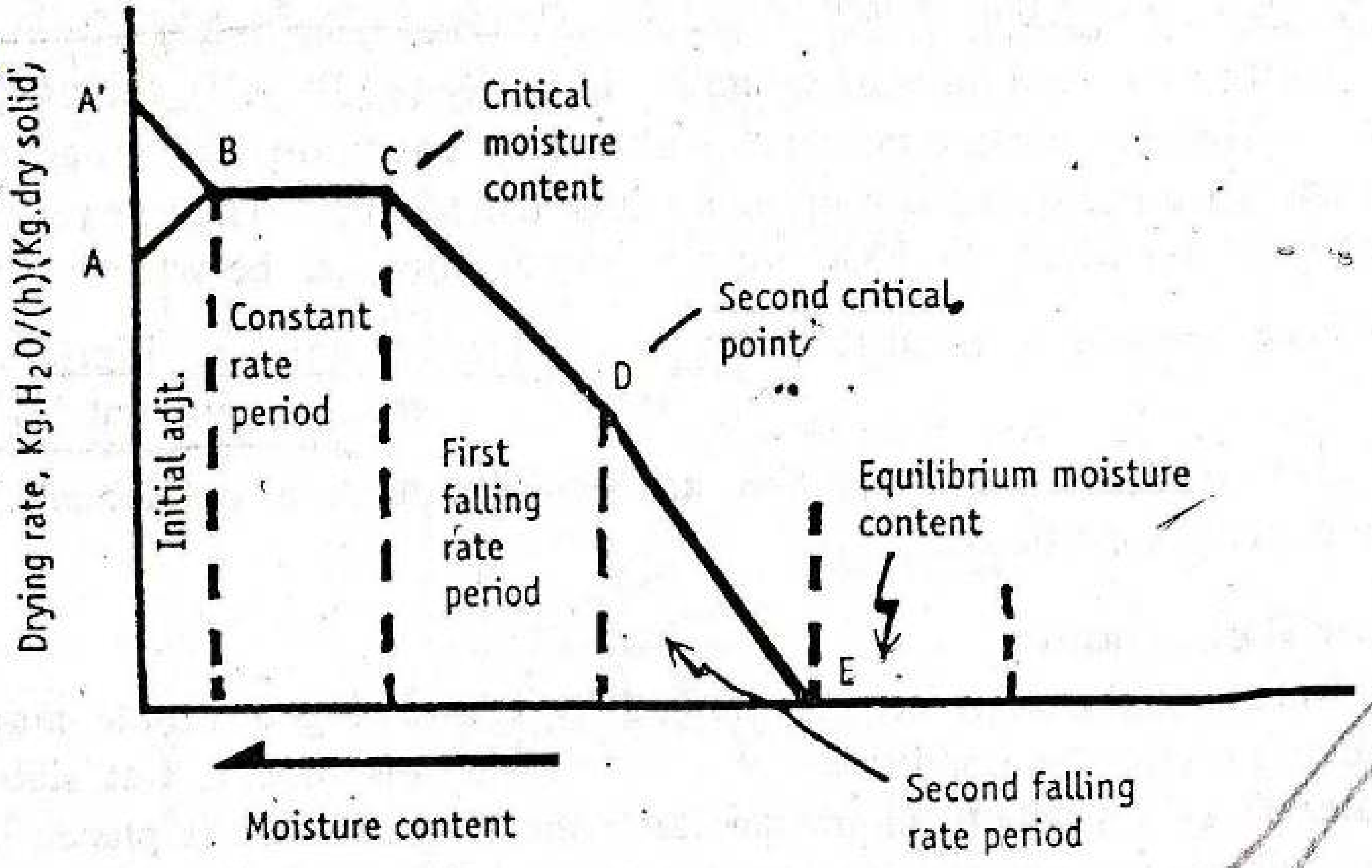
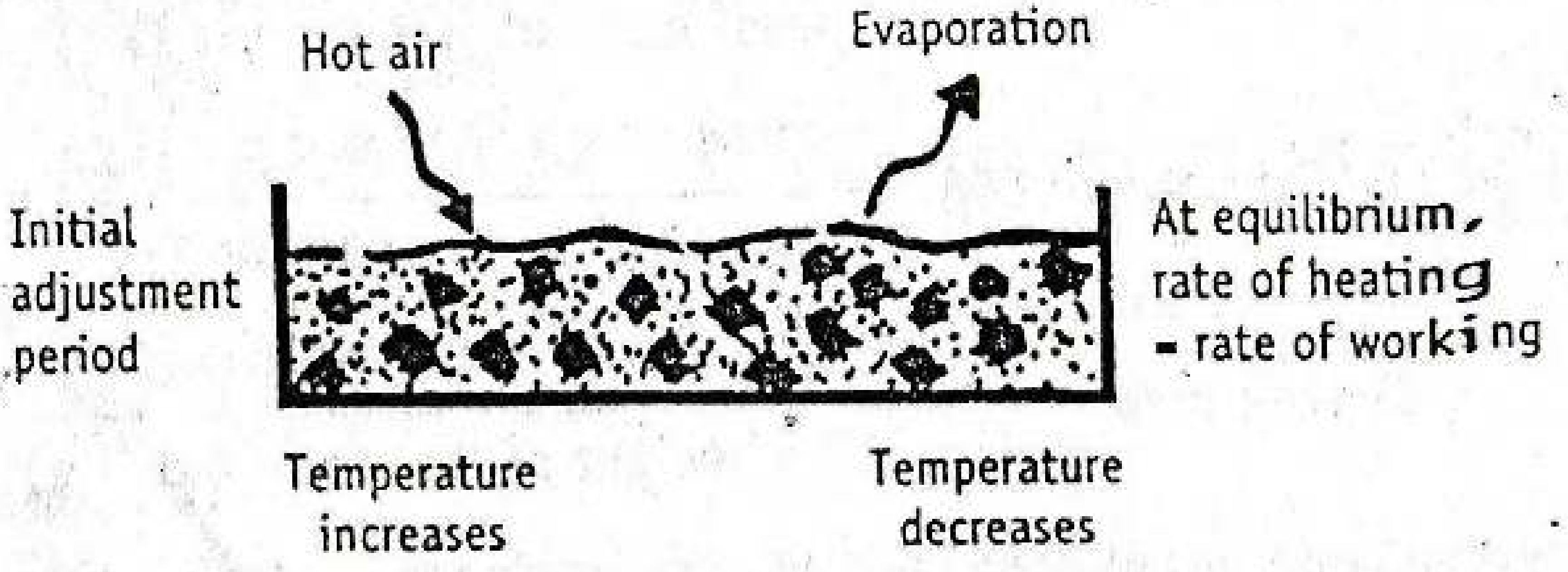
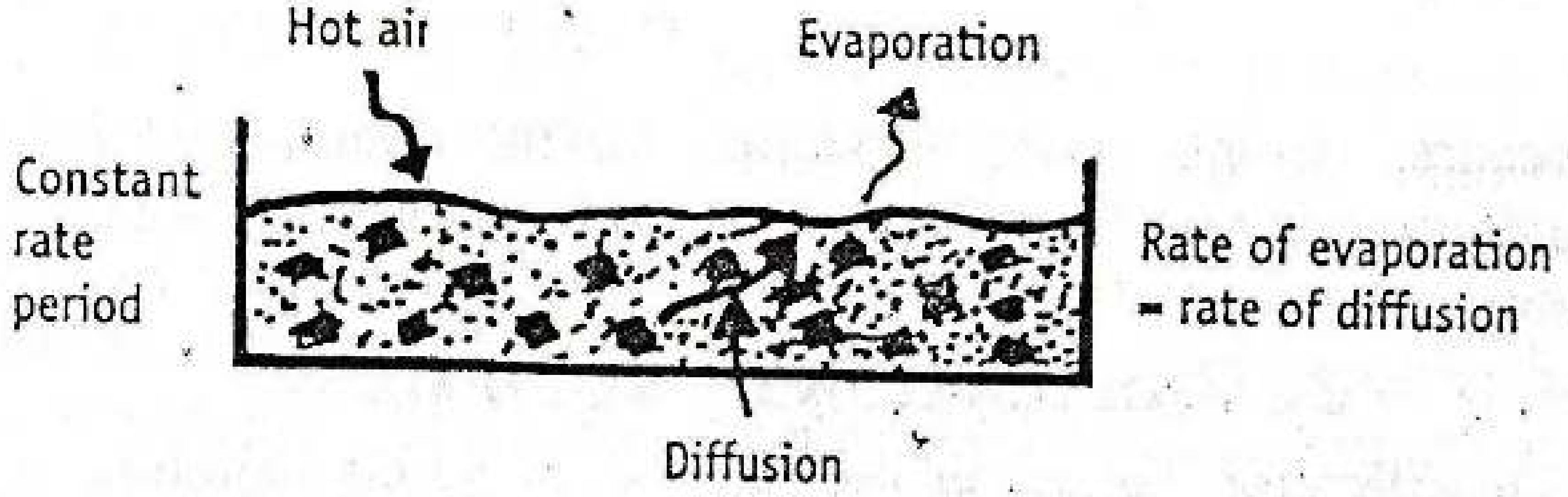


Figure 14-2. FMC curve.

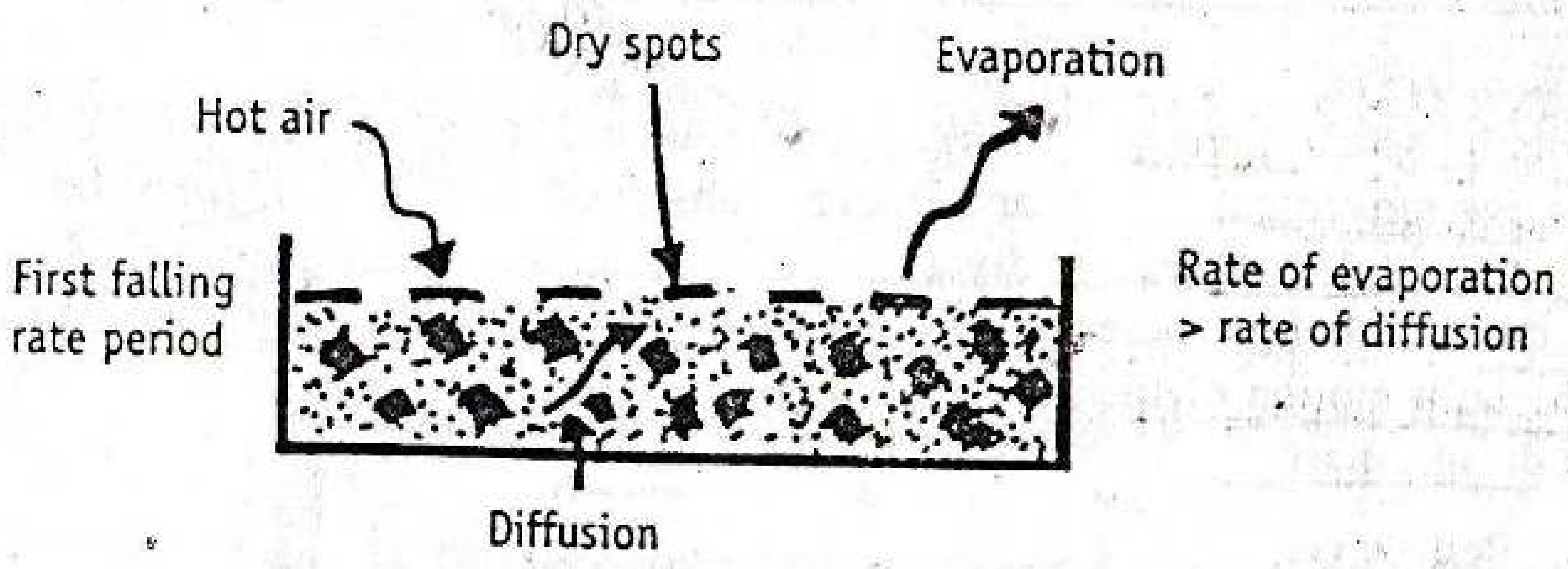
(1) The time corresponding to AB represents the *initial adjustment period*. During this period, the solids absorb heat and the temperature increases. At the same time, the moisture begins to evaporate and thus tends to cool the drying solid. After some time, the temperature stabilises (heating and cooling rates become equal). This temperature is equal to the wet bulb temperature of the drying air and is referred by the point B.



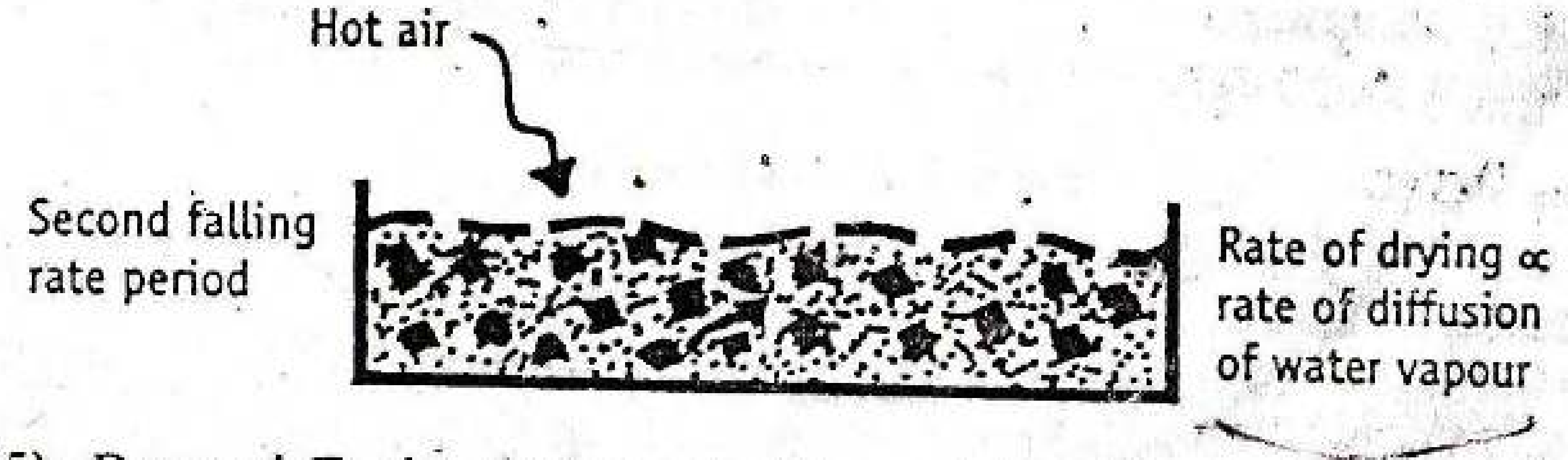
(2) The time corresponding to BC represents the *constant rate period*. The temperature remains constant and rate of drying is constant. The moisture evaporating from the surface is replaced by the water diffusing from the interior of the solid. The rate of diffusion is equal to the rate of evaporation. The moisture content at the end of constant rate (point C) is referred to as the *critical moisture content* (CMC).



(3) The time corresponding to CD represents the *first falling rate period* (or unsaturated surface drying). During this period, the surface water is no longer replaced at a rate fast enough to maintain a continuous film on the surface. Dry spots begin to appear and the rate of drying begins to fall off. The point D is referred to as the *second critical point*. At this point, the film of surface water is completely evaporated.



(4) The time corresponding to DE represents the *second falling rate period*. During this period, the rate of drying falls even more rapidly than the first falling rate. During this period, the rate of drying is dependent on the rate of diffusion of vapour of moisture to the surface of the solid. Point E is referred to as the *equilibrium moisture content*.



(5) Beyond E, the drying rate is equal to zero. Therefore, temperature and moisture content remain constant. Beyond, E, continued drying is waste of time and energy.

The curves may have different shapes for different levels of moisture. If the drying is carried above the level of CMC, only constant rate period occurs. If the drying is started for the material whose initial moisture content is less than CMC, then falling rate period occurs.

CLASSIFICATION OF EQUIPMENT

The classification based on the method of solids handling is more suitable when special attention is given to the nature of material to be dried. Dryers are classified as given in Table 14-1.

TABLE 14-1

Classification of Dryers—Mechanism, Examples, Advantages and Disadvantages

Type of dryer and mechanism	*Examples*	*Advantages*	*Disadvantages*
Static Bed Dryer Systems in which there is no relative movement among the solid particles being dried, although there may be bulk motion of the entire drying mass.	Tray dryer and freeze dryer	Attrition is not observed	Only a fraction of the solid particles is directly exposed
Moving Bed Dryer Systems in which the drying particles are partially separated so that they flow over each other	Drum dryer	The entire material is continuously exposed to heat source	Attrition is possible
Fluidised Bed Dryer Systems in which the solid particles are partially suspended in an upward moving heated gas system	Fluidised bed dryer	Solid-gas contact is excellent, uniform drying	Attrition of particles takes place
Pneumatic Dryer Systems in which drying particles are entrained and conveyed at a high velocity gas stream	Spray dryer	Efficient and rapid drying	

EQUIPMENT

TRAY DRYER

Principle : In tray dryer, hot air is continuously circulated. Forced convection heating takes place to remove moisture from the solids placed in trays. Simultaneously, the moist air is removed partially.

Construction : The construction of a tray dryer is shown in Figure 14-3. It consists of a rectangular chamber whose walls are insulated. Trays are placed inside the heating chamber. The number of trays may vary with the size of the dryer. Dryers of laboratory size may contain a minimum of three trays, where as dryers of industry size may contain more than 20 trays. Each tray is rectangular or square and about 1.2 to 2.4 metres square in area. Trays are usually loaded from 10.0 to 100.0 millimetres deep. The distance between the bottom of upper tray and (upper) surface of the substance loaded in the subsequent tray must be 40.0 millimetres.

Alternately the trays can be placed in trucks on wheels, which can be rolled into and out of chamber. Two such trucks can be arranged inside dryer. Dryer is fitted with a fan for circulating air over the trays. Electrically heated elements are provided inside (rather than outside) to heat the air (steam also can be used as it is cheaper). In the corner of the chamber, direction vanes (not shown in Figure 14-3) are placed to direct air in the expected path.

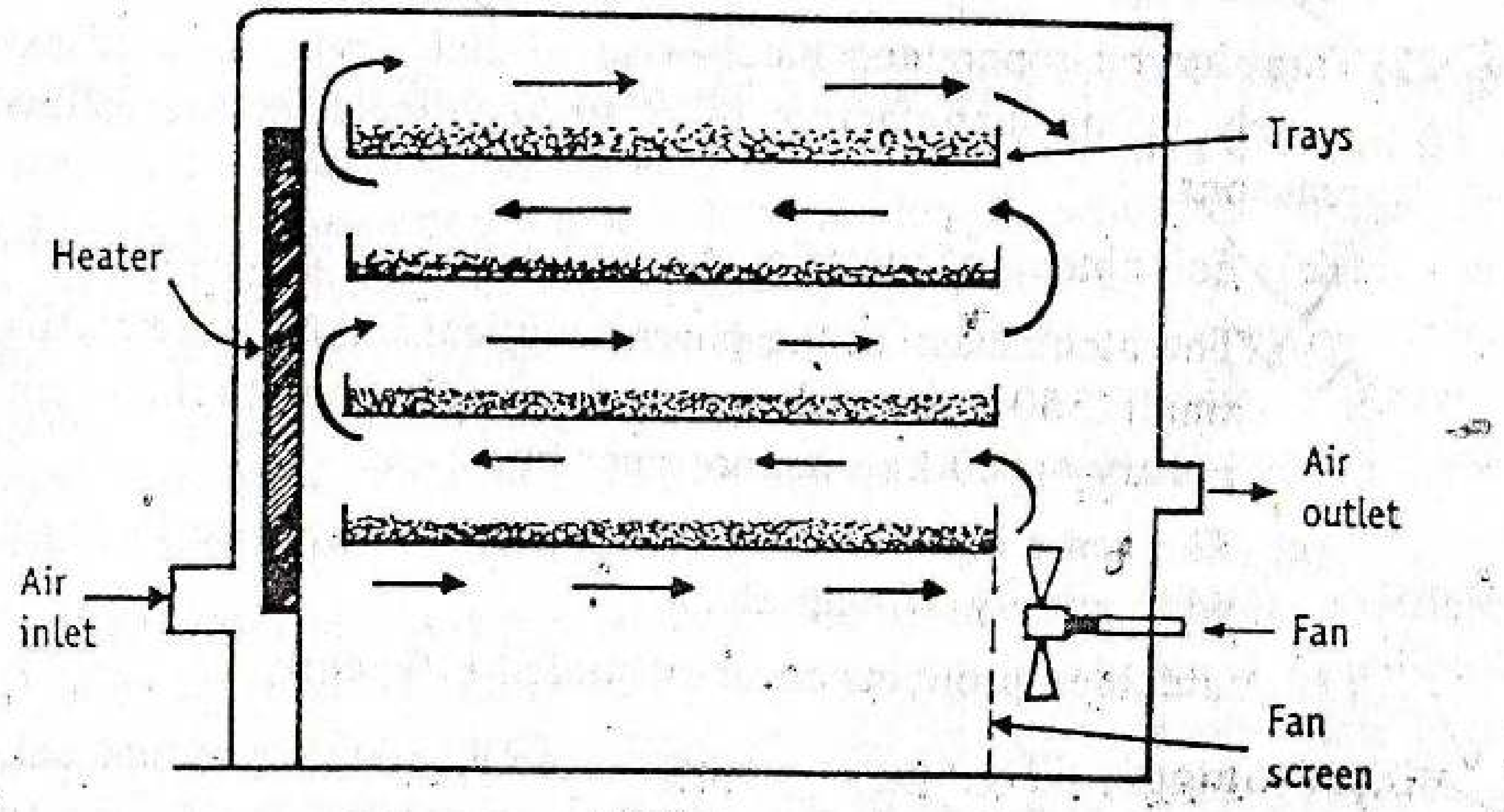


Figure 14-3. Tray dryer.

Working : Wet solid is loaded into trays. Trays are placed in the chamber. Fresh air is introduced through inlet, which passes through the heaters and gets heated up. The hot air is circulated by means of fans at 2 to 5 metre per second. Turbulent flow lowers the partial vapour pressure in the atmosphere and also reduces the thickness of the air boundary layer. The water is picked up by air. As water evaporates from the surface, the water diffuses from the interior of the solid by capillary action. These events occur in a single pass of air. The time of contact is short and the amount of water picked up in a single pass is small. Therefore the discharged air to the tune of 80 to 90% is circulated back through fans. Only 10 to 20% of fresh air is introduced. Moist air is discharged through outlet. Thus constant temperature and uniform airflow over the material can be maintained for achieving uniform drying.

In case of wet granules (as in tablets and capsules) drying is continued until the desired moisture content is obtained. At the end of drying, trays (trucks) are pulled out of the chamber and taken to a tray dumping station.

Uses : Sticky materials, plastic substances, granular mass or crystalline materials, precipitates and pastes can be dried in a tray dryer. Crude drugs, chemicals, powders, tablet granules or parts of equipment are dried.

Advantages : (1) In tray dryer, handling of materials (loading and unloading) can be done without losses.

(2) Tray dryer is operated batch-wise. Batch drying is used extensively in the manufacture of pharmaceuticals for the following reasons.

(a) Each batch of material can be handled as a separate entity.

(b) The batch sizes in the pharmaceutical industry are relatively small (250 kg or less per batch) compared with the chemical industry (1000 kg or more per hour).

(c) The same equipment is readily adjusted for use in drying a wide variety of materials.

(d) Valuable products can be handled efficiently.

Disadvantages : Tray dryer requires more labour to load and unload. Hence, cost increases. The process is time consuming.

Variants : Tray dryer may be operated under vacuum, often with indirect heating. This is done in special vacuum tray dryers for drying vitamins and other heat-sensitive products.

Tunnel dryer : In this type, trucks are loaded with wet material at one end of the tunnel. The tunnel comprised of a number of units, each of which is electro-statically controlled. The solids get dried and the product is discharged at the other end of the tunnel.

DRUM DRYER OR ROLLER DRYER
(or Film Drum Dryer)

Principle : In drum dryer, a heated hollow metal drum rotates on its longitudinal axis, which is partially dipped in the solution to be dried. The solution is carried as a film on the surface of the dryer and dried to form a layer. A suitable knife scraps the dried material, while the drum is rotating.

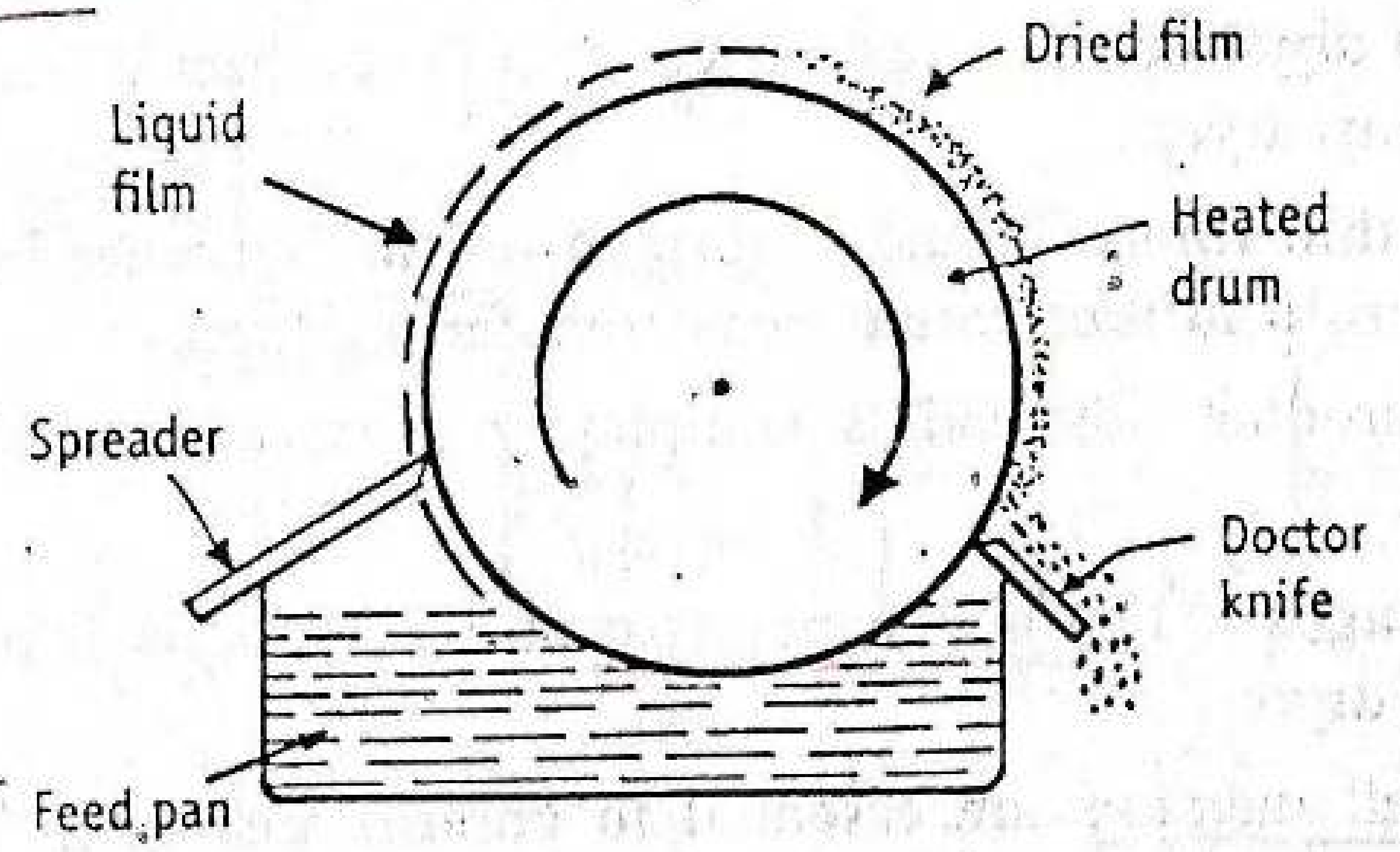


Figure 14-4. Drum dryer.

Construction : The construction of a drum dryer is shown in Figure 14-4. It consists of a horizontally mounted hollow steel drum of 0.6 to 3.0 metres diameter and 0.6 to 4.0 metres length, whose external surface is smoothly polished. Below the drum, feed pan is placed in such a way that the drum dips partially into the feed. On one side of the drum a spreader is placed and on the other side a doctor's knife is placed to scrap the dried material. A storage bin (or a conveyor) is placed connecting the knife to collect the material.

Working : Steam is passed inside the drum. Heat transfer coefficient of the drum metal is high. Drying capacity is directly proportional to the surface area of the drum. Heat is transferred by conduction to the material. Simultaneously drum is rotated at a rate of 1-10 revolutions per minute. The liquid material present in the feed pan adheres as a thin layer to the external surface of the drum during its rotation. The material is completely dried during its journey in slightly less than one rotation (i.e., from one side to another side of the drum). The dried material is scrapped by the doctor's knife, which then falls into a storage bin. The time of contact of the material with hot metal is 6 to 15 seconds only. Therefore, processing conditions such as film thickness, steam temperature are closely controlled.

Uses : Drum dryer is used for drying solutions, slurries, suspensions etc. The products dried are milk products, starch products, ferrous salts, suspensions of zinc oxide, suspension of kaolin, yeast, pigments, malt extracts, antibiotics, glandular extracts, insecticides, DDT, calcium and barium carbonates.

Advantages : (1) In drum dryer, drying time is less, only a few seconds. Therefore, heat sensitive materials can be dried.

(2) Drum dryer occupies less space, as it is compact when compared to spray dryer.

(3) As a thin film of liquid is formed on the large heating surface, rates of heat transfer and mass transfer are high.

(4) The product obtained is completely dried and is in the final form.

Disadvantages : (1) Maintenance cost of a drum dryer is higher than spray dryer.

(2) Skilled operators are essential to control feed rate, film thickness, speed of rotation and temperature.

(3) It is not suitable for solutions of salts with less solubility.

Variants : A vacuum drum dryer encloses both drum and feed line in a vacuum chamber to facilitate drying of heat sensitive materials. It is suitable for drying of drugs susceptible to oxidation and to recover solvents.

In a large scale, instead of one drum, two drums are set in parallel, rotating in opposite directions with a common feed inlet. The feed can be introduced on to the drum either by spraying it on the top or by introducing from the bottom.

SPRAY DRYER

Principle : In spray dryer, the fluid to be dried is atomized into fine droplets, which are thrown radially into a moving stream of hot gas. The temperature of the droplets is immediately increased and fine droplets get dried instantaneously in the form of spherical particles. This process completes in a few seconds before the droplets reach the wall of the dryer.

Construction : The construction of a spray dryer is shown in Figure 14-5. It consists of a large cylindrical drying chamber with a short conical bottom, made up of stainless steel (diameter of the drying chamber ranges between 2.5 to 9.0 metres and height is 25.0 metres or more). An inlet for hot air is placed in the roof of the chamber. Another inlet carrying spray-disk atomizer is set in the roof (shown in Figure 14-5). The spray disk atomizer is about 300 millimetres in diameter and rotates at a speed of 3,000 to 50,000 revolutions per minute. Bottom of the dryer is connected to a cyclone separator.

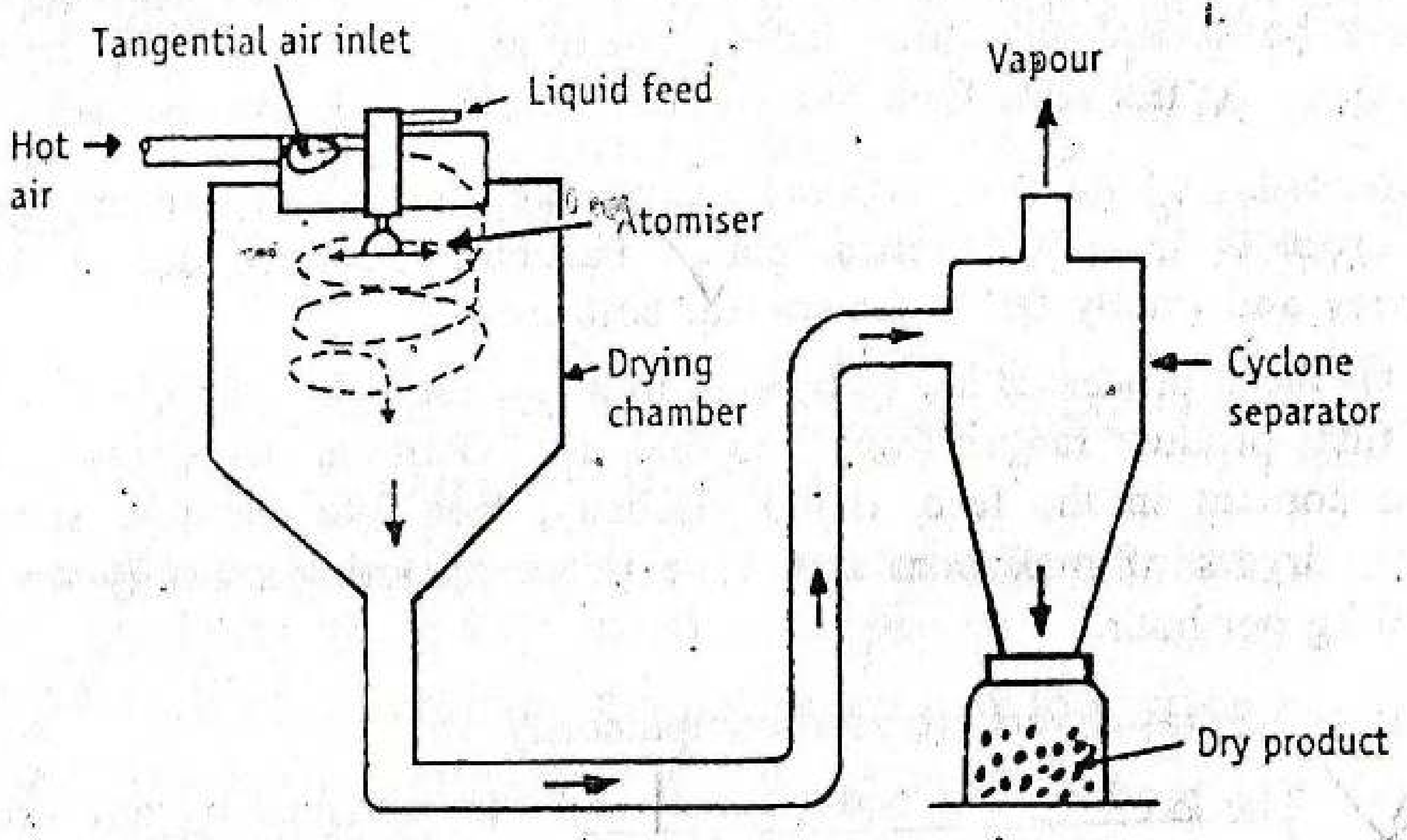


Figure 14-5. Spray dryer.

Working : Drying of the material in spray dryer involves 3 stages.

(1) Atomization of the liquid.

(2) Drying of the liquid droplets.

(3) Recovery of the dried product.

Atomization of the liquid to form liquid droplets : The feed is introduced through the atomizer either by gravity or by using suitable pump to form fine droplets. The properties of the final product depend on the droplet form, hence, the selection of the type of atomizer is important. Atomizer of any type: pneumatic atomizer, pressure nozzle and spinning disc atomizer may be used.

The rate of feed is adjusted in such a way that the droplets should be completely dried before reaching the walls of the drying chamber. At the same time, the product should not be over heated.

