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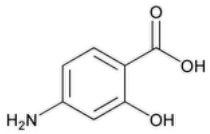
Aminosalicylic Acid



$C_7H_7NO_3$ 153.14

Benzoic acid, 4-amino-2-hydroxy-;

4-Aminosalicylic acid CAS RN®: 65-49-6; UNII: 5B2658E0N2.

DEFINITION

Aminosalicylic Acid contains NLT 98.5% and NMT 100.5% of aminosalicylic acid ($C_7H_7NO_3$), calculated on the anhydrous basis.

[CAUTION—Under no circumstances use a solution prepared from Aminosalicylic Acid if its color is darker than that of a freshly prepared solution.]

IDENTIFICATION

• **A.**

Sample stock solution: Dissolve 250 mg in 3 mL of 1 N sodium hydroxide, transfer to a 500-mL volumetric flask, and dilute with water to volume.

Sample solution: Transfer a 5-mL aliquot of the *Sample stock solution* to a 250-mL volumetric flask containing 12.5 mL of pH 7 phosphate buffer (see *Reagents, Indicators, and Solutions—Buffer Solutions*), and dilute with water to volume.

Analysis: Compare the *Sample solution* in a suitable spectrometer against a blank of the same buffer in the same concentration.

Acceptance criteria: The *Sample solution* exhibits absorbance maxima at 265 ± 2 and 299 ± 2 nm, and the ratio A_{265}/A_{299} is 1.50–1.56.

• **B.**

Sample: 1 g

Analysis: Place the *Sample* in a small, round-bottom flask, and add 10 mL of acetic anhydride. Heat the flask on a steam bath for 30 min, add 40 mL of water, filter, cool, and allow to stand until the diacetyl derivative has crystallized. Collect the precipitate on a filter, wash well with water, and dry at 105° for 1 h.

Acceptance criteria: The diacetyl derivative melts at 191°–197°.

• **C.**

Sample: 0.1 g

Analysis: Shake the *Sample* with 10 mL of water, and filter. To 5 mL of the filtrate add 1 drop of ferric chloride TS.

Acceptance criteria: A violet color is produced.

ASSAY

• PROCEDURE

Solution A: 12.7 mg/mL of tetrabutylammonium hydroxide in methanol

Mobile phase: *Solution A*, 0.05 M dibasic sodium phosphate, and 0.05 M monobasic sodium phosphate (150:425:425)

Internal standard solution: 5 mg/mL of acetaminophen in *Mobile phase*

Standard solution: 0.5 mg/mL of aminosalicylic acid prepared as follows. Transfer 12.5 mg of USP Aminosalicylic Acid RS to a 25-mL low-actinic volumetric flask, add 15 mL of *Mobile phase*, and swirl to dissolve. Add 2.5 mL of the *Internal standard solution*, and dilute with *Mobile phase* to volume.

Sample solution: 0.5 mg/mL of Aminosalicylic Acid prepared as follows. Transfer 12.5 mg of Aminosalicylic Acid to a 25-mL low-actinic volumetric flask, add 15 mL of *Mobile phase*, and swirl to dissolve. Add 2.5 mL of the *Internal standard solution*, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for acetaminophen and aminosalicylic acid are 0.83 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.7 between aminosalicylic acid and acetaminophen

Relative standard deviation: NMT 1.0% for the peak response ratio of aminosalicylic acid to acetaminophen

Analysis

Samples: *Standard solution* and *Sample solution*

After use, wash the column for 30 min with a mixture of methanol, water, and phosphoric acid (77:23:0.6), and then wash for 30 min with a mixture of methanol and water (50:50).

Calculate the percentage of aminosalicylic acid ($C_7H_7NO_3$) in the portion of Aminosalicylic Acid taken:

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

R_U = peak response ratio of aminosalicylic acid to acetaminophen from the *Sample solution*

R_S = peak response ratio of aminosalicylic acid to acetaminophen from the *Standard solution*

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

C_U = concentration of Aminosalicylic Acid in the *Sample solution* (mg/mL)

Acceptance criteria: 98.5%–100.5% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Chloride and Sulfate,** *Chloride*⟨221⟩

Sample solution: 25 mg/mL in a mixture of nitric acid and water (5:15)

Acceptance criteria: NMT 0.042%; the solution shows no more chloride than corresponds to 0.30 mL of 0.020 N hydrochloric acid.

- **Limit of *m*-Aminophenol**

Solution A: 12.7 mg/mL of tetrabutylammonium hydroxide in methanol

Mobile phase: *Solution A*, 0.05 M dibasic sodium phosphate, and 0.05 M monobasic sodium phosphate (150:425:425)

Internal standard solution: 5 µg/mL of sulfanilamide in *Mobile phase*

Standard stock solution: 12 µg/mL of USP *m*-Aminophenol RS in *Mobile phase*

Standard solution: 1.2 µg/mL of USP *m*-Aminophenol RS prepared as follows. Transfer 10.0 mL of the *Standard stock solution* and 10.0 mL of the *Internal standard solution* to a 100-mL low-actinic volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: 0.5 mg/mL of Aminosalicylic Acid prepared as follows. Transfer 50 mg of Aminosalicylic Acid to a 100-mL low-actinic volumetric flask, add 50 mL of *Mobile phase*, and swirl to dissolve. Add 10.0 mL of the *Internal standard solution*, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 10-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for sulfanilamide and *m*-aminophenol are about 0.66 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.5 between *m*-aminophenol and sulfanilamide

Relative standard deviation: NMT 7%

Analysis

Samples: *Standard solution* and *Sample solution*

After use, wash the column for 30 min with a mixture of methanol, water, and phosphoric acid (77:23:0.6), and then wash for 30 min with a mixture of methanol and water (50:50).

Calculate the percentage of *m*-aminophenol in the portion of Aminosalicylic Acid taken:

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

R_U = peak response ratio of *m*-aminophenol to sulfanilamide from the *Sample solution*

R_S = peak response ratio of *m*-aminophenol to sulfanilamide from the *Standard solution*

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

C_U = concentration of the *Sample solution*, as determined in the *Assay* (mg/mL)

Acceptance criteria: NMT 0.25%

SPECIFIC TESTS

- **pH ⟨791⟩:** 3.0–3.7, in a saturated solution
- **Water Determination, *Method I*⟨921⟩:** NMT 0.5%
- **Hydrogen Sulfide, Sulfur Dioxide, and Amyl Alcohol**

  Sample: 500 mg

  Analysis: Dissolve the *Sample* in 5 mL of 1 N sodium hydroxide, add 6 mL of 3 N hydrochloric acid, and stir vigorously.

  Acceptance criteria: No odor of hydrogen sulfide or sulfur dioxide is perceptible, and NMT a faint odor of amyl alcohol is perceptible. A piece of moistened lead acetate test paper held over the mixture does not become discolored.
- **Clarity and Color of Solution**

  Sample 1: 1 g

  Analysis 1: Dissolve *Sample 1* in 10 mL of sodium bicarbonate solution (1 in 15).

  Acceptance criteria 1: The resulting solution is clear and has NMT a faint yellow color.

  Sample 2: 1 g

  Analysis 2: Dissolve *Sample 2* in 50 mL of freshly prepared 1.6 M nitric acid.

  Acceptance criteria 2: The resulting solution is clear and has NMT a slight color.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers at a temperature not exceeding 30°.
- **USP Reference Standards ⟨11⟩**

  USP *m*-Aminophenol RS

  USP Aminosalicylic Acid RS

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

Topic/Question	Contact	Expert Committee
AMINOSALICYLIC ACID	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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