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Doxepin Hydrochloride Capsules

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DEFINITION

Doxepin Hydrochloride Capsules contain an amount of Doxepin Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of doxepin ($C_{19}H_{21}NO$).

IDENTIFICATION

- **A.** The retention times of the major peaks for the (E)- and (Z)-isomers of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- **B.** The UV spectra of the major peaks for the (E)- and (Z)-isomers of doxepin in the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Solution A: 27.6 g/L of [monobasic sodium phosphate](#) in [water](#)

Mobile phase: [Methanol](#) and *Solution A* (30:70). Adjust with diluted [phosphoric acid](#) to a pH of 2.5.

Standard solution: 0.11 mg/mL of [USP Doxepin Hydrochloride RS](#) (equivalent to 0.1 mg/mL of doxepin) in *Mobile phase*

Sample stock solution: Nominally 0.57 mg/mL of doxepin hydrochloride (equivalent to 0.5 mg/mL of doxepin) from the contents of NLT 20 Capsules in *Mobile phase*, prepared as follows. Remove, as completely as possible, the contents of NLT 20 Capsules. Mix the combined contents, and transfer a suitable quantity of the powder, equivalent to 50 mg of doxepin, to a 100-mL volumetric flask. Add 70 mL of *Mobile phase*, and shake by mechanical means for 30 min. Dilute with *Mobile phase* to volume, and filter. Use the filtrate.

Sample solution: Nominally 0.1 mg/mL of doxepin from *Sample stock solution* in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4-mm × 12.5-cm; 5-μm packing [L7](#)

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 μL

Run time: NLT 2 times the retention time of the first peak of doxepin

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for the (E)- and (Z)-isomers are 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the (E)- and (Z)-isomers

Tailing factor: NMT 2.0 each for the (E)- and (Z)-isomers

Relative standard deviation: NMT 2.0% each for the (E)- and (Z)-isomers

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = [(r_{U(Z)} + r_{U(E)}) / (r_{S(Z)} + r_{S(E)})] \times (C_S / C_U) \times (M_1 / M_2) \times 100$$

$r_{U(Z)}$ = peak response of the (Z)-isomer from the *Sample solution*

$r_{U(E)}$ = peak response of the (E)-isomer from the *Sample solution*

$r_{S(Z)}$ = peak response of the (Z)-isomer from the *Standard solution*

$r_{S(E)}$ = peak response of the (E)-isomer from the *Standard solution*

C_s = concentration of doxepin hydrochloride 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%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#).

Test 1

Medium: [Water](#); 900 mL

Apparatus 1: 50 rpm

Time: 30 min

Standard solution: [USP Doxepin Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary, to the same concentration as the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 292 nm

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (A_u/A_s) \times C_s \times D \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

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)

D = dilution factor of the *Sample solution*, if necessary

M_{r1} = molecular weight of doxepin, 279.38

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of doxepin ($C_{19}H_{21}NO$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.15% w/v pepsin (1:10000 with albumin substrate) in [water](#); 900 mL. [NOTE—The *Medium* may appear hazy.]

Apparatus 1: 50 rpm

Time: 30 min

Dilute phosphoric acid: Transfer 6.5 mL of [phosphoric acid](#) to a 100-mL volumetric flask and dilute with [water](#) to volume.

Buffer: 1.42 g/L of [anhydrous dibasic sodium phosphate](#) in [water](#), adjust with dilute phosphoric acid to a pH of 7.7

Mobile phase: [Acetonitrile](#) and *Buffer* (60:40)

Standard stock solution: 0.63 mg/mL of [USP Doxepin Hydrochloride RS](#) (equivalent to 0.6 mg/mL of doxepin) prepared as follows. Transfer a suitable quantity of [USP Doxepin Hydrochloride RS](#) to an appropriate volumetric flask. Add 70% of the flask volume of *Medium*. Sonicate for about 5 min and dilute with *Medium* to volume.

Standard solution: ($L/800$) mg/mL of [USP Doxepin Hydrochloride RS](#) (equivalent to [$L/900$] mg/mL of doxepin) from *Standard stock solution*, where L is the label claim in mg/Capsule, prepared as follows. Transfer a portion of *Standard stock solution* to an appropriate volumetric flask and dilute with *Medium* to volume. Pass the resulting solution through a suitable filter discarding the first few milliliters.

Sample solution: Pass a portion of the solution under test through a suitable filter discarding the first few milliliters.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3.5-μm packing [L1](#)

Column temperature: 40°