ANALYTICAL METHOD VALIDATION

PROTOCOL

FOR

ASSAY OF ETORICOXIB TABLET

ANALYTICAL METHOD VALIDATION PROTOCOL FOR ASSAY OF ETORICOXIB TABLETS

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1.0 DOCUMENT CHANGE HISTORY:

Previous Version	Current Version	Reason for Change

2.0 PROTOCOL CUM REPORT APPROVAL SHEET:

	Department	Name	Designation	Sign. & Date
Prepared By	Quality Control			

	Department	Name	Designation	Sign. & Date
Reviewed By	Quality Control			

	Department	Name	Designation	Sign. & Date
Approved By	Quality Assurance			

ANALYTICAL METHOD VALIDATION PROTOCOL FOR ASSAY OF ETORICOXIB TABLETS

3.0 OBJECTIVE:

3.1 The objective of validation of analytical procedure is to demonstrate that it is suitable for its intended purpose.

4.0 SCOPE:

4.1 This Analytical method validation protocol cum report is applicable for assay method of Etoricoxib Tablet.

5.0 RESPONSIBILITY:

5.1 Quality Control Analyst

5.1.1 To ensure availability of required reagents, working standard/ reference standard /column/ instrument.

5.1.2 To perform and record the analytical method validation.

5.2 Quality Control Head or Designee

5.2.1 To review and ensure correct analytical method validation

5.2.2 To provide the required reagents / material / column/instruments.

5.3 Quality Assurance Head

5.3.1 To approve the protocol cum report.

6.0 CHARACTERISTICS OF ANALYTICAL PROCEDURE:

6.1 Following characteristics should be considered during analytical method validation for Assay.

6.1.1 Specificity

6.1.2 Precision (System Precision, Repeatability, Intermediate precision)

6.1.3 Accuracy

6.1.4 Linearity and Range

6.1.5 Solution Stability

6.1.6 Robustness

6.1.7 System Suitability

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7.0 REVALIDATION CRITERIA:

7.1 Revalidation may be necessary in the following circumstances

7.1.1 Changes in the synthesis of the drug substance.

7.1.2 Changes in the composition of the finished product

7.1.3 Changes in the Analytical procedure.

8.0 DESCRIPTION OF ANALYTICAL METHOD:

8.1 The detailed analytical method for the determination of Etoricoxib Tablet is described below:

8.2 PRODUCT DETAILS

Name of API	Etoricoxib
Pharmacopoeial status	In House
Molecular formula	$C_{18}H_{15}ClN_2O_2S$
Description	An off white to creamish coloured powder.
Solubility	Freely soluble in tetrahydrofuran, demethylsulphoxide and in dimethyl formamide, soluble in methanol and in acetone, sparingly soluble in ethanol.
Label claim	Each film coated tablet contains: Etoricoxib 90/120 mg*

* = This method is applicable for both Etoricoxib 90 mg /120 mg strength

8.3 INSTRUMENTS / EQUIPMENTS / CHEMICALS / GLASSWARES:

INSTRUMENTS / EQUIPMENTS	
HPLC Make: Shimadzu Model : Prominence-*i* Instrument ID: _____	**Analytical Balance** Make: …… Model : ……. Instrument ID : _____
Ultrasonic Bath Make: Scientific international Model : 3.5L100H Instrument ID : _____	
CHEMICALS & GLASSWARE	
0.05 Ammonium Acetate	0.45µ membrane filters
Acetonitrile (HPLC grade)	Whatmen filter paper No.1
Water (HPLC grade)	Glasswares (A Grade)

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8.4 ANALYTICAL METHODOLOGY

Chromatographic system

Column : A stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),

Flow Rate : 1.0 ml/minute

Detector : UV at 220 nm

Injection volume : 20 µl

Preparation of Mobile Phase: A mixture of 55 volumes of buffer solution prepared by dissolving 6.8 g of potassium dihydrogen orthophosphate in 1000 ml of water, adjusted to pH 3.5 with Orthophosphoric acid and 45 volumes of acetonitrile.

