Analytical Method Validation Report

Dried Aluminium Hydroxide, Magnesium Hydroxide and Simethicone Gel

PHARMA DEVILS

QUALITY CONTROL DEPARTMENT

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

CONTRIBUTIONS:
This protocol is a team effort of Quality control Laboratory chemists to achieve the objective of validating the analytical methods carried out to estimate the contents of pharmaceutical products.

Analytical Method Validation Protocol Number			
Validation Frequency	Analytical Methods should be validated during and at the end of development process and after any significant change in analytical method.		
	Designation	**Name of the Person**	**Sign /Date**
Prepared By	Officer QC		
Checked By	Manager QC		
Reviewed By	Manager QA		
Approved By	Operation Head		

What is Validation?

Validation is the evaluating of processes, products or analytical methods to ensure compliance with Product or method requirements. One of the most popular definitions of Validation came from the 'US FDA' General Principle of Validation **"Establishing documented evidence which provides a high Degree of assurance that a specific process will consistently produce a product meeting its Predetermined specifications and quality attributes."**

The term Validation & Qualification are often mixed up and there is also some overlap. Equipment Qualification means checking an instrument for compliance with previously defined functional and Performance specifications. For Operational Qualification generic standards and analytical conditions are used rather than real sample conditions. Validation relates more to the entire but sample specific process including sample preparation, analysis, and data evaluation.

Validation efforts in the analytical laboratory should be broken down into separate components addressing the equipment and the analytical methods run on that equipment. After these have been verified separately they should be checked together to confirm expected performance limits **(System Suitability Testing),** and finally the sample analysis data collected on such a system should be authenticated with suitable validation checkouts. All methods / equipment that are used to create,
Modify, maintain, archive or distribute critical data for cGMP/GLP.

Analytical method should be validated prior to routine use and after changing method parameters. Peoples involved in Validation exercise should be qualified for their jobs. This includes education, training and/or experience.

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Validation of an analytical method is the process by which it is established, by laboratory studies, that the performance characteristics of the method meet the requirements for the intended analytical applications.

Typical analytical performances characteristics that should be considered in the validation of the types of methods are as follows.

- **Accuracy**
- **Precision**
- **Specificity**
- **Detection Limit**
- **Quantitation Limit**
- **Linearity**
- **Range**

USP 30 in "(1225) Validation of compendial procedures" says Category I (Analytical methods for Quantization of major components of bulk drug substances or active ingredients including preservative in finished pharmaceutical products) should comply with **Accuracy, Precision, Specificity, Linearity, Robustness, & Range.**

However after discussions with many experts & referring some of the IDAM – APA magazines, we have decided to at least comply with **Accuracy,, Linearity, Precision, Robustness .**

Validation Report:

Once the method has been validated, a validation report should be prepared that includes.

- Objective & scope of the method (applicability, type).
- Summary of the methodology.
- Type of compound & matrix.
- All chemical, reagents, reference standards, detailed instruction on their preparation.
- Method parameters.
- Detailed condition on how the experiments were conducted including sample preparation. The report must be detailed enough to ensure that it can be reproduced by a competent technician with comparable equipment.
- Statistical procedures & representative calculations.
- Representative plots
- Performance data for acceptance limit
- Criteria for revalidation
- Summary & conclusions
- Approval with name, designations, date & signatures of those responsible for the review & approval of the analytical test procedure.

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Validation Report for Dried Aluminium Hydroxide, Magnesium Hydroxide and Simethicone Gel:

OBJECTIVE: The efficacy & safety of a medicinal product can only be assured by analytical monitoring of its quality.

SCOPE: The scope of analytical validation is to ensure that the procedure under consideration is capable of giving reproducible and reliable results.

Product Name	Dried Aluminium Hydroxide, Magnesium Hydroxide and Simethicone Gel USP
Ingredient	Dried Aluminium Hydroxide, Magnesium Hydroxide and Simethicone
Label Claim	Each 10ml contains: Dried Aluminium Hydroxide Gel BP------- 830.0 mg Magnesium Hydroxide BP----------185.0mg Simethicone USP----------50.0 mg

(A)Test Method — By Titramatric Method

Dried Aluminium Hydroxide Gel BP

Specificity (Diluents Interference):

Placebo Preparation:

A placebo solution was prepared same as the formulation except for the addition of the active ingredients. Here used as the placebo solution. Consume volume in titration used is approximately equal in sample and blank titration. Observation Result: Nil

Conclusion for Specificity:

We observed that consumed volume in titration of blank, there is no significant change consumed volume in placebo (Diluents) for Dried Aluminium Hydroxide Gel assay method. Therefore specificity of the method considered acceptable.

System Accuracy:

The system precision of the above method was carried out by taking consumed volume for six times of the sample preparation.

Test Data collection:

S. No.	Titrate Volume		
	Blank (ml)	Sample (ml)	Difference (ml)
1.	24.8	16.7	8.1
2.	24.8	16.7	8.1
3.	24.8	16.6	8.2
4.	24.9	16.7	8.2

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

5.	24.8	16.6	8.2
6.	24.9	16.7	8.2
Mean	24.833	16.67	8.17
RSD	0.208%	0.309%	0.632%

Acceptance Criteria: RSD is not more than 2.0%.

Range:

Definition:

The Range of an analytical method is the interval between the upper & lower level of analyte that have been demonstrated with precision, accuracy & linearity using the method as written. The Range is normally expressed in same units as test results e.g. Percent or Parts per million, obtained by the analytical method.

Assay:

Dried Aluminium Hydroxide Gel BP**:** Label Claim 830 mg / 10 ml
(Limit: 90.0 % to 110.0 % of the labeled amount).

Sample Preparation:

Transfer an accurately weight of sample, previously well-shaken in its original container, equivalent to about 830 mg of aluminum hydroxide, to a suitable beaker. Add 20 mL of water, stir, and slowly add 10 mL of hydrochloric acid. Heat gently, if necessary, to aid solution, cool, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask; add water to volume, and mix.

Procedure— Pipette 10 mL of the Assay preparation into a 250-mL beaker, add 20 mL of water, then add, in the order named and with continuous stirring, 25.0 mL of Edetate disodium titrant and 20 mL of acetic acid-ammonium acetate buffer TS, and heat near the boiling temperature for 5 minutes. Cool, add 50 mL of alcohol and 2 mL of dithiazone TS, and mix. Titrate with 0.05 M zinc sulfate VS until the color changes from green-violet to rose-pink. Perform a blank determination, substituting 10 mL of water for the Assay preparation, and making any necessary correction.

