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Oxycodone Hydrochloride Oral Solution

DEFINITION

Oxycodone Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectrum of the oxycodone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

Delete the following:

▲• **B. Thin-Layer Chromatography**

Standard solution: Evaporate 5 mL of the *Standard solution* obtained from *Identification* test *A* just to dryness. Dissolve the residue in 1.0 mL of chloroform.

Sample solution: Evaporate 5 mL of the *Sample solution* obtained from *Identification* test *A* just to dryness. Dissolve the residue in 1.0 mL of chloroform.

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 20 µL

Developing solvent system: Acetone, toluene, ether, and ammonium hydroxide (6:4:1:0.3)

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the plate until the solvent front has moved about three-fourths of the length of the plate, remove it, mark the solvent front, allow the solvent to evaporate, and spray with iodoplatinate TS.

Acceptance criteria: The principal spot from the *Sample solution* corresponds in color, size, and R_F value to that from the solution from the *Standard solution*, and no other spots are observed. ▲(USP 1-May-2021)

Change to read:

• ▲**B.**▲ (USP 1-May-2021) The retention time of the oxycodone peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

Mobile phase: Acetonitrile, 0.01 M sodium 1-hexanesulfonate, and glacial acetic acid (25:74:1). Adjust with 5 N sodium hydroxide to a pH of 3.5.

Standard solution: 0.045 mg/mL of USP Oxycodone RS in *Mobile phase*

Sample solution: Nominally 0.05 mg/mL of oxycodone hydrochloride in *Mobile phase* from Oral Solution. Pass a portion of this mixture through a filter of 0.5-µm or finer pore size, and use the clear filtrate as the *Sample solution*.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm. ▲For *Identification A*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2021)

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.7 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$) in the portion of Oral Solution 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 = nominal 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 free base, 315.37

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Add the following:

▲• Organic Impurities

Buffer: Dissolve 0.54 g of monobasic potassium phosphate in 1000 mL of water. Adjust with hydrochloric acid to a pH of 3.5. Add 6.5 g of anhydrous octanesulfonic acid sodium salt and readjust with hydrochloric acid to a pH of 3.5.

Solution A: Acetonitrile and *Buffer* (8:92)

Solution B: Acetonitrile and *Buffer* (45:55)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
8	78	22
18	78	22
47	0	100
47.01	100	0
55	100	0

Diluent: Acetonitrile and 0.1 N hydrochloric acid (20:80)

System suitability solution: 0.45 mg/mL of USP Oxycodone RS and 0.001 mg/mL of USP Oxycodone Related Compound A RS in *Diluent*

Sensitivity solution: 0.225 µg/mL of USP Oxycodone RS in *Diluent*

Standard solution: 0.0045 mg/mL of USP Oxycodone RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of oxycodone hydrochloride from Oral Solution in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 10-cm; 2.6-µm packing L1

Column temperature: 45°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for oxycodone related compound A and 7-methyloxycodone (4,5α-Epoxy-14-hydroxy-3-methoxy-7,17-dimethylmorphinan-6-one) are 1.05 and 1.17, respectively.]

Suitability requirements

Resolution: NLT 2.0 between oxycodone and oxycodone related compound A, *System suitability solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual degradation product in the portion of Oral Solution 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 individual degradation product from the *Sample solution*

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

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

C_U = nominal 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 free base, 315.37

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxycodone *N*-oxide (oxycodone related compound B)	0.42	1.14	1.0
Oxycodone	1.00	—	—
Any unspecified degradation product	—	1.00	0.2
Total degradation products	—	—	2.0

▲ (USP 1-May-2021)

OTHER COMPONENTS

• **ALCOHOL DETERMINATION** ⟨611⟩, *Procedures, Method II* (if present): 85.0%–115.0% of the labeled amount of alcohol (C_2H_5OH), determined by the gas–liquid chromatographic method, using acetone as the internal standard

PERFORMANCE TESTS

• **Uniformity of Dosage Units** ⟨905⟩

For Oral Solution packaged in single-unit containers: Meets the requirements

• **Deliverable Volume** ⟨698⟩

For Oral Solution packaged in multiple-unit containers: Meets the requirements

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 1.4–4.6

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-May-2021)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Oxycodone RS

▲ USP Oxycodone Related Compound A RS

4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-7-ene-6-one.

$C_{18}H_{19}NO_4$ 313.35▲ (USP 1-May-2021)

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

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

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