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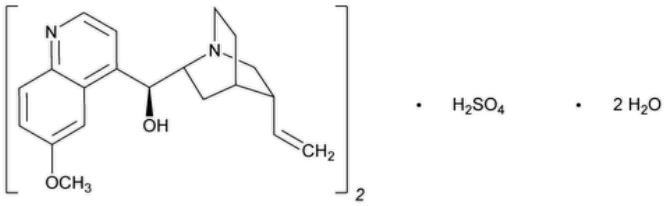
Quinidine Sulfate



$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$ 782.94
$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4$ 746.93
Cinchonan-9-ol, 6'-methoxy-, (9*S*)-, sulfate (2:1) (salt), dihydrate;
Quinidine sulfate (2:1) (salt) dihydrate CAS RN®: 6591-63-5; UNII: J13S2394HE.
Anhydrous CAS RN®: 50-54-4; UNII: 140CU2322K.

DEFINITION

Quinidine Sulfate is the sulfate of an alkaloid obtained from various species of *Cinchona* and their hybrids and from *Remijia pedunculata* Flückiger (Fam. Rubiaceae), or prepared from quinine. It contains NLT 99.0% and NMT 101.0% of total alkaloid salt, calculated as Quinidine Sulfate $[(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4]$, on the anhydrous basis.

IDENTIFICATION

• **A.**

Sample solution: 1-in-2000 solution of Quinidine Sulfate in dilute sulfuric acid (1 in 350)

Acceptance criteria: The *Sample solution* 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 from the *Sample solution* corresponds to that from the *Standard solution*, as obtained in *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 solution: Dissolve 200 mg of Quinidine Sulfate in 20 mL of glacial acetic acid, heating if necessary, and cool the solution.

Titrimetric system

Mode: Titrimetry

Titrant: 0.1 N perchloric acid VS

Endpoint detection: Visual

Analysis: To the *Sample solution* add 20 mL of acetic anhydride and 4 drops of *p*-naphtholbenzein TS, and titrate with *Titrant* from a 10-mL microburet to a green endpoint. Perform a blank determination, and make any necessary corrections. Each mL of 0.1 N perchloric acid is equivalent to 24.90 mg of total alkaloid salt, calculated as quinidine 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%

• **Organic Impurities**

Standard solution A: 6 mg/mL of USP Quinidine Sulfate RS in diluted alcohol

Standard solution B: 0.06 mg/mL of USP Quinidine Sulfate RS in diluted alcohol from *Standard solution A*

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

Sample solution: 6 mg/mL of Quinidine 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 (50:40:10)

Analysis

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

Proceed as directed in the chapter. The solvent chamber is used without previous equilibration. When the solvent front has moved 15 cm, remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray with glacial acetic acid. Locate the spots on the plate by examination under long-wavelength UV light. Then spray the plate with potassium iodoplatinate TS.

Acceptance criteria: Any spot produced by the *Sample solution* at the R_F value of a spot produced by *Standard solution C* is not greater in size or intensity than that corresponding spot. Apart from these spots and from the spots appearing at the R_F value of quinidine sulfate and dihydroquinidine sulfate (the two spots most evident from *Standard solution A*), any additional fluorescent spot is not greater in size or intensity than the principal spot of *Standard solution B*. After the treatment 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 C*.

• **Limit of Dihydroquinidine 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: Dilute 10.0 mL of diethylamine with water to 100 mL.

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

System suitability solution: 0.2 mg/mL each of USP Quinidine Sulfate RS and dihydroquinidine hydrochloride prepared as follows. Dissolve a suitable quantitiy of each USP Quinidine Sulfate RS and dihydroquinidine hydrochloride in about 10% of total volume of methanol, and dilute with *Mobile phase* to volume.

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

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 3.9-mm × 30-cm; packing L1

Injection volume: 50 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for quinidine and dihydroquinidine are 1 and 1.5, respectively.]

Suitability requirements

Resolution: NLT 2.5 between quinidine and dihydroquinidine

Relative standard deviation: NMT 2.0%

Analysis

Sample: *Sample solution*

Acceptance criteria: 20.0%; the response of the dihydroquinidine peak is NMT 0.25 that of the quinidine peak.

SPECIFIC TESTS

• **Chloroform–Alcohol-Insoluble Substances**

Sample solution: Warm 2 g of Quinidine Sulfate with 15 mL of chloroform and dehydrated alcohol mixture (2:1) at 50° for 10 min.

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

Acceptance criteria: NMT 0.1%; the weight of the residue does not exceed 2 mg.

• **Optical Rotation,** *Specific Rotation⟨781S⟩*

Sample solution: 20 mg/mL of Quinidine Sulfate in 0.1 N hydrochloric acid

Acceptance criteria: +275° to +288° on the anhydrous basis

• **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 Quinidine Sulfate RS

USP Quininone RS

Cinchonan-9-one, 6'-methoxy-, (8-alpha)-.

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

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

Topic/Question	Contact	Expert Committee
QUINIDINE SULFATE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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