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Quinidine Sulfate Tablets

DEFINITION

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

IDENTIFICATION

- **A.**

  Analysis: Shake the equivalent to 100 mg of quinidine sulfate from powdered Tablets, with 10 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 of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in *Organic Impurities*.

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

  Analysis: Shake the equivalent to 100 mg of quinidine sulfate from powdered Tablets, with 10 mL of dilute hydrochloric acid (1 in 100), and filter.

  Acceptance criteria: The filtrate meets the requirements.

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: 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.

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

  Sample stock solution: Weigh and finely powder NLT 20 Tablets. Transfer a portion of the powder, nominally equivalent to 160 mg of quinidine sulfate, to a 100-mL volumetric flask. Add 80 mL of methanol, and shake the flask by mechanical means for 30 min. Dilute with methanol to volume, and filter, discarding the first 10 mL of filtrate.

  Sample solution: Nominally equivalent to 0.192 mg/mL of quinidine 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

  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

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of the labeled amount of quinidine sulfate (quinidine sulfate and dihydroquinidine sulfate) in the portion of the 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 response of quinidine from the *Sample solution*

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

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

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

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

C_U = nominal concentration of quinidine 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: 30 min

Standard solution: USP Quinidine Sulfate RS in *Medium*

Sample solution: Dilute with *Medium* to a concentration that is similar to the *Standard solution.* Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

Mode: UV

Analytical wavelength: 248 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 85% (*Q*) of the labeled amount of quinidine 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

Standard solution: 40 µg/mL of USP Quinidine Sulfate RS in dilute hydrochloric acid (1 in 100)

Sample solution: Transfer a crushed Tablet to a 250-mL volumetric flask, add 175 mL of dilute hydrochloric acid (1 in 100), and shake by mechanical means for 30 min. Add dilute hydrochloric acid (1 in 100) to volume. Filter a portion of the mixture, discarding the first 20 mL of the filtrate. Dilute quantitatively, if necessary.

Instrumental conditions

Mode: UV

Cell: 1 cm

Analytical wavelength: 345 nm

Blank: Water

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the percentage of the labeled amount of quinidine sulfate and dihydroquinidine sulfate, calculated as quinidine 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 Quinidine Sulfate RS in the *Standard solution* (mg/mL)

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

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **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: Equivalent to 6 mg/mL of quinidine sulfate in diluted alcohol prepared as follows. Shake an amount equivalent to 150 mg of quinidine sulfate from a suitable amount of powdered Tablets in 25 mL of diluted alcohol for 10 min, and filter.

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*.

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-, (8alpha)-.

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

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

Topic/Question	Contact	Expert Committee
QUINIDINE SULFATE TABLETS	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

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