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Quinine Sulfate Capsules

DEFINITION

Quinine Sulfate Capsules 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 the contents of Capsules

Analysis: Shake the *Sample* 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.

Delete the following:

▲ **B.** The R_f value of the principal spot from the *Sample solution* corresponds to that from *Standard solution A*, as obtained in the test for

Organic Impurities. ▲ (USP 1-May-2021)

Change to read:

• **▲ B.** ▲ (USP 1-MAY-2021) [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Sulfate](#)

Sample: Nominally 20 mg of quinine sulfate from the contents of Capsules

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

Acceptance criteria: The filtrate meets the requirements.

Change to read:

• **▲ C.** ▲ (USP 1-MAY-2021) The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• 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 A*, *Solution B*, and [water](#) (100:20:20:860). 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 in [methanol](#) prepared as follows. Transfer an amount, equivalent to 160 mg of quinine sulfate from the contents of NLT 20 Capsules, 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 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; ▲10-μm ▲ (USP 1-May-2021) 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 ($C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$, calculated as the sum of quinine sulfate and dihydroquinine sulfate, in the portion of Capsules taken:

$$\text{Result} = [(r_{b,U} + r_{d,U}) / (r_{b,S} + r_{d,S})] \times (C_S / C_U) \times (M_{r1} / M_{r2}) \times 100 \quad (\text{USP 1-May-2021})$$

 $r_{b,U}$ = peak response of quinine from the *Sample solution* $r_{d,U}$ = peak response of dihydroquinine from the *Sample solution* $r_{b,S}$ = peak response of quinine from the *Standard solution* $r_{d,S}$ = peak 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) M_{r1} = molecular weight of quinine sulfate, 782.94 M_{r2} = molecular weight of anhydrous quinine sulfate, 746.92 (USP 1-May-2021)**Acceptance criteria:** 90.0%–110.0%**PERFORMANCE TESTS****Change to read:**

- [DISSOLUTION \(711\)](#)

Test 1**Medium:** [0.1 N hydrochloric acid](#); 900 mL**Apparatus 1:** 100 rpm**Time:** 45 min**Detector:** 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****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of quinine sulfate ($C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$ dissolved:

$$\text{Result} = (r_U / r_S) \times (C_S / L) \times (M_{r1} / M_{r2}) \times D \times V \times 100$$

 r_U = absorbance of the *Sample solution* r_S = absorbance of the *Standard solution* C_S = concentration of [USP Quinine Sulfate RS](#) in the *Standard solution* (mg/mL) L = label claim (mg/Capsule) M_{r1} = molecular weight of quinine sulfate, 782.94 M_{r2} = molecular weight of anhydrous quinine sulfate, 746.92 D = dilution factor of the *Sample solution*, as needed

V = volume of *Medium*, 900 mL ▲ (USP 1-May-2021)

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.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: [0.1 N hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Solution A: Add 7.0 mL of [methanesulfonic acid](#) to 4.0 mL of [glacial acetic acid](#), and dilute with [water](#) to 100 mL.

Solution B: Dissolve 10.0 mL of [diethylamine](#) in [water](#) to obtain 100 mL of solution.

Mobile phase: [Water](#), [acetonitrile](#), *Solution A*, and *Solution B* (81:15:2:2). Adjust with *Solution B* to a pH of 3.0.

Standard solution: Prepare a solution of known concentration of [USP Quinine Sulfate RS](#) in *Medium*.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, and suitably dilute with *Medium*.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Flow rate: 1.2 mL/min

Injection volume: 10 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for the quinine peak

Relative standard deviation: NMT 2.0% for the sum of the quinine and dihydroquinine peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of quinine sulfate $(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$ dissolved.

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times (M_{r1}/M_{r2}) \times D \times V \times 100$$

r_U = sum of the peak responses of quinine and dihydroquinine from the *Sample solution*

r_S = sum of the peak responses of quinine and dihydroquinine from the *Standard solution*

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

L = label claim (mg/Capsule)

M_{r1} = molecular weight of quinine sulfate, 782.94

M_{r2} = molecular weight of anhydrous quinine sulfate, 746.92

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (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.

Test 3: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.

Medium: [0.1 N hydrochloric acid](#); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: 0.0144 mg/mL of [USP Quinine Sulfate RS](#) in *Medium*

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

Instrumental conditions

Mode: UV

Analytical wavelength: 248 nm

Cell: 1 cm

Blank: *Medium*

Analysis