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Orphenadrine Citrate, Aspirin, and Caffeine Tablets

DEFINITION

Orphenadrine Citrate, Aspirin, and Caffeine Tablets contain NLT 90.0% and NMT 110.0% each of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$), aspirin ($C_9H_8O_4$), and caffeine ($C_8H_{10}N_4O_2$).

IDENTIFICATION

• **A.** The retention times of the orphenadrine, aspirin, and caffeine peaks in the chromatogram of the *Sample solution* correspond to those of the orphenadrine, aspirin, and caffeine peaks in the chromatogram of the *Standard solution*, as obtained in the *Orphenadrine Citrate* and *Aspirin and Caffeine* tests in the *Assay*.

ASSAY

• ORPHENADRINE CITRATE

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.6. To each L of this solution add 5.8 g of sodium dodecyl sulfate, and dissolve.

Mobile phase: Acetonitrile and *Buffer* (50:50)

Diluent: Methanol and glacial acetic acid (92:8)

Standard solution: 0.1 mg/mL of [USP Orphenadrine Citrate RS](#) prepared as follows. Transfer the weighed amount of standard to a suitable volumetric flask with the aid of methanol. Add glacial acetic acid to fill 8% of final volume and methanol to fill 75% of final volume. Sonicate with occasional shaking for NLT 15 min. Allow the solution to equilibrate to room temperature. Dilute with methanol to volume. Filter a portion through a suitable filter of 0.45-μm pore size, discarding at least the first 3 mL of the filtrate.

Sample stock solution: Nominally 0.5 mg/mL of orphenadrine citrate from Tablets (NLT 5), prepared as follows. To the volumetric flask containing the Tablets, add glacial acetic acid to fill 8% of final volume and methanol to fill 75% of final volume. Sonicate with occasional hand shaking for NLT 15 min. Shake mechanically for NLT 15 min. Allow the solution to equilibrate to room temperature. Dilute with methanol to volume. [NOTE—This solution also contains 7.7 mg/mL of aspirin and 0.6 mg/mL of caffeine.]

Sample solution: Nominally 0.1 mg/mL of orphenadrine citrate by diluting a suitable portion of the *Sample stock solution* with *Diluent*. Filter a portion through a suitable filter of 0.45-μm pore size, discarding at least the first 3 mL of the filtrate. [NOTE—This solution also contains 1.5 mg/mL of aspirin and 0.1 mg/mL of caffeine.]

Chromatographic system

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

Mode: LC

Detector: UV 257 nm

Column: 3.9-mm × 30-cm; 10-μm packing L1

Flow rate: 2 mL/min

Injection volume: 15 μL

Run time: 1.5 times the retention time of orphenadrine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

• **ASPIRIN AND CAFFEINE**

Buffer: Dissolve 0.8 g/L of hexanesulfonic acid sodium salt in water. Adjust with glacial acetic acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (40:60)

Diluent: Methanol and glacial acetic acid (92:8)

Standard solution: 1.5 mg/mL of [USP Aspirin RS](#) and 0.1 mg/mL of [USP Caffeine RS](#) prepared as follows. Transfer the weighed amount of standards to a suitable volumetric flask with the aid of methanol. Add glacial acetic acid to fill 8% of final volume and methanol to fill 75% of final volume. Sonicate with occasional hand shaking for NLT 15 min. Allow the solution to equilibrate to room temperature. Dilute with methanol to volume. Filter a portion through a suitable filter of 0.45- μ m pore size, discarding at least the first 3 mL of the filtrate.

Sample stock solution: Nominally 7.7 mg/mL of aspirin from Tablets (NLT 5), prepared as follows. To the volumetric flask containing the Tablets, add glacial acetic acid to fill 8% of final volume and methanol to fill 75% of final volume. Sonicate with occasional hand shaking for NLT 15 min. Allow the solution to equilibrate to room temperature. Dilute with methanol to volume. [NOTE—This solution also contains 0.6 mg/mL of caffeine and 0.5 mg/mL of orphenadrine citrate.]

Sample solution: Nominally 1.5 mg/mL of aspirin by diluting a suitable portion of the *Sample stock solution* with *Diluent*. Filter a portion through a suitable filter of 0.45- μ m pore size, discarding at least the first 3 mL of the filtrate. [NOTE—This *Sample solution* also contains 0.1 mg/mL of caffeine and 0.1 mg/mL of orphenadrine citrate.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm $\times$ 30-cm; 10- μ m packing L1

Flow rate: 1.2 mL/min

Injection volume: 15 μ L

Run time: 3 times the retention time of aspirin

System suitability

[NOTE—The relative retention time for caffeine and for aspirin is 0.70 and 1.0, respectively.]

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between caffeine and aspirin peaks

Relative standard deviation: NMT 2.0% each for both the caffeine and aspirin peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of aspirin ($C_9H_8O_4$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Calculate the percentage of the labeled amount of caffeine ($C_8H_{10}N_4O_2$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_s = peak response from the *Standard solution*

C_s = concentration of [USP Caffeine RS](#) in the *Standard solution* (mg/mL)

C_u = nominal concentration of caffeine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% each of aspirin and caffeine

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Times: 45 min for aspirin and caffeine; 60 min for orphenadrine

Separate dissolution baths must be run for the different time points.

Orphenadrine citrate

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.6. To each L of this solution add 5.8 g of sodium dodecyl sulfate, and dissolve.

Mobile phase: Acetonitrile and *Buffer* (50:50)

Standard solution: ($L/900$) mg/mL of [USP Orphenadrine Citrate RS](#) in *Medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 257 nm

Column: 3.9-mm × 30-cm; 10-μm packing L1

Flow rate: 2 mL/min

Injection volume: 100 μL

Run time: 1.2 times the retention time of orphenadrine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 3.0%

Calculate the percentage (Q) of the labeled amount of orphenadrine citrate ($C_{18}H_{23}NO \cdot C_6H_8O_7$) dissolved:

$$\text{Result} = (r_u/r_s) \times (C_s/L) \times V \times 100$$

r_u = peak response for orphenadrine from the *Sample solution*

r_s = peak response for orphenadrine from the *Standard solution*

C_s = concentration of [USP Orphenadrine Citrate RS](#) in the *Standard solution* (mg/mL)

L = label claim for orphenadrine (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (Q) of the labeled amount of orphenadrine is dissolved in 60 min.

Aspirin and caffeine

Buffer: 0.8 g/L of hexanesulfonic acid sodium salt in water

Mobile phase: Methanol and *Buffer* (40:60). Adjust with glacial acetic acid to a pH of 3.0.

Standard stock solution: 1.0 mg/mL of [USP Aspirin RS](#), 0.1 mg/mL of [USP Caffeine RS](#), and 0.1 mg/mL of [USP Salicylic Acid RS](#) prepared as follows. Transfer the weighed amount of standards to a suitable volumetric flask with the aid of methanol. Add glacial acetic acid to fill 8% of final volume and methanol to fill 75% of final volume. Sonicate with occasional shaking for NLT 15 min. Allow the solution to equilibrate to room temperature. Dilute with methanol to volume.

Standard solution: Dilute a suitable volume of the *Standard stock solution* with methanol to obtain a final concentration of about 0.25 mg/mL of [USP Aspirin RS](#) and 0.025 mg/mL each of [USP Caffeine RS](#) and [USP Salicylic Acid RS](#).

Sample solution: At the time specified, withdraw the solution under test and pass through a suitable filter. If necessary, dilute the filtrate with methanol to obtain a final concentration similar to that of the *Standard solution*.