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Amitriptyline Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-amitriptyline-hcl-tabs-20230630.

DEFINITION

Amitriptyline Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** 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: 11.04 g of [monobasic sodium phosphate](#) in 900 mL of [water](#). Adjust with [phosphoric acid](#) to a pH of 2.5 ± 0.5 , and dilute to make 1000 mL.

Mobile phase: [Acetonitrile](#) and *Buffer* (42:58)

Standard solution: 0.2 mg/mL of [USP Amitriptyline Hydrochloride RS](#) in *Mobile phase*

Sample solution: Nominally 0.2 mg/mL of amitriptyline hydrochloride in *Mobile phase*, prepared as follows. Transfer NLT 20 Tablets to a suitable volumetric flask, add 50% of the flask volume of *Mobile phase*, and shake the mixture for 1 h or until the Tablets have disintegrated. Dilute with *Mobile phase* to volume, and filter. Dilute the clear filtrate with *Mobile phase* to obtain a solution with a nominal concentration of 0.2 mg/mL of amitriptyline hydrochloride.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification A*, use a diode array detector in the range of 220–400 nm.

Column: 3.9-mm $\times$ 30-cm; 10- μ m packing [L1](#)

Flow rate: 2 mL/min

Injection volume: 20 μ L

Run time: NLT 1.5 times the retention time of amitriptyline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) in each Tablet 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 Amitriptyline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#)

▲**Test 1**▲ (RB 26-May-2023)

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: ($L/900$) mg/mL of [USP Amitriptyline Hydrochloride RS](#) in *Medium*, where L is the Tablet label claim in milligrams. Dilute with *Medium*, if necessary.

Sample solution: Pass a portion of solution under test through a suitable filter. Dilute with *Medium*, if necessary.

Instrumental conditions

Analytical wavelength: UV 239 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of [USP Amitriptyline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

D = dilution factor, if necessary

Tolerances: NLT 75% (Q) of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) is dissolved.

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

Medium: 0.1 N [hydrochloric acid](#); 500 mL, deaerated, if necessary

Apparatus 1: 100 rpm

Time: 30 min

Diluted phosphoric acid: [Phosphoric acid](#) and [water](#) (1:10)

Buffer: Dissolve 0.87 g of [potassium phosphate dibasic](#) in 1 L of [water](#). Adjust with *Diluted phosphoric acid* to a pH of 7.0. Add 1.0 mL of [triethylamine](#). Adjust with *Diluted phosphoric acid* to a pH of 7.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (35:65)

Standard solution: ($L/500$) mg/mL of [USP Amitriptyline Hydrochloride RS](#) in *Medium*, where L is the label claim in mg/Tablet. Sonicate to dissolve, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, discarding the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: NLT 1.5 times the retention time of amitriptyline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

r_U = peak response of amitriptyline from the *Sample solution*

r_S = peak response of amitriptyline from the *Standard solution*

C_S = concentration of [USP Amitriptyline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

V = volume of the *Medium*, 500 mL