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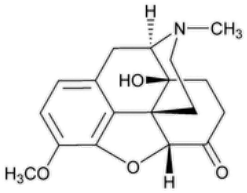
Oxycodone Hydrochloride



• HCl

$C_{18}H_{21}NO_4 \cdot HCl$ 351.82

Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17- methyl-, hydrochloride, (5α)-;

4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6- one hydrochloride CAS RN®: 124-90-3; UNII: C1ENJ2TE6C.

DEFINITION

Oxycodone Hydrochloride contains NLT 97.0% and NMT 103.0% of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$), calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

Change to read:

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

Sample: Dissolve 250 mg of Oxycodone Hydrochloride in 25 mL of water. Render 25 mL of the resulting solution 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 at 105° for 2 h.

Acceptance criteria: Meets the requirements

• **B.** The retention time of the oxycodone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: 0.005 M sodium 1-hexanesulfonate, methanol, triethylamine, and phosphoric acid (900:100:2:5). Adjust with 50% sodium hydroxide solution to a pH of 2.5 ± 0.1 and filter.

System suitability solution: 13 µg/mL of USP Codeine Phosphate RS and 9 µg/mL of USP Oxycodone RS in *Mobile phase*

Standard solution: 0.9 mg/mL of USP Oxycodone RS in *Mobile phase*

Sample solution: 1 mg/mL of Oxycodone Hydrochloride in *Mobile phase*. [Note—Pass a portion of this solution through a filter of 0.5-µm or finer pore size, and use the filtrate as the *Sample solution*.]

Chromatographic system

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

Mode: LC

Detector: UV 206 nm

Column: 3.9-mm × 15-cm; 4-µm packing L7

Column temperature: 50°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of oxycodone

System suitability

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

[Note—The relative retention times for codeine and oxycodone are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between codeine and oxycodone, *System suitability solution*

Tailing factor: 0.75–1.25, *Standard solution*

Relative standard deviation: NMT 1.10%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$) in the portion of Oxycodone Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of oxycodone hydrochloride, 351.82

M_{r2} = molecular weight of oxycodone base, 315.37

Acceptance criteria: 97.0%–103.0% on the anhydrous, solvent-free basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.05%

[Note—Use of sulfuric acid is omitted.]

[Note—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 1* is recommended if 8β-hydroxyoxycodone (7,8-dihydro-8β-14-dihydroxycodeinone) is a potential impurity.]

• **Organic Impurities, Procedure 1**

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Oxycodone Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_T = sum of the responses of all the peaks from the *Sample solution*

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Oxymorphone	0.31	0.15
Noroxymorphone[a]	0.33	0.15
10-Hydroxyoxycodone[b]	0.53	0.15
6-α Oxycodol[c]	0.67	0.25
8β-Hydroxyoxycodone (7,8-dihydro-8β-14-dihydroxycodeinone)[d]	0.71	0.15

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Oxycodone	1.00	—
Hydrocodone	1.19	0.15
Individual unspecified impurity	—	0.10
Total impurities	—	2.0

[a] 4,5α-Epoxy-3,14-dihydroxymorphinan-6-one.

[b] 4,5α-Epoxy-10α,14-dihydroxy-3-methoxy-17-methylmorphinan-6-one.

[c] 4,5α-Epoxy-3-methoxy-17-methylmorphinan-6α,14-diol.

[d] 4,5α-Epoxy-8β,14-dihydroxy-3-methoxy-17-methylmorphinan-6-one.

- **Organic Impurities, Procedure 2**

Buffer: Mix 4.0 mL of heptafluorobutyric acid with 2000 mL of water and adjust with ammonium hydroxide to a pH of 2.3 ± 0.1.

Solution A: Methanol and *Buffer* (23:77)

Solution B: Methanol, tetrahydrofuran, and *Buffer* (20:3:77)

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	0
2	100	0
30	0	100
55	0	100
55.1	100	0
65	100	0

Diluent: Trifluoroacetic acid and water (3:1000)

System suitability solution: 0.0067 mg/mL each of USP Hydrocodone RS and USP Oxycodone Related Compound A RS, and 3.0 mg/mL of USP Oxycodone Hydrochloride RS in *Diluent*

Standard solution: 0.0067 mg/mL of USP Hydrocodone RS in *Diluent*

Sample solution: 3.0 mg/mL of Oxycodone Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 3-µm packing L1

Column temperature: 38°

Flow rate: 0.8 mL/min

Injection volume: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between oxycodone and hydrocodone; NLT 1.0 between hydrocodone and oxycodone related compound A, *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 Oxycodone Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

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

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

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

M_{r1} = molecular weight of hydrocodone hydrochloride, 335.83

M_{r2} = molecular weight of hydrocodone, 299.36

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. Disregard any peaks below 0.03%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxymorphone hydrochloride	0.54	0.93	0.15
1-Hydroxyoxycodone hydrochloride[a]	0.69	1.00	0.15
6-Oxycodol hydrochloride[b]	0.79	1.16	0.25
Oxycodone hydrochloride	1.00	—	—
Hydrocodone hydrochloride	1.14	1.00	0.50
14-Hydroxycodeinone hydrochloride (oxycodone related compound A hydrochloride)[c]	1.18	0.99	0.25
Noroxycodone hydrochloride[d]	1.26	0.94	0.50
Individual unspecified impurity	—	—	0.10
Total impurities	—	—	1.5

[a] 4,5α-Epoxy-1,14-dihydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

[b] 4,5α-Epoxy-3-methoxy-17-methylmorphinan-6,14-diol hydrochloride.

[c] 4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-7-ene-6-one hydrochloride (oxycodone related compound A hydrochloride salt).

[d] 4,5α-Epoxy-14-hydroxy-3-methoxymorphinan-6-one hydrochloride.

SPECIFIC TESTS

• **Content of Chloride**

Sample solution: 6 mg/mL of Oxycodone Hydrochloride in methanol

Analysis: To 50 mL of the *Sample solution*, add 5 mL of glacial acetic acid and titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically. Each milliliter of 0.1 N silver nitrate is equivalent to 3.545 mg of chloride.

Acceptance criteria: 9.8%–10.4% on the anhydrous, solvent-free basis

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

Sample solution: 25 mg/mL of Oxycodone Hydrochloride in water on the anhydrous, solvent-free basis

Acceptance criteria: −137° to −149°

- **Water Determination** ⟨921⟩, *Method I*: NMT 7.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **Labeling:** The label states with which *Organic Impurities* procedure the article complies if *Organic Impurities*, *Procedure 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Codeine Phosphate RS
USP Hydrocodone RS
USP Oxycodone RS
USP Oxycodone Hydrochloride RS
USP Oxycodone Related Compound A RS

Also known as 14-Hydroxycodeinone;
4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-7-ene-6-one.

$C_{18}H_{19}NO_4$ 313.35

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

Topic/Question	Contact	Expert Committee
OXYCODONE HYDROCHLORIDE	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

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