Metformin (Immediate Release) & Sitagliptin Tablets

Analytical Profile No.: MetI Sit 073/074/AP 021

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

1. Identification:

1.1. Metformin HCl: In the assay, the principle peak in the chromatogram obtained with the test solution should correspond to the peak in the chromatogram obtained with the reference solution of Metformin HCl.

1.2. Sitagliptin: In the assay, the principle peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution of Sitagliptin.

2. Dissolution

2.1 Metformin: *Determine by UV Spectroscopy*

2.1.1 Dissolution Parameters:

Apparatus: Basket
Medium: 1000 ml phosphate buffer pH 6.8
Speed and Time: 100 rpm & 45 minutes
Temperature: 37 ºC

Withdraw a suitable volume of the medium and filter

2.1.2 Test Solution: Use the filtrate, dilute if necessary with dissolution medium to obtain a solution having similar concentration to that of reference solution.

2.1.3 Reference solution: Weigh accurately about 25 mg Metformin hydrochloride reference standard 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.

2.1.4 Procedure: Measure the absorbance of the standard and sample solution at about 232 nm. Calculate the percentage of drug release in the tablet.

2.1.5 Limit: Not less than 70 % (D) of the stated amount

2.2 Sitagliptin: *Determine by liquid chromatography*

2.2.1 Dissolution Parameters:

Apparatus: Basket
Medium: 900 ml of water
Temperature: 37 ± 0.5 ℃

Withdraw a suitable volume of the medium and filter

2.2.2 Test Solution: Use the filtrate.

2.2.3 Reference Solution: Weigh accurately about 36.885 mg of Sitagliptin Phosphate Monohydrate reference standard eq. to 27.75 mg Sitagliptin and dissolve in water to produce 50 ml. Dilute 5 ml to 50 ml with water (55.5 ppm).

2.2.4 Chromatographic system: *Proceed as directed under Assay*

2.2.5 Procedure: Separately inject 20 µl of standard and sample solution and blank solution (dissolution medium) and obtain the respective chromatograms. Measure the peak responses. Calculate the % release of the drug.

2.2.6 Limit: Not less than 75 % (D) of the stated amount.

3. Uniformity of the content (Sitagliptin): *Determine by Liquid chromatography*

3.1 Test Solution: Take a single tablet, crush and transfer to 100 ml volumetric flask with the help of 70 ml diluents. Sonicate for 30 min and dilute to 100 ml with diluents. Filter the solution and dilute 5 ml of filtrate to 50 ml with the diluent. Filter the final solution through 0.2 µm membrane filter. Prepare similarly for 9 more tablets.

3.2 Reference Solution: Weigh accurately about 33 mg of Sitagliptin Phosphate Monohydrate reference standard eq. to 25 mg Sitagliptin in 50 ml volumetric flask and add 35 ml diluents. Dissolve by sonication and dilute to 50 ml with diluents. Dilute 5 ml resulting solution to 50 ml with diluents (50 ppm). Filter the resulting standard solution through 0.2 µm membrane filter.

3.3 Chromatographic system: *Proceed as directed under Assay*

3.4 Procedure: Inject 20 µl of reference and sample solution separately and obtain the respective chromatogram. Measure the peak responses. Calculate the content of Sitagliptin in each tablet.

3.5 Limit: 85-115 % of the stated amount of Sitagliptin

4. Assay:

4.1 Test Solution: Weigh individually 20 tablets & crush them into fine powder. Weigh accurately the powder eq. to 50 mg of Metformin HCl and in 100 ml flask, add 70 ml of diluents & sonicate for 15 minutes to dissolve. After sonication, dilute to 100 ml with diluents and stir for 20 minutes, filter through filter paper and dilute 5 ml filtrate to 25 ml with diluents. 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 Sitagliptin Tablet.

4.2 Reference Solution (850 mg metformin+ 50 mg Sitagliptin Tablet):

4.2.1 Metformin HCl Reference solution: Weigh accurately about 25 mg Metformin HCl reference standard and transfer into 50 ml volumetric flask. Add about 35 ml of diluent and sonicate for about 10 minutes and make up the volume to 50 ml with diluents.

4.2.2 Sitagliptin Reference solution: Weigh accurately about 30 mg eq. of Sitagliptin from Sitagliptin Phosphate reference standard into separate 100 ml volumetric flask. Add about 70 ml of diluent and sonicate for about 10 minutes and make up the volume to 100 ml with diluents. Dilute 5 ml of Sitagliptin standard solution to 50 ml with diluents.

4.2.3 Reference solution combination: Pipette 5 ml of Metformin HCl reference solution & Sitagliptin reference solution into 25 ml volumetric flask and make up the volume to 25 ml with diluent. Filter the final solution through 0.2 µm membrane filter.

4.3 Chromatographic system

Column:	Octyldecylsilane (C18), (250*4.6 mm), 5 µm
Flow rate:	1.0 ml/min
Wavelength:	205 nm
Injection volume:	20 µl
Column temperature:	30 °C
Detector:	UV Detector

Buffer: Weigh 1.36 gm KH_2PO_4, dissolve in 900 ml water and add 2.5 ml of triethylamine. Adjust to pH 3.5 with orthophosphate and dilute to 1000 ml with water.

Mobile phase: Buffer: Acetonitrile (75:25)

Diluents: 5 volume of Acetonitrile: 95 volume of 0.1% v/v orthophosphoric acid in water.

4.4 Procedure: Inject the reference solution five times. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0, the relative standard deviation for replicate injections in not more than 2.0 % and resolution between two peaks should be not less than 2. Inject 20 µl of sample solution separately and obtain the respective chromatogram. Measure the peak responses. Calculate the content of Metformin and Sitagliptin in the tablets.

5. Other tests: As per pharmacopoeial requirement.