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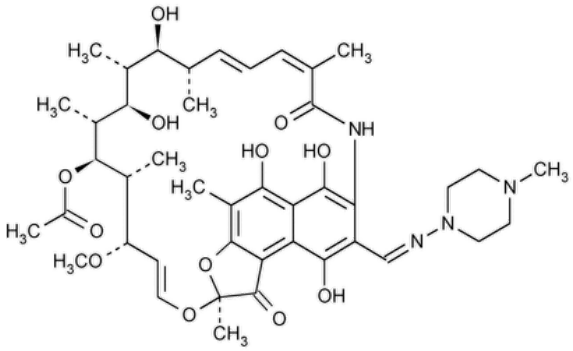
Rifampin



$C_{43}H_{58}N_4O_{12}$ 822.94

Rifamycin, 3-[[(4-methyl-1-piperazinyl)imino]methyl]-.

5,6,9,17,19,21-Hexahydroxy-23-methoxy-2,4,12,16,18,20,22-heptamethyl-8-[*N*-(4-methyl-1-piperazinyl)formimidoyl]-2,7-(epoxypentadeca[1,11,13]trienimino)naphtho[2,1-*b*]furan-1,11-(2*H*)-dione 21-acetate CAS RN®: 13292-46-1; UNII: VJT6J7R4TR.

» Rifampin contains not less than 95.0 percent and not more than 103.0 percent of $C_{43}H_{58}N_4O_{12}$, calculated on the dried basis.

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

USP Reference Standards ⟨11⟩—
USP Rifampin RS
USP Rifampin Quinone RS

Change to read:

Identification, ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: 197M▲ (CN 1-May-2020)

Crystallinity ⟨695⟩: meets the requirements.

pH ⟨791⟩: between 4.5 and 6.5, in a suspension (1 in 100).

Loss on drying ⟨731⟩—Dry about 100 mg in a capillary-stoppered bottle in vacuum at 60° for 4 hours: it loses not more than 2.0% of its weight.

Related substances—

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

Stock test preparation—Transfer about 200 mg of Rifampin to a 100-mL volumetric flask, dissolve in and dilute with acetonitrile to volume, and mix. Sonicate for about 30 seconds, if necessary, to ensure dissolution. [Note—Use this solution within 2 hours.]

Test preparation—Transfer 5.0 mL of *Stock test* to a 50-mL volumetric flask, dilute with *Solvent mixture* to volume, and mix. [Note—Prepare this solution immediately prior to injection into the chromatograph.]

Dilute test preparation—Transfer 10.0 mL of *Stock test preparation* to a 100-mL volumetric flask, dilute with acetonitrile to volume, and mix. Transfer 5.0 mL of the resulting solution to a 50-mL volumetric flask, dilute with acetonitrile to volume, and mix. Transfer 5.0 mL of this solution to another 50-mL volumetric flask, dilute with *Solvent mixture* to volume, and mix. [Note—Prepare this final dilution immediately prior to injection into the chromatograph.]

Procedure—Separately inject equal volumes (about 50 µL) of the *Test preparation* and the *Dilute test preparation* into the chromatograph, record the chromatograms, and measure the responses for all of the peaks. Calculate the percentage of each related substance by the formula:

$$r_{Ti}/(r_D + 0.01\Sigma r_{Ti})$$

in which r_{Ti} is the area of the peak of the individual related substance in the chromatogram obtained from the *Test preparation*, r_D is the area of the rifampin peak in the chromatogram obtained from the *Dilute test preparation*, and Σr_{Ti} is the sum of the areas of all of the peaks of the related substances obtained in the chromatogram of the *Test preparation:* not more than 1.5% of rifampin quinone is found, not more than

1.0% of any other individual related substance is found, and a total of not more than 3.5% of all individual related substances, other than rifampin quinone, having retention times of up to 3 in relation to the retention time of rifampin is found.

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.

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 water, acetonitrile, 1.0 M dibasic potassium phosphate, 1.0 M monobasic potassium phosphate, and 1.0 M citric acid (640:250:77:23:10).

Standard preparation—Transfer about 40 mg of USP Rifampin RS, accurately weighed, to a 200-mL volumetric flask. Dissolve in and dilute with acetonitrile to volume, and mix. Sonicate for about 30 seconds, if necessary, to ensure dissolution. [NOTE—Use this solution within 5 hours.] Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with *Solvent mixture* to volume, and mix. [NOTE—Prepare this final dilution immediately prior to injection into the chromatograph.]

Assay preparation—Using Rifampin, proceed as directed for *Standard preparation*.

Resolution solution—Dissolve suitable quantities of USP Rifampin RS and USP Rifampin Quinone RS in acetonitrile to obtain a solution containing about 0.1 mg of each per mL. Transfer 1.0 mL of this solution to a 10-mL volumetric flask, dilute with *Solvent mixture* 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 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 column efficiency determined from the rifampin peak is not less than 1000 theoretical plates, and 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. The relative retention times are about 0.6 for rifampin quinone and 1.0 for rifampin. Calculate the quantity, in mg, of rifampin ($C_{43}H_{58}N_4O_{12}$) in the portion of Rifampin taken to prepare the *Assay preparation* by the formula:

$$2000C(r_U/r_S)$$

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