Each mL of 0.05 M Edetate disodium titrant consumed is equivalent to 3.900 mg of Al (OH) 3.

Calculation:

$$\frac{TVb - TVs \times \text{actual Molarity} \times 200 \times \text{Weight per ml} \times 10 \times 3.9 \times 100 \times 100}{0.05 \times \text{Sample Weight} \times \text{Sample taken volume} \times 76.5 \times 830} = \quad \%$$

Test Data collection:

Sr. No.	Titrate Volume				% Assay
	Blank (ml)	Sample (ml)	Difference (ml)	Mean (ml)	

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

1.	25.0	16.8	8.2	8.15	100.078
2.	24.9	16.8	8.1		

Linearity/ Accuracy:

Definition:

The Linearity of an analytical method is its ability to elicit test results that are directly, or by a well

Defined mathematical transformation, proportional to the concentration of the analyte in samples within a given range. Linearity is usually expressed in terms of the variance around the slope of the regression line calculated according to an established mathematical relationship from test results obtained by the analysis of sample with varying concentration of analyte.

Sample Preparation:

Transfer an accurately weight of sample as required quantity, previously well-shaken in its original container, up to 80.0% to 120.0% of equivalent to label claim of aluminum hydroxide, to a suitable beaker. Add 20 mL of water, stir, and slowly add 10 mL of hydrochloric acid. Heat gently, if necessary, to aid solution, cool, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask; add water to volume, and mix.

Procedure— Pipette 10 mL of the Assay preparation into a 250-mL beaker, add 20 mL of water, then add, in the order named and with continuous stirring, 25.0 mL of Edetate disodium titrant and 20 mL of acetic acid-ammonium acetate buffer TS, and heat near the boiling temperature for 5 minutes. Cool, add 50 mL of alcohol and 2 mL of dithiazone TS, and mix. Titrate with 0.05 M zinc sulfate VS until the color changes from green-violet to rose-pink. Perform a blank determination, substituting 10 mL of water for the Assay preparation, and making any necessary correction.

Each mL of 0.05 M Edetate disodium titrant consumed is equivalent to 3.900 mg of Al (OH) 3.

Calculation:

$$\frac{TVb - TVs \times \text{actual Molarity} \times 200 \times \text{Weight per ml} \times 10 \times 3.9 \times 100 \times 100}{0.05 \times \text{Sample Weight} \times \text{Sample taken volume} \times 76.5 \times 830} = \quad \%$$

Test Data collection:

S. No.	Concentration	Titrate Volume		
		Blank (ml)	Sample (ml)	Difference (ml)
1.	80.0%	25.0	18.5	6.5
2.	90.0%	24.9	17.7	7.2
3.	100.0%	25.0	16.9	8.1
4.	110.0%	24.9	16.0	8.9
5.	120.0%	24.9	15.2	9.7

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ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

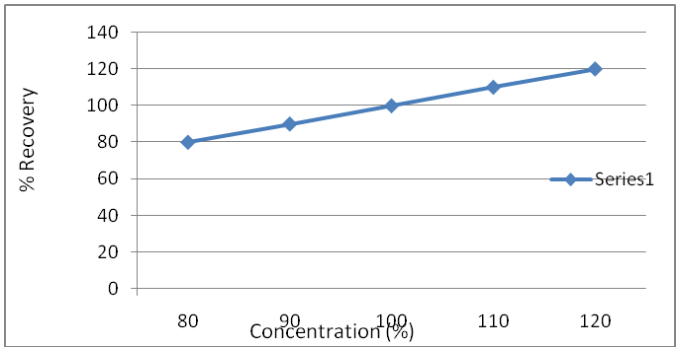
Data Collection:

% Concentration	Corr. Coefficient	Sample Difference volume (ml)	% Recovery	Corr. Coefficient
80.0	1.0	6.5	79.81	0.99996
90.0		7.2	89.74	
100.0		8.1	99.67	
110.0		8.9	109.75	
120.0		9.7	119.71	

From the above results, draw a curve.

Linearity plot for Dried Aluminium Hydroxide:

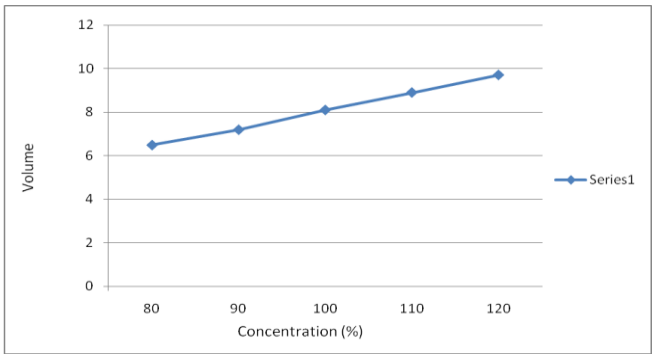
Concentration (%)	Recovery %
	79.81
80.0	89.74
90.0	99.67
100.0	109.75
110.0	119.71
120.0	



Linearity plot for Dried Aluminium Hydroxide:

Concentration (%)	Volume (ml)
80.0	6.5
90.0	7.2
100.0	8.1
110.0	8.9
120.0	9.7

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL



R-squared value (R^2)

The R-squared value, also known as the coefficient of determination, is an indicator that ranges in value from 0 to 1 and reveals how closely the estimated values for the trend line correspond to your actual data. A trend line is most reliable when its R-squared value is at or near 1.

Linearity Equation

Equations for calculating trend line

Calculates the least squares fit for a line represented by the following equation:

y = m x + b

Where m is the slope and b is the intercept.

x = concentration

y = Absorbance Value

Sample

Therefore, from Linearity Equation, **y = mx + b, m** ⟶ 0.999x

b ⟶ 0.163

We can arrive sample concentration from the above equation is 100 mcg

Calculation:

TVb - TVs X actual Molarity X 200 X Weight per ml X 10 X 3.9 X 100 X 100
0.05 X Sample Weight X Sample taken volume X 76.5 X 830

= %

Conclusion for Linearity:

The graphical representation & data collected during this exercise proves Dried Aluminium Hydroxide for demonstrate linearity in the range of 80% to 120% when determined by UV method.

Precision:

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple sampling of a homogeneous sample. The precision of the analytical method is usually expressed as Standard deviation or relative standard deviation (coefficient of variation) of a series measurement. The precision may be measured of either the degree of reproducibility or of repeatability of the analytical method on the normal operating condition.

