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Oxycodone Hydrochloride Extended-Release Tablets

DEFINITION

Oxycodone Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$).

IDENTIFICATION

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

Add the following:

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

ASSAY

Change to read:

• **Procedure**

▲**Buffer solution:** 7.8 g/L of potassium phosphate, monobasic in water, adjusted with phosphoric acid to a pH of 3.0

Mobile phase: Acetonitrile and *Buffer solution* (10:90)

Diluent: Acetonitrile and simulated gastric fluid TS without enzyme (10:20)

0.85% phosphoric acid: 10 mL/L of phosphoric acid in water

Standard stock solution: 0.9 mg/mL of USP Oxycodone RS in *0.85% phosphoric acid*

Standard solution: 0.09 mg/mL of USP Oxycodone RS in *Diluent* from the *Standard stock solution*

Sample stock solution: Nominally (*L*/100) mg/mL of oxycodone hydrochloride where *L* is the label claim in mg/Tablets. Transfer 10 Tablets into a 1000-mL volumetric flask, and add 900 mL of *Diluent*. Stir until the Tablets are completely dispersed. Dilute with *Diluent* to volume. Physically manipulate the Tablets as necessary to ensure complete dispersion within 24 h with stirring in *Diluent*. Protect this solution from light.

Sample solution: Nominally about 0.1 mg/mL of oxycodone hydrochloride in *Diluent* from the *Sample stock solution*. Pass through a suitable filter of 0.45-µm pore size. For Tablets labeled to contain 10 mg, use the *Sample stock solution* directly.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm. For *Identification B*, use a diode array detector in the range of 200–350 nm.

Column: 3.0-mm × 25-cm; 5-µm packing L1

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: NLT 1.4 times the retention time of oxycodone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.7–1.2

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 Tablets taken:

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

r_U = peak response of oxycodone from the *Sample solution*

r_S = peak response of oxycodone 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 base, 315.36▲ (USP 1-Dec-2021)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Medium:** Simulated gastric fluid TS without enzymes; 900 mL

Apparatus 1: 100 rpm. Include a stainless-steel spring across the underside of the top of each of the baskets to prevent Tablet adhesion to the underside of the top of the baskets during the test.

Times: 1, 4, and 12 h

0.85% phosphoric acid: 10 mL/L of phosphoric acid in water

Mobile phase: Transfer 28.0 g of potassium phosphate, monobasic into a 4-L flask, and dissolve with 3600 mL of water. Adjust with phosphoric acid to a pH of 3.0. Add 400 mL of acetonitrile, and mix.

Standard stock solution: 0.9 mg/mL of USP Oxycodone RS in *0.85% phosphoric acid*

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a solution having a concentration of 0.009 mg/mL of USP Oxycodone RS for Tablets labeled to contain 10, 15, 20, 30, and 40 mg, and 0.063 mg/mL of USP Oxycodone RS for Tablets labeled to contain 60 and 80 mg.

Sample solution: Pass the solution under test through a suitable filter of 1.0- or 10-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 3.0-mm × 25-cm; 5-µm packing L1

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: NLT 3.7 times the retention time of oxycodone

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.7–1.2

Relative standard deviation: NMT 2%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of oxycodone from the *Sample solution*

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

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

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

M_{r2} = molecular weight of oxycodone base, 315.36

Calculate the percentage of the labeled amount of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$) released at each time point (*i*):

$$Result_1 = C_1 \times V \times (1/L) \times 100$$

$$Result_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$Result_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of oxycodone hydrochloride in the portion of the sample withdrawn at time point *i* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Medium* (mL)

Tolerances: See *Table 1* for Tablets labeled to contain 10, 15, 20, and 60 mg; see *Table 2* for Tablets labeled to contain 30 and 40 mg; see *Table 3* for Tablets labeled to contain 80 mg.

Table 1

Time Point (*i*)	Time (h)	Amount Released (%)
1	1	15–35
2	4	55–75
3	12	NLT 85

Table 2

Time Point (*i*)	Time (h)	Amount Released (%)
1	1	15–35
2	4	60–80
3	12	NLT 85

Table 3

Time Point (*i*)	Time (h)	Amount Released (%)
1	1	15–35
2	4	52–72
3	12	NLT 85

The percentages of the labeled amount of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.▲ (USP 1-Dec-2021)

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

Delete the following:

▲• **Limit of Oxycodone Related Compound B (Oxycodone *N*-Oxide)**

Diluent: 10 mL/L of phosphoric acid in water

Buffer: 6.8 g/L of monobasic potassium phosphate. Add 1.2 mL of triethylamine, and adjust with *Diluent* to a pH of 3.0 ± 0.1.

Mobile phase: Methanol, *tert*-butyl methyl ether, and *Buffer* (30:1:170)

Standard solution: 0.18 mg/mL of USP Oxycodone RS and 0.002 mg/mL of USP Oxycodone Related Compound B RS in *Diluent*. [NOTE—Prepare fresh daily.]

Sample stock solution: Transfer 10 Tablets into a 500-mL volumetric flask, add 50 mL of *Diluent* and 50 mL of alcohol, and sonicate for 90 min to extract the active ingredient. Dilute with *Diluent* to volume.

Sample solution: 0.2 mg/mL of oxycodone hydrochloride from the *Sample stock solution* in *Diluent*. Pass a portion of the solution through a suitable filter, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 4.5 between the oxycodone and oxycodone related compound B peaks

Relative standard deviation: NMT 3.0% for oxycodone related compound B

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of oxycodone related compound B in the portion of Tablets taken:

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

r_U = peak area of oxycodone related compound B from the *Sample solution*

r_S = peak area of oxycodone related compound B from the *Standard solution*

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

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

Acceptance criteria: NMT 1%▲ (USP 1-Dec-2021)

Add the following:

▲• ORGANIC IMPURITIES

Buffer solution, Mobile phase, Diluent, 0.85% phosphoric acid, Standard stock solution, Sample stock solution, and **Sample solution:** Prepare as directed in the *Assay*.

Standard solution: 0.9 µg/mL of USP Oxycodone RS in *Diluent* from the *Standard stock solution*

Sensitivity solution: 0.0001 mg/mL of USP Oxycodone RS in *Diluent* from the *Standard solution*

System suitability stock solution: 0.1 mg/mL of USP Oxycodone Related Compound B RS in *0.85% Phosphoric acid*

System suitability solution: 0.9 µg/mL of USP Oxycodone RS and 0.001 mg/mL of USP Oxycodone Related Compound B RS prepared by diluting the *System suitability stock solution* with the *Standard solution*

Chromatographic system

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

Mode: LC

Detector: UV 206 nm

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

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: NLT 4.5 times the retention time of oxycodone

System suitability

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

Suitability requirements

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

Resolution: NLT 8.0 between oxycodone and oxycodone related compound B, *System suitability solution*

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

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

r_U = peak response of each degradation product from the *Sample solution*

r_S = peak response of oxycodone 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)

F = relative response factor of each degradation product (see *Table 4*)

Acceptance criteria: See *Table 4*. The reporting threshold is 0.1%.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxycodone	1.0	1.00	—
Oxycodone related compound B	1.6	0.94	0.5
Any unspecified degradation product	—	1.00	0.2
Total degradation products	—	—	1.0▲ (USP 1-Dec-2021)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

Delete the following:

▲• **Labeling:** When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.▲ (USP 1-Dec-2021)

• **USP Reference Standards** ⟨11⟩

USP Oxycodone RS

USP Oxycodone Related Compound B RS

4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one *N*-oxide.

$C_{18}H_{21}NO_5$ 331.36

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

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

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