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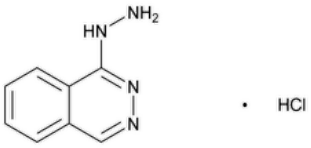
Hydralazine Hydrochloride



$C_8H_8N_4 \cdot HCl$ 196.64

Phthalazine, 1-hydrazino-, monohydrochloride;

1-Hydrazinophthalazine monohydrochloride CAS RN®: 304-20-1; UNII: FD171B778Y.

DEFINITION

Hydralazine Hydrochloride contains NLT 98.0% and NMT 102.0% of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)
- **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: 0.25 mg/mL of Hydralazine Hydrochloride in water

  Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

  Mobile phase: Dissolve 1.44 g of sodium dodecyl sulfate and 0.75 g of tetrabutylammonium bromide in 770 mL of water, and add 230 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 3.0.

  Diluent: 0.1 N acetic acid

  System suitability stock solution: 0.25 mg/mL of USP Hydralazine Hydrochloride RS and 0.05 mg/mL of USP Phthalazine RS in *Diluent*

  System suitability solution: 25 µg/mL of USP Hydralazine Hydrochloride RS and 5 µg/mL of USP Phthalazine RS in *Diluent* from the *System suitability stock solution*

  Standard stock solution: 0.4 mg/mL of USP Hydralazine Hydrochloride RS in *Diluent*

  Standard solution: 40 µg/mL of USP Hydralazine Hydrochloride RS in *Diluent* from the *Standard stock solution*

  Sample stock solution: 0.4 mg/mL of Hydralazine Hydrochloride in *Diluent*

  Sample solution: 40 µg/mL of Hydralazine Hydrochloride in *Diluent* prepared as follows. Transfer a suitable amount of the *Sample stock solution* to a suitable volumetric flask. Dilute with *Diluent* to volume and filter, discarding the first 10 mL of the filtrate.

  Chromatographic system

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

  Mode: LC

  Detector: UV 230 nm

  Column: 4.0-mm × 25-cm; 10-µm packing L10

  Flow rate: 1 mL/min

  Injection volume: 25 µL

  System suitability

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

  [Note—The relative retention times for phthalazine and hydralazine hydrochloride are 0.65 and 1.0, respectively.]

  Suitability requirements

  Resolution: NLT 4.0 between the phthalazine and hydralazine peaks, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$) in the portion of Hydralazine Hydrochloride taken:

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

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

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

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

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Mobile phase, Diluent, and **System suitability solution:** Prepare as directed in the *Assay*.

Standard solution: 0.001 mg/mL of USP Hydralazine Hydrochloride RS in *Diluent*. Sonication may be necessary for complete dissolution.

Sample solution: 0.5 mg/mL of Hydralazine Hydrochloride in *Diluent* prepared as follows. Transfer a suitable amount of Hydralazine Hydrochloride to a suitable volumetric flask. Add *Diluent* to fill about 60% of the total volume, and sonicate to dissolve. Cool, and dilute with *Diluent* to volume.

Chromatographic system: Proceed as directed in the *Assay*, except for *Injection volume*.

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 4.0 between the phthalazine and hydralazine peaks, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Hydralazine Hydrochloride taken:

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

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

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

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
1-Phthalazinone	0.55	2.3	0.15
2-Formyl benzoic acid	0.60	1.1	0.15

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Phthalazine	0.75	3.6	0.15
1-Chlorophthalazine	0.83	1.5	0.15
Hydralazine	1.00	—	—
Any unspecified impurity	—	1.0	0.10
Total impurities[a]	—	—	1.0

[a] Total impurities include specified and unspecified impurities.

• **Limit of Hydrazine**

Buffer: Dissolve 5.82 g of dibasic sodium phosphate and 3.81 g of monobasic potassium phosphate in 1 L of water, and adjust with either 1 N sodium hydroxide or 1 N phosphoric acid to a pH of 7.0 ± 0.1.

Mobile phase: Dissolve 300 mg of edetate disodium in 300 mL of water in a 1-L volumetric flask. Dilute with acetonitrile to volume.

Benzaldehyde solution: Transfer 1.0 mL of benzaldehyde to a 100-mL volumetric flask, and dilute with a mixture of methanol and water (9:1) to volume.

Acetonitrile solution: Transfer 300 mL of water to a 1000-mL volumetric flask, and dilute with acetonitrile to volume.

Standard stock solution: 0.65 mg/mL of hydrazine dihydrochloride in water

Standard solution 1: 0.325 µg/mL of hydrazine dihydrochloride in water from *Standard stock solution*

Standard solution 2: Transfer 1.0 mL of *Standard solution 1* to a 10-mL flask. Add 4.0 mL of *Benzaldehyde solution,* and shake by mechanical means for 20 min.

Standard solution 3: Transfer 2.0 mL of *Standard solution 2* to a 5-mL volumetric flask, and dilute with *Acetonitrile solution* to volume.

Extraction column: Use a freshly conditioned solid phase extraction column containing benzenesulfonic acid strong cation-exchange packing with a sorbent-mass to column volume ratio of 500 mg/3 mL, or equivalent. The column is conditioned as follows. Wash the column with two 2.0-mL portions of hexanes, and dry under vacuum for 2 min. Wash the column with two 2.0-mL portions of methanol, two 2.0-mL portions of water, and two 2.0-mL portions of *Buffer*. At no time after the hexanes wash should the column be allowed to dry out.

Sample solution: Transfer about 20 mg of Hydralazine Hydrochloride to a 10-mL reaction vessel, and dissolve in 1.0 mL of water. Add 4.0 mL of *Benzaldehyde solution*, and shake by mechanical means for 20 min. Pipet 2.0 mL of this solution into the *Extraction column* and elute into a 5-mL volumetric flask. Wash the *Extraction column* with two 1.5-mL portions of the *Acetonitrile solution*, collecting the washings with the eluate, and dilute with *Acetonitrile solution* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 310 nm

Column: 4.0-mm × 25-cm; 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution 3*

[Note—The relative retention times for hydralazine and hydrazine are about 1.0 and 1.5, respectively.]

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution 3* and *Sample solution*

Calculate the percentage of hydrazine in the portion of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$) taken:

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

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

r_S = peak response of hydrazine from *Standard solution 3*

C_S = concentration of hydrazine dihydrochloride in *Standard solution 3* (µg/mL)

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

M_{r1} = molecular weight of hydrazine, 32.05

M_{r2} = molecular weight of hydrazine dihydrochloride, 104.97

Acceptance criteria: NMT 0.001%

SPECIFIC TESTS

- **pH** ⟨791⟩

Sample solution: 20 mg/mL of Hydralazine Hydrochloride in water

Acceptance criteria: 3.5–4.2

- **Loss on Drying** ⟨731⟩

Analysis: Dry at 110° for 15 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

USP Hydralazine Hydrochloride RS

USP Phthalazine RS $C_8H_6N_2$ 130.15

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

Topic/Question	Contact	Expert Committee
HYDRALAZINE HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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