Precision – Method precision:

Dried Aluminium Hydroxide Gel BP**:** Label Claim 830mg / 10ml

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

(Limit: 90.0 % to 110.0 % of the labeled amount).

Sample Preparation:

Transfer an accurately weight of sample, previously well-shaken in its original container, equivalent to about 830 mg of aluminum hydroxide, to a suitable beaker. Add 20 mL of water, stir, and slowly add 10 mL of hydrochloric acid. Heat gently, if necessary, to aid solution, cool, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask; add water to volume, and mix.

Procedure— Pipette 10 mL of the Assay preparation into a 250-mL beaker, add 20 mL of water, then add, in the order named and with continuous stirring, 25.0 mL of Edetate disodium titrant and 20 mL of acetic acid-ammonium acetate buffer TS, and heat near the boiling temperature for 5 minutes. Cool, add 50 mL of alcohol and 2 mL of dithiazone TS, and mix. Titrate with 0.05 M zinc sulfate VS until the color changes from green-violet to rose-pink. Perform a blank determination, substituting 10 mL of water for the Assay preparation, and making any necessary correction.

Each mL of 0.05 M Edetate disodium titrant consumed is equivalent to 3.900 mg of Al (OH) 3.

Sample Dilutions:

By "……":

(A) Take 11.21gm of sample and proceed as per above.

(B) Take 11.16gm of sample and proceed as per above.

(C) Take 11.26gm of sample and proceed as per above.

(D) Take 11.14gm of sample and proceed as per above.

(E) Take 11.31gm of sample and proceed as per above.

(F) Take 11.29gm of sample and proceed as per above.

Test Data collection:

S. No.	Samples	Titrate Volume		
		Blank (ml)	Sample (ml)	Difference (ml)
1.	A	24.9	16.8	8.1
2.	B	24.9	16.9	8.0
3.	C	24.9	16.8	8.1
4.	D	24.9	16.9	8.0
5.	E	24.9	16.8	8.1
6.	F	24.9	16.8	8.1

Calculation:

TVb - TVs X actual Molarity X 200 X Weight per ml X 10 X 3.9 X 100 X 100

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

0.05 X Sample Weight X Sample taken volume X 76.5 X 830

= %

Estimated Amount of Dried Aluminium Hydroxide:-

- Assay on % of Theory for sample A---- 99.36%
- Assay on % of Theory for sample B---- 98.58%
- Assay on % of Theory for sample C-----98.93%
- Assay on % of Theory for sample D-----98.76%
- Assay on % of Theory for sample E-----98.49%
- Assay on % of Theory for sample F-----98.67%

Table for Six Replicate Assays

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.36	98.798%	0.318%
Sample B	98.58		
Sample C	98.93		
Sample D	98.76		
Sample E	98.49		
Sample F	98.67		

Acceptance Criteria: NMT 2% (% of Relative Standard Deviation)

Conclusion for precision:
The overall % Relative standard deviation 0.318% for Dried Aluminium Hydroxide there is no significant difference. Therefore Repeatability of the method considered acceptable as it well within 2 % Relative Standard Deviation.

Intermediate Precision –
(Within laboratory variations such as different days, analyst & equipments):

Sample Preparation:
Transfer an accurately weight of sample, previously well-shaken in its original container, equivalent to about 830 mg of aluminum hydroxide, to a suitable beaker. Add 20 mL of water, stir, and slowly add 10 mL of hydrochloric acid. Heat gently, if necessary, to aid solution, cool, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask; add water to volume, and mix.

Procedure— Pipette 10 mL of the Assay preparation into a 250-mL beaker, add 20 mL of water, then add, in the order named and with continuous stirring, 25.0 mL of Edetate disodium titrant and 20 mL of acetic acid-ammonium acetate buffer TS, and heat near the boiling temperature for 5 minutes. Cool, add 50 mL of alcohol

and 2 mL of dithiazone TS, and mix. Titrate with 0.05 M zinc sulfate VS until the color changes from green-violet to rose-pink. Perform a blank determination, substituting 10 mL of water for the Assay preparation, and making any necessary correction.

Each mL of 0.05 M Edetate disodium titrant consumed is equivalent to 3.900 mg of Al (OH) 3.

Sample Dilutions:

Analyst (II) by "……."

(A) Take 11.13gm of sample and proceed as per above.

(B) Take 11.16gm of sample and proceed as per above.

(C) Take 11.11gm of sample and proceed as per above.

(D) Take 11.13gm of sample and proceed as per above.

(E) Take 11.22gm of sample and proceed as per above.

(F) Take 11.26gm of sample and proceed as per above.

Test Data collection:

S.No.	Samples	Titrate Volume		
		Blank (ml)	Sample (ml)	Difference (ml)
1.	A	24.9	16.8	8.1
2.	B	24.9	16.8	8.1
3.	C	24.9	16.9	8.0
4.	D	24.9	16.9	8.0
5.	E	24.9	16.8	8.1
6.	F	24.9	16.8	8.1

Calculation:

$$\frac{TVb - TVs \times \text{actual Molarity} \times 200 \times \text{Weight per ml} \times 10 \times 3.9 \times 100 \times 100}{0.05 \times \text{Sample Weight} \times \text{Sample taken volume} \times 76.5 \times 830} = \quad \%$$

Estimated Amount Dried Aluminium Hydroxide:

- Assay on % of Theory for sample A ----100.08%
- Assay on % of Theory for sample B ----99.82%
- Assay on % of Theory for sample C ----99.03%
- Assay on % of Theory for sample D ----98.85%
- Assay on % of Theory for sample E ----99.28%
- Assay on % of Theory for sample F -----98.93%

Test Data analyst by "……."

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	100.08	99.33%	0.510%
Sample B	99.82		
Sample C	99.03		
Sample D	98.85		
Sample E	99.28		
Sample F	98.93		

Relative standard deviation of two different analysts and days:

Test Data analyst by "……"

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.36	98.798%	0.318%
Sample B	98.58		
Sample C	98.93		
Sample D	98.76		
Sample E	98.49		
Sample F	98.67		

Test Data analyst by "……."

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	100.08	99.33%	0.510%
Sample B	99.82		
Sample C	99.03		
Sample D	98.85		
Sample E	99.28		
Sample F	98.93		

Acceptance Criteria: NMT 2 % (% of Relative Standard Deviation).

