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Oxycodone and Aspirin Tablets

» Oxycodone and Aspirin Tablets contain Oxycodone Hydrochloride and Aspirin, or Oxycodone Hydrochloride, Oxycodone Terephthalate, and Aspirin. Tablets contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of oxycodone ($C_{18}H_{21}NO_4$), and not less than 90.0 percent and not more than 110.0 percent of the labeled amount of aspirin ($C_9H_8O_4$).

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—Label the Tablets to state both the content of the oxycodone active moiety and the content or contents of the salt or salts of oxycodone used in formulating the article.

USP Reference standards ⟨11⟩—

USP Aspirin RS
USP Oxycodone RS
USP Salicylic Acid RS

Identification—The retention times of the oxycodone peak and the aspirin peak in the chromatograms of the respective *Assay preparations* correspond to those of the corresponding analytes of the respective *Standard preparations*, as obtained in the *Assay for oxycodone* and the *Assay for aspirin*, respectively.

Dissolution, *Procedure for a Pooled Sample* ⟨711⟩—

Medium: 0.05 M acetate buffer, prepared by mixing 2.99 g of sodium acetate trihydrate and 1.66 mL of glacial acetic acid with water to obtain 1000 mL of solution having a pH of 4.50 ± 0.05; 500 mL.

Apparatus 1: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{18}H_{21}NO_4$ dissolved using the method for *Assay for oxycodone*, making any necessary volumetric adjustments. Determine the amount of $C_9H_8O_4$ dissolved from UV absorbances at the wavelength of the isobestic point of aspirin and salicylic acid at about 265 nm of filtered portions of the solution under test, suitably diluted with *Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Aspirin RS in the same medium. [Note—Prepare the Standard solution at the time of use. An amount of alcohol not to exceed 1% of the total volume of the Standard solution may be used to bring the Reference Standard into solution prior to dilution with *Medium*.]

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{18}H_{21}NO_4$ is dissolved in 30 minutes and not less than 75% *(Q)* of the labeled amount of $C_9H_8O_4$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Salicylic acid—

Mobile phase—Dissolve 2 g of sodium 1-heptanesulfonate in a mixture of 850 mL of water and 150 mL of acetonitrile, and adjust with glacial acetic acid to a pH of 3.4. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluting solution—Prepare a mixture of acetonitrile and formic acid (99:1).

Standard preparation—Dissolve an accurately weighed quantity of USP Salicylic Acid RS in *Diluting solution* to obtain a solution having a known concentration of about 0.008 mg per mL.

Test preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed quantity of the powder, equivalent to about 380 mg of aspirin, to a 100-mL volumetric flask, add about 20 mL of *Diluting solution*, and sonicate for about 15 minutes. Dilute with *Diluting solution* to volume, and mix. Centrifuge a portion of this mixture, and use the clear supernatant as the *Test preparation*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 299-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 4.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Test preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the responses for the salicylic acid peaks. Calculate the percentage of salicylic acid in the portion of

Tablets taken by the formula:

$$10{,}000(C/a)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Salicylic Acid RS in the *Standard preparation*, a is the quantity, in mg, of aspirin in the portion of Tablets taken, as determined in the *Assay for aspirin*, and r_U and r_S are the salicylic acid peak responses obtained from the *Test preparation* and the *Standard preparation*, respectively: not more than 3.0% is found.

Assay for aspirin—[NOTE—Volumetric flasks should be dried at 105° for not less than 1 hour, and cooled in a desiccator before use.]

Mobile phase—Prepare a mixture of *n*-heptane and glacial acetic acid (96:4), and filter through a filter of 0.5 µm or finer porosity. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Internal standard solution—Prepare solution of 1-naphthol in chloroform containing about 1 mg per mL. [NOTE—Protect this solution from light.]

Standard preparation—Transfer about 163 mg of USP Aspirin RS, accurately weighed, to a 50-mL volumetric flask. Add 2.5 mL of glacial acetic acid, and swirl. Add 25 mL of chloroform, and shake for 10 minutes. Add 5.0 mL of *Internal standard solution*, dilute with chloroform to volume, and mix. [NOTE—Protect this solution from light.]

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 325 mg of aspirin, to a 100-mL volumetric flask, add 5 mL of glacial acetic acid, and swirl. Add 50 mL of chloroform, and shake for 10 minutes. Add 10.0 mL of the *Internal standard solution*, dilute with chloroform to volume, mix, and filter. [NOTE—Prepare the *Assay preparation* and the *Standard preparation* concomitantly, and protect from light.]

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 300-nm detector and a 4.6-mm × 25-cm column containing packing L3. The flow rate is about 4 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between the 1-naphthol peak and the aspirin peak is not less than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—[NOTE—Use peak areas where peak responses are indicated.] Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.65 for 1-naphthol and 1.0 for aspirin. Calculate the quantity, in mg, of Aspirin ($C_9H_8O_4$) in the portion of Tablets taken by the formula:

$$100C(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP Aspirin RS in the *Standard preparation*, and R_U and R_S are the ratios of the aspirin peak response to the 1-naphthol peak response obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Assay for oxycodone—

Mobile phase—Dissolve 2.2 g of sodium 1-octanesulfonate in 740 mL of water, add 260 mL of methanol, 10 mL of glacial acetic acid, and 0.1 mL of triethylamine. Mix, and adjust with 5 N sodium hydroxide to a pH of 6.5 ± 0.1. Filter through a suitable filter of 0.5 µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Diluting solution—Use 0.1 N hydrochloric acid.

Internal standard solution—Transfer about 50 mg of ethylparaben to a 500-mL volumetric flask, add 10 mL of methanol, and swirl to dissolve. Dilute with *Diluting solution* to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Oxycodone RS in *Diluting solution*, and dilute quantitatively with *Diluting solution* to obtain a stock solution having a known concentration of about 0.75 mg per mL. Transfer 15.0 mL of this stock solution to a second 100-mL volumetric flask, add 20.0 mL of *Internal standard solution*, dilute with *Diluting solution* to volume, and mix to obtain a *Standard preparation* having a known concentration of about 0.112 mg of USP Oxycodone RS per mL.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 11.2 mg of oxycodone, to a suitable glass-stoppered conical flask, add 50.0 mL of *Diluting solution*, and shake by mechanical means for about 30 minutes. Filter this solution, transfer 25.0 mL of the clear filtrate to a 50-mL volumetric flask, add 10.0 mL of *Internal standard solution*, dilute with *Diluting solution* to volume, and mix. Use this solution as the *Assay preparation.*

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm × 15-cm column that contains packing L1 and is maintained at a temperature of 50 ± 1.0°. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure:* the column efficiency, determined from the oxycodone peak, is not less than 1800 theoretical plates, the resolution, *R,* between the oxycodone and the ethylparaben peaks is not less than 6, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 30 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.5 for oxycodone and 1.0 for ethylparaben. Calculate the quantity, in mg, of oxycodone ($C_{18}H_{21}NO_4$) in the portion of Tablets taken by the formula:

$$100C(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP Oxycodone RS in the *Standard preparation*, and R_U and R_S are the ratios of the responses of the oxycodone peak and the ethylparaben peak obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

Topic/Question	Contact	Expert Committee
OXYCODONE AND ASPIRIN 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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