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Rifampin Capsules

» Rifampin Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{43}H_{58}N_4O_{12}$.

Packaging and storage—Preserve in tight, light-resistant containers, protected from excessive heat.

USP Reference standards ⟨11⟩—

USP Rifampin RS
USP Rifampin Quinone RS

Identification—

A: Triturate a quantity of Capsule contents, equivalent to about 50 mg of rifampin, with 5 mL of chloroform, and filter. Apply 3 µL each of the filtrate (test solution) and of a solution of USP Rifampin RS in chloroform containing 10 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in an equilibrated chromatographic chamber containing a solvent system consisting of a mixture of chloroform and methanol (90:10) until the solvent front has moved about one-half of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the red spots on the plate: the R_F value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

B: The chromatogram of the *Assay preparation* exhibits a major peak for rifampin, the retention time of which corresponds to that exhibited in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Dissolution ⟨711⟩—

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{43}H_{58}N_4O_{12}$ dissolved from absorbances at the wavelength of maximum absorbance at about 475 nm on filtered portions of the solution under test, suitably diluted, if necessary, with *Dissolution Medium*, in comparison with a Standard solution having a known concentration of USP Rifampin RS, calculated on the dried basis, in the same *Medium*, prepared concomitantly and held in the water bath for the *Time* specified.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{43}H_{58}N_4O_{12}$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—

Phosphate buffer,*Mobile phase*, *Solvent mixture*, *Diluent*, *Standard preparation*, *Resolution solution*, and *Chromatographic system*—Proceed as directed in the *Assay*.

Test preparation—Transfer the contents of 1 Capsule to a suitable volumetric flask so that when diluted to volume as directed below, each mL of solution contains about 1.5 mg of rifampin. Rinse the Capsule shell with a small quantity of *Solvent mixture*, and add the washing to the volumetric flask. Add *Solvent mixture* until the flask is about four-fifths full. Proceed as directed for *Assay preparation* in the *Assay*, beginning with "Sonicate for about 5 minutes."

Procedure—Proceed as directed for *Procedure* in the *Assay*. Calculate the quantity, in mg, of $C_{43}H_{58}N_4O_{12}$ in the Capsule content by the formula:

$$(LC/D)(r_U/r_S)$$

in which L is the labeled quantity, in mg, of rifampin in the Capsule, C is the concentration, in mg per mL, of USP Rifampin RS, calculated on the dried basis, in the *Standard preparation*, D is the concentration, in mg per mL, of rifampin in the *Test preparation*, based on the labeled quantity per Capsule and the extent of dilution, and r_U and r_S are the rifampin peak responses obtained from the *Test preparation* and the *Standard preparation*, respectively.

Loss on drying ⟨731⟩—Dry about 100 mg of Capsule contents in a capillary-stoppered bottle in vacuum at 60° for 3 hours: it loses not more than 3.0% of its weight.

Assay—

Phosphate buffer—Dissolve 136.1 g of monobasic potassium phosphate in about 500 mL of water, add 6.3 mL of phosphoric acid, dilute with water to 1000 mL, and mix (pH 3.1 ± 0.1).

Mobile phase—Prepare a suitable mixture of water, acetonitrile, *Phosphate buffer*, 1.0 M citric acid, and 0.5 M sodium perchlorate (510:350:100:20:20), filter through a suitable filter of 0.7 µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Solvent mixture—Prepare a mixture of acetonitrile and methanol (1:1).

Diluent—Prepare a suitable mixture of water, acetonitrile, 1.0 M dibasic sodium phosphate, 1.0 M monobasic potassium phosphate, and 1.0 M citric acid (640:250:77:23:10).

Standard preparation—Dissolve an accurately weighed quantity of USP Rifampin RS in *Solvent mixture* to obtain a solution having a known concentration of about 1.5 mg per mL, sonicating for about 30 seconds, if necessary, to ensure dissolution. Transfer 10.0 mL of this solution to a 50-mL volumetric flask, dilute with acetonitrile to volume, and mix. [Note—Use this working solution within 5 hours.] Transfer 5.0 mL of the working solution to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix. Each mL of this solution contains about 0.03 mg of USP Rifampin RS. [Note—Inject this *Standard preparation* into the chromatograph within 30 to 60 seconds after preparation.]

Assay preparation—Remove, as completely as possible, the contents of not less than 20 Capsules, and weigh accurately. Mix the Capsule contents, and transfer an accurately weighed portion of the powder, equivalent to about 300 mg of rifampin, to a 200-mL volumetric flask, and add about 180 mL of *Solvent mixture*. Sonicate for about 5 minutes, allow to equilibrate to room temperature, dilute with *Solvent mixture* to volume, and mix. Transfer 10.0 mL of the resulting solution to a 50-mL volumetric flask, dilute with acetonitrile to volume, and mix. [Note—Use this solution within 5 hours.] Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix. [Note—Inject this *Assay preparation* into the chromatograph within 30 to 60 seconds after preparation.]

Resolution solution—Dissolve USP Rifampin Quinone RS in *Solvent mixture* to obtain a solution containing about 0.1 mg per mL. Transfer 1.5 mL of this solution and 5.0 mL of the working solution used to prepare the *Standard preparation* to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 10-cm column that contains 5-µm packing L7. The flow rate is about 1.5 mL per minute. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for rifampin quinone and 1.0 for rifampin, and the resolution, *R*, between the rifampin quinone and rifampin peaks is not less than 4.0. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of $C_{43}H_{58}N_4O_{12}$ in the portion of Capsules taken by the formula:

$$10{,}000C(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Rifampin RS, calculated on the dried basis, in the *Standard preparation*, and r_U and r_S are the rifampin peak area responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
RIFAMPIN CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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