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Tramadol Soluble Tablets

Details for the public consultation of this monograph are as follows:

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Notes	New Monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

μ-Opioid receptor (OP_3, MOR) agonist and noradrenaline reuptake inhibitor; analgesic.

DEFINITION

Tramadol Soluble Tablets contain Tramadol Hydrochloride.

The Soluble Tablets comply with the requirements stated under Tablets and with the following requirements.

Content of tramadol hydrochloride, $C_{16}H_{25}NO_2,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of powdered tablets containing 50 mg of Tramadol Hydrochloride with 20 mL of *water* for 5 minutes, filter and add 5 mL of 1M *sodium hydroxide* and extract with 25 mL of *dichloromethane*. Collect the organic extract, dry with *anhydrous sodium sulfate* and evaporate to dryness. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the reference spectrum of tramadol *(RS XXX)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of a solution containing 0.2% w/v of sodium chloride in a mixture of 7 volumes of 1M *hydrochloric acid* and 1000 volumes of *water*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

Solution A 30 volumes of *acetonitrile* and 70 volumes of 0.2% w/v of *trifluoroacetic acid* in *water*.

(1) After 10 minutes withdraw a sample of the medium and filter. Dilute with the dissolution medium, if necessary, to produce a solution containing 0.0056% w/v of Tramadol Hydrochloride.
(2) 0.0056% w/v of *tramadol hydrochloride BPCRS* in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Luna C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 270 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase 270 volumes of *acetonitrile* and 730 volumes of 0.2% w/v of *trifluoracetic acid in water*.

DETERMINATION OF CONTENT

Calculate the total content of tramadol hydrochloride, $C_{16}H_{25}NO_2$,HCl in the medium from the chromatograms obtained and using the declared content of $C_{16}H_{25}NO_2$,HCl in *tramadol hydrochloride BPCRS*.

LIMITS

The amount of tramadol hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in solution A.

Solution A 30 volumes of *acetonitrile* and 70 volumes of 0.2% w/v of *trifluoroacetic acid* in *water*.

(1) Mix with the aid of ultrasound and shaking, a quantity of powdered tablets containing 50 mg of Tramadol Hydrochloride in 80 mL and further dilute to 100 mL. Centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 500 volumes.
(3) 0.005% w/v each of *tramadol hydrochloride BPCRS* and *tramadol impurity A BPCRS*.
(4) Dilute 1 volume of solution (2) to 2 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (7.5 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3.5 µm) (Symmetry C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 270 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.2% w/v of *trifluoroacetic acid* in *water*.

Mobile phase B 0.2 volumes of *trifluoroacetic acid*, 20 volumes of *water* and 80 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-15	90→70	10→30	linear gradient
15-30	70→10	30→90	linear gradient
30-31	10→90	90→10	linear gradient
31-37	90	10	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless in the chromatogram obtained with solution (3), the *resolution* between impurity A and tramadol is at least 1.5.

The test is not valid unless, in the chromatogram obtained with solution (4), the *signal-to-noise ratio* of the peak due to tramadol is at least 15.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of tramadol hydrochloride in solution (2).

For the reporting threshold, use the concentration of tramadol hydrochloride in solution (4).

Tramadol retention time: about 12 minutes.

Relative retention: impurity D, about 0.6; impurity A, about 0.9; impurity C, about 1.5; impurity B, about 1.6 and impurity 1, about 1.1.

Correction factor: impurity 1, multiply by 1.5.

LIMITS

Unspecified impurities: 0.2%.

Total impurities: 1.0%.

Reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Mix with the aid of ultrasound and shaking, a quantity of powdered tablets containing 50 mg of Tramadol Hydrochloride with 40 mL of the mobile phase. Add sufficient mobile phase to produce 100 mL and centrifuge. Further dilute 1 volume of the supernatant liquid to 10 volumes with the mobile phase.
(2) 0.005% w/v of *tramadol hydrochloride BPCRS* in the mobile phase.
(3) 0.005% w/v each of *tramadol hydrochloride BPCRS* and *tramadol impurity A BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity A and tramadol is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{16}H_{25}NO_2$,HCl in the tablets from the chromatograms obtained and using the declared content of $C_{16}H_{25}NO_2$,HCl in *tramadol hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A - D listed under *Tramadol Hydrochloride* and:


1. 1-[(1S,2S)-2-hydroxy-2-(3-methoxyphenyl)cyclohexyl]-N,N-dimethylmethanamine oxide, Tramadol N-oxide

1. 1-[(1S,2S)-2-hydroxy-2-(3-methoxyphenyl)cyclohexyl]-N,N-dimethylmethanamine oxide, Tramadol N-oxide