Conclusion for Intermediate Precision:

The overall % Relative standard deviation of two different analysts are 0.318% & 0.510% Dried Aluminium Hydroxide there is no significant difference between two analysts Within laboratory variations such as different days, analyst & equipments.

Therefore reproducibility of the method considered to be acceptable.

(B) Test Method By Titramatric Method

Magnesium Hydroxide BP

Specificity (Diluents Interference):

Placebo Preparation:

A placebo solution was prepared same as the formulation except for the addition of the active ingredients. Here used as the placebo solution. Consume volume in titration used is approximately equal in sample and blank titration. Observation Result: Nil

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Conclusion for Specificity:
We observed that consumed volume in titration of blank, there is no significant change consumed volume in placebo (Diluents) for Magnesium Hydroxide BP assay method. Therefore specificity of the method considered acceptable.

System Accuracy:
The system precision of the above method was carried out by taking consumed volume for six times of the sample preparation.
Test Data collection:

S. No.	Titrate Volume (ml)
1.	12.7
2.	12.6
3.	12.7
4.	12.6
5.	12.6
6.	12.6
Mean	12.63
RSD	0.409%

Acceptance Criteria: RSD is not more than 2.0%.

Range:
Definition:

The Range of an analytical method is the interval between the upper & lower level of analyte that have been demonstrated with precision, accuracy & linearity using the method as written. The Range is normally expressed in same units as test results e.g. Percent or Parts per million, obtained by the analytical method.

Assay:
Magnesium Hydroxide BP**:** Label Claim 185mg / 10ml
(Limit: 90.0 % to 110.0 % of the labeled amount).

Sample Preparation: — Prepare as directed in the Assay for aluminum hydroxide.

Procedure— Pipette a volume of the Assay preparation, equivalent to about 40 mg of magnesium hydroxide, into a 400-mL beaker, add 200 mL of water and 20 mL of triethanolamine, and stir. Add 10 mL of ammonia-ammonium chloride buffer TS and 3 drops of an eriochrome black indicator solution prepared by dissolving 200 mg of eriochrome black T in a mixture of 15 mL of triethanolamine and 5 mL of dehydrated alcohol, and mix. Cool the solution to between 3 and 4 by immersion of the beaker in an ice bath, then remove, and titrate with 0.05 M edetate disodium VS to a blue endpoint. Perform a blank determination, substituting water for the Assay preparation, and make any necessary correction.

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Each mL of 0.05 M edetate disodium consumed is equivalent to 2.916 mg of Mg (OH) 2.

Calculation:

TV X actual Molarity X 200 X Weight per ml X 10 X 2.916 X 100

0.05 X Sample Weight X Sample taken volume X 185

= %

Test Data collection:

S. No.	Titrate Volume (ml)	Mean	% Assay
1.	12.7	12.65	99.92
2.	12.6		

Linearity/ Accuracy:

Definition:

The Linearity of an analytical method is its ability to elicit test results that are directly, or by a well

Defined mathematical transformation, proportional to the concentration of the analyte in samples within a given range. Linearity is usually expressed in terms of the variance around the slope of the regression line calculated according to an established mathematical relationship from test results obtained by the analysis of sample with varying concentration of analyte.

Sample Preparation: — Prepare as directed in the Assay for aluminum hydroxide.

Procedure— Pipette a volume of the Assay preparation, equivalent to about 40 mg of magnesium hydroxide, into a 400-mL beaker, add 200 mL of water and 20 mL of triethanolamine, and stir. Add 10 mL of ammonia-ammonium chloride buffer TS and 3 drops of an eriochrome black indicator solution prepared by dissolving 200 mg of eriochrome black T in a mixture of 15 mL of triethanolamine and 5 mL of dehydrated alcohol, and mix. Cool the solution to between 3 and 4 by immersion of the beaker in an ice bath, then remove, and titrate with 0.05 M edetate disodium VS to a blue endpoint. Perform a blank determination, substituting water for the Assay preparation, and make any necessary correction.

Each mL of 0.05 M edetate disodium consumed is equivalent to 2.916 mg of Mg (OH) 2.

Calculation:

TV X actual Molarity X 200 X Weight per ml X 10 X 2.916 X 100

0.05 X Sample Weight X Sample taken volume X 185

= %

Test Data collection:

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

S. No.	Concentration	Titrate Volume (ml)
1.	80.0%	10.1
2.	90.0%	11.4
3.	100.0%	12.6
4.	110.0%	13.9
5.	120.0%	15.2

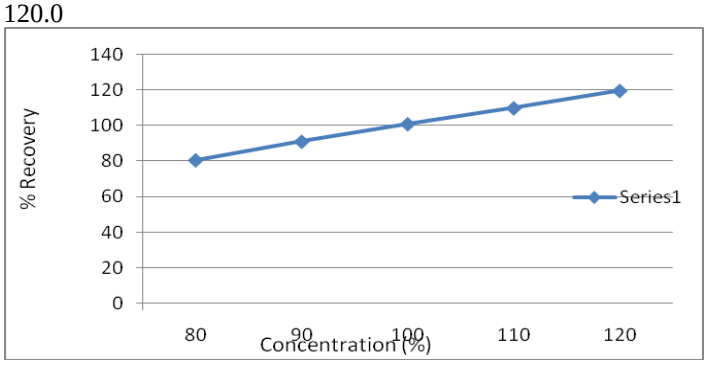
Data Collection:

% Concentration	Corr. Coefficient	Sample Difference volume (ml)	% Recovery	Corr. Coefficient
80.0	1.0	10.1	80.35	0.99967
90.0		11.4	90.86	
100.0		12.6	100.79	
110.0		13.9	109.80	
120.0		15.2	119.64	

From the above results, draw a curve.

