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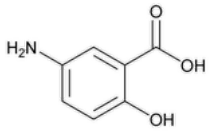
# Mesalamine



$C_7H_7NO_3$ 153.14

Benzoic acid, 5-amino-2-hydroxy-;

5-Aminosalicylic acid CAS RN®: 89-57-6; UNII: 4Q81I59GXC.

## DEFINITION

Mesalamine contains NLT 98.5% and NMT 101.5% of mesalamine ($C_7H_7NO_3$), calculated on the dried basis.

## IDENTIFICATION

***Change to read:***

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

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

## ASSAY

• **Procedure**

**Buffer:** Transfer 7.1 g of anhydrous dibasic sodium phosphate and 6.9 g of monobasic sodium phosphate to a 1000-mL volumetric flask, add 500 mL of water, and swirl to dissolve. Add 7.5 mL of a solution of tetrabutylammonium hydroxide 30-hydrate in methanol (1 in 4), dilute with water to volume, and mix.

**Mobile phase:** Methanol and *Buffer* (15:85)

**System suitability solution:** 0.25 mg/mL of 4-aminosalicylic acid and 0.4 mg/mL of USP Mesalamine RS in *Mobile phase*

**Standard stock solution:** 1 mg/mL of USP Mesalamine RS in *Mobile phase*

**Standard solution:** 0.4 mg/mL of USP Mesalamine RS in *Mobile phase* from the *Standard stock solution*

**Sample stock solution:** 1 mg/mL of Mesalamine in *Mobile phase*

**Sample solution:** 0.4 mg/mL of Mesalamine in *Mobile phase* from the *Sample stock solution*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 254 nm

**Column:** 4-mm × 30-cm; 10-µm packing L1

**Flow rate:** 2 mL/min

**Injection volume:** 15 µL

**System suitability**

**Samples:** *System suitability solution* and *Standard solution*

**Suitability requirements**

**Resolution:** NLT 2.0 between 4-aminosalicylic acid and mesalamine, *System suitability solution*

**Tailing factor:** NMT 2.5, *Standard solution*

**Relative standard deviation:** NMT 0.73%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of mesalamine ($C_7H_7NO_3$) in the portion of Mesalamine taken:

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

$r_U$ = peak response of mesalamine from the *Sample solution*

$r_S$ = peak response of mesalamine from the *Standard solution*

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

$C_U$ = concentration of Mesalamine in the *Sample solution* (mg/mL)

**Acceptance criteria:** 98.5%–101.5% on the dried basis

**IMPURITIES**

• **Chloride and Sulfate, *Chloride*⟨221⟩**

**Sample solution:** Disperse 500 mg in 40 mL of water, sonicate for 5 min, and filter the dispersion. Use the filtrate.

**Analysis:** Add 1 mL of nitric acid to the *Sample solution*.

**Acceptance criteria:** No more chloride than corresponds to 0.7 mL of 0.020 N hydrochloric acid (0.1%)

• **Chloride and Sulfate, *Sulfate*⟨221⟩**

**Sample solution:** Dissolve 500 mg in water. Filter if necessary. Use the filtrate.

**Acceptance criteria:** The *Sample solution* shows no more sulfate than corresponds to 1.0 mL of 0.02 N sulfuric acid (0.2%).

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

• **Hydrogen Sulfide and Sulfur Dioxide**

**Analysis:** Dissolve about 500 mg in 5 mL of 1 N sodium hydroxide, add 6 mL of 3 N hydrochloric acid, and stir vigorously. Hold a piece of moistened lead acetate test paper over the mixture.

**Acceptance criteria:** The test paper so obtained does not become discolored.

• **Content of 3-Aminosalicylic Acid and Other Related Impurities**

[Note—Use this test to measure 3-aminosalicylic acid and other related impurities not measured in the test for *Content of Aniline, 2-Aminophenol, and 4-Aminophenol*.]

**Mobile phase:** Dissolve 1.36 g of monobasic potassium phosphate and 2.2 g of sodium 1-octanesulfonate in 890 mL of water, and adjust with phosphoric acid to a pH of 2.2. Pass through a filter of 0.5-µm or finer pore size. To the filtrate add 80 mL of methanol and 30 mL of acetonitrile.

**Standard solution:** 1 µg/mL each of USP Mesalamine RS and 3-aminosalicylic acid in *Mobile phase*

**Sample solution:** 0.5 mg/mL of Mesalamine in *Mobile phase*. Initially add about 75% of the final volume of *Mobile phase*, and sonicate briefly to dissolve. Dilute with *Mobile phase* to volume, and mix.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm × 15-cm; 5-µm packing L7

**Flow rate:** 1.2 mL/min

**Injection volume:** 20 µL

**Run time:** 3 times the retention time of mesalamine

**System suitability**

**Sample:** *Standard solution*

[Note—See *Table 1* for the relative retention times.]

