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Aspirin and Codeine Phosphate Tablets

» Aspirin and Codeine Phosphate Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of aspirin ($C_9H_8O_4$) and codeine phosphate hemihydrate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$).

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

USP Reference standards ⟨11⟩—

USP Aspirin RS
USP Codeine Phosphate RS
USP Salicylic Acid RS

Identification—Dissolve a suitable quantity of USP Aspirin RS in the *Solvent mixture* prepared as directed under *Assay for aspirin and codeine phosphate and limit of free salicylic acid* to obtain a *Standard aspirin solution* containing about 3.3 mg per mL. Dissolve a suitable quantity of USP Codeine Phosphate RS in the *Solvent mixture* to obtain a *Standard codeine phosphate solution* containing about 1 mg per mL. Chromatograph these solutions as directed for *Procedure* in the *Assay for aspirin and codeine phosphate and limit of free salicylic acid*. The retention times of the major peaks in the chromatogram of the *Assay preparation,* obtained as directed in the *Assay for aspirin and codeine phosphate and limit of free salicylic acid,* correspond to those in the chromatograms of the *Standard aspirin solution* and the *Standard codeine phosphate solution,* respectively.

Dissolution ⟨711⟩—

Medium: 0.05 M acetate buffer, prepared by mixing 2.99 g of sodium acetate trihydrate and 1.66 mL of glacial acetic acid with water to obtain 1000 mL of solution having a pH of 4.50 ± 0.05; 900 mL.

Apparatus 2: 75 rpm.

Time: 30 minutes.

Determine the amounts of aspirin ($C_9H_8O_4$) and codeine phosphate hemihydrate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$) dissolved by employing the following method.

Mobile phase, Solvent mixture, and *Aspirin* and *codeine phosphate standard preparation*—Prepare as directed in the *Assay for aspirin and codeine phosphate and limit of free salicylic acid.*

Internal standard solution—Dissolve phenacetin in methanol to obtain a solution having a concentration of about 0.07 mg per mL.

Standard solution A—Prepare a solution of USP Aspirin RS in *Solvent mixture* having an accurately known concentration of about 0.36 mg per mL.

Standard solution B—Transfer about 12 mg of USP Codeine Phosphate RS and 25 mg of USP Salicylic Acid RS, each accurately weighed, to a 50-mL volumetric flask, add 2.5 mL of methanol, and mix. Add *Medium* to volume, and mix. Pipet 10 mL of the resulting solution into a 100-mL volumetric flask, add *Medium* to volume, and mix.

Standard preparations A and *B*—Pipet 10 mL of *Standard solution A* and 10 mL of *Standard solution B* into separate containers, add 3.0 mL of the *Internal standard solution* to each container, and mix.

Test preparation—Withdraw a portion of the solution under test and filter, discarding the few mL of the filtrate. Pipet 10 mL of the filtrate and 3.0 mL of the *Internal standard solution* into a suitable container, and mix.

Chromatographic system—Proceed as directed for *Chromatographic system* in the *Assay for aspirin and codeine phosphate and limit of free salicylic acid,* except to use only the *Aspirin and codeine phosphate preparation* for evaluation of the suitability of the system.

Procedure—Proceed as directed in the *Assay for aspirin and codeine phosphate and limit of free salicylic acid,* except to inject about 50 µL of the *Standard preparations* and the *Test preparation.* The relative retention times are 0.3 for salicylic acid, 0.6 for aspirin, 0.8 for codeine phosphate, and 1.0 for phenacetin. Calculate the amount of codeine phosphate dissolved by comparison of the relative peak response ratios for the codeine phosphate peaks, obtained from *Standard preparation B* and the *Test preparation.* Calculate the percentage of aspirin dissolved by the formula:

$$[0.9C(R_U/R_S) + 0.9C'(R'_U/R'_S)(180.16/138.12)]/3.25$$

in which C is the concentration, in µg per mL, of USP Aspirin RS in *Standard solution A;* R_U and R_S are the peak response ratios for the aspirin component obtained from the *Test preparation* and *Standard preparation A,* respectively; C' is the concentration, in µg per mL, of USP Salicylic Acid RS in *Standard solution B;* R'_U and R'_S are the peak response ratios for the salicylic acid component obtained from the *Test preparation* and *Standard preparation B,* respectively; and 180.16 and 138.12 are the molecular weights of aspirin and salicylic acid, respectively.

Tolerances—Not less than 75% *(Q)* of the labeled amounts of aspirin ($C_9H_8O_4$) and codeine phosphate hemihydrate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$) is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements for *Content Uniformity* with respect to aspirin and codeine phosphate.

