Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 302 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*
Suitability requirements
Tailing factor: NMT 1.6
Relative standard deviation: NMT 3.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of salicylic acid ($C_7H_6O_3$) relative to the labeled amount of aspirin 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 the *Standard solution*
C_S = concentration of USP Salicylic Acid RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of aspirin in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 3.0%

- **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 Aspirin RS
  USP Caffeine RS
  USP Salicylic Acid RS

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.