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Tramadol Hydrochloride Tablets

DEFINITION

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

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample solution: Transfer powdered Tablets, equivalent to 200 mg of tramadol hydrochloride, into a 50-mL volumetric flask, add 20 mL of dichloromethane, and sonicate. Filter, and transfer the clear supernatant to a separating funnel. Extract the dichloromethane layer with two 10-mL portions of 2 N sodium hydroxide, and discard the aqueous layer. Dry the dichloromethane layer over anhydrous sodium sulfate, and filter. Evaporate this solution to dryness under a stream of nitrogen.

Acceptance criteria: Meet the requirements

• **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**

Solution A: Dissolve 5 mL of perchloric acid in 950 mL of water in a 1-L volumetric flask. Add 4 mL of 25% ammonia water, dilute with water to volume, and mix. Adjust with 25% ammonia water to a pH of 2.2 ± 0.2.

Mobile phase: Acetonitrile and *Solution A* (23:77)

Standard solution: 0.1 mg/mL of USP Tramadol Hydrochloride RS in 0.1 N hydrochloric acid

Sample solution: Finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to 50 mg of tramadol hydrochloride, into a 100-mL volumetric flask. Add 70 mL of 0.1 N hydrochloric acid, sonicate for 5 min, and shake for 10 min. Dilute with 0.1 N hydrochloric acid to volume, and mix. Pass a portion of this solution through a suitable filter, discarding the first 20 mL of the filtrate. Transfer 10 mL of the clear filtrate into a 50-mL volumetric flask, dilute with 0.1 N hydrochloric acid to volume, and mix.

Chromatographic system

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

Mode: LC

Detector: UV 273 nm

Column: 3.9-mm × 15-cm; packing L7

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *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 from the *Sample solution*

r_S = peak response 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 *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Solution A, Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Standard solution: 0.055 mg/mL of USP Tramadol Hydrochloride RS in *Medium*

Sample solution: Withdraw 9 mL from the dissolution vessel, and pass through a suitable filter. Discard the first 3 mL of the filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

Procedure for content uniformity

Solution A, Mobile phase, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: Transfer 1 whole Tablet to a 100-mL volumetric flask, add 70 mL of 0.1 N hydrochloric acid, sonicate until the Tablet is completely disintegrated, and shake for 10 min. Dilute with 0.1 N hydrochloric acid to volume, and mix. Pass a portion of this solution through a suitable filter, discarding the first 20 mL of the filtrate. Transfer 10 mL of the clear filtrate into a 50-mL volumetric flask, dilute with 0.1 N hydrochloric acid to volume, and mix.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) in the 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 Tramadol Hydrochloride RS in the *Standard solution* (mg/mL)

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

IMPURITIES

Organic Impurities

• **Procedure**

Solution A and **Mobile phase:** Prepare as directed in the *Assay*.

System suitability solution: 0.2 mg/mL each of USP Tramadol Hydrochloride RS and USP Tramadol Related Compound A RS in *Mobile phase*

Standard solution: 6 µg/mL of USP Tramadol Hydrochloride RS in *Mobile phase*

System sensitivity solution: Transfer 5 mL of the *Standard solution* into a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Sample solution: Finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to 200 mg of tramadol hydrochloride, into a 50-mL volumetric flask. Add about 35 mL of *Mobile phase,* sonicate for 5 min, and shake for 10 min. Dilute with *Mobile phase* to volume, and mix. Pass a portion of this solution through a suitable filter, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 273 nm

Column: 3.9-mm × 15-cm; packing L7

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Samples: *System suitability solution*, *Standard solution*, and *System sensitivity solution*

Suitability requirements

Resolution: NLT 2.0 between tramadol related compound A and tramadol, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*; NMT 10%, *System sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each individual impurity from the *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 *Sample solution* (mg/mL)

F = relative response factor (see *Impurity Table 1*)

[NOTE—Disregard any peak that is shown to be due to solvents or excipients.]

Acceptance criteria

Individual unspecified impurities: See *Impurity Table 1*.

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
RS,SR-1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohexanol hydrochloride[a]	0.85	1.0	0.2
Tramadol hydrochloride	1.00	—	—
1-(3-Methoxyphenyl)-2-(dimethylaminomethyl) cyclohex-1-ene hydrochloride	5.27	1.0	0.2
1-(3-Methoxyphenyl)-2-(dimethylaminomethyl) cyclohex-6-ene hydrochloride	4.27	1.27	0.2
Individual unspecified impurity	—	1.0	0.2
Total impurities	—	—	0.7%

[a] Tramadol related compound A.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Tramadol Hydrochloride RS

USP Tramadol Related Compound A RS

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

Topic/Question	Contact	Expert Committee
TRAMADOL HYDROCHLORIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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