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Acetaminophen and Caffeine Tablets

DEFINITION

Acetaminophen and Caffeine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and caffeine ($C_8H_{10}N_4O_2$).

IDENTIFICATION

• **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, relative to the internal standard, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: Methanol and glacial acetic acid (95:5)

Mobile phase: Methanol, glacial acetic acid, and water (28:3:69)

Internal standard solution: 6 mg/mL of benzoic acid in methanol

Standard stock solution: 0.25 mg/mL of USP Acetaminophen RS and 0.25*J* mg/mL of USP Caffeine RS in *Solution A*; *J* being the ratio of the labeled amount, in mg, of caffeine to the labeled amount, in mg, of acetaminophen per Tablet

Standard solution: 0.1 mg/mL of USP Acetaminophen RS and 0.1*J* mg/mL of USP Caffeine RS, prepared by transferring 20.0 mL of *Standard stock solution* and 3.0 mL of *Internal standard solution* to a 50-mL volumetric flask, and diluting with *Solution A* to volume

Sample stock solution: Nominally 2.5 mg/mL of acetaminophen in *Solution A*, prepared as follows. Transfer a portion of the powder equivalent to 250 mg of acetaminophen, from NLT 20 finely powdered Tablets, to a 100-mL volumetric flask. Add 75 mL of *Solution A*, and shake by mechanical means for 30 min. Dilute with *Solution A* to volume.

Sample solution: Transfer 2.0 mL of the *Sample stock solution* and 3.0 mL of *Internal standard solution* to a 50-mL volumetric flask, and dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 10-cm; 5-µm packing L1

Column temperature: 45 ± 1°

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for acetaminophen, caffeine, and benzoic acid are about 0.3, 0.5, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.4 between any of the analyte and internal standard peaks

Tailing factor: NMT 1.2 for each analyte peak

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate individually the percentages of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and 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 ratio of acetaminophen or caffeine to the internal standard from the *Sample solution*

R_S = peak response ratio of acetaminophen or caffeine to the internal standard from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0% of acetaminophen ($C_8H_9NO_2$) and caffeine ($C_8H_{10}N_4O_2$)

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: 100 rpm

Time: 60 min

Solution A, Mobile phase, Internal standard solution, Standard stock solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Standard solution: Transfer 20.0 mL of the *Standard stock solution*, 3.0 mL of *Internal standard solution*, and 20 mL of water to a 50-mL volumetric flask, and allow to stand for 30 s. Dilute with *Solution A* to volume. Use within 8 h.

Sample solution: Transfer an aliquot of a filtered portion of the solution under test to a 50-mL volumetric flask to obtain an expected concentration of 0.1 mg/mL of acetaminophen and 0.1*J* mg/mL of caffeine, where *J* is defined for the *Standard stock solution*. Add 3.0 mL of *Internal standard solution* and 20 mL of *Solution A*, and allow to stand for 30 s. Dilute with *Solution A* to volume.

Analysis: Proceed as directed in the *Assay*, using the *Standard solution* and *Sample solution* prepared within the *Dissolution* test. Calculate the percentages of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and caffeine ($C_8H_{10}N_4O_2$) dissolved:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of acetaminophen or caffeine to the internal standard from the *Sample solution*

R_S = peak response ratio of acetaminophen or caffeine to the internal standard from the *Standard solution*

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

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

Tolerances: NLT 75% (*Q*) of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and caffeine ($C_8H_{10}N_4O_2$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **4-Aminophenol in Acetaminophen-Containing Drug Products** ⟨227⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Acetaminophen RS

USP Caffeine RS

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

Topic/Question	Contact	Expert Committee
ACETAMINOPHEN AND CAFFEINE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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