Oxycodeone Hydrochloride

C₁₈H₂₁NO₄ · HCl · 351.82
Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-1, hydrochloride, (5α)-4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride [124-90-3].

DEFINITION
Oxycodeone Hydrochloride contains NLT 97.0% and NMT 103.0% of C₁₈H₂₁NO₄ · HCl, calculated on the anhydrous, solvent-free basis.

IDENTIFICATION
\[ \bullet \ \text{A. PROCEDURE} \]

Sample solution: Dissolve 250 mg in 25 mL of water. Analysis: Render the 25 mL of Sample 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°C.

Acceptance criteria: The precipitate so obtained melts between 218° and 223°, but the range between the beginning and the end of melting does not exceed 2° (see Melting Range or Temperature (741)).

\[ \bullet \ \text{B. INFRARED ABSORPTION (197K):} \] Use a portion of the dried precipitate obtained in Identification test A.

ASSAY
\[ \bullet \ \text{PROCEDURE} \]

Mobile phase: 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 codeine phosphate and 9 µg/mL of oxycodone in Mobile phase

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

Sample solution: 1 mg/mL of Oxycodeone Hydrochloride in Mobile phase. [NOTE—Pass a portion of this solution through a filter having a 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°C

Flow rate: 1.5 mL/min

Injection size: 10 µL

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

Tailing factor: 0.75–1.25, Standard solution

Relative standard deviation: NMT 2.0% from replicate injections, Standard solution

Analysis
Sample: 10% NMT 2.0% from replicate injections.

Calculation: The percentage of C₁₈H₂₁NO₄ · HCl in the portion of Oxycodeone Hydrochloride taken:

\[
\text{Result} = \left( \frac{r_s}{r_U} \right) \times \left( \frac{C_s}{C_U} \right) \times \left( \frac{M_2}{M_1} \right) \times 100
\]

\[
r_s = \text{peak response from the Sample solution}
\]

\[
r_U = \text{peak response from the Standard solution}
\]

\[
C_s = \text{concentration of USP Oxycodeone RS in the Standard solution (mg/mL)}
\]

\[
C_U = \text{concentration of Oxycodeone Hydrochloride in the Sample solution (mg/mL)}
\]

\[
M_1 = \text{molecular weight of oxycodone base, } 315.37
\]

\[
M_2 = \text{molecular weight of oxycodone hydrochloride, } 351.82
\]

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

IMPURITIES
Inorganic Impurities

\[ \bullet \ \text{RESIDUE ON IGNITION (281):} \] NMT 0.05%. [NOTE—Use of sulfuric acid is omitted.]

Change to read:

Organic Impurities

\[ \bullet \ \text{PROCEDURE 1: LIMIT OF ALCOHOL} \]

Internal standard stock solution: Pipet 3.0 mL of the Internal standard stock solution to a 100-mL volumetric flask, and dilute with water to volume. [NOTE—The isopropyl alcohol must be free of alcohol impurities.]

Internal standard solution: Transfer 6.0 mL of the Internal standard solution to a 15-mL centrifuge tube, add 5.0 mL of the Internal standard solution, and mix to dissolve.

Chromatographic system
(See Chromatography (621), System Suitability.)

Mode: GC

Detector: Flame ionization

Column: 4-mm × 1.8-m glass; packed with 80- to 100-mesh support S3

Carrier gas: Helium

Temperature

Column: 150°C. [NOTE—Condition the column overnight at 235°C with a slow flow of carrier gas.]

Injector: 170°C

Detector: 170°C

Injection size: 5 µL

System suitability
Sample: Standard solution

Suitability requirements
Resolution: NLT 2 between isopropyl alcohol and alcohol

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2 Oxycodone

Tailing factor: NMT 1.5
Relative standard deviation: NMT 2.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of USP Oxycodone Hydrochloride in the portion of Oxycodone Hydrochloride taken:

$$\text{Result} = \left( \frac{R_U}{R_I} \times \frac{C_I}{C_U} \right) \times 100$$

$$R_U = \text{peak response ratio of the alcohol peak to the isopropyl alcohol from the Sample solution}$$

$$R_I = \text{peak response ratio of the alcohol peak to the isopropyl alcohol from the Standard solution}$$

$$C_I = \text{concentration of USP Oxycodone Hydrochloride in the Standard solution (\(\mu g/mL\))}$$

$$C_U = \text{concentration of Oxycodone Hydrochloride in the Sample solution (\(\mu g/mL\))}$$

Acceptance criteria: NMT 1.0%

*PROCEDE 2

Analysis: Use the chromatogram of the Sample solution in the Assay, to calculate the percentage of each impurity in the portion of Oxycodone Hydrochloride taken:

$$\text{Result} = \left( \frac{r_U}{r_T} \right) \times 100$$

$$r_U = \text{peak response for each impurity}$$

$$r_T = \text{sum of the responses of all the peaks}$$

Acceptance criteria

Individual impurities: The impurities meet the requirements listed in Impurity Table 1.