Drying of the liquid droplets : Fine droplets are dried in the drying chamber by supplying hot air through the inlet.

The surface of the liquid drop is dried immediately to form a tough shell. Further, the liquid inside must escape by diffusing through the shell at a particular rate. At the same time, heat transfer from outside to inside takes place at a rate greater than liquid diffusion rate. As a result, heat inside mounts up which allows the liquid to evaporate at a faster rate. This tendency of a liquid leads to rise in the internal pressure, which causes the droplets to swell. The shell's thickness decreases where as permeability for vapour increases. If the shell is neither elastic nor permeable, it ruptures and the internal pressure escapes.

The temperature of air is adjusted in such a way that the droplets should be completely dried before reaching the walls of the drying chamber. At the same time, the product should not be over heated.

Recovery of the dried product : Centrifugal force of atomizer drives the droplets to follow helical path. Particles are dried during their journey and finally fall at the conical bottom.

All these processes are completed in a few seconds. Particle size of the final product ranges from 2 to 500 mm. Particle size depends on solid content in the feed, liquid viscosity, feed rate and disc speed. Spray dryers of maximum size have got evaporating capacity up to 2000 kg per hour.

Uses : Spray dryers are used compulsorily, if:

(1) The product is a better form than that obtained by any other dryer.

(2) The quantity of the material to be dried is large.

(3) The product is thermolabile, hygroscopic, or undergoes chemical decomposition.

A few products that are dried using spray dryer are:

acacia
adrenaline
bacitracin
barium sulphate
blood
borax
boric acid
calcium sulphate
chloramphenicol succinate
citric acid
coffee extract
detergents
dextran
extracts
ferrous sulphate
fruit juices
gelatin
hexamine
hormones
lactose
methyl cellulose
milk
pancreatin
penicillin
pepsin
plasma
serum
soaps
sodium phosphate
starch
sulphur
vaccines
vitamins
yeast

Advantages : (1) Spray drying is a continuous process and drying is very rapid. Drying completes within 3 to 30 seconds.

(2) Labour costs are low as it combines the function of an evaporator, a crystllizer, a dryer, a size reduction unit and a classifier.

(3) By using suitable atomizer, the product of uniform and controllable size can be obtained. Free flowing product of uniform spheres is formed which is very convenient for tabletting process.

(4) Fine droplets formed provide large surface area for heat and mass transfer. Product shows excellent solubility.

(5) Either the solution or suspension or thin paste can be dried in one step to get the final product ready for package.

(6) It is suitable for the drying of sterile products.

(7) Reconstituted product appears more or less similar to the fresh material.

(8) Globules of an emulsion can be dried with the dispersed phase inside and layer of the continuous phase outside. On reconstitution, the emulsion will be formed.

Disadvantages : (1) Spray dryer is very bulky (height of 25.0 metres and diameter of 9.0 metres) and expensive.

(2) Such a huge equipment is not always easy to operate.

(3) The thermal efficiency is low, as much heat is lost in the discharged gases.

Variants : (1) Spray dryer can be constructed in such a way as to suit sterile products.

(2) It can be operated under closed conditions to recover solvents.

(3) It can be operated under oxygen free environment.

(4) It can be constructed in such a way that the flow of liquid and gas may be co-current, counter current or a combination of both in the same unit.

(5) The same equipment can be used for spray congealing.

(6) It is useful for encapsulation (coating) of solid and liquid particles.

FLUIDISED BED DRYER (FBD)

Principle : In fluidised bed dryer, hot air (gas) is passed at high pressure through a perforated bottom of the container containing granules to be dried. The granules are lifted from the bottom and suspended in the stream of air. This condition is called *fluidized state*. The hot gas is surrounding every granule to completely dry them. Thus, materials or granules are uniformly dried.

Construction : Two types of bed dryers are available, vertical fluid bed dryer and horizontal fluid bed dryer.

The construction of a vertical fluidised bed dryer is shown in Figure 14-6. The dryer is made up of stainless steel or plastic. A detachable bowl is placed at the bottom of the dryer, which is used for charging and discharging. The bowl has a perforated bottom with a wire mesh support for placing materials to be dried. A fan is mounted in the upper part for circulating hot air. Fresh air inlet, prefilter and heat exchanger are connected serially to heat the air to the required temperatures. The temperature of hot air and exit air are monitored. Bag filters are placed above the drying bowl for the recovery of fines.

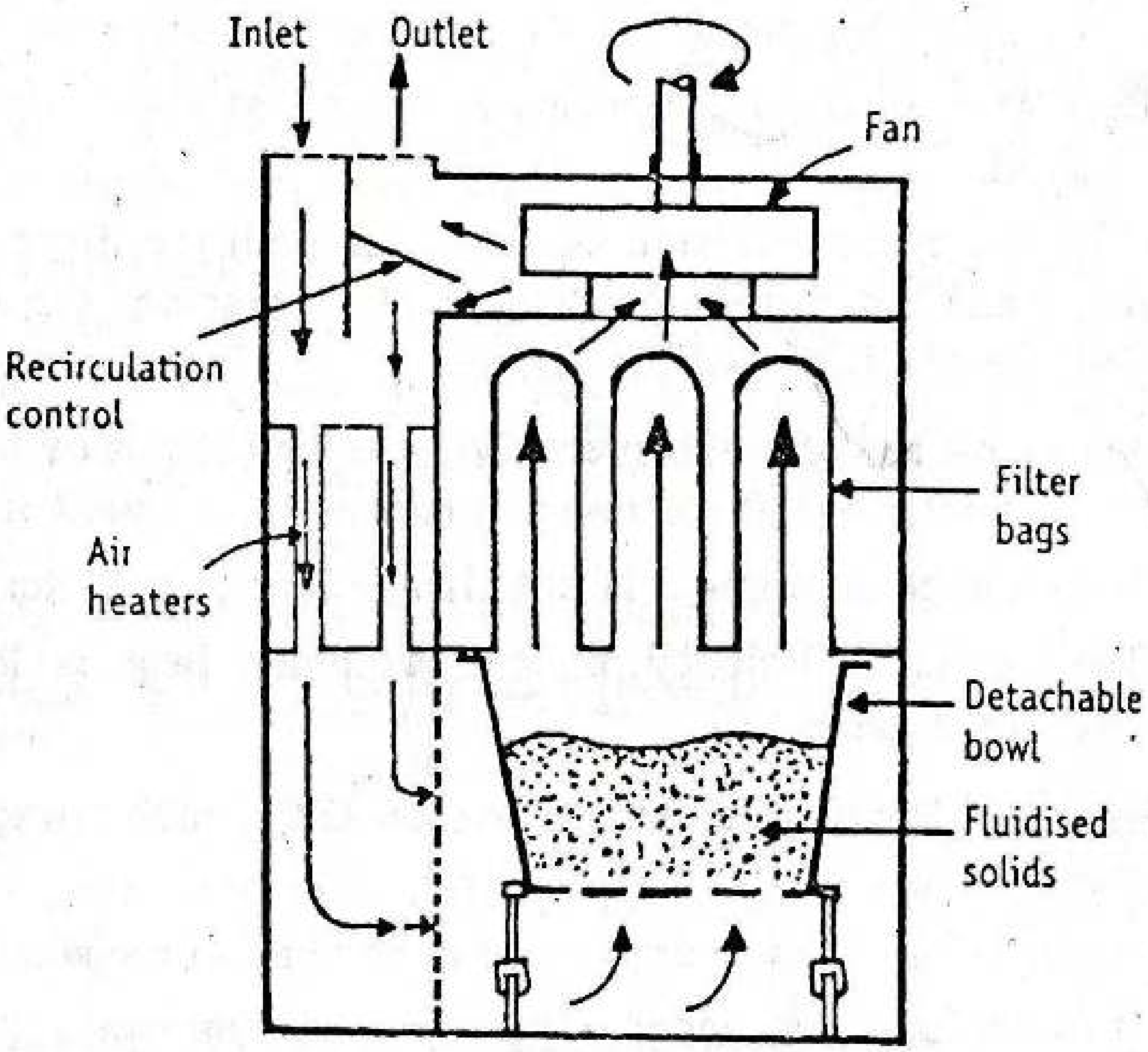


Figure 14-6. Fluidised bed dryer.

Working : The wet granules to be dried are placed in the detachable bowl. The bowl is pushed into the dryer. Fresh air is allowed to pass through a prefilter, which subsequently gets heated by passing through a heat exchanger. The hot air flows through the bottom of the bowl. Simultaneously fan is allowed to rotate. The air velocity is gradually increased.

When the velocity of the air is greater than settling velocity of granules, the granules remain partially suspended in the gas stream. After some time, a point of pressure is reached at which frictional drag on the particles is equal to the force of gravity. The granules rise in the container because of high velocity gas (1.5 to 7.5 metres per minute) and later fall back in a random boiling motion. This condition is said to be *fluidised state*. The gas surrounds every granule to completely dry them. The air leaves the dryer by passing through the bag filter. The entrained particles remain adhered to the inside surface of the bags. Periodically the bags are shaken to remove the entrained particles.

Intense mixing between granules and hot gas provides uniform conditions of temperature, composition and particle size distribution. Drying is achieved at constant rate and falling rate period is very short. Any attempt to increase the air velocity may result in entrainment.

The residence time for drying is about 40 minutes. The material is left for some time in the dryer for reaching ambient temperature. The bowl is taken out for discharging. The end product is free flowing.

Uses : Fluidised bed dryer is popularly used for drying of granules in the production of tablets. Fluidised bed dryer can be used for three operations such as mixing, granulation and drying. It is modified for coating of granules.

Advantages : (1) Fluidised bed dryer requires less time to complete drying, i.e., 20 to 40 minutes compared to 24 hours of tray dryer. Handling time is also short. It is 15 times faster than the tray dryer.

(2) It is available in different sizes with the drying capacity ranging from 5 to 200 kg per hour.

(3) The drying containers are mobile, making handling simple and reducing labour costs.

(4) The thermal efficiency is 2 to 6 times than tray dryer.

(5) It is also used for mixing the ingredients and its mixing efficiency is also high.

(6) Hot spots are not observed in the dryer, because of its excellent mixing and drying capacities.

(7) Higher drying temperatures can be used that are not possible in tray dryer and truck dryer.

(8) It facilitates the drying of thermolabile substances, since the contact time for drying is short.

(9) It can be used either as batch type or continuous type.

(10) It has a high output from a small floor space.

(11) The free movement of individual particles eliminates the risk of soluble material migrating as may occur in static beds.

Disadvantages : Many organic powders develop electrostatic charges during drying. To avoid this, efficient electrical earthing of the dryer is essential. The turbulence of the fluidised state of granules may cause attrition of some materials resulting in the production of fines. But using a suitable binding agent this problem can be solved. Fine particles may become entrained and must be collected by bag filters.

Variants : *Plug flow dryer* : It is a rectangular fluid bed dryer having different compartments for fluidisation. The material is made to move from inlet through different compartments to outlet. Different drying conditions can be maintained in the compartments. Often the last compartment is fluidised with cold gas to cool the solids before discharge.

VACUUM DRYER

Principle : In vacuum dryer, material is dried by the application of vacuum. When vacuum is created, the pressure is lowered so that water boils at a lower temperature. Hence, water evaporates faster. The heat transfer becomes efficient, i.e., rate of drying enhances substantially.

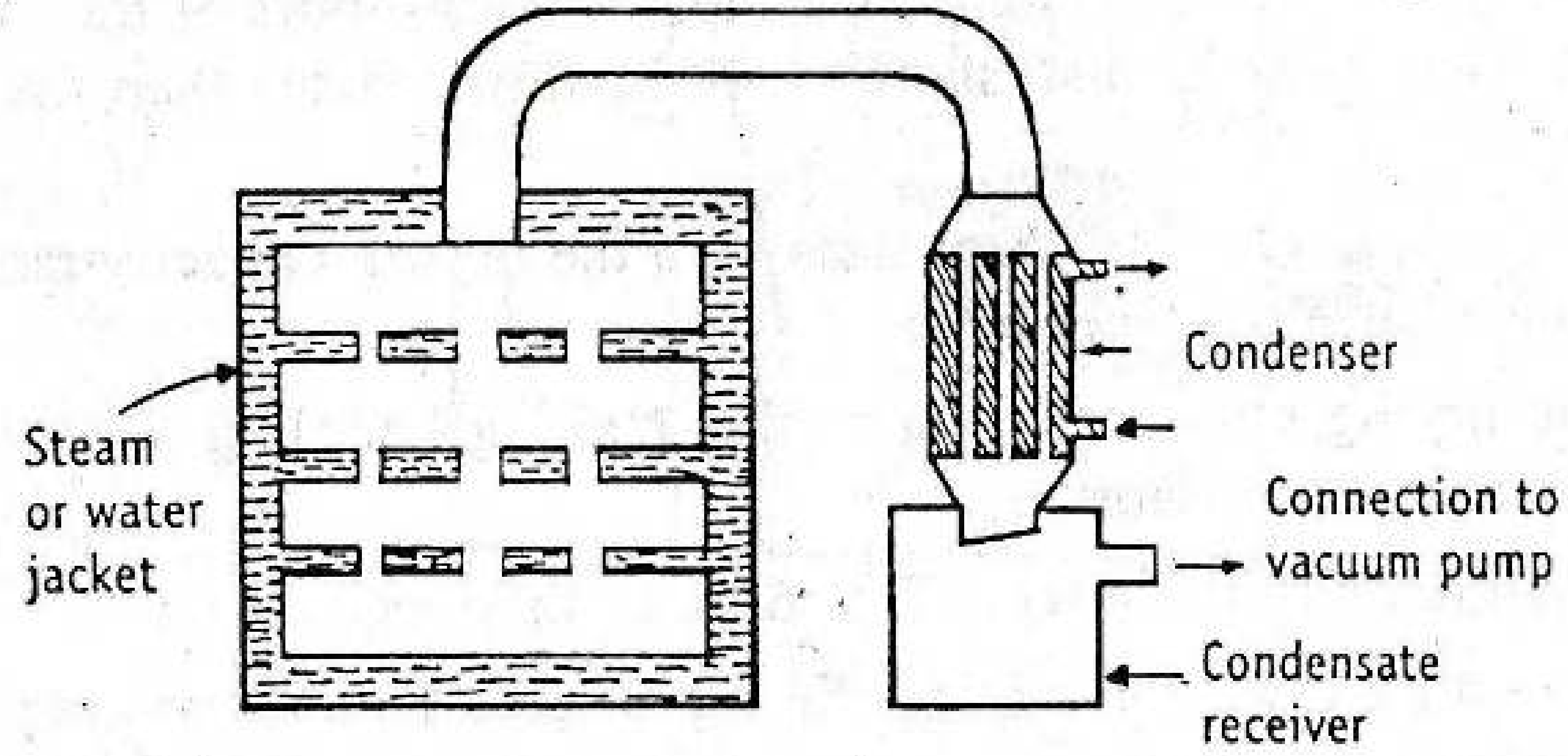


Figure 14-7. Vacuum dryer.

Construction : The construction of a vacuum dryer is shown in Figure 14-7. It is made of a cast iron heavy-jacketed vessel. It is so strong that it can withstand high vacuum within the oven and steam pressure in the jacket. The enclosed space (approximately 1.5 metre cube) is divided into a number of portions by means of 20 hollow shelves, which are part of the jacket. These shelves provide larger surface area (about 45 to 50 metre square) for conduction of heat. Over the shelves, metal trays are placed for keeping the material. The oven door can be locked tightly to give an air tight seal. The oven is connected to a vacuum pump by placing condenser in between.

Working : The material to be dried is spread on trays. The trays are placed on the shelves. Pressure is decreased up to 30 to 60 kilopascals by means of a vacuum pump. Door is closed firmly. Steam or hot air is supplied into the hollow space of jacket and shelves. Heat transfer by conduction takes place. At this vacuum, evaporation of water from the material takes place at 25-30°C, on account of lowering of boiling point. Water vapour passes into the condenser where condensation takes place.

At the end of the drying, vacuum line is disconnected. The material is collected from the trays.

Uses : Vacuum dryer can be used for drying of the following:

(1) Heat sensitive materials, which undergo decomposition.

(2) Dusty and hygroscopic materials.

(3) Drugs containing toxic solvents. These can be separated into closed containers.

(4) Feed containing valuable solvents. These are recovered by condensation.

(5) Drugs which are required as porous end products.

(6) Friable dry extracts.

Advantages : (1) Vacuum dryer provides large surface area for heat transfer.

(2) Handling of the material, trays and equipment is easy.

(3) It is easy for switching over to the next materials.

(4) Hot water of desired temperatures can be supplied.

(5) Electrically heated hollow shelves can be used.

Disadvantages : (1) In vacuum dryer, heat transfer coefficients are low.

(2) It has a limited capacity and used for batch process.

(3) It is more expensive than tray dryer. Labour and running costs are also high.

(4) Sometimes, there is a danger of over heating as the material is in contact with steam heated surface for longer period.

FREEZE DRYER

Freeze drying is also known as *lyophilization*, i.e., system is made solvent loving for removing the same.

Principle : In freeze drying, water is removed from the frozen state by *sublimation*, i.e., direct change of water from solid into vapour without conversion to a liquid phase. Solid-liquid-vapour equilibrium phase diagram of water is useful to decide the experimental conditions. The drying is achieved by subjecting the material to temperature and pressures below the triple point (in practice, below eutectic temperature is essential). Under these conditions, any heat transferred is used as latent heat and ice sublimes directly into vapour state. The water vapour is removed from the system by condensation in a cold trap maintained at a temperature lower than the frozen material. //

Construction : The construction of a freeze dryer is shown in Figure 14-8. It consists of:

(1) Drying chamber in which trays are loaded.
(2) Heat supply in the form of radiation source, heating coils.
(3) Vapour condensing or adsorption system.
(4) Vacuum pump or steam ejector or both.

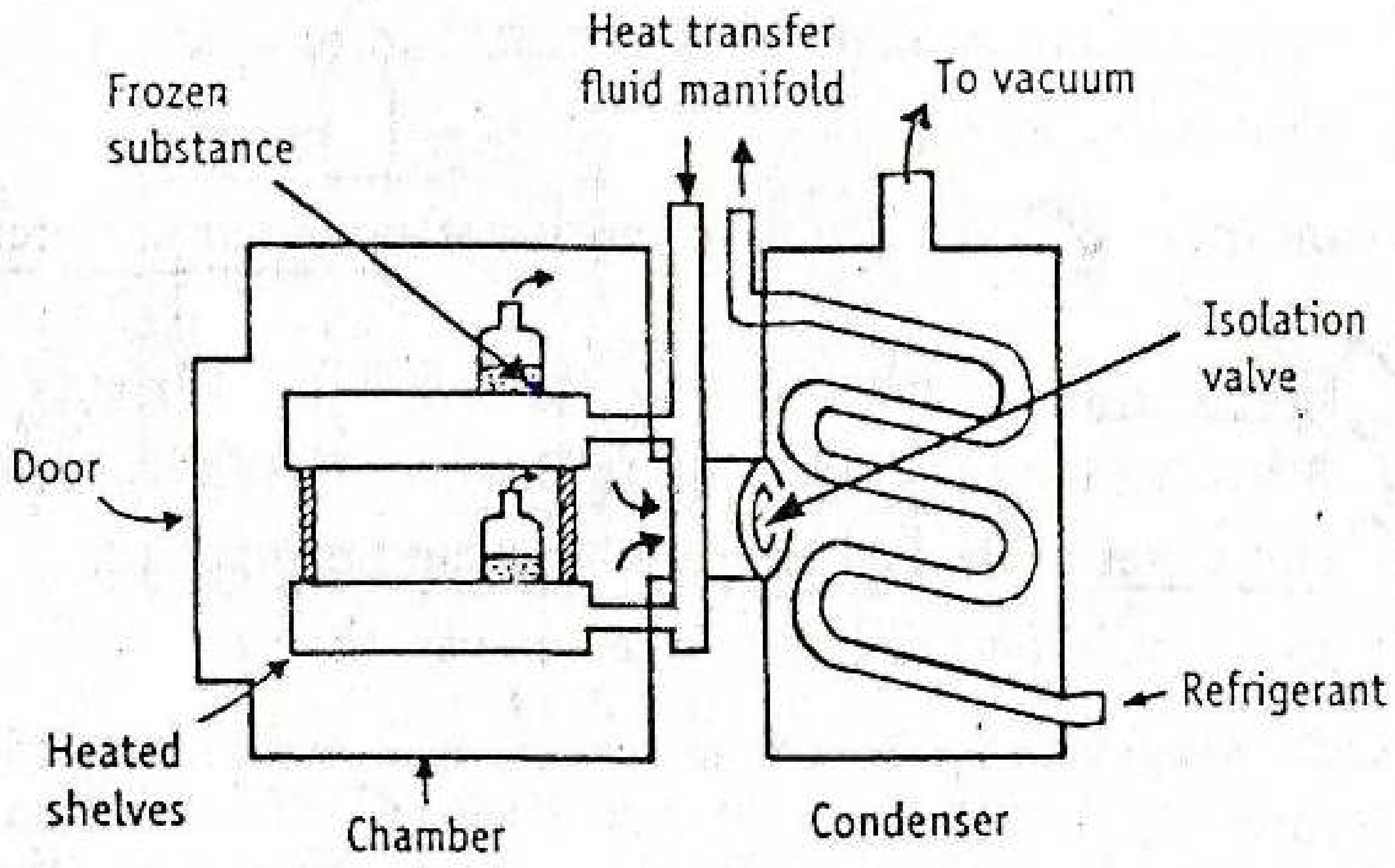


Figure 14-8. Schematic diagram of freeze dryer.

The chamber for vacuum drying is generally designed for batch operation. It consists of shelves for keeping the material. The distance between subliming surface and condenser must be less than the mean path of molecules. This increases the rate of drying. The condenser consists of a relatively large surface cooled by solid carbon dioxide slurred with acetone or ethanol. The temperature of the condenser must be much lower than the evaporated surface of frozen substance. In order to maintain this condition, the condenser surface is cleaned repeatedly.

19/10

Working : The working of freeze dryer consists of the following steps.

(1) Preparation and pretreatment
(2) Prefreezing for solidifying water
(3) Primary drying (sublimation of ice under vacuum)
(4) Secondary drying (removal of residual moisture under high vacuum)
(5) Packing

Preparation and pretreatment : The volume of solution introduced into the container is limited by its capacity. Satisfactory freeze drying beyond a certain limit of depth of liquid is not possible. Therefore pretreatment is essential. The solution is pre-concentrated under normal vacuum tray drying. This reduces the actual drying by 8 to 10 times. The final product becomes more porous. Liquid or solid desiccants are also used for this purpose.

Prefreezing to solidify water : Vials, ampoules or bottles in which the aqueous solution is packed are frozen in cold shelves (about –50°C). During this stage, cabinet is maintained at low temperature and atmospheric pressure. The normal cooling rate is about 1 to 3 Kelvin per minute so that large ice crystals with relatively large holes are formed on sublimation of ice. This is also responsible for giving a porous product.

Primary drying (sublimation of ice under vacuum) : In this step, the material to be dried is spread as much large surface as possible for sublimation. The temperature and pressure should be below the triple point of water, i.e., 0.0098°C and 0.533 kilopascals, (4.58 mmHg) for the sublimation, when water alone is present.

When a solution of solid is dried, the depression of freezing point of water occurs. Hence, it is essential that the temperature be brought below the eutectic point. The pressure and temperature at which the frozen solid vaporises without conversion to a liquid is referred to as the *eutectic point*. Depending on the drug substance dissolved in water, the eutectic point is determined. The usual range is from –10°C to 30°C. The condition of 1 to 8 K below eutectic point is sufficient.

Vacuum is applied to the tune of about 3 mmHg (0.4 kilopascals) on the frozen sample. The temperature is linearly increased to about 30°C in a span of 2 hours.

Heat (about 2900 kilojoules per kg) is supplied which transfers as latent heat and ice sublimes directly into vapour state. The heat controls the movements of ice layer inwards. It has to be controlled in such a

Principle : In freeze drying, water is removed from the frozen state by *sublimation*, i.e., direct change of water from solid into vapour without conversion to a liquid phase. Solid-liquid-vapour equilibrium phase diagram of water is useful to decide the experimental conditions. The drying is achieved by subjecting the material to temperature and pressures below the triple point (in practice, below eutectic temperature is essential). Under these conditions, any heat transferred is used as latent heat and ice sublimes directly into vapour state. The water vapour is removed from the system by condensation in a cold trap maintained at a temperature lower than the frozen material.

Construction : The construction of a freeze dryer is shown in Figure 14-8. It consists of:

(1) Drying chamber in which trays are loaded.
(2) Heat supply in the form of radiation source, heating coils.
(3) Vapour condensing or adsorption system.
(4) Vacuum pump or steam ejector or both.

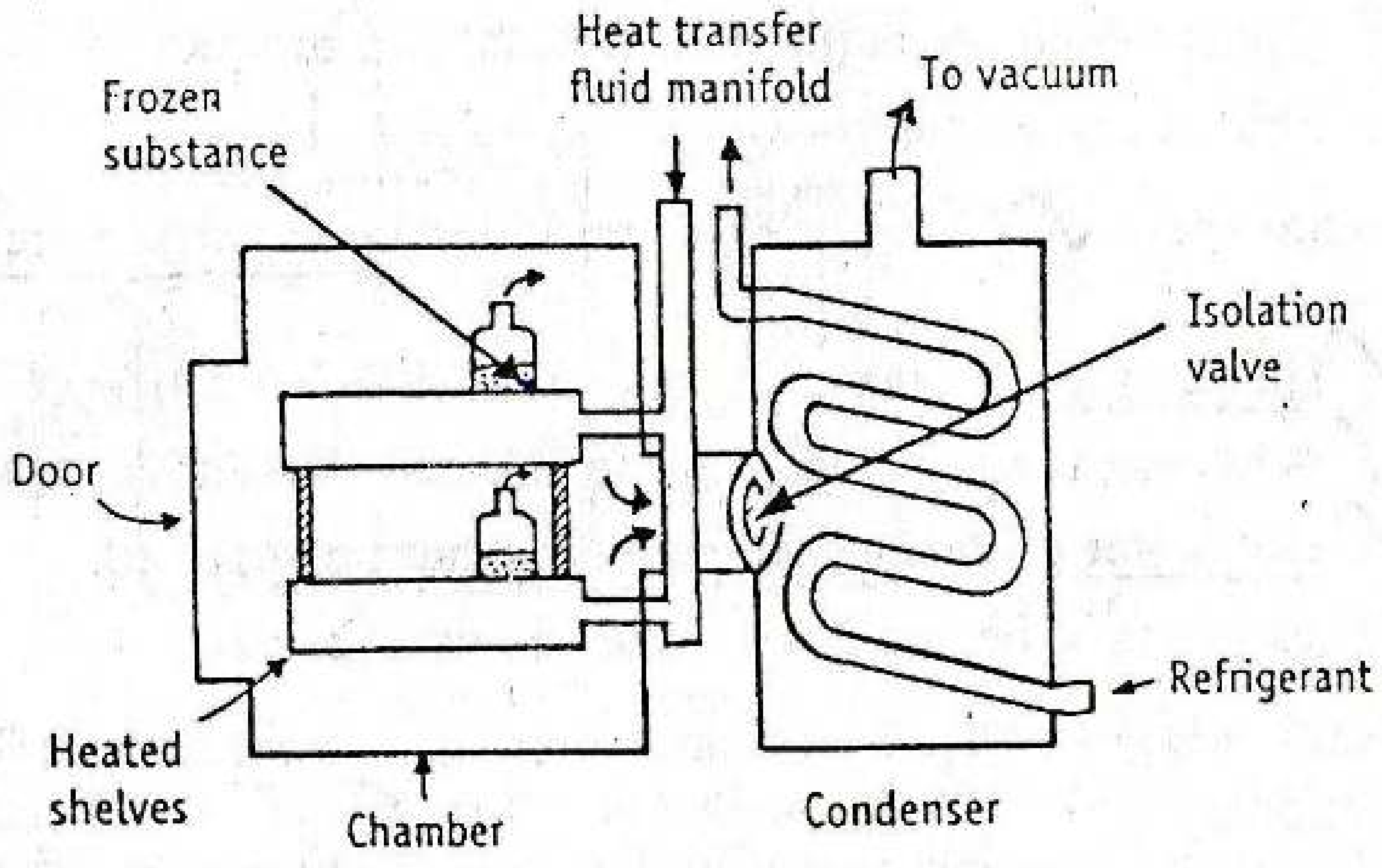


Figure 14-8. Schematic diagram of freeze dryer.

The chamber for vacuum drying is generally designed for batch operation. It consists of shelves for keeping the material. The distance between subliming surface and condenser must be less than the mean path of molecules. This increases the rate of drying. The condenser consists of a relatively large surface cooled by solid carbon dioxide slurred with acetone or ethanol. The temperature of the condenser must be much lower than the evaporated surface of frozen substance. In order to maintain this condition, the condenser surface is cleaned repeatedly.

M 10

Working : The working of freeze dryer consists of the following steps.

(1) Preparation and pretreatment
(2) Prefreezing for solidifying water
(3) Primary drying (sublimation of ice under vacuum)
(4) Secondary drying (removal of residual moisture under high vacuum)
(5) Packing

Preparation and pretreatment : The volume of solution introduced into the container is limited by its capacity. Satisfactory freeze drying beyond a certain limit of depth of liquid is not possible. Therefore pretreatment is essential. The solution is pre-concentrated under normal vacuum tray drying. This reduces the actual drying by 8 to 10 times. The final product becomes more porous. Liquid or solid desiccants are also used for this purpose.

Prefreezing to solidify water : Vials, ampoules or bottles in which the aqueous solution is packed are frozen in cold shelves (about –50°C). During this stage, cabinet is maintained at low temperature and atmospheric pressure. The normal cooling rate is about 1 to 3 Kelvin per minute so that large ice crystals with relatively large holes are formed on sublimation of ice. This is also responsible for giving a porous product.

Primary drying (sublimation of ice under vacuum) : In this step, the material to be dried is spread as much large surface as possible for sublimation. The temperature and pressure should be below the triple point of water, i.e., 0.0098°C and 0.533 kilopascals, (4.58 mmHg) for the sublimation, when water alone is present.

When a solution of solid is dried, the depression of freezing point of water occurs. Hence, it is essential that the temperature be brought below the eutectic point. The pressure and temperature at which the frozen solid vaporises without conversion to a liquid is referred to as the *eutectic point*. Depending on the drug substance dissolved in water, the eutectic point is determined. The usual range is from –10°C to 30°C. The condition of 1 to 8 K below eutectic point is sufficient.

Vacuum is applied to the tune of about 3 mmHg (0.4 kilopascals) on the frozen sample. The temperature is linearly increased to about 30°C in a span of 2 hours.

Heat (about 2900 kilojoules per kg) is supplied which transfers as latent heat and ice sublimes directly into vapour state. The heat controls the movements of ice layer inwards. It has to be controlled in such a manner so as to get highest possible water vapour at ice surface without melting the material. As soon as vapour molecules are formed, these are removed. The overall driving force is the temperature difference (also vapour pressure difference) between evaporating surface and condenser.

As the drying proceeds, thickness of the frozen layer decreases and the thickness of partially dried solids increases. Primary drying stage removes easily removable moisture. During this stage, about 98% to 99% water is removed. Still traces of moisture is present in the sample.

Secondary drying (Removal of residual moisture under high vacuum) : During this stage, traces of moisture is removed. The temperature of the solid is raised to as high as 50 to 60°C, but vacuum is lowered below that is used in primary drying (50 mmHg). The rate of drying is very low and it takes about 10 to 20 hours.

Packing : After vacuum is replaced by inert gas, the bottles and vials are closed.

Uses : Freeze dryer is most commonly used in the production of dosage forms, such as injections, solutions and suspensions. It is used for drying of a number of products.

(1) Blood plasma and its fractionated products.
(2) Bacterial and viral cultures.
(3) Human tissue (arteries and corneal tissue).
(4) Antibiotics and plant extracts.
(5) Steroids, vitamins and enzymes.

Several other products such as food items (prawns, mushrooms, meat and poultry products), coffee and tea concentrates and citrus fruit juices are dried.

Advantages : The entire operation is carried out well below the freezing point. This offers several advantages.

(1) Thermolabile materials (heat sensitive materials) can be dried.
(2) The product retains its bulk volume. It is porous and uniform. The reconstitution of the material is easy.
(3) Denaturation does not occur.
(4) Migration of salts and other solutes does not take place.
(5) Loss of volatile material is less.
(6) Moisture level can be kept as low as possible without decomposition.

(7) Material can be dried in its final container such as single dose and multiple dose vials.
(8) Sterility can be maintained.
(9) The final product can be stored at ambient temperature, if well sealed by providing inert atmosphere.

Disadvantages : (1) The product is prone to oxidation, due to high porosity and large surface area. Therefore, the product should be packed in vacuum or using inert gas or in a container impervious to gases.

(2) Equipment and running costs are high.
(3) It is difficult to adopt the method for solutions containing non-aqueous solvents.
(4) The period of drying is high (rarely less than 10 hours). Time cannot be shortened.

QUESTION BANK

Each question carries 2 marks

1. Distinguish between drying and evaporation.
2. Give suitable dryers.
   (i) Granular free flowing solids
   (ii) Wet bricks before sending to kilns
   (iii) Sticky pastes
   (iv) Food products like Horlicks.
3. Define critical moisture content and equilibrium moisture content.
4. Define bound moisture and free moisture content.
5. Mention the factors affecting constant drying rate.
6. Classify dryers giving suitable examples.
7. List the critical conditions for drying of various substances.
8. Define drying. Give its importance in the formulation of dosage forms.
9. Explain how agitator dryers are useful to dry pasty and sludgy materials.
10. How do you obtain the rate of drying curve for a given drying operation? Give its applications.

Each question carries 5 marks

1. Recommend a suitable dryer for drying the following substances and substantiate your answer with at least two reasons.
   (A) Liver extracts
   (B) Granular solids
   (C) Pasty materials

(D) Granules of heat sensitive drugs
(E) Vitamin B complex granules
(F) Colloidal solution

2. Describe the drying rate curve for a nonporous granular solid.
3. Describe the principle with the help of a labeled diagram of fluidised bed dryer.
4. List the pharmaceutical applications of freeze drying process. Give salient features of the process.
5. Describe the construction and working of a fluidized bed dryer.
6. Explain the principle of spray drying with suitable labeled diagram.
7. Describe the drying rate curve. Explain its applications.
8. Explain the principle and working of drum dryer.
9. Compare spray drying with drying in a vacuum shell dryer.
10. Explain the factors to be considered in the selection of a suitable dryer.
11. Explain the operation and applications of fluidised bed dryer.
12. Describe the function of drum dryer and its uses.
13. Describe the rate of drying curve for a crude fibrous drug.
14. Explain the principle of freeze drying. What are its applications in pharmacy?
15. Compare the operations of spray dryer and tray dryer.
16. Describe the concept of spray dryer. What are its advantages? Compare the spray drying with other methods of drying.

Each question carries 10 marks

1. Explain the construction, operational details of freeze dryer. Describe its applications in pharmacy.
2. Describe the concept of spray drying. Describe the specific advantages of spray dried product over drum dried material. Also list the pharmaceutical applications.
3. How do you classify dryers? Describe in detail the constant rate and falling rate periods. Add a note on critical moisture content.
4. For drying of milk, we can use either drum dryers or spray dryers. Which dryer will you prefer and why? Discuss drum dryers in detail.
5. Discuss the construction, working. advantages and disadvantages of spray dryer.
6. Explain the theory behind drying and rate of drying with suitable graphs.

