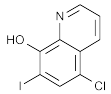
Clioquinol



C_9H_5ClINO 305.50
8-Quinolinol, 5-chloro-7-iodo-.
5-Chloro-7-iodo-8-quinolinol [130-26-7].

» Clioquinol, dried over phosphorus pentoxide for 5 hours, contains not less than 93.0 per cent and not more than 100.5 per cent of C_9H_5ClINO (the 5-chloro-7-iodo-8-quinolinol isomer).

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Clioquinol RS

Identification—

A: Prepare a Standard solution as directed for *Standard preparation* in the *Assay*, except to use 1.0 mL of pyridine instead of the *Internal standard solution*, and chromatograph as directed in the *Assay:* the chromatogram of the *Assay preparation* obtained in the *Assay* exhibits a peak for clioquinol, the retention time of which corresponds with that exhibited by the Standard solution.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 5 µg per mL.

Medium: 3 N hydrochloric acid.

Absorptivities at 267 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: Heat 100 mg with 5 mL of sulfuric acid: copious violet vapors of iodine are evolved.

Loss on drying ⟨731⟩**—**Dry it over phosphorus pentoxide for 5 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.5%.

Free iodine and iodide—Shake 1.0 g with 20 mL of water for 30 seconds, allow to stand for 5 minutes, and filter. To 10 mL of the filtrate add 1 mL of 2 N sulfuric acid, then add 2 mL of chloroform, and shake: no violet color appears in the chloroform (*free iodine*). To the mixture add 5 mL of 2 N sulfuric acid and 1 mL of potassium dichromate TS, and shake for 15 seconds: the color in the chloroform layer is no deeper than that produced in a control test made in the following manner: Dilute 2.0 mL of potassium iodide solution (1 in 6000) with water to 10 mL, add 6 mL of 2 N sulfuric acid, 1 mL of potassium dichromate TS, and 2 mL of chloroform, and shake for 15 seconds (*0.05% of iodide*).

Assay—

Internal standard solution—Prepare a solution of pyrene in pyridine containing 2 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Clioquinol RS in a mixture of pyridine and *n*-hexane (4:1) to obtain a Standard solution having a known concentration of about 3 mg per mL. Transfer 1.0 mL of the Standard solution to a screw-capped glass vial fitted with a septum, add 1.0 mL of bis(trimethylsilyl)acetamide and 1.0 mL of *Internal standard solution*, attach the cap, and mix. Heat in a water bath at 50° for 15 minutes, and then cool to ambient temperature.

Assay preparation—Transfer about 75 mg of Clioquinol, previously dried and accurately weighed, to a 25-mL volumetric flask, dissolve in a mixture of pyridine and *n*-hexane (4:1), dilute with the same solvent to volume, and mix. Transfer 1.0 mL of this solution to a screw-capped glass vial fitted with a septum, add 1.0 mL of bis(trimethylsilyl)acetamide and 1.0 mL of *Internal standard solution*, attach the cap, and mix. Heat in a water bath at 50° for 15 minutes, then cool to ambient temperature.

Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector, and contains a 1.83-m × 2-mm glass column packed with 3% liquid phase G3 on 80- to 100-mesh support S1AB. The injection port and detector temperatures are maintained at 170° and 250°, respectively, and the initial column temperature is 200° for a conditioning period of not less than 16 hours (not connected to the detector) and is then reduced to 165 °. Helium is used as the carrier gas at a flow rate of about 30 mL per minute, and hydrogen and air are introduced into the detector at rates of 25 mL and 500 mL per minute, respectively. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the resolution, *R,* between the clioquinol and the internal standard peaks is not less than 3.

Procedure—Separately inject equal volumes (about 1 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times for clioquinol and pyrene are about 0.6 and 1.0, respectively. Calculate the quantity, in mg, of C_9H_5ClINO in the Clioquinol taken by the formula:

$$25C(R_U / R_S)$$

in which *C* is the concentration, in mg per mL, of USP Clioquinol RS in the Standard solution used to prepare the *Standard preparation*; and R_U and R_S are the ratios of the peak responses of the clioquinol peak to the internal standard peak obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Clioquinol Cream

» Clioquinol Cream contains not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of C_9H_5ClINO in a suitable cream base.

Packaging and storage—Preserve in collapsible tubes or tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Clioquinol RS

Identification—

A: Prepare a Standard solution as directed for *Standard preparation* in the *Assay*, except to use 1.0 mL of pyridine instead of the *Internal standard solution*, and chromatograph as directed in the *Assay:* the chromatogram of the *Assay preparation* obtained in the *Assay* exhibits a peak for clioquinol, the retention time of which corresponds with that exhibited by the Standard solution.

B: Place a quantity of Cream, equivalent to about 25 mg of clioquinol, in a 100-mL volumetric flask, add about 75 mL of dilute hydrochloric acid (1 in 4), and heat on a steam bath to melt the cream, shaking vigorously to extract the clioquinol. Cool under running water, and add dilute hydrochloric acid (1 in 4) to volume. Filter through paper, and dilute 3 mL of the filtrate with dilute hydrochloric acid (1 in 4) to 100 mL: the UV absorption spectrum of this solution exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Clioquinol RS, concomitantly measured.

Assay—

Internal standard solution, *Standard preparation*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Clioquinol*.

Assay preparation—Transfer an accurately weighed portion of Cream, equivalent to about 150 mg of clioquinol, to a 60-mL separator. Place the separator on its side in a vacuum oven at a