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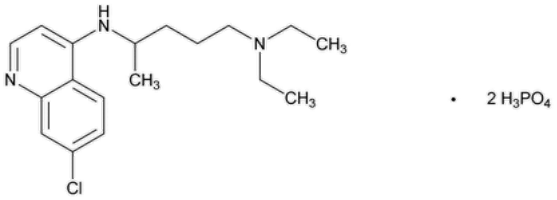
# Chloroquine Phosphate



$C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$ 515.86

1,4-Pentanediamine, $N^4$-(7-chloro-4-quinolinyl)-$N^1$,$N^1$-diethyl-, phosphate (1:2);

7-Chloro-4-[[4-(diethylamino)-1-methylbutyl]amino]quinoline phosphate (1:2) CAS RN®: 50-63-5; UNII: 6E17K3343P.

## DEFINITION

Chloroquine Phosphate contains NLT 98.0% and NMT 102.0% of chloroquine phosphate ($C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$), calculated on the dried basis.

## IDENTIFICATION

***Change to read:***

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K▲ (CN 1-May-2020)

***Change to read:***

• **B.** ▲Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U▲ (CN 1-May-2020)

**Medium:** Dilute hydrochloric acid (1 in 1000)

**Sample solution:** 10 µg/mL

**Ratio:** $A_{343}/A_{329}$, 1.00–1.15

• **C.** 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**

**Buffer:** 1.4 g/L of anhydrous dibasic sodium phosphate in water. Adjust with 10% phosphoric acid to a pH of 3.0.

**Mobile phase:** 0.4% triethylamine in methanol and *Buffer* (70:30)

**System suitability solution:** 2.0 µg/mL each of USP Chloroquine Phosphate RS, USP Phenol RS, USP Hydroxychloroquine Sulfate RS, USP Chloroquine Related Compound A RS, USP Chloroquine Related Compound D RS, USP Chloroquine Related Compound E RS, and USP Chloroquine Related Compound G RS in *Mobile phase*

**Standard solution:** 0.3 mg/mL of USP Chloroquine Phosphate RS in *Mobile phase*. Sonicate to dissolve if necessary.

**Sample solution:** 0.3 mg/mL of Chloroquine Phosphate in *Mobile phase*. Sonicate to dissolve if necessary.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 260 nm

**Column:** 4.6-mm × 25-cm; 5-µm packing L1

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**System suitability**

**Samples:** *System suitability solution* and *Standard solution*

[Note—See *Table 1* for the corresponding relative retention times.]

**Suitability requirements**

**Resolution:** NLT 2.0 between chloroquine and chloroquine related compound A, *System suitability solution*

**Tailing factor:** NMT 2.0 for chloroquine, *Standard solution*

**Relative standard deviation:** NMT 0.7% for chloroquine, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of chloroquine phosphate ($C_{18}H_{26}ClN_3 \cdot 2H_3PO_4$) in the portion of Chloroquine Phosphate taken:

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

$r_U$ = peak response from the *Sample solution*

$r_S$ = peak response from the *Standard solution*

$C_S$ = concentration of USP Chloroquine Phosphate RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Chloroquine Phosphate in the *Sample solution* (mg/mL)

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

## IMPURITIES

• **Organic Impurities**

**Mobile phase, System suitability solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**Standard solution:** Use the *System suitability solution*.

**Sample solution:** 2 mg/mL of Chloroquine Phosphate in *Mobile phase*

**System suitability**

**Sample:** *System suitability solution*

[Note—See *Table 1* for the corresponding relative retention times.]

**Suitability requirements**

**Resolution:** NLT 2.0 between chloroquine and chloroquine related compound A and NLT 2 between adjacent impurities

**Tailing factor:** NMT 2.0 for peaks corresponding to chloroquine phosphate, phenol, hydroxychloroquine sulfate, chloroquine related compound A, chloroquine related compound D, chloroquine related compound E, and chloroquine related compound G

**Relative standard deviation:** NMT 5.0% for chloroquine phosphate, phenol, hydroxychloroquine sulfate, chloroquine related compound A, chloroquine related compound D, chloroquine related compound E, and chloroquine related compound G

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity, other than chloroquine related compound G, in the portion of Chloroquine Phosphate taken:

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

$r_U$ = peak response of each impurity from the *Sample solution*

$r_S$ = peak response of the corresponding USP Reference Standard from the *Standard solution*

$C_S$ = concentration of the corresponding USP Reference Standard in the *Standard solution* (mg/mL)

$C_U$ = concentration of Chloroquine Phosphate in the *Sample solution* (mg/mL)

Calculate the percentage of chloroquine related compound G and any other unspecified impurity in the portion of Chloroquine Phosphate taken:

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

$r_U$ = peak response of chloroquine related compound G or any other impurity from the *Sample solution*

$r_S$ = peak response of USP Chloroquine Phosphate RS from the *Standard solution*

$C_S$ = concentration of USP Chloroquine Phosphate RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Chloroquine Phosphate in the *Sample solution* (mg/mL)

**Acceptance criteria:** See *Table 1*. Disregard any peak less than 0.05%.

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Phenol | 0.2 | 0.1 |
| Chloroquine related compound G | 0.27 | 0.1 |
| Chloroquine related compound D | 0.42 | 0.50 |

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Hydroxychloroquine sulfate | 0.49 | 0.1 |
| Chloroquine related compound A | 0.73 | 0.1 |
| Chloroquine phosphate | 1.0 | — |
| Chloroquine related compound E | 1.5 | 0.1 |
| Any other individual impurity | — | 0.10 |
| Total impurities | — | 2.0 |

**SPECIFIC TESTS**

• **Loss on Drying** ⟨731⟩

**Analysis:** Dry a sample at 105° for 16 h.

**Acceptance criteria:** NMT 2.0%

**ADDITIONAL REQUIREMENTS**

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP Chloroquine Phosphate RS

USP Chloroquine Related Compound A RS

4,7-Dichloroquinoline.

$C_9H_5Cl_2N$ 198.05

USP Chloroquine Related Compound D RS

Monoethyl chloroquine;

7-Chloro-4-{[4-(ethylamino)-1-methylbutyl]amino}quinoline.

$C_{16}H_{22}ClN_3$ 291.82

USP Chloroquine Related Compound E RS

5-Chloroquine isomer;

*N*$^4$-(5-Chloroquinolin-4-yl)-*N*$^1$,*N*$^1$-diethylpentane-1,4-diamine oxalate.

$C_{18}H_{26}ClN_3 \cdot C_2H_2O_4$ 409.91

USP Chloroquine Related Compound G RS

4-[(7-Chloroquinolin-4-yl)amino]-*N*,*N*-diethylpentan-1-amine oxide sulfate.

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

USP Hydroxychloroquine Sulfate RS

USP Phenol RS



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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| CHLOROQUINE PHOSPHATE | Documentary Standards Support | SM12020 Small Molecules 1 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM12020 Small Molecules 1 |

**Chromatographic Database Information:** Chromatographic Database

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