15

Humidification and Dehumidification

Humidity Charts and its Utility
Humidification
Dehumidification
Refrigeration
Air Conditioning

Humidification is a unit operation, which involves the transfer of liquid water into water vapour.

Though the definition describes the transfer of liquid into vapour, the reverse process is also possible. The process in which the moisture (humidity) is decreased (transfer of vapour to liquid state) in the air is known as *dehumidification*.

These transfer processes depend on temperature and humidity that are already present in the air. Therefore, it is an equilibrium process. In humidification, the dry air is passed over a liquid, so that liquid evaporates into the gas stream. In case of drying of wet solids, the reduction of the moisture content of the solids is the main aim. The humidification of the air stream also occurs, which is a secondary effect. In dehumidification, liquid vapour from the air is removed by condensation as in the distillation process. Air conditioning and drying also involve humidification and dehumidification operations.

In the normal environmental conditions, the air has a certain humidity. Different seasons, day and night timings also exhibit variations in the humidity and temperature. Such variations influence the characteristics of raw materials, finished products and processing conditions.

The behaviour of solids in the presence of moisture (when these are present in the ambient conditions) is of considerable importance in pharmacy. Based on their reactions, substances are classified as:

(*a*) *Hygroscopic substances* have the natural tendency of absorbing moisture or water. Examples are vegetable drugs such as digitalis leaves and chemicals such as sodium sulphate. Liquids such as glycerin, absolute alcohol and concentrated sulphuric acid are also hygroscopic.

(b) *Deliquescent substances* have the natural tendency to absorb water and liquefy. Examples are calcium chloride, potassium carbonate etc.

(c) *Efflorescent substances* have the natural tendency to loose water. Examples are borax, caffeine, quinidine sulphate etc.

Applications

Preservation of pharmaceuticals : The effect of humidity on the materials is as follows.

(1) The substances absorb moisture and undergo chemical degradation such as hydrolysis and oxidation, when they are exposed to excessive humidity.

(2) Physical stability of drugs and dosage forms can be affected. For example, gelatin capsules absorb moisture and become soft and sticky. Suppositories and creams become liquids.

(3) Low humidity has adverse effects. For example, hard gelatin capsules loose water and become dry and brittle.

Therefore, controlled humidity should be maintained.

Evaluation of dosage forms : Environmental test chambers are designed to carry out stability and shelf life testing of drugs. The test chambers offer reproducible temperature and humidity conditions. Climatic conditioning is also required for herbal research, pesticide research and zoology.

Processing conditions in unit operations : In case of normal drying and freeze drying, experimental conditions are chosen based on humidity consideration.

Maintenance of animals and equipment : According to the Drugs and Cosmetics Act and Rules, in many cases the animal house should be air-conditioned. Sophisticated electronic (analytical) equipment are placed and the work is carried in air-conditioned rooms.

Fabrication of environmental conditioners : The principles have been applied for the construction of equipment such as dehumidifiers, air conditioners and refrigerators. Some manufacturing areas where humidity is controlled are given below.

Compression of tablets : In the granulation section, air conditioning is optional, if necessary the conditions are 45% RH and 22°C. In the tabletting section, the conditions are less than 20% RH and 22°C.

Manufacture of soft gelatin capsules : The temperature is usually in the range of 20° C to 22°C and the humidity is controlled to a maximum of 40% RH in the processing areas and between 20 and 30% RH in the drying areas.

The composition and properties of mixture of air and water vapour are essential to maintain the desired environmental conditions. The thermal properties of such a mixture are also important. The discussion in this chapter is devoted to air-water systems; however, the principles can be applied to liquid gases also.

Definitions

The basic definitions of different terms involved are discussed in order to appreciate the theory, practice, handling of equipment etc.

Humidity (H) : It is also known as *humidity ratio*. It is mathematically expressed under any given set of conditions as:

$$\textit{Humidity, } H = \frac{\text{mass of vapour present in the air (kg)}}{\text{mass of dry air (kg)}} \qquad (1)$$

Normally, the amount of vapour is measured in terms of pressure, but not in weight terms. Let the partial pressure of water vapour in the sample of air in question be p_A kilopascals. Then humidity in equation (1) may be expressed as:

$$\textit{Humidity, } H = \frac{\begin{array}{c}\text{partial vapour pressure}\\ \text{of water in air}\end{array}}{\begin{array}{c}\text{partial vapour pressure}\\ \text{of dry air}\end{array}} = \frac{p_A}{(1-p_A)} \qquad (2)$$

Since molecular weights of water and air are 18 and 29, respectively, then humidity at the temperature and pressure can also be written as:

$$H = \frac{M_A p_A}{M_B(1-p_A)} = \frac{18 p_A}{29\ (1-p_A)} \qquad (3)$$

where M_A = molecular weight of gas or vapour (water)
M_B = molecular weight of air

Humidity at saturated gas (air) (H_s) : At a given temperature and pressure, if the gas in vapour (air) is in equilibrium with the liquid gas, then that gas is said to be *saturated*. If H_s is the saturated humidity and P_A is the vapour pressure of the liquid, then,

$$H_s = \frac{M_A P_A}{M_B(1 - P_A)} \qquad (4)$$

Percent humidity (H_A) : Percentage of humidity may be expressed, at certain temperature and pressure, as:

$$\textit{Percent humidity } (H_A) = \frac{\text{actual humidity (H)}}{\text{saturation humidity (H}_S\text{)}} \times 100 \qquad (5)$$

At humidities other than 0 and 100 percent, the percent humidity is less than relative humidity.

Relative humidity (H_R) : Relative humidity is expressed as a percentage. It is defined mathematically at a temperature as:

$$\textit{Relative humidity, } H_R = \frac{\begin{array}{c}\text{actual partial pressure of water}\\ \text{vapour in the air-water mixture } (p)\end{array}}{\begin{array}{c}\text{partial pressure of water}\\ \text{vapour at saturation } (p_S)\end{array}} \times 100 \qquad (6)$$

Humid volume (V) : It is the volume occupied by a unit mass of dry gas and its associated vapour

Humid heat : It is the heat required to raise unit mass of dry gas and its associated vapour through one unit difference in temperature at constant pressure.

Mathematically it is expressed as:

$$s = C_a + HC_w \qquad (7)$$

where s = humid heat, kJ/kg·K

C_a = specific heat capacity of gases, kJ/kg·K

C_w = specific heat capacity of vapour, kJ/kg·K

H = humidity

For air-water system

Humid heat = 1.00 + 1.9 H kJ/kg·K

Saturated volume : It is humid volume of saturated vapour.

Enthalpy : Enthalpy of air-water vapour is the heat content of 1 kg of dry air and its associated moisture (water vapour) expressed as kilojoules per kg of dry air.

Dew point : It is the temperature to which a mixture of air-water vapour must be cooled (at constant humidity) to become saturated (i.e., to be in equilibrium with liquid at the dew point).

Dry bulb temperature : It is the temperature of moist air when it is measured at rest by any instrument, which is not affected by the moisture content of air or by radiation.

Wet bulb temperature–Theory : Wet bulb temperature is the dynamic equilibrium temperature attained by a water surface when exposed to air under adiabatic conditions.

Consider a case in which the air is unsaturated at a given temperature and humidity. Such a stream of air is passed over a wet surface under adiabatic conditions, i.e., no heat is received from or given to the surroundings during the operation.

The initial temperature of the wet surface is approximately that of the air. A partial pressure difference (driving force) is set up between air and wetted surface. The water tends to evaporate from the surface and increases the humidity of the air. As a result, the temperature of the surface decreases and sensible heat will be transferred from the air to wetted surface. Ultimately a steady state will be reached at which the loss of heat due to the heat of evaporation is exactly balanced by the heat passing from the air into the water as *sensible heat*. Under these conditions, the temperature of water remains constant. This temperature is called wet bulb temperature.

If the initial temperature of the wetted surface is less than wet bulb temperature, it will rise to the wet bulb temperature. Since heat transfer and mass transfer are observed in the above process, their coefficients are important and are effected by many factors. The wet bulb temperature depends upon the temperature and humidity of air.

HUMIDITY CHARTS AND ITS UTILITY

Humidity Charts

For engineering calculations, the properties of mixture of air and water vapour are necessary. *Humidity charts* or *psychometric charts* are helpful for this purpose. Three types of plots are shown in Figure 15-1.

Humidity vs. temperature : In this chart, humidity (expressed as kg of water per kg of dry air) is plotted on y-axis and temperature (in °C) is plotted on x-axis at atmospheric pressure. The plots are curved and each represents a definite humidity value. The following information may be obtained from the chart.

(a) Any point on the chart represents the temperature and humidity of the sample of air.

(b) The curved line marked 100% gives the humidity of saturated air at various temperatures.

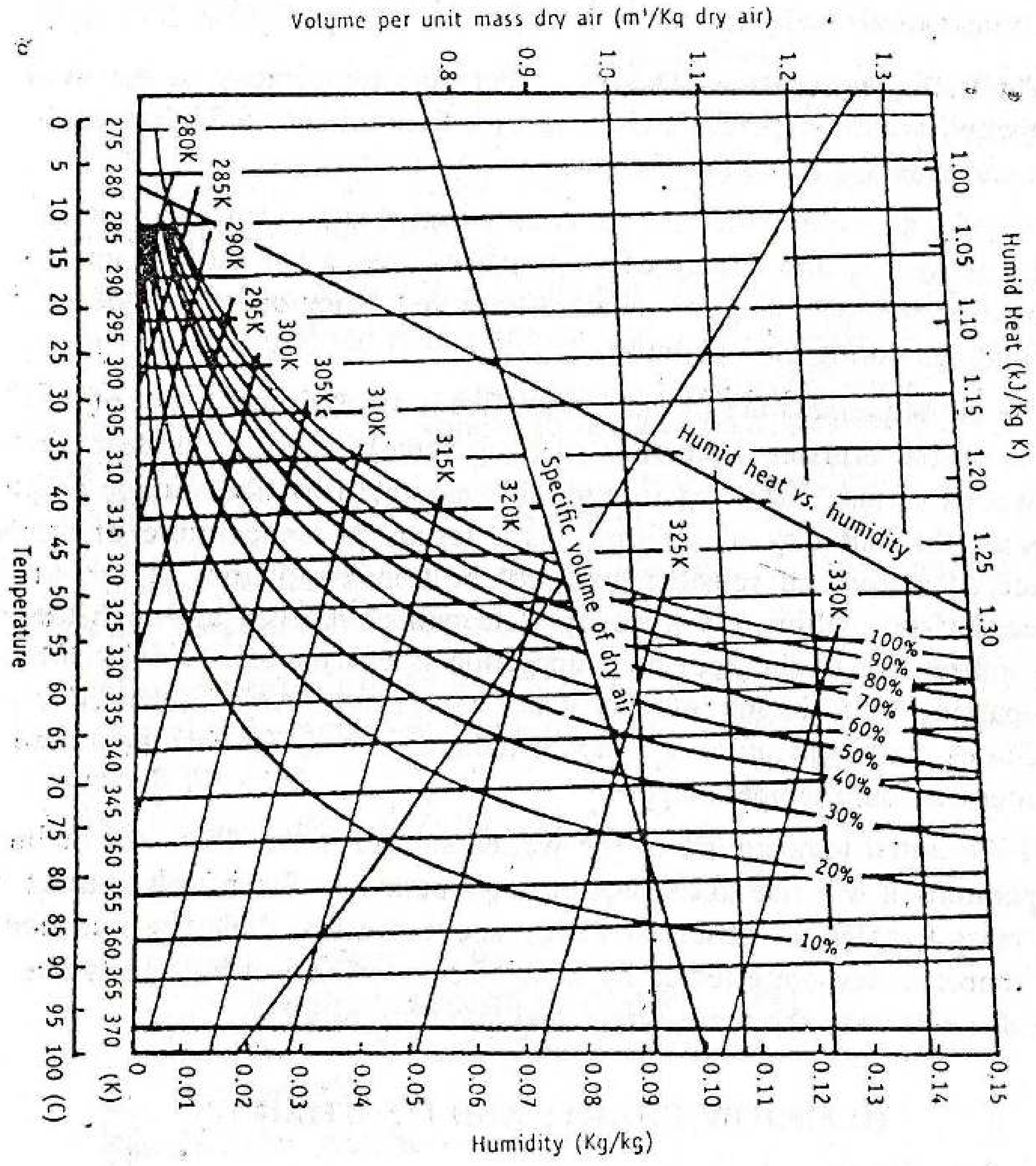


Figure 15-1. Humidity chart, air-water at 1 atmosphere.

(c) To the left of the saturation curve (100% RH), mixtures of air and water vapour can not exist.

(d) Curved lines below the saturated air curve (100% RH) represent various percents of humidity, namely 60%, 40% etc.

Humid heat vs. Humidity : This line is plotted by taking humidity on the right-hand edge (y-axis) and humid heat (kilojoules per kg·Kelvin) along the top of the chart (x-axis). These lines are useful for designing the air conditioners.

Specific volume vs. temperature : The line for specific volume of dry air (and for the saturated volume) is plotted with temperature on x axis and metre cube per kg dry air along the left edge of chart on y axis. The humid volume of a sample of air at a given temperature and humidity can be found by linear interpolation to the humidity-temperature curve.

Adiabatic cooling lines : The groups of lines, which are right side of the saturation curve, are the adiabatic cooling curves. These curves serve two very useful purposes. Firstly, they can be used to determine humidity from the knowledge of wet-bulb and dry-bulb temperatures. Secondly, these curves show the changes in humidity during drying under adiabatic conditions.

Use of Humidity Chart

Humidity chart is a source of data on a definite air-water mixture. A portion of the chart is shown in Figure 15-2. Assume that a given stream of unsaturated air is having a temperature, t_1. It can be represented by point A. By moving vertically downwards, the axis gives the temperature, t_1 which is dry-bulb temperature. Point A is used to illustrate the usefulness of chart. The following types of data can be obtained from the chart.

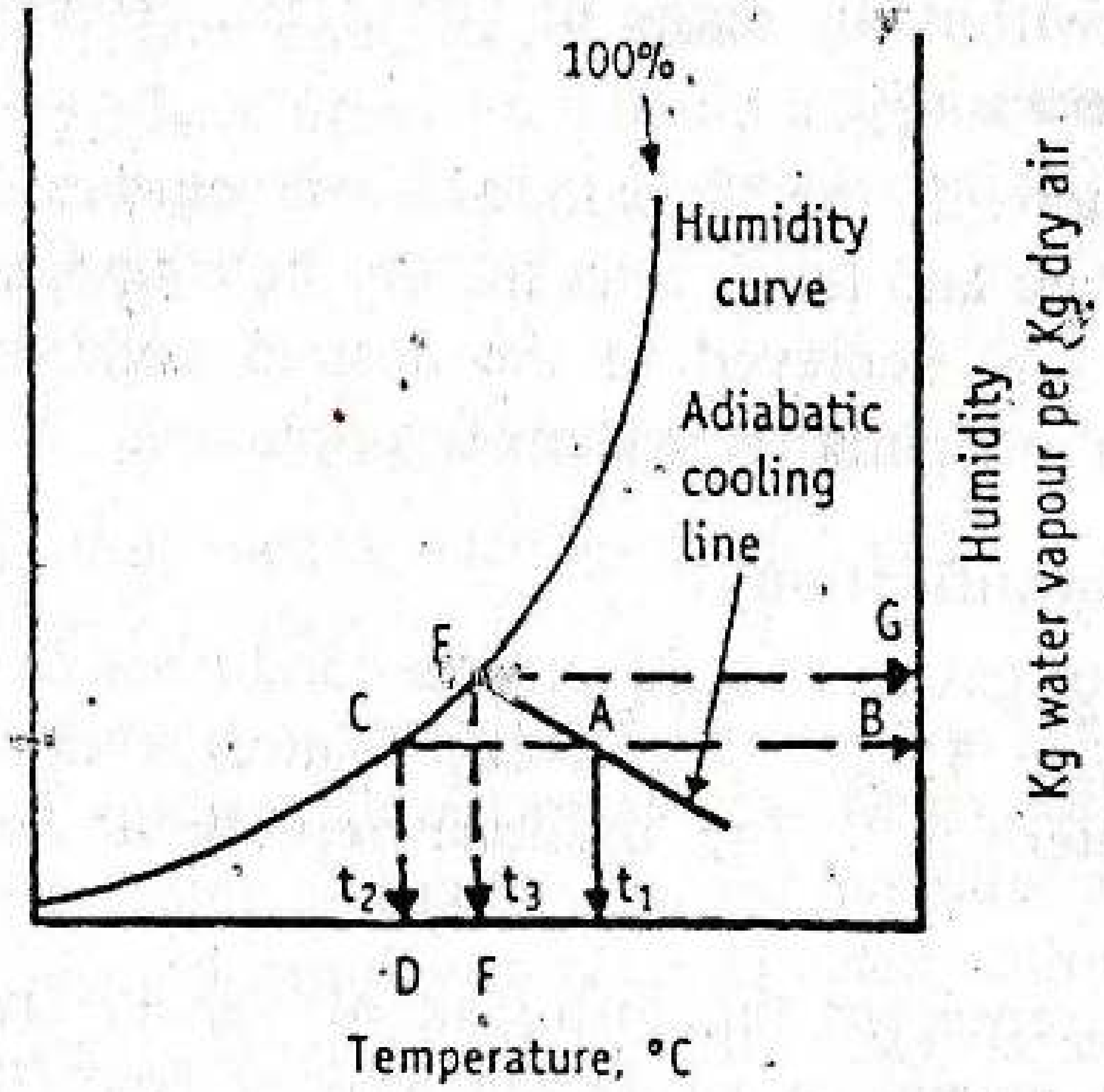


Figure 15-2. Use of humidity chart.

(1) **Humidity :** From point A moving horizontally towards humidity axis gives an intercept point B on axis, which is the humidity of the sample.

(2) **Dew point :** From point A moving horizontally towards left to the 100% line gives an intersection point C. Moving vertically from C downwards to temperature axis gives an intercept point D, which is the dew point temperature, t_2.

(3) **Adiabatic-saturation temperature :** From point A moving along the adiabatic cooling line towards the 100% line gives an intersection point E. Moving vertically from point E downwards to temperature axis gives an intercept point F, which is the adiabatic-saturation temperature t_3.

(4) **Humidity at adiabatic-saturation** : From point E moving horizontally towards humidity axis gives an intersection point G, which is the humidity at adiabatic saturation line.

In a similar manner, humid volume and humid heat can be obtained, by considering the corresponding lines, humid volume and humid heat lines, respectively, as shown in Figure 15-1.

HUMIDIFICAITON

Humidification is the process of increasing the moisture in the air.

Applications

In pharmaceutical industry, if special conditions are not prescribed, the humidity required for various operations is from 20 to 30% RH and the temperature is within the range of 20°–27°C. Hence, dry weather humidification is necessary.

By spraying water into the air path, at a temperature higher than the dew point temperature and lower than the dry bulb temperature, cooling and humidification are achieved to the desired conditions. For this purpose, absorption refrigeration system is employed.

Mechanism of Humidification

The interaction of gas and liquid and the conditions of humidification are shown in Figure 15-3. The x-axis indicates the perpendicular distance to the interface. The ordinate represents temperature and humidity.

Broken arrows represent the diffusion of vapour through the gas phase. Continuous arrows represent the flow of heat (both latent and sensible) through the gas and liquid phases.

In adiabatic humidification, the air is in contact with the liquid at constant temperature. The humidity at the interface (H_i) must be greater than humidity (H_y) of the gas, so that the air gets humidified. Since water is vaporised, the latent heat is transferred from the liquid to gas. The gas temperature (t_y) must be higher than the interface temperature (t_i) in order that sensible heat may flow to the interface. (Heating or cooling without the addition or subtraction of moisture content is called sensible heating or cooling).

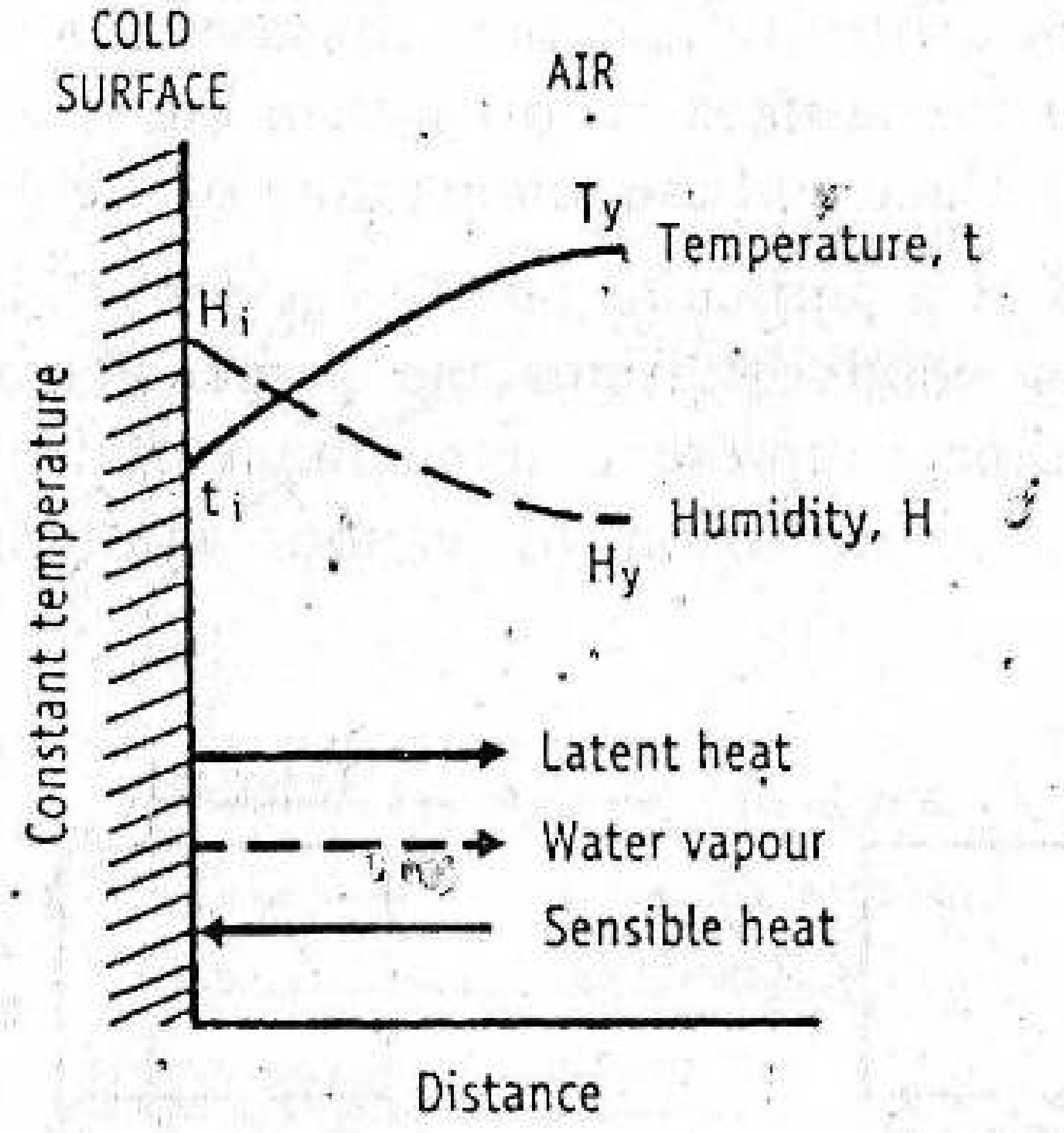


Figure 15-3. Conditions in adiabatic humidifier.

H_i and t_i represent equilibrium conditions of interface (saturation conditions). Latent heat flows from liquid to gas and sensible heat flows from gas to liquid get balanced. Therefore, there is no temperature gradient in the liquid.

DEHUMIDIFICATION

Dehumidification means decreasing of humidity (removal of moisture) from the air.

Dehumidification is accomplished by bringing the moist air in contact with a cold surface (liquid or solid). Many large air conditioner plants incorporate automatic control of the humidity and temperature of the issuing air. Temperature control is effected with the aid of thermocouple or resistance thermometer. Humidity is controlled using a thermocouple recording of the difference between the wet and dry-bulb temperatures.

Applications

Dehumidifiers are used in special heat transfer devices to liquefy vapour by removing their latent heat. Such systems are called *condensers*.

In pharmaceutical industry, many operations are carried at a stated humidity to get optimum results. In many parts of India (e.g., Bengal, Kerala etc.) the air is very humid and it becomes difficult to carry on operation with hygroscopic substances even in air-conditioned room. Hence, dehumidifiers are installed for certain operations.

Mechanism of Dehumidification

The principle of dehumidification is illustrated in the Figure 15-4. If the temperature of the surface is lower than the dew point of the gas, condensation takes place and the temperature of the gas falls.

The conditions at a particular point in a dehumidifier are shown in Figure 15-5. The *x*-axis indicates the perpendicular distance to the interface. The ordinate represents temperature and humidity. (Broken arrows represent the diffusion of vapour through the gas phase. Unbroken arrows represent the flow of heat (both latent and sensible) through the gas and liquid phase).

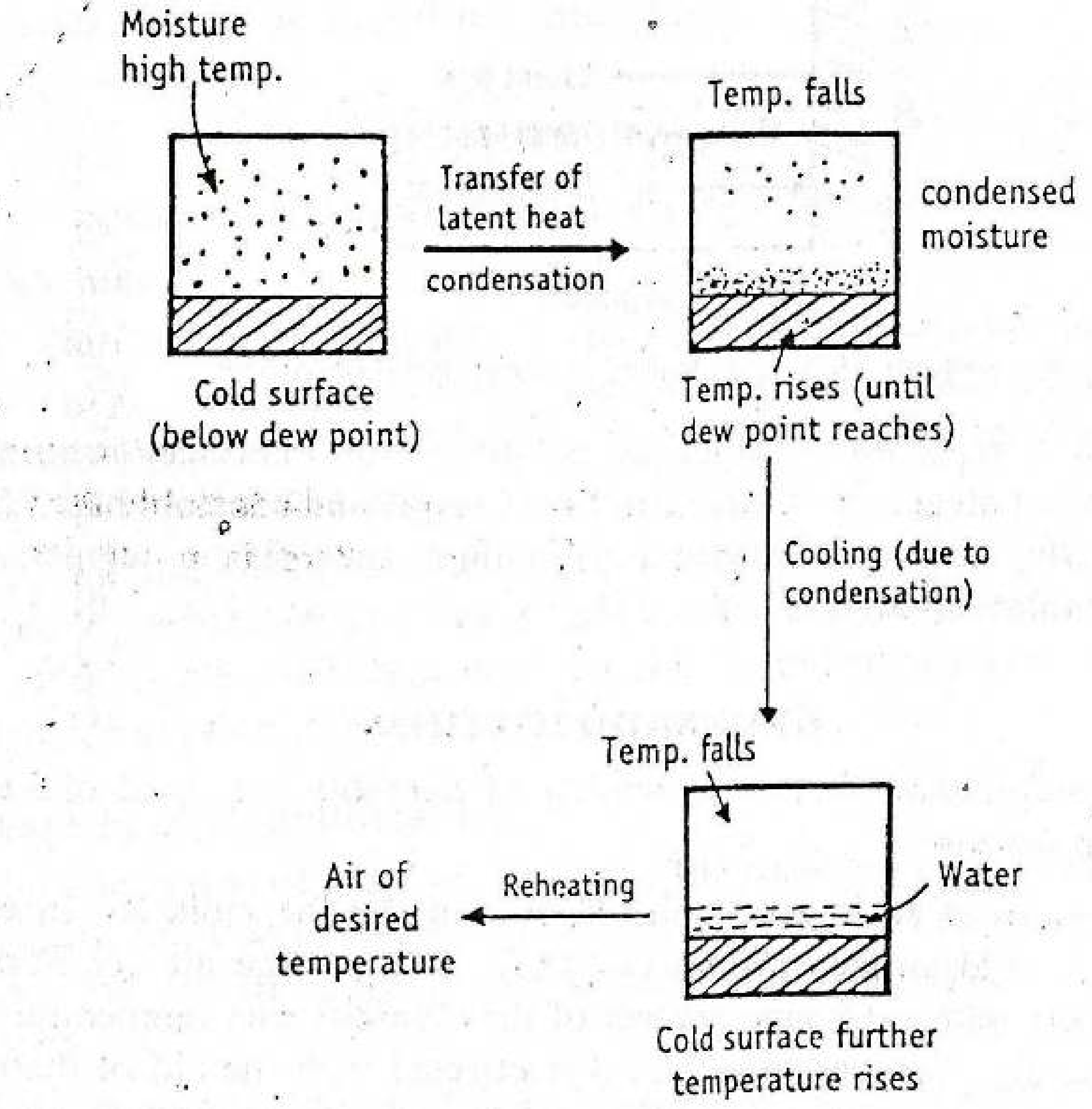


Figure 15-4. Principle of dehumidification process. Temperature and humidity are reduced simultaneously.

In this case, humidity of air, H_y, is greater than the humidity at interface, H_i and, therefore, water vapour diffuses to the interface. Since vapour is condensed to water, latent heat is transferred to the water. So the temperature of the surface tends to rise and that of the air decreases. It would be expected that the air would cool at constant humidity, until the dew point is reached (Figure 15-4).

Since t_i and H_i represent saturated air, t_y must be greater than t_i. Hence the bulk of the air would be saturated with water vapour at that temperature. The sensible heat is transferred into the water.

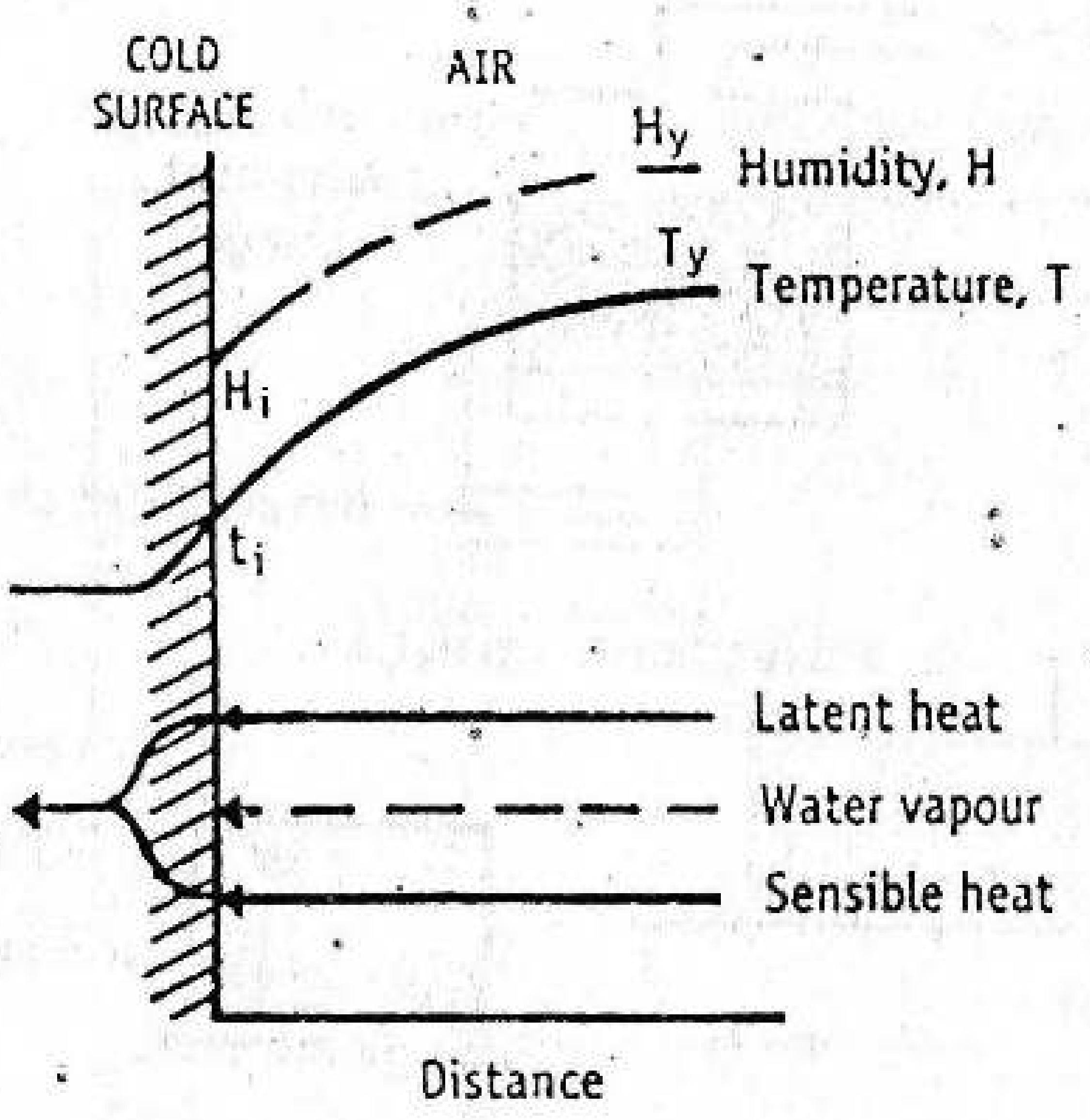


Figure 15-5. Condition of dehumidifier.

The air in contact with the surface is cooled below its dew point. Subsequently, air from a distant place condenses, which requires time to cool. Therefore, effective mixing enhances the dehumidification. Normally, the temperature and humidity are reduced simultaneously throughout the process. After dehumidification, the gas can be reheated to its original dry-bulb temperature.

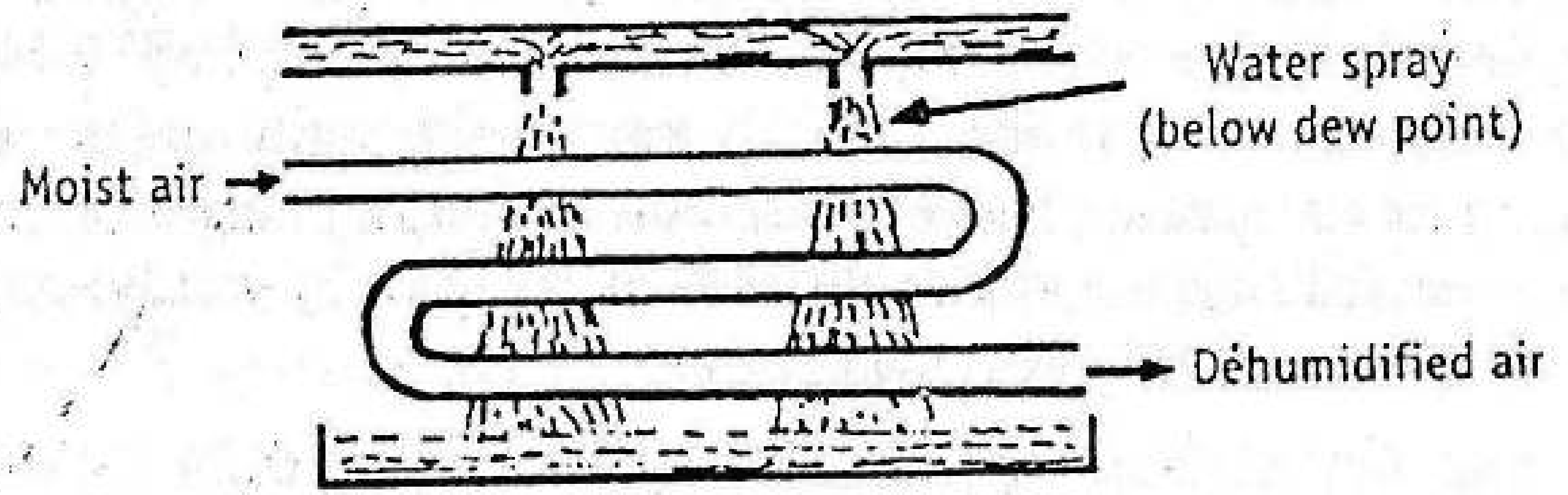
Approaches to Dehumidification

Different approaches to dehumidification are described in Fig. 15-6.