Assay for aspirin and codeine phosphate and limit of free salicylic acid—

Mobile phase—Dissolve 225 mg of tetramethylammonium hydroxide pentahydrate and 200 mg of sodium 1-octanesulfonate in 700 mL of water. Add 150 mL of methanol, 150 mL of acetonitrile, and 1.0 mL of glacial acetic acid, and stir. Pass through a membrane filter, and degas. [Note—The amounts of sodium 1-octanesulfonate, methanol, and acetonitrile may be varied to obtain acceptable chromatography.]

Solvent mixture—To 15 g of anhydrous citric acid add 200 mL of methanol and 20 mL of glacial acetic acid, dilute with chloroform to 1000 mL, and mix until the citric acid is dissolved.

Internal standard solution—Dissolve phenacetin in *Solvent mixture* to obtain a solution having a concentration of about 2 mg per mL.

Salicylic acid stock standard solution—Dissolve an accurately weighed quantity of USP Salicylic Acid RS in *Solvent mixture,* and quantitatively dilute with *Solvent mixture* to obtain a solution having a known concentration of about 1 mg per mL.

Salicylic acid standard preparation—Transfer 5.0 mL of *Salicylic acid stock standard solution* to a 50-mL volumetric flask, add 5.0 mL of *Internal standard solution,* dilute with *Solvent mixture* to volume, and mix.

Codeine phosphate stock standard solution—Transfer about 325*J* mg of USP Codeine Phosphate RS, accurately weighed, to a 25-mL volumetric flask, *J* being the ratio of the labeled amount, in mg, of codeine phosphate to the labeled amount, in mg, of aspirin per Tablet. Dissolve in and dilute with *Solvent mixture* to volume, and mix.

Aspirin and *codeine phosphate standard preparation*—Transfer about 65 mg of USP Aspirin RS, accurately weighed, to a 10-mL volumetric flask. Add 5.0 mL of *Codeine phosphate stock standard solution,* 1.0 mL of *Salicylic acid stock standard solution,* and 1.0 mL of *Internal standard solution,* dilute with *Solvent mixture* to volume, and mix.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 325 mg of aspirin, to a screw-capped, 120-mL bottle, add 5.0 mL of *Internal standard solution* and 45.0 mL of *Solvent mixture,* mix, and sonicate for 2 to 5 minutes. Centrifuge, and use a portion of the resultant clear solution as the *Assay preparation.* Use on the day prepared.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm × 30-cm column that contains 10-µm packing L1. The flow rate is about 2 mL per minute. Chromatograph replicate injections of the *Salicylic acid standard preparation* and the *Aspirin and codeine phosphate standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times for salicylic acid, aspirin, codeine, and phenacetin are about 0.3, 0.5, 0.8, and 1.0, respectively; the resolution, *R,* between salicylic acid and aspirin, between aspirin and codeine, and between codeine and phenacetin is not less than 2.0; the tailing factor for each analyte peak is not more than 2.0; and the relative standard deviation of the ratios of the peak responses of salicylic acid, aspirin, and codeine to the peak response of phenacetin is not more than 3.0%.

Procedure—Separately inject equal volumes (about 5 µL) of the *Salicylic acid standard preparation, Aspirin and codeine phosphate standard preparation,* and *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of aspirin ($C_9H_8O_4$) in the portion of Tablets taken by the formula:

$$50C(R_U/R_S)$$

in which *C* is the concentration, in mg per mL, of USP Aspirin RS in the *Aspirin and codeine phosphate standard preparation;* and R_U and R_S are the ratios of the peak responses of aspirin and phenacetin obtained from the *Assay preparation* and the *Aspirin and codeine phosphate 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 the portion of Tablets taken by the formula:

$$(406.37/397.37)(50C)(R_U/R_S)$$

in which 406.37 and 397.37 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 *Aspirin and codeine phosphate standard preparation;* and R_U and R_S are the ratios of the peak responses of codeine phosphate and phenacetin obtained from the *Assay preparation* and the *Aspirin and codeine phosphate standard preparation,* respectively. Calculate the percentage of free salicylic acid in the Tablets taken by the formula:

$$5000(C/a)(R_U/R_S)$$

in which *C* is the concentration, in mg per mL, of USP Salicylic Acid RS in the *Salicylic acid standard preparation; a* is the quantity, in mg, of aspirin in the portion of powdered Tablets taken, based on the labeled amount; and R_U and R_S are the ratios of the peak responses of salicylic acid and phenacetin obtained from the *Assay preparation* and the *Salicylic acid standard preparation,* respectively: not more than 3.0% is found.

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

Topic/Question	Contact	Expert Committee
ASPIRIN AND CODEINE PHOSPHATE TABLETS	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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