ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON PHARMACOPOEIAL PRODUCT

DEPARTMENT OF DRUG ADMINISTRATION

Illaprazole enteric coated tablets

Illaprazole tablet contain not less than 90 % and not more than 110 % of the stated amount of Illaprazole.

1. Identification:

In the assay, the principle peak in the chromatogram obtained with the sample solution should correspond to the peak in the chromatogram obtained with the reference standard solution of Illaprazole.

2. Dissolution Test:

2.1 Dissolution Parameter (Acid phase):

2.1.1 Medium : 0.1 M HCl
2.1.2 Apparatus : Paddle
2.1.3 Rotation : 100 RPM
2.1.4 Temperature : 37˚C ± 0.5˚C
2.1.5 Time : 2 hrs

2.1.6. Dissolution Medium Preparation: Dissolve 8.5 ml of hydrochloric acid to 1000 ml with water.

2.1.7 Standard Preparation:

Weigh accurately about 28 mg of working standard of Illaprazole and transfer into 100 ml volumetric flask. Dissolve with 0.1 N HCl and make up the volume to 100 ml with 0.1 N HCl. Pipette 2 ml of this solution and transfer into 50 ml volumetric flask and make up the volume to 50 ml with 0.1 M HCl.

2.1.8. Sample preparation

Place 1 tablet in each dissolution vessel and run the apparatus as per above condition and collect the sample solution from each jar at specified time. After the completion of the dissolution, filter the resulting solution. Remove each tablet from individual vessels and subject them to the test in buffer stage.

2.1.9. Procedure:

Measure absorbance of both the standard and sample preparation at about 220 nm using 0.1 M HCl as blank. Calculate the percentage release of Illaprazole in acid medium by using the following formula.

2.1.10. Calculation:

Illaprazole (%):

$$=\frac{Abs\ of\ spl}{Abs\ of\ std} \times \frac{conc.of\ std}{conc.of\ spl} \times std\ potency\ \% \times \frac{100-LOD/WC}{100} \quad x\ \mathbf{100}\ \%$$

2.1.11 Tolerance Limit: Not more than 10 % D of the stated amount

2.2 Dissolution Parameter (Buffer phase):

2.2.1 Medium : Tris-Acetate buffer pH 8.5
2.2.2 Apparatus : Paddle
2.2.3 Rotation : 100 RPM
2.2.4 Temperature : 37˚C ± 0.5˚C
2.2.5 Time : 45 minutes

2.2.6. Dissolution Medium Preparation: Dissolve 0.249 g of calcium chloride and 12.11 g of tris(hydroxymethyl) aminomethane in 1000 ml water. Adjust pH to 8.5± 0.05 with 5 M acetic acid.

2.2.7 Standard Preparation:

Weigh accurately about 28 mg of working standard of Illaprazole and transfer into 50 ml volumetric flask. Dissolve with methanol and make up the volume to 50 ml with methanol. Pipette 2 ml of this solution and transfer into 100 ml volumetric flask and make up the volume to 100 ml with dissolution medium.

2.2.8 Sample preparation

Place 1 tablet (taken out from the acid stage) in each dissolution vessel and run the apparatus as per above condition and collect the sample solution from each jar at specified time. After the completion of the dissolution, filter the resulting solution.

2.2.9. Procedure:

Measure absorbance of both the standard and sample preparation at about 220 nm using dissolution medium as blank. Calculate the percentage release of Illaprazole in buffer medium by using the following formula.

