Status: Currently Official on 14-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-CEC9AD9E-CF48-4DD3-B89E-9FA16AFF60BB_1_en-US
DOI: https://doi.org/10.31003/USPNF_M13385_01_01
DOI Ref: 8s5pp

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 ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$).

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 80*J* 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: 3.2*J* 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: 0.16*J* 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 × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 50 µL

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 ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$) 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 ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$)

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 90*J* 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-µm or

finer pore size, and swirl to dissolve. Dilute with water to volume.

Aspirin: 0.36 mg/mL of USP Aspirin RS

Carisoprodol: 0.36*J* 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

System suitability solution: 0.36 mg/mL of salicylic acid in the *Standard solution*

Sample solution: Pass a portion of the solution under test through a suitable filter, and use the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Refractive index

Column: 3.9-mm × 30-cm; packing L1

Temperatures

Detector: 30 ± 1°

Column: 30 ± 1°

Flow rate: 2 mL/min

Injection volume: 300 µL

System suitability

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

[NOTE—The relative retention times for aspirin and carisoprodol are 0.4 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between aspirin and salicylic acid; NLT 1.5 between carisoprodol and salicylic acid, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of aspirin ($C_9H_8O_4$) and carisoprodol ($C_{12}H_{24}N_2O_4$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

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

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

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

V = volume of the *Medium,* 900 mL

L = label claim of aspirin or carisoprodol (mg/Tablet)

Procedure for codeine phosphate

Buffer: 4.0 g/L of docusate sodium and 1.5 g/L of ammonium nitrate in water

Mobile phase: Acetonitrile and *Buffer* (45:55)

Standard solution: 0.018 mg/mL of USP Codeine Phosphate RS in water

Sample solution: Pass a portion of the solution under test through a suitable filter, and use the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

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

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

V = volume of the *Medium*, 900 mL

L = label claim of codeine phosphate (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amounts of aspirin ($C_9H_8O_4$), carisoprodol ($C_{12}H_{24}N_2O_4$), and codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot ½H_2O$) are dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements for *Content Uniformity* with respect to aspirin, carisoprodol, and codeine phosphate

IMPURITIES

• **Organic Impurities**

Limit of free salicylic acid

Mobile phase, Diluent, Standard solution B, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* for *Aspirin and Carisoprodol*.

Analysis

Samples: *Standard solution B* and *Sample solution*

Calculate the percentage of free salicylic acid in the portion of Tablets taken:

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

r_U = peak response of salicylic acid from the *Sample solution*

r_S = peak response of salicylic acid from *Standard solution B*

C_S = concentration of USP Salicylic Acid RS in *Standard solution B* (mg/mL)

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

Acceptance criteria: NMT 3.0% of free salicylic acid

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards ⟨11⟩**

USP Aspirin RS

USP Carisoprodol RS

USP Codeine N-Oxide RS

7,8-Didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol *N*-oxide.
$C_{18}H_{21}NO_4$ 315.37

USP Codeine Phosphate RS

USP Salicylic Acid RS

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

Topic/Question	Contact	Expert Committee
CARISOPRODOL, ASPIRIN, AND 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

Current DocID: GUID-CEC9AD9E-CF48-4DD3-B89E-9FA16AFF60BB_1_en-US

DOI: https://doi.org/10.31003/USPNF_M13385_01_01

DOI ref: 8s5pp