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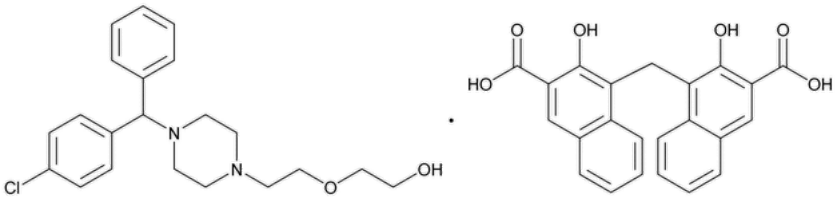
Hydroxyzine Pamoate



$C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$ 763.27

Ethanol, 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, (±)-, compd. with 4,4'-methylenebis[3-hydroxy-2-naphthalenecarboxylic acid] (1:1);

(±)-2-[2-[4-(*p*-Chloro-α-phenylbenzyl)-1-piperazinyl]ethoxy]ethanol 4,4'-methylenebis[3-hydroxy-2-naphthoate] (1:1) CAS RN®: 10246-75-0; UNII: M20215MUFR.

DEFINITION

Hydroxyzine Pamoate contains NLT 97.0% and NMT 102.0% of hydroxyzine pamoate ($C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$), calculated on the anhydrous basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** [Note—Methods described in ⟨197K⟩ or ⟨197A⟩ may be used.]

• **B.** The retention time of the hydroxyzine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: To each L of water, add 1.0 mL of stronger ammonia water.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
6	80	20
20	20	80
25	20	80
26	80	20
30	80	20

Diluent: Acetonitrile and *Solution A* (80:20)

System suitability solution: 1 µg/mL of USP Hydroxyzine Pamoate RS, 3 µg/mL of USP Hydroxyzine Related Compound A RS, and 1 µg/mL of USP 4-Chlorobenzophenone RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Hydroxyzine Pamoate RS in *Diluent*

Sample solution: 0.1 mg/mL of Hydroxyzine Pamoate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

[NOTE—Rinse the column with a solution of acetonitrile and water (20:80) and then with a solution of acetonitrile and water (80:20) after each analysis.]

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention time for 4-chlorobenzophenone is 1.1. See *Table 2* for the relative retention times for other compounds.]

Suitability requirements

Resolution: NLT 1.5 between hydroxyzine and hydroxyzine related compound A; NLT 1.5 between hydroxyzine related compound A and 4-chlorobenzophenone, *System suitability solution*

Tailing factor: NMT 1.5 for hydroxyzine, *Standard solution*

Relative standard deviation: NMT 0.73% for hydroxyzine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydroxyzine pamoate ($C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$) in the portion of Hydroxyzine Pamoate taken:

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

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

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

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

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

Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%

Change to read:

• **ORGANIC IMPURITIES**

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

Standard solution: 1 µg/mL of USP Hydroxyzine Pamoate RS, 3 µg/mL of USP Hydroxyzine Related Compound A RS, and 1 µg/mL of USP 4-Chlorobenzophenone RS in *Diluent*

Sample solution: 1000 µg/mL of Hydroxyzine Pamoate in *Diluent*

System suitability

Sample: *Standard solution*

[NOTE—The relative retention time for 4-chlorobenzophenone is 1.1. See *Table 2* for the relative retention times for other compounds.]

Suitability requirements

Resolution: NLT 1.5 between hydroxyzine and hydroxyzine related compound A; NLT 1.5 between hydroxyzine related compound A and ▲4-chlorobenzophenone▲ (ERR 1-Jun-2021)

Relative standard deviation: NMT 5.0% each for hydroxyzine and hydroxyzine related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydroxyzine related compound A in the portion of Hydroxyzine Pamoate taken:

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

r_U = peak response of hydroxyzine related compound A from the *Sample solution*

r_S = peak response of hydroxyzine related compound A from the *Standard solution*

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

C_U = concentration of Hydroxyzine Pamoate in the *Sample solution* (µg/mL)

Calculate the percentage of decloxizine and each unspecified impurity in the portion of Hydroxyzine Pamoate taken:

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

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

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

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

C_U = concentration of Hydroxyzine Pamoate in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pamoic acid[a]	0.05	—
Decloxizine[b]	0.90	0.15
Hydroxyzine	1.0	—
Hydroxyzine related compound A	1.05	0.15
Any individual unspecified impurity	—	0.10
Total impurities	—	0.50

[a] This peak is due to the pamoate counterion; hence it is not an impurity and should not be included in the total impurities.

[b] 2-[2-(4-Benzhydrylpiperazin-1-yl)ethoxy]ethanol.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store below 30°.

• **USP Reference Standards ⟨11⟩**

USP 4-Chlorobenzophenone RS

4-Chlorobenzophenone.

$C_{13}H_9ClO$ 216.66

USP Hydroxyzine Related Compound A RS

1-[(4-Chlorophenyl)phenylmethyl]piperazine.

$C_{17}H_{19}ClN_2$ 286.80

USP Hydroxyzine Pamoate RS

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

Topic/Question	Contact	Expert Committee
HYDROXYZINE PAMOATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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