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Lidocaine Hydrochloride Topical Solution

DEFINITION

Lidocaine Hydrochloride Topical Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$).

IDENTIFICATION

Change to read:

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

Sample: Place in a separator a volume of Topical Solution, nominally equivalent to 200 mg of lidocaine hydrochloride, and extract with four 15-mL portions of chloroform, discarding the chloroform extracts. Add 2 mL of 2 N sodium hydroxide to the aqueous solution remaining in the separator, and extract with four 15-mL portions of chloroform. Combine the chloroform extracts, and evaporate to dryness. Dissolve the crystals in solvent hexane, evaporate the solvent, and dry the residue under vacuum over silica gel for 24 h. [Note—A rotary evaporator may be used.]

Acceptance criteria: The residue obtained from the *Sample* 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**

Solution A: *water* and glacial acetic acid (930:50). Adjust with 1 N sodium hydroxide to a pH of 3.4.

Mobile phase: *Acetonitrile* and *Solution A* (20:80)

Standard solution: 1.7 mg/mL of USP Lidocaine RS (equivalent to 2 mg/mL of lidocaine hydrochloride) in *Mobile phase*, prepared as follows. Transfer a weighed quantity of USP Lidocaine RS to a suitable volumetric flask, and add 1 N hydrochloric acid to fill 1% of the final volume. Warm if necessary, and dilute with *Mobile phase* to volume.

System suitability stock solution: 220 µg/mL of USP Methylparaben RS in *Mobile phase*

System suitability solution: Mix 2 mL of *System suitability stock solution* with 20 mL of the *Standard solution*.

Sample solution: Nominally 2 mg/mL of lidocaine hydrochloride from Topical Solution in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between lidocaine and methylparaben, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$) in the portion of Topical Solution taken:

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

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

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

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

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

M_{r1} = molecular weight of lidocaine hydrochloride, 270.80

M_{r2} = molecular weight of lidocaine, 234.34

Acceptance criteria: 95.0%–105.0%

IMPURITIES

• **Organic Impurities**

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

Standard solution: 0.0017 mg/mL of USP Lidocaine RS (equivalent to 0.002 mg/mL of lidocaine hydrochloride), 0.0026 mg/mL of USP Ropivacaine Related Compound A RS (equivalent to 0.002 mg/mL of 2,6-dimethylaniline), and 0.002 mg/mL of USP Lidocaine Related Compound H RS in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between the lidocaine related compound H and 2,6-dimethylaniline (ropivacaine related compound A free base) peaks

Relative standard deviation: NMT 2.0% for lidocaine, lidocaine related compound H, and 2,6-dimethylaniline

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of lidocaine related compound H in the portion of Topical Solution taken:

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

r_U = peak response of lidocaine related compound H from the *Sample solution*

r_S = peak response of lidocaine related compound H from the *Standard solution*

C_S = concentration of USP Lidocaine Related Compound H RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of 2,6-dimethylaniline in the portion of Topical Solution taken:

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

r_U = peak response of 2,6-dimethylaniline from the *Sample solution*

r_S = peak response of 2,6-dimethylaniline from the *Standard solution*

C_S = concentration of USP Ropivacaine Related Compound A RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of 2,6-dimethylaniline, 121.18

M_{r2} = molecular weight of ropivacaine related compound A, 157.64

Calculate the percentage of any unspecified degradation product in the portion of Topical Solution taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

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

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

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

M_{r1} = molecular weight of lidocaine hydrochloride, 270.80

M_{r2} = molecular weight of lidocaine, 234.34

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lidocaine	1.0	—
2,6-Dimethylaniline	3.2	0.5
Lidocaine related compound H	3.8	0.5
Any unspecified degradation product	—	0.5
Total degradation products	—	2.0

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 5.0–7.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Lidocaine RS

USP Lidocaine Related Compound H RS

2-Chloro-*N*-(2,6-dimethylphenyl)acetamide.

$C_{10}H_{12}ClNO$ 197.66

USP Methylparaben RS

USP Ropivacaine Related Compound A RS

2,6-Dimethylaniline hydrochloride.

$C_8H_{11}N \cdot HCl$ 157.64

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

Topic/Question	Contact	Expert Committee
LIDOCAINE HYDROCHLORIDE TOPICAL SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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