ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON PHARMACOPOEIAL PRODUCT
DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory

Metformin (Sustained Release) & Linagliptin Tablets

Analytical Profile No.: LMS 074/075/AP 029

Metformin (Sustained Release) & Linagliptin Tablets contain not less than 90% and not more than 110% of the stated amount of Metformin and Linagliptin.

1. Identification:

1.1. Metformin HCl:

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 Metformin HCl.

1.2. Linagliptin:

In the assay, the principle peak in the chromatogram obtained with the sample solution corresponds to the peak in the chromatogram obtained with the reference standard solution of Linagliptin.

2. Dissolution

4.1 Linagliptin: Determine by liquid chromatography

4.1.1 Dissolution Parameters:

Apparatus: Basket

Medium: 0.1N HCl

Volume: 900 ml

Speed and Time: 50rpm for 45 min

Chromatographic condition (Linagliptin):

Column: C18, 150*4.6 mm, 5 µm

Flow rate: 1.0 ml/min

Wavelength: 295 nm

Injection volume: 20 µl

Column temperature: 25 °C

Detector: PDA Detector

4.1.2 Test Solution:

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.

4.1.3 Reference Solution:

Weigh accurately about 13.5 mg of working standard of Linagliptin and transfer into 100 ml volumetric flask. Add about 60 ml of 0.1 N HCl, sonicate for 15 minutes, cool and make up the volume to 100 ml with 0.1 N HCl. Dilute 2 ml of the resulting solution to 100 ml with 0.1 N HCl. Filter the resulting standard solution through a membrane filter of 0.2 µm.

4.1.4 Procedure:

Linagliptin:

Separately inject 20 µl of standard and sample solution and blank solution (dissolution medium) and obtain the respective chromatograms. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0%. Measure the peak responses. Measure the peak responses and calculate the % release of the drug.

4.1.5 Limit:

D. Not less than 80 % of the stated amount

4.2 Metformin Sustained release tablet: Determine by UV Spectroscopy

4.2.1 Dissolution test condition

Apparatus: Basket

Medium: 1000 ml phosphate buffer pH 6.8

Speed: 100 rpm

Time: 1 hour, 3 hours and 10 hours

4.2.2 Reference solution:

Weigh accurately about 25 mg of working standard of metformin hydrochloride and transfer into 100 ml volumetric flask. Dissolve with water and make up the volume to 100 ml with water. Dilute 2 ml of the standard solution to 100 ml with dissolution medium.

4.2.3 Test solution:

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.

4.2.4 Procedure:

Dilute 1 ml of the filtrate to 100 ml with dissolution medium. Measure the absorbance of the standard and sample solution at about 232 nm. Calculate the percentage of drug release in the tablet.

4.2.6 Limit:

1st hr: 25% to 50% of the stated amount

3rd hr: 45% to 70% of the stated amount

8th hr: NLT 80% of the stated amount

3. Uniformity of the content (Linagliptin): Determine by liquid chromatography

3.1 Chromatographic system:

Same as Assay

3.2 Test Solution:

Take 10 tablets and transfer individually to 100ml volumetric flask. Add 60ml of mobile phase and sonicate for 15 min to disperse the tablet. Make up the volume with mobile phase. Filter the final solution through 0.2 µm membrane filter. (25ppm)

3.3 Reference Solution:

Weigh accurately about 12.5 mg Linagliptin working standard in 50 ml volumetric flask and add 35 ml mobile phase. Dissolve by sonication and dilute to 50 ml with mobile phase. Dilute 5 ml resulting solution to 50 ml with mobile phase. Filter the resulting standard solution through 0.2 µm membrane filter. (25ppm)

3.4 Chromatographic Procedure:

Inject 20 µl of standard and sample solution separately and obtain the respective chromatogram. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0%. Measure the peak responses. Measure the peak responses and calculate the content of Linagliptin in each tablet.

3.5 Limit:

85-115% of the stated amount

4Assay: Determine by liquid chromatography

4.1 Chromatographic system

Column: C18, (150*4.6 mm), 5 µm

Flow rate: 1.0 ml/min

Wavelength: 265 nm (Metformin) & 295 nm (Linagliptin)

Injection volume: 20 µl

Detector: PDA Detector

Column temperature: 25 °C

Buffer: 0.02M Phosphate buffer

Mobile phase: Buffer: Acetonitrile (70:30)

4.2 Test Solution:

Weigh individually 20 tablets & crush the tablet into fine powder. Weigh accurately the powder eq. to 500 mg of Metformin HCl in 100 ml flask, add 70 ml of mobile phase & sonicate for 15 minutes to dissolve. After sonication, cool to room temperature and make volume to 100 ml with mobile phase. Filter the final solution through 0.2 µm membrane filter.

Note: Adjust the concentration of the standard preparation and sample preparation depending upon the strength of Metformin and Linagliptin Tablet.

4.3 Reference Solution:

Metformin HCl Standard solution: Weigh accurately about 42.5 mg of working standard of Metformin HCl and transfer into 20 ml volumetric flask and sonicate to dissolve.

Linagliptin Standard solution: Weigh accurately about 12.5 mg Linagliptin working standard into separate 100 ml volumetric flask. Add about 70 ml of mobile phase and sonicate for about 10 minutes and make up the volume to 100 ml with mobile phase.

Mix Reference Solution:

Pipette 2 ml of Linagliptin standard solution to 20 ml with mobile phase in a volumetric flask of Metformin HCl and make up to mark with mobile phase.

4.4 Procedure:

Inject 20µl of standard solution as per above mentioned chromatographic condition. In the chromatogram obtained from the standard preparation, the column efficiency determined from the major peak should not be less than 2000 theoretical plates, the tailing factor should be not more than 2.0 and the relative standard deviation of replicate injections should not be more than 2.0 %. Inject 20µl of the sample preparation and chromatograph as per above mentioned chromatographic condition. and resolution between two peaks should be not less than 2. Calculate the content of Linagliptin and Metformin per tablet.

5. Other test: As per pharmacopoieal requirement.