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Carisoprodol, Aspirin, and Codeine Phosphate Tablets

DEFINITION

Carisoprodol, Aspirin, and Codeine Phosphate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of carisoprodol ($C_{12}H_{24}N_2O_4$), aspirin ($C_9H_8O_4$), and codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot \frac{1}{2}H_2O$).

IDENTIFICATION

- **A.** The retention times of the aspirin, carisoprodol, and codeine phosphate peaks of the *Sample solutions* correspond to those of the *Standard solutions* obtained as directed in the *Assay for Aspirin and Carisoprodol* and the *Assay for Codeine Phosphate*.

ASSAY

• ASPIRIN AND CARISOPRODOL

Buffer: Combine 5 mL of glacial acetic acid and 500 mL of water, and pass the mixture through a membrane filter of 0.5-μm or finer pore size. Use the filtrate.

Mobile phase: Methanol and *Buffer* (64:36)

Diluent: Acetonitrile, glacial acetic acid, and water (40:1:59)

Standard solution A: USP Reference Standards in *Diluent* as listed below and prepared as follows. Transfer 80 mg of [USP Aspirin RS](#) and 80J mg of [USP Carisoprodol RS](#) to a 25-mL volumetric flask. Add 15 mL of *Diluent*, swirl for 5 min, and sonicate for 25–30 s. Dilute with *Diluent* to volume.

Aspirin: 3.2 mg/mL of [USP Aspirin RS](#)

Carisoprodol: 3.2J mg/mL of [USP Carisoprodol RS](#), where J is the ratio of the labeled amount, in mg, of carisoprodol to the labeled amount of aspirin

Standard solution B: 0.016 mg/mL of [USP Salicylic Acid RS](#) in *Diluent*

System suitability solution: 0.5 mg/mL of salicylic acid in *Standard solution A*

Sample solution: Nominally 3.25 mg/mL of aspirin from NLT 20 Tablets prepared as follows. Finely powder NLT 20 Tablets. Transfer a portion of powder, equivalent to 325 mg of aspirin, to a 100-mL volumetric flask. Add 50 mL of *Diluent*, and swirl for 5 min. Sonicate for 25–30 s, shake by mechanical means for 30 min, and dilute with *Diluent* to volume. Pass a portion of this solution through a membrane filter of 0.5-μm or finer pore size, and use the filtrate.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector

Aspirin and carisoprodol: Refractive index

Salicylic acid: UV 313 nm

Column: 4.6-mm × 25-cm; packing L7

Temperatures

Refractive index detector: 30 ± 1°

Column: 30 ± 1°

Flow rate: 1 mL/min

Injection volume: 50 μL

System suitability

Samples: *Standard solution A*, *Standard solution B*, and *System suitability solution*

[NOTE—The relative retention times for aspirin, salicylic acid, and carisoprodol are about 0.6, 0.7, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.2 between the solvent and aspirin peaks; NLT 1.5 between aspirin and salicylic acid, *System suitability solution* using the refractive index detector

Relative standard deviation: NMT 2.0% for *Standard solution A* using the refractive index detector; NMT 5.0% for *Standard solution B* at 313 nm

Analysis

Samples: *Standard solution A* and *Sample solution*

Calculate the percentages of the labeled amounts of aspirin ($C_9H_8O_4$) and carisoprodol ($C_{12}H_{24}N_2O_4$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of aspirin or carisoprodol from the *Sample solution*

r_S = peak response of aspirin or carisoprodol from *Standard solution A*

C_S = concentration of [USP Aspirin RS](#) or [USP Carisoprodol RS](#) in the *Standard solution A* (mg/mL)

C_U = nominal concentration of aspirin or carisoprodol in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amounts of aspirin ($C_9H_8O_4$) and carisoprodol ($C_{12}H_{24}N_2O_4$)

• CODEINE PHOSPHATE

Solution A: 3.7 g/L of docusate sodium in methanol

Solution B: 2 g/L of ammonium nitrate in water

Mobile phase: *Solution A* and *Solution B* (60:40) adjusted with glacial acetic acid to a pH of 3.3 ± 0.05

Diluent: Methanol and 0.01 N sulfuric acid (50:50)

System suitability solution: 0.16 mg/mL of [USP Codeine Phosphate RS](#) and 0.12 mg/mL of [USP Codeine N-Oxide RS](#) in *Diluent*

Standard solution: USP Reference Standards in *Diluent* as listed below. Swirl for 5 min, and sonicate for 25–30 s.

Codeine phosphate: 0.16 mg/mL of [USP Codeine Phosphate RS](#)

Aspirin: 0.16J mg/mL of [USP Aspirin RS](#), where J is the ratio of the labeled amount, in mg, of aspirin to that of codeine phosphate

Sample solution: Nominally 0.16 mg/mL of codeine phosphate prepared as follows. Finely powder NLT 20 Tablets. Transfer an amount of powder equivalent to 16 mg of codeine phosphate to a 100-mL volumetric flask. Add 50 mL of *Diluent*, sonicate for 30 min, shake by mechanical means for 30 min, and dilute with *Diluent* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm $\times$ 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 50 μ L

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for codeine N-oxide and codeine phosphate are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.2 between codeine phosphate and codeine N-oxide, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot \frac{1}{2}H_2O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Codeine Phosphate RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of the *Sample solution* (mg/mL)

M_{r1} = molecular weight of codeine phosphate hemihydrate, 406.37

M_{r2} = molecular weight of anhydrous codeine phosphate, 397.37

Acceptance criteria: 90.0%–110.0% of the labeled amount of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot \frac{1}{2}H_2O$)

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: Water; 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Procedure for aspirin and carisoprodol

Buffer: Glacial acetic acid in water (1 in 50)

Mobile phase: Methanol and *Buffer* (51:49)

Standard solution: USP Reference Standards as listed below and prepared as follows. Transfer 90 mg of [USP Aspirin RS](#) and 900 mg of [USP Carisoprodol RS](#) to a 250-mL volumetric flask. Add 5 mL of acetonitrile, previously passed through a membrane filter of 0.5- μ m or