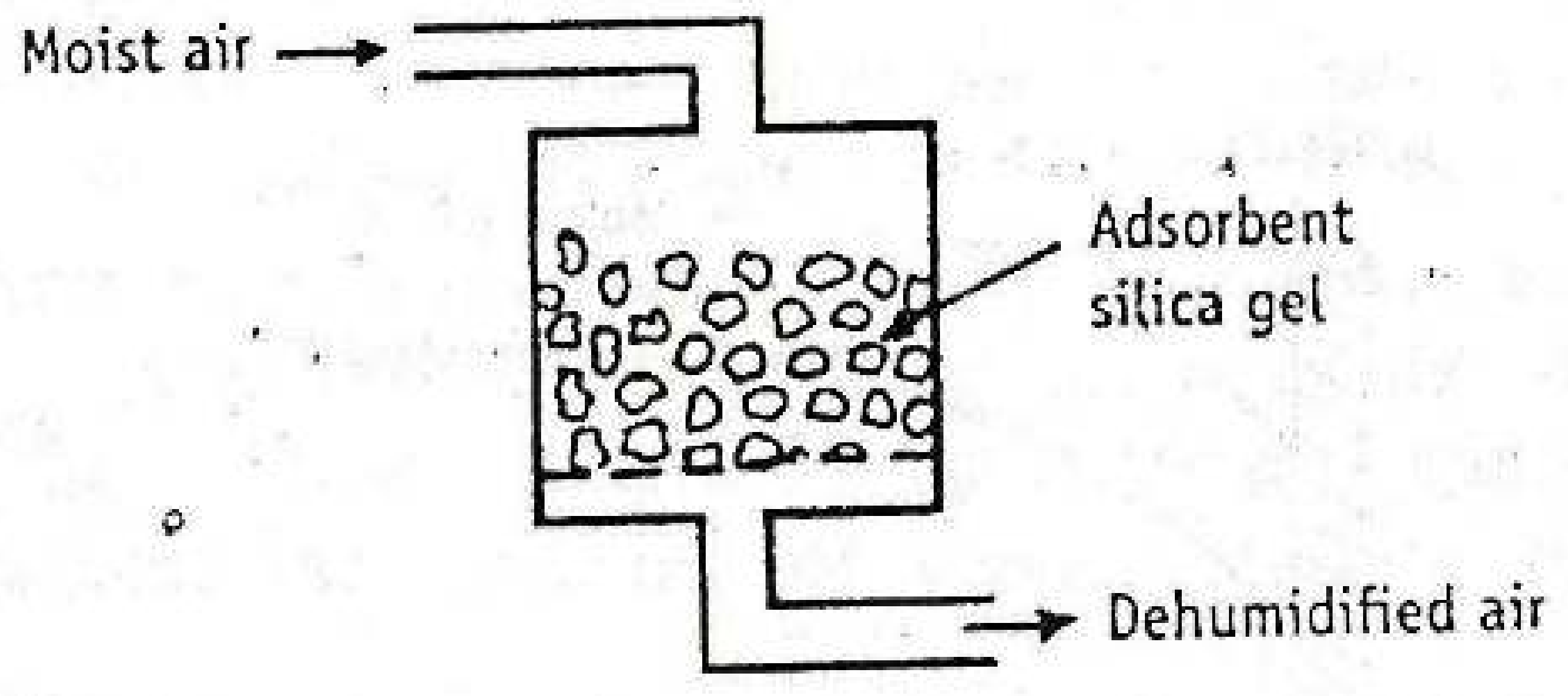
(a) Moist air is brought in contact with a spray of cold water, whose temperature is lower than the dew point of the entering air. (Figure 15-6a)

(b) Humidity can be reduced by compressing the air (Figure 15-6c). During compression, the partial pressure of the vapour increases.

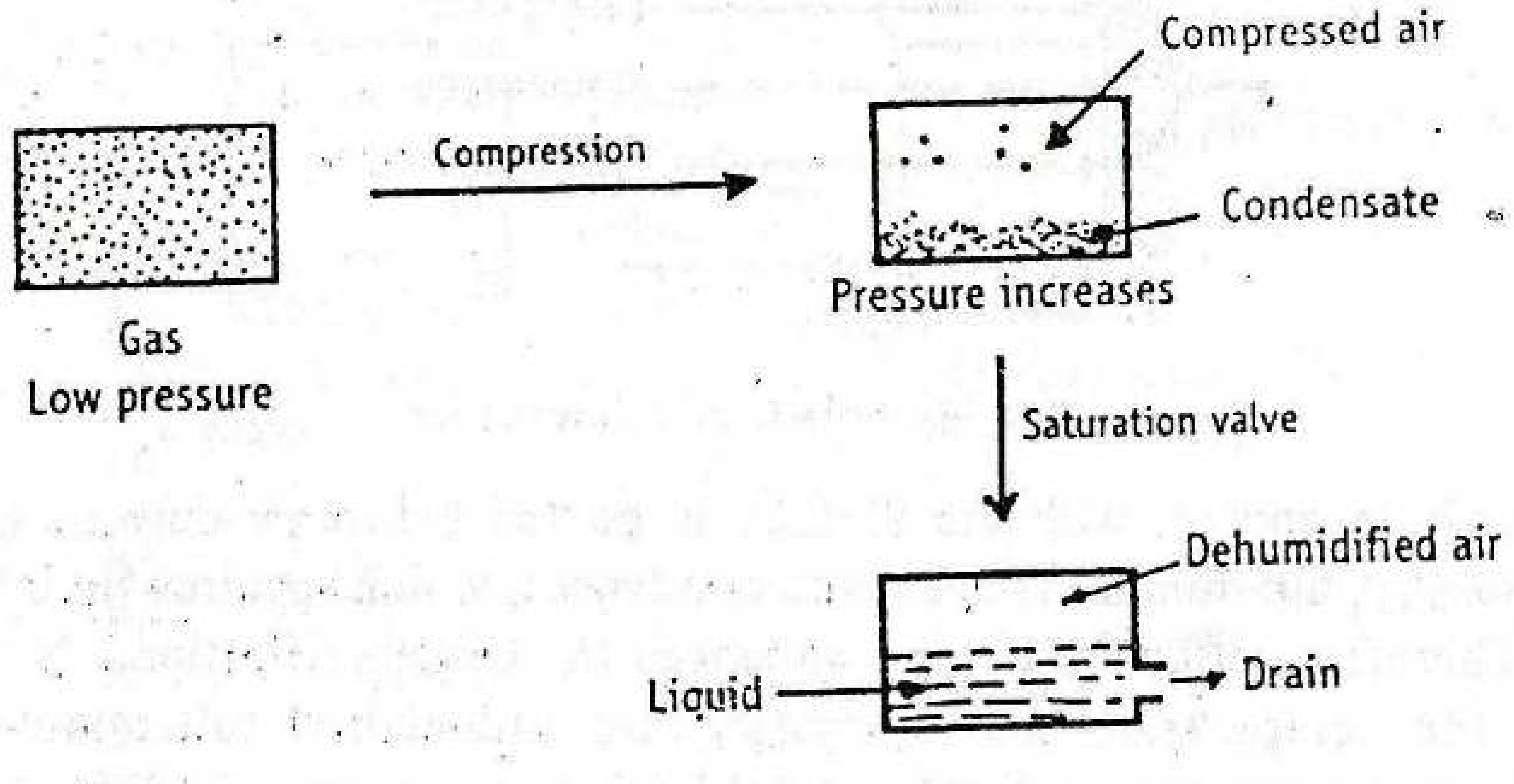
As soon as it reaches the saturation value, condensation takes place. The water gets liquefied and drained off.



(a) Spraying of water on moist air.



(b) Adsorption of moist air.



(c) Compression of moist air.

Figure 15-6. Approaches for achieving dehumidification.

(c) Moist air is passed over a solid adsorbent surface or through a liquid adsorbent spray (Figure 15-6b). Dehumidification occurs due to the lowering of water vapour pressure. The adsorbents used are silica gel or activated alumina. The liquid adsorbents are solutions of inorganic salts (brine, lithium chloride) or organic compounds such as ethylene glycol. Reactivation of adsorbents

is necessary. It is done intermittently or continuously. Silica gel has to be regenerated as soon as or even before it adsorbs 40% of its weight of water.

REFRIGERATION

Mechanical refrigeration is a process of lowering the temperature of a substance less than that of its surroundings.

The simplest form of refrigeration observed in daily life is the use of ice. Ice absorbs heat from the surroundings and melt. During this process the surrounding area becomes cool due to the loss of heat. The capacity of refrigeration is expressed in tonne.

A *tonne of refrigeration* is defined as the rate of heat removal from the surroundings equivalent to the heat required for melting 1 tonne of ice in one day.

If the latent heat of fusion of ice is taken as 336 kilojoules per kg, one tonne is equivalent to heat removal at a rate of 14,000 kilojoules per hour.

Applications

Refrigeration is used extensively in air conditioning plants in the areas for comfort and processing areas. It is used in several other areas as given below.

(1) Removal of heat from chemical reactions.

(2) Preservation of thermolabile substances. For example, insulin, ACTH, pituitary hormones and vaccines are stored in refrigerator. It is extremely important to store all blood products such as whole human blood at as low a temperature as possible above freezing point.

(3) Liquefy processing gas.

(4) Separation of vapour by distillation.

(5) Purification of products.

(6) Preferential freeze-out of one component from a liquid mixture.

Refrigerants

Refrigerant is a liquid which readily absorbs heat when evaporated at a low temperature and pressure and gives out heat on condensing at a higher temperature and pressure. Refrigerants may be primary or secondary.

Primary refrigerants are those liquids that change from a liquid to a gas after absorbing heat.

A number of refrigerants are available, which permits the selection for a specific application. Examples of primary refrigerants and their chemical constitution are given below.

Numerical designation	*Chemical name*
R11	Trichlorofluoromethane (Cl_3FC)
R12 (Freon 12)	Dichlorodifluoromethane (Cl_2F_2C)
R13	Chlorotrifluoromethane (ClF_3C)
R21	Dichlorofluoromethane (Cl_2FCH)
R22 (Freon 22)	Chlorodifluoromethane (ClF_2CH)
R113	Dichlorotetrafluoroethane
R1150	Ethylene
R1270	Propylene
	Ammonia

Secondary refrigerants are those liquids, which act only as heat carriers. Examples are brine, air and water.

The choice of a suitable refrigerant depends upon many factors, although a few are mentioned below.

(1) The latent heat of vaporisation should be large so that the desired cooling effect is produced.

(2) At normal temperature and pressure, refrigerant must be in vapour phase and on compression and cooling it should be liquefied easily.

(3) The pressure required to liquefy the vapour of the refrigerant in the condenser section must be so as to maintain it usually at room temperature.

(4) The vapour pressure of refrigerant liquid in the evaporator section must be maintained at about −15°C greater than the atmospheric pressure.

(5) The specific volume of the refrigerant vapour should not be large.

VCC

Principle

The refrigeration cycle is also known as vapour compression cycle. This is illustrated using single-stage vapour compression.

The basic construction of refrigeration cycles is shown in Figure 15-7. The cycle operates at two pressures, high and low, to enable the process to produce a continuous cooling effect. The sequence of events in the refrigeration cycle is explained by taking basic components in order.

(a) *Receiver or condenser* : The liquid refrigerant is kept in a container namely condenser. The refrigerant is under pressure and the vapour and liquid phases are in equilibrium.

(b) *Expansion valve* : It is a device, which controls the rate of flow of refrigerant into the evaporator, converting the refrigerant from high pressure to low pressure. The refrigerant enters a low-pressure zone.

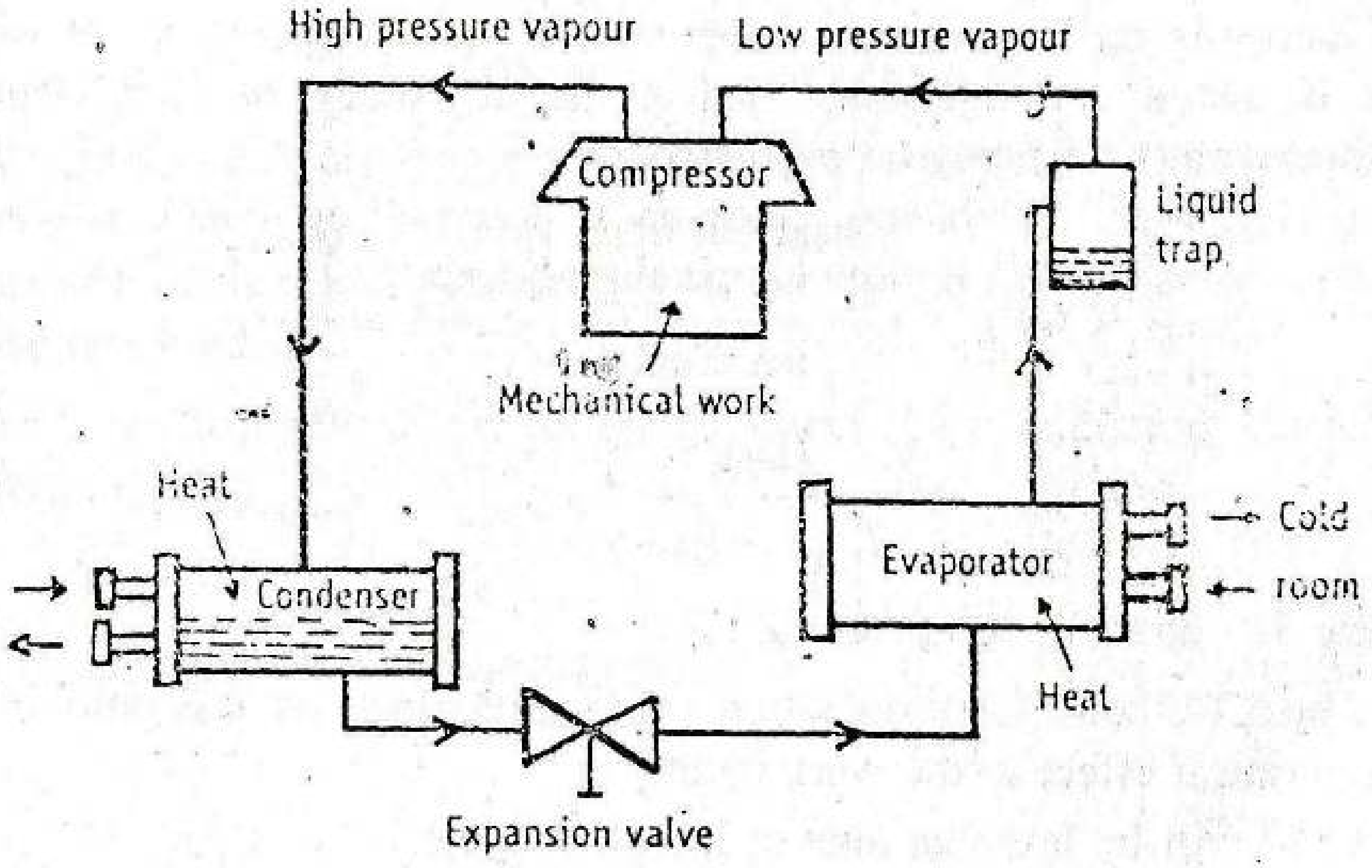


Figure 15-7. Basic construction of refrigeration cycle.

(c) *Evaporator* : Subsequently, a mixture of vapour and liquid enters the evaporator, which consists of coils. Here the refrigerant evaporates by absorbing heat from the space. The molecules move apart by breaking intermolecular forces. The energy (heat) required for this process is taken from the surrounding environment, i.e., space, which is to be cooled. In this step, liquid vaporises completely, though some liquid still remains.

(d) *Liquid trap* : A liquid trap is used to remove liquid, which is then returned to receiver (condenser).

(e) *Compressor* : The saturated vapour is allowed to pass through the compressor. During compression, heat of compression is added to vapour and the pressure raises. The compression is adiabatic and on the discharge side it produces a supersaturated gas. The valve should be opened very slowly. A part of the liquid vaporises to give a stream of high velocity.

(f) *Condenser* : The supersaturated vapour flows to the condenser where the gas is liquefied. These condensers can be air-cooled or water-cooled.

Thus, one cycle is completed as shown in Figure 15-7 and the process continues.

Theory

An ideal refrigeration cycle is a reversal of Carnot cycle as per the second law of thermodynamics. Similar to Carnot cycle, refrigeration also depends on the working temperatures, i.e., temperatures at which heat is added and rejected. Hence, the efficiency or coefficient of performance (COP) may be expressed as:

$$COP_R = \frac{\text{heat absorbed from low temperature source}}{\text{net work input}} = \frac{Q_{low}}{W} \qquad (18)$$

$$= \frac{T_{high}}{T_{high} - T_{low}} \qquad (19)$$

where T = absolute temperature, K.

The *COP* of the refrigeration cycle is defined as the ratio of the refrigeration effect to the work input.

COP will be less than that of the ideal cycle.

As mentioned in the working of a refrigerator, the refrigeration process can be understood from the pressure-enthalpy (heat content) charts. During this process, the refrigerant undergoes a change in enthalpy. Essentially the refrigeration process consists of evaporation and compression.

(i) As the liquid evaporates, it takes heat from the environment (the interior of refrigerator or substance placed in it) so that environment gets cooled. The *net refrigerant effect* (RE) accomplished in the evaporator may be written as:

$$\textit{Net refrigerating effect, } Q_{low} = h_g - h_f \qquad (20)$$

where h_g = enthalpy of gas (vapour) leaving the evaporator, kJ/kg
h_f = enthalpy of liquid leaving the condenser, kJ/kg

The refrigerant effect is defined as the amount of heat removed from the surroundings per unit mass flow of refrigerant.

(ii) Work is being done on the refrigerant vapour to compress it. Heat of compression is expressed as:

$$\textit{Heat of compression, } W = h_d - h_g \qquad (21)$$

where h_d = enthalpy of the discharge, kJ/kg
h_g = enthalpy of inlet compressor, kJ/kg

The work of compression is determined by multiplying the heat of compression by the mass of flow.

Combining equations (20) and (21), COP can be written as:

$$COP = \frac{\text{refrigerating effect}}{\text{work input for compression}} \qquad (22)$$

Two parameters are important for the performance of a refrigerator. The rate at which refrigeration is obtained depends on the weight and volume of a refrigerant circulated per tonne, though several other factors are also involved.

The mass flow rate of the refrigerant circulated per tonne of capacity is determined by:

$$\textit{Refrigerant mass flow rate, } (\text{kg/h}) = \frac{\text{Rate of removal of heat (kJ/h)}}{\text{Refrigerant effect (kJ/kg)}} \qquad (23)$$

$$= \frac{14000 \text{ kJ/h}}{Q_{low}}$$

The theoretical volume of vapour to be handled per tonne may be expressed as:

$$\textit{Theoretical volume of vapour } (\text{m}^3/\text{h}) = \text{mass flow rate} \times v_g \qquad (24)$$

where v_g = specific volume of the suction vapour entering the compressor, m^3/kg.

In order to achieve low temperature effect, it is necessary to have a high compression ratio. A single stage refrigeration cycle cannot yield low temperature effect. To avoid high compression ratio, it is necessary to have several stages of compression. It is necessary for low temperature applications.

A refrigeration system that consists of more than one stage of compression is defined as *multistage refrigeration system*.

Temperatures from −101.1 to −78°C can be obtained by using refrigeration system containing multistage systems.

AIR CONDITIONING

Air conditioning is the process of treating air so as to control its temperature, humidity, cleanliness and distribution simultaneously to meet the requirements of the conditioned space.

In the production area, a desired environment, i.e., humidity and temperature, is maintained. Therefore, air conditioning facilities are essential. Today many offices and pharmaceutical plants are equipped with air conditioners.

Applications

Promoting the human comfort : Human body feels comfort when the heat produced by metabolism of human body is balanced by the sum of the heat dissipated to the surroundings and the heat stored in human body. Air purity is of utmost importance. For example, increase in carbon dioxide adds discomfort. The efficiency and health of workers should be maintained at safe tolerance limits.

Maintenance of proper conditions for the manufacture, processing and preserving of material and equipment : The following areas are identified.

Compression of tablets : In the granulation section, the air conditioning is optional, if necessary the conditions are 45% RH and 22°C. In the tabletting section, the conditions are less than 20% RH and 22°C. In the production of effervescent products, dry syrups, controlling humidity is a vital factor. The relative humidity should not exceed 10 to 15% and temperature is at 22°C.

Manufacture of soft gelatin capsules : The temperature is usually in the range of 20°C to 22°C and the humidity is controlled to a maximum of 40% in the operating areas and between 20 and 30% in the drying areas.

Manufacture of sterile products : In case of parenterals and ophthalmic products, the environmental conditions are much more stringent in filling and sealing rooms. Therefore, the standards of clean air quality are of greater importance. In the production of all biological products (Schedule C & C_1) air conditioning is essential.

Environmental test chambers : These are designed to carry out stability and shelf life testing of drugs. They offer reproducible temperature and humidity conditions. Climatic conditioning is also required for herbal research, pesticide research and zoology.

Maintenance of animals and equipment : According to the Drugs and Cosmetics Act and Rules, the animal houses should be air-conditioned. Sophisticated electronic (analytical) equipment are stored and the work is carried out in air conditioned rooms.

Approaches for Achieving Air Conditioning

Normally the air is allowed to reach complete saturation by providing appropriate conditions. Then humidity is fixed. In commercial equipment, the conditions are somewhat indeterminate and the exit humidity is not quite saturated. Therefore the exit humidity is fixed by varying water temperature according to the characteristics of the specific piece of equipment at hand. This can be achieved by re-heating to the desired temperature.

Consider the following example. When air is entering the equipment, let the initial dry bulb temperature of the air be t_1 and humidity be H_1. It is represented by point A. Let the desired dry-bulb temperature be t_2 and humidity be H_2 at the exit point air (point B). The exit air attains the desired conditions in any one of the following methods.

(A) The sequence of steps is shown in Figure 15-8. The air is first allowed to attain the desired humidity by treating with water using humidity chart. It is represented by point C (wet bulb temperature, t_3).

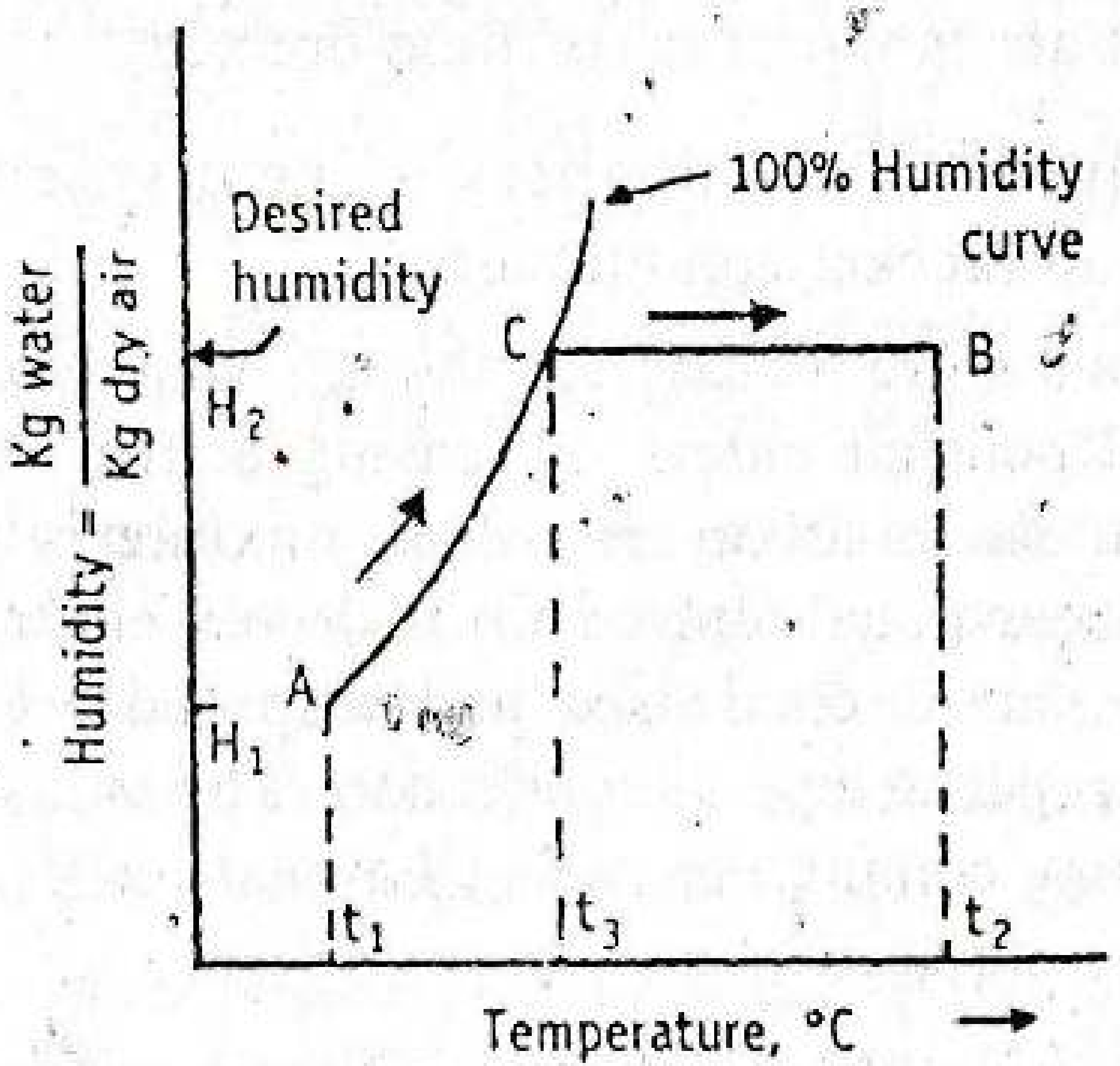


Figure 15-8. Changes in air temperature and humidity for air conditioning process (Approach A), using 100% humidity line of the psychometric chart.

Then it is heated to attain the desired temperature of t_2 at the same humidity. This path of air is represented by ACB in Figure 15-8.

(B) The sequence of steps is shown in Figure 15-9. In the second approach, air is preheated to a temperature, t_4. Subsequently, the air is cooled along the adiabatic cooling line, until it reaches the desired humidity. It is then reheated so as to reach the desired temperature of t_2. This corresponds to path ADCB in Figure 15-9.

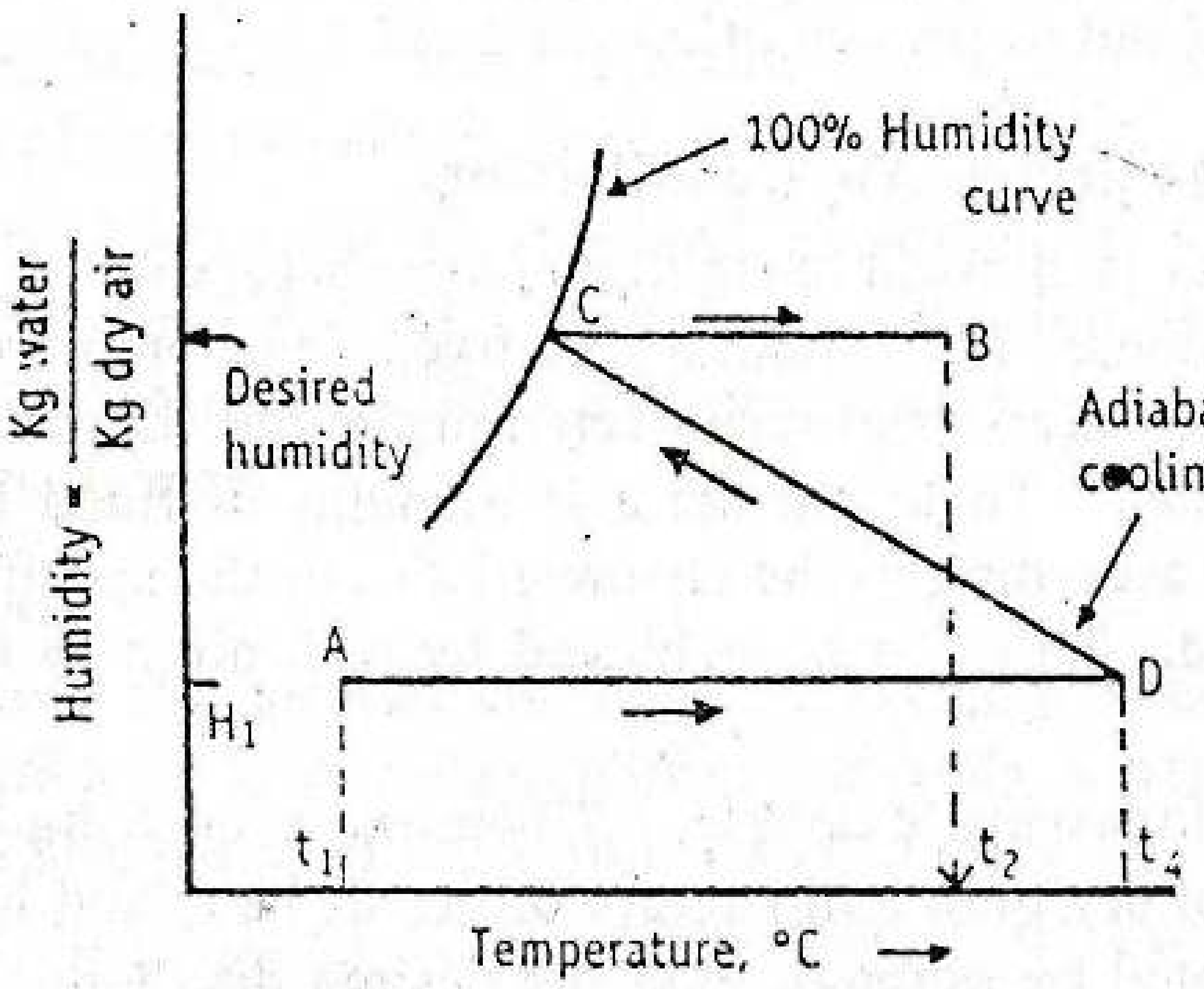


Figure 15-9. Changes in air temperature and humidity for air conditioning process (Approach B), based on adiabatic cooling line.

Types of Equipment

Modern air conditioning equipment generally fall into two classes.

1. Self contained air conditioner (unitary or packaged)
2. Central air conditioner (or field erected).

1. Self contained air conditioners : These systems include window mounted or wall bracket conditioners.

Most of these units are air cooled, though water-cooled types have also been made. Room air enters the casing at the front panel. It is mixed with part of the outdoor air. This mixture is forced over the cooling coils by a centrifugal fan, which is driven electrically. Some of the moisture in the air is condensed and disposed off by means of a single ring of the propeller type of condenser. The units are hermetically sealed. Reciprocating compressors using nontoxic refrigerant and driven by capacitor motors are used.

2. Central air conditioning system : These systems may serve one or several areas with conditioned air being supplied through duct network.

Air cleaning is usually provided using filters, which can be cleaned for reuse or disposable. Cooling is achieved using either water or by direct expansion in refrigerated coils or air washers. Steam or hot water coils are used for heating. Humidification systems may be provided by surface type water nozzles, steam humidifiers or sprayed coils.

Equipment : Air conditioning involves specialised applications of basic thermodynamics, hydrodynamics and fluid flow principles.

Principle : In this type of air conditioner, approach (B) is used. The air is heated to a higher temperature, followed by cooling along an adiabatic cooling line to reach the desired humidity. It is then reheated to the desired temperature at constant humidity. Thus the path ADCB is followed.

Construction : The construction of the equipment is shown in Figure 15-10.

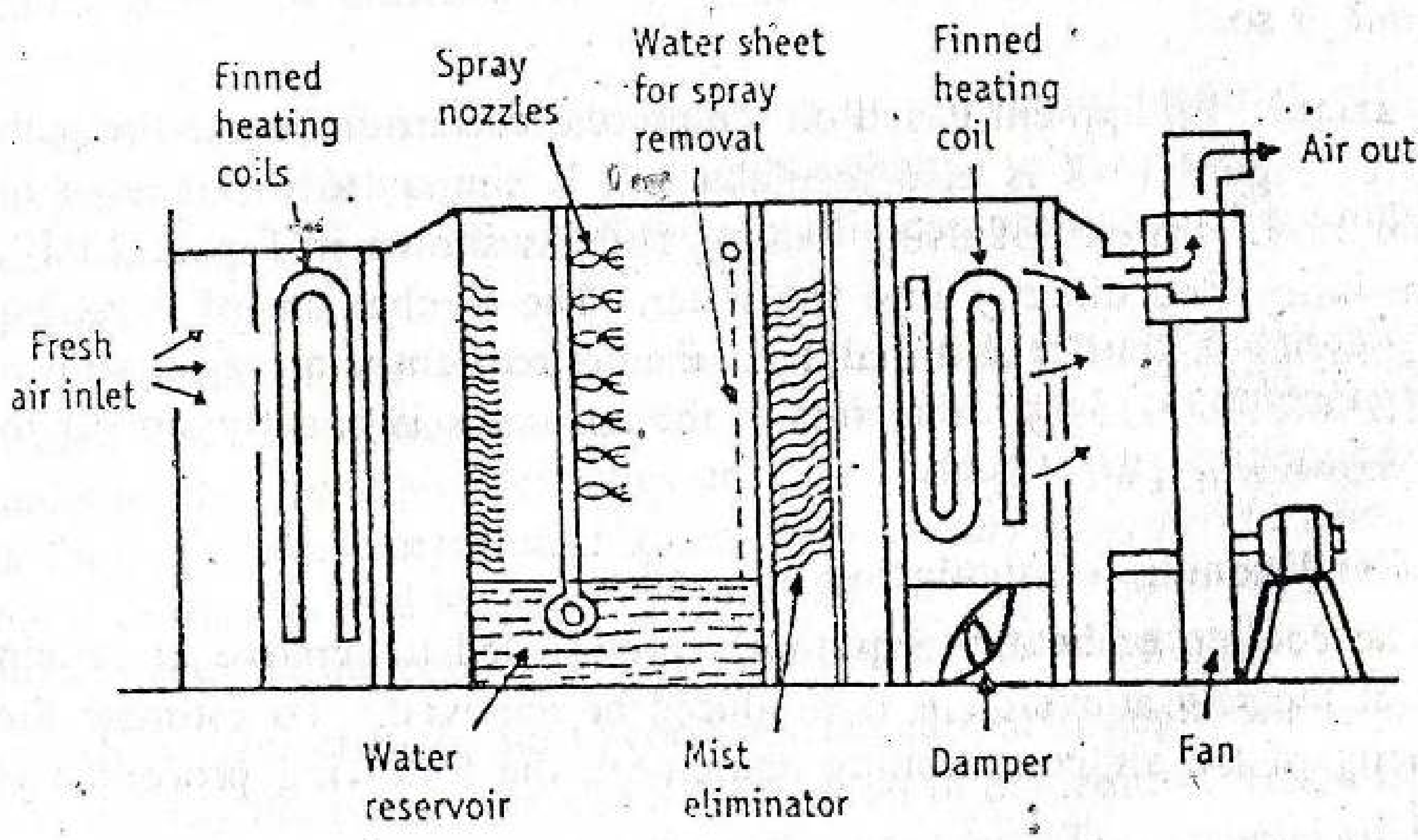


Figure 15-10. Typical, central-stationed air conditioning unit and control systems.

