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Hydroxyzine Pamoate Capsules

DEFINITION

Hydroxyzine Pamoate Capsules contain hydroxyzine pamoate ($C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$).

IDENTIFICATION

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

ASSAY

Change to read:

- **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 (equivalent to 0.6 µg/mL of hydroxyzine hydrochloride), 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 (equivalent to 0.06 mg/mL of hydroxyzine hydrochloride) in *Diluent*

Sample stock solution: Nominally 1.0 mg/mL of hydroxyzine pamoate from Capsules (equivalent to 0.6 mg/mL of hydroxyzine hydrochloride) prepared as follows. Transfer a portion of the powder from NLT 10 Capsules to a suitable volumetric flask. Add 75% of the flask volume of *Diluent*, sonicate for NLT 15 min, and shake by mechanical means for NLT 30 min. Dilute with *Diluent* to volume. Centrifuge a portion of the solution and use the supernatant. [Note—The use of a centrifuge speed of 3000 rpm for 10 min may be suitable.]

Sample solution: Nominally 0.1 mg/mL of hydroxyzine pamoate (equivalent to 0.06 mg/mL of hydroxyzine hydrochloride) from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm. For *Identification B*, use a diode array detector in the range of 200–400 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

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

[NOTE—The relative retention times for decloxizine and 4-chlorobenzophenone are 0.90 and 1.1, respectively. 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), *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 the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) in the portion of Hydroxyzine Pamoate Capsules taken:

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

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 = equivalent concentration of hydroxyzine hydrochloride in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of hydroxyzine hydrochloride, 447.83

M_{r2} = molecular weight of hydroxyzine pamoate, 763.27

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DISSOLUTION ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Mobile phase: Methanol and 0.05 M monobasic sodium phosphate (60:40)

Standard solution: USP Hydroxyzine Hydrochloride RS in *Medium*

Sample solution: Use a filtered portion of the solution under test. Dilute with *Medium*, if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 232 nm

Column: 4.6-mm × 25-cm; 10-µm packing L9

Flow rate: 1.9 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times D \times V \times (1/L) \times 100$$

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 Hydrochloride RS in the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution*, if needed

V = volume of the *Medium*, 900 mL

L = label claim (mg/Capsule)

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Tolerances: NLT 75% (*Q*) of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

- **Organic Impurities**

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

Standard solution: 1 µg/mL of USP Hydroxyzine Pamoate RS (equivalent to 0.6 µg/mL of hydroxyzine hydrochloride), 3 µg/mL of USP Hydroxyzine Related Compound A RS, and 1 µg/mL of USP 4-Chlorobenzophenone RS in *Diluent*

Sample solution: Nominally 1000 µg/mL of hydroxyzine pamoate from Capsules (equivalent to 600 µg/mL of hydroxyzine hydrochloride) prepared as follows. Transfer a portion of the powder from NLT 10 Capsules to a suitable volumetric flask. Add 75% of the flask volume of *Diluent*, sonicate for NLT 15 min, and shake by mechanical means for NLT 30 min. Dilute with *Diluent* to volume. Centrifuge a portion of the solution and use the supernatant. [Note—The use of a centrifuge speed of 3000 rpm for 10 min may be suitable.]

System suitability

Sample: *Standard solution*

[Note—The relative retention times for decloxizine and 4-chlorobenzophenone are 0.90 and 1.1, respectively. 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

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 Capsules 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 = equivalent concentration of hydroxyzine hydrochloride in the *Sample solution* (µg/mL)

Calculate the percentage of each unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each unspecified degradation product 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 = equivalent concentration of hydroxyzine hydrochloride in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of hydroxyzine hydrochloride, 447.83

M_{r2} = molecular weight of hydroxyzine pamoate, 763.27

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	—
Hydroxyzine	1.0	—
Hydroxyzine related compound A	1.05	0.2

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Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any individual unspecified degradation product	—	0.20
Total degradation products	—	1.0

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

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP 4-Chlorobenzophenone RS
4-Chlorobenzophenone.
$C_{13}H_9ClO$ 216.66

USP Hydroxyzine Hydrochloride RS

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 CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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