Standard solution: Weigh about 50.0 mg of Etoricoxib working standard and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol. Further dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45 µm filter.

Test Solution: Weigh and powdered 20 Tablet. Weigh accurately a quantity of Tablet powder containing about 50.0 mg of Etoricoxib and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol. Further dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45 µm filter.

Procedure:

System Suitability: Inject standard solution.

Tailing factor: The tailing factor of the principal peak should not more than 2.0.

Theoretical plates: The theoretical plates of the principal peak should not less than 2000.

Relative standard deviation: Relative standard deviation for replicate injections should not more than 2.0 %.

Inject the standard solution as five replicates and the test solution in duplicate.

Calculate the content of Etoricoxib in the Tablet.

Calculation:

For Etoricoxib(in mg/Tablet) =

$$\frac{\text{Mean Peak area of Test X Weight of Std. X 5 X 100 X 50 X Potency X Avg. weight}}{\text{Mean Peak area of Standard X 100 X 50 X Weight of sample X 5 X100}}$$

For Etoricoxib (in percent/Tablet)

= Etoricoxib (in mg/Tablet)

---------- X 100

Label Claim

Acceptance Criteria: 90.00 % to 110.00 %

9.0 ANALYTICAL PERFORMANCE PARAMETER:

9.1 SPECIFICITY

Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix, etc.

Placebo study of analytical method use for drug product is checking the positive or negative interference due to placebo on final results of analytical method. Placebo study of the Etoricoxib Tablet shall be established by analyzing the placebo as per assay method and calculating the % interference of the same.

Standard Solution: Weigh about 50.0 mg (……. mg) of Etoricoxib working standard and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with Methanol. And filter through whatman filter paper. Dilute 5ml of filtrate to 50 ml with methanol and filter through 0.45 µm filter.

Placebo Solution: Dissolve about 172.2 mg of placebo (…….. mg) in 100 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45 µm filter.

Sample Solution: Weigh about 50.0mg (……..mg) of Etoricoxib working standard and about 172.2 mg of placebo (……. mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45 µm filter.

Procedure: Inject as single run, Blank solution (diluent), Placebo solution, test solution and Standard solution. Record observation as per table No.-01.

Acceptance Criteria: No peak shall be observed in the blank and placebo solution at the retention time of principal peak of Etoricoxib.

Table-01: Specificity

Name of Sample	Retention Time (RT) in minutes	Peak area
Blank solution (diluent)	Nil	Nil
Placebo Solution	Nil	Nil
Standard Solution	5.647	4220348
Sample Solution	5.648	4221730
Conclusion:		

9.2 PRECISION

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

9.2.1 SYSTEM PRECISION

Determine the system precision for method by six replicates of standard solution and calculate the mean and relative standard deviation (RSD) of the response obtained.

"Prepare the standard solution described as under specificity."

Acceptance criteria: Relative standard deviation of six Replicates should not be more than 2.0 %.

Record observation as per Table No.-02.

Table-02: System Precision

Sample ID	Peak Retention Time	Mean Peak Area	% RSD
Standard Inj.-1	5.645	4233118	**0.273**
Standard Inj.-2	5.646	4238202	
Standard Inj.-3	5.646	4250628	
Standard Inj.-4	5.646	4240302	
Standard Inj.-5	5.647	4246014	
Standard Inj.-6	5.646	4265822	

Conclusion:

9.2.2 REPEATABILITY

Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision.

Prepare six different sample of 100% concentration.

Standard Solution: Weigh about 50.0 mg (……..mg) of Etoricoxib working standard and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol. And filter through whatman filter paper. Dilute 5ml of filtrate to 50 ml with methanol.