Working : The principle employed in this equipment is approach B. Outdoor air and room air is drawn into the equipment using a fan. Air quality is maintained by allowing the air to pass through the filters in order to remove suspended particles. Air is then allowed to pass through finned coils and heated (as indicated from point A to D in Figure 15-9).

The hot air is then passed through water sprays and is adiabatically cooled and humidified (line DC in Figure 15-9). The pump draws water from the reservoir below and sprays on the air stream. The pump also delivers water to give a curtain of water to eliminate most of the entrained sprays. The air then enters the eliminator baffles where the last entrained water is removed. In the pump discharge, there may be a heater or a provision for steam injection to adjust the water temperature.

A second set of coils performs the final re-heating (line CB in Figure 15-9). The final temperature may be regulated by controlling the steam in the second set of coils or by controlling a bypass damper as shown in Figure 15-9. A fan draws the air through the apparatus and discharges it to the point of use. From this point, the air is sent to the required areas through ducts.

Temperature is regulated by thermostatically controlled heating or cooling units or by a combination of heating-cooling units.

Circulation takes place naturally within area, but it is necessary to use mechanical means to re-circulate air (to replenish air periodically with fresh air) or by ventilation, which circulates fresh air only once in an hour or so.

Variant : Equipment based on the process corresponding to the path ACB of Figure 15-8 is also available. It is similar to that shown in Figure 15-9. Instead of using heating coils as shown in Figure 15-10, steam is injected directly into the water. The mechanism of pumping and spraying is similar and maintains the desired temperature (as shown by CB in Figure 15-8). The rest of the apparatus is exactly similar to that shown in Figure 15-10.

Air Conditioning—Calculation of Load

The cooling or heating equipment is provided to remove or to add heat at the rate at which it is produced or removed. To estimate the capacity of the air conditioning equipment, the following procedure is used.

Step 1. The temperature conditions (outdoor and indoor temperature) are designed for winter and summer outdoor temperatures.

Step 2. Space cooling load is calculated.

(a) Direction and magnitude of wind velocity.
(b) Outside humidity and temperature.
(c) The nature of construction materials.
(d) Orientation of openings, windows and doors.
(e) Period of occupancy and the number of persons in the room and their activities.

Hence, air conditioning is provided under assumed conditions keeping variables fixed. Allowances have to be made for changes in the assumed conditions.

Glossary of Symbols

C_a = Specific heat capacity of gases, kJ/kg.
C_w = Specific heat capacity of vapour, kJ/kg.
COP = Coefficient of performance.
H = Humidity, kg/kg.
H_A = Per cent humidity.
H_R = Relative humidity.
H_s = Humidity at saturated gas (Air).
h = Hour
h_d = Enthalpy of discharge leaving compressor, kJ/kg.
h_g = Enthalpy of gas leaving evaporator, kJ/kg.
h_f = Enthalpy of liquid leaving the condenser, kJ/kg.
M_A = Molecular weight of gas or vapour.
M_B = Molecular weight of air.
P_A = Vapour pressure of liquid, kPa.
P_B = Vapour pressure of the air, kPa.
p_A = Partial pressure of water in air, kPa.
Q = Heat absorbed from low temperature source (net refrigerating effect), kJ/kg.
T = Absolute temperature, K.
V = Humid volume, m^3/kg.
v_g = Specific volume, m^3/kg.
s = Humid heat, kJ/kg·K.
w = Weight of moisture, kg.
W = Heat of compression (net work input), kJ/kg.

QUESTION BANK

Each question carries 2 marks

1. What are humidity charts? Write their uses in pharmacy.
2. Draw a humidity chart and give its significance.
3. Define the terms, humidity and dew point.
4. Write the utility of humidity charts.
5. Differentiate between humidity and relative humidity.
6. What are the applications of dehumidification/humidification?
7. Explain the principle of dehumidification
8. Explain the principle of humidification.
9. Differentiate dry bulb temperature and wet bulb temperatures.
10. What are the applications of air conditioning?

Each question carries 5 marks

1. Describe the important features of humidity charts.
2. Describe the working of a refrigerator.
3. What do the term dehumidification means? Write a note on the applications of dehumidification.
4. With a neat diagram explain principle and working of an air conditioner.

16

Corrosion

- Theories of Corrosion
- Factors Influencing Corrosion
- Types of Corrosion
- Prevention and Control of Corrosion

.Metals spontaneously undergo gradual destruction when exposed to the atmosphere. In chemical terminology, such destruction is known as corrosion.

Corrosion is defined as the reaction of a metallic material with its environment, which causes a measurable change to the material and can result in a functional failure of the metallic component or of a complete system.

Exposure of the surface to air, water, and caustic chemicals are responsible for corrosion. Since metals are good conductors, they undergo electrochemical changes on their surfaces. The compound that is formed during corrosion is referred to as *corrosion product* and the metal surface is said to be *corroded*. The *corrosion media* are generally liquids (mostly aqueous solutions), but also solids and gases.

The surface changes due to corrosion are carried through the equipment and destroy the performance and fabrication in due course. Some times, the leached metal may contaminate the product. The material of construction must be resistant to corrosion and erosion. Hence, adequate attention should be paid while selecting the materials for construction of equipment.

Corrosion can be either dry or wet type.

Dry corrosion : It involves the direct attack of dry gases (air and oxygen) on the metals through chemical reactions. As a result an oxide layer is formed over the surface. This type of corrosion is not common.

Wet corrosion : It involves the direct attack of aqueous media (strong or dilute, acidic or alkaline) on metal through electrochemical reactions. The moisture and oxygen are also responsible. This type of corrosion is quite common.

Applications

Knowledge of corrosion is helpful in certain areas to prevent problems.

Dies and punches : In the compression of tablets, dies and punches should be free from rust and corrosion. Chromium plated dies and punches are used, so that the problems such as pits and abrasion can be avoided.

Milling equipment : In these equipment, a perfect fit between the moving parts should be maintained for effective size reduction. Though corrosion does not effect the performance of the mill or product, surface imperfections do not facilitate proper cleaning of the equipment. Hence, the associated problems persist.

Chemical processing reactors : Diverse nature of solutions which come in contact with the reactor surface often lead to corrosion on account of corrosive media and environmental conditions.

Fermenters : Glass, glass-lined and stainless steel (S.S.) materials are used for the construction of the fermentors. During fermentation, the release of trace metals from the equipment may have deleterious effects on the enzyme system and metabolic pathways of the organisms. The possible corrosion aspects in fermentors are pits and crevices, which make it difficult to clean and remove the contamination. Most of the operations are conducted at normal temperatures and the pH of the media would be around neutral. Maintenance of hygiene, need for sterility and prevention of contamination are important considerations in the construction of fermenters.

Storage containers : Prolonged storage of reactive chemicals leads to corrosion of the containers.

This chapter highlights the general aspects of corrosion such as corrosive environments, principles, types of corrosion and measures to prevent corrosion.

THEORIES OF CORROSION

The metal surface undergoes an electrochemical reaction with the moisture and oxygen in the atmosphere. This theory is known as *electrochemical theory of corrosion*. The mechanism involves the formation of a galvanic cell (anodic and cathodic areas), by different metals (for example, Fe and Cu) or in different areas on the same piece of metal (for example, iron).

When galvanic cells are formed on different metals, the corrosion is known as *galvanic corrosion*. These reactions are illustrated using the metals in the presence of eletrolyte solution such as hydrochloric acid.

Corrosion Reactions on Single Metal

Electrochemical reactions are illustrated by considering the corrosion on a piece of iron in hydrochloric acid. Anodic and cathodic areas are formed on the surface of iron, owing to surface imperfections (localised stresses, grain orientation, inclusions in the metals) or due to variations in the environment. Numerous tiny reactions may occur (Figure 16-1).

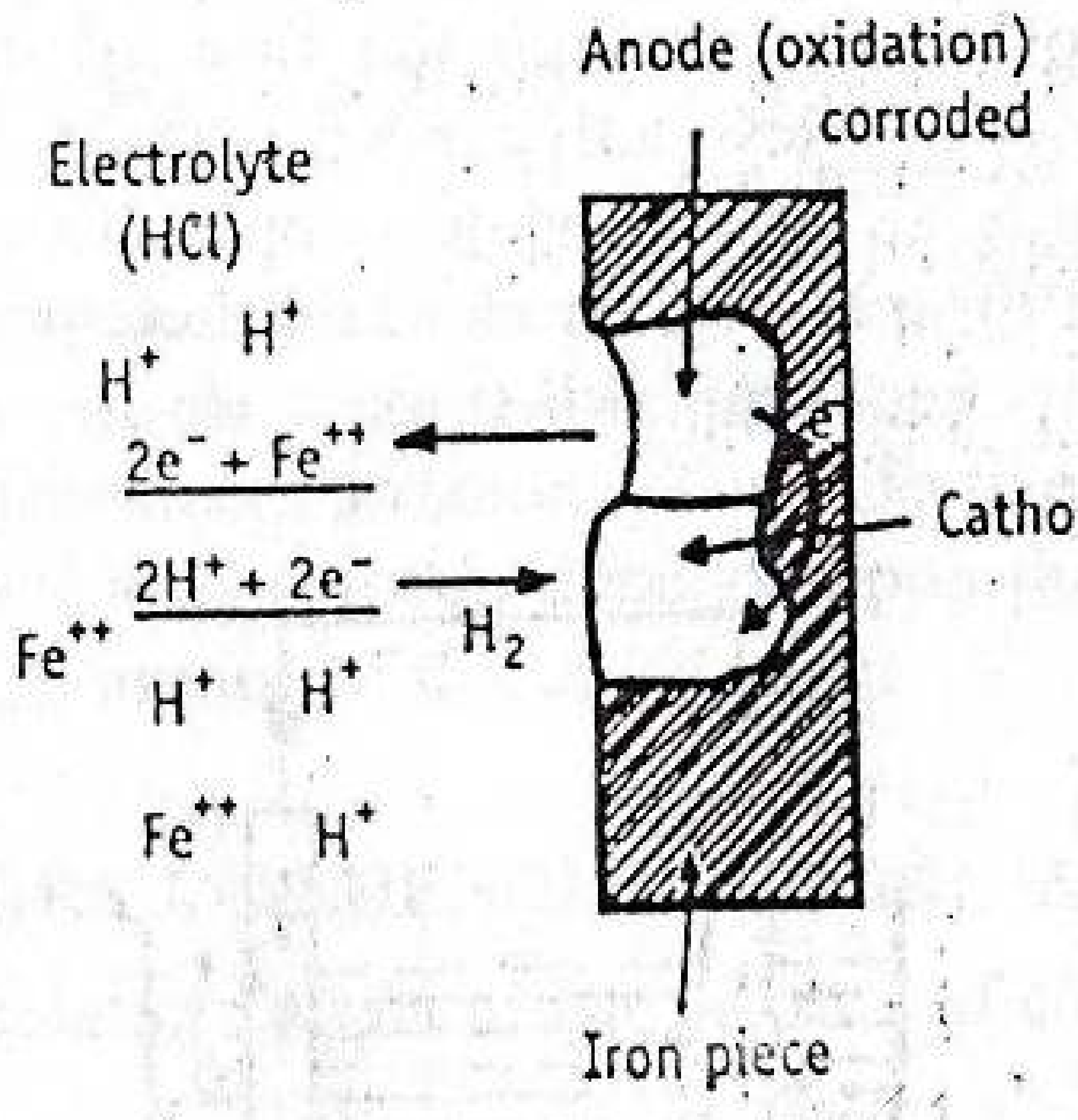


Figure 16-1. Electrochemical mechanism of corrosion. Different areas on the iron piece are illustrated.

Reaction at anode : Oxidation takes place with the release of electrons. Positively charged iron atoms get detached from the solid surface and enter into solution (electrolyte) as positive ions.

At anode: $Fe \longrightarrow Fe^{++} + 2e^-$ (indicated by rough surface)
(oxidation)

The released free electrons (negative charge) pass round the external circuit.

Reaction at cathode : Reduction of constituents occurs with the taking up of electrons. The free electrons reach the cathode and react with some positively charged species such as hydrogen ions in the electrolyte solution. In the absence of acid, water itself dissociates to generate H^+ ions.

At cathode: $2H^+ + 2e^- \longrightarrow H_2\uparrow$ (indicated by formation of bubbles at the surface)
(Reduction)

The amount of metal (iron) which is dissolved in the electrolyte is proportional to the number of electrons flowing, which in turn is dependent upon the potential and resistance of the metal.

The overall reaction: $Fe + 2H_2O \longrightarrow \underset{\text{Red brown rust}}{Fe(OH)_2} + H_2\uparrow$

High evolution of H_2 accompanies rapid corrosion such as hydrogen embrittlement. Depletion of hydrogen also enhances corrosion. In moderate concentrations of H_2, corrosion slows down.

Corrosion Reactions Between Metals

Galvanic corrosion results from the flow of current from a more active metal (anode) to a less active metal (cathode). For example, zinc dissolves and forms an anode, while copper (Cu) forms the cathode. These two metals form two electrodes and their presence in an electrolytic solution forms a galvanic cell (Figure 16-2).

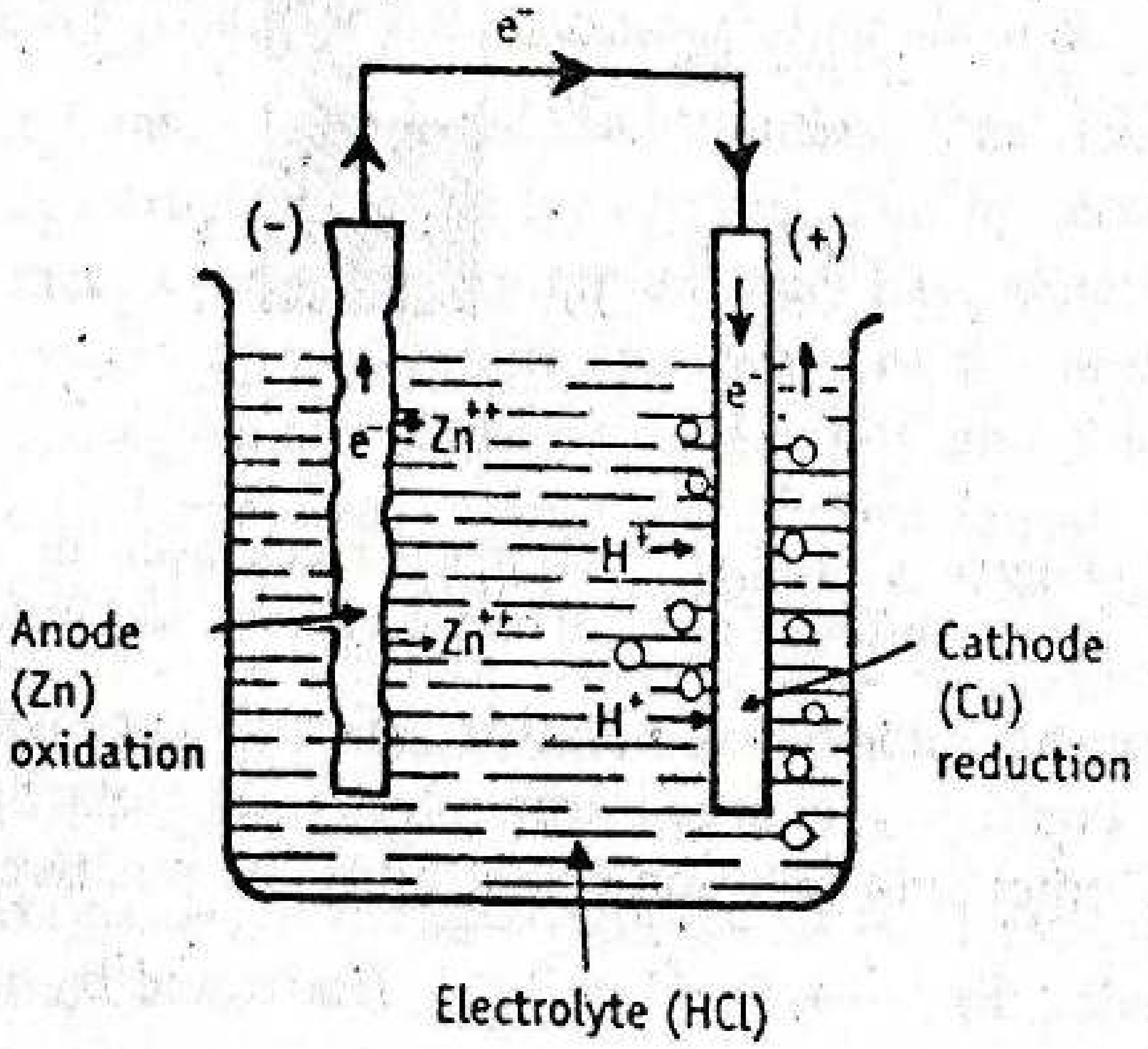


Figure 16-2. Galvanic mechanism of corrosion. Reactions between different kinds of metals.

Spontaneous reaction can occur when two electrodes are connected through an external wire. Reactions at anode and cathode are:

At anode: $Zn \longrightarrow Zn^{++} + 2.e^-$ (indicated by rough surface)
(oxidation)

At cathode: $2H^+ + 2e^- \longrightarrow H_2\uparrow$ (indicated by formation of bubbles at the surface)
(Reduction)

The corrosion current flows at the expense of the anode metal, which gets corroded continuously, where as the cathode metal is protected.

In some cases, evolution of the hydrogen gas is slow. The accumulation of a layer of hydrogen on the cathode surface slows down the corrosion. This is called *cathodic polarisation*. It forms an insulating layer that slows down or stops the electrochemical reaction.

Corrosion Involving Oxygen

The oxygen dissolved in an electrolyte can react with accumulated hydrogen to form water. Depletion of hydrogen layer allows corrosion to proceed.

At cathode: $O_2 + 2H_2 \longrightarrow 2H_2O$ Corrosion proceeds due to depletion of hydrogen

The above reaction takes place in acid media. When the corrosion media is alkaline or neutral, oxygen is absorbed. The presence of moisture (or water) promotes corrosion. The effective concentration of oxygen in water adjacent to cathode depends upon the degree of aeration, temperature and presence of dissolved salts.

FACTORS INFLUENCING CORROSION

A number of processing factors affect the rate of corrosion.

Solution pH

The pH affects the rate of corrosion of metals by one of the three general patterns.

(1) Metals such as iron dissolve rapidly in acidic solution. In the middle pH range (4 to 10), the concentration of H^+ ions is low. Hence, the corrosion rate is controlled by the rate of transport of oxidizer (oxygen).

(2) Certain amphoteric metals dissolve rapidly in either acidic or basic solutions. Examples are aluminium and zinc. Corrosion proceeds.

(3) Noble metals are not affected by pH. Examples are gold and platinum.

The H^+ ions have a tendency to take up electrons to form H_2 gas. Therefore, H^+ ions capture electrons and promote anodic corrosion.

Oxidising Agents

Oxidising agents may accelerate the corrosion of one class of materials, whereas retard another class.

Oxidizing agents such as oxygen (O_2) react with hydrogen to form water. Once hydrogen is removed, corrosion is accelerated. For example, copper in sodium chloride solution follows this mechanism.

Oxidising agents retard corrosion due to formation of surface oxide films, which makes the surface more resistant to chemical attack. Therefore, adsorbed oxygen layer is essential. Thus a balance between the power of oxidising compounds to preserve the protective film and their tendency to destroy the protective film determine the corrosion of the metal. For example, an oxide film is rapidly formed on stainless steel. This film cannot be dissolved or destroyed easily even in severe operating conditions. However, sulphuric acid and hydrochloric acid can easily destroy this oxide film.

Temperature

The rate of corrosion tends to increase with rising temperature. It has a secondary effect. The influence of temperature on corrosion may follow several of these mechanisms.

(1) Increase in temperature reduces the solubility of oxygen or air. The released oxygen enhances the corrosion.

(2) Increase in temperature induces phase changes, which enhances the rate of corrosion. At high temperatures, organic chemicals are saturated with water. As the temperature decreases, water gets condensed.

(3) Oxygen is needed for maintaining iron oxide film, which prevents corrosion. In the absence of oxygen (due to increase in temperature), the corrosion of stainless steel increases.

(4) Copper-based alloys do not depend on the oxide film for corrosion.

Velocity

When the corrosive medium moves at a high velocity along the metallic surface, the rate of corrosion frequently increases. High velocity has the following effects.

(1) Corrosion products are formed rapidly, because chemicals (including oxidising substances) are brought to the corroding surface at a higher rate.

(2) The accumulation of insoluble film on the metallic surface is prevented. Therefore, corrosion resistance of these films decreases.

(3) The corrosion products (or film) are easily stifled and carried away, thereby exposing the new surfaces for corrosion.

Thus corrosion proceeds unhindered. This factor is responsible for the corrosion of a number of equipment parts, such as condensers, evaporator pipes (in the vicinity of bends in the pipes), propellers, agitators and centrifugal pumps. Corrosion occurs frequently in small diameter tubes/pipes through which corrosive liquid may be circulated at high speeds as shown in the above examples.

Surface Films

Once corrosion is started, its further progress is often controlled by the nature of surface films. A variety of surface films have been observed.

Thin oxide films are formed on the surface of stainless steel (rusting). These films tend to retain or absorb moisture, which delays the time of drying. Hence, the surface exposure to atmosphere or corrosive vapour increases the extent of corrosion. The rust films formed on low alloy steels are more protective than those formed on unalloyed steel.

Insoluble salts such as carbonates and sulphates may be precipitated from hot solutions on the metal surfaces. These protect the metal surfaces.

If the film is porous (example is zinc oxide), corrosion continues. Nonporous films (example is chromium oxide film on iron) prevent further corrosion.

Oil and grease films may occur on the surfaces either intentionally or naturally. These films protect the surface from direct contact with corrosive substances. Examples are metals submerged in sewage or equipment used for processing oily substances.

Other Factors

The concentration of corrosive chemicals in the environment influences the rate of corrosion. In equipment such as distillation columns, reactors and evaporators, the concentration can change continuously, making prediction of corrosion rate difficult. In addition, corrosion rates are seldom linear over a wide range. Concentration is important during plant shut-down. The presence of moisture that collects during cooling

TYPES OF CORROSION

Pure metals and their alloys tend to enter into chemical union with the components of a corrosive medium to form stable compounds. Corrosion can be broadly classified as follows.

1. Fluid corrosion, General
2. Fluid corrosion, Localised
3. Fluid corrosion, Structural
4. Fluid corrosion, Biological

Fluid Corrosion : General

When corrosion is generally confined to a metal surface, it is known as *general corrosion*. This type occurs in a uniform fashion over the entire exposed surface area at a wide range of temperatures. General corrosion is of two types.

Physicochemical corrosion : The effects of this type are swelling, crazing, cracking, softening etc. Examples are plastics and nonmetallic material.

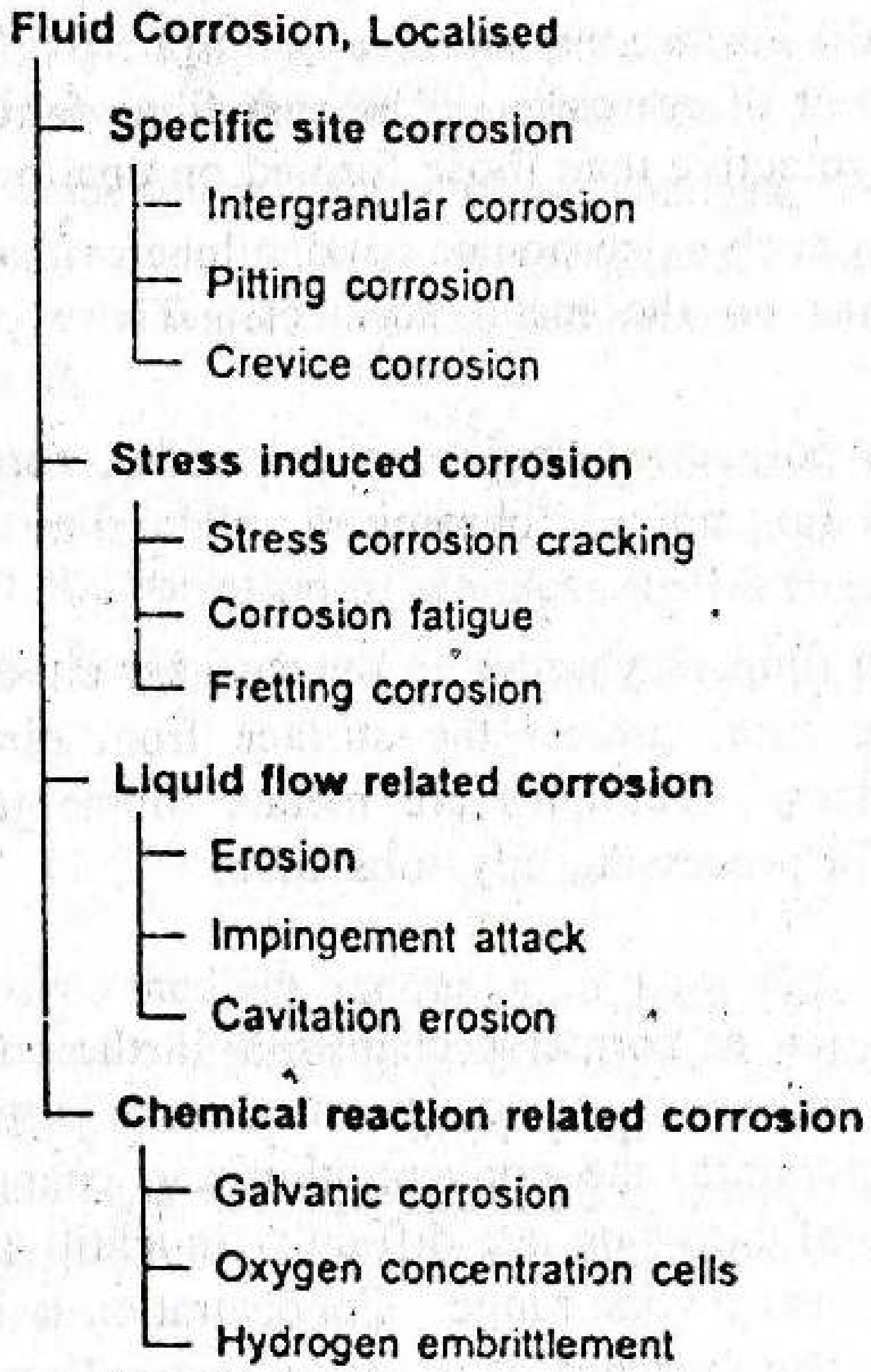


Figure 16-3. Classification of localised fluid corrosion

Electrochemical corrosion : This type of corrosion occurs at discrete points of metallic surfaces when electricity flows from cathodic area to anodic area. Metallic surface gets divided into anodic portion or cathodic portion.

Fluid Corrosion : Localised

Fluid corrosion is the most frequently observed on different locations in a material. It occurs in numerous ways. It is further classified as given in Figure 16-3.

Specific site corrosion : Mechanically weak spots or dead spots in a reaction vessel cause specific site corrosion.

Inter-granular corrosion : Selective corrosion that occurs in the grain boundaries in a metal/alloy is called as *intergranular corrosion.* Microscopic examination can reveal clearly the intergranular corrosion. When severe, this attack causes a loss of strength and ductility out of proportion to the amount of metal actually destroyed by corrosion. Crystalline grain structure as such is not attacked appreciably. One example is:

$$\begin{matrix}\text{Austenitic} \\ \text{stainless steel}\end{matrix} + \begin{matrix}\text{Nitric} \\ \text{acid}\end{matrix} \xrightarrow{\text{hot condition}} \begin{matrix}\text{Grain boundary} \\ \text{precipitation}\end{matrix}$$

Stainless steel is stabilized by incorporation of niobium/titanium or carbon (less than 0.03%).

Pitting corrosion : This type of corrosion results in development of pits and cavities. They range from deep cavities of small diameter to shallow depressions. Example is:

$$\begin{matrix}\text{Alloy of aluminium} \\ \text{or stainless steel}\end{matrix} + \begin{matrix}\text{Aqueous} \\ \text{solution}\end{matrix} \xrightarrow{\text{chlorides}} \text{Cavities}$$

Pitting of a metal occurs when there is a break in the protective oxide layer and imperfections on the underlying metal. Inhibitors are sometimes helpful in preventing pitting corrosion.

Crevice corrosion : In this type, corrosion occurs in crevices because solutions are retained at such places, which takes longer time to dry out. When this occurs, the intensity of attack is usually more severe than surrounding areas of the same surface. Crevices are formed because of the metal contact with another piece of the same or other metal or with a nonmetallic material. Corrosion in the crevices is due to a number of reasons as given below:

- Deficiency of oxygen.
- Acidity changes.
- Buildup of ions.
- Depletion of inhibitor.

Stress induced corrosion : Residual internal stress in the metal or external applied stress accelerates the corrosion. Residual internal stress is produced by:

- Deformation during fabrication.
- Unequal rate of cooling from high temperatures.
- Internal stress rearrangements involving volume changes.
- Stress induced by rivets, bolts and shrink fits.

Eliminating high stress areas prevents this type of corrosion. The external stress can be kept at minimum by employing suitable experimental conditions.

Stress corrosion cracking : At the surface, if the tensile stress is equal to or more than the yield stress, the surface develops cracks. This is known as *stress corrosion cracking*. Examples are:

- Cold-formed brass develops crack in the environment of ammonia.
- Embrittlement cracking of steel is observed in caustic solution.

Corrosion fatigue : Corrosion fatigue is the ability of a metal surface to withstand repeated cycles of corrosion. The metal surface is stressed and simultaneously attacked by the corrosive media. Pits (concentration points) indicating corrosion are formed initially, which further develop into cracks. As this process continues, the surface looses its fatigue resistance and ultimate failure of equipment.

The protective surface oxide film reduces corrosion. Under cyclic or repeated stress conditions, rupture of protective oxide films takes place at a higher rate than at which new protective films can be formed. Therefore, the rate of corrosion is enhanced.

Fretting corrosion : Fretting corrosion occurs when metals slide over each other and cause mechanical damage to one or both. During relative movement of metals, two processes may occur, (i) frictional heat is generated, which oxidizes the metal to form oxide films (ii) removal of the protective films resulting in exposure of fresh surface to corrosion attack.

This can be avoided by using harder materials, minimising friction by lubrication or by proper designing of the equipment, so that no relative movement of parts takes place.

Flow related corrosion : Liquid metals can cause corrosion. Usually the driving force is the tendency of the liquid to dissolve solids or penetrating the metal along the grain boundaries at places of wetting. Corrosion rate is enhanced at high temperatures. A few examples are:

- Mercury attack on aluminium alloys.
- Molten zinc on stainless steel.

Impingement corrosion : This is also referred to as *erosion-corrosion* or *velocity accelerated corrosion*. It is accelerated by removal of corrosive products (such as oxide films), which would otherwise tend to stifle the corrosion reaction.

Erosion : Erosion is the destruction of a metal by abrasion and attrition caused by the flow of liquid/gas (with or without suspended solids). The additional factors that can influence erosion include:

- Alloy contents of the steel (for example, chromium, copper, manganese etc.).
- Pipe system design and component geometry.
- Water and steam composition (especially pH and oxygen content).

The use of harder metals and changes in velocity or environment are used to prevent erosion.

Cavitation erosion : Formation of transient voids or vacuum bubbles in a liquid stream passing over a surface is known as *cavitation*. The bubbles may collapse on the metal surface thereby causing severe impact or explosive effect. Therefore, considerable damage and corrosion is observed. The protective films also get destroyed due to impact.

Cavitation erosion is observed around propellers, rudders in pumps etc. Redesign, use of a more resistant metal and protective coatings are required to avoid this type of corrosion.

Chemical reaction related corrosion : Corrosion involves chemical reactions such as oxidation and reduction at anode and cathode, respectively.

Galvanic corrosion : Galvanic corrosion is associated with the flow of current to a less-active metal (copper cathode) from a more-active metal (zinc anode) in the same environment. Coupling of two metals, which are widely separated in the electrochemical series, generally produces an accelerated attack on the more active metal, zinc, i.e., anodic corrosion. Therefore, a combination of metals which are as close as possible in the electrochemical series should be chosen.

In galvanic corrosion, the effect of area is very important. For example, steel rivets on copper (Cu) plates will corrode much more rapidly than a steel plate with copper rivets. Corrosion at the anode may be 100 to 1000 times higher, if the two areas are same.

Protective oxide films tend to reduce galvanic corrosion. Insulating materials can be placed between two metal faces to prevent corrosion. For example, plates when bolted together, specially designed plastic washers can be used.

Oxygen concentration cell : This type of corrosion is due to the presence of oxygen electrolytic cell, i.e., a difference in the amount of oxygen in solution at one point exists when compared to another. Corrosion is accelerated where oxygen concentration is least, for example, under gaskets, stuffing boxes etc., because formation of an oxide film is not possible. This also occurs under solid substances that may be deposited on a metal surface as ready access to oxygen is shielded. Redesign/change in mechanical conditions must be used to overcome this situation.

Hydrogen embrittlement : Hydrogen can penetrate carbon steel and reacts with carbon to form methane. The removal of carbon results in decreased strength. Corrosion is possible at elevated temperatures as significant hydrogen partial pressure is generated. This causes a loss of ductility, (hydrogen embrittlement) and failure by cracking or blistering of the steel. Resistance to this type of attack is improved by alloying with chromium/molybdenum.

Hydrogen damage can also result from hydrogen generated by electrochemical corrosion reaction. The atomic hydrogen formed on the metal surface diffuses into the metal and forms molecular hydrogen at micro-voids. The result is failure by embrittlement, cracking and blistering. This phenomenon is observed in solution of specific weak acids such as hydrogen sulphide and hydrocyanic acid.

Fluid Corrosion : Structural

In structural fluid corrosion type, the structural (mechanical) strength is reduced on account of corrosion. This may occur when one component of the alloy is removed or released into the solution. The corrosion products may remain in the plant. Two examples are presented here.

Graphite corrosion : Graphite is an allotropy of carbon. Graphite corrosion occurs in gray cast iron. The metallic iron is converted into corrosive products leaving a residue of intact graphite mixed with iron corrosive products and other insoluble constituents of cast iron. When the layer of graphite and corrosive products is impervious, corrosion will cease or slow down. If the layer is porous, the corrosion will progress by galvanic behaviour between graphite and iron.

When carbon steel is heated for prolonged periods at temperatures higher than 455°C, carbon may get segregated, which is then transformed into graphite. Hence, the structural strength of steel is affected. Employing killed steel or low alloyed steels of chromium and molybdenum or chromium and nickel can prevent this type of corrosion.

