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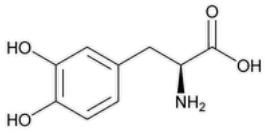
Levodopa



$C_9H_{11}NO_4$ 197.19

L-Tyrosine, 3-hydroxy-;

(−)-3-(3,4-Dihydroxyphenyl)-L-alanine CAS RN®: 59-92-7; UNII: 46627O600J.

DEFINITION

Levodopa contains NLT 98.0% and NMT 102.0% of levodopa ($C_9H_{11}NO_4$), 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*.

ASSAY

• **Procedure**

Protect all solutions from light, and maintain them at 10° until they are injected into the chromatograph.

Diluent: 0.1% trifluoroacetic acid in water

Mobile phase: Tetrahydrofuran and *Diluent* (3:97)

System suitability solution: 10 µg/mL each of USP Levodopa RS, USP Levodopa Related Compound B RS, and USP L-Tyrosine RS in *Diluent*

Standard solution: 0.4 mg/mL of USP Levodopa RS in *Diluent*

Sample solution: 0.4 mg/mL of Levodopa in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm L1 packing

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—Refer to *Table 1* in the test for *Organic Impurities* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between levodopa and L-tyrosine

Tailing factor: NMT 2.0 for levodopa

Relative standard deviation: NMT 2.0% for levodopa

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levodopa ($C_9H_{11}NO_4$) in the portion of the sample taken:

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

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

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

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

IMPURITIES

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

Change to read:

• **Organic Impurities**

Protect all solutions from light, and maintain them at 10° until they are injected into the chromatograph.

Diluent, Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Levodopa taken:

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

r_U = peak area for any impurity in the *Sample solution*

r_S = peak area for Levodopa in the *Standard solution*

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

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

F = relative response factor of each impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Levodopa related compound A[a]	0.9	0.41	0.1
Levodopa	1.0	—	—
L-Tyrosine	1.3	0.44	0.1
Levodopa related compound B	1.6	0.83	0.5
L-Veratrylglycine[b]	2.7	0.76	0.1
Individual unknown impurity	—	1.0	0.1
Total impurities	—	—	1.1

[a] 3-(3,4,6-Trihydroxyphenyl)alanine▲; also known as 3-(2,4,5-Trihydroxyphenyl)-L-alanine.▲ (ERR 1-Nov-2018)

[b] 3-(3,4-Dimethoxyphenyl)-L-alanine.

SPECIFIC TESTS

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

Sample solution: 500 mg of Levodopa in a 25-mL volumetric flask. Add 10 mL of 1 N hydrochloric acid to dissolve the solid, add 5 g of methenamine, swirl the contents to dissolve the methenamine, and add 1 N hydrochloric acid to volume.

Analysis: Allow the *Sample solution* to stand in the dark at 25° for 3 h, and measure the rotation.

Acceptance criteria: −160° to −167°

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, store in a dry place, and prevent exposure to excessive heat.

• **USP Reference Standards ⟨11⟩**

USP Levodopa RS

USP Levodopa Related Compound B RS

3-Methoxytyrosine.

$C_{10}H_{13}NO_4$	211.22

USP L-Tyrosine RS

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

Topic/Question	Contact	Expert Committee
LEVODOPA	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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