Sample Solution_1: Weigh about 50.0 mg (……..mg) of Etoricoxib working standard and about 172.2 mg of placebo (……..mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_2: Weigh about 50.0 mg (……mg) of Etoricoxib working standard and about 172.2 mg of placebo (…….mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_3: Weigh about 50.0 mg (……mg) of Etoricoxib working standard and about 172.2 mg of placebo (……mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter

paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_4: Weigh about 50.0 mg (…….. mg) of Etoricoxib working standard and about 172.2 mg of placebo (……. mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_5: Weigh about 50.0 mg (……..mg) of Etoricoxib working standard and about 172.2 mg of placebo (…….mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_6: Weigh about 50.0 mg (……mg) of Etoricoxib working standard and about 172.2 mg of placebo (…….. mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Procedure: Inject the standard solution in five replicates and sample solution in duplicate. Calculate the Relative standard deviation of the Results.

Calculate the content of Etoricoxib.

For Etoricoxib (in mg/Tablet) =

$$\frac{\text{Mean Peak area of Test X Weight of Std. X 5 X 100 X 50 X Potency X Avg. weight}}{\text{Mean Peak area of Standard X 100 X 50 X Weight of sample X 5 X100}}$$

For Etoricoxib (in percent/Tablet) =

$$\frac{\text{Etoricoxib (in mg/Tablet)}}{\text{Label Claim}} \times 100$$

Acceptance criteria: The relative standard deviation (RSD) for Assay % should not be more than 2.0.

Record observation as per table No.-03.

Table- 03: Repeatability

Sample ID	Mean Peak Area	% Assay	% RSD
Sample - 1	4231846	99.54	0.216
Sample - 2	4209495	99.46	
Sample - 3	4214670	99.81	
Sample - 4	4189658	99.44	
Sample - 5	4226088	99.94	
Sample -6	4195899	99.45	

Conclusion:

9.2.3 INTERMEDIATE PRECISION: (DAY - 2)

Intermediate precision expresses within-laboratories variations: different days, different analysts, different equipment, etc.

Standard Solution: Weigh about 50.0 mg (mg.) of Etoricoxib working standard and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol. And filter through whatman filter paper. Dilute 5ml of filtrate to 50 ml with methanol.

Prepare six different sample of 100% concentration for Day - 2

Sample Solution_1: Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_2: Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_3: Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2

mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_4: Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_5: Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution_6: Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Procedure: Inject the standard solution in five replicates and sample solution in duplicate. Calculate the Relative standard deviation of the Results.

Calculate the content of Etoricoxib.

For Etoricoxib (in mg/Tablet) =

$$\frac{\text{Mean Peak area of Test X Weight of Std. X 5 X 100 X 50 X Potency X Avg. weight}}{\text{Mean Peak area of Standard X 100 X 50 X Weight of sample X 5 X100}}$$

For Etoricoxib (in percent/Tablet) =

$$\frac{\text{Etoricoxib (in mg/Tablet)}}{\text{Label Claim}} \times 100$$

Acceptance Criteria: The relative standard deviation (RSD) of the result obtained from six preparations should not more than 2.0 and overall RSD (for 12 sample of Repeatability and inter mediate precision) should not be more than 2.0.

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Record observation as per table No. 04.

Table- 04: Repeatability &Intermediate Precision

Sample ID	Day -1 (From Repeatability)	Day -2 (Intermediate precision)
	% assay of Etoricoxib	% assay of Etoricoxib
Sample-1	99.54	99.46
Sample-2	99.46	99.64
Sample-3	99.81	99.81
Sample-4	99.44	100.32
Sample-5	99.94	99.48
Sample-6	99.45	100.05
Mean	99.61	99.79
SD	0.215	0.340
% RSD	0.216	0.340
Overall mean of 12 sample	99.70	
Overall SD of 12 sample	0.288	
Overall RSD of 12 sample	0.289	
Conclusion:		

9.3 ACCURACY

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found.

Accuracy should be assessed using a minimum of 9 determinations over a minimum of 3 concentration levels covering the specified range (e.g.: 3 concentrations /3 replicates each of the total analytical procedure).

"Prepare the standard solution described under Precision."

