

**ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON
PHARMACOPOEIAL PRODUCT**

DEPARTMENT OF DRUG ADMINISTRATION

Rifaximin Tablets

Rifaximin Tablets contain not less than 90-110% 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.

2. Dissolution Test: Rifaximin

2.1 Dissolution Parameter:

- 2.1.1 Medium** : 0.1 M Sodium phosphate buffer pH 7.4 containing 0.8 % SLS
- 2.1.2 Apparatus** : Paddle
- 2.1.3 Rotation** : 75 RPM
- 2.1.4 Temperature** : $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$
- 2.1.5 Time** : 60 minutes

2.1.6. Dissolution Medium Preparation: Dissolve 3.5 g of sodium dihydrogen phosphate dehydrate 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.

2.1.7 Standard Preparation:

Weigh accurately about 27.5 mg of working standard of Rifaximin 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 0.22 micron filter paper.

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. Dilute 5 ml of the filtrate to 25 ml with mobile phase and again filter through 0.22 micron filter paper

2.1.9. Chromatographic system:

- 2.1.9.1 Column:** 250 X 4.6 mm (Phenyl Column)
- 2.1.9.2 Flow rate:** 1.0 ml/min
- 2.1.9.3 Wave length:** 300 nm
- 2.1.9.4 Injection volume:** 20 μl
- 2.1.9.5 Column Oven Temperature:** 35°C

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2.1.10 Mobile phase

2.1.10.1 Buffer: 0.025 M sodium dihydrogen phosphate in water, adjust pH to 3.0 with orthophosphoric acid.

2.1.10.1 Mobile phase: Buffer: ACN (45:55)

Mix buffer and Acetonitrile, cool to room temperature and filter the solution through 0.2 micron filter paper using vacuum pump.

2.1.10.2 Procedure:

Inject 20 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 is not more than 2.0%. After the completion of the system suitability test parameter, inject 20 µl of each of the sample solution separately. Calculate the release of drug in the Rifaximin tablet by using following formula:

2.1.11 Calculation:

Rifaximin (%):

$$\frac{\text{Area of spl}}{\text{Area of std}} \times \frac{\text{conc of std}}{\text{conc of spl}} \times \text{std potency \%} \times \frac{100 - \text{LOD/WC}}{100} \times 100 \%$$

Result: Rifaximin in %

2.1.12 Tolerance Limit: NLT 80 % of the labeled amount

3. Assay: Rifaximin tablet

3.1 Chromatographic system:

3.1.1 Column: 250 X 4.6 mm (Phenyl Column)

3.1.2 Flow rate: 1.0 ml/min

3.1.3 Wave length: 300 nm

3.1.4 Injection volume: 20 µl

3.1.5 Column Oven Temperature: 35°C

3.1.6 Mobile phase

3.1.6.1 Buffer: 0.025 M sodium dihydrogen phosphate in water, adjust pH to 3.0 with orthophosphoric acid.

3.1.6.2 Mobile phase: Buffer: ACN (45:55)

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: Mobile phase

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3.3 Standard Preparation:

Weigh accurately about 50 mg of working standard of Rifaximin 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 0.22 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 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 diluents. Centrifuge the solution. Dilute 5 ml of the resulting solution to 50 ml with diluent. Filter the solution with 0.22 micron nylon membrane filter paper.

3.5 Procedure

Inject 20 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 is not more than 2.0%. After the completion of the system suitability test parameter, inject 20 µl of each of the sample solution separately. Calculate the content of Rifaximin in each tablet by using following formula:

Rifaximin per tablet:

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