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Quinine Sulfate Tablets

DEFINITION

Quinine Sulfate Tablets contain amounts of quinine sulfate and dihydroquinine sulfate totaling NLT 90.0% and NMT 110.0% of the labeled amount of quinine sulfate, calculated as $(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$.

IDENTIFICATION

- **A.**

  Sample: Nominally 100 mg of quinine sulfate from powdered Tablets

  Analysis: Shake the *Sample* well with 100 mL of dilute sulfuric acid (1 in 350), and filter.

  Acceptance criteria: An appropriate dilution of the filtrate 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 A*, as obtained in the test for *Organic Impurities*.

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

  Sample: Nominally 20 mg of quinine sulfate from powdered Tablets

  Analysis: Shake *Sample* with 10 mL of dilute hydrochloric acid (1 in 100), and filter

  Acceptance criteria: The filtrate meets the requirements.

- **D.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

  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 B*, *Solution A*, and water (10:2:2:86). Adjust with *Solution B* to a pH of 2.6 if the pH is found to be lower.

  System suitability solution: 0.2 mg/mL each of USP Quinine Sulfate RS and dihydroquinine, dissolved in 10% of the final volume of methanol. Dilute with *Mobile phase* to volume.

  Standard solution: 0.2 mg/mL of USP Quinine Sulfate RS in *Mobile phase*

  Sample stock solution: Nominally 1.6 mg/mL of quinine sulfate prepared as follows. Transfer an equivalent to 160 mg of quinine sulfate from NLT 20 powdered Tablets to a 100-mL volumetric flask, add 80 mL of methanol, and shake by mechanical means for 30 min. Dilute with methanol to volume, and filter, discarding the first 10 mL of the filtrate.

  Sample solution: Nominally 0.2 mg/mL of quinine sulfate in *Mobile phase* from the *Sample stock solution*

  Chromatographic system

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

  Mode: LC

  Detector: UV 235 nm

  Column: 3.9-mm × 30-cm; packing L1

  Flow rate: 1 mL/min

  Injection volume: 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

  Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of quinine sulfate and dihydroquinine sulfate in the portion of Tablets taken:

$$\text{Result} = [(r_{B,U} + r_{D,U})/(r_{B,S} + r_{D,S})] \times (C_S/C_U) \times 100$$

$r_{B,U}$ = peak area response of quinine from the *Sample solution*

$r_{D,U}$ = peak area response of dihydroquinine from the *Sample solution*

$r_{B,S}$ = peak area response of quinine from the *Standard solution*

$r_{D,S}$ = peak area response of dihydroquinine from the *Standard solution*

C_S = concentration of USP Quinine Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of quinine sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Detection: UV maximum at about 248 nm

Standard solution: Prepare a solution of known concentration of USP Quinine Sulfate RS in *Medium*.

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium*

Analysis: Determine the percentage of the labeled amount of quinine sulfate [$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot H_2O$] dissolved.

Tolerances: NLT 75% (*Q*) of the labeled amount of quinine sulfate [$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$] is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

Diluent: Hydrochloric acid (1 in 100)

Standard solution: 40 µg/mL of USP Quinine Sulfate RS in *Diluent*

Sample solution: Transfer the contents of one powdered Tablet to a 250-mL volumetric flask, add 175 mL of *Diluent*, and shake by mechanical means for 30 min. Add *Diluent* to volume. Filter a portion of the mixture, discarding the first 20 mL of the filtrate.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Cell: 1 cm

Analytical wavelength: Maximum at about 345 nm

Blank: Water

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of quinine sulfate [$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$], in the Tablet taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Quinine Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of quinine sulfate in the *Sample solution* (mg/mL)

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **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 *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: Nominally 6 mg/mL of quinine sulfate prepared as follows. Shake the equivalent of 150 mg of quinine sulfate from powdered Tablets with 25 mL of diluted alcohol for 10 min, and filter.

Chromatographic system

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

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). [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 from *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*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed 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 TABLETS	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

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