Sample Solution -1 (80%): Weigh about 40.0mg (mg) of Etoricoxib working standard and about 182.2 mg of placebo (mg.) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution -2 (80%): Weigh about 40.0mg (mg) of Etoricoxib working standard and about 182.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution -3 (80%): Weigh about 40.0mg (mg) of Etoricoxib working standard and about 182.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution-1 (100%): Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution-2 (100%): Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution-3 (100%): Weigh about 50.0mg (mg) of Etoricoxib working standard and about 172.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution-1 (120%): Weigh about 60.0mg (mg) of Etoricoxib working standard and about 162.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution-2 (120%): Weigh about 60.0mg (mg) of Etoricoxib working standard and about 162.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman

filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution-3 (120%): Weigh about 60.0 mg (mg) of Etoricoxib working standard and about 162.2 mg of placebo (mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Procedure: Inject the standard solution in five replicates and sample solution in duplicate. Calculate the percentage recovery in each sample.

Calculation for Etoricoxib

$$\frac{\text{Mean Peak area of Test X Weight of Std. X 5 X 100 X 50 X Potency X Avg. weight}}{\text{Mean Peak area of Standard X 100 X 50 X Weight of sample X 5 X100}}$$

Acceptance Criteria: The % recovery of Etoricoxib should be in between 98.00 % to 102.00 %.

Record observation as per table No - 05.

Table-05: Accuracy

S. No.	Accuracy Level (w.r.t target conc.)	Weight of standard (Etoricoxib)	Weight of sample with placebo (mg)	(%) Recovery of Etoricoxib
1.	80%	50.3 mg	171.2	99.44
2.	80%	50.3 mg	173.9	99.77
3.	80%	50.3 mg	175.3	99.98
4.	100%	50.3 mg	176.9	99.80
5.	100%	50.3 mg	168.1	99.53
6.	100%	50.3 mg	175.9	99.72
7.	120%	50.3 mg	168.3	99.21
8.	120%	50.3 mg	169.3	99.68
9.	120%	50.3 mg	167.8	99.39
Mean				99.61
SD				0.240
% RSD				0.241
Conclusion:				

9.4 LINEARITY AND RANGE:

Linearity indicates the ability to produce results that are directly proportional to the concentration of the analyte in samples. A series of samples should be prepared in which the analyte concentrations span the claimed range of the procedure. If there is a linear relationship, test results should be evaluated by appropriate statistical methods. A minimum of five concentrations should be used.

Range is an expression of the lowest and highest levels of analyte that have been demonstrated to be determinable for the product. The specified range is normally derived from linearity studies.

Prepare the Concentration of Etoricoxib of 80%, 90%, 100%, 110% and 120%.

Stock solution: Weigh about 50.0 mg (……mg) of Etoricoxib working standard in 100 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol. Filter the solution through whatman filter paper.

Test Solution (80%): Dilute 4.0 ml of stock solution to 50.0 ml with methanol.

Test Solution (90%): Dilute 4.5 ml of stock solution to 50.0 ml with methanol.

Test Solution (100%): Dilute 5.0 ml of stock solution to 50.0 ml with methanol.

Test Solution (110%): Dilute 5.5 ml of stock solution to 50.0 ml with methanol.

Test Solution (120%): Dilute 6.0 ml of stock solution to 50.0 ml with methanol.

Procedure: Inject each solution in duplicate and plot the linearity graph for average area of Etoricoxib peak.

Record all the results as per Table- 06.

Acceptance Criteria: Correlation Coefficient: NLT 0.99 for Etoricoxib peak.

Table- 06

Parameters	**Etoricoxib**	
Sample ID	Mean Area	Correlation Coefficient
80 %	3351689	0.9987
90 %	3706271	
100 %	4140093	
110 %	4493525	
120 %	4953440	
Conclusion:		

9.5 SOLUTION STABILITY

Prepare standard and sample solution and Inject the standard and sample solution initially, after 6 hours, after 12 hours, and 24 hours at each time point. Keep the standard and sample solution at room temperature, calculate the absolute (%) difference at each time point from initial time point.

