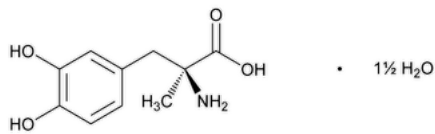


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Methyldopa



$C_{10}H_{13}NO_4 \cdot 1\frac{1}{2}H_2O$ 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 $\times$ 25-cm; 5- μ m packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 μ L

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°