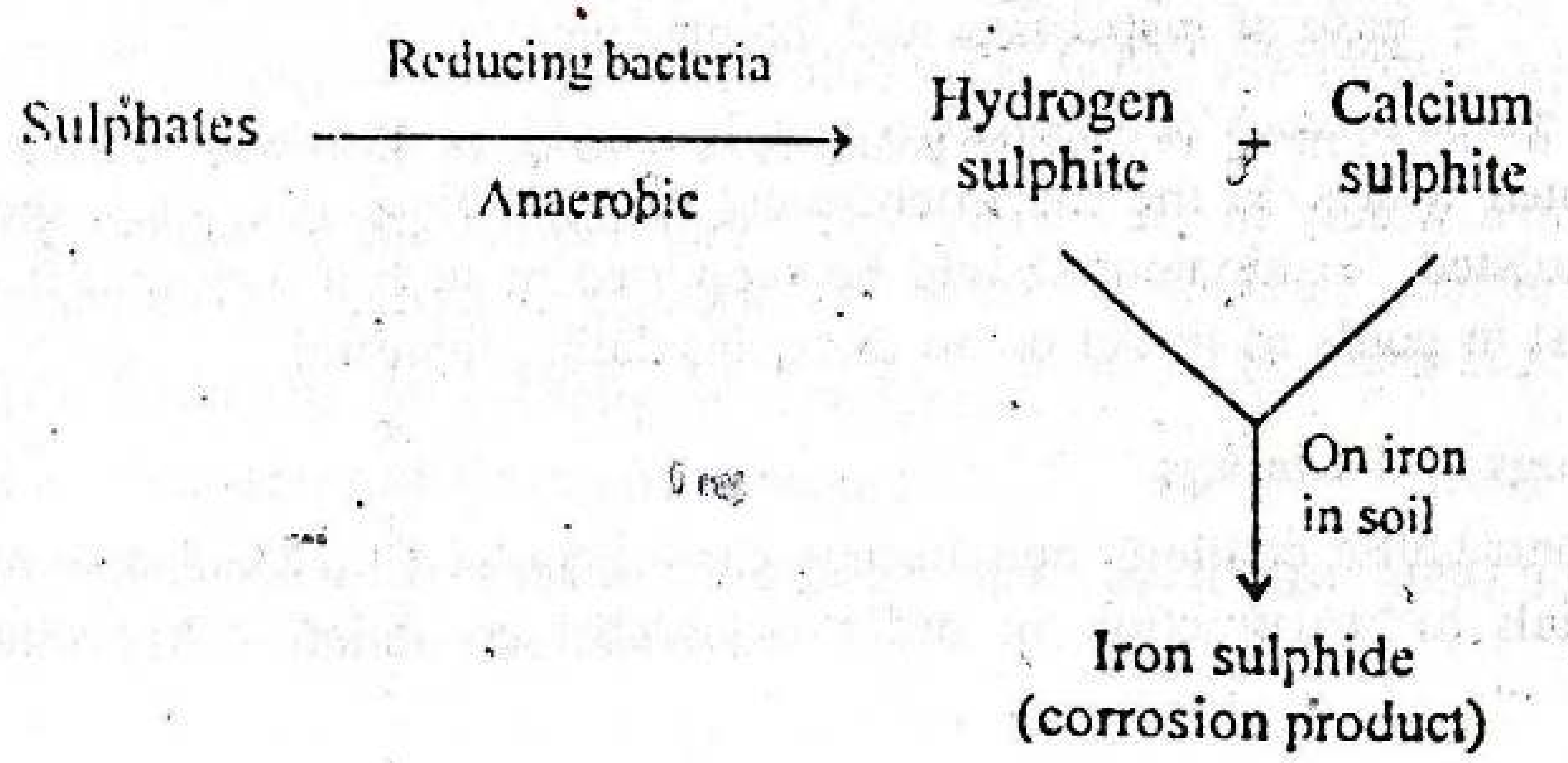
Dezincification : This type of corrosion is seen in brass that contains more than 15% zinc. In brass, the principal product of corrosion is metallic copper, which may redeposit on the plant. Another mechanism involves the formation of zinc corrosion products leaving the copper residue.

Corrosion may occur as plug filling pits (plug type) or as continuous layers surrounding the unaffected core of brass (general type). It can be reduced by the addition of small amount of arsenic, antimony or phosphorus to the alloy.

Fluid Corrosion : Biological

The metabolic action of microorganisms can either directly or indirectly cause deterioration of a metal. Such a process is called *biological corrosion*. Microorganisms associated with corrosion are either aerobic or anaerobic. The causes for biological corrosion are:

(1) Producing corrosive environment or altering environmental composition.
(2) Creating electrolyte-concentration cells on the metal surface.
(3) Altering resistance to surface films.
(4) Influencing the rate of anodic/cathodic reaction.



The role of biological corrosion may be explained, using anaerobic sulphate reducing bacteria in slightly acidic or alkaline soils.

As these bacteria thrive under these conditions, they will continue to promote this reaction until failure of the pipe occurs.

PREVENTION AND CONTROL OF CORROSION

Selection of Proper Material

Corrosion should not be permitted in fine mesh wire-screens, orifices and other items in which dimensions are critical and changes are not permitted.

In many cases, non-metallic materials will be useful and attractive from the point of view of economics and performance. These should be considered if their strength, temperature and design specifications are satisfactory.

Permissible corrosion rates are important factors and differ with equipment. Appreciable corrosion can be permitted for tanks and lines, if anticipated and allowed for thickness in its design.

The corrosion characteristics of chemicals and limitations of construction materials must be considered from the literature before selecting equipment. In addition, processing conditions to which the material is exposed should also be considered. For this purpose, relevant literature should be consulted.

Proper Design of Equipment

In the design of equipment, a number of fittings such as baffles, stiffeners, drain nozzles, location of valves and pumps should be considered. Corrosion can be minimised, if the equipment design facilitates:

- Elimination of crevices
- Complete drainage of liquids
- Ease of cleaning
- Ease of inspection and maintenance

A direct contact between two metals should be avoided, if they are separated widely in the electrochemical series. Otherwise, they should be insulated. Equipment should be supported in such a way that it will not rest in pools of liquid or on damp insulating material.

Coatings and Linings

Nonmetallic coatings and linings can be applied on steel and other materials of construction in order to combat corrosion. Appropriate methods such as electroplating, cladding, organic coatings should be considered. The thickness of the linings is important (100 mils). Effective linings can be obtained by bonding directly to substrate metal or building multiple layers or lamination.

Organic coatings are used as linings in equipment such as tanks, piping, pumping lines and shipping containers. Some examples of the linings are:

- Ceramic
- Elastic
- Carbon brick
- Glass-coated
- Plastic
- Organic

A thin non-reinforced paint-like coating of less than 0.75 mm thickness should not be used in services for which full protection is required from corrosion. Some examples of linings and uses are:

Tin coated steel (tin plate)	– food containers
Lead (Pb) coating (Terne plate)	– roofings
Aluminium (Al) coated steel	– high temp conditions
Zinc (Zn) coated steel	– many atmospheric conditions

The cladding (i.e., mechanical bonding) of steel with an alloy is another approach to this problem. For instance, special glasses can be bonded to steel so that the liner is of 1.5 mm thick which is impervious. Equipment and pipings are lined in this manner and routinely used in severely corrosive acid services.

Altering Environment

Corrosion can be combated or reduced by employing the following environmental conditions.

(1) Removing air from boiler feed water prevents the influence of water on steel.

(2) Reducing aeration prevents the formation of passive oxide film in stainless steel alloys by acidic media.

(3) Pumping of inert gas into solutions prevents the contact of air or oxygen as in case of nickel based alloys.

(4) Reducing the temperature.

(5) Eliminating the moisture.

(6) Reducing the velocity or turbulence.

(7) Shortening the time of exposure.

Addition of acid media should be done as a last step, so that maximum dilution can be obtained.

Inhibitors

The corrosion inhibitors are added to the environment to decrease corrosion of metals. These form protective films.

Adsorption type, for example, adsorbed on the metal.
Scavenger type, for example, remove corrosion agents.
Vapour phase type, for example, sublime and condense on metal surface.

Examples of inhibitors are given below.

Inhibitors	*Material protected in the media*
Chromates, phosphates, silicates	– iron and steel in aqueous solution.
Organic sulphides, amines	– iron and steel in acidic medium.
Copper sulphate	– stainless steel in hot diluted solution of sulphuric acid

Inhibitors are generally used in quantities less than 0.1% by weight. In some cases, the amount of inhibitor used is critical.

Cathodic Protection

The cathodic protection is based on the galvanic action between the metal(s) of the plant (cathode) and anode suspended in the solution. The metal to be protected is made a cathode, i.e., electrons are supplied, there by dissolution of metal is suppressed. This can be achieved by two methods.

(1) Sacrificial anode method
(2) Impressed emf method

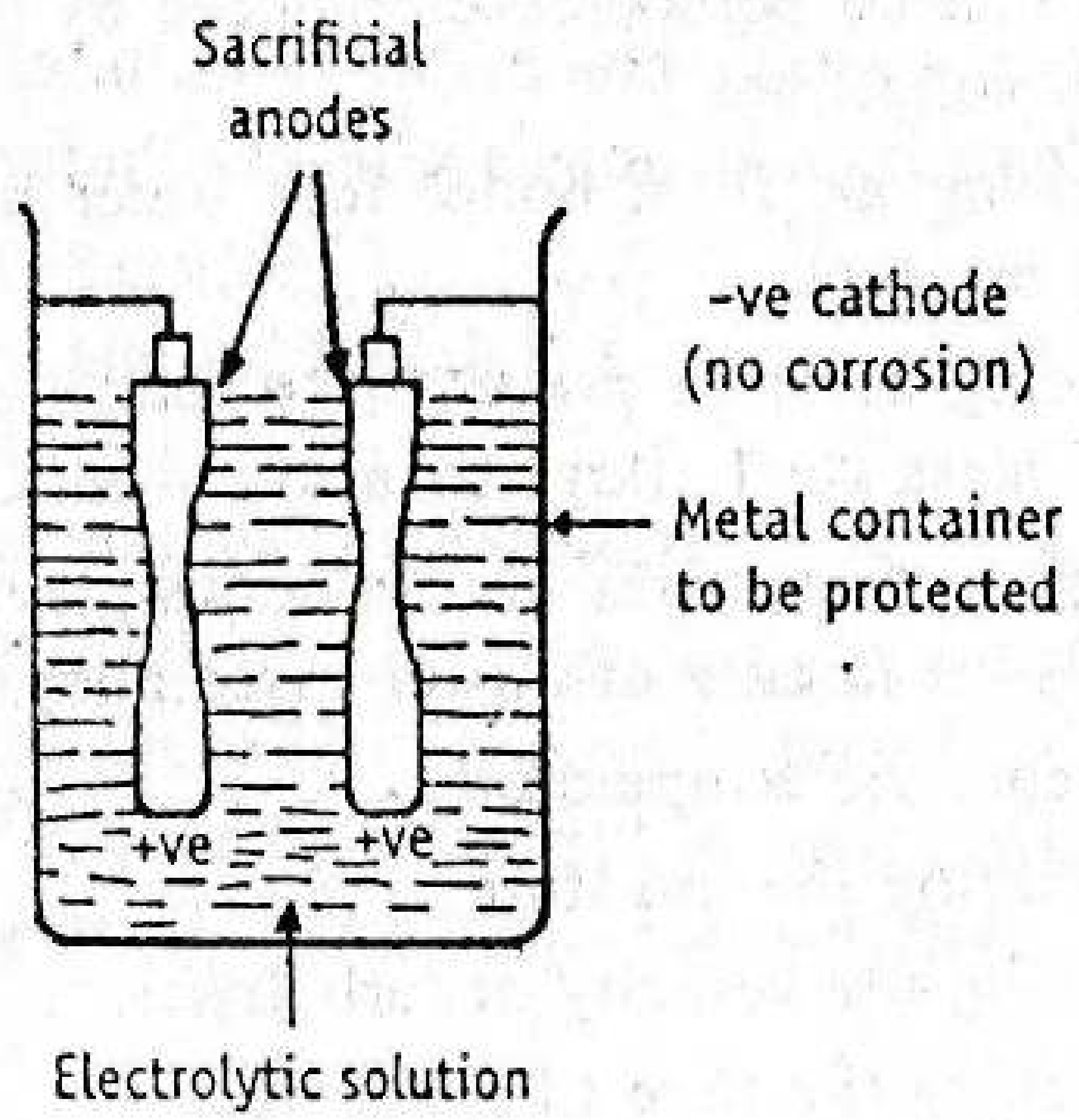


Figure 16-4. Simple sacrificial anodes.

Sacrificial anode method : In this method, anodes are kept in electrical contact with the metal to be protected (cathode). The anodes are sacrificed, since it goes into solution (Figure 16-4). For example, for the protection of iron and steel tanks, the metals such as zinc, aluminium, magnesium and their alloys are used as sacrificial anodes. These are used in limited pH range when high solution rate is acceptable, since these are amphoteric.

Anode metal is selected from the electrochemical series amongst the metals present below the tank metal. The anode should not be poisonous and not detrimental to the product.

Impressed emf Method : This is also known as *applied current system*, i.e., external voltage is impressed between tank and electrodes. The negative terminal of power supply is connected to the material to be protected. Therefore, the natural galvanic effect is avoided and the anode is maintained positive (Figure 16-5).

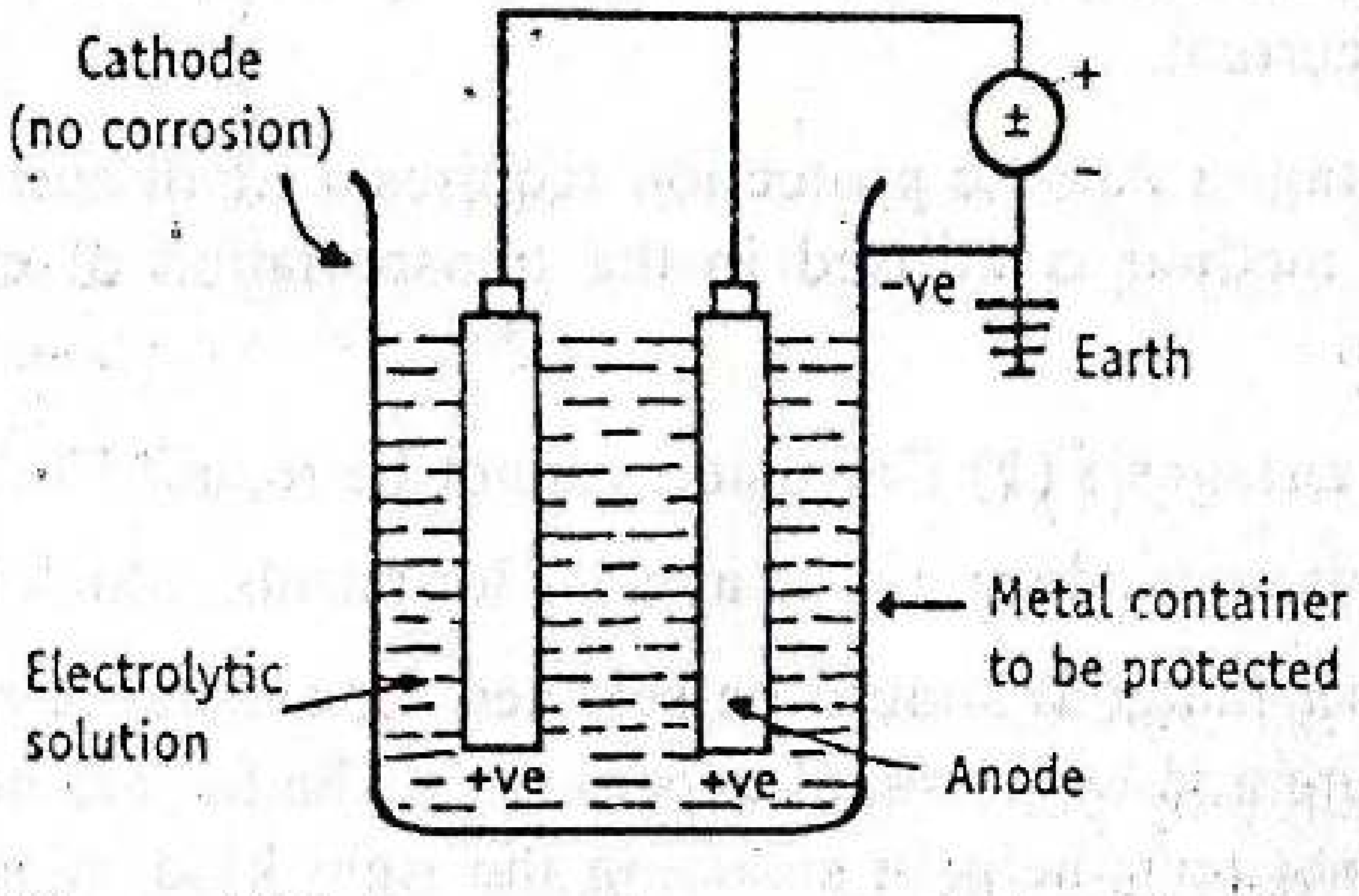


Figure 16-5. Impressed current cathode protection.

Since anode is not consumed, any conducting material, metal or non-corrodable alloys can be used. For example, in case of sulphuric acid and deionised water, graphite and high silicon steel are compressed. The anodes can be buried in the ground or suspended in the aqueous solution of electrolyte.

Advantages : (1) This method is used for large tanks to store mild corrosive liquors. In these cases, mild steel is used with negligible corrosion.

(2) Cathodic protection method is simple and the most effective.

(3) It is inexpensive. It enables the use of cheaper material for plant construction.

Disadvantage : Corrosion cannot be reduced to zero.

Anodic Protection

In the method, a predetermined potential is applied to the metal specimen and the corresponding current changes are observed. During the initial stage, the current increases indicating the dissolution (corrosion) of the metal. When the current reaches a critical point, passivisation occurs, i.e., the oxide layer sets in a suitable oxidising environment. The potential at critical point is called *passivating potential*. Above this passivating potential, the current flow decreases to a very small value called passivating current.

The *passivating current* is defined as the minimum protective current density required to maintain passivisation.

At this stage, an increase in potential will not corrode the metal since the latter is in a highly passive state. For example, in case of stainless steel, titanium becomes easily passive and cannot offer cathodic protection. In such cases, the corrosion rate may be slowed down by the use of anodic current.

Advantage : Anodic protection requires a small current. The anodic protection method is utilised in the transportation of concentrated sulphuric acid.

Disadvantages : (1) Corrosion cannot be reduced to zero.

(2) This method cannot be applied for metals, which do not passivate.

A proper material should be selected for a specific process based on the literature and by personal experience. The factors influencing corrosion will not only help in selecting the right kind of material, but also suggest the processing conditions. It is equally essential to identify the type of corrosion, if it occurs. Since the theories of corrosion are known, it is possible to adopt appropriate preventive measures.

QUESTION BANK

Each question carries 2 marks

1. Explain the terms ' pitting corrosion' and 'galvanic corrosion'.
2. Give the applications of protective linings and coatings with respect to corrosion control with suitable examples.
3. What is the role of plastic washers in the corrosion of metals?
4. How oxide films are formed? What are its advantages?
5. Highlight the role of oxygen in the corrosion of metals

Each question carries 5 marks

1. What is corrosion? Mention the factors that influence rate of corrosion.
2. Explain measures you suggest to check the problems of corrosion.
3. Write electrochemical theory of corrosion.
4. Describe the biological corrosion and suggest the preventive measures.
5. Describe the mechanism of corrosion of iron.
6. Define corrosion. Give its causes. Classify corrosion.

Each question carries 10 marks

1. What is corrosion? Name the various types of corrosion. How can corrosion be prevented?
2. Discuss various types of corrosion and suggest the methods to tackle the same in pharmaceutical industries.

17

Materials of Construction

A number of equipment are used in the manufacture of pharmaceuticals, bulk drugs, antibiotics, biological products etc. In addition, several accessories such as containers for processing and packing of finished products are essential. A wide variety of materials can be utilised for the construction of equipment. The success or failure of a new chemical plant or in the improvement of an existing facility depends on:

1. Design of equipment
2. Selection of material
3. Technique of fabrication

The design (construction) and working of equipment employed in unit operations have been discussed vividly in various chapters. The knowledge on the properties of materials is essential for selecting the right kind of materials.

The purpose of this chapter is to provide a working knowledge on some of the major types of materials available for construction. This will determine whether a process is expensive or complex. It also decides the profit and utility of the end product. The technical details on the fabrication are not within the scope of this chapter, because it needs special expertise, which may not be relevant.

The selection of a material for the construction of equipment depends on the following properties.

1. Chemical resistance
2. Structural strength
3. Resistance to physical shock i.e., operating pressure

4. Resistance to thermal shock i.e., operating temperature
5. Ease of fabrication
6. Cost
7. Maintenance

Selecting satisfactory materials for the construction of plant encounters problems involving chemical, physical and economic factors.

FACTORS INFLUENCING SELECTION OF MATERIALS

Chemical Factors

The container or equipment should protect the integrity of the contents. At the same time, the contents should not alter the properties of the material with which the vessel is made. When these are in contact with each other, the effects may be understood in two ways:

(a) The contents may react and thus get contaminated with the material of the plant.

(b) The drugs and chemicals may destroy the material of the plant.

Contamination of the product : The impurities in chemical substances or bulk drugs may be from different sources. The solvent action may cause corrosion, so that the traces of metal ions used in construction tend to pass into solution and contaminate the product. Substances such as glass, silica, lead, cast iron, steel, tinned iron and a variety of alloys are used in the construction of a chemical plant and most of them produce contamination.

Even though impurities are present in traces, these may cause the product to decompose. For example, heavy metals inactivate penicillin. The appearance of the product may also be effected by changes in colour. Glass vessels may give up traces of alkali to the solvent, though this is unlikely, if the vessels are of hard glass. Sometimes, product contamination may be innocuous and non-toxic.

Influence of chemicals on the material of the plant : The solutions that come into contact with the equipment are generally corrosive in nature. In addition, equipment are exposed to extremes of pH, temperatures and pressures. As a result, the material gets corroded, losing its strength and durability. Therefore, the life of the equipment is reduced.

The knowledge of materials of plant construction assists greatly in providing a plant that will be resistant to attack of acids, alkalis, oxidizing agents, tannins etc. New alloys having special physical and chemical properties have been developed to meet the problems of chemical reactions.

Physical Factors

Strength : The material should have sufficient strength so that it can withstand the stresses or rigours to which the material is subjected in the production. Iron and stainless steel can satisfy these properties. For example, in the compression of tablets, the dies and punches should have sufficient mechanical strength to transmit the applied pressure, otherwise tablets are poorly formed. Glass satisfies the property of strength, but is breakable.

Generally tablets, capsules and vials are preserved in blister packing. The packing materials should withstand the rigors of handling, shipment and transportation. Plastic materials are used, because these offer sufficient mechanical strength.

Aerosol containers must withstand pressure as high as 960 kPa to 1.20 MPa at 55°C. Tin plate containers can satisfy this condition, while plastic containers cannot be used due to its poor mechanical strength.

Mass : Many times, the equipment should be transported or moved from one place to another. This is possible when the material is light in weight, when other factors are satisfactory. Similarly, plastic material is employed for the manufacture of containers for use of pharmaceuticals and cosmetics on account of its light weight. As a result the cost of transportation reduces.

Wear properties : These properties become important, when there is a possibility of friction between the moving parts. For example, during milling and grinding, the grinding surfaces wear off and these materials will be incorporated into powder as impurities. Such type of mills should be avoided, when drugs of high purity are required. The risk of contamination is more due to wear of ceramic or iron equipment (sieves etc.).

During tabletting operations, the upper and lower punches rotate continuously. In this process, the wearing of these punches is high.

Thermal conductivity : In chemical industries, several equipment such as evaporators, dryers, stills and heat exchangers are used. The material employed for their fabrication should have good thermal conductivity. However, the resistant films greatly retard the process of heat transfer. For example, iron, glass or graphite tubes are used in the fabrication of heat exchangers, so that effective heat transfer is possible.

Thermal expansion : If the material has high coefficient of expansion, the design of plants may be greatly complicated. This increases stresses and the risk of fracture when temperature changes. The material should be able to maintain size and shape of equipment at working temperatures.

Ease of fabrication : During fabrication, the materials undergo various processes such as casting, welding, forging and machinisation etc. For example, glass and plastics can be easily moulded into containers of different shapes and sizes. Glass can be used as a lining material for reaction vessels used in the chemical industry. Iron and steel undergo various rigours of processing during fabrication.

Cleansing : Smooth and polished surfaces allow the process of cleansing easy. Materials that can be obtained with such a finishing are ideal, when scrupulous cleanliness is necessary. For example, stainless steel and glass are suitable for this purpose.

Sterilisation : In the production of parenterals, ophthalmic products, antibiotics and biologicals, sterilisation is an essential step, which is obtained by autoclaving. The material should be capable of withstanding the necessary treatment, usually steam and pressure.. In most cases, cleansing is a preliminary step to the sterilisation of apparatus and plant. For example, equipment and vessels are made of stainless steel, because they can be sterilised.

Transparency : Transparency may be a useful property because it permits the visual observation of the changes during a process. For this reason, borosilicate glass has been increasingly used in the construction of reactors, fermentors etc.

Economic factors : Initial costs and maintenance of the plant must be economical. Here the main concern is not simply to obtain the least cost material. Low wearing qualities and lower maintenance may well mean that a higher initial cost is more economical in the long run.

CLASSIFICATION OF MATERIALS FOR PLANT CONSTRUCTION

Materials of pharmaceutical plant construction can be classified as shown in Figure 17-1.

Different materials and their properties are discussed so that right kind of materials can be selected for the desired purpose and function.

FERROUS METALS

Iron metal is one of the widely used materials for the construction of plants because of its mechanical strength, abundant availability and lower cost. Some varieties of iron are discussed.

CAST IRON

Cast iron consists of iron with a proportion of carbon (beyond 1.5%). The properties of iron depend on the amount of carbon present in it. Cast iron is abundantly available, inexpensive and therefore widely used. A number of types of cast iron are available (Table 17-1).

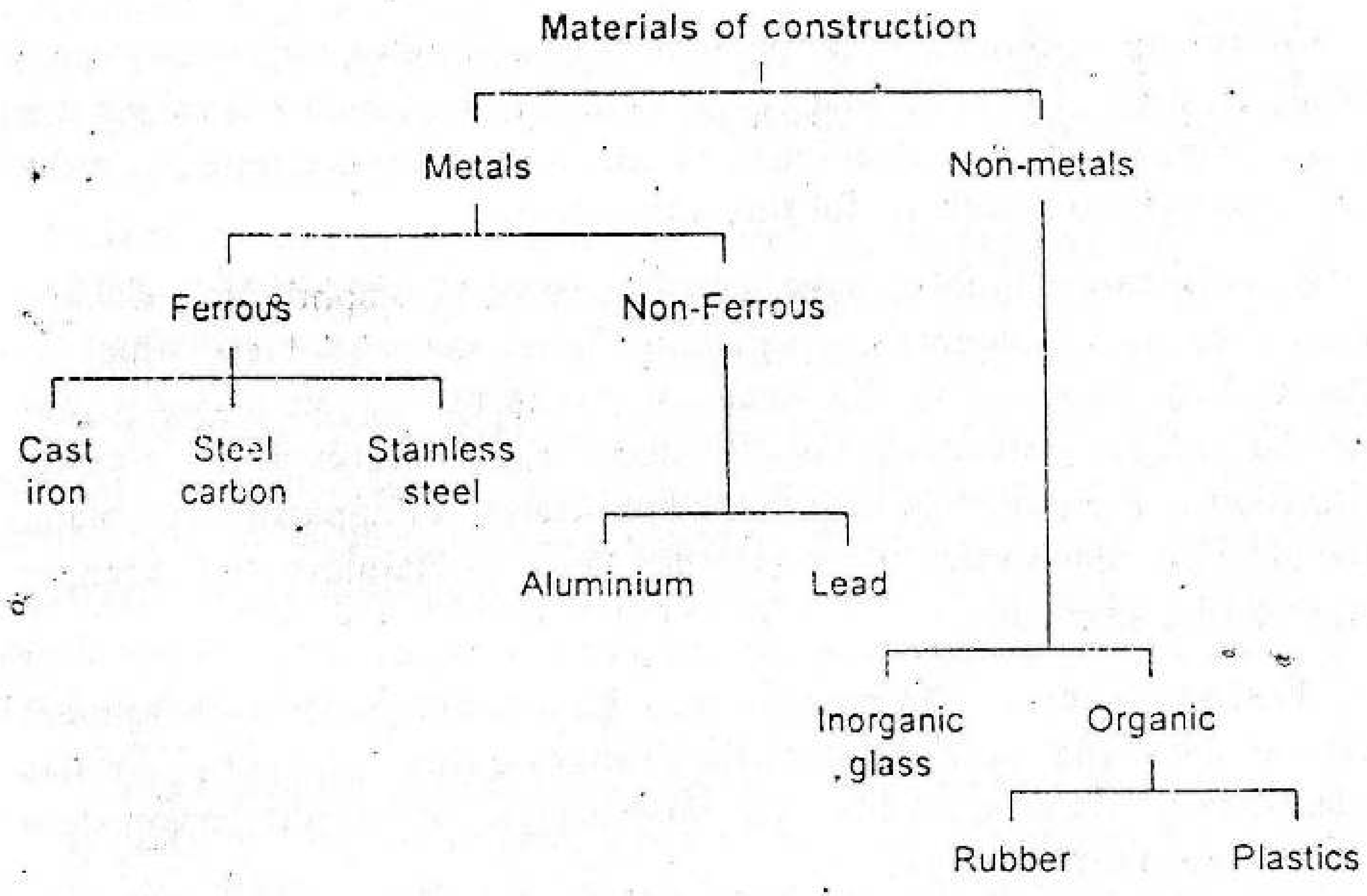


Figure 17-1. Classification of materials used for the construction of plant.

Advantages : (1) Cast iron is cheap. Therefore, it is used in place of expensive plant material with coatings or linings of enamel or plastic.

(2) It is resistant to concentrated sulphuric acid, nitric acid and dilute alkalis.

(3) Since cast iron has low thermal conductivity, it is used for the construction of outer surface of jackets of steam pans.

Disadvantages : (1) Cast iron is very hard and brittle. Therefore, it is difficult to machine. This disadvantage can be overcome by the addition of different materials to improve its performance.

(2) Cast iron is attacked by dilute sulphuric acid, dilute nitric acid and dilute as well as concentrated hydrochloric acid.

(3) Since cast iron has low thermal conductivity, it cannot be used for heat transfer in stills.

Uses : It is commonly used for the construction of:

(1) Supports for plant

(2) Jackets of steam pans

(3) Linings with enamel, plastic or suitable protective material

Modifications of cast iron : Cast iron is not considered corrosion resistant. The characteristics of cast iron can be altered by alloying with other elements such as silicon, nickel and chromium. (see Table 17-1)

Commercial Types : Duriron and Durichlor.

TABLE 17-1

Different Types of Cast Iron Alloys

Types of cast iron	*Composition*	*Properties*	*Disadvantages*
Gray cast iron	Carbon silicon	Low cost, easy to cast into intricate shapes and linings. For grinding balls, dies, impellers.	Brittle, poor resistance to impact and shock
Maleable iron	white cast iron carbon–2.5%	Corrosion resistant Type I easy to machine	Type II less easy to machine
High silicon cast iron	Silicon-13-16% cast iron	Resistant to corrosion, oxidising environment, reducing environment. Used in sulphuric acid services.	Not easily machined and welded
Nickel resistant cast iron		Superior toughness, impact resistant, easy to weld and machine. Corrosion resistant and heat resistant.	Oxidising agents such as nitric acid are highly detrimental. There is little attack from neutral or alkaline solution

CARBON STEEL OR MILD STEEL

Carbon steel is an iron alloy, which contains only a small percentage of carbon. **Advantages** of carbon steel are:

(1) Carbon steel is cheapest. Therefore, it is preferred.

(2) It is easily weldable and is frequently used in fabrication.

Disadvantages of carbon steel are:

(1) Carbon steel has limited resistance to corrosion. This property can be improved by preparing alloys.

(2) It reacts with caustic soda, brine and sea-water. Alloying it can reduce this reactivity.

Uses : Carbon steel is used for the construction of bars, pipes and plates. It is used to fabricate large storage tanks for water, sulphuric acid, organic solvents etc. It is used for supporting structures such as grinders and bases for plant vessels.

Variants of carbon steel : The properties of carbon steel can be altered by alloying it with other metals. Some of the metals and their properties are:

Nickel (Ni) – improves toughness, corrosion resistance and low temperature properties.

Chromium (Cr) – increases hardness, more abrasive resistance and resistance to oxidation.

Silicon (Si) – increases hardness, more abrasive resistance and resistance to oxidation.

Molybdenum (Mb) – provides strength at elevated temperatures

The types of alloys of carbon steel are given in Table 17-2.

TABLE 17-2

Different Types and Alloys of Carbon Steel

Variety of carbon steel	*Composition*	*Advantages*
Low alloy steel	Low concentration of iron, carbon, manganese, nickel, chromium and molybdenum	– High mechanical strength – Corrosions resistant to environments. – Walls of plant can be thin.
Alloying with nickel	nickel	– Increased hardness – High corrosion resistance – Improved low temperature properties.
Alloying with silicon chromium	nickel chromium	– Abrasion resistant – Corrosion resistant – Resistant to oxidation

STAINLESS STEEL

Stainless steel is an alloy of iron. Usually, it contains chromium and nickel, which make the steel corrosion resistant. Stainless steel is stabilised by the addition of titanium, niobium or tantalum. Minor amounts of other elements such as copper, molybdenum and selenium are added. Stainless steel also has the advantage of ease in fabrication.

The abundant use of stainless steel is due to the properties such as:

- heat resistance
- corrosion resistance
- ease of fabrication
- cleaning and sterilisation
- tensile strength

Depending on the composition, stainless steel alloys are available in three groups, viz., martensitic, ferritic and austenitic. These are given in Table 17-3.

TABLE 17-3

Different Types of Stainless Steel

Composition	*Advantages*	*Disadvantages*	*Uses*
Martensitic (e.g: Type 410)			
Chromium : 12-20% Carbon : 0.2- 0.4% Nickle upto 2.0%	Mildly corrosion resistant, atmospheric and organic exposures	Ductility is poor	Sinks, bench tops, storage tanks, buckets, mixing elements etc.
Ferritic (α-form) (e.g: Type 430)			
Chromium : 15-30% Carbon : 0.1% Nickel : nil	Better corrosion resistant; easy to machine; resistant to oxidation and temperature. (upto 800°C)	not good against reducing agents, hydrochloric acid	Tower linings, baffles, separator, tower, heat exchanger, tubings, condensers, furnace parts, pumps shafts, valve parts.
Austenitic (γ-form)			
Chromium : 13-20% Nickel : 6-22 % Carbon : 0.1% < 0.25%	Highly corrosion resistant; readily cleaned; sterilizable; easy to weld; non-magnetic	Not easy to machine	Fermentors, storage vessels, evaporators, extraction vessels, small apparatus (funnels, buckets etc.)

NON-FERROUS METALS

ALUMINIUM

A number of aluminium items are used in regular day to day life. Aluminium is cheap, light in weight and offers adequate mechanical strength. In addition, aluminium equipment can be easily fabricated. Further, aluminium can be strengthened by cold working. Their maintenance and cleaning is also easy. Hence, its utility is mostly recommended. However, the use of aluminium in the construction of plant and equipment is limited.

Advantages : (1) High resistance to atmospheric conditions, industrial fumes, vapour and fresh or salt waters. Aluminium can be used with concentrated nitric acid (above 82%) and acetic acid.

(2) Thermal conductivity of aluminium is 60% that of pure copper.

Disadvantages : (1) The mechanical strength decreases greatly above 150°C.

(2) Aluminium cannot be used with strong caustic solution.

