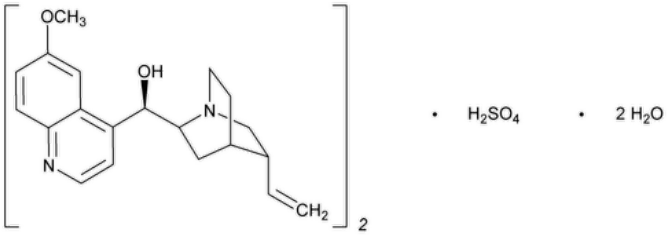
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Jan-2018
Document Type: USP Monographs
DocId: GUID-281F0F56-096C-4764-9BFE-F9BC72CB6A97_3_en-US
DOI: https://doi.org/10.31003/USPNF_M72820_03_01
DOI Ref: 81395

Quinine Sulfate



$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$ 782.94

Cinchonan-9-ol, 6'-methoxy-, (8α,9*R*)-, sulfate (2:1) (salt), dihydrate;

Quinine sulfate (2:1) (salt) dihydrate CAS RN®: 207671-44-1.

Anhydrous 746.93 CAS RN®: 804-63-7; UNII: M4XCR57IWG.

DEFINITION

Quinine Sulfate is the sulfate of an alkaloid obtained from the bark of species of *Cinchona*. It contains NLT 99.0% and NMT 101.0% of total alkaloid salt, calculated as $(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4$, on the anhydrous basis.

IDENTIFICATION

• **A.** A 0.5-mg/mL solution in dilute sulfuric acid (1 in 350) exhibits a vivid blue fluorescence. On the addition of a few drops of hydrochloric acid, the fluorescence disappears.

• **B.** The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard stock solution*, as obtained in the test for *Organic Impurities*.

• **C.** **Identification Tests—General**, *Sulfate*⟨191⟩

Sample solution: 20-mg/mL solution made with the aid of a few drops of hydrochloric acid

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Sample: 200 mg of Quinine Sulfate

Analysis: Dissolve the *Sample* in 20 mL of acetic anhydride, and add 4 drops of *p*-naphtholbenzein TS. Titrate with 0.1 N perchloric acid VS from a 10-mL microburet to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 24.90 mg of total alkaloid salt, calculated as quinine sulfate $[(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4]$.

Acceptance criteria: 99.0%–101.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition** ⟨281⟩**:** NMT 0.1%

• **Chloroform–Alcohol-Insoluble Substances**

Sample: 2 g

Analysis: Warm the *Sample* with 15 mL of a mixture of chloroform and dehydrated alcohol (2:1) at 50° for 10 min. Pass through a tared, sintered-glass filter, using gentle suction. Wash the filter with five 10-mL portions of the chloroform–alcohol mixture, dry at 105° for 1 h, and weigh.

Acceptance criteria: The weight of the residue is NMT 2 mg (0.1%).

• **Organic Impurities**

Standard stock solution: 6 mg/mL of USP Quinine Sulfate RS, in diluted alcohol

Standard solution A: 0.06 mg/mL of USP Quinine Sulfate RS from the *Standard stock solution*, in diluted alcohol

Standard solution B: 0.05 mg/mL of USP Quininone RS (corresponding to 0.06 mg/mL of the sulfate), and 0.10 mg/mL of cinchonidine (corresponding to 0.12 mg/mL of the sulfate), in diluted alcohol

Sample solution: 6 mg/mL of Quinine Sulfate, in diluted alcohol

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Chloroform, acetone, and diethylamine (5:4:1). [NOTE—The solvent chamber being used without previous equilibration.]

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Proceed as directed for *Chromatography ⟨621⟩, Thin-Layer Chromatography*. Allow the spots to dry, and develop the chromatogram in a solvent system until the solvent front has moved 15 cm. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by spraying with glacial acetic acid, and examine under long-wavelength UV light.

Acceptance criteria: Any spot produced by the *Sample solution* at the R_F value of a spot produced by *Standard solution B* is not greater in size or intensity than that corresponding spot. Apart from these spots and from the spot appearing at the R_F value of quinine, any additional fluorescent spot is not greater in size or intensity than the spot of *Standard solution A*. Spray the plate with potassium iodoplatinate TS. Any spot produced by the *Sample solution* is not greater in size or intensity than a corresponding spot from *Standard solution B*.

• **DIHYDROQUININE SULFATE**

Solution A: Add 35.0 mL of methanesulfonic acid to 20.0 mL of glacial acetic acid, and dilute with water to 500 mL.

Solution B: Dissolve 10.0 mL of diethylamine in water to obtain 100 mL of solution.

Mobile phase: Acetonitrile, *Solution A*, *Solution B*, and water (100:20:20:860). Adjust with *Solution B* to a pH of 2.6 if found to be lower.

System suitability solution: 0.2 mg/mL of USP Quinine Sulfate RS and 0.2 mg/mL dihydroquinine prepared as follows. Dissolve in methanol using 5% of the final volume, and dilute with *Mobile phase* to volume.

Sample solution: 0.2 mg/mL of Quinine Sulfate in *Mobile phase*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: 235 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1 mL/min

Injection size: 50 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for quinine and dihydroquinine are 1 and 1.5, respectively.]

Suitability requirements

Resolution: NLT 1.2 between quinine and dihydroquinine

Relative standard deviation: NMT 2.0% for the quinine peak

Analysis

Sample: *Sample solution*

Calculate the percentage of dihydroquinine in the portion of Quinine Sulfate taken:

$$\text{Result} = r_U/(r_U + r_S) \times 100$$

r_U = peak response of dihydroquinine from the *Sample solution*

r_S = peak response of quinine from the *Sample solution*

Acceptance criteria: NMT 10.0% of dihydroquinine

SPECIFIC TESTS

• **OPTICAL ROTATION,** *Specific Rotation⟨781S⟩*

Sample solution: 20 mg/mL, in 0.1 N hydrochloric acid

Acceptance criteria: −235° to −245°

• **Water Determination, *Method I*⟨921⟩:** 4.0%–5.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

• **USP Reference Standards ⟨11⟩**

USP Quinine Sulfate RS

USP Quininone RS

Cinchonan-9-one, 6'-methoxy-, (8α)-.

$C_{20}H_{22}N_2O_2$ 322.40

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

Topic/Question	Contact	Expert Committee
QUININE SULFATE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 37(3)

Current DocID: GUID-281F0F56-096C-4764-9BFE-F9BC72CB6A97_3_en-US
Previous DocID: GUID-281F0F56-096C-4764-9BFE-F9BC72CB6A97_1_en-US
DOI: https://doi.org/10.31003/USPNF_M72820_03_01
DOI ref: 81395