Linearity plot for Magnesium Hydroxide BP:

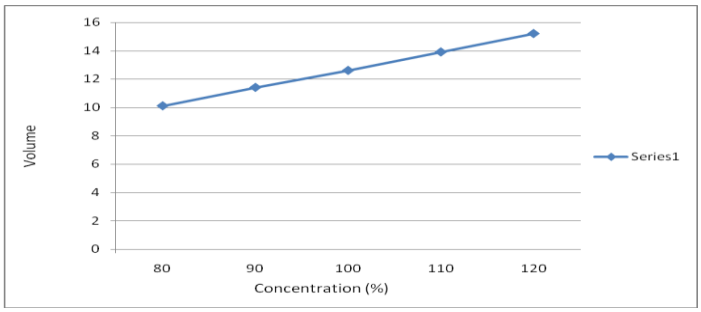
Concentration (%)	Recovery %
	80.35
80.0	90.86
90.0	100.79
100.0	109.80
110.0	119.64
120.0	



Linearity plot for Magnesium Hydroxide BP:

Concentration (%)	Volume (ml)
80.0	10.1
90.0	11.4
100.0	12.6
110.0	13.9
120.0	15.2

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL



R-squared value (R^2)

The R-squared value, also known as the coefficient of determination, is an indicator that ranges in value from 0 to 1 and reveals how closely the estimated values for the trend line correspond to your actual data. A trend line is most reliable when its R-squared value is at or near 1.

Linearity Equation

Equations for calculating trend line

Calculates the least squares fit for a line represented by the following equation:

y = m x + b

Where m is the slope and b is the intercept.

x = concentration

y = Absorbance Value

Sample

Therefore, from Linearity Equation, **y = mx + b, m** ⟶ 0.999x

b ⟶ 0.163

We can arrive sample concentration from the above equation is 100 mcg

Calculation:

TV X actual Molarity X 200 X Weight per ml X 10 X 2.916 X 100

0.05 X Sample Weight X Sample taken volume X 185

= %

Conclusion for Linearity:

The graphical representation & data collected during this exercise proves Magnesium Hydroxide BP for demonstrate linearity in the range of 80% to 120% when determined by UV method.

Precision:

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple sampling of a homogeneous sample. The precision of the analytical method is usually expressed as Standard deviation or relative standard deviation (coefficient of variation) of a series measurement. The precision may be measured of either the degree of reproducibility or of repeatability of the analytical method on the normal operating condition.

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Precision – Method precision:

Magnesium Hydroxide BP**:** Label Claim 185mg / 10ml
(Limit: 90.0 % to 110.0 % of the labeled amount).

Sample Preparation: — Prepare as directed in the Assay for aluminum hydroxide.

Procedure— Pipette a volume of the Assay preparation, equivalent to about 40 mg of magnesium hydroxide, into a 400-mL beaker, add 200 mL of water and 20 mL of triethanolamine, and stir. Add 10 mL of ammonia-ammonium chloride buffer TS and 3 drops of an eriochrome black indicator solution prepared by dissolving 200 mg of eriochrome black T in a mixture of 15 mL of triethanolamine and 5 mL of dehydrated alcohol, and mix. Cool the solution to between 3 and 4 by immersion of the beaker in an ice bath, then remove, and titrate with 0.05 M edetate disodium VS to a blue endpoint. Perform a blank determination, substituting water for the Assay preparation, and make any necessary correction.

Each mL of 0.05 M edetate disodium consumed is equivalent to 2.916 mg of Mg (OH) 2.

Sample Dilutions:

By "……..":

(A) Take 11.11gm of sample and proceed as per above.

(B) Take 11.20gm of sample and proceed as per above.

(C) Take 11.17gm of sample and proceed as per above.

(D) Take 11.31gm of sample and proceed as per above.

(E) Take 11.23gm of sample and proceed as per above.

(F) Take 11.08gm of sample and proceed as per above.

Test Data collection:

Sr. No.	Samples	Titrate Volume (ml)
1.	A	12.5
2.	B	12.6
3.	C	12.6
4.	D	12.7
5.	E	12.6
6.	F	12.5

Calculation:

$$\frac{TV \times \text{actual Molarity} \times 200 \times \text{Weight per ml} \times 10 \times 2.916 \times 100}{0.05 \times \text{Sample Weight} \times \text{Sample taken volume} \times 185} = \quad \%$$

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

= %

Estimated Amount of Magnesium Hydroxide BP:-

- Assay on % of Theory for sample A---- 99.62%
- Assay on % of Theory for sample B---- 99.61%
- Assay on % of Theory for sample C-----99.89%
- Assay on % of Theory for sample D-----99.43%
- Assay on % of Theory for sample E-----99.35%
- Assay on % of Theory for sample F-----99.89%

Table for Six Replicate Assays

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.62	99.63%	0.226%
Sample B	99.61		
Sample C	99.89		
Sample D	99.43		
Sample E	99.35		
Sample F	99.89		

Acceptance Criteria: NMT 2% (% of Relative Standard Deviation)

Conclusion for precision:
The overall % Relative standard deviation 0.226% for Magnesium Hydroxide BP there is no significant difference. Therefore Repeatability of the method considered acceptable as it well within 2 % Relative Standard Deviation.

Intermediate Precision –
(Within laboratory variations such as different days, analyst & equipments):

Sample Preparation: — Prepare as directed in the Assay for aluminum hydroxide.

Procedure— Pipette a volume of the Assay preparation, equivalent to about 40 mg of magnesium hydroxide, into a 400-mL beaker, add 200 mL of water and 20 mL of triethanolamine, and stir. Add 10 mL of ammonia-ammonium chloride buffer TS and 3 drops of an eriochrome black indicator solution prepared by dissolving 200 mg of eriochrome black T in a mixture of 15 mL of triethanolamine and 5 mL of dehydrated alcohol, and mix. Cool the solution to between 3 and 4 by immersion of the beaker in an ice bath, then remove, and titrate with 0.05 M edetate disodium VS to a blue endpoint. Perform a blank determination, substituting water for the Assay preparation, and make any necessary correction.

Each mL of 0.05 M edetate disodium consumed is equivalent to 2.916 mg of Mg (OH) 2.

Sample Dilutions: Analyst (II) By "……..":

(A) Take 11.24gm of sample and proceed as per above.

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

(B) Take 11.27gm of sample and proceed as per above.

(C) Take 11.14gm of sample and proceed as per above.

(D) Take 11.21gm of sample and proceed as per above.

(E) Take 11.16gm of sample and proceed as per above.

(F) Take 11.33gm of sample and proceed as per above.

Test Data collection:

S. No.	Samples	Titrate Volume (ml)
1.	A	12.6
2.	B	12.6
3.	C	12.5
4.	D	12.6
5.	E	12.6
6.	F	12.7

Calculation:

TV X actual Molarity X 200 X Weight per ml X 10 X 2.916 X 100

0.05 X Sample Weight X Sample taken volume X 185

= %

Estimated Amount Magnesium Hydroxide BP:

- Assay on % of Theory for sample A ----99.26%
- Assay on % of Theory for sample B ----99.00%
- Assay on % of Theory for sample C ----99.36%
- Assay on % of Theory for sample D ----99.53%
- Assay on % of Theory for sample E ----99.98%
- Assay on % of Theory for sample F -----99.26%

Test Data analyst by "……..."

