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# Tramadol Hydrochloride Extended-Release Tablets

## DEFINITION

Tramadol Hydrochloride Extended-Release 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

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

**Change to read:**

- **B.**  [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy: 197U](#)  (CN 1-MAY-2020)

**Sample solution:** Use the *Sample solution* from the Assay.

**Analysis:** Using separate 1-cm cells, record the UV spectrum of the *Sample solution* and *Standard solution*.

**Acceptance criteria:** The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same wavelength as that of a similar solution of the *Standard solution*.

## ASSAY

### PROCEDURE

**Mobile phase:** Tetrahydrofuran, trifluoroacetic acid, triethylamine, and water (10:0.1:0.1:90). [NOTE—Maintain at a pH range of 2.2–2.4.]

**Standard stock solution:** 1 mg/mL of [USP Tramadol Hydrochloride RS](#) prepared by dissolving in 20% of the flask volume of methanol.

Sonicate if necessary, and dilute with water to volume.

**Standard solution:** 0.13 mg/mL of [USP Tramadol Hydrochloride RS](#) in *Mobile phase*, from the *Standard stock solution*

**Sample solution:** Nominally 0.13 mg/mL of tramadol hydrochloride in *Mobile phase*. Prepare by dissolving 10 Tablets in 20% of the flask volume of methanol, in a water bath for 60 min, at about 60° with intermittent shaking. Sonicate for 10 min. Add 40% of the flask volume of water, and sonicate for 30 min. If all Tablets are not fully disintegrated, then continue to sonicate until disintegration is completed. Shake the flask vigorously for 10 min using a mechanical shaker, and dilute with water to volume. Centrifuge a portion of the solution, pass through a suitable nylon filter, and collect the filtrate after discarding the first 2 mL. Pipet 5.0 mL of the filtrate into a 200-mL volumetric flask, and dilute with *Mobile phase* to volume.

### Chromatographic system

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

**Mode:** LC

**Detector:** UV 216 nm

**Column:** 4.6-mm × 15-cm; 5-μm packing L11

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 10 μL

### System suitability

**Sample:** *Standard solution*

#### Suitability requirements

**Column efficiency:** NLT 2000 theoretical plates

**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 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

**Change to read:**

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

### Test 1

**Medium:** 0.1 N hydrochloric acid; 900 mL

**Apparatus 1:** 75 rpm

**Times:** 2, 4, 8, 10, and 16 h

**Standard solution:** ( $L/900$ ) mg/mL of [USP Tramadol Hydrochloride RS](#) in *Medium*, where  $L$  is the label claim in mg/Tablet

**Sample solution:** Withdraw 10 mL of the solution under test, and pass through a suitable filter of 0.45- $\mu$ m pore size, discarding the first 4 mL of the filtrate. Replace the volume withdrawn with the same volume of *Medium* preheated at  $37.0 \pm 0.5^\circ$ .

### Instrumental conditions

**Mode:** UV

**Analytical wavelength:** 271 nm

**Cell:**  $\blacktriangle 5$  mm  $\blacktriangle$  (ERR 1-May-2019)

**Blank:** *Medium*

### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the concentration ( $C_i$ ), in mg/mL, of tramadol hydrochloride ( $C_{16}H_{25}NO_2 \cdot HCl$ ) in the sample withdrawn from the vessel at each time point ( $i$ ):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

$A_U$  = absorbance of the *Sample solution*

$A_S$  = absorbance of the *Standard solution*

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

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

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_5 = \{(C_5 \times V) + [(C_4 + C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$C_i$  = concentration of tramadol hydrochloride in the portion of the sample withdrawn at the specified time point (mg/mL)

$V$  = volume of *Medium*, 900 mL

$L$  = label claim (mg/Tablet)

$V_S$  = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

**Tolerances:** See [Table 1](#).

**Table 1**

| Time Point<br>(i) | Time<br>(h) | Amount<br>Dissolved<br>(%) |
|-------------------|-------------|----------------------------|
| 1                 | 2           | NMT 15                     |
| 2                 | 4           | 10–40                      |
| 3                 | 8           | 50–85                      |
| 4                 | 10          | 65–95                      |
| 5                 | 16          | NLT 80                     |

The percentages of the labeled amount of tramadol hydrochloride ( $C_{16}H_{25}NO_2 \cdot HCl$ ) released at the times specified conform to

[Dissolution \(711\)](#), [Acceptance Table 2](#).

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

**Medium:** 0.1 N hydrochloric acid; 900 mL

**Apparatus 1:** 75 rpm

**Times:** 2, 4, 8, 10, and 16 h

**Standard stock solution:** 5 mg/mL of [USP Tramadol Hydrochloride RS](#) in *Medium*. Sonicate if necessary.

**Standard solution:** Dilute the *Standard stock solution* with *Medium* to obtain a concentration of [USP Tramadol Hydrochloride RS](#) (see [Table 2](#)).

**Table 2**

| Label Claim<br>(mg/Tablet) | Concentration of<br><a href="#">USP Tramadol Hydrochloride RS</a><br>(mg/mL) |
|----------------------------|------------------------------------------------------------------------------|
| 100                        | 0.075                                                                        |
| 200                        | 0.100                                                                        |
| 300                        | 0.200                                                                        |

**Sample solution:** Pass a portion of the solution under test through a suitable filter.

**Instrumental conditions**

**Mode:** UV

**Analytical wavelength:** 271 nm

**Cell**

**For Tablets labeled to contain 100 mg:** 1 cm

**For Tablets labeled to contain 200 and 300 mg:** 0.5 cm

**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 at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

$A_U$  = absorbance of the *Sample solution*

$A_S$  = absorbance of the *Standard solution*

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

$V$  = volume of *Medium*, 900 mL

$L$  = label claim (mg/Tablet)