**Suitability requirements**

**Resolution:** NLT 2 between mesalamine and 3-aminosalicylic acid

**Relative standard deviation:** NMT 5.0% for both mesalamine and 3-aminosalicylic acid

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of 3-aminosalicylic acid:

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

$r_U$ = peak response of 3-aminosalicylic acid from the *Sample solution*

$r_S$ = peak response of 3-aminosalicylic acid from the *Standard solution*

$C_S$ = concentration of 3-aminosalicylic acid in the *Standard solution* (µg/mL)

$C_U$ = concentration of Mesalamine in the *Sample solution* (µg/mL)

Calculate the percentage of any other impurity:

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

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

$r_S$ = peak response of mesalamine from the *Standard solution*

$C_S$ = concentration of USP Mesalamine RS in the *Standard solution* (µg/mL)

$C_U$ = concentration of Mesalamine in the *Sample solution* (µg/mL)

**Acceptance criteria:** See *Table 1*.

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Mesalamine | 1.0 | — |
| 3-Aminosalicylic acid | 1.3 | 0.2 |
| Any other impurity | — | 0.2 |
| Total impurities | — | 1.0 |

- **Content of Aniline, 2-Aminophenol, and 4-Aminophenol**

**Standard stock solution:** 0.05 mg/mL of aniline, 2 mg/mL of 2-aminophenol, and 2 mg/mL of USP 4-Aminophenol RS in methanol

**Standard solution:** 0.5 µg/mL of aniline, 20 µg/mL of 2-aminophenol, and 20 µg/mL of USP 4-Aminophenol RS from the *Standard stock solution* in methylene chloride

**Sample solution:** 100 mg/mL of Mesalamine in methylene chloride. Allow to settle, and use the clear methylene chloride solution.

**Chromatographic system**

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

**Mode:** GC

**Detector:** Flame ionization

**Column:** 0.53-mm × 10-m fused-silica capillary; 2.65-µm film of G27

**Temperatures**

**Injection port:** 280°

**Detector:** 300°

**Column:** See *Table 2*.

**Table 2**

| Initial Temperature (°) | Temperature Ramp (°/min) | Final Temperature (°) | Hold Time at Final Temperature (min) |
|---|---|---|---|
| 70 | — | 70 | 2 |
| 70 | 30 | 150 | 1 |

**Carrier gas:** Helium

**Flow rate:** 15 mL/min

**Injection volume:** 2 µL

**System suitability**

**Sample:** *Standard solution*

[Note—See *Table 3* for the relative retention times.]

**Suitability requirements**

**Resolution:** NLT 2.0 between aniline and 2-aminophenol; NLT 2.0 between 2-aminophenol and 4-aminophenol

**Relative standard deviation:** NMT 10.0% for aniline, 2-aminophenol, and 4-aminophenol

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of aniline, 2-aminophenol, and 4-aminophenol in the portion of Mesalamine taken:

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

$r_U$ = peak response of aniline, 2-aminophenol, or 4-aminophenol from the *Sample solution*

$r_S$ = peak response of aniline, 2-aminophenol, or 4-aminophenol from the *Standard solution*

$C_S$ = concentration of aniline, 2-aminophenol, or USP 4-Aminophenol RS in the *Standard solution* (µg/mL)

$C_U$ = concentration of Mesalamine in the *Sample solution* (µg/mL)

**Acceptance criteria:** See *Table 3*.

**Table 3**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Aniline | 0.5 | 0.0005 |
| 2-Aminophenol | 0.9 | 0.02 |
| 4-Aminophenol | 1.0 | 0.02 |

## SPECIFIC TESTS

- **Clarity of Solution**

  **Sample solution:** Freshly prepare a solution of 0.25 g of Mesalamine in 10 mL of 1 N hydrochloric acid.

  **Acceptance criteria:** The *Sample solution* is clear.

- **Loss on Drying ⟨731⟩**

  **Analysis:** Dry under vacuum at 105° for 3 h.

  **Acceptance criteria:** NMT 0.5%

- **pH ⟨791⟩**

  **Sample:** A suspension (1 in 40)

  **Acceptance criteria:** 3.5–4.5

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **USP Reference Standards ⟨11⟩**

  USP 4-Aminophenol RS

  4-Aminophenol.

  $C_6H_7NO$ 109.13

  USP Mesalamine RS



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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| MESALAMINE | Documentary Standards Support | SM22020 Small Molecules 2 |

**Chromatographic Database Information:** Chromatographic Database

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