DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Rifaximin tablet

Analytical Profile No.: RIF 074/075/AP 026

Rifaximin tablets contain not less than 90 per cent and not more than 110 per cent of the stated amount of Rifaximin.

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 Rifaximin.

Tests:

2. Dissolution Test: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 1000 ml of 0.1 M sodium phosphate buffer pH 7.4 containing 0.8 per cent SLS Dissolve 3.5 g of sodium dihydrogen phosphate dihydrate and 10.9 g of anhydrous disodium hydrogen phosphate in 1 litre of water and adjust the pH of the solution to 7.4. To it add 8 g of sodium lauryl sulphate and dissolve.

Speed and time: 75 rpm and 60 minutes

Temperature: 37±0.5℃

Withdraw the suitable volume of the medium and filter.

2.2 Test solution: Dilute 5 ml of the filtrate to 25 ml with mobile phase and filter through 0.2 micron filter paper.

2.3 Reference solution: Weigh accurately about 27.5 mg Rifaximin reference standard and transfer into 50 ml volumetric flask. Dissolve with mobile phase and make up the volume to 100 ml with mobile phase. Pipette 5 ml of this solution and transfer into 25 ml volumetric

flask, add 5 ml of dissolution medium and make up the volume to 25 ml with mobile phase. Filter through 0.2 micron filter paper.

2.4 Chromatographic system: Use the chromatographic system as described under assay

2.5 Procedure: Inject 20 µl of reference solution five times and obtain the respective chromatogram. Measure the peak responses. The test is not valid unless the column efficiency determined from the major peak is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation of replicate injections is not more than 2.0 %. After injecting reference solution inject 20 µL of test solution and blank solution. Calculate the per cent release of rifaximin from each tablet.

2.6 Limit: Not less than 80 per cent (D) of the stated amount.

3. Assay: *Determine by liquid chromatography*

3.1 Diluent (Buffer) : 0.025 M sodium dihydrogen phosphate in water, adjust pH to 3.0 with orthophosphoric acid**.**

3.2 Test Solution: Weigh individually 20 tablets and crush them into fine powder. Weigh accurately the powder equivalent to 50 mg of Rifaximin and transfer into 50 ml volumetric flask. Add about 35 ml of diluent, sonicate for about 10 minutes and cool the solution to room temperature and make up the volume to 50 ml with diluent. Centrifuge the solution. Dilute 5 ml of the resulting solution to 50 ml with diluent. Filter the solution with 0.2 micron membrane filter paper.

3.3 Reference solution: Weigh accurately about 50 mg Rifaximin reference standard and transfer into 50 ml volumetric flask. Dissolve in the mobile phase and make up the volume to 50 ml with mobile phase. Dilute 5 ml of the resulting solution to 50 ml with mobile phase. Filter through 0.2 micron membrane filter paper.

3.4 Chromatographic system:

Column: a stainless steel column 25 cm x 4.6 mm, Phenyl column,

Injection volume: 20 µl,

Flow rate: 1.0 ml per minute,

Detector: spectrophotometer set at 300 nm,

Column temperature: 35 ºC

Mobile phase: a mixture of 45 volumes of buffer solution (0.025 M sodium dihydrogen phosphate in water, adjust pH to 3.0 with orthophosphoric acid) and 55 volumes of acetonitrile,

3.5 Procedure: Inject 20 µl of reference solution five times. The test is not valid unless the column efficiency determined from the major peak is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation of replicate injections is not more than 2.0 %. After injecting reference solution, inject 20 µl of test solution and blank solution and obtain the respective chromatogram. Measure the peak responses. Calculate the content of Rifaximin in each tablet.

4. Other tests: As per pharmacopoeial requirements.