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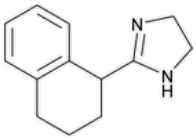
Tetrahydrozoline Hydrochloride



• HCl

$C_{13}H_{16}N_2 \cdot HCl$ 236.74

1*H*-Imidazole, 4,5-dihydro-2-(1,2,3,4-tetrahydro-1-naphthalenyl)-, monohydrochloride;

2-(1,2,3,4-Tetrahydro-1-naphthyl)-2-imidazoline monohydrochloride CAS RN®: 522-48-5; UNII: 0YZT43HS7D.

DEFINITION

Tetrahydrozoline Hydrochloride contains NLT 98.0% and NMT 102.0% of tetrahydrozoline hydrochloride ($C_{13}H_{16}N_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K

• **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***

Sample solution: 5 mg/mL

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Buffer: 2.64 g/L of dibasic ammonium phosphate in water; adjusted with ammonium hydroxide to a pH of 9.0

Mobile phase: Acetonitrile and *Buffer* (15:85)

Standard solution: 0.025 mg/mL of USP Tetrahydrozoline Hydrochloride RS in water

Sample solution: 0.025 mg/mL of Tetrahydrozoline Hydrochloride in water

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 37°

Flow rate: 1.2 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tetrahydrozoline hydrochloride ($C_{13}H_{16}N_2 \cdot HCl$) in the portion of Tetrahydrozoline Hydrochloride taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

▲**Buffer:** Dissolve 4 g of sodium dodecyl sulfate in 600 mL water. Add 3 mL of triethylamine and adjust with orthophosphoric acid to a pH of 2.0.

Mobile phase: Methanol, acetonitrile, and *Buffer* (26.5: 26.5: 47)

System suitability solution: 2 mg/mL of USP Tetrahydrozoline Hydrochloride RS, and 2 µg/mL each of USP Tetrahydrozoline Related Compound A RS, USP Tetrahydrozoline Related Compound B RS, USP Tetrahydrozoline Related Compound C RS, USP Tetrahydrozoline Related Compound D RS, and USP Tetrahydrozoline Related Compound E RS in *Mobile phase*

Standard solution: 2 µg/mL of USP Tetrahydrozoline Hydrochloride RS in *Mobile phase*

Sensitivity solution: 1 µg/mL of USP Tetrahydrozoline Hydrochloride RS in *Mobile phase* from the *Standard solution*

Sample solution: 2 mg/mL of Tetrahydrozoline Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 4-µm packing L87

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of tetrahydrozoline

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between tetrahydrozoline and tetrahydrozoline related compound B, *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 any individual impurity in the portion of Tetrahydrozoline Hydrochloride taken:

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

r_U = peak response of any individual impurity from the *Sample solution*

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

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

C_U = concentration of Tetrahydrozoline Hydrochloride in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria NMT (%)
Tetrahydrozoline related compound C	0.4	1.0	0.10
Tetrahydrozoline related compound A	0.5	1.0	0.1
Naphthyl imidazoline[a]	0.8	4.3	0.10
Tetrahydrozoline	1.0	—	—
Tetrahydrozoline related compound B	1.1	1.6	0.10
Tetrahydrozoline related compound E	1.3	0.8	0.10
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.2

[a] 2-(Naphthalen-1-yl)-4,5-dihydro-1*H*-imidazole.

▲ (USP 1-May-2022)

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Tetrahydrozoline Hydrochloride RS

▲ USP Tetrahydrozoline Related Compound A RS

1,2,3,4-Tetrahydronaphthalene-1-carbonitrile.

$C_{11}H_{11}N$ 157.21

USP Tetrahydrozoline Related Compound B RS

2-(1,2,3,4-Tetrahydronaphthalen-1-yl)-1*H*-imidazole.

$C_{13}H_{14}N_2$ 198.27

USP Tetrahydrozoline Related Compound C RS

1,2,3,4-Tetrahydronaphthalene-1-carboxylic acid.

$C_{11}H_{12}O_2$ 176.22

USP Tetrahydrozoline Related Compound D RS

2-(Naphthalen-1-yl)-4,5-dihydro-1*H*-imidazole hydrochloride.

$C_{13}H_{12}N_2 \cdot HCl$ 232.71

USP Tetrahydrozoline Related Compound E RS

N-(2-Aminoethyl)-1,2,3,4-tetrahydronaphthalene-1-carboxamide.

$C_{13}H_{18}N_2O$ 218.30▲ (USP 1-May-2022)

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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