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Tramadol Hydrochloride and Acetaminophen Tablets

DEFINITION

Tramadol Hydrochloride and Acetaminophen Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) and acetaminophen ($C_8H_9NO_2$).

IDENTIFICATION

- **A.** The retention times of the *Tramadol sample solution* and the *Acetaminophen sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Mobile phase: [Tetrahydrofuran](#), [triethylamine](#), [water](#), and [trifluoroacetic acid](#) (8:0.1:92:0.1). The apparent pH of the final solvent mixture should be between 2.2 and 2.4.

Diluent: [Methanol](#) and [water](#) (1:9)

Standard solution: 0.065 mg/mL of [USP Acetaminophen RS](#) and 0.075 mg/mL of [USP Tramadol Hydrochloride RS](#) in *Diluent*. Sonication may be used to aid dissolution.

Sample stock solution: Weigh NLT 20 Tablets, and determine the average Tablet weight. Grind the Tablets into a fine powder, and transfer an amount equivalent to one Tablet to a 50-mL volumetric flask. Add 30 mL of *Diluent* with continuous shaking to disperse the powder. Sonicate for 15 min with intermittent shaking, and shake the flask on a mechanical shaker for 30 min. Dilute with *Diluent* to volume, and mix well. Centrifuge the suspension, and use the supernatant for subsequent dilutions.

Tramadol sample solution: Nominally 75 µg/mL of tramadol hydrochloride in *Diluent* from the *Sample stock solution*

Acetaminophen sample solution: Nominally 65 µg/mL of acetaminophen in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 216 nm for tramadol hydrochloride and UV 249 nm for acetaminophen

Column: 4.6-mm × 15-cm; 5-µm packing [L11](#)

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: 4 times the retention time of acetaminophen

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 10.0 between acetaminophen and tramadol

Tailing factor: NMT 2.0 for each analyte

Relative standard deviation: NMT 2.0% for each analyte

Analysis

Samples: *Standard solution*, *Tramadol sample solution*, and *Acetaminophen sample solution*

Calculate the percentage of the labeled amount of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of tramadol from the *Tramadol sample solution*

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

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

C_u = nominal concentration of tramadol hydrochloride in the *Tramadol sample solution* (mg/mL)

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of acetaminophen from the *Acetaminophen sample solution*

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

C_s = concentration of [USP Acetaminophen RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of acetaminophen in the *Acetaminophen sample solution* (mg/mL)

Acceptance criteria

Tramadol hydrochloride: 90.0%–110.0% of the labeled amount of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$)

Acetaminophen: 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$)

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

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

Apparatus 2: 50 rpm

Time: 30 min

Buffer solution: 6.8 mg/mL of [monobasic potassium phosphate](#) in water. Adjust with phosphoric acid to a pH of 2.50.

Mobile phase: [Acetonitrile](#) and *Buffer solution* (1:4)

Standard solution: 0.36 mg/mL of [USP Acetaminophen RS](#) and 0.04 mg/mL of [USP Tramadol Hydrochloride RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 272 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L7](#)

Column temperature: 25°

Flow rate: 1 mL/min

Injection volume: 25 μL

Run time: 2 times the retention time of tramadol

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for acetaminophen and tramadol are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 5.0 between the acetaminophen and tramadol peaks

Relative standard deviation: NMT 2.0% for both the acetaminophen and tramadol peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) and tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) dissolved:

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

r_U = peak response of acetaminophen or tramadol from the *Sample solution*

r_S = peak response of acetaminophen or tramadol from the *Standard solution*

C_s = concentration of [USP Acetaminophen RS](#) or [USP Tramadol Hydrochloride RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim for acetaminophen or tramadol hydrochloride (mg/Tablet)