Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-6F3832BE-55D9-4220-BC36-F2117DB6BC2C_3_en-US
DOI: https://doi.org/10.31003/USPNF_M37780_03_01
DOI Ref: 5wd96

Hydralazine Hydrochloride Tablets

DEFINITION
Hydralazine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample: Transfer an amount equivalent to about 100 mg of hydralazine hydrochloride from finely powdered Tablets to a glass-stoppered flask. Add 40 mL of 1 N hydrochloric acid, shake by mechanical means for 5 min, and filter. Discard the first few milliliters of the filtrate. Place 20 mL of the filtrate in a separator, wash with 10 mL of methylene chloride, and discard the washing. Mix the aqueous solution in the separator with 2 mL of 14 mg/mL sodium nitrite solution, add 10 mL of methylene chloride, shake by mechanical means for 5 min, and allow the layers to separate. Pass the methylene chloride layer through a filter of anhydrous sodium sulfate previously washed with methylene chloride and collect the solution in a 50-mL beaker. Evaporate to dryness with the aid of gentle heat and a stream of dry nitrogen.

Acceptance criteria: Meet the requirements

• **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

• **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 solution: 25 µg/mL of USP Hydralazine Hydrochloride RS and 5 µg/mL of USP Phthalazine RS in *Diluent*

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

Sample stock solution: Nominally 0.4 mg/mL of hydralazine hydrochloride from NLT 20 finely powdered Tablets in *Diluent*. Centrifuge the solution and use the clear supernatant.

Sample solution: Nominally 40 µg/mL of hydralazine hydrochloride in *Diluent* from the *Sample stock solution*

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 are about 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 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$) in the portion of Tablets 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 = nominal concentration of hydralazine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: A known concentration of USP Hydralazine Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter and dilute with *Medium*, if necessary, to a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 260 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$) dissolved.

Tolerances: NLT 75% (*Q*) of the labeled amount of hydralazine hydrochloride ($C_8H_8N_4 \cdot HCl$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

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

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

Standard stock solution: 0.1 mg/mL of USP Hydralazine Hydrochloride RS in *Diluent*, prepared as follows. To a suitable amount of USP Hydralazine Hydrochloride RS, add 60% of the total volume of *Diluent*, sonicate to dissolve, cool to room temperature, and then dilute with *Diluent* to volume.

Standard solution: 0.001 mg/mL of USP Hydralazine Hydrochloride RS in *Diluent* from the *Standard stock solution*

Sample solution: Nominally 0.5 mg/mL of hydralazine hydrochloride from NLT 20 powdered Tablets in *Diluent*, prepared as follows. To a suitable amount of powdered Tablets, add 60% of the total volume of *Diluent* and sonicate for 15 min with occasional swirling. Cool to room temperature, dilute with *Diluent* to volume, and pass through a suitable filter of 0.45-µm pore size.

Chromatographic system: Proceed as directed in the *Assay* except for the following.

Injection volume: 20 µL

Run time: NLT 5.8 times the retention time of hydralazine

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 any unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of any unspecified degradation product 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 = nominal 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[a]	0.55	2.3	—
2-Formylbenzoic acid[a]	0.60	1.1	—
Phthalazine[a]	0.75	3.6	—
1-Chlorophthalazine[a]	0.83	1.5	—
Hydralazine	1.00	—	—
Any unspecified degradation product	—	1.0	0.20
Total impurities[b]	—	—	1.5

[a] Process-related impurity.

[b] Total impurities include process-related impurities and degradation products.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **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 TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(5)

Current DocID: GUID-6F3832BE-55D9-4220-BC36-F2117DB6BC2C_3_en-US

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