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Hydroxyzine Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-hydroxyzine-hcl-tabs-20240329.

DEFINITION

Hydroxyzine Hydrochloride Tablets contain 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 main peak of the *Sample solution* corresponds to that of the hydroxyzine peak of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: Trifluoroacetic acid and water (0.1: 99.9)

Solution B: Trifluoroacetic acid and acetonitrile (0.05: 99.95)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
12	55	45
16	55	45
21	20	80
25	20	80
26	90	10
30	90	10

Diluent: Acetonitrile and water (30:70)

Standard solution: 0.05 mg/mL of USP Hydroxyzine Hydrochloride RS in *Diluent*

Sample stock solution: Nominally 0.5 mg/mL of hydroxyzine hydrochloride from Tablets in *Diluent* prepared as follows. Transfer a portion of finely powdered Tablets (NLT 10), equivalent to 50 mg of hydroxyzine hydrochloride, to a 100-mL volumetric flask and add 80 mL of *Diluent*. Sonicate for 30 min to dissolve and dilute with *Diluent* to volume. Centrifuge 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 0.05 mg/mL of hydroxyzine hydrochloride from the *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: 2.1-mm × 15-cm; 1.8-µm packing L1

Flow rate: 0.3 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: USP Hydroxyzine Hydrochloride RS in *Medium*

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

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 230 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) dissolved from the UV absorbances.

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

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: Water; 250 mL

Apparatus 3: 30 dips/min

Time: 45 min

Standard solution: USP Hydroxyzine Hydrochloride RS in *Medium*

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

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 230 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) dissolved from the UV absorbances.

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

▲**Test 3:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: Dissolve 1.38 g of potassium phosphate, monobasic in 1 L of water. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Standard solution: 0.02 mg/mL of USP Hydroxyzine Hydrochloride RS in *Medium*. Sonicate to dissolve, if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter of 10-µm pore size. Dilute with *Medium* to a concentration similar to that of the *Standard solution*, if necessary. Pass through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2.7 times the retention time of hydroxyzine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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)

V = volume of the *Medium*, 500 mL

D = dilution factor of the *Sample solution*, if necessary

L = label claim (mg/tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) is dissolved▲ (RB 1-Apr-2024)

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

IMPURITIES

• **Organic Impurities**

Solution A, Solution B, Mobile phase, and **Diluent:** Proceed as directed in the *Assay*.

Standard stock solution: 25.0 µg/mL each of USP Hydroxyzine Hydrochloride RS, USP Hydroxyzine Related Compound A RS, and USP 4-Chlorobenzophenone RS in *Diluent*

Standard solution: 1.0 µg/mL each of USP Hydroxyzine Hydrochloride RS, USP Hydroxyzine Related Compound A RS, and USP 4-Chlorobenzophenone RS from the *Standard stock solution* in *Diluent*

Sample solution: Nominally 500 µg/mL of hydroxyzine hydrochloride from Tablets prepared as follows. Transfer a portion of finely powdered Tablets (NLT 10), equivalent to 50 mg of hydroxyzine hydrochloride, to a 100-mL volumetric flask. Add 80 mL of *Diluent*. Sonicate 30 min to dissolve and dilute with *Diluent* to volume. Centrifuge the solution and use the supernatant. [Note—The use of a centrifuge speed of 3000 rpm for 10 min may be suitable.]

Chromatographic system

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

Mode: LC

Detectors

Hydroxyzine and hydroxyzine related compound A: UV 230 nm

4-Chlorobenzophenone: UV 254 nm

Column: 2.1-mm × 15-cm; 1.8-µm packing L1

Flow rate: 0.3 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 5.0 between hydroxyzine related compound A and hydroxyzine

Relative standard deviation: NMT 3.0% each for hydroxyzine related compound A, hydroxyzine, and 4-chlorobenzophenone

Analysis

Samples: *Standard solution* and *Sample solution*

For degradation products detected at UV 230 nm

Calculate the percentage of any individual unspecified degradation product in the portion of Tablets taken:

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

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

C_U = nominal concentration of hydroxyzine hydrochloride in the *Sample solution* (µg/mL)

For 4-chlorobenzophenone detected at UV 254 nm

Calculate the percentage of 4-chlorobenzophenone in the portion of Tablets taken:

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

r_U = peak response of 4-chlorobenzophenone from the *Sample solution*

r_S = peak response of 4-chlorobenzophenone from the *Standard solution*

C_S = concentration of USP 4-Chlorobenzophenone RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of hydroxyzine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.03%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Decloxizine[a]	0.87	—
Hydroxyzine related compound A[a]	0.96	—
Hydroxyzine	1.0	—
4-Chlorobenzophenone	1.4	0.2
Any individual unspecified degradation product	—	0.3
Total degradation products	—	0.5

[a] These are process impurities that are controlled in the drug substance. They are not to be reported or included in the total degradation products.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **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;

Also known as *p*-Chlorobenzhydrylpiperazine.

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

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

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

Chromatographic Database Information: Chromatographic Database

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