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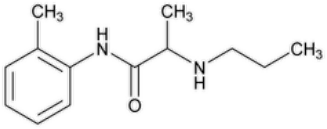
Prilocaine



$C_{13}H_{20}N_2O$ 220.31

Propanamide, *N*-(2-methylphenyl)-2-(propylamino)-;

2-(Propylamino)-*o*-propionotoluidide;

(*RS*)-*N*-(2-Methylphenyl)-2-(propylamino)propanamide CAS RN®: 721-50-6; UNII: 046O35D44R.

DEFINITION

Prilocaine contains NLT 98.0% and NMT 102.0% of prilocaine ($C_{13}H_{20}N_2O$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

Analysis: Because of the low melting point of prilocaine, the mortar, pestle, and potassium bromide must be at ambient temperature. Record the IR spectrum using the diffuse reflectance technique.

Acceptance criteria: Meets 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**

Buffer: 0.18 g/L of monobasic sodium phosphate and 2.89 g/L of dibasic sodium phosphate dihydrate in water

Mobile phase: Acetonitrile and *Buffer* (27:73)

System suitability solution: 2.5 µg/mL of USP Prilocaine RS and 3.0 µg/mL of USP Prilocaine Related Compound B RS in *Mobile phase*

Standard solution: 0.3 mg/mL of USP Prilocaine Hydrochloride RS in *Mobile phase*

Sample solution: 0.25 mg/mL of Prilocaine in *Mobile phase*

[Note—Sonication may be needed to aid dissolution for the *Standard solution* and the *Sample solution*.]

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: At least 1.3 times the retention time of prilocaine

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between prilocaine and prilocaine related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.73, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of prilocaine ($C_{13}H_{20}N_2O$) in the portion of Prilocaine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

C_U = concentration of Prilocaine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of prilocaine, 220.31

M_{r2} = molecular weight of prilocaine hydrochloride, 256.77

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Limit of Prilocaine Related Compound A**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 1.3 µg/mL of USP Prilocaine Related Compound A RS in *Mobile phase*

Sample solution: 10 mg/mL of Prilocaine in *Mobile phase*

System suitability

Sample: *Standard solution*

Suitability requirements

Signal-to-noise ratio: NLT 10

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: Any peak corresponding to prilocaine related compound A (*o*-toluidine) in the *Sample solution* is NMT the response of the major peak in the *Standard solution* (0.01%).

- **Organic Impurities**

Buffer, Mobile phase, and **System suitability solution:** Proceed as directed in the *Assay*.

Sample solution: 2.5 mg/mL of Prilocaine in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay*, except for the run time.

Run time: At least 1.5 times the retention time of prilocaine

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for prilocaine and prilocaine related compound B are about 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 3.0 between prilocaine and prilocaine related compound B

Signal-to-noise ratio: NLT 10 for prilocaine

Analysis

Sample: *Sample solution*

Check the stability of the baseline by injecting *Mobile phase*.

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

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = individual peak response for each impurity

r_T = sum of all the peak responses

Acceptance criteria

Individual impurity: NMT 0.2% of any individual impurity; NMT one impurity exceeds 0.1%.

Total impurities: NMT 0.5%

SPECIFIC TESTS

- **Water Determination, *Method Ia* ⟨921⟩**

Sample: 1.00 g

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store below 25°.
- **USP Reference Standards** ⟨11⟩

USP Prilocaine RS

USP Prilocaine Hydrochloride RS

USP Prilocaine Related Compound A RS

o-Toluidine hydrochloride.

$C_7H_9N \cdot HCl$ 143.62

USP Prilocaine Related Compound B RS

(*RS*)-*N*-(4-Methylphenyl)-2-(propylamino)propanamide.

$C_{13}H_{20}N_2O$ 220.31

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

Topic/Question	Contact	Expert Committee
PRILOCAINE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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