Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2022
Document Type: USP Monographs
DocId: GUID-5AEBD2FD-B10B-4EAF-9378-C7D52DD559DA_6_en-US
DOI: https://doi.org/10.31003/USPNF_M82020_06_01
DOI Ref: 4ey5h

Tetrahydrozoline Hydrochloride Ophthalmic Solution

DEFINITION

Tetrahydrozoline Hydrochloride Ophthalmic Solution is a sterile, isotonic solution of Tetrahydrozoline Hydrochloride in water. It contains NLT 90.0% and NMT 110.0% of the labeled amount of tetrahydrozoline hydrochloride ($C_{13}H_{16}N_2 \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

• **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

Change to read:

• **Procedure**

Solution A: 20 mM dibasic ammonium phosphate in water. Adjust with ammonium hydroxide to a pH of 9.0.

Mobile phase: Acetonitrile and *Solution A* (15:85)

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

Sample solution: Nominally 0.025 mg/mL of tetrahydrozoline hydrochloride prepared as follows. Transfer a suitable volume of Ophthalmic Solution to a suitable volumetric flask. Dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm. ▲For *Identification A*, use a diode array detector in the range of 195–400 nm.▲ (USP 1-May-2022)

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

Column temperature: 37°

Flow rate: 1.2 mL/min

Injection volume: 25 µL

Run time: NLT 2 times the retention time of tetrahydrozoline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tetrahydrozoline hydrochloride ($C_{13}H_{16}N_2 \cdot HCl$) in the portion of Ophthalmic Solution taken:

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

r_U = peak response of tetrahydrozoline 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* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: 20 mM dibasic ammonium phosphate in water. Adjust with ammonium hydroxide to a pH of 9.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
11.0	85	15
12.0	60	40
26.0	60	40
27.0	30	70
41.0	30	70
42.0	85	15
50.0	85	15

▲**System suitability solution:** 250 µg/mL of USP Tetrahydrozoline Hydrochloride RS and 5 µg/mL each of USP Tetrahydrozoline Related Compound A RS, USP Tetrahydrozoline Related Compound C RS, and USP Tetrahydrozoline Related Compound E RS in water▲ (USP 1-May-2022)

Standard solution: 5 µg/mL of USP Tetrahydrozoline Hydrochloride RS▲▲ (USP 1-May-2022) in water

Sensitivity solution: 0.25 µg/mL of USP Tetrahydrozoline Hydrochloride RS in water, from the *Standard solution*

Sample solution: Nominally 250 µg/mL of tetrahydrozoline hydrochloride in water prepared as follows. Transfer a suitable volume of Ophthalmic Solution to a suitable volumetric flask. Dilute with water to volume and mix.

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: 50 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

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

Suitability requirements

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 specified and any unspecified degradation product in the portion of Ophthalmic Solution taken:

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

r_U = peak response of each specified and any unspecified degradation product 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 = nominal concentration of tetrahydrozoline hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.1%.▲ (USP 1-May-2022)

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲Tetrahydrozoline related compound C▲ (USP 1-May-2022)	0.8	2.0
Tetrahydrozoline	1.0	—
▲Tetrahydrozoline related compound E▲ (USP 1-May-2022)	1.8	2.0
Tetrahydrozoline related compound A▲▲ (USP 1-May-2022)	4.4	2.0
Tetrahydrozoline methyl ester[a]	5.3	2.0
Any unspecified degradation product	—	1.0
Total degradation products	—	3.0

[a] Methyl 1,2,3,4-tetrahydronaphthalene-1-carboxylate.

SPECIFIC TESTS

- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 5.8–6.5

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 C RS

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

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

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)

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

Topic/Question	Contact	Expert Committee
TETRAHYDROZOLINE HYDROCHLORIDE OPHTHALMIC SOLUTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(3)

Current DocID: GUID-5AEBD2FD-B10B-4EAF-9378-C7D52DD559DA_6_en-US

DOI: https://doi.org/10.31003/USPNF_M82020_06_01

DOI ref: 4ey5h