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Oxycodone and Acetaminophen Tablets

DEFINITION

Oxycodone and Acetaminophen Tablets contain Oxycodone Hydrochloride and Acetaminophen. Tablets contain the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of oxycodone ($C_{18}H_{21}NO_4$), and NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$).

IDENTIFICATION

• **A. Thin-Layer Chromatography**

Standard solution A: 0.5 mg/mL of USP Oxycodone RS in a mixture of methanol and water (4:1)

Standard solution B: 0.5*J* mg/mL of USP Acetaminophen RS in a mixture of methanol and water (4:1). [Note—*J* is the ratio of the labeled amount, in mg, of acetaminophen to the labeled amount, in mg, of oxycodone per Tablet.]

Sample solution: Nominally equivalent to 2.5 mg of oxycodone from powdered Tablets in a 5-mL mixture of methanol and water (4:1). Sonicate for 5 min, and shake by mechanical means for 15 min. Allow to settle, and use the clear supernatant.

Chromatographic system

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

Adsorbent: 0.25-mm layer of silica gel mixture

Application volume: 20 µL

Developing solvent system: Butyl alcohol, glacial acetic acid, and water (4:1:2)

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Proceed as directed in the chapter. Develop the chromatographic plate until the solvent front has moved about three-fourths of the length of the plate. Mark the solvent front, and allow the plate to air-dry for about 30 min. Expose the plate to iodine vapors in a closed chamber, and locate the spots.

Acceptance criteria: The R_F values of the principal spots from the *Sample solution* correspond to those from the respective *Standard solutions*.

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

ASSAY

• **Procedure**

Solution A: Methanol and 0.05 M dibasic potassium phosphate (1:9). Adjust with phosphoric acid to a pH of 4.0.

Buffer: 0.95 mg/mL of monobasic potassium phosphate in water, phosphoric acid, and *n*-nonylamine (1000:1:1). Prepare as follows: Add 950 mg of monobasic potassium phosphate to 1000 mL of water. Add 1 mL of phosphoric acid, and stir until dissolved. While stirring, add 1 mL of *n*-nonylamine, and stir until a clear solution is obtained. Adjust with potassium hydroxide TS to a pH of 4.9 ± 0.1.

Mobile phase: Methanol and *Buffer* (1:9)

Oxycodone standard stock solution: 0.075 mg/mL of USP Oxycodone RS in *Solution A*

Standard stock solution: 0.03*J* mg/mL of USP Acetaminophen RS and 0.03 mg/mL of USP Oxycodone RS in *Solution A*. Prepare by adding 40% of the flask volume of *Solution A* to the appropriate quantity of USP Acetaminophen RS, and then adding 40% of the flask volume of *Oxycodone standard stock solution* and diluting with *Solution A* to volume. [Note—*J* is the ratio of the labeled amount, in mg, of acetaminophen to that of oxycodone equivalent.]

Standard solution: 0.003*J* mg/mL of USP Acetaminophen RS and 0.003 mg/mL of USP Oxycodone RS in *Mobile phase* from *Standard stock solution*

Sample stock solution: Nominal equivalent of 0.03 mg/mL of oxycodone, from powdered Tablets (NLT 20), in *Solution A* in a suitable container. Shake by mechanical means for 1 h.

Sample solution: 0.003 mg/mL of oxycodone in *Mobile phase* from *Sample stock solution*. Pass the resulting solution through a membrane filter of 0.5-µm or finer pore size, discarding the first 10 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for oxycodone and acetaminophen are about 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.4 between acetaminophen and oxycodone

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of oxycodone ($C_{18}N_{21}NO_4$) in the portion of Tablets taken:

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

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 in the *Sample solution* (mg/mL)

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0% of the labeled amount of oxycodone ($C_{18}H_{21}NO_4$), and 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$)

PERFORMANCE TESTS

• **DISSOLUTION,** *Procedure for a Pooled Sample*⟨711⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* as needed.

Analysis: Determine the amounts of oxycodone ($C_{18}H_{21}NO_4$) and acetaminophen ($C_8H_9NO_2$) dissolved, using the procedure in the *Assay*, and making any necessary volumetric adjustments, including adjusting the solution under test to a pH of about 5.5 before injecting.

Tolerances: NLT 75% (*Q*) of the labeled amounts of oxycodone ($C_{18}H_{21}NO_4$) and acetaminophen ($C_8H_9NO_2$) is dissolved.

• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.

• **LABELING:** The Tablets may be labeled to indicate the content of oxycodone hydrochloride ($C_{18}H_{21}NO_4 \cdot HCl$) equivalent. Each mg of oxycodone is equivalent to 1.116 mg of oxycodone hydrochloride.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Acetaminophen RS
USP Oxycodone RS

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

Topic/Question	Contact	Expert Committee
OXYCODONE AND ACETAMINOPHEN TABLETS	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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