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.26	99.40%	0.335%
Sample B	99.00		
Sample C	99.36		
Sample D	99.53		
Sample E	99.98		
Sample F	99.26		

Relative standard deviation of two different analysts and days:
Test Data analyst by "……"

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.62	99.63%	0.226%
Sample B	99.61		
Sample C	99.89		
Sample D	99.43		
Sample E	99.35		
Sample F	99.89		

Test Data analyst by "……."

Sample Number	% Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.26	99.40%	0.335%
Sample B	99.00		
Sample C	99.36		
Sample D	99.53		
Sample E	99.98		
Sample F	99.26		

Acceptance Criteria: NMT 2 % (% of Relative Standard Deviation).

Conclusion for Intermediate Precision:

The overall % Relative standard deviation of two different analysts is 0.226% & 0.335% Magnesium Hydroxide BP there is no significant difference between two analysts within laboratory variations such as different days, analyst & equipments.

Therefore reproducibility of the method considered to be acceptable.

(C)Test Method By Infrared spectrophotometry
Simethicone USP

Specificity (**Diluents Interference**)

Placebo Preparation:

A placebo solution was prepared same as the formulation except for the addition of the active ingredients. Here used as the placebo solution. Absorbance at about 800nm, Observation Result: Nil

Conclusion for Specificity:

We observed that at wavelength about 800 nm there is no significant Absorbance for placebo (Diluents) for Simethicone USP assay method. Therefore specificity of the method considered acceptable.

System Accuracy:

The system precision of the above method was carried out by taking Absorbance for six times of the sample preparation.

Test data collection:

Serial No.	Absorbance of Simethicone
1.	0.485

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

2.	0.482
3.	0.483
4.	0.484
5.	0.485
6.	0.483
Mean	0.484
RSD	**0.269%**

Acceptance Criteria: RSD is not more than 2.0%.

Range:

Definition:

The Range of an analytical method is the interval between the upper & lower level of analyte that have been demonstrated with precision, accuracy & linearity using the method as written. The Range is normally expressed in same units as test results e.g. Percent or Parts per million, obtained by the analytical method.

Assay:

Simethicone USP: Label Claim 50.0mg / 10ml

(Limit: 90.0 % to 110.0 % of the labeled amount).

Sample Preparation:

Transfer an accurately measured volume of Oral Suspension, equivalent to about 50 mg of Simethicone, to a suitable round, narrow-mouth, screw-capped, 120-mL bottle, add 40 mL of 0.1 N sodium hydroxide, and swirl to disperse. Add 25.0 mL of toluene, close the bottle securely with a cap having an inert liner, and shake for 15 minutes, accurately timed, on a reciprocating shaker (e.g., about 200 oscillations per minute and a stroke of 38 ± 2 mm). Transfer the mixture to a 125-mL separator. Remove about 5 mL of the upper, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture until a clear supernatant (Assay preparation) is obtained.

Prepare a Standard preparation similarly, except to dissolve about 50 mg of Simethicone WS, accurately weighed, in 25.0 mL of toluene, add 40 mL of 0.1 N sodium hydroxide, and add a volume of water equal to that of the specimen of Oral Suspension taken. Prepare a blank by mixing 10 mL of toluene with 0.5 g of anhydrous sodium sulfate and centrifuging to obtain a clear supernatant. Concomitantly determine the absorbance of the solutions in 0.5-mm cells at the wavelength of maximum absorbance at about 7.9 µm, with a suitable IR

spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of [–(CH3)2SiO–]n in each mL of the Oral Suspension taken by the formula:

$$(W / V)(AU / AS)$$

in which W is the weight, in mg, of USP Polydimethylsiloxane WS used in preparing the Standard preparation; V is the volume, in mL, of Oral Suspension taken; and AU and AS are the absorbance of the Assay preparation and the Standard preparation, respectively.

Test data collection:

Samples	Sample absorbance	Mean	% Assay
01	0.341	0.341	101.21
02	0.341		

Linearity/ Accuracy:

Definition:

The Linearity of an analytical method is its ability to elicit test results that are directly, or by a well defined mathematical transformation, proportional to the concentration of the analyte in samples within a given range. Linearity is usually expressed in terms of the variance around the slope of the regression line calculated according to an established mathematical relationship from test results obtained by the analysis of sample with varying concentration of analyte.

Sample Preparation:

Transfer an accurately measured volume of Oral Suspension, equivalent to as required quantity of Simethicone, to a suitable round, narrow-mouth, screw-capped, 120-mL bottle, add 40 mL of 0.1 N sodium hydroxide, and swirl to disperse. Add 25.0 mL of toluene, close the bottle securely with a cap having an inert liner, and shake for 15 minutes, accurately timed, on a reciprocating shaker (e.g., about 200 oscillations per minute and a stroke of 38 ± 2 mm). Transfer the mixture to a 125-mL separator. Remove about 5 mL of the upper, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture until a clear supernatant (Assay preparation) is obtained.

Prepare a Standard preparation similarly, except to dissolve about 50 mg of Simethicone WS, accurately weighed, in 25.0 mL of toluene, add 40 mL of 0.1 N sodium hydroxide, and add a volume of water equal to that of the specimen of Oral Suspension taken. Prepare a blank by mixing 10 mL of toluene with 0.5 g of anhydrous sodium sulfate and centrifuging to obtain a clear supernatant. Concomitantly

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

determine the absorbance of the solutions in 0.5-mm cells at the wavelength of maximum absorbance at about 7.9 µm, with a suitable IR spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of [–(CH3)2SiO–]n in each mL of the Oral Suspension taken by the formula:

$$(W / V)(AU / AS)$$

in which W is the weight, in mg, of USP Polydimethylsiloxane WS used in preparing the Standard preparation; V is the volume, in mL, of Oral Suspension taken; and AU and AS are the absorbance of the Assay preparation and the Standard preparation, respectively.

