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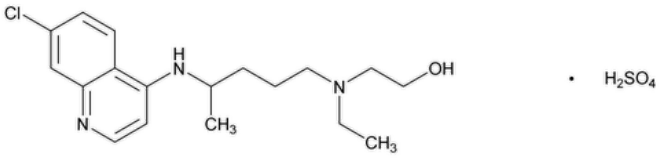
Hydroxychloroquine Sulfate



$C_{18}H_{26}ClN_3O \cdot H_2SO_4$ 433.95

Ethanol, 2-[[4-[(7-chloro-4-quinolinyl)amino]pentyl]ethyl] amino-, (±)-, sulfate (1:1) (salt);

(±)-2-[[4-[(7-Chloro-4-quinolyl)amino]pentyl]ethylamino] ethanol sulfate (1:1) (salt) CAS RN®: 747-36-4.

DEFINITION

Hydroxychloroquine Sulfate contains NLT 98.0% and NMT 102.0% of hydroxychloroquine sulfate ($C_{18}H_{26}ClN_3O \cdot H_2SO_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

Change to read:

• **B.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (Official 1-Jun-2021)

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

Sample solution: 10 mg/mL of Hydroxychloroquine Sulfate in water

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** Acetonitrile, water, and phosphoric acid (100:900:2)

Solution B: Acetonitrile, water, and phosphoric acid (800:200:1)

Mobile phase: *Solution A* and *Solution B* (97:3)

Standard solution: 0.01 mg/mL of USP Hydroxychloroquine Sulfate RS in *Solution A* prepared as follows. Transfer a suitable quantity of USP Hydroxychloroquine Sulfate RS to a suitable volumetric flask and add about 75% of the flask volume of *Solution A*. Sonicate for NLT 5 min or until solids are dissolved. Dilute with *Solution A* to volume.

Sample solution: 0.01 mg/mL of Hydroxychloroquine Sulfate in *Solution A* prepared as follows. Transfer a suitable quantity of Hydroxychloroquine Sulfate to a suitable volumetric flask and add about 75% of the flask volume of *Solution A*. Sonicate for NLT 5 min or until solids are dissolved. Dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 2.0-mm × 10-cm; 2-µm packing L1

Column temperature: 35°

Flow rate: 0.8 mL/min

Injection volume: 3 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydroxychloroquine sulfate ($C_{18}H_{26}ClN_3O \cdot H_2SO_4$) in the portion of Hydroxychloroquine Sulfate taken:

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

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

r_S = peak response of hydroxychloroquine from the *Standard solution*

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

C_U = concentration of Hydroxychloroquine Sulfate in the *Sample solution* (mg/mL)▲ (Official 1-Jun-2021)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Delete the following:

▲• **Ordinary Impurities** ⟨466⟩

Standard solution: Prepare in 10% water in methanol.

Sample solution: Prepare in 10% water in methanol.

Eluant: A mixture of alcohol, water, and ammonium hydroxide (80:16:4)

Visualization: 1

Acceptance criteria: Meets the requirements▲ (Official 1-Jun-2021)

Add the following:

▲• **Organic Impurities**

Solution A and **Solution B:** Prepare as directed in the *Assay*.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	97	3
1.8	97	3
2.5	5	95
3.5	5	95
4.0	97	3
6.0	97	3

Standard stock solution: Use the *Standard solution* from the *Assay*.

Standard solution: 0.001 mg/mL of USP Hydroxychloroquine Sulfate RS in *Solution A* from the *Standard stock solution*

Sample solution: 0.1 mg/mL of Hydroxychloroquine Sulfate in *Solution A* prepared as follows. Transfer a suitable quantity of Hydroxychloroquine Sulfate to a suitable volumetric flask and add about 75% of the flask volume of *Solution A*. Sonicate for NLT 5 min or until solids are dissolved. Dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 2.0-mm × 10-cm; 2-µm packing L1

Column temperature: 35°

Flow rate: 0.8 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Hydroxychloroquine Sulfate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of any individual impurity from the *Sample solution*

r_S = peak response of hydroxychloroquine from the *Standard solution*

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

C_U = concentration of Hydroxychloroquine Sulfate in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desethyl hydroxychloroquine[a]	0.87	1.3	0.5
Hydroxychloroquine	1.0	—	—
Hydroxychloroquine acetate (if present)[b]	1.52	0.81	0.5
Sulfohydroxychloroquine[c]	2.32	1.0	0.5
Chloroquine related compound A[d]	4.46	2.4	0.15
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0▲ (Official 1-Jun-2021)

[a] 2-({4-[(7-Chloroquinolin-4-yl)amino]pentyl}amino)ethan-1-ol.

[b] 2-({4-[(7-Chloroquinolin-4-yl)amino]pentyl}ethylamino)ethyl acetate. This process impurity may be present if acetic acid or acetates are used in the synthesis.

[c] 2-({4-[(7-Chloroquinolin-4-yl)amino]pentyl}ethylamino)ethyl hydrogen sulfate.

[d] 4,7-Dichloroquinoline.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers.
- **USP Reference Standards** ⟨11⟩
  USP Hydroxychloroquine Sulfate RS

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

Topic/Question	Contact	Expert Committee
HYDROXYCHLOROQUINE 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

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