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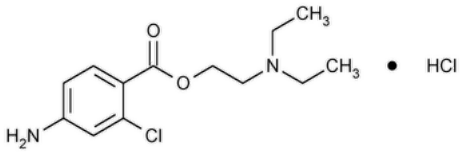
Chloroprocaine Hydrochloride



$C_{13}H_{19}ClN_2O_2 \cdot HCl$ 307.22

Benzoic acid, 4-amino-2-chloro-, 2-(diethylamino)ethyl ester, monohydrochloride;

2-(Diethylamino)ethyl 4-amino-2-chlorobenzoate monohydrochloride CAS RN®: 3858-89-7; UNII: LT7Z1YW11H.

DEFINITION

Chloroprocaine Hydrochloride contains NLT 98.0% and NMT 102.0% of chloroprocaine hydrochloride ($C_{13}H_{19}ClN_2O_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

ASSAY

- **Procedure**

Buffer: 1.26 g/L of ammonium formate in water. Adjust with formic acid to a pH of 3.5.

Solution A: Acetonitrile and *Buffer* (10:90)

Solution B: Acetonitrile

Mobile phase: See *Table 1*. A re-equilibration time of NLT 20 min to the initial conditions after the gradient is recommended.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	30	70
16	100	0
23	100	0

Diluent: Acetonitrile and water (10:90)

Standard solution: 0.1 mg/mL of USP Chloroprocaine Hydrochloride RS in *Diluent*. Sonication may be necessary for complete dissolution.

Sample solution: 0.1 mg/mL of Chloroprocaine Hydrochloride in *Diluent*. Sonication may be necessary for complete dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 294 nm

Column: 4.6-mm × 25-cm, 5-µm; packing L1

Column temperature: 40°

Flow rate: 1.8 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chloroprocaine hydrochloride ($C_{13}H_{19}ClN_2O_2 \cdot HCl$) in the portion of Chloroprocaine Hydrochloride taken:

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

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

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

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

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

Change to read:

• **Organic Impurities**

Buffer, Solution A, Solution B, Mobile phase, and **Diluent:** Prepare as directed in the *Assay*

System suitability solution: 0.03 mg/mL each of USP Chloroprocaine Hydrochloride RS and USP Procaine Hydrochloride RS in methanol. Sonication may be necessary for complete dissolution.

Standard solution: 0.0032 mg/mL of USP Chloroprocaine Hydrochloride RS in methanol. Sonication may be necessary for complete dissolution.

Sensitivity solution: 0.0016 mg/mL of USP Chloroprocaine Hydrochloride RS in *Diluent* from *Standard solution*

Sample solution: 3.2 mg/mL of Chloroprocaine Hydrochloride in methanol. Sonication may be necessary for complete dissolution.

Chromatographic system: Proceed as directed in the *Assay* except for the *Injection volume*.

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

Injection volume: 2 µL

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 10 between chloroprocaine and procaine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Chloroprocaine Hydrochloride taken:

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

r_U = peak response of each impurity from the *Sample solution*

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

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Procaine	0.72	1.39	0.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Chloroprocaine	1.00	1.00	—
4-Amino-2-chlorobenzoic acid	1.36	1.27	0.15
▲Isopropyl 4-amino-2-chlorobenzoate▲ (CN 1-Aug-2024)	2.88	0.92	0.15
Any individual unspecified impurity	—	1.00	0.10
Total impurities	—	—	1.0

SPECIFIC TESTS

• **Acidity:**

Sample solution: Dissolve 1.0 g of Chloroprocaine Hydrochloride in 25 mL of water.

Analysis: Add 2 drops of methyl red TS, and titrate with 0.020 N sodium hydroxide.

Acceptance criteria: NMT 1.8 mL is required to produce a yellow color.

• **Loss on Drying ⟨731⟩**

Sample: 500 mg

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards ⟨11⟩**

USP Chloroprocaine Hydrochloride RS

USP Procaine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
CHLOROPROCAINE HYDROCHLORIDE	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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