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Oxymorphone Hydrochloride Tablets

DEFINITION

Oxymorphone Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$).

IDENTIFICATION

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

• **B.** The UV absorption spectra of the oxymorphone peak of the *Sample solution* and that of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the *Assay*.

ASSAY

• **Procedure**

Protect all solutions containing oxymorphone from light and use clear glass HPLC vials.

Solution A: Dissolve 2.02 g of sodium 1-heptanesulfonate in 900 mL of water and add 100 mL of acetonitrile. Adjust with phosphoric acid to a pH of 2.1.

Solution B: Dissolve 2.02 g of sodium 1-heptanesulfonate in 750 mL of water and add 250 mL of acetonitrile. Adjust with phosphoric acid to a pH of 2.1.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
35	0	100
40	0	100
40.1	100	0
50.1	100	0

Standard solution: 0.14 mg/mL of USP Oxymorphone RS in *Solution A*. Sonicate to dissolve if necessary.

Sample solution: Nominally 0.16 mg/mL of oxymorphone hydrochloride in *Solution A* prepared as follows. Transfer NLT 8 Tablets to a suitable volumetric flask and add about 50% of the final volume of *Solution A*. Sonicate for at least 15 min with occasional vigorous shaking until the Tablets disintegrate completely. Then shake for at least 20 min. Immediately dilute with *Solution A* to volume, and mix well. Immediately pass the solution through a suitable filter of 0.45-µm pore size, discard the first 5 mL of the filtrate, and use the filtrate for analysis.

Chromatographic system

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

Mode: LC

Detectors

Assay: UV 230 nm

Identification test B: Diode array UV 200–360 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L1

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Column temperature: 40°

Flow rate: 1.0 mL/min

Injection volume: 30 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 oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) 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 oxymorphone from the *Sample solution*

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

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

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

M_{r1} = molecular weight of oxymorphone hydrochloride, 337.80

M_{r2} = molecular weight of oxymorphone, 301.34

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: Dissolve 2.02 g of sodium 1-heptanesulfonate in 800 mL of water and add 200 mL of acetonitrile. Adjust with phosphoric acid to a pH of 2.1.

Standard stock solution: 0.1 mg/mL of USP Oxymorphone RS in 0.1 N hydrochloric acid

Standard solution: (L/1000) mg/mL of USP Oxymorphone RS in water from the *Standard stock solution*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1.0 mL/min

Injection volume: 60 µL

Run time: NLT 2.7 times the retention time of oxymorphone

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 oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of oxymorphone hydrochloride, 337.80

M_{r2} = molecular weight of oxymorphone, 301.34

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 20 min

Buffer: Dissolve 26.4 g of dibasic ammonium phosphate in 2 L of water.

Mobile phase: Acetonitrile, methanol, and *Buffer* (5:25:70)

Diluent: *Buffer*

Standard stock solution: 0.05 mg/mL of USP Oxymorphone RS in *Medium*

Standard solution: 0.0025 mg/mL of USP Oxymorphone RS in *Diluent* from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute this solution with *Diluent* to obtain a solution with a similar concentration as that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 212 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 1.6 times the retention time of oxymorphone

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 oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) dissolved:

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

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

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

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

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of oxymorphone hydrochloride, 337.80

M_{r2} = molecular weight of oxymorphone, 301.34

L = label claim (mg/Tablet)

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Tolerances: NLT 85% (*Q*) of the labeled amount of oxymorphone hydrochloride ($C_{17}H_{19}NO_4 \cdot HCl$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Protect all solutions containing oxymorphone from light and use clear glass HPLC vials.

Solution A, Solution B, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay.*

System suitability stock solution A: 0.2 mg/mL of USP Oxymorphone Related Compound A RS prepared as follows. Transfer an amount of USP Oxymorphone Related Compound A RS to a suitable volumetric flask. Dissolve with 24% of the flask volume of 0.1 N hydrochloric acid and dilute with acetonitrile to volume.

System suitability stock solution B: 0.02 mg/mL of USP Oxymorphone Related Compound A RS in acetonitrile from *System suitability stock solution A*

System suitability stock solution C: 0.14 mg/mL of USP Oxymorphone RS in *Solution A*

System suitability solution: 0.0008 mg/mL of USP Oxymorphone Related Compound A RS in *System suitability stock solution C* from *System suitability stock solution B*

Standard solution: 0.00014 mg/mL of USP Oxymorphone RS in *Solution A* from *System suitability stock solution C*

System suitability

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

Suitability requirements

Resolution: NLT 2 between oxymorphone related compound A and oxymorphone, *System suitability solution*

Relative standard deviation: NMT 10%, *Standard solution*

Analysis

Sample: *Sample solution*

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

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

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

r_T = sum of peak responses from the *Sample solution*

F = relative response factor of each individual degradation product (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
10-Hydroxyoxymorphone[a]	0.58	1.00	0.2
Oxymorphone related compound A (oxymorphone *N*-oxide)	0.81	1.09	0.2
Oxymorphone	1.00	1.00	—
10-Ketooxymorphone[b]	1.42	0.93	0.2
Oxycodone[c]	2.11	—	—
1-Bromooxymorphone[c,d]	2.22	—	—

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2,2'-Bisoxymorphone[e]	2.36	1.61	0.2
Any individual unspecified degradation product	—	1.00	0.2
Total degradation products	—	—	1.5

[a] 4,5α-Epoxy-3,10,14-trihydroxy-17-methylmorphinan-6-one.

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

[c] Process impurities, not included in the total degradation products.

[d] 1-Bromo-4,5α-epoxy-3,14-dihydroxy-17-methylmorphinan-6-one.

[e] 2,2'-Bioxymorphone.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at 25°, excursions permitted between 15° and 30°.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Oxymorphone RS

USP Oxymorphone Related Compound A RS

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

$C_{17}H_{19}NO_5$ 317.34

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

Topic/Question	Contact	Expert Committee
OXYMORPHONE HYDROCHLORIDE 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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