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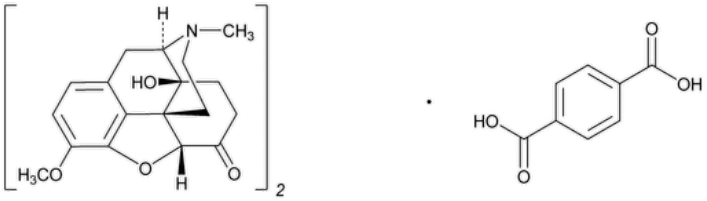
Oxycodone Terephthalate



$(C_{18}H_{21}NO_4)_2 \cdot C_8H_6O_4$ 796.86

Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-, 1,4-benzenedicarboxylate (2:1 salt), (5α);

4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one 1,4-benzenedicarboxylate (2:1 salt) CAS RN®: 64336-55-6.

DEFINITION

Oxycodone Terephthalate contains NLT 97.0% and NMT 103.0% of oxycodone terephthalate $(C_{18}H_{21}NO_4)_2 \cdot C_8H_6O_4$, calculated on the dried basis.

IDENTIFICATION

• **A. Melting Range or Temperature ⟨741⟩**

Sample solution: Transfer 50 mL of the filtrate retained from the test for *Content of Terephthalate Acid* to a 125-mL conical flask. Render the solution alkaline with 6 N ammonium hydroxide. Allow the mixture to stand until a precipitate is formed. Filter, wash the precipitate with 50 mL of cold water, and dry for 2 h at 105°.

Acceptance criteria: The precipitate melts between 218° and 223°, but the range between the beginning and end of the melting does not exceed 2°.

Change to read:

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

Sample: Use a portion of the dried precipitate obtained in *Identification* test *A*.

Acceptance criteria: Meets the requirements

Change to read:

• **C. ▲Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U▲** (CN 1-May-2020)

Sample solution: 150 µg/mL in 0.1 N hydrochloric acid

Acceptance criteria: Exhibits a maxima at 280 nm

ASSAY

• **Procedure**

Mobile phase: To 2.2 g of sodium 1-octanesulfonate in 740 mL of water add 260 mL of methanol, 10 mL of glacial acetic acid, and 0.1 mL of triethylamine. Mix, and adjust with 5 N sodium hydroxide to a pH of 6.5 ± 0.1. Pass through a filter of 0.5-µm or finer pore size.

Diluent: 0.1 N hydrochloric acid

Internal standard solution: 0.1 mg/mL of ethylparaben prepared by dissolving in 2% of the flask volume of methanol and diluting with *Diluent* to volume

Standard stock solution: 0.75 mg/mL of USP Oxycodone RS in *Diluent*

Standard solution: 0.11 mg/mL of USP Oxycodone RS prepared as follows. Transfer 15.0 mL of *Standard stock solution* to a 100-mL volumetric flask, add 20.0 mL of *Internal standard solution*, and dilute with *Diluent* to volume.

Sample stock solution: 0.71 mg/mL of Oxycodone Terephthalate in *Diluent*. Filter, discarding the first 5 mL.

Sample solution: 0.14 mg/mL of Oxycodone Terephthalate prepared as follows. Transfer 10.0 mL of the *Sample stock solution* to a 50-mL volumetric flask, add 10.0 mL of *Internal standard solution*, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.9-mm × 15-cm; packing L1

Column temperature: 50 ± 1.0°

Flow rate: 1 mL/min

Run time: Twice the retention time of the main oxycodone peak

Injection size: 30 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 6 between oxycodone and ethylparaben

Column efficiency: NLT 1800 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of oxycodone terephthalate $(C_{18}H_{21}NO_4)_2 \cdot C_8H_6O_4$ in the portion of Oxycodone Terephthalate taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

R_U = peak response ratio of oxycodone to ethylparaben from the *Sample solution*

R_S = peak response ratio of oxycodone to ethylparaben from the *Standard solution*

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

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

M_{r1} = one-half of the molecular weight of oxycodone terephthalate, 398.43

M_{r2} = molecular weight of oxycodone, 315.37

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 1%
- **Organic Impurities**

Solution A: 2.2 g of sodium 1-octanesulfonate in 850 mL of water. Add 150 mL of methanol, 20 mL of glacial acetic acid, and 1.0 mL of triethylamine. Pass through a filter of 0.5-µm or finer pore size.

Solution B: 2.2 g of sodium 1-octanesulfonate in 500 mL of water. Add 500 mL of methanol, 20 mL of glacial acetic acid, and 1.0 mL of triethylamine. Pass through a filter of 0.5-µm or finer pore size.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
30	80	20
50	0	100
55	0	100

Diluent: 0.1 N hydrochloric acid

Standard stock solution: 0.9 mg/mL of USP Oxycodone RS in *Diluent*

Standard solution: 0.09 mg/mL of USP Oxycodone RS from the *Standard stock solution*, prepared by adding to 20% of the flask volume of methanol, and diluting with *Diluent* to volume

System suitability stock solution: 0.05 mg/mL of 4-hydroxybenzoic acid isopropyl ester in methanol

System suitability solution: 0.01 mg/mL of 4-hydroxybenzoic acid isopropyl ester and 0.09 mg/mL of USP Oxycodone RS in *Diluent* from the *System suitability stock solution* and *Standard stock solution*, respectively

Sample solution: 11 mg/mL of Oxycodone Terephthalate in methanol prepared as follows. Transfer the required amount of sample to a suitable volumetric flask. Add 80% of the flask volume of methanol, and shake by mechanical means for about 20 min to dissolve. Dilute with methanol to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.9-mm × 15-cm; packing L1

Column temperature: 45 ± 1°

Flow rate: 1.5 mL/min

Injection size: 25 µL

System suitability

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

Suitability requirements

Resolution: NLT 8 between the oxycodone and 4-hydroxybenzoic acid isopropyl ester peaks, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak area of an individual impurity from the *Sample solution*

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

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

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

M_{r1} = one-half of the molecular weight of oxycodone terephthalate, 398.43

M_{r2} = molecular weight of oxycodone, 315.37

[Note—If any impurity is found having a retention time of about 2 in relation to that of the oxycodone peak, divide its apparent percentage by 4.8.]

Acceptance criteria

Individual impurities: NMT 1.0%

Total impurities: NMT 2.0%

SPECIFIC TESTS

• **Content of Terephthalic Acid**

Sample solution: Transfer 1 g into a 50-mL beaker. Add 25 mL of 0.2 N hydrochloric acid, and heat to boiling with continuous stirring. Cover the beaker with a watch glass, and allow to cool to room temperature. Pass the suspension through a tared, medium-porosity filtering crucible. Transfer any material remaining in the beaker to the crucible with the aid of small portions of cold 0.2 N hydrochloric acid. Wash the material in the crucible with several portions of cold 0.2 N hydrochloric acid. [Note—Reserve the combined filtrates for use in *Identification* test *A*.]

Analysis: Dry the material in the crucible at 105° for 1 h, allow to cool, and reweigh. The material in the crucible is terephthalic acid. Determine the weight of terephthalic acid, and calculate the percentage of terephthalic acid.

Acceptance criteria: Between 20.2% and 21.5% of terephthalic acid ($C_8H_6O_4$) in Oxycodone Terephthalate on the dried basis

• **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 4 h: it loses NMT 1.5% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨11⟩

  USP Oxycodone RS

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

Topic/Question	Contact	Expert Committee
OXYCODONE TEREPHTHALATE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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