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Acetaminophen Tablets

DEFINITION

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

IDENTIFICATION

• **A.** The retention time of the acetaminophen peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV spectrum of the acetaminophen peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 1% (v/v) glacial acetic acid in water

Solution B: Methanol

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system for 4 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
4.0	90	10
4.1	20	80
6.0	20	80

Diluent: Methanol and water (10:90)

Standard solution: 0.01 mg/mL of USP Acetaminophen RS in *Diluent*

Sample stock solution: Nominally 0.1 mg/mL of acetaminophen in *Diluent* prepared as follows. Transfer an appropriate amount of acetaminophen from NLT 10 Tablets to a suitable volumetric flask and dilute with *Diluent* to volume. Centrifuge or pass a portion of this solution through a suitable filter. [Note—Sonication or shaking may be necessary.]

Sample solution: Nominally 0.01 mg/mL of acetaminophen in *Diluent* from the *Sample stock solution*. Pass a portion of this solution through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 243 nm. For *Identification B*, use a diode array detector in the range of 220–400 nm.

Column: 3.0-mm × 10-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

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

r_U = peak response of acetaminophen from the *Sample solution*

r_S = peak response of acetaminophen from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: A known concentration of USP Acetaminophen RS in *Medium*

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium* to obtain a concentration similar to that of the *Standard solution*

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 243 nm

Analysis

Samples: *Standard solution* and *Sample solution*

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

Tolerances: NLT 80% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) is dissolved.

For Tablets labeled as chewable

Medium: pH 5.8 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*); 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Standard solution, Sample solution, Instrumental conditions, and **Analysis:** Proceed as directed above.

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

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

IMPURITIES

Change to read:

• **Organic Impurities**

It is suggested to protect all solutions containing acetaminophen or 4-aminophenol from light.

Buffer: Dissolve 1.9 g of ammonium formate in 1 L of water. Add 1.0 mL of formic acid.

Solution A: Dissolve 3.1 g of ammonium acetate in 1 L of water. Add 1.0 mL of trifluoroacetic acid.

Solution B: Acetonitrile, methanol, and water (10:75:15)

Solution C: Dissolve 3.1 g of ammonium acetate in 1000 mL of *Solution B*. Add 1.0 mL of trifluoroacetic acid.

Mobile phase: See *Table 2*. Return to original conditions and re-equilibrate the system for 4 min.

Table 2

Time (min)	Solution A (%)	Solution C (%)
0	97	3
5	70	30
10	10	90
11	10	90

Diluent: Methanol and *Buffer* (5:95)

Sensitivity solution: 0.000175 mg/mL of USP 4-Aminophenol RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.00175 mg/mL of USP 4-Aminophenol RS and 0.0035 mg/mL of USP Acetaminophen RS in *Diluent*. Sonicate to dissolve, if necessary.

Sample stock solution: Nominally 5 mg/mL of acetaminophen in *Diluent* from NLT 10 Tablets. [Note—It is recommended to shake on a flat bed at low speed (180 oscillations/min) to dissolve, if necessary.]

Sample solution: Nominally 3.5 mg/mL of acetaminophen in *Diluent* prepared as follows. Pass a portion of the *Sample stock solution* through a suitable filter of 0.2-µm pore size. Discard the first 2 mL of the filtrate. Dilute a suitable volume of the filtrate with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 272 nm ▲▲ (ERR 1-Oct-2021)

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 0.9 mL/min

Injection volume: 25 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0% for 4-aminophenol and acetaminophen, *Standard solution*

Signal-to-noise ratio: NLT 10 for 4-aminophenol, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 4-aminophenol in the portion of Tablets taken:

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

r_U = peak response of 4-aminophenol from the *Sample solution*

r_S = peak response of 4-aminophenol from the *Standard solution*

C_S = concentration of USP 4-Aminophenol RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Tablets taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

r_S = peak response of acetaminophen from the *Standard solution*

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

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

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
4-Aminophenol	0.53	0.15
Acetaminophen	1.0	—
Any unspecified impurity	—	0.15
Total impurities	—	0.60

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **Labeling:** Label Tablets that must be chewed to indicate that they are to be chewed before swallowing.
- **USP Reference Standards ⟨11⟩**

USP Acetaminophen RS

USP 4-Aminophenol RS

4-Aminophenol.

C_6H_7NO 109.13

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

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

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