(3) Many mineral acids attack aluminium.

(4) Oxide and hydro-oxide films are formed rapidly, when its surface is exposed. Normally this film is thickened by chemical and electrolytic means. These provide so called anodised finishes.

Uses : A super grade is preferred for food and pharmaceutical use. It is used in many heat transfer applications. These are used as meat storage containers.

Aluminium alloys and modifications : A number of aluminium alloys are available with improved qualities and mechanical properties. Aluminium alloys are used in the construction of equipment producing medicinal substances, since aluminium does not affect the salts.

Aluminium is non-toxic to microorganisms. It has considerable use in biosynthetic processes such as the production of citric acid gluconic acid and streptomycin by deep culture methods. It is most useful for the construction of containers namely drums, barrels, rail tankers etc.

LEAD

Lead has the lowest cost and is used as collapsible tube material particularly for non-food products such as adhesives, inks, paints and lubricants. Lead tubes with internal linings are sometimes used for fluoride tooth-paste. Lead chamber process is used in the manufacture of sulphuric acid.

Disadvantages : (1) Lead has low melting point and hence possesses poor structural qualities.

(2) It has high coefficient of expansion. Therefore, temperature strain results in permanent deformation.

In pharmaceutical practice, lead has little use, because of the risk of contamination even in traces produces toxicity and of cumulative nature. It is used for the construction of cold water pipes, waste pipes and dilution tanks for laboratories.

Lead alloys and modifications : Lead alloys with superior performance qualities have been established. For example, acid lead and copper lead are used in chemical industries. Some metals are added to lead for altering properties.

Silver and copper – improves corrosion resistance.
improves creep and fatigue resistance.
Antimony, tin, arsenic – hardens, still melting point is low.

Lead-lined steel structures are used for the construction of pipes, valves, vessels designed for operations at high temperatures, fluctuating temperatures or vacuum.

NONMETALS—INORGANIC

GLASS

A number of glass articles are used in daily life. Glass has the advantages of superior protective qualities, attractiveness and low cost. It is chemically inert to a large extent and available in a variety of sizes, shapes and colours. Glass containers practically offer excellent barrier against every element except light. UV rays and sunlight are harmful to certain ingredients and bring about chemical deterioration. Protective action against light can be achieved by amber-coloured glass. Protection against IR rays can be obtained by using green glass. The disadvantages are its fragility and weight.

Glass is considered as a super-cooled liquid, though it is seen in solid state. The constituents are present in amorphous state. Glass is composed of the following constituents.

Sand - silica pure (silicon dioxide, SiO_2) - base material
Soda ash - sodium carbonate (Na_2CO_3) - improves the properties
Lime stone - calcium carbonate ($CaCO_3$) - improves the properties
Cullet - broken glass - fusion agent

Silicon dioxide is having a tetrahedron structure. The glass that is prepared by silicon dioxide alone is the most resistant, but relatively brittle. It can be melted and moulded at high temperatures. Therefore, cations such as sodium, potassium, calcium, magnesium, aluminium, boron, iron etc., are added. These cations (available as oxides) modify the physicochemical properties of glass, so that it is suitable for the manufacture of glass with desired characteristics. However, this glass has low chemical resistance. Some varieties of glasses are given in Table 17-4.

TABLE 17-4

Some Varieties of Glasses

Type of glass	*Composition*	*Advantages or uses*
Soft glass (soda glass)	Sodium silicate Calcium silicate	Making glass bulbs and window glasses
Hard glass (potash glass)	Potassium silicate Calcium silicate	Glass apparatus, which resists the action of acids
Flint glass (Potash lead glass)	Potassium silicate Lead silicate	Optical instrument because of its refractive index
Jena glass	Zinc silicate Barium borosilicate	Laboratory glassware, because of its resistance to acids and alkali
Pyrex glass	Silicon dioxide Boron oxide Sodium oxide Small amounts of potassium calcium magnesium	Laboratory glassware and reactor vessels, because of its resistance to heat
Quartz glass	Pure silica	Silica crucibles, distilled water stills (for high purity), because of its low coefficient of expansion. It withstands temperature shock upto 1000°C.

Glass containers used for pharmaceutical purposes are given in Table 17-5. These types are classified into four groups. These have varied degree of chemical resistance. The reasons for the low chemical resistance are as follows. Most of the alkali oxides such as Na_2O, K_2O, MgO and CaO enter the spaces within the structures and reduce the strength of inter-atomic forces between silicon and oxygen. The oxides decrease the melting point of glass and are comparatively free to migrate. This behaviour creates a number of problems in their use. These are:

(a) Oxides leach into the solution, raises the pH, hydrolyse or catalyse chemical reactions.

(b) Some times, glass flakes are formed in the solution.

However, boron oxide enters into the structural configuration of glass and does not leach out and hence is used in parenteral packings.

TABLE 17-5

Types of Glass used in Pharmaceutical Industry IP

Types	*General description*	*Properties*	*Uses*
I	Highly resistant Borosilicate (Alkali and earth cations are replaced by boron)	Resistant to alkali leaching, less brittle, low thermal expansion easy to clean and sterilise.	Containers for buffered and unbuffered, aqueous solutions and injectables
II	Treated soda-lime glass.	Surface alkali is neutralised by sulphur dioxide vapours. Glass surface is resistant to water.	Containers for buffered, aqueous solution with pH below 7.0, dry powders, oleogenous solutions.
III	Soda-lime glass	It releases comparatively more alkali. It offers moderate hydrolytic resistance.	Dry powders, oleogenous solutions.
IV	General purpose soda lime glass		Not for parenterals, used as containers for tablets, oral solutions, suspensions, ointments and liquids for external use.

GLASSED STEEL

Glassed steel is an inorganic product of fusion, which is cooled to a rigid condition without crystallising. It requires special considerations in its design and use. These surfaces are applied to heavy vessels. Normally, several coatings are fused in a furnace. Glassed steel combines the corrosion resistance of glass with the working strength of steel.

Advantages of glassed steel are:

(1) It has excellent resistance to all acids except hydrofluoric acid and hot concentrated sulphuric acid.

(2) It can be attacked by hot alkaline solution. Particularly suitable for piping when transparency is desirable.

(3) It is brittle and gets damaged by thermal shock. Hence it is protected using glass lined with epoxy polyester fibre glass.

(4) A nucleated crystallised ceramic metal composite form of glass has superior mechanical properties compared with conventional glassed steel.

(5) Glass linings are resistant to:

(a) All concentrations of hydrochloric acids upto 120°C.

(b) Dilute concentrations of sulphuric acid up to the boiling point.

(c) All concentrations of nitric acid upto boiling point.

(d) Acid resistant glass with improved alkali resistance (up to pH 12).

Uses : Glass lined steel is used for handling of strong acids, alkalis and saline solutions. For small-scale manufacture and pilot plant work, glassed steel vessels are used.

NONMETALS—ORGANIC

RUBBER

Rubber is used as such or as lining materials for the construction of plants. Both natural and synthetic rubbers are used.

Natural Rubber : Rubber is a naturally occurring polymer, which is obtained as latex from rubber trees. It is a common example of an elastomer. *Elastomer* is a substance that can be stretched readily and when released, rapidly regains its original form.

Soft Rubber : The naturally occurring polymer is known as *soft rubber*. It is a polymer of monomeric isoprene (C_5H_8). Thus, rubber is a polyisoprene with a formula $(C_5H_8)_n$. Soft rubber has the advantages of being resistant to dilute mineral acids, dilute alkalis and salts. The disadvantage is that soft rubber can be attacked by oxidising media, oils and organic solvents. Soft rubber is used as lining materials for plants, as it can bond easily to the steel.

Addition of carbon black to the soft rubber gives hardened rubber. It is used for making tyres, tubes and conveyor belts.

Hard Rubber : When soft rubber is mixed with sulphur, warmed and set into a given shape, it retains its form. The sulphur combines with the polymeric chains of rubber and cross-links between them. This process is called *vulcanisation*. Soft rubber with 25 % or more sulphur is known as *hard rubber*. Hard rubber has the advantages of hardness and strength. So it is used for making gloves, bands, tubes and stoppers.

Synthetic Rubber : Synthetic rubber has taken greater importance over natural rubber due to its superiority in properties such as resistance to oxidation, solvents, oils and other chemicals. Some synthetic rubber materials with their properties are reported in Table 17-6.

TABLE 17-6

Some Varieties of Rubber

Synthetic rubber	*Properties*	*Uses*
1. Neoprene (polychloroprene)	• Does not burn readily like natural rubber. • Stable at high temperature.	Insulating material in electric cables, conveyor belts in coal mines, making hoses in the transportation of oils. Rubber stoppers, cap-liners, dropper assemblies for eye drops etc.
2. Nitrile rubber	• Resistant to oil and solvents.	
3. Butyl rubber	• Resistant to - mineral acids & alkalis concentrated acids (except nitric and sulphuric acid)	Used for closures of freeze dried product containers because of its low water vapour permeability.
4. Silicon rubber (polysiloxanes)	• Resistant to - high & low temperatures. - attack to aliphatic solvents, oils and greases	
5. Polyisoprene	• Stable at high temperature, translucent, flexinile.	

Synthetic rubber is thermoplastic, but when mixed with sulphur, warmed and set into a given shape, it retains its form. *Vulcanization* of rubber is possible. It is used for making gloves, bands and tubes, caps for vials.

Rubber is a soft material, but can be hardened by adding carbon black. Hardened rubber is used for making tubes, tyres and conveyor belts.

PLASTICS

Plastic materials have been in common use in various ways in our daily life. These are light in weight so that transportation is easy and cheap. These are available in a variety of shapes implying that it can be easily fabricated. Plastic containers are used for storing a number of substances such as inorganic salts and weak mineral acid. In machines, plastic materials are preferred wherever moving parts are present indicating that it offers less friction. These have better resistance to environmental factors. In a similar manner, plastic materials also used in the construction of plants.

Plastics are synthetic resins containing long chains of atoms linked to form giant or macromolecules (polymers). They have high molecular weight (10^3 to 10^7).

Plastics have several **advantages**. These are:

(1) Low thermal and electrical resistance.
(2) Excellent resistance to weak mineral acids.
(3) Unaffected by inorganic salts.
(4) Resistance to slight changes in pH.

Plastics have **disadvantages** also. These are:

(1) Low mechanical strength
(2) High expansion rates

Basically, two types of plastics are used in pharmaceutical industry.

Thermosetting plastics : *Thermosetting plastics* can be formed under heat and pressure. But these cannot be softened or remoulded, once hardened. Some thermosetting plastics are made of phenolic and urea resins.

Thermoplastic plastics : *Thermoplastic plastics* are formed by the application of heat and pressure and can be softened and remoulded. This is a specific advantage. Scrap and rejected articles can be worked again to get new materials.

Some thermoplastic materials and their uses are given below:

Polyethylene – cables, buckets, pipes
Polypropylene – milk cartons, ropes
Polyvinyl chloride – gloves, water proof garments
Teflon – gaskets, coatings

Based on the *utility* of plastics in plant construction, these can be categorised as:

1. Rigid materials
2. Flexible materials
3. Metallic surfaces
4. Plastic cements
5. Special case plastics

1. Rigid materials : These are phenolic resins with various inert fillers. These are used in the fabrication of a number of items. For example, Keebush is a rigid material (phenolic plastic) and is used for gears, bearing etc. It is light in weight. Some of its applications are:

- Gears
- Pipes
- Pumps
- Bearing
- Fittings
- Ducts
- Vessels
- Valves
- Filter presses

Disadvantages : These are resistant to corrosion except oxidising substances and strong alkalis.

2. Flexible materials : These are thermoplastic materials. These materials can be rigid or flexible depending upon the amount of plasticizer added. These are used in the fabrication of:

- Tanks
- Funnels
- Pipes
- Buckets
- Ducts

3. Metallic surfaces : Plastics of polyethelene or polyvinyl chloride types are used along with plasticizers for the coating of metallic surfaces. These are used to protect the metal from corrosion. These linings are applied on:

- Tanks
- Stirrers
- Vessels
- Fans

4. Plastic cements : These are used for spaces between acid resistant tiles and bricks

5. Special cases : Plastics are used as guards for moving parts of machinery. Nylon and PVC fibres are woven into filter cloths and are used for aseptic screening.

QUESTION BANK

Each question carries 2 marks

1. Write the usefulness of glass lined equipment in the pharmaceutical plant.

Each question carries 5 marks

1. Explain the importance of stainless steel in pharmaceutical industry.
2. Write a note on the utility of glass and stainless steel in pharmaceutical industry.
3. Describe steel as a material of plant construction.
4. Name five important classes of plastics. Mention their applications in pharmaceutical industry.
5. Describe the steel alloys used in pharmacy practice.
6. What are the properties of glass? What are its applications as material of construction?
7. Describe various types of iron as materials of construction.

18

Pharmaceutical Industry—Establishment

Pharmaceutical Industry
Plant Location
Plant Layout
Utilities and Services
Industrial Pollution and Control
Industrial Hazards and Safety

The development of a complete plant design requires consideration of many factors. The role of costs and profits is very important. The application of engineering principles in the design of individual equipment is equally important. In addition, many factors such as plant location, layout, operations and control, utility and safety should be considered.

PHARMACEUTICAL INDUSTRY

The pharmaceutical industry differs from most other industries in that there exist a considerable degree of specialisation in it. Since products are so varied, no firm engages in all aspects of pharmaceutical manufacture. The products can be classified arbitrarily on the following lines.

Crude and processed botanical drugs : India grows a large number of vegetable drugs and supplies them to manufacturing houses in India and abroad. There is a steady demand for drugs consumed by Ayurvedic and Unani Practitioners of medicine.

Fine chemicals and pharmaceuticals : In India, a large number of pharmaceutical manufacturing houses purchase fine chemicals and industrial chemicals from firms, which specialise in their manufacture, for converting them into tablets, ointments, capsules, injections and other pharmaceutical preparations.

Proprietary drugs : With the decline of dispensed medicines, the pre-packed products such as tablets, capsules and parenteral products, are now prescribed and consumed in large quantities by hospitals and nursing homes. Hence, a number of firms engage in preparing proprietary drugs. Some manufacturers have built a name for the pharmaceutical industry and for themselves, by their research activities. Thus efforts are continued to develop better formulations of old drugs and discovery of new drugs. However, such manufacturers are limited in India.

Definitions of Manufacturers

Manufacturers are engaged in the mechanical or chemical transformation of inorganic and organic substances into new products.

The above definition also includes assembling of components or products. Pharmaceutical manufacturing has been divided into three kinds.

1. Biological products
2. Medicines and botanicals
3. Pharmaceutical preparations

The *biological products industry* includes "establishments engaged primarily in the production of bacterial and viral vaccines, toxins and analogous products (such as allergenic extracts), serum, plasma and other blood derivatives for human and veterinary use."

The *medicinal and botanicals industry* includes "establishments engaged primarily in the manufacture of bulk medicines, organic and inorganic chemicals, their derivatives and processing (grading, grinding and milling) of bulk botanical drugs and herbs."

The *pharmaceutical preparations industry* includes "establishments engaged primarily in manufacture, fabrication or processing into pharmaceutical preparations for human and veterinary use."

PLANT LOCATION

The selection of a location for the construction of a pharmaceutical or chemical plant is a vital decision to be taken, because it determines the balancing of investments and profits. Therefore, location of the plant has a strong influence on the success of an industrial venture. Care should be exercised in choosing the plant size. Primarily the plant should be located where the cost of production and distribution can be minimum. But other factors such as room for expansion and general living conditions are also important.

1. Fundamental (Primary) factors
2. Derived (Secondary) factors

Normally, primary factors exercise greater influence than secondary factors. However, it will be difficult to make a clear-cut decision between these types of factors. Sometimes, the secondary factors may have greater influence on location.

Fundamental or Primary Factors

1. Raw materials
2. Market
3. Energy availability
4. Transportation facility
5. Labour supply

1. Raw Materials : The availability of raw materials and cost of its transportation will be major determinants. Pharmaceutical industry uses the following types of raw materials.

(a) Crude drugs
(b) Inorganic chemicals
(c) Organic chemicals

It would be economical to locate the plant nearer to the source of raw materials particularly when they are consumed in large volumes. For example, raw materials for perfume industry are aromatic plants. These cannot be transported because important active principles may be lost and materials get spoiled. Hence, the industries undertaking extraction are located nearer to the place of cultivation as in Himachal Pradesh and hilly areas of UP.

If raw materials are not locally available or dangerous chemicals, the freight charges and risk of dangers increase enormously. If raw materials are stable, other factors take importance over this factor.

2. Market : Market exercises a strong influence on the establishment of industries. Where market is regional, the industry is located nearer to the market. The bulk drug industry is located in a place where drug formulation industries are located, since bulk drugs are the feed for the formulations and buyers are found nearby.

3. Energy availability : Fuel and power are the energy sources, which exert the same kind of influence as the raw materials. Now-a-days, electricity and diesel engines have been developed and are available at many places. In many cases, plants create power on their own for the smooth functioning of the industry. Therefore, industry can be located remote to the power generation plants.

4. Transportation facility : Transport is the lifeline of modern industry. Transport facilities are needed for bringing raw materials and distribution of finished products. An industry tends to be localised at places, which have a developed means of transport such as railway, road and seaport. These facilities are normally available in metropolitan cities or mega-cities such as Bombay, Calcutta, Madras, Hyderabad and Bangalore. Hence, most of the industries are located in these cities.

If the sale price of the finished product is very high, because of technical considerations as compared with freight charges, transportation may not outweigh other factors. The kind and amount of products and raw materials determine the most suitable type of transportation facility. There is also a need for transportation facilities for the personnel.

5. Labour supply : Low wages and abundant labour help in localisation of certain industries such as tea. However, pharmaceutical and chemical plants require skilled labour, who are better paid and often highly mobile. Therefore, industries can be located away from areas of labour concentration.

Consideration should be given to prevailing pay rates, restrictions on number of hours of work per week, competing industries that can cause dissatisfaction or high turn over rates among the workers, racial problems and variations in the skill and intelligence of the workers.

Derived (Secondary) Factors

1. Climate and soil
2. Government concessions
3. Water supply
4. Waste disposal
5. Site characteristics
6. Flood and fire protection
7. Community factors

1. Climate and soil : Climate and soil are very important for industries based on agriculture. For example, Ayurvedic drugs are mainly plant-based products. The soil and climate are suitable for cultivation of medicinal plants in the state of Kerala. These formulations are largely produced in that state.

In pharmaceutical industry, many operations have to be carried out in air-conditioned rooms, in dust free environment and under humidity control. A location which is very hot during summer would not be suitable as it is subjected to dust storms and drying up of water supplies. Further an area where the humidity is very high would not be suitable from the point of cost, contamination, difficulties of maintaining laboratory animals in proper condition and the efficiency of labour and supervisory force.

Industries based on production of antibiotics etc. are normally located in a place wherein the microbial contamination in the environment is low and the ambient temperatures throughout the year are cool. For example, IDPL antibiotics plant is located in Rishikesh (in UP) and Karnataka Antibiotics and Pharmaceuticals Limited (KAPL) is located in Bangalore, Karnataka State.

If the plant is located in a cold climate, costs may be increased by the necessity of constructing protective shelters around the process equipment. Special cooling towers or a/c equipment may be required, if the prevailing temperature is high.

2. Government concessions : Government subsidies and tax concessions have been provided for the industries located in certain notified areas. These areas have been declared as industrially backward and the government offers incentives such as low wages, cheap power, tax concessions etc. Previously such areas were not economically feasible, but now due to government concessions, these areas are developing fast.

3. Water supply : The processing industries use large quantities of water for cooling, washing, steam generation and also as a raw material (liquid orals). The plant, therefore, must be located where a dependable supply of water is available. A study should be conducted regarding the supply position of underground water and/or surface water and their seasonal variations. The quality of the water is also very important in pharmaceutical industry, as purified water is consumed in large quantities.

The temperature, mineral content, silt or sand content, bacteriological content, cost of supply and purification treatment must also be considered while choosing a water supply. A detailed estimate of water requirements both for the present and future must be made.

4. Waste disposal : In recent years, many legal restrictions have been placed on the methods for disposing of waste materials from the processing industries.

(a) When organic or inorganic chemicals are manufactured, there may occur problems of noxious gases being produced and discharged in to the atmosphere or into the sea.

(b) If the industry is engaged in the manufacture of biological products from raw materials obtained from slaughter houses

- or pathogenic organisms, the waste disposal does pose a problem, but a minor one, because the raw material handled is not in huge quantities.

The site selected for a plant should have adequate capacity and facilities for correct waste disposal. Attention should also be given to potential requirements for additional waste treatment facilities.

5. Site characteristics : The topography of the land and soil structure should be considered, since both may have a pronounced effect on construction costs. The cost of the land, local building costs and living conditions are important. Future changes may make it desirable or necessary to expand the plant facilities.

6. Flood and fire protection : Many industrial plants are located along large bodies of water and there are risks of flood or hurricane damage. Before choosing a plant site, the regional history of natural events of this kind should be examined. In case of major fire, assistance from the fire departments should be easily available. Fire hazards in the immediate surrounding area of the plant site must not be overlooked.

7. Community factors : The character and facilities of a community can have quite an effect on the location of the plant. Cultural facilities of the community are important for sound growth. Churches, temples, libraries, schools, civic theatres, concert associations and other similar groups, if active and dynamic, do much to make a community progressive. If a minimum number of facilities for satisfactory living of plant personnel do not exist, it often becomes a burden for the plant to subsidize such facilities.

Special Provisions of Factory Premises—Location

The factory shall be located in a sanitary place remote from filthy surroundings. The factory shall be situated in a place which:

(a) Shall not be adjacent to an open sewage, drain or public lavatories.

(b) Shall not be adjacent to a factory, which produces disagreeable or obnoxious odours or fumes.

(c) Shall not be adjacent to a factory, which emits large quantities of soot, dust or smoke.

The factory shall not constitute undue danger to adjacent life and property. State laws and other related laws should be consulted.

No location can meet all the requirements ideally, but the best compromise has to be made by considering various points objectively and gathering relevant information. After considering all the above points, a project report has to be prepared. It becomes necessary for the entrepreneur to acquaint himself with all the legal controls, which are existing. A few such acts are:

Indian Factories Act.
Drugs and Cosmetics Act and Rules.

PLANT LAYOUT

Once the location of plant is decided, the problem of layout has to be tackled.

Plant layout is a coordinated effort to achieve the final objective to integrate machines, materials and personnel for economic production.

Layout can be described as location of different departments and arrangement of machinery in a department. A proper layout has the advantage from the point of workers, labour costs, other production costs, production controls, supervision and capital investment. Layouts are of two types.

(a) Process layout or functional layout
(b) Product or straight line layout

Process layout or functional layout : In this type, all machines of a particular class doing a particular type of work or process are arranged together in a separate department. For example, all cutting machines may be placed in one department, i.e., cutting department. The advantages of this type are:

(a) More effective supervision can be achieved.
(b) Division of labour or specialised work can be provided.
(c) Less disruption of production is possible.
(d) Good scope for expansion.

This type of layout may not be possible in the pharmaceutical and chemical industry, because a number of unit operations should be performed in a sequence.

Product or straight line layout : In this type, all machines doing various operations are arranged in a line. The advantages of this type of layout are:

(a) Facilitates quick and smooth processing of work.
(b) Reduces cost of material handling using conveyor.

(c) Reduces manufacturing time and speeds up the manufacturing cycle.
(d) Facilitates proper use of floor space.
(e) Reduces inventory of work-in progress.
(f) Reduces inventory of finished goods.

This type of layout is more suitable for the pharmaceutical and chemical industries. Some times, a combination of these two layouts is also used.

Procedures of Layout

The procedures of plant layout are shown in Figure 18-1. A proper layout in each case includes arrangement of processing areas, storage areas and handling areas for efficient coordination. The layout of processing units in a plant, the equipment within these units must be planned. Then detailed piping, structural and electrical design should be developed. This layout can play an important part in determining construction and manufacturing costs. Thus, these must be planned carefully with attention being given to future problems that may arise.

Some factors which guide the layout are:

(a) New site development or additions to a developed site.
(b) Type and quantity of products to be produced.
(c) Type of process and product control.
(d) Space available and space required.
(e) Operational convenience and accessibility.
(f) Economic distribution of utilities and services.
(g) Type of buildings and building code requirements.
(h) Health and safety considerations.
(i) Waste disposal problems.
(j) Auxiliary equipment.
(k) Possible future expansion.

Scale drawings indicating complete description with elevation can be used for determining the best location for equipment and facilities. Elementary layouts are developed first. By analysing all the factors that are involved in the plant layout, detailed recommendations can be presented finally. Drawings and elevations including isometric drawings of the piping systems can be prepared.

In the recent years, three-dimensional models are often made for making proposed plant layouts. These have the advantage of indicating errors in a plant layout easily. In addition, models are useful in improving the layout during plant construction. Models are also useful for instruction and orientation purposes after the plant is completed.

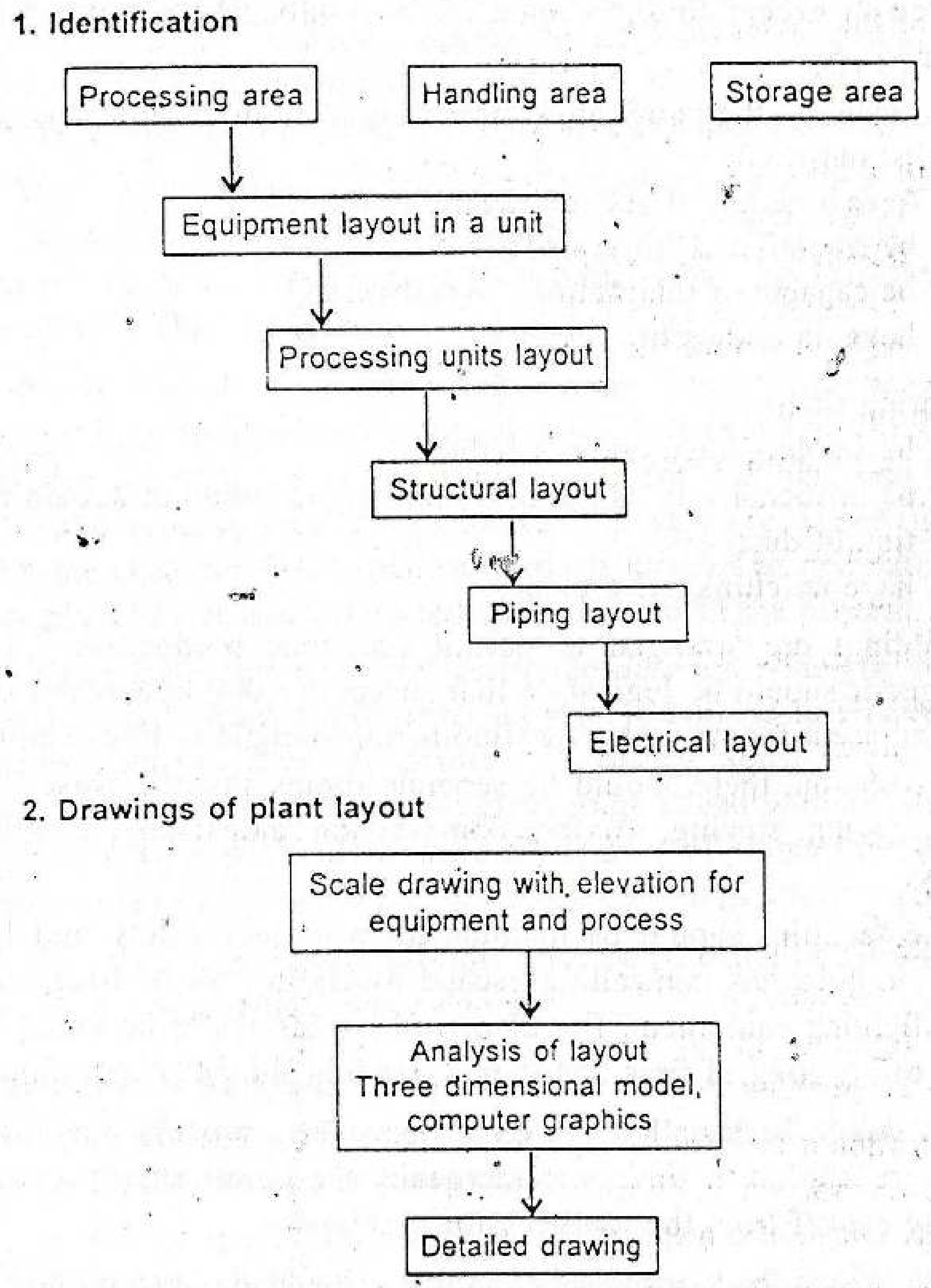


Figure 18-1. Flow diagram of procedures for an appropriate design of plant layout.

Special Provisions of Plant Layout

The premises should be suitable for the purpose of drug manufacturing. It means that all possible measures should be taken to prevent confusion or mixing-up of substances or materials and contamination. The building for the factory shall be constructed so as to permit the production under hygienic conditions. They shall conform to the conditions laid down in the Factories Act, 1948 (63 of 1948).

1. The part of the building used for manufacture shall not be used as sleeping place.
2. No sleeping place adjoining the building shall communicate therewith except through open air and through an intervening open space.
3. The walls of the room in which manufacturing operations are carried out shall
   - (a) have a height of six feet from the floor.
   - (b) be smooth and waterproof.
   - (c) be capable of maintaining cleanliness.
   - (d) have no chinks or crevices.

The flooring shall:

- (a) be smooth, even and washable
- (b) be in such a way as not to permit any retention or accumulation of dust
- (c) have no chinks or crevices.

The buildings are arranged to permit economic production. The routing of goods should be logical so that successive unit operations can be done in adjacent rooms with superfluous transportation. For example in the tablet section, there should be separate rooms situated closer for granulation, drying, sieving, mixing, compression and, if any, coating, successively.

Adequate facilities should be maintained to provide safety and fire protection. Regulations controlling escape routes in case of fires, providing fire fighting equipment, fire alarms and measures to be taken for prevention of breaking of fires and their spreading should be complied.

Devices should be installed in every room where process operations are carried on, so that in times of emergency the power supply can be immediately cut off from the transmission machinery.

Building meant for storing and handling should be segregated and isolated. These satisfy the provisions of the act.

UTILITIES AND SERVICES

Utilities

The basic utilities required for an industrial plant are power and water.

The primary sources of energy for the supply of power are heat of combustion of fuels. Fuel burning plants are of greater industrial significance than hydro-electric fuels, because the physical location of fuel burning plants is not restricted.

In chemical industries, power is supplied primarily in the form of electrical energy. Agitators, pumps, hoists, conveyers, compressors and similar equipment are usually operated by electric motors. Sometimes, internal combustion engines and hydraulic turbines are employed.

When a new plant is being set up, a decision must be made on either to use purchased power or to set up its own power unit. It may be possible to obtain steam as a by-product from the self-generation of electricity. This factor may influence the final decision.

Power can be transmitted in various forms, such as mechanical energy, heat energy and pressure energy. It is essential to recognise these different methods for transmitting power and the best one to suit the particular process should be chosen. For example, steam is generated from the cheapest fuel expanded through turbines to generate the necessary plant power and exhausted steam is used in the process heat.

Water for industrial purposes can be obtained either from the plant's own source or from a municipal supply. If demand for water is large, it can be obtained from the plant's own drilled wells, rivers, lakes, dam streams. Before the company agrees to go ahead with any new project, it must ensure itself of a sufficient supply of water for all industrial, sanitary and safety demands for both present and future.

The water used in manufacture shall be pure and of drinkable quality, free from pathogenic microorganisms.

Maintenance Services

Many of the problems involved in maintenance are due to the faulty design and layout of plant and equipment.

Sufficient space and facilities for maintenance work must be provided in the plant layout. It is essential to consider maintenance regulations while making decisions on equipment. Too often the design engineer is conscious only on installation costs and fails to recognize the maintenance costs. On several occasions, the maintenance costs can easily nullify the advantages of a cheap initial installation. For example, a compact system of piping, valves and equipment may be cheap and convenient for the operator's use, but maintenance of the system may be costly and involves time consuming dismantling operations.

Instruments are used in the chemical industry to measure process variables such as temperature, pressure and density. Automatic control has been accepted as the best and the resultant savings in labour combined with improved ease and efficiency of operations has more than offset the added expense for instrumentation (Use of high speed computers). In general, one centrally located control room is used for the recording and regulation of the process variables.

Storage

1. Adequate storage facilities for raw materials, intermediates, recycle materials, rejected materials and fuels are essential for the operation of a processing plant.
2. Bulk storage of liquids is generally handled by a closed spherical or cylindrical tanks so as to prevent the escape of volatile material and minimizing contamination.
3. Liquids with vapour pressures above atmospheric pressure must be stored in vented tanks. Flame arrest mechanisms must be installed in all openings.
4. Gases are stored at atmospheric pressure in wet or dry seal gas-holders.
5. High pressure gases are stored in spherical or horizontal cylindrical vessels under pressure.
6. Solid products and raw materials are either stored in weather tight tanks with sloping roofs or in out door bins and mounds.

INDUSTRIAL POLLUTION AND CONTROL

Thermal Pollution and Control

Various off-stream cooling systems are required to handle thermal discharges from processes because:

1. Changes in temperature cause potential damage to the aquatic environment.
2. High temperature causes reduction in the assimilative capacity of organic wastes.
3. Federal enactments are more stringent regarding water temperature standards.

Cooling towers are most often considered for this service followed by cooling ponds and spray ponds in that order.

1. In *wet cooling towers*, the condensed cold water and ambient air are intimately mixed. Cooling results from the evaporation of a portion of water.

2. In *dry cooling towers*, the temperature of the condensed water decreases due to conduction and convection for the transfer of heat from the water to the air.
3. *Cooling ponds* are generally considered for heat removal when suitable land is available at a reasonable price. It is normally assumed that heat discharged to a cooling pond is lost through the air water interface.
4. *Spray ponds* provide a viable alternative to cooling ponds when land costs are too high. It is estimated that a spray pond required only about 5 to 10% the area of a cooling pond due to the more air water contact. In addition, drift losses and corrosion problems are less severe than in cooling towers.

Water Pollution Abatement

The problems of handling a liquid waste effluent is more complex than handling a waste gas effluent. The waste liquid may contain dissolved gases/solids or it may be slurry in either concentrated or diluted forms. Because of this complexity, priority should be given to the possibility of recovering part or all of the waste products for reuse or for sale.

Frequently, it is economical to install recovery facilities rather than waste treatment equipment. If product recovery is not capable of solving the waste disposal problem, waste treatment should be done. One of the functions of the design engineer is to decide which treatment process or combination of processes will best perform the necessary task of cleaning up the waste water effluent. This treatment could be physical, chemical or biological in nature, depending upon the type of waste involved and the amount of removal necessary.

Physical treatment : Large floating or suspended particles are removed first. Sedimentation and gravity settling methods are employed using circular clarifiers, with continuous chain sludge scrapers. Adsorption process is employed using activated carbon for the removal of refractory organic substances, toxic substances and colour. Three different membrane processes, viz., ultrafiltration, reverse osmosis and electro-dialysis are used as the final treatment and for in-plant recovery systems.

Chemical treatment : Chemical methods are generally used to remove colloidal matter, colour, odour, acids, alkalis, heavy metals and oil. Such a treatment is generally brought about by coagulation, flocculation, emulsion breaking, precipitation and neutralization.

Biological treatment : If common bacteria are found in water, many organic materials will be oxidized to form carbon dioxide, water, sulphate and similar materials. This treatment consumes oxygen that is dissolved in water and may cause a depletion of dissolved oxygen.

