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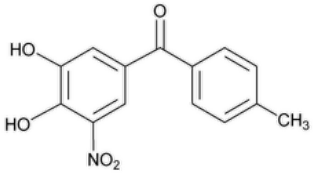
Tolcapone



$C_{14}H_{11}NO_5$ 273.24

Methanone, (3,4-dihydroxy-5-nitrophenyl)(4-methylphenyl)-;

3,4-Dihydroxy-4'-methyl-5-nitrobenzophenone CAS RN®: 134308-13-7; UNII: CIF6334OLY.

DEFINITION

Tolcapone contains NLT 98.5% and NMT 101.5% of tolcapone ($C_{14}H_{11}NO_5$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (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**

Diluent: Methanol and acetonitrile (24:15)

Buffer: Transfer 6.8 g of monobasic potassium phosphate into a 1-L volumetric flask. Dissolve in about 980 mL of water. Adjust with phosphoric acid to a pH of 2.0. Dilute with water to volume.

Mobile phase: Acetonitrile, methanol, and *Buffer* (25:40:35)

System suitability stock solution: 5 µg/mL of USP Tolcapone Related Compound A RS, 5 µg/mL of USP Tolcapone RS, and 10 µg/mL of USP Tolcapone Related Compound B RS in *Diluent*

System suitability solution: 0.1 µg/mL of USP Tolcapone Related Compound A RS, 0.1 µg/mL of USP Tolcapone RS, and 0.2 µg/mL of USP Tolcapone Related Compound B RS from *System suitability stock solution* prepared as follows. Transfer a suitable volume of *System suitability stock solution* to a suitable volumetric flask. Add 63% of the flask volume of *Diluent* and dilute with water to volume.

Standard stock solution: 1.0 mg/mL of USP Tolcapone RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Tolcapone RS from *Standard stock solution* prepared as follows. Transfer a suitable volume of *Standard stock solution* to a suitable volumetric flask. Add 55% of the flask volume of *Diluent* and dilute with water to volume.

Sample stock solution: 1.0 mg/mL of Tolcapone in *Diluent*

Sample solution: 0.1 mg/mL of Tolcapone from *Sample stock solution* prepared as follows. Transfer a suitable volume of *Sample stock solution* to a suitable volumetric flask. Add 55% of the flask volume of *Diluent* and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.0-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times are given in *Table 1*.]

Suitability requirements

Resolution: NLT 4.0 between tolcapone related compound B and tolcapone, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tolcapone ($C_{14}H_{11}NO_5$) in the portion of Tolcapone taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

Acceptance criteria: 98.5%–101.5% on the anhydrous and solvent-free basis

IMPURITIES

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

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 Tolcapone taken:

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

r_U = peak area of any impurity from the *Sample solution*

r_S = peak area of tolcapone from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tolcapone related compound A	0.6	0.87	0.1
Tolcapone	1.0	—	—
Tolcapone related compound B	1.4	1.0	0.2
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.5

SPECIFIC TESTS

• **Water Determination,** *Method I* ⟨921⟩**:** NMT 0.1%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards** ⟨11⟩

USP Tolcapone RS

USP Tolcapone Related Compound A RS

4'-Methyl-3,4-dihydroxybenzophenone.

$C_{14}H_{12}O_3$ 228.24

USP Tolcapone Related Compound B RS

4-Hydroxy-3-methoxy-4'-methyl-5-nitrobenzophenone.

$C_{15}H_{13}NO_5$ 287.27

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

Topic/Question	Contact	Expert Committee
TOLCAPONE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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