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Hydrocodone Bitartrate and Acetaminophen Tablets

» Hydrocodone Bitartrate and Acetaminophen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of hydrocodone bitartrate disesquihydrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2½H_2O$) and acetaminophen ($C_8H_9NO_2$).

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

Labeling—The labeling indicates the *Dissolution* test with which the product complies.

USP Reference standards ⟨11⟩—
USP Acetaminophen RS
USP Hydrocodone Bitartrate RS

Identification—

A: Finely powder 1 Tablet, and transfer about half of the powder to a test tube. Add 1 mL of 1 N sodium hydroxide and 10 mL of water, and centrifuge. Add 5 or 6 drops of ferric chloride TS: a deep blue color develops, and almost immediately a gray-black precipitate forms *(presence of acetaminophen)*.

B: The retention times of the hydrocodone bitartrate peak and the acetaminophen peak in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

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

TEST 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*.

Medium: pH 5.8 ± 0.05 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Proceed as directed in the *Assay*, making any necessary modifications.

Tolerances—Not less than 80% *(Q)* each of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and hydrocodone bitartrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2½H_2O$) are dissolved in 30 minutes.

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

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus, Time, and *Procedure*—Proceed as directed under *Test 1*.

Tolerances—Not less than 80% *(Q)* each of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and hydrocodone bitartrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2½H_2O$) is dissolved in 30 minutes.

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

Assay—

Buffer solution—Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (85:15), and add 0.2 mL of triethylamine per L of *Mobile phase.* Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Hydrocodone bitartrate standard stock preparation—Dissolve an accurately weighed quantity of USP Hydrocodone Bitartrate RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 35 µg per mL.

Standard preparation—Transfer about 38 mg of USP Acetaminophen RS, accurately weighed, to a 50-mL volumetric flask. Add an accurately measured volume of *Hydrocodone bitartrate standard stock preparation* containing about 38000*J* µg of USP Hydrocodone Bitartrate RS, *J* being the ratio of the labeled amount, in mg, of hydrocodone bitartrate to that of acetaminophen per Tablet, dilute with *Mobile phase* to volume, and mix. This solution contains about 0.76 mg of USP Acetaminophen RS per mL and about 760*J* µg of USP Hydrocodone Bitartrate RS per mL.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 76 mg of acetaminophen, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Pass a portion of this mixture through a membrane having a 0.45-µm or finer porosity, discarding the first 5 mL of the filtrate.

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Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a detector set at 210 nm for hydrocodone bitartrate and 295 nm for acetaminophen and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for acetaminophen and 2.0 for hydrocodone; the resolution, *R,* between hydrocodone and acetaminophen is not less than 5.0; the tailing factor for the hydrocodone peak is not more than 1.6; and the relative standard deviation for replicate injections determined from both acetaminophen and hydrocodone is not more than 2.0% each.

Procedure—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. From the responses obtained at 210 nm, calculate the quantity, in mg, of hydrocodone bitartrate ($C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2½H_2O$) in the portion of Tablets taken by the formula:

$$(494.49/449.46)(0.1C)(r_U/r_S)$$

in which 494.49 is the molecular weight of hydrocodone bitartrate disesquihydrate; 449.46 is the molecular weight of anhydrous hydrocodone bitartrate; C is the concentration, in µg per mL, of USP Hydrocodone Bitartrate RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively. From the responses obtained at 295 nm, calculate the quantity, in mg, of acetaminophen ($C_8H_9NO_2$) 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 Acetaminophen RS in the *Standard preparation;* and r_U and r_S are the peak responses 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
HYDROCODONE BITARTRATE AND ACETAMINOPHEN TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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