Air Pollution Control

Air pollution control can essentially be classified into two major categories.

- Those suitable for removing particulate matter.
- Those associated with removing gaseous pollutants.

Air pollutants are removed by chemical and physical means in the following manner.

1. Coarse diameter particulate matter can be removed with low-energy devices such as settling chambers, cyclones and spray chambers.
2. Sub-micron particles must be removed with high-energy units such as bag filters, electrostatic precipitators and venturi scrubbers.
3. Intermediate particles can be removed with impingement separators or low-energy wet collectors.
4. Gaseous pollutants can be removed from air streams either by absorption, adsorption, condensation or incineration.

INDUSTRIAL HAZARDS AND SAFETY

Toxic and corrosive chemicals, fire, explosions and plant personnel falling to accidents are the major health and safety hazards encountered in the operations of plants in processing industries.

Chemical Hazards

Tough many common substances are apparently innocuous, prolonged breathing and/or skin contact produce irritation and may bring about permanent impairment of health or even death.

Many chemicals can cause severe burns, if these come into contact with living tissue. Living tissue may be destroyed by chemical reactions such as:

(a) Dehydration by strong dehydrating agents.
(b) Digestion by strong acids and bases.
(c) Oxidation by strong oxidizing agents.

Eyes and mucous membranes of the throat are particularly susceptible to the effect of corrosive dust, mist and gases. In addition, many chemicals are very toxic, flammable or detonable.

Chloroform, benzene, chlorinated hydrocarbons, low-boiling fractions of petroleum are some of the common solvents used in pharmaceutical industry. Solvents used in the extraction of plants, purification of synthetic drugs and in chemical analysis should be handled with care.

In pharmaceutical industry, most of the dermatitis can be attributed to synthetic drugs, especially to acridines and phenothiazine compounds. It has been noticed that fair people are generally more susceptible to skin irritation than dark people. The only protection from skin reactions is to observe cleanliness and to remove the people from the areas as soon as the first sign of skin reactions is noticed. Wherever practicable, application of barrier creams before commencing the work has been found useful in protecting individuals.

While grinding vegetable drugs, dust evolved is irritating. For example, capsicum and podophyllum affect the eyes and irritation is painful. Therefore, goggles are to be worn. Some individuals are so sensitive to ipecacuanha that they develop symptoms of asthma, when exposed even to minute traces of its dust.

Tolerance levels for toxic chemicals have been set by Federal Regulations. Flammability and detonability of chemicals are available in most handbooks. Hazards due to industrial chemicals can be minimised if there is strict observance of safety regulations and protective measures of good house-keeping principles, besides their full and intelligent cooperation in the handling of dangerous chemicals and drugs.

Dust Explosion

In pharmaceutical industry, a number of grinding operations is employed. If iron or stone pieces get into the disintegrator or other similar grinding mills, sparks are emitted, which might bring about explosion with some easily combustible materials. Therefore, suitable precautions against accumulation of dust should be taken. It has been found that in pharmaceutical and ancillary factories, dust of starch and dextrin besides organic substances are extremely hazardous.

The methods used for controlling dust in the pharmaceutical industry are:

(a) Filtration
(b) Inertial separation
(c) Electrostatic precipitation

Filtration : In this method, air which contains dust is sucked or blown through a suitable mechanical barrier whose pore size is sufficiently small to retain particles. Materials used for this purpose include paper, felt, wool, cotton-wool and nylon. The filters often take the form of pads or panels fitted to the walls and windows of building. A large variety of filter bags are available, which can be attached to a particular machine where dust is produced.

Inertial separators : Example is a cyclone separator. In this method, air is allowed to circulate in a spiral manner through a cone-shaped vessel. Due to centrifugal force, particles of drugs are thrown outwards to the walls of the cyclone separator. They slide down to a hopper, which can be subsequently withdrawn. Cyclone separators are particularly suitable for attaching to machines. These can form an integral part of the design of certain mills and mixers.

Electrostatic precipitators : It consists of a number of earthed tubes. Fine metal wires are stretched between the tubes. Several thousand volts of direct current is applied on metal wires. The high potential difference between the tubes and the wires ionizes the dust particles that are carried by air stream. The dust is deposited on metal plates from which it is collected periodically.

Fire and Explosion Hazards

A single fire or explosion can spread to adjoining units. Careful plant layout and judicious choice of constructional materials can reduce such events. Hazardous operations should be isolated by conducting them in separate buildings or by the use of brick firewalls. Brick or reinforced concrete walls can limit the effects of an explosion, particularly if the roof is designed to lift easily under an explosive force.

Equipment should be designed to meet the specifications and codes of recognized authorities such as Indian Standards Association, American Petroleum Institute (API) and American Society of Testing Materials. The design and construction of pressure vessels and storage tanks should follow API and ASME codes.

Adequate venting is necessary and it is advisable to provide protection by using both spring-loaded valves and rupture discs. Possible sources of fire are reduced by eliminating the unnecessary ignition sources such as flames, sparks, heated materials, matches, smoking, welding, cutting and static electricity. Spontaneous combustion and non-explosion proof electrical equipment are the potential ignition sources. The installation of sufficient fire alarms, temperature alarms, fire-fighting equipment and sprinkler systems must be specified in design.

Every type of mechanical device should be examined periodically by a competent person.

Noise Abatement

The design engineer should include noise studies in the design stage of any industrial facility.

To attain efficient, effective and practical noise control, it is necessary to understand noise sources in the process, their acoustic properties and characteristics and how they interact to create the overall noise situation. Table 18-1 presents typical process design equipment providing high noise levels and potential solutions to this problem.

TABLE 18-1

Equipment Noise Sources, Levels and Potential Control Solutions

Equipment	*Sound level in dBA at 3 feet*	*Possible noise control treatments*
Air coolers	87-94	Aerodynamic fan blades, decrease revolutions per minute, increase pitch, include tip and hub seals, decrease pressure drop
Compressors	90-120	Install mufflers on intake and exhaust, enclose the machine with casing, vibration isolation and lagging of piping system
Electric motors	90-110	Acoustically lined fan covers, enclosures and motor mutes.
Heaters and furnaces	95-110	Acoustic plenums, intake mufflers, lined and damped ducts.
Valves	<80-108	Avoid sonic velocities, limit pressure drop and mass flow, replace with special low noise valves, vibration isolation and lagging.
Pipes	9-105	Inline silencers, vibration isolation and lagging.

Safety Regulations

Safety must be a paramount consideration in the design of pharmaceutical industry. The factories Act, 1948 is very comprehensive. It includes provisions on cleanliness, ventilation, lighting and heating and the prevention of over-crowding.

The intention of the Occupational Safety and Health Act (OSHA) of 1970 is "to assure so far as possible every working man and woman in the nation safe and healthy working conditions and to preserve our human resources." Two of the standards directly related to workers health and important in design work are:

(1) toxic hazardous substances.
(2) occupational noise exposure.

The first factor concerns with the normal release of toxic and carcinogenic substances carried via vapour, fumes, dust fibres or other media. Compliance with the act requires the designer to make calculations of concentrations and exposure time of plant personnel to toxic chemicals during normal operation of a process or a plant. Their release could emanate from various types of seals, control valve packing or other similar sources. Normally, the designer can meet the limits set for exposure to toxic substances by specifying special valves, seals, vapour recovery systems and appropriate ventilation systems.

The Federal Register should be examined closely for the list of materials declared hazardous, acceptable material exposure time and concentration before beginning the detailed design of a project.

The occupational noise exposure standard requires well planned timely execution of steps. It is best to prepare two noise specifications during plant design itself. One to define the designers own scope of work and the other to set vendor noise-level requirements for various pieces of equipment.

Other standards in the safety area most often cited by OSHA are the National Electric Code and Machinery and Machinery Guarding, which must be considered in detailed designs.

Personal Safety

Every attempt should be made to incorporate facilities for health and safety, protection of personnel in the plant design. This includes (but it is not limited to) protected walkways, platforms, stairs and work area. Any unavoidable physical hazards must be clearly defined. In such areas, means for exit must be unmistakable. All machinery must be guarded with protective devices. In all cases, medical devices and first aid must be readily available for all workers.

QUESTION BANK

Each question carries 5 marks

1. What are possible industrial hazards? How can they be controlled?
2. What methods are employed for preventing the hazards of handling and use of poisonous chemicals in industry?
3. Explain industrial pollution and control.
4. What methods are employed for preventing the hazards of handling and use of poisonous chemicals in industry?
5. Write a note on plant location.

Each question carries 10 marks

1. Describe the factors that should be considered regarding plant location and layout.

APPENDIX–I

FRACTIONS AND MULTIPLICATIONS OF UNITS

(A) Greek Alphabets

Α	α	Alpha	Ν	ν	Nu
Β	β	Beta	Ξ	ξ	Xi
Γ	γ	Gamma	Ο	ο	Omicron
Δ	δ	Delta	Π	π	Pi
Ε	ε	Epsilon	Ρ	ρ	Rho
Ζ	ζ	Zeta	Σ	σ	Sigma
Θ	θ	Theta	Υ	υ	Upsilon
Ι	ι	Iota	Φ	ϕ	Phi
Κ	κ	Kappa	Χ	χ	Chi
Λ	λ	Lambda	Ψ	ψ	Psi
Μ	μ	Mu	Ω	ω	Omega

(B) SI Units

Fraction	*Prefix*	*Abbreviation*	*Power*	*Prefix*	*Abbreviation*
10^{-1}	deci	d	10^{1}	deca	da
10^{-2}	centi	c	10^{2}	hecta	h
10^{-3}	milli	m	10^{3}	kilo	k
10^{-6}	micro	μ	10^{6}	mega	M
10^{-9}	nano	n	10^{9}	giga	G
10^{-12}	pico	p	10^{12}	terra	T
10^{-15}	femto	f			
10^{-18}	atto	a			

APPENDIX II

(A) Some Notations of Units and their Abbreviations in SI Units

Property	*Units in full names*	*Abbreviations for the units*
Acceleration due to gravity	metre per second square	m/s^2
Amount of heat	joule	J
Capacity of a pump	metre cube per hour	m^3/h
Centrifugal force	newton	N
Concentration	Moles	Mol
	Molarity	M
	Normality	N
	Molality	m
Density	kilogram per metre cube	kg/m^3
Displacement in pump	metre cube per minute	m^3/min
Drop in head	metre	m
Energy	joule	J
Enthalpy per unit mass	joules per kilogram	J/kg
Film coefficient or Surface coefficient	watt per metre square·Kelvin	$W/m^2{\cdot}K$
Force	newton	N
Frequency	hertz	Hz
Gravitational force	newton	N
Heat transfer	joule	J
Heat transfer coefficient	watt per metre square·Kelvin	$W/m^2{\cdot}K$
Heat transfer rate	joule per second	J/s
Height or length	metre	m
Length	metre	m
Mass	kilogram	kg
Power	watt	W
Pressure	pascal	Pa
Pressure drop	pascal	Pa
Pressure head	metre	m

Property	*Units in full names*	*Abbreviations for the units*
Rate of discharge of liquid	meter cube per minute	m^3/min
Rate of drying	kilogram per hour	kg/h
Rate of entry of feed	kilogram per hour	kg/h
Specific energy	millijoule per kilogram	mJ/kg
Specific surface	metre square per meter cube	m^2/m^3
Speed of rotation	Revolutions per second	r/s
Steam pressure	pascal	Pa
Stefan Boltzmann constant	watt per metre square Kelvin^4	$W/m^2{\cdot}K^4$
Surface area	metre square	m^2
Surface energy	millijoules per metre square	mJ/m^2
Temperature	Degree Kelvin Degree Celsius	K °C
Tensile strength	megapascal	Mpa
Thermal conductivity	watt per metre square·Kelvin	$W/m^2{\cdot}K$
Time	second (or minute or hour)	s (or min or h)
Velocity	metre per second	m/s
Viscosity	pascal.second	Pa·s
Volume	metre cube (or litre)	m^3 (or l)
Work done	watt hour	W·h
Young's modulus	megapascal	Mpa

(B) Some Important conversions in SI Units

Pascal (Pa) $= N/m^2$ $= kg/m{\cdot}s^2$

Newton (N) $= kg/m$

Joule (J) $= N{\cdot}m$ $= kg.m^2/s^2$

$N{\cdot}m = J$

$N{\cdot}m/s = J/s = W$

$J/s = W$

$W = N{\cdot}m/s$

APPENDIX–III

INTER-CONVERSION OF UNITS

TABLE-1
FPS to SI Units

Measurement	*Unit*	*Conversion factor*	*Reciprocal*
Area	1 ft^2	9.290×10^{-2} m^2	10.764
	1 in^2	6.452×10^{-4} m^3	1550
Density	1 lb/ft^3	16.0185 kg/m^3	6.243×10^{-2}
	1 lb/in^3	27.680 kg/m^3	3.613×10^{-5}
Energy, work and power	1 Btu	1.055×10^3 joules	9.4781×10^{-4}
Force	1 lbf	4.448 N	0.225
Heat transfer coefficient	$Btu/s \cdot ft^2$ °F	20.44 $kW/m^2 \cdot K$	4.89×10^{-2}
Length	1 foot	0.3048 meter	3.2808
	1 inch	2.54×10^{-2} meter	39.370
Mass	1 pound (lb)	0.4536 kg	2.2046
	1 US ton	9.072×10^{-4} kg	11.02×10^2
Mass flow rate	1 lb/s	0.454 kg/s	2.205
Power	1 ft.lbf/s	1.356 W	0.738
	1 lbf·ft	1.355×10^{-3} kJ	7.38×10^2
Pressure	1 lbf/in^2	6895 Pa	1.45×10^{-4}
	1 atm.	1.013×10^2 kPa	9.87×10^{-3}
	1 bar	100 kPa	0.01
	1 inHg	3386 Pa	2.95×10^{-4}
Stress	1 lbf/in^2	6.8948×10^3 kPa	1.4504×10^{-4}
Thermal conductivity	1 $Btu \cdot ft/h \cdot ft^2 \cdot °F$	1.730 $W/m \cdot K$	0.578
	1 $Btu \cdot in/h \cdot ft^2 \cdot °F$	0.1442 $W/m \cdot K$	6.935
Thermal resistance	1 $°F \cdot ft^2 \cdot h/Btu$	1.761×10^2 $K \cdot m^2/kW$	5.679×10^{-3}
	1 lbf/ft^2	4.788×10^{-2} kPa	20.886
Vacuum	1 inHg (60°F)	3.377 kPa	0.2961
	1 inH_2O (39.2°F)	0.2491 kPa	4.0145
Velocity	1 ft/s	0.305 m/s	3.281
	1 in/s	0.0254 m/s	39.37

Measurement	*Unit*	*Conversion factor*	*Reciprocal*
Viscosity	1 $lbf \cdot s/in^2$	6.894×10^3 $Pa \cdot s$	1.451×10^{-4}
	1 $lbf \cdot s/ft^2$	47.88 $Pa \cdot s$	2.0886×10^{-2}
Volume	1 ft^3	2.832×10^{-2} m^3	35.315
	1 in^3	1.693×10^{-5} m^3	61.024
	1 US gallon	4.54×10^{-3} m^3	220.264

TABLE–2
Interconversion of Units (Fundamental and Derived) with Conversion Factors

Unit	*Conversion factor × unit*	*Reciprocal*
1 foot	= 30.48 cm (or ml)	0.03281
1 pound (lb)	= 453.6 gram	2.2046×10^{-3}
1 cm^2	= 1.639×10^{-5} m^2	6.1024×10^4
1 dyne	= 0.01 mN	100
1 $dyne/cm^2$	= 0.1 Pa	10
1 cm H_2O (4°C)	= 9.80×10^{-2} kPa	10.205
1 cal	= 4.184×10^{-3} kJ	239.00
1 erg	= 1.0×10^{-7} J	10^7
1 $°C \cdot m^2 \cdot h/kcal$	= 8.604×10^2 $K \cdot m^2/kW$	1.162×10^{-3}
1 $cal \cdot m/s \cdot cm^2 \cdot °C$	= 4.184×10^2 $W/m \cdot K$	2.39×10^{-3}
1 mmHg	= 6.895 kPa	0.145
1 $cal/s \cdot cm^2 \cdot °C$	= 41.84 $kW/m^2 \cdot K$	2.39×10^{-2}

TEMPERATURES

TABLE-3
Interconversion of Temperature and Relevant Equations

1 R (Rankine) = (1/18) K (Kelvin)
1 K (Kelvin) = 1.8 R (Rankine)
T R (Rankine) = T°F + 459.67
T°F (Fahrenheit) = T R – 459.67
T°C (Celcius) = (°F – 32)/1.8°C
T°F (Fahrenheit) = 32 +1.8°C
ΔT°C = 1.8 ΔT°F = ΔT K

APPENDIX-IV

DEFINITIONS AND MEANINGS

Actual screen : A screen which does not give perfect separation about the cut diameter of the powder.

Agitation : Refers to the induced motion of a material in a specified way, usually in a circulatory pattern inside a container.

Air binding: In centrifugal pumps, the entry of air into the pump at the initial stage practically stops delivering the liquid. This phenomenon is known as air binding.

Amorphous solids : These are the solids which do not have specific shape.

Attrition : It involves breaking down of the material by rubbing action between two surfaces.

Axial angle : It is an angle between the two perpendiculars to the intersecting faces in a crystal.

Axial flow of liquids : The flow of liquid that acts in a direction parallel to the impeller shaft.

Axial length : It is the distance between centres of two atoms in a crystal.

Azeotropic distillation : It is a distillation method in which azeotropic mixture is broken by the addition of a third substance, which forms a new azeotrope with one of the components.

Azeotropic solution : It is a solution which distils unchanged at a, constant temperature.

Belt idlers : These are supporting rollers, which are arranged on a shaft below the belt.

Bernoulli's theorem: States that in a steady state, ideal flow of a incompressible fluid, the total energy per unit mass, which consists of pressure energy, kinetic energy and datum energy, at any point of the fluid is constant.

Binary liquids : Are those liquids which are miscible with one another in all proportions.

Biological corrosion : The metabolic action of microorganisms can either directly or indirectly causes deterioration of a metal (corrosion).

Black body : It is a body that radiates maximum possible amount of energy at a given temperature.

Blending : It is mixing of powders smoothly and inseparably together.

Bound water : Is the minimum water held by the material that exerts an equilibrium vapour pressure less than the pure water at the same temperature.

Bulk transport : Is the movement of a large portion of a material from one location to another location in a given system.

Calandria : It is a steam compartment, which consists of a number of tubes fitted in a vessel and is included in the evaporator.

Caking : Is the process of formation of clumps or cakes when crystals are improperly stored.

Cavitation : It is a phenomenon of formation of vapour bubbles and their sudden collapse in a pump.

Centrifugal effect : It is expressed as a ratio of centrifugal force to gravitational force.

Centrifugal force : It is due to inertia of a rotating body and it acts on the rotating body in a direction away from the point or axis of rotation or revolution.

Centrifugal pump : An hydraulic machine which converts the mechanical energy into pressure energy by means of centrifugal force.

Centrifugation : It is a unit operation employed for separating the constituents present in a dispersion with the aid of centrifugal force.

Clarification : It is a process of separation of liquids containing solids not exceeding 1.0%.

Coefficient of thermal conductivity : Is defined as the quantity of heat flowing per second across one square metre area of cross section of a slab of the material of one metre thickness, whose faces are maintained at a steady temperature difference of one degree Kelvin.

Compression : It is a means by which the material is crushed between rollers by the application of pressure.

Conduction : It is a process in which heat flow in a body is achieved by the transfer of the momentum of individual atoms or molecules without mixing.

Convection : It is a process in which heat flow is achieved by actual mixing of warmer portions with cooler portions of the same material.

Corrosion : Is a reaction of a metallic material with its environment, which causes a measurable change to the material and can result in a functional failure of the metallic component or of a complete system.

Critical humidity : Is the humidity above which crystals absorb moisture and below which they do not absorb moisture.

Crystal : It is a solid particle, which is formed by the solidification (crystallisation) process (under suitable environment) of a substance in which structural units are arranged by a fixed geometric pattern or lattice.

Crystal growth : It is a diffusion of solute molecules or ions from solution to reach the faces of a crystal, which helps in their growth.

Crystal hydrate : It is a solid substance which associates with water.

Crystal lattice : It is the orderly internal arrangement of particles in three dimensional space.

Crystallization : Is a spontaneous arrangement of the particles into a repetitive orderly array, i.e., regular geometric patterns.

Cutting : It is a means of tearing the material by a sharp blade.

Dalton's law : It states that the total pressure exerted by an ideal gaseous mixture is equal to the sum of the individual partial pressures of the component gases, if alone were present and occupied the total volume.

Depth filtration : It is a filtration process, in which the slurry penetrates to a point where the diameter of solid particles is greater than that of the tortuous void or channel.

Destructive distillation : It is a distillation method in which the distillate is a decomposition product of the constituents of the organic matter burnt in the absence of air.

Diaphragm : It is a flexible physical barrier.

Distilland : The feed liquid mixture to be distilled.

Distillate (condensate) : The liquid condensed during distillation.

Distillation : It is a separation of the components of a liquid mixture by processes involving vaporisation and subsequent condensation at another place.

Double acting pump : It is a pump that displaces water on both halves of the cycle of the movement of the pumping element (piston or plunger), i.e., during up-stroke and down-stroke.

Drop-wise condensation : It is a process in which the condensed liquid collects as drops that may range from microscopic size up to drops that are seen with the naked eye.

Drying : It is a process of removal of small amounts of water or other liquid from a material by the application of heat.

Energy : The energy of a body is measure of the capacity or ability of the body to do work.

Energy balance : The law of conservation of energy states that the energy output must be same as the energy input in any process.

Equilibrium moisture content (EMC) : Is the amount of water present in the solid, which exerts a vapour pressure equal to the vapour pressure of the atmosphere surrounding it.

Erosion : It is the destruction of a metal by abrasion and attrition caused by the flow of liquids or gases.

Eutectic point : The temperature and pressure at which the frozen solid vaporises without conversion to a liquid.

Evaporation : It is a process of vaporising large quantities of volatile liquid to get a concentrated product.

Extractive distillation : It is a distillation method in which azeotropic mixture is broken by the addition of a third substance which is relatively nonvolatile liquid compared to the components to be separated.

Film type condensation : A process in which the condensed liquid wets the surface on which it is condensing and forms a continuous film of condensate.

Filter aid : It forms a surface deposit which screens out the solids and also prevents plugging of the supporting filter medium.

Filter cake : The accumulated solids that are retained on the filter medium.

Filter medium : Is a porous medium used to retain the solids.

Filtrate : The clear liquid that has passed through the filter medium.

Filtration : Is a process of separation of solids from a fluid by passing the same through a porous medium that retains the solid but allows the fluid to pass through.

Filtration centrifuge : A centrifuge in which solids pass through the porous medium based on the difference in the densities of the solid and liquid phases on application of centrifugal force.

Flash distillation (equilibrium distillation) : It is a distillation process in which the entire liquid mixture is suddenly vaporised (flash) by passing the feed from a high pressure zone to a low pressure zone.

Flaw in a particle : It is a structural weakness that may develop into a crack under strain.

Flight in conveyor : The conveying mechanism such as screw element used in the screw conveyor.

Fluid dynamics : It deals with the study of fluids in motion.

Fluid flow : It is the study of flow of substances that do not permanently resist distortion.

Fluid statics : It deals with the fluids at rest in equilibrium.

Fluidised state : It is a state in which solids are suspended in a stream of air.

Forced convection : It is a heat transfer process in which mixing of fluid is obtained by a stirrer or agitator or pumping the fluid for recirculation.

Fourier's law : This law states that the rate of heat flow through a uniform metal is proportional to the area, the temperature drop and inversely proportional to the length of the path of flow

Fractional distillation : It is a distillation process in which vaporisation of liquid mixture gives rise to a mixture of constituents from which the desired one is separated in pure form.

Fractionating column : It is a special type of still-head in which condensation and revaporisation take place simultaneously.

Free moisture content (FMC) : Is the amount of water that is free (easy) to evaporate from the surface.

Galvanic corrosion : Corrosion associated with the flow of current to a less-active metal (cathode) from a more-active metal (anode) in the same environment.

Grey body : It is a body whose absorptivity is constant at all wavelengths of radiation, at a given temperature.

Heat exchanger : It is a heating device used for transferring heat from one fluid (hot gas or steam) to another fluid through a metal wall.

Heat interchanger : It is a heating device used for transferring heat from one liquid to another liquid or from one gas to another gas through a metal wall.

Ideal screen : A screen which sharply separates the feed mixture in such a way that the smallest particle in the oversize will be just larger than the largest particle in the undersize.

Ideal solution (perfect solution) : It is a solution in which the attractions between unlike molecules are of the same order as between like molecules.

Impact : It involves the operation of splitting the material apart, when a lump of material strikes against the rotating hammers.

Inertia : It is the intrinsic property of a body by virtue of which it cannot change by itself its state of rest or uniform motion along a straight line.

Isomorphism : It is a phenomenon in which two or more substances possess the same crystalline form and crystals of one such substance can be grown in the saturated solution of the other.

Kinetic energy : Of a body is the energy possessed by the body by virtue of its motion.

Laminar flow (viscous flow) : It is a flow in which the fluid particles move in layers or laminar with one layer sliding over the other.

Laminar mixing : Is the mixing of two dissimilar liquids through laminar flow, i.e., the applied shear stretches the interface between them.

Latent heat of vaporisation : Is defined as the quantity of heat required to convert a unit mass of the liquid at its boiling point from the liquid to the vapour state without a change in temperature.

Manometers : These are the devices used for the measurement of pressure difference at a point of fluid.

Material balance : The law of conservation of matter states that material cannot be destroyed or created, it can be changed from one form to another.

Mier's supersaturation theory : Postulates a definite relationship between concentration and temperature at which crystals will spontaneously form in an initially unseeded solution.

Miscible liquids : These liquids are miscible in all proportions.

Mixing : Putting together in one mass or assemblage with more or less thorough diffusion of the constituent elements among one another.

Mixing : Is a process that tends to result in a randomization of dissimilar particles within a system.

Molecular diffusion : Is the mixing at molecular level in which molecules diffuse due to thermal motion.

Molecular distillation (short path distillation or evaporative distillation) : It is a distillation method in which each molecule in the vapour phase travels mean free path and gets condensed individually without intermolecular collisions on application of vacuum.

Natural convection : It is a heat transfer process in which mixing of fluids is accomplished by the natural currents set up, when body of fluid is heated.

Nucleation : It refers to the birth of very small bodies of a new phase within a homogenous supersaturated liquid phase, which is responsible for crystallisation.

Over-size powder : The material that remains on the given screening surface.

Partially miscible liquids : These are the liquids, which are miscible in one another at one particular proportion.

Permeability : It is the flow rate of a liquid of unit viscosity across a unit area of cake thickness under a pressure gradient of unity.

Pitch : It is the distance the propeller would move through the fluid per revolution, if slippage does not occur.

Polymorph : It is a chemical substance, which can exist in more than one crystalline form.

Potential energy : It is the energy possessed by the body by virtue of its position or configuration.

Power pump : It is a pump in which the moving element (piston or plunger) is actuated by some form of energy other than steam.

Pressure head : It is defined as the height of a column of liquid of known density, which is numerically equal to a pressure term.

Pseudomorph : It is a solid form, which arise because of inclusion of small amounts of solvent of crystallisation.

Radial flow of liquid : It is the flow of liquid that acts in a direction vertical to the impeller shaft.

Radiation : It is a process in which heat flows through space by means of electromagnetic waves.

Raoult's law : It states that the partial vapour pressure of each volatile constituent is equal to the vapour pressure of the pure constituent multiplied by its mole fraction in the solution at a given temperature.

Real solution (perfect solution) : The solution which does not obey ideal solution behaviour or which do not obey Raoult's law.

Reciprocating pump : It is a pump in which the pumping element moves in a forward and backward directions in a cylinder.

Reducing valves : These are the valves used in order to maintain uniform pressure in one part of the system at a level lower than the pressure in another part of the system.

Reynolds number : It is a ratio of inertial force to viscous force of a flowing fluid.

Rotary positive displacement pump : It is a pump in which liquid is mechanically displaced by the rotation of one or more elements within a stationary housing.

Sedimentation centrifuge : A centrifuge that produces sedimentation of solids based on the difference in the densities of two or more phases of the mixture.

Self-priming pump : It is a pump, which can remove air from casing by suitable mechanism.

Sieve number : It indicates the number of meshes per linear length of 0.0254 m (one inch).

Simple distillation : Is a process of converting a single constituent from a liquid (or mixture) into its vapour, transferring the vapour to another place and recovering the liquid by condensing the vapour, usually by allowing it to come in contact with the cold surface.

Single acting pump : It is a pump, which displaces water on one half of the cycle of the movement of the pumping element (piston or plunger), i.e., during the down stroke.

Size reduction : Is a process of reducing large solid unit masses (vegetable or chemical substances) into small unit masses, coarse particles or fine particles.

Size separation : It is a unit operation, that involves the separation of a mixture of various sizes of particles into two or more portions by means of screening surfaces.

Steady state system : The system is said to be in steady state, if the operating conditions do not vary with time.

Steam distillation : It is a method of distillation carried with the aid of steam and is used for the separation of high boiling substances from nonvolatile impurities.

Stoichiometry : It means carrying out of calculations based on quantitative relationships.

Sublimation : It is a process in which direct change of water from solid into vapour takes place without conversion into a liquid phase.

Supersaturated solution : Is one that contains more of the dissolved solute than it would normally contain in a saturated solution at a definite temperature.

Surface coefficient : It is the conductive capacity of the stagnant film for the transfer of heat.

Surface filtration : It is a screening action (filtration process) by which pores or holes of the medium prevent the passage of solids.

Tangential flow of liquid : It is the flow of liquid that acts in a direction tangent to the circle of rotation around the impeller shaft.

Thermal conductivity : It is the reciprocal of thermal resistance.

Turbulent flow : A flow is said to be turbulent, if the Reynolds number is more than 4000 in a pipe.

Turbulent flow : It is the flow in which the fluid particles continuously transfer momentum to adjacent layers.

Turbulent mixing : is mixing due to turbulent flow, which results in random fluctuation of the fluid velocity at any given point within the system.

Unbound water : Is the amount of water (moisture) held by the material that exerts an equilibrium vapour pressure equal to that of pure water at the same temperature.

Under-size powder : The material that can pass through the screening surface

Unit cell : It is the smallest geometric portion of the crystal, which repeats to build up the whole crystal.

Unit operation : A process frequently consists of a fewer number of distinct individual steps. Each step is called unit operation.

Unit process : It is one in which several unit operations are combined in a sequence to achieve the objectives of a chemical or physical process.

Unsteady state : If the operating conditions are varying with time, then the system is said to be in unsteady state.

Validation : It is a procedure that demonstrates the ability of consistently producing a product with the established specifications under ideal conditions.

Valve : It is a device used to control the rate of flow of fluid in a pipeline.

Variable area meter : It is a device that measures the area of flow, so as to produce a constant head differential.

Variable head meter : It is a device that measures the variation in the pressure across a fixed constriction placed in the path of flow consisting of a constant area.

Viscous flow : A flow is said to be viscous if the Reynolds number is less than 2000 in a pipe or the fluid flows in layers.

Volatility : Of any substance in solution may be defined as the equilibrium partial pressure of the substance in the vapour state divided by the mole fraction of the substance in the solution.

Vortex : It is a strong circulatory flow pattern manifests near the impeller shaft.

Young's modulus : The ratio of the longitudinal stress to the longitudinal strain within elastic limits.

Zeotropic mixture : It is a mixture whose total vapour pressure is always intermediate between those of pure components.

APPENDIX-V

BIBLIOGRAPHY

1. E.A Rawlins, *Bentley's Textbook of Pharmaceutics*, 8th edition, Bailiere Tindall, London, 1977.
2. S.J. Carter, *Copper & Gunn's Tutorial Pharmacy*, 6th edition, The Kothari Book Depot, Bombay, 1972.
3. J. Polderman, *Introduction to Pharmaceutical Production*, Novib, The Hague, 1990.
4. M.E. Aulton, *Pharmaceutics*, ELBS Churchill Livingstone, 1988.
5. L. Lachman, H.A. Lieberman and J.L. Kanig, *The Theory and Practice of Industrial Pharmacy*, 2nd & 3rd editions, Lea & Febiger, Philadelphia, 1970 & 1985.
6. A.L. Gennaro, *Remington's Pharmaceutical Sciences*, 8th edition, Mack. Publishing Company, Pennsylvania, 1990.
7. J.I. Wells, *Pharmaceutical Preformulations*, Ellis Horwood Limited, Chickester, 1988.
8. *Indian Pharmacopoeia*, 3rd edition, The Controller of Publications, Delhi, 1985.
9. W.L., Badger and J.T. Banchero, *Introduction to Chemical Engineering*, McGraw-Hill Book Company, Singapore, 1955.
10. W.L. McCabe, J.C. Smith and P. Harriott, *Unit Operations of Chemical Engineering*, 5th edition, McGraw-Hill Book Company, Singapore, 1993.
11. R.H. Perry and D. Green, *Perry's Chemical Engineer's Handbook*, 6th edition, McGraw-Hill Book Company, Singapore, 1984.
12. J.M. Coulson, J.F. Richardson, J.R. Backhurst and J.H. Harker, *Chemical Engineering*, Volume 2, 1st, and 2nd edition, Asian Book Private Limited, New Delhi, 1998.
13. H.A. Lieberman and L. Lachman, *Pharmaceutical Dosage Forms, Tablets*, Volume 2, Marcel Dekker, Inc., New York, 1981.
14. K.E. Avis, H.A. Lieberman and L. Lachman, *Pharmaceutical Dosage Forms, Parenteral Medications*, Volume 2, 2nd edition, Marcel Dekker, Inc., New York, 1993.
15. C.V.S. Subrahmanyam, *Textbook of Physical Pharmaceutics*, 2nd edition, Vallabh Prakashan, Delhi, 2000.
16. M.L. Schroff, *General Pharmacy*, Part 1, National Book Centre, Calcutta, 1970.

17. R.M. Mehta, *Pharmaceutics-I*, 2nd edition, Vallabh Prakashan, Delhi, 1998.
18. B.M. Mithal, *Textbook of Forensic Pharmacy*, 10th edition, Vallabh Prakashan, 1999.
19. O.P. Khanna and M. Lal, *A Text book of Material Science and Metallurgy*, Dhanpat Rai & Sons,
20. B.S. Jaiprakash and R. Venugopal, *Chemistry for Engineering Students*, Subash Publications,
21. M. Peters, and K.D. Tirmerhaus, *Plant Design and Economics for Chemical Engineers*, 3rd edition, McGraw-Hill International Book Company, 1981.
22. G.T. Austin, *Shreve's Chemical Process Industries*, 5th edition, McGraw-Hill Book Company, 1986.
23. R.K. Bansal, *A Textbook of Fluid Mechanics and Hydraulic Machines*, 6th edition, Laxmi Publications (P) Ltd., New Delhi, 1998.
24. O.A. Hougen, K.M. Watson and R.A. Ragatz, *Chemical Process Principles*, Part I and Part II, CBS Publishers & Distributors, New Delhi, 1995.
25. P.K. Nag, *Engineering Thermodynamics*, 2nd edition, Tata McGraw-Hill Publishing Company Limited, New Delhi, 1995.
26. Indian Standard: Quantities and Units, Bureau of Indian Standards, New Delhi, 1995.

SUBJECT INDEX