Test data collection:

Samples	Sample absorbance	Mean
Sample-A-01 80.0%	0.388	
Sample-A-02 80.0%	0.386	0.387
Sample-A-03 80.0%	0.387	
Sample-B-01 90.0%	0.437	
Sample-B-02 90.0%	0.435	0.436
Sample-B-03 90.0%	0.436	
Sample-C-03 100.0%	0.484	
Sample-C-02 100.0%	0.485	0.484
Sample-C-03 100.0%	0.483	
Sample-D-01 110.0%	0.534	
Sample-D-02 110.0%	0.532	0.534
Sample-D-03 110.0%	0.536	
Sample-E-01 120.0%	0.582	
Sample-E-02 120.0%	0.583	0.583
Sample-E-03 120.0%	0.584	

Data Collection:

Concentration in %	Corr. Coefficient	Sample Mean Abs.	% Recovery	Corr. Coefficient
80	1.0	0.387	80.16	
90		0.436	89.97	
100		0.484	99.81	
110		0.534	109.79	
120		0.583	119.88	

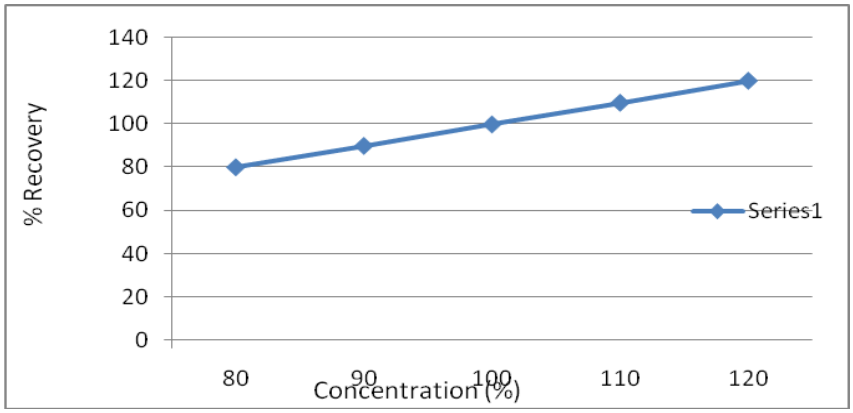
From the above results, draw a curve.

Linearity plot for Simethicone:

Concentration (%)	Recovery %
80	80.16
90	89.97
100	99.81
110	109.79

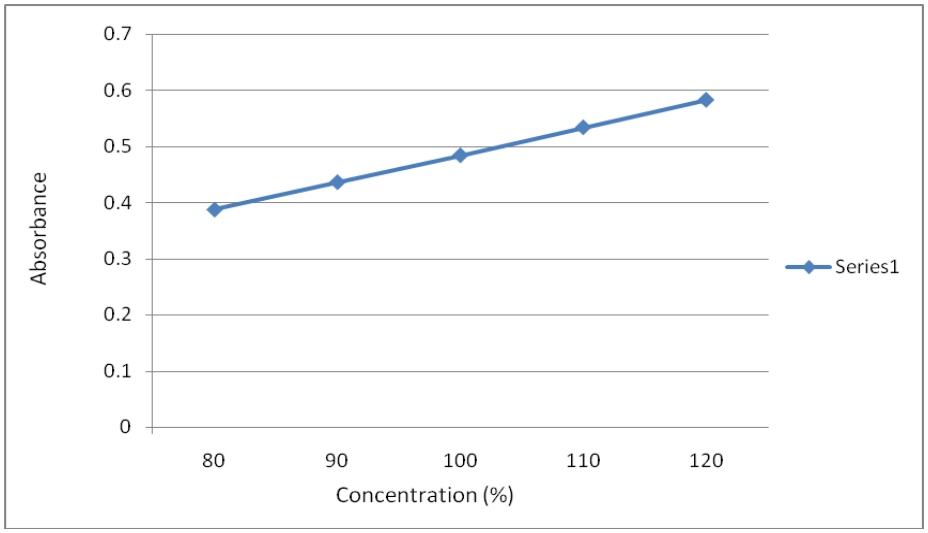
ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

120 119.88



Linearity plot for Simethicone:

Concentration (%)	Absorbance
80	0.387
90	0.436
100	0.484
110	0.534
120	0.583



ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

R-squared value (R^2)

The R-squared value, also known as the coefficient of determination, is an indicator that ranges in value from 0 to 1 and reveals how closely the estimated values for the trend line correspond to your actual data. A trend line is most reliable when its R-squared value is at or near 1.

Linearity Equation

Equations for calculating trend line
Calculates the least squares fit for a line represented by the following equation:
$y = m x + b$
Where m is the slope and b is the intercept.
x = concentration
y = Absorbance Value
Sample
Therefore, from Linearity Equation, **y = mx + b, m** ⟶ 0.999x
b ⟶ 0.163
We can arrive sample concentration from the above equation is 100 mcg
Calculation : Each mL of the Oral Suspension taken by the formula:

$$(W / V)(AU / AS)$$

in which W is the weight, in mg, of USP Polydimethylsiloxane WS used in preparing the Standard preparation; V is the volume, in mL, of Oral Suspension taken; and AU and AS are the absorbance of the Assay preparation and the Standard preparation, respectively.

Conclusion for Linearity:

The graphical representation & data collected during this exercise proves Simethicone for demonstrate linearity in the range of 80% to 120% when determined by UV method.

Precision:

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple sampling of a homogeneous sample. The precision of the analytical method is usually expressed as Standard deviation or relative standard deviation (coefficient of variation) of a series measurement. The precision may be measured of either the degree of reproducibility or of repeatability of the analytical method on the normal operating condition.

Precision – Method precision:

Simethicone USP: Label Claim 50.0mg / 10ml (Limit: 90.0 % to 110.0 % of the labeled amount).

Sample Preparation:

Transfer an accurately measured volume of Oral Suspension, equivalent to about 50 mg of Simethicone, to a suitable round, narrow-mouth, screw-capped, 120-mL bottle, add 40 mL of 0.1 N sodium hydroxide, and

swirl to disperse. Add 25.0 mL of toluene, close the bottle securely with a cap having an inert liner, and shake for 15 minutes, accurately timed, on a reciprocating shaker (e.g., about 200 oscillations per minute and a stroke of 38 ± 2 mm). Transfer the mixture to a 125-mL separator. Remove about 5 mL of the upper, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture until a clear supernatant (Assay preparation) is obtained.

