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Acetaminophen and Aspirin Tablets

DEFINITION

Acetaminophen and Aspirin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$).

IDENTIFICATION

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

ASSAY

• **Procedure**

[Note—Use clean and dry glassware. Inject the *Standard solution* and the *Sample solution* promptly after preparation.]

Solution A: Chloroform, methanol, and glacial acetic acid (78:20:2)

Mobile phase: Transfer 225 mg of tetramethylammonium hydroxide pentahydrate to a 1000-mL flask. Add 750 mL of water, 125 mL of methanol, 125 mL of acetonitrile, and 1.0 mL of glacial acetic acid. Stir for 3 min, and pass through a membrane filter of 0.5-µm or finer pore size.

Internal standard solution: 20 mg/mL of benzoic acid in *Solution A*

Standard solution: 3.25 mg/mL each of USP Acetaminophen RS and USP Aspirin RS, and 2.0 mg/mL of benzoic acid, from *Internal standard solution*, in *Solution A*

Sample solution: Nominally 3.25 mg/mL of acetaminophen in *Solution A*, prepared as follows. Transfer an equivalent of 325 mg of acetaminophen, from NLT 20 finely powdered Tablets, to a 100-mL volumetric flask. Add 10.0 mL of *Internal standard solution* and 50 mL of *Solution A*, and sonicate for 3 min. Dilute with *Solution A* to volume. Pass a portion of this solution through a filter of 2.5-µm or finer pore size. Use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

[Note—The retention times for acetaminophen, salicylic acid (if present), aspirin, and benzoic acid are about 2, 3, 5, and 8 min, respectively.]

Suitability requirements

Relative standard deviation: NMT 3.0% for acetaminophen or aspirin for four replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate individually the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) and 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 ratio of acetaminophen or aspirin to benzoic acid from the *Sample solution*

R_S = peak response ratio of acetaminophen or aspirin to benzoic acid from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$)

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Procedure for a pooled sample

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Solution A, Mobile phase, and **Chromatographic system** (except for *Injection volume*)**:** Proceed as directed in the *Assay*.

Injection volume: 20 µL

Internal standard solution: 1 mg/mL of benzoic acid in methanol

Standard stock solution A: 70 µg/mL of USP Salicylic Acid RS in *Solution A*

Standard solution A: Combine 4.0 mL of *Standard stock solution A* and 1.0 mL of *Internal standard solution*.

Standard stock solution B: 360 µg/mL each of USP Acetaminophen RS and USP Aspirin RS in *Solution A*

Standard solution B: Combine 4.0 mL of *Standard stock solution B* and 1.0 mL of *Internal standard solution*.

Sample stock solution: Filtered portions of sample suitably diluted with *Medium* to a concentration that is similar to that of *Standard stock solution A* or *Standard stock solution B*

Sample solution: Combine 4.0 mL of the *Sample stock solution* and 1.0 mL of *Internal standard solution*.

Analysis

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

[NOTE—The relative retention times for acetaminophen, salicylic acid, aspirin, and benzoic acid are about 0.3, 0.4, 0.6, and 1.0, respectively.]

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved:

$$\text{Result} = (R_U/R_S) \times (C/W) \times 90$$

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

R_S = relative peak response ratio of acetaminophen to the internal standard from *Standard solution B*

C = concentration of USP Acetaminophen RS in *Standard solution B* (µg/mL)

W = labeled amount of acetaminophen (mg)

Calculate the percentage of the labeled amount of aspirin ($C_9H_8O_4$) dissolved:

$$\text{Result} = \{[90C_1 \times (R_{U1}/R_{S1})] + [90C_2 \times (R_{U2}/R_{S2}) \times 1.3044]\}/W$$

C_1 = concentration of USP Aspirin RS in *Standard solution B* (µg/mL)

R_{U1} = relative peak response ratio of aspirin to the internal standard from the *Sample solution*

R_{S1} = relative peak response ratio of aspirin to the internal standard from *Standard solution B*

C_2 = concentration of USP Salicylic Acid RS in *Standard solution A* (µg/mL)

R_{U2} = relative peak response ratio of salicylic acid to the internal standard from the *Sample solution*

R_{S2} = relative peak response ratio of salicylic acid to the internal standard from *Standard solution A*

W = labeled amount of aspirin (mg)

Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$) is dissolved.

• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩, *Content Uniformity*: Meet the requirements with respect to acetaminophen and to aspirin

IMPURITIES

• **LIMIT OF SALICYLIC ACID**

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

Standard stock solution: 1.0 mg/mL of USP Salicylic Acid RS in *Solution A*

Standard solutions: Transfer 1.0-, 5.0-, and 10.0-mL portions of *Standard stock solution* to separate 100-mL volumetric flasks. Add 10.0 mL of *Internal standard solution* to each flask, and dilute with *Solution A* to volume.

Analysis

Samples: *Sample solution* and *Standard solutions*

Plot the ratios of the peak responses for salicylic acid and benzoic acid for each of the *Standard solutions* versus concentrations, in mg/mL, of salicylic acid, and draw the straight line best fitting the three plotted points. From the graph so obtained, and from the ratio of the peak responses for salicylic acid and benzoic acid from the *Sample solution* as obtained in the *Assay*, determine the concentration, in mg/mL, of salicylic acid ($C_7H_6O_3$) in the *Sample solution*.

Calculate the percentage of salicylic acid in relation to the concentration of aspirin in the *Sample solution*, as obtained in the *Assay*.

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 Salicylic Acid RS

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

Topic/Question	Contact	Expert Committee
ACETAMINOPHEN AND ASPIRIN TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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