Edition: BP 2025 (Ph. Eur. 11.6 update)

Hydroxychloroquine Tablets

General Notices

Action and use

Antiprotozoal (malaria); used in the treatment of rheumatoid arthritis.

DEFINITION

Hydroxychloroquine Tablets contain Hydroxychloroquine Sulfate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of hydroxychloroquine sulfate, $C_{18}H_{26}ClN_3O,H_2SO_4$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Dissolve a quantity of the powdered tablets containing 0.1 g of Hydroxychloroquine Sulfate in a mixture of 10 mL of *water* and 2 mL of 2M *sodium hydroxide* and extract with two 20-mL quantities of *chloroform*. Wash the chloroform extracts with *water*, dry with *anhydrous sodium sulfate*, evaporate to dryness and dissolve the residue in 2 mL of *chloroform IR*. The *infrared absorption spectrum* of the resulting solution, Appendix II A, is concordant with the *reference spectrum* of hydroxychloroquine *(RS 182)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.022% w/v of Hydroxychloroquine Sulfate, at the maximum at 343 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.022% w/v solution of *hydroxychloroquine sulfate BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of hydroxychloroquine sulfate, $C_{18}H_{26}ClN_3O,H_2SO_4$, in the medium from the absorbances obtained and using the declared content of $C_{18}H_{26}ClN_3O,H_2SO_4$ in *hydroxychloroquine sulfate BPCRS*.

LIMITS

The amount of hydroxychloroquine sulfate released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase A.

(1) Shake a quantity of the powdered tablets containing 0.2 g of Hydroxychloroquine Sulfate in 150 mL of mobile phase A, dilute to 200 mL and filter. Dilute 1 volume of the resulting solution to 10 volumes.
(2) Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume to 5 volumes.
(3) 0.00004% w/v of *2-[4-[(7-chloro-4-quinolinyl)amino]pentyl] amino ethanol sulfate BPCRS* (impurity C).
(4) 0.0001% w/v of *hydroxychloroquine sulfate BPCRS* and 0.0001% w/v of *2-[4-[(7-chloro-4-quinolinyl)amino]pentyl] amino ethanol sulfate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5µm) (Inertsil ODS3 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.2 volumes of *orthophosphoric acid*, 10 volumes of *acetonitrile R1* and 90 volumes of *water*.

Mobile phase B 0.1 volumes of *orthophosphoric acid*, 20 volumes of *water* and 80 volumes of *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-2	100	0	isocratic
2-10	100→85	0→15	linear gradient
10-18	85→100	15→0	linear gradient
18-25	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to hydroxychloroquine (retention time about 5 minutes) are: impurity C, about 0.95; impurity B, about 1.5 and impurity G, about 2.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity C and hydroxychloroquine is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.4%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%).

the sum of the areas of any *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase A.

(1) Weigh and powder 20 tablets. Shake a quantity of the powdered tablets containing 0.2 g of Hydroxychloroquine Sulfate with 150 mL of mobile phase A, dilute to 200 mL and filter. Dilute 1 volume of the filtrate to 10 volumes.
(2) 0.01% w/v of *hydroxychloroquine sulfate BPCRS*.
(3) 0.0001% w/v of *hydroxychloroquine sulfate BPCRS* and 0.0001% w/v of *2-[4-[(7-chloro-4-quinolinyl)amino]pentyl] amino ethanol sulfate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity C and hydroxychloroquine is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of hydroxychloroquine sulfate, $C_{18}H_{26}ClN_3O,H_2SO_4$, in the tablets using the declared content of $C_{18}H_{26}ClN_3O,H_2SO_4$ in *hydroxychloroquine sulfate BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities B, C and G listed under Hydroxychloroquine Sulfate.