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Codeine Phosphate Tablets

» Codeine Phosphate Tablets contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$.

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

USP Reference standards ⟨11⟩—
USP Codeine Phosphate RS

Change to read:

Identification—

A: Digest a quantity of finely powdered Tablets, equivalent to about 100 mg of codeine phosphate, with 15 mL of water and 5 mL of 2 N sulfuric acid for 1 hour. Filter, if necessary, and wash any undissolved residue with a few mL of water. Render the filtrate alkaline with 6 N ammonium hydroxide ▲and▲ (ERR 1-Aug-2021) extract with several small portions of chloroform. ▲Evaporate the combined chloroform extracts on a steam bath to dryness, and dry at 80° for 4 hours: the IR absorption spectrum of a potassium bromide dispersion of the residue so obtained exhibits maxima at the same wavelengths as that of the codeine obtained by similarly treating 1 mL of a solution of USP Codeine Phosphate RS (1 in 100).▲ (ERR 1-Aug-2021)

B: To a quantity of finely powdered Tablets, equivalent to about 100 mg of codeine phosphate, add 10 mL of water and 2 drops of 2 N sulfuric acid. Digest, with frequent shaking, for 15 minutes, and filter. Neutralize 5 mL of the filtrate with 6 N ammonium hydroxide, and add silver nitrate TS: a yellow precipitate of silver phosphate is formed, and it is soluble in diluted nitric acid and in 6 N ammonium hydroxide.

Dissolution ⟨711⟩—
Medium: water; 900 mL.
Apparatus 2: 50 rpm.
Time: 45 minutes.
Procedure—Determine the amount of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 284 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Codeine Phosphate RS in the same *Medium*.
Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.
Procedure for content uniformity—Transfer 1 Tablet, previously crushed or finely powdered, to a 50-mL volumetric flask, add 25 mL of water, and shake to dissolve. Dilute with water to volume, and filter, if necessary, discarding the first 20 mL of the filtrate. Transfer an aliquot of the filtrate, equivalent to about 6 mg of codeine phosphate, to a 50-mL volumetric flask containing 2 mL of 3 N hydrochloric acid, and dilute with water to volume. Dissolve an accurately weighed quantity of USP Codeine Phosphate RS in 0.1 N hydrochloric acid, and dilute quantitatively and stepwise with the same solvent to obtain a Standard solution having a known concentration of about 120 µg per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 284 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$ in the Tablet taken by the formula:

$$2.5(C/V)(A_U/A_S)(406.37/397.37)$$

in which C is the concentration, in µg per mL, of USP Codeine Phosphate RS in the Standard solution; V is the volume, in mL, of the aliquot taken of the solution of the Tablet; A_U and A_S are the absorbances of the solution from the Tablet and the Standard solution, respectively; and 406.37 and 397.37 are the molecular weights of codeine phosphate hemihydrate and anhydrous codeine phosphate, respectively.

Change to read:

Limit of morphine—▲Dissolve about 50 mg of potassium ferricyanide in 10 mL of water, and add 1 drop of ferric chloride TS and a 1-mL▲ (ERR 1-Aug-2021) portion of the filtrate from *Identification* test *B*▲: no blue color is produced immediately.▲ (ERR 1-Aug-2021)

Assay—Weigh and finely powder not fewer than 20 Tablets. Accurately weigh a portion of the powder, equivalent to about 150 mg of codeine phosphate, and transfer to a 100-mL volumetric flask. Add 20 mL of 0.5 N sulfuric acid, and shake the mixture occasionally during 2 hours. Add water to volume, mix, and filter through a filtering crucible. Transfer to a separator an accurately measured portion of the filtrate, equivalent to not less than 75 mg of codeine phosphate, render the solution alkaline with 6 N ammonium hydroxide, and completely extract the alkaloid with successive 15-mL portions of chloroform. Evaporate the combined chloroform solution on a steam bath nearly to dryness. Dissolve the residue in about 2 mL of methanol, heating, if necessary, add methyl red TS, and titrate with 0.02 N sulfuric acid VS to a faint pink color. Add about 40 mL of freshly boiled, cooled water, and complete the titration with 0.02 N sulfuric acid VS. Each mL of 0.02 N sulfuric acid is equivalent to 8.128 mg of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot \frac{1}{2}H_2O$.

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

Topic/Question	Contact	Expert Committee
CODEINE PHOSPHATE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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