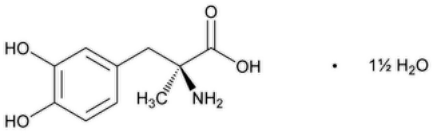
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Aug-2023
Document Type: USP Monographs
DocId: GUID-6F614343-3DFB-4E85-A12A-4F90AD685333_7_en-US
DOI: https://doi.org/10.31003/USPNF_M52340_07_01
DOI Ref: e6rf3

Methyldopa



$C_{10}H_{13}NO_4 \cdot 1½H_2O$ 238.24
$C_{10}H_{13}NO_4$ 211.22
L-Tyrosine, 3-hydroxy-α-methyl-, sesquihydrate;
L-3-(3,4-Dihydroxyphenyl)-2-methylalanine sesquihydrate CAS RN®: 41372-08-1; UNII: 56LH93261Y.
Anhydrous CAS RN®: 555-30-6; UNII: M4R0H12F6M.

DEFINITION

Methyldopa contains NLT 98.0% and NMT 102.0% of methyldopa ($C_{10}H_{13}NO_4$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K
- **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**

[Note—Freshly prepare the *Standard solution* and *Sample solution* before use.]

Buffer: 0.1 M monobasic sodium phosphate. Adjust with phosphoric acid to a pH of 3.0.
Mobile phase: *Buffer* and methanol (850:150)
Diluent: 0.1 N hydrochloric acid
Standard solution: 0.4 mg/mL of USP Methyldopa RS in *Diluent*
Sample solution: 0.4 mg/mL of Methyldopa in *Diluent*
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1.0 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: 0.9–1.5
Relative standard deviation: NMT 0.73%
Analysis
Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methyldopa ($C_{10}H_{13}NO_4$) in the portion of Methyldopa taken:

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

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

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

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

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

[Note—Freshly prepare the *Standard solution* and *Sample solution* before use.]

Buffer, Mobile phase, and **Diluent:** Prepare as directed in the *Assay*.

System suitability solution: 4 µg/mL of USP Methyldopa RS and 6 µg/mL each of USP 3-*O*-Methylmethyldopa RS, USP Methyldopa Related Compound B RS, and USP Methyldopa Related Compound C RS in *Diluent*

Standard solution: 4 µg/mL of USP Methyldopa RS in *Diluent*

Sample solution: 4 mg/mL of Methyldopa in *Diluent*

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run time*.

Run time: NLT 6 times the retention time of methyldopa

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between methyldopa related compound B and methyldopa related compound C, *System suitability solution*

Relative standard deviation: NMT 5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Methyldopa 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 methyldopa from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 1*. Disregard any peaks below 0.03%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Methyldopa	1.0	1.0	—
3-*O*-Methylmethyldopa[a]	1.9	1.0	0.15
Methyldopa related compound B[b]	4.3	0.38	0.15
Methyldopa related compound C[c]	4.9	0.77	0.15
Any individual unspecified impurity	—	1.0	0.05
Total impurities	—	–	0.5

[a] (*S*)-2-Amino-3-(4-hydroxy-3-methoxyphenyl)-2-methylpropanoic acid.

[b] (*S*)-2-Amino-3-(4-methoxyphenyl)-2-methylpropanoic acid.

[c] (*S*)-2-Amino-3-(3,4-dimethoxyphenyl)-2-methylpropanoic acid.

SPECIFIC TESTS

• **Optical Rotation ⟨781S⟩, *Procedures, Specific Rotation***

Sample solution: 44 mg/mL, in a solvent that is a solution of aluminum chloride hexahydrate in water (2 in 3) that previously has been treated with activated charcoal, filtered, and adjusted with 0.25 N sodium hydroxide to a pH of 1.5

Acceptance criteria: −25° to −28°

• **Acidity**

Sample solution: Dissolve 1.0 g in carbon dioxide-free water with the aid of heat, and add 1 drop of methyl red TS.

Analysis: Titrate the *Sample solution* with 0.10 N sodium hydroxide to a yellow endpoint.

Acceptance criteria: NMT 0.50 mL is required.

• **Water Determination ⟨921⟩, *Method I*:** 10.0%–13.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Methyldopa RS

USP Methyldopa Related Compound B RS

(*S*)-2-Amino-3-(4-methoxyphenyl)-2-methylpropanoic acid hydrochloride.

$C_{11}H_{15}NO_3 \cdot HCl$ 245.70

USP Methyldopa Related Compound C RS

(*S*)-2-Amino-3-(3,4-dimethoxyphenyl)-2-methylpropanoic acid hydrochloride.

$C_{12}H_{17}NO_4 \cdot HCl$ 275.73

USP 3-*O*-Methylmethyldopa RS

(*S*)-2-Amino-3-(4-hydroxy-3-methoxyphenyl)-2-methylpropanoic acid ▲monohydrate.▲ (CN 1-Aug-2023)

$C_{11}H_{15}NO_4$ ▲$\cdot H_2O$ 243.26▲ (CN 1-Aug-2023)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(2)

Current DocID: GUID-6F614343-3DFB-4E85-A12A-4F90AD685333_7_en-US

DOI: https://doi.org/10.31003/USPNF_M52340_07_01

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