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Rifampicin Oral Suspension

General Notices

Action and use

Rifamycin antituberculosis drug.

DEFINITION

Rifampicin Oral Suspension is a suspension of Rifampicin in powder of suitable fineness in a suitable flavoured vehicle.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements.

Content of rifampicin, $C_{43}H_{58}N_4O_{12}$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

To a quantity containing 0.1 g of Rifampicin add 30 mL of *water* and shake with two 50 mL quantities of *chloroform*. Dry the combined extracts with *anhydrous sodium sulfate*, filter and evaporate the filtrate to dryness at a temperature not exceeding 70°. The residue, after washing with 1 mL of *ether* and drying at 70°, complies with the following tests.

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of rifampicin (*RS 312*).
B. Dissolve 10 mg of the residue in 10 mL of *methanol* and dilute 2 mL to 100 mL with *phosphate buffer pH 7.4*. The *light absorption* of the resulting solution, Appendix II B, in the range 240 to 500 nm exhibits three maxima, at 254, 334 and 475 nm.

TESTS

Acidity

pH, 4.2 to 4.8, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the solvent mixture described below. To 10 volumes of a 21.01% w/v solution of *citric acid* add 23 volumes of a 13.61% w/v solution of *potassium dihydrogen orthophosphate*, 77 volumes of a 17.42% w/v solution of *dipotassium hydrogen orthophosphate*, 250 volumes of *acetonitrile* and 640 volumes of *water* and mix. Prepare the solutions immediately before use.

(1) Add 5 mL of *water* to a quantity of the oral suspension containing 20 mg of Rifampicin and extract with four 10-mL quantities of *dichloromethane*, filter the combined extracts and evaporate to dryness at a temperature not exceeding 40°. Dissolve the residue in 10 mL of *acetonitrile* and dilute 5 mL of the solution to 50 mL with the solvent mixture.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.00030% w/v of *rifampicin quinone EPCRS*.

(4) 0.00020% w/v of *rifampicin* N-*oxide BPCRS*.
(5) 0.0010% w/v of *3-formylrifamycin SV BPCRS*.
(6) Dilute 1 volume of solution (3) to 1.5 volumes and mix 1 volume of the resulting solution with 1 volume of solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Partisil C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for at least 3 times the retention time of the peak due to rifampicin.

MOBILE PHASE

35 volumes of *acetonitrile* and 65 volumes of a solution containing 0.1% v/v of *orthophosphoric acid*, 0.19% w/v of *sodium perchlorate*, 0.59% w/v of *citric acid* and 2.09% w/v of *potassium dihydrogen orthophosphate*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (6), the *resolution factor* between the two principal peaks is at least 4.0. If necessary, adjust the concentration of *acetonitrile* in the mobile phase.

LIMITS

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) (1.5%);

the area of any peak corresponding to rifampicin *N*-oxide is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (1%);

the area of any peak corresponding to 3-formylrifamycin SV is not greater than the area of the principal peak in the chromatogram obtained with solution (5) (5%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peaks eluting before the peak due to rifampicin quinone.

ASSAY

Dilute a weighed quantity containing 0.4 g of Rifampicin to 500 mL with *methanol*, mix thoroughly, dilute 2 mL to 100 mL with *phosphate buffer pH 7.4* and measure the *absorbance* of the resulting solution at the maximum at 475 nm, Appendix II B. Calculate the content of $C_{43}H_{58}N_4O_{12}$ taking 187 as the value of A(1%, 1 cm) at 475 nm. Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{43}H_{58}N_4O_{12}$, weight in volume.