Edition: BP 2025 (Ph. Eur. 11.6 update)

Rifampicin Capsules

General Notices

Action and use

Rifamycin antituberculosis drug.

DEFINITION

Rifampicin Capsules contain Rifampicin.

The capsules comply with the requirements stated under Capsules and with the following requirements.

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

92.5 to 107.5% of the stated amount.

IDENTIFICATION

A. Shake a quantity of the contents of the capsules containing 0.15 g of Rifampicin with 5 mL of *chloroform*, filter and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of rifampicin (*RS 312*).
B. The *light absorption*, Appendix II B, in the range 220 to 500 nm of the final solution obtained in the Assay exhibits four maxima, at 237, 254, 334 and 475 nm.

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

After 45 minutes withdraw a 10 mL sample of the medium and filter. Measure the *absorbance* of the filtered sample, diluted if necessary with 0.1M *hydrochloric acid*, at the maximum at 336 nm, Appendix II B, using 0.1M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of rifampicin, $C_{43}H_{58}N_4O_{12}$, in the medium taking 263 as the value of A(1%, 1 cm) at the maximum at 336 nm.

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) Shake a quantity of the contents of the capsules containing 20 mg of Rifampicin with 10 mL of *acetonitrile*, centrifuge and dilute 5 mL of the clear supernatant liquid to 50 mL with the solvent mixture.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.00080% w/v of *rifampicin quinone EPCRS*.
(4) 0.00030% w/v of *rifampicin* N-*oxide BPCRS*.
(5) 0.00010% w/v of *3-formylrifamycin SV BPCRS*.
(6) Dilute 1 volume of solution (3) to 4 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) (4%);

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) (1.5%);

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) (0.5%);

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%).

ASSAY

Shake a quantity of the mixed contents of 20 capsules containing 0.1 g of Rifampicin with 80 mL of *methanol*, add sufficient *methanol* to produce 100 mL and filter. Dilute 2 mL of the filtrate 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.