"Prepare the standard solution described under specificity."

Sample Solution : Weigh about 50.0 mg (…….. mg) of Etoricoxib working standard and about 172.2 mg of placebo (…… mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter

Acceptance criteria: The absolute % difference in assay with respect to initial at each time point should not be more than 2.0.

Record observation as per table No.- 06.

Table- 06: Solution Stability for Etoricoxib at Room Temperature

Time in Hour	% Assay of Etoricoxib	Absolute difference (%) at each time point from initial time point
0	99.57	-
6	98.35	1.22
12	98.16	1.41
24	97.62	1.95

Conclusion:

9.6 ROBUSTNESS

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

Carry out one set of analysis, using the same homogeneous sample. Select the changes to be made in the analytical procedure from the below list, as applicable.

- Change in pH of buffer (pH specified in method ± 0.2)

- Change in mobile phase composition of each component (Absolute 2 %)
- Change in flow rate (flow specified in method ± 0.1)

Standard Solution: Weigh about 50.0 mg (……. mg) of Etoricoxib working standard and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Sample Solution: Weigh about 50.0mg (……mg) of Etoricoxib working standard and about 172.2 mg of placebo (……..mg) and transfer into a 100.0 ml volumetric flask, add about 60.0 ml methanol, sonicate to dissolve and dilute up to mark with methanol and filter through whatman filter paper. Dilute 5 ml of filtrate to 50 ml with methanol and filter through 0.45µm filter.

Procedure: For each set inject the standard solution in five replicates and duplicate run of sample solution. Calculate the result of assay for each set of analysis. Determine the absolute difference in the results obtained in Robustness study and Repeatability study (Sample 1).

Acceptance criteria: The absolute difference in the results obtained in robustness study and repeatability study (Sample 1) shall not be more than 2.0%.

Table- 07: Robustness study for Etoricoxib

Changes	% Result of repeatability study (Sample 1)	% Result of Etoricoxib	Absolute Difference (%)
	Etoricoxib		
Change in pH of buffer (+0.2)	99.54	100.03	-0.49
Change in pH of buffer (-0.2)		99.94	-0.40
Change in mobile phase composition		99.59	-0.05
Change in Flow rate (+0.1)		99.94	-0.40
Change in Flow rate (-0.1)		99.86	-0.32
Conclusion:			

9.8 SYSTEM SUITABILITY:

Inject Standard Solution for System Suitability describe under Specificity.

Acceptance criteria: The system suitability shall comply as per methodology.

System Suitability Parameter	Observation	Acceptance criteria
	Etoricoxib	
Tailing Factor	1.071	NMT 2.0%
Theoretical Plates	9474	NLT 2000
Relative Standard Deviation	0.273	NMT 2.0%

10.0 DOCUMENTATION:

After completion of activity of analytical method validation, detailed reports including result findings shall be prepared as per the above outlined protocol cum report which shall cover the details of analytical method, selection of analytical performance parameters, acceptance criteria and complete details about the validation procedure and plan.

11.0 ABBREVIATION:

1	HPLC	High Performance Liquid Chromatography
2	API	Active Pharmaceutical ingredients
3	STP	Standard Testing Procedure
4	mg	Milligram
5	ml	Milliliter
6	NLT	Not Less Than
7	NMT	Not More Than

12.0 CONCLUSION:

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

Approved By (Head QC)
Sign. & Date

13.0 ANNEXURE:

Composition of placebo: (In mg/Tablet)

S.No.	Raw material used	Quantity (in mg)
1.	Dibasic Calcium Phosphate BP	100
2.	Microcrystalline Cellulose BP	174
3.	Croscarmelose Sodium BP	20
4.	Povidone BP	6
5.	Isopropyl Alcohol BP	Q.S.
6.	Lactose BP	4
7.	Colloidal Anhydrous Silica BP	2
8.	Magnesium Stearate BP	4