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Doxepin Hydrochloride Oral Solution

DEFINITION

Doxepin Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of doxepin ($C_{19}H_{21}NO$).

IDENTIFICATION

• **A.**

Mobile phase: Add 0.2 mL of diethylamine to a solution containing 250 mL of chloroform and 750 mL of acetonitrile in a vacuum flask. Before use, degas the contents of the flask by stirring vigorously with a magnetic stirrer, while applying vacuum, for 10 min.

Standard solution: 0.44 mg/mL of USP Doxepin Hydrochloride RS in *Mobile phase*

Sample solution: To 5.0 mL of the Oral Solution in a 60-mL separator add 1 mL of sodium hydroxide solution (1 in 25), 1 g of sodium chloride, and 5.0 mL of ethyl acetate. Shake the mixture vigorously for 1 min. Allow the phases to separate, transfer 1.0 mL of the clear upper phase to a 25-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 2-mm × 50-cm; packed with silica microspheres

Flow rate: 0.4 mL/min

Injection volume: 4 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The chromatogram of the *Sample solution* exhibits two peaks having retention times that are identical with those obtained with the *Standard solution*.

ASSAY

• **Procedure**

Diluent: Dilute hydrochloric acid (1 in 120)

Standard stock solution: 1.1 mg/mL of USP Doxepin Hydrochloride RS (1.0 mg/mL of doxepin) in *Diluent*

Standard solution: Dilute 4.0 mL of *Standard stock solution* to 50 mL using *Diluent*. Transfer 15.0 mL of the resulting solution to a 125-mL separator, and extract with two 20-mL portions of ether. Dilute 10.0 mL of the extracted aqueous phase to 25.0 mL using *Diluent*.

Sample stock solution: Nominally 1 mg/mL of doxepin from Oral Solution in *Diluent*

Sample solution: Dilute 4.0 of *Sample stock solution* to 50 mL using *Diluent*. Transfer 15.0 mL of the resulting solution to a 125-mL separator, and extract with two 20-mL portions of ether. Dilute 10.0 mL of the extracted aqueous phase to 25.0 mL using *Diluent*.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 292 nm

Cell: 1 cm

Blank: Diluent

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxepin ($C_{19}H_{21}NO$) in the Oral Solution taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

C_U = nominal concentration of doxepin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of doxepin, 279.38

M_{r2} = molecular weight of doxepin hydrochloride, 315.84

Acceptance criteria: 90.0%–110%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements for Oral Solution packaged in single-unit containers

• **Deliverable Volume ⟨698⟩:** Meets the requirements for Oral Solution packaged in multiple-unit containers

SPECIFIC TESTS

• **pH ⟨791⟩**

Analysis: Allow the portion of Oral Solution under test to remain in contact with the electrodes for 15 min before the measurement.

Acceptance criteria: 4.0–7.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **Labeling:** Label the Oral Solution to indicate that each dose is to be diluted with water or other suitable fluid to approximately 120 mL just before administration.

• **USP Reference Standards ⟨11⟩**

USP Doxepin Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
DOXEPIN HYDROCHLORIDE ORAL SOLUTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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