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Terpin Hydrate and Codeine Oral Solution

» Terpin Hydrate and Codeine Oral Solution contains, in each 100 mL, not less than 1.53 g and not more than 1.87 g of terpin hydrate ($C_{10}H_{20}O_2 \cdot H_2O$), and not less than 180 mg and not more than 220 mg of codeine ($C_{18}H_{21}NO_3 \cdot H_2O$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Terpin Hydrate RS
USP Codeine Phosphate RS

Identification—

Developing solvent—Prepare a mixture of methylene chloride and methanol (9:1).

Standard solution A—Dissolve a suitable quantity of USP Terpin Hydrate RS in methylene chloride to obtain a solution having a concentration of about 3 mg per mL. [Note—A small volume of methanol may be used to aid dissolution of the terpin hydrate.]

Standard solution B—Transfer 20 mg of USP Codeine Phosphate RS to a suitable separator containing 10 mL of water, add 1 mL of 1 N sodium hydroxide, and mix. Add 10 mL of methylene chloride, and shake for 1 minute. Allow the layers to separate, and drain the lower organic layer into a suitable flask. Discard the aqueous layer.

Test solution—Transfer 10 mL of Oral Solution to a suitable separator containing 10 mL of water, and add 1 mL of 1 N sodium hydroxide. Add 10 mL of methylene chloride, shake for 1 minute, and allow the layers to separate. Use the clear lower organic layer as the *Test solution*.

Procedure—Apply separately 5 µL of *Standard solution A*, *Standard solution B*, and the *Test solution* to a suitable thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram in a chromatographic chamber containing the *Developing solvent* until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the chromatographic chamber, mark the solvent front, and allow the plate to dry. Examine the plate under short-wavelength UV light, and mark the location of the codeine spots. Spray the plate with phosphomolybdic acid TS, and heat at 105° for 5 minutes. The terpin hydrate spots appear blue on a yellow background. The R_F values of the spots due to terpin hydrate and codeine obtained from the *Test solution* correspond to those obtained from *Standard solutions A* and *B*, respectively.

Alcohol Determination, *Method II* ⟨611⟩: between 90.0% and 110.0% of the labeled amount of C_2H_5OH.

Assay for terpin hydrate—

Internal standard solution—Prepare a chloroform solution containing 20 mg of biphenyl and 2.6 mg of *N*-phenylcarbazole in each mL.

Standard preparation—Transfer about 26 mg of USP Codeine Phosphate RS and about 170 mg of USP Terpin Hydrate RS, both accurately weighed, to a separator, add 5 mL of alcohol, shake to dissolve the terpin hydrate, add 25 mL of water to dissolve the codeine phosphate, add 10 mL of 5 N sodium hydroxide, and extract with three 25-mL portions of chloroform, filtering each, successively, through cotton. Rinse the cotton with chloroform. To the combined rinse and extracts add 5.00 mL of *Internal standard solution*, and mix.

Assay preparation—Pipet 10 mL of Oral Solution into a separator, add 20 mL of water and 10 mL of 5 N sodium hydroxide, and extract with three 25-mL portions of chloroform, filtering each, successively, through cotton. Rinse the cotton with chloroform. To the combined rinse and extracts add 5.00 mL of *Internal standard solution*, and mix.

Chromatographic system and *System suitability*—Proceed as directed in the *Assay* under *Terpin Hydrate*. [Note—Heat the column to 230° to remove the *N*-phenylcarbazole and codeine from prior injections.]

Procedure—Inject about 1 µL of the *Standard preparation* into a suitable gas chromatograph, and record the chromatogram. Similarly, inject about 1 µL of the *Assay preparation*, and record the chromatogram. Calculate the quantity, in mg, of terpin hydrate ($C_{10}H_{20}O_2 \cdot H_2O$) in each mL of the Oral Solution taken by the formula:

$$0.1(190.28/172.27)W_S(R_U/R_S)$$

in which 190.28 and 172.27 are the molecular weights of terpin hydrate ($C_{10}H_{20}O_2 \cdot H_2O$) and anhydrous terpin ($C_{10}H_{20}O_2$); respectively, W_S is the weight, in mg, of USP Terpin Hydrate RS, calculated on the anhydrous basis; and R_U and R_S are the area-ratios of terpin to biphenyl obtained from the chromatograms for the *Assay preparation* and the *Standard preparation,* respectively.

Assay for codeine—

Internal standard solution—Prepare as directed under *Assay for terpin hydrate*.

Standard preparation—Evaporate the remaining *Standard preparation* for Oral Solution from the *Assay for terpin hydrate* nearly to dryness, and dissolve the residue in about 20 mL of chloroform.

Assay preparation—Evaporate the remaining *Assay preparation* for Oral Solution from the *Assay for terpin hydrate* nearly to dryness, and dissolve the residue in about 20 mL of chloroform.

Chromatographic system and *System suitability*—Proceed as directed in the *Assay* under *Terpin Hydrate*, except to maintain the temperature of the column at 230° instead of 120°.

Procedure—Proceed as directed under *Assay for terpin hydrate*, except to maintain the temperature of the column at 230° instead of 120°. The retention times for *N*-phenylcarbazole and codeine are about 7 minutes and 10 minutes, respectively. Calculate the quantity, in mg, of codeine ($C_{18}H_{21}NO_3 \cdot H_2O$) in each mL of the Oral Solution taken by the formula:

$$0.1(317.39/397.37)W_S(R_U/R_S)$$

in which 317.39 and 397.37 are the molecular weights of codeine ($C_{18}H_{21}NO_3 \cdot H_2O$) and codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4$), respectively; W_S is the weight, in mg, of USP Codeine Phosphate RS; and R_U and R_S are the area-ratios of codeine to *N*-phenylcarbazole obtained from the chromatograms for 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
TERPIN HYDRATE AND CODEINE ORAL SOLUTION	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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