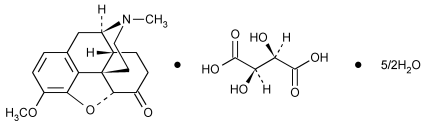
Hydrocodone Bitartrate



$C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2^1/_2H_2O$ 494.490

Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-, (5α)-, [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1 : 1), hydrate (2 : 5).

4,5α-Epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1 : 1) hydrate (2 : 5) [*34195-34-1; 6190-38-1*].

Anhydrous 449.46 [*143-71-5*].

» Hydrocodone Bitartrate, dried in vacuum at 105° for 2 hours, contains not less than 98.0 percent and not more than 102.0 percent of $C_{18}H_{21}NO_3 \cdot C_4H_6O_6$.

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

USP Reference standards ⟨11⟩**—***USP Dihydrocodeine Bitartrate RS. USP Hydrocodone Bitartrate RS. USP Hydrocodone Bitartrate Related Compound A RS.*

Identification—

A: *Infrared Absorption* ⟨197M⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 100 µg per mL.

Medium: 0.1 N sulfuric acid.

Specific rotation ⟨781S⟩**:** between –79° and –84°.

Test solution: 20 mg, undried, per mL, in water. Calculate the result on the basis of the undried aliquot.

pH ⟨791⟩**:** between 3.2 and 3.8, in a solution (1 in 50).

Loss on drying—Dry it in vacuum at 105° for 2 hours [NOTE—See the *Note* in the *Assay* for precautions regarding handling of the dried material.]: it loses not less than 7.5% and not more than 12.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Chloride—To 10 mL of a solution (1 in 100), acidified with nitric acid, add a few drops of silver nitrate TS: no opalescence is produced immediately.

Organic volatile impurities, *Method I* ⟨467⟩**:** meets the requirements.

(Official until July 1, 2008)

Assay—[NOTE—Dry both the USP Hydrocodone Bitartrate RS and the Hydrocodone Bitartrate materials in vacuum at 105° for 2 hours. Immediately transfer the dried materials to a desiccator containing phosphorus pentoxide. Weigh each dried material individually within 1 minute, and proceed with the *Assay*.]

Mobile phase—Prepare a mixture of acetonitrile, water, and diethylamine (800 : 4 : 1). Prepare a filtered and degassed mixture of this solution and methanol (55 : 45). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer about 10 mg of previously dried USP Hydrocodone Bitartrate RS, accurately weighed, to a 10-mL volumetric flask, add 5 mL of water, and mix to dissolve. Dilute with methanol to volume, and mix to obtain a solution having a known concentration of about 1 mg per mL.

Assay preparation—Transfer an accurately weighed quantity of previously dried Hydrocodone Bitartrate, equivalent to about 100 mg of hydrocodone bitartrate, $C_{18}H_{21}NO_3 \cdot C_4H_6O_6$, to a 100-mL volumetric flask, add 50 mL of water, and mix to dissolve. Dilute with methanol to volume, and mix.

Resolution solution—Prepare a solution in methanol containing about 0.4 mg of USP Dihydrocodeine Bitartrate RS and 0.6 mg of USP Hydrocodone Bitartrate RS per mL. Prepare a mixture of this solution and water (1 : 1).

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains packing L3. The flow rate is about 1.5 mL per minute. Chromatograph the *Resolution solution*, and record the responses as directed for *Procedure:* the relative retention times are about 0.7 for hydrocodone and 1.0 for dihydrocodeine; and the resolution, *R*, between hydrocodone and dihydrocodeine is not less than 3.0. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 1.0%.

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. Calculate the quantity, in mg, of $C_{18}H_{21}NO_3 \cdot C_4H_6O_6$ in the portion of Hydrocodone Bitartrate taken by the formula:

$$(100C)(r_U / r_S)$$

in which C is the concentration, in mg 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.