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Bromodiphenhydramine Hydrochloride and Codeine Phosphate Oral Solution

» Bromodiphenhydramine Hydrochloride and Codeine Phosphate Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of bromodiphen hydramine hydrochloride ($C_{17}H_{20}$ BrNO · HCl) and codeine phosphate hemihydrate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$).

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

Labeling—Label it to indicate the alcohol content.

USP Reference standards ⟨11⟩—

USP Bromodiphenhydramine Hydrochloride RS
USP Codeine Phosphate RS

Identification—

A: *Thin-Layer Chromatographic Identification Test ⟨201⟩*—

Test solution—Transfer a volume of Oral Solution, equivalent to about 10 mg of codeine phosphate, to a separator, and add 5 mL of water, 5 mL of methylene chloride, and 1 mL of ammonium hydroxide. Shake for 1 minute, allow the layers to separate, and use the clear, lower layer.

Standard solution—Prepare a solution of USP Bromodiphenhydramine Hydrochloride RS and USP Codeine Phosphate RS in methanol containing 10 mg of each per mL.

Developing solvent system: a mixture of alcohol and ammonium hydroxide (49:1).

B: The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Microbial enumeration tests ⟨61⟩ and Tests for specified microorganisms ⟨62⟩—It meets the requirements of the tests for absence of *Salmonella* species, *Escherichia coli, Staphylococcus aureus,* and *Pseudomonas aeruginosa*. The total aerobic microbial count does not exceed 100 cfu per mL, and the total combined molds and yeasts count does not exceed 50 cfu per mL.

pH ⟨791⟩: between 4.5 and 6.5.

Alcohol Determination, *Method II* ⟨611⟩: between 4.0% and 6.0% is found.

Assay—

Diluent—Prepare a mixture of methanol and water (80:20).

Mobile phase—Prepare a filtered and degassed mixture of methanol, water, 0.1 N ammonium hydroxide solution, and 0.1 N ammonium nitrate solution (27:3:2:1). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve accurately weighed quantities of USP Bromodiphenhydramine Hydrochloride RS and USP Codeine Phosphate RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having known concentrations of about 100 µg per mL and 80 µg per mL, respectively.

Assay preparation—Using a pipet calibrated "to contain", transfer an accurately measured volume of Oral Solution, equivalent to about 10 mg of bromodiphenhydramine hydrochloride and 8 mg of codeine phosphate, to a 100-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30.0-cm column that contains packing L3. The flow rate is about 1.0 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 bromodiphenhydramine and 1.4 for codeine; the resolution, *R,* between bromodiphenhydramine and codeine is not less than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

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 peak responses for bromodiphenhydramine and codeine. Calculate the quantity, in mg, of bromodiphen hydramine hydrochloride ($C_{17}H_{20}$BrNO · HCl) in each mL of the Oral Solution taken by the formula:

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

in which C is the concentration, in mg per mL, of USP Bromodiphenhydramine Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of Oral Solution taken to prepare the *Assay preparation;* and r_U and r_S are the bromodiphenhydramine peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively. Calculate the quantity, in mg, of codeine phosphate hemihydrate ($C_{18}H_{21}NO_3 \cdot$

$H_3PO_4 \cdot ½H_2O$) in each mL of the Oral Solution taken by the formula:

$$(406.37/397.36)(100C/V)(r_U/r_S)$$

in which 406.37 and 397.36 are the molecular weights of codeine phosphate hemihydrate and anhydrous codeine phosphate, respectively; *C* is the concentration, in mg per mL, of USP Codeine Phosphate RS in the *Standard preparation; V* is the volume, in mL, of Oral Solution taken to prepare the *Assay preparation;* and r_U and r_S are the codeine 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
BROMODIPHENHYDRAMINE HYDROCHLORIDE AND CODEINE PHOSPHATE ORAL SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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