Total impurities: NMT 2.0%

<table>
<thead>
<tr>
<th>Impurity Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
</tr>
<tr>
<td>Oxymorphine</td>
</tr>
<tr>
<td>Noroxymorphine</td>
</tr>
<tr>
<td>10-Hydroxyoxycodone</td>
</tr>
<tr>
<td>6-(\alpha) Oxycodol</td>
</tr>
<tr>
<td>7,8-Dihydro-8(\beta)-14-dihydroxycodeinone</td>
</tr>
<tr>
<td>Hydrocodone</td>
</tr>
</tbody>
</table>

Individual unspecified impurity — — 0.10

*PROCEDE 3: LIMIT OF OXYCODONE RELATED COMPOUND A (14-HYDROXYCODEINONE) AND OXYCODONE RELATED COMPOUND C (CODEINONE)

Solution A: Dissolve 3.45 g of monobasic sodium phosphate in 1000 mL of water. Add 5.41 g of sodium dodecyl sulfate, and mix. Filter, and adjust with 50% (w/v) sodium hydroxide solution to a pH of 7.50 ± 0.05.

Solution B: Water and phosphoric acid (9:1)

Diluent: Prepare a mixture of water and Solution B (9:1).

Mobile phase: Prepare a mixture of acetonitrile, methanol, and Solution A (15.8:12.0:72.2), and adjust with Solution B to a pH of 7.80 ± 0.01.

Standard solution: 50 mg/mL of USP Oxycodone Hydrochloride RS and 0.5 µg/mL each of USP Oxycodone Related Compound A RS and USP Oxycodone Related Compound C RS in Diluent

Unspiked oxycodone hydrochloride solution: 50 mg/mL of USP Oxycodone Hydrochloride RS in Diluent

System suitability solution: 100 µg/mL of USP Oxycodone Hydrochloride RS and 5 µg/mL each of USP Oxycodone Related Compound A RS and USP Oxycodone Related Compound C RS in Diluent

Sample solution: 50 mg/mL of Oxycodone Hydrochloride in Diluent

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 220 nm

Column: 3.0-mm × 15-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 0.7 mL/min

Injection size: 5 µL

System suitability

Samples: Standard solution and System suitability solution

[NOTE—The relative retention times for oxycodone related compound C, oxycodone related compound A, and oxycodone are about 0.44, about 0.85, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4 between oxycodone related compound A and oxycodone related compound C, System suitability solution

Tailing factor: NMT 2.0, System suitability solution

Relative standard deviation: NMT 20% for oxycodone related compound A and C, Standard solution

Analysis

Samples: Diluent, Standard solution, Unspiked oxycodone hydrochloride solution, and Sample solution

Calculate the percentage of oxycodone related compound A and oxycodone related compound C in the portion of Oxycodone Hydrochloride taken:

$$\text{Result} = \left( \frac{r_U}{r_T} \right) \times 100$$

$$r_U = \text{peak response of oxycodone related compound A or oxycodone related compound C from the Sample solution}$$

$$r_T = \text{peak response of oxycodone related compound A or oxycodone related compound C minus the response of the Unspiked oxycodone hydrochloride solution from the Standard solution}$$

$$C_I = \text{concentration of USP Oxycodone Related Compound A RS or USP Oxycodone Related Compound C RS in the Standard solution (\(\mu g/mL\))}$$

$$C_U = \text{concentration of Oxycodone Hydrochloride in the Sample solution (\(\mu g/mL\))}$$

Acceptance criteria

Individual impurities: See Impurity Table 2.

<table>
<thead>
<tr>
<th>Impurity Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
</tr>
<tr>
<td>Oxycodone related compound A</td>
</tr>
<tr>
<td>Oxycodone related compound C</td>
</tr>
<tr>
<td>Oxycodone</td>
</tr>
</tbody>
</table>

+14-Hydroxycodeinone (C9H19NO3)

+Codeinone (C22H23NO3)

(Postponed indefinitely)

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ing the endpoint potentiometrically. Each mL of 0.1 N silver nitrate is equivalent to 3.545 mg of Cl.

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

- **Optical Rotation, Specific Rotation (781S):** −137° to −149°
  Sample solution: 25 mg/mL of Oxycodone Hydrochloride, in water, on the anhydrous, solvent-free basis

- **Water Determination, Method I (921):** NMT 7.0%

### ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.

Change to read:

- **USP Reference Standards (11)**
  - USP Oxycodone RS
  - USP Oxycodone Hydrochloride RS
  - USP Oxycodone Related Compound A RS
  - USP Oxycodone Related Compound C RS ▲USP33