2.2.10. Calculation:

Illaprazole (%):

$$=\frac{Abs\ of\ spl}{Abs\ of\ std}\times\frac{conc.of\ std}{conc.of\ spl}\times std\ potency\ \%\ \times\ \frac{100-LOD/WC}{100}\ \ x\ \mathbf{100}\ \%$$

2.2.11. Tolerance Limit: More than 75 % D of the stated amount

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3. Assay: Illaprazole tablet

3.1 Chromatographic system:
3.1.1 Column: 150 X 4.6 mm (C 18)
3.1.2 Flow rate: 1.0 ml/min
3.1.3 Wave length: 237 nm
3.1.4 Injection volume: 10 µl
3.1.5 Column Oven Temperature: Ambient

3.1.6 Mobile phase
3.1.6.1 Buffer: Solution containing 2.727 g potassium dihydrogen phosphate and 1 g sodium hydroxide in 1000 ml water.

3.1.6.2 Mobile phase: Buffer: ACN (50:50)
Mix buffer and Acetonitrile, cool to room temperature and filter the solution through 0.45 micron Nylon membrane filter paper using vacuum pump.

3.2 Diluents: Methanol

3.3 Standard Preparation:

Weigh accurately about 25 mg of working standard of Illaprazole and transfer into 50 ml volumetric flask. Dissolve in the methanol and make up the volume to 50 ml with methanol. Dilute 5 ml of the resulting solution to 50 ml with methanol. Filter through 0.22 micron nylon membrane filter paper.

3.4 Sample Preparation:
Weigh individually 20 tablets and crush the tablet to fine powder. Weigh accurately the powder equivalent to 50 mg of Illaprazole and transfer into 100 ml volumetric flask. Add about 60 ml of methanol, sonicate for about 10 minutes and cool the solution to room temperature and make up the volume to 100 ml with diluents. Centrifuge the solution. Dilute 5 ml of the resulting solution to 25 ml with diluent. Filter the solution with 0.22 micron nylon membrane filter paper.

3.5 Procedure

Inject 10 µl of standard preparation five/six times. The test is not valid unless the column efficiency is not less than 2000 theoretical plates. The tailing factor is not more than 2.0 and the relative standard deviation for replicate injections in not more than 2.0%. After the completion of the system suitability test parameter, inject 10 µl of each of the sample solution separately. Calculate the content of Illaprazole in each tablet by using following formula:

Illaprazole per tablet:

$$\frac{Spl\ Peak\ Area}{Std\ Peak\ Area} \times \frac{conc.of\ std}{conc.of\ spl} \times std\ potency\ \% \times \frac{100-LOD/WC}{100}\ \ x\ Average\ weight$$

4.0 Uniformity of content

4.1 Standard Preparation:

Weigh accurately about 25 mg of working standard of Illaprazole and transfer into 50 ml volumetric flask. Dissolve in the methanol and make up the volume to 50 ml with methanol. Dilute 5 ml of the resulting solution to 50 ml with methanol. Filter through 0.22 micron nylon membrane filter paper.

4.2 Sample Preparation:

Place one tablet in a 100 ml volumetric flask; add about 60 ml of methanol to dissolve with the help of sonicator. Cool and make up the volume to 100 ml with methanol. Filter through 0.22 micron nylon membrane filter paper.

4.3 Mobile phase: Same asAssay

4.4 Chromatographic condition: Same as Assay

4.5 Procedure

Inject 10 µl of standard preparation five/six times. The test is not valid unless the column efficiency is not less than 2000 theoretical plates. The tailing factor is not more than 2.0 and the relative standard deviation for replicate injections in not more than 2.0%. After the completion of the system suitability test parameter, inject 10 µl of each of the sample solution separately. Calculate the content of Illaprazole in each tablet by using following formula:

Illaprazole per tablet:

$$\frac{\textbf{Spl Peak Area}}{\textbf{Std Peak Area}} \textbf{X} \frac{\textbf{Std wt}}{\textbf{Std Dil.}} \textbf{X} \frac{\textbf{Spl Dil.}}{\textbf{Spl wt}} \textbf{X Avg wt X Std Pot.} (\%) \textbf{X} \frac{\textbf{100} - \textbf{Std W.C}}{\textbf{100}} \textbf{X} \frac{\textbf{1}}{\textbf{Label Claim}} \textbf{X 100}\%$$