Rifampicin tablets (Rifampicini compressi)

Category. Antituberculosis drug.

Storage. Rifampicin tablets should be kept in a tightly closed container, protected from light.

Additional information. Strengths in the current WHO Model list of essential medicines: 150 mg, 300 mg. Strengths in the current WHO Model list of essential medicines for children: 150 mg, 300 mg.

The tablets are usually coated.

Requirements

Comply with the monograph for "Tablets".

Definition. Rifampicin tablets contain Rifampicin. They contain not less than 90.0% and not more than 110.0% of the amount of rifampicin ($C_{43}H_{58}N_4O_{12}$) stated on the label.

Identity tests

-Either test A alone or any two of tests B, C and D may be applied.

A. To a quantity of the powdered tablets containing about 20 mg of Rifampicin add 5 mL of dichloromethane R and shake. Filter and evaporate the filtrate to dryness. Dissolve rifampicin RS in a small amount of dichloromethane R and evaporate to dryness. Carry out the examination with the residues as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from the rifampicin RS residue.

B. To a quantity of the powdered tablets containing 1 mg of Rifampicin add 3 mL of water R, shake and filter. To the filtrate add 3 drops of copper(II) sulfate (160 g/l) TS, shake and heat to boiling; a violet colour is produced.

C. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R5 as the coating substance and a mixture of 85 volumes of dichloromethane R and 15 volumes of methanol R as the mobile phase. Apply separately to the plate 3 µl of each of the following 2 solutions in dichloromethane R. For solution (A) shake a quantity of the powdered tablets containing about 50 mg of Rifampicin with 5 mL of dichloromethane R and filter. Solution (B) contains 10 mg of rifampicin RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in a current of air and examine the chromatogram in daylight.

The principal spot obtained with solution A corresponds in position, appearance and intensity to that obtained with solution B.

D. See the test described below under Assay method A. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that of the principal peak in the chromatogram obtained with solution (2).

Dissolution. Carry out the test as described under 5.5 Dissolution test for solid oral dosage forms, using as the dissolution medium, 500 mL of dissolution buffer, pH 6.8, 0.25% SDS TS and rotating the paddle at 75 revolutions per minute. At 30 minutes withdraw a sample of about 10 mL of the medium through an in-line filter. Measure the absorbance (1.6) of a 1 cm layer of the filtered sample, suitably diluted if necessary, immediately after withdrawal at the maximum at about 475 nm. At the same time measure the absorbance at the maximum at about 475 nm of a suitable solution of rifampicin RS in dissolution buffer, pH 6.8, 0.25% SDS TS using the same buffer as the blank.

For each of the six tablets tested calculate the total amount of rifampicin ($C_{43}H_{58}N_4O_{12}$) in the medium. The amount in solution for each tablet is not less than 80% of the amount declared on the label. If the amount obtained for one of the six tablets is less than 80%, repeat the test using a further six tablets; the average amount for all 12 tablets tested is not less than 75% and the amount obtained for no tablet is less than 60%.

Related substances

Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, preparing the solutions and using the conditions given below under Assay method A.

Inject 20 µl each of solutions (1), (3) and (4).

In the chromatogram obtained with solution (4) the following peaks are eluted at the following relative retention with reference to rifampicin (approximate retention time 25 minutes): rifampicin quinone about 0.7; 3-formylrifamycin about 0.9. The test is not valid unless the resolution between the peaks due to rifampicin and 3-formylrifamycin is at least 1.5.

In the chromatogram obtained with solution (1) the area of any peak corresponding to rifampicin quinone is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (4.0%), and the area of any peak corresponding to 3-

formylrifamycin is not greater than 0.125 times the area of the principal peak obtained with solution (3) (0.5%). The area of any other peak is not greater than 0.375 times the area of the principal peak obtained with solution (3) (1.5%). The sum of the areas of all the peaks, other than the principal peak, is not greater than 1.5 times the area of the peak in the chromatogram obtained with solution (3) (6.0%). Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (3) (0.4%) and any peak with relative retention less than 0.23 with reference to rifampicin.

Assay

-Either method A or method B may be applied. For either method prepare fresh solutions and perform the assay without delay. Low-actinic glassware is recommended.

A. Determine by *1.14.1 Chromatography*, High-performance liquid chromatography, using a stainless steel column (25 cm x 4.6 mm) packed with particles of silica gel the surface of which has been modified with chemically bonded octadecylsilyl groups (5 µm). As the mobile phase use a mixture of 6 volumes of methanol R and 4 volumes of phosphate buffer pH 7.0 (potassium dihydrogen phosphate R (0.01 mol/l), adjusted with sodium hydroxide (0.1 mol/l) VS).

Prepare the following solutions in a mixture of 4 volumes of methanol R and 6 volumes of phosphate buffer pH 7.0. For solution (1) weigh and powder 20 tablets, shake a quantity of the powder containing about 40 mg of Rifampicin, accurately weighed, in 200 mL and filter. Solution (2) contains 0.20 mg of rifampicin RS per mL. For solution (3) dilute a suitable volume of solution (1) to obtain a concentration of 8 µg of Rifampicin per mL. Solution (4) contains 0.2 mg of rifampicin RS per mL, 0.2 mg of rifampicin quinone RS per mL and 0.2 mg of 3-formylrifamycin RS per mL.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of about 254 nm.

Inject 20 µl of solution (4). The assay is not valid unless the resolution between the peaks due to rifampicin and 3-formylrifamycin is at least 1.5.

Inject alternately 20 µl each of solutions (1) and (2).

Measure the areas of the peak responses obtained in the chromatograms from solutions (1) and (2) and calculate the content of rifampicin ($C_{43}H_{58}N_4O_{12}$).

B. Weigh and powder 20 tablets. Transfer a quantity of the powder containing about 0.10 g of Rifampicin, accurately weighed, to a 100 mL volumetric flask, add about 80 mL of methanol R and shake. Dilute to volume with methanol R, mix, filter and discard the first 20 mL of the filtrate. Dilute 2 mL of the filtrate to 100 mL with phosphate buffer, pH 7.4, TS. Measure the absorbance of the resulting solution in a 1 cm layer at the maximum at about 475 nm, using as the blank phosphate buffer, pH 7.4, TS. Calculate the content of rifampicin ($C_{43}H_{58}N_4O_{12}$) using the absorptivity value of 18.7 ($A^{1\%}_{1cm}$ = 187).