Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-76F3F896-F4E7-4824-A0DF-05ED3552B283_4_en-US
DOI: https://doi.org/10.31003/USPNF_M17270_04_01
DOI Ref: q52l5

Cholestyramine Resin

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CAS RN®: 11041-12-6; UNII: 4B33BGI082.

» Cholestyramine Resin is a strongly basic anion-exchange resin in the chloride form, consisting of styrene-divinylbenzene copolymer with quaternary ammonium functional groups. Each g exchanges not less than 1.8 g and not more than 2.2 g of sodium glycocholate, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Cholestyramine Resin RS

Change to read:

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

pH ⟨791⟩**:** between 4.0 and 6.0, in a slurry (1 in 100).

Loss on drying ⟨731⟩—Dry over phosphorus pentoxide at a pressure not exceeding 50 mm of mercury at 70° for 16 hours: it loses not more than 12.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Dialyzable quaternary amines—

pH 9.2 Buffer—Transfer 3.80 g of sodium borate decahydrate to a 1000-mL volumetric flask, dissolve in and dilute with water to volume, and mix.

Bromothymol blue solution—Transfer 150 mg of bromothymol blue and 405 mg of sodium carbonate to a 100-mL volumetric flask, dilute with water to volume, and mix.

Standard solution—Take 1 mL of 60% benzyltrimethylammonium chloride solution, accurately pipeted, and dilute quantitatively, and stepwise, with water to obtain a stock solution having a concentration of 0.2 ± 0.01 mg per mL [Note—Prepare this solution fresh]. Cut a 20- to 25-cm piece of cellulose dialysis tubing* having a molecular weight cut-off that falls within the 6,000 to 14,000 range and a dry flat width of 5 to 9 cm, and place it in water to hydrate until pliable, appropriately sealing one end. Pipet 5 mL of the stock solution into the tubing, add 5 mL of water, appropriately seal the open end, place the tube in a suitable vessel containing 100 mL of water so that it is completely immersed in the water, and stir the fluid for 16 hours to effect dialysis.

Test solution—Cut a 20- to 25-cm piece of cellulose dialysis tubing* having a molecular weight cut-off that falls within the 6,000 to 14,000 range and a dry flat width of 5 to 9 cm, and place it in water to hydrate until pliable, appropriately sealing one end. Weigh 2 ± 0.01 g of Cholestyramine Resin, and carefully transfer the specimen into the tubing, taking care to ensure that none adheres to the upper walls of the tubing. Add 10 mL of water to the contents of the tube, appropriately seal the open end, and place the tube in a suitable vessel containing 100 mL of water so that it is completely immersed in the water. Stir the fluid for 16 hours to effect dialysis.

Procedure—Pipet the following into each of three separators: Separator 1—5 mL of *Standard solution,* 5 mL of *pH 9.2 Buffer,* 1 mL of *Bromothymol blue solution,* and 10 mL of chloroform; Separator 2—5 mL of *Test solution,* 5 mL of *pH 9.2 Buffer,* 1 mL of *Bromothymol blue solution,* and 10 mL of chloroform; Separator 3—5 mL of water, 5 mL of *pH 9.2 Buffer,* 1 mL of *Bromothymol blue solution,* and 10 mL of chloroform. Shake each separator vigorously for 1 minute, allow the phases to separate until the chloroform phase is clear, and collect the chloroform extracts in separate 25-mL volumetric flasks. Repeat the extraction process with a second 10-mL portion of chloroform, and combine with the previous extracts. Dilute each solution with chloroform to volume, if necessary, and mix. Concomitantly determine the absorbances of the *Test solution* and the *Standard solution* at the wavelength of maximum absorbance at about 420 nm, with a suitable spectrophotometer, using the solution from Separator 3 as the blank: the absorbance of the *Test solution* does not exceed that of the *Standard solution* (0.05% as benzyltrimethylammonium chloride).

Chloride content—To about 750 mg of Cholestyramine Resin, accurately weighed, add 100 mL of water and 50 mg of potassium nitrate. Add, with stirring, 2 mL of nitric acid, and titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically, and using a silver-glass

electrode system. Each mL of 0.1 N silver nitrate is equivalent to 3.545 mg of Cl. Not less than 13.0% and not more than 17.0% of Cl, calculated on the dried basis, is found.

Exchange capacity—

Mobile phase—Prepare a filtered and degassed mixture of 0.08 M monobasic potassium phosphate and acetonitrile (65:35). Adjust with phosphoric acid to a pH of 3.0. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Potassium phosphate buffer—Transfer about 4 g of monobasic potassium phosphate and about 12 g of dibasic potassium phosphate to a 1-liter volumetric flask. Dissolve in and dilute with water to volume, and mix.

Sodium glycocholate solution—Transfer about 15 g of sodium glycocholate to a 500-mL volumetric flask, and dissolve in and dilute with *Potassium phosphate buffer* to volume.

Reference solution—Pipet 4.0 mL of *Sodium glycocholate solution* into a 100-mL volumetric flask, and dilute with water to volume.

Standard solution—Transfer about 100 mg of USP Cholestyramine Resin RS, accurately weighed, to a 25-mL conical flask. Pipet 15.0 mL of *Sodium glycocholate solution* into the flask, and stir by mechanical means for 2 hours. Transfer the contents to a centrifuge tube, and centrifuge for 15 minutes. Transfer 5.0 mL of the supernatant to a 50-mL volumetric flask, and dilute with water to volume.

System suitability solution—Prepare a solution in water containing, in each mL, about 0.6 mg of sodium glycocholate and about 0.3 mg of taurodeoxycholic acid.

Test solution—Transfer about 100 mg of anhydrous Cholestyramine Resin, accurately weighed, to a 25-mL conical flask. Pipet 15.0 mL of *Sodium glycocholate solution* into the flask, and stir by mechanical means for 2 hours. Transfer the contents to a centrifuge tube, and centrifuge for 15 minutes. Transfer 5.0 mL of the supernatant to a 50-mL volumetric flask, and dilute with water to volume.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 214-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R*, between sodium glycocholate and taurodeoxycholic acid is not less than 1.5. Chromatograph the *Reference solution*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.5; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Reference solution*, the *Standard solution*, and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of sodium glycocholate absorbed on each g of the Resin taken by the formula:

$$M(2.5r_R - r_U)W_S/(2.5r_R - r_S)W_U$$

in which M is the stated value, in mg, of sodium glycocholate absorbed per g of USP Cholestyramine Resin RS; r_R, r_U, and r_S are the peak responses obtained from the *Reference solution*, the *Test solution*, and the *Standard solution*, respectively; W_U is the weight, in mg, of Cholestyramine Resin, calculated on the dried basis, taken to prepare the *Test solution;* and W_S is the weight, in mg, of USP Cholestyramine Resin RS taken to prepare the *Standard solution.*

* A suitable tubing is Spectra/Por 1, Item # 132665, available from Spectrum Laboratories, Inc. (www.spectrapor.com), or equivalent.

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

Topic/Question	Contact	Expert Committee
CHOLESTYRAMINE RESIN	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 32(2)

Current DocID: GUID-76F3F896-F4E7-4824-A0DF-05ED3552B283_4_en-US
DOI: https://doi.org/10.31003/USPNF_M17270_04_01
DOI ref: q52l5