Prepare a Standard preparation similarly, except to dissolve about 50 mg of Simethicone WS, accurately weighed, in 25.0 mL of toluene, add 40 mL of 0.1 N sodium hydroxide, and add a volume of water equal to that of the specimen of Oral Suspension taken. Prepare a blank by mixing 10 mL of toluene with 0.5 g of anhydrous sodium sulfate and centrifuging to obtain a clear supernatant. Concomitantly determine the absorbance of the solutions in 0.5-mm cells at the wavelength of maximum absorbance at about 7.9 µm, with a suitable IR spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of [–(CH3)2SiO–]n in each mL of the Oral Suspension taken by the formula:

$$(W / V)(AU / AS)$$

in which W is the weight, in mg, of USP Polydimethylsiloxane WS used in preparing the Standard preparation; V is the volume, in mL, of Oral Suspension taken; and AU and AS are the absorbance of the Assay preparation and the Standard preparation, respectively.

Sample Dilutions:

By "……":

(A) Take 11.22gm of sample and proceed as per above.

(B) Take 11.13gm of sample and proceed as per above.

(C) Take 11.20gm of sample and proceed as per above.

(D) Take 11.25gm of sample and proceed as per above.

(E) Take 11.19gm of sample and proceed as per above.

(F) Take 11.17gm of sample and proceed as per above.

Test Data Collection:

Samples		Sample Absorbance	Mean
Sample A	T1	0.485	0.485
	T2	0.485	
Sample B	T1	0.484	0.484
	T2	0.484	

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

Sample C	T1	0.485	0.485
	T2	0.485	
Sample D	T1	0.486	0.486
	T2	0.486	
Sample E	T1	0485	0.485
	T2	0.485	
Sample F	T1	0.485	0.485
	T2	0.485	

Estimated Amount of Simethicone:-

- Assay on % of Theory for sample A---- 99.79%
- Assay on % of Theory for sample B---- 99.60%
- Assay on % of Theory for sample C-----99.56%
- Assay on % of Theory for sample D-----99.85%
- Assay on % of Theory for sample E-----99.56%
- Assay on % of Theory for sample F-----99.56%

Table for Six Replicate Assays

Sample Number	Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.79%	99.67%	0.138%
Sample B	99.60%		
Sample C	99.56%		
Sample D	99.85%		
Sample E	99.56%		
Sample F	99.56%		

Acceptance Criteria: NMT 2% (% of Relative Standard Deviation)

Conclusion for precision:

The overall % Relative standard deviation 0.138% for Simethicone there is no significant difference. Therefore Repeatability of the method considered acceptable as it well within 2 % Relative Standard Deviation.

Intermediate Precision –

(Within laboratory variations such as different days, analyst & equipments):

Sample Preparation:

Transfer an accurately measured volume of Oral Suspension, equivalent to about 50 mg of Simethicone, to a suitable round, narrow-mouth, screw-capped, 120-mL bottle, add 40 mL of 0.1 N sodium hydroxide, and swirl to disperse. Add 25.0 mL of toluene, close the bottle securely with a cap having an inert liner, and shake for 15 minutes, accurately timed, on a reciprocating shaker (e.g., about 200 oscillations per minute and a stroke of 38 ± 2 mm). Transfer the mixture to a 125-mL separator. Remove about 5 mL of the upper, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube

with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture until a clear supernatant (Assay preparation) is obtained.

Prepare a Standard preparation similarly, except to dissolve about 50 mg of Simethicone WS, accurately weighed, in 25.0 mL of toluene, add 40 mL of 0.1 N sodium hydroxide, and add a volume of water equal to that of the specimen of Oral Suspension taken. Prepare a blank by mixing 10 mL of toluene with 0.5 g of anhydrous sodium sulfate and centrifuging to obtain a clear supernatant. Concomitantly determine the absorbance of the solutions in 0.5-mm cells at the wavelength of maximum absorbance at about 7.9 µm, with a suitable IR spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of [–(CH3)2SiO–]n in each mL of the Oral Suspension taken by the formula:

$$(W / V)(AU / AS)$$

in which W is the weight, in mg, of USP Polydimethylsiloxane WS used in preparing the Standard preparation; V is the volume, in mL, of Oral Suspension taken; and AU and AS are the absorbance of the Assay preparation and the Standard preparation, respectively.

Analyst: "……..."

(A) Take 11.24gm of sample and proceed as per above.

(B) Take 11.16gm of sample and proceed as per above.

(C) Take 11.30gm of sample and proceed as per above.

(D) Take 11.22gm of sample and proceed as per above.

(E) Take 11.13gm of sample and proceed as per above.

(F) Take 11.21gm of sample and proceed as per above.

Calculate the content of $C_{21}H_{21}N$, HCl taking 355 as the specific absorbance at 286 nm.

Test Data Collection:

Samples		Sample Absorbance	Mean
Sample A	T1	0.486	0.486
	T2	0.486	
Sample B	T1	0.485	0.485
	T2	0.485	
Sample C	T1	0.485	0.485
	T2	0.485	
Sample D	T1	0.485	0.485
	T2	0.485	
Sample E	T1	0.485	0.485
	T2	0.485	
Sample F	T1	0.485	0.485

ANALYTICAL METHOD VALIDATION REPORT FOR DRIED ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETHICONE GEL

	T2	0.485	

Estimated Amount of Simethicone"

- Assay on % of Theory for sample A ----99.80%
- Assay on % of Theory for sample B ----99.58%
- Assay on % of Theory for sample C ----99.58%
- Assay on % of Theory for sample D ----99.58%
- Assay on % of Theory for sample E ----99.58%
- Assay on % of Theory for sample F -----99.58%

Relative standard deviation of two different analysts and days:

Test Data analyst by "……"

Sample Number	Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.80%	99.62%	0.098%
Sample B	99.58%		
Sample C	99.58%		
Sample D	99.58%		
Sample E	99.58%		
Sample F	99.58%		

Test Data analyst by "……."

Sample Number	Estimated Amount	Mean	Relative Standard Deviation (RSD)
Sample A	99.79%	99.67%	0.138%
Sample B	99.60%		
Sample C	99.56%		
Sample D	99.85%		
Sample E	99.56%		
Sample F	99.56%		

Acceptance Criteria: NMT 2 % (% of Relative Standard Deviation).

Conclusion for Intermediate Precision:

The overall % Relative standard deviation of two different analysts are 0.098% & 0.138% Simethicone there is no significant difference between two analysts Within laboratory variations such as different days, analyst & equipments.

Therefore reproducibility of the method considered to be acceptable.

CONCLUSION:

All the analytical parameter are checked as per the approved validation process and found well within specified acceptance criteria. Hence, it is concluded that, this method is suitable for accurate & precise results for routine analysis.