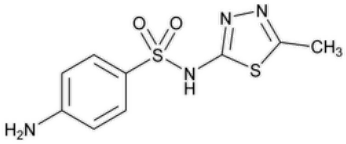
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2022
Document Type: USP Monographs
DocId: GUID-40B5E90B-09DC-48E8-914C-0BDDB1183B56_5_en-US
DOI: https://doi.org/10.31003/USPNF_M79150_05_01
DOI Ref: rj9xr

Sulfamethizole



$C_9H_{10}N_4O_2S_2$ 270.33

Benzenesulfonamide, 4-amino-*N*-(5-methyl-1,3,4-thiadiazol-2-yl)-;

N^1-(5-Methyl-1,3,4-thiadiazol-2-yl) sulfanilamide CAS RN®: 144-82-1; UNII: 25W8454H16.

DEFINITION

Sulfamethizole contains NLT 98.0% and NMT 101.0% of sulfamethizole ($C_9H_{10}N_4O_2S_2$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M
- **B.**

  Sample: 0.1 g

  Analysis: Add 5 mL of 3 N hydrochloric acid to the *Sample*, and boil gently for 5 min. Cool in an ice bath, then add 4 mL of 1% sodium nitrite solution, add water to make 10 mL, and place the mixture in an ice bath for 10 min. To 5 mL of the cooled mixture add a solution of 50 mg of 2-naphthol in 2 mL of 10% sodium hydroxide solution.

  Acceptance criteria: An orange-red precipitate is formed, and it darkens on standing.
- **C.**

  Sample: 20 mg

  Analysis: Suspend the *Sample* in 5 mL of water, add dropwise 1 N sodium hydroxide until dissolved, then add 2 or 3 drops of cupric sulfate TS.

  Acceptance criteria: A light green precipitate is formed, and it does not change on standing.
- **D.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

  Mobile phase: Methanol, glacial acetic acid, and water (30:1:69)

  Standard stock solution: 0.4 mg/mL of USP Sulfamethizole RS in methanol

  Standard solution: 8 µg/mL of USP Sulfamethizole RS from the *Standard stock solution* in *Mobile phase*

  Sample stock solution: 0.4 mg/mL of Sulfamethizole in methanol

  Sample solution: 8 µg/mL of Sulfamethizole from the *Sample stock solution* in *Mobile phase*

  Chromatographic system

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

  Mode: LC

  Detector: UV 254 nm

  Column: 3.9-mm × 30-cm; 10-µm packing L1

  Flow rate: 1 mL/min

  Injection volume: 50 µL

  System suitability

  Sample: *Standard solution*

  Suitability requirements

  Column efficiency: NLT 2000 theoretical plates

  Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sulfamethizole ($C_9H_{10}N_4O_2S_2$) in the portion of Sulfamethizole taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–101.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Chloride and Sulfate ⟨221⟩, *Chloride***

  Sample solution: A 25.0-mL portion of the filtrate prepared in the test for *Acidity*

  Acceptance criteria: 0.014%; shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid
- **Chloride and Sulfate ⟨221⟩, *Sulfate***

  Sample solution: A 25.0-mL portion of the filtrate prepared in the test for *Acidity*

  Acceptance criteria: 0.04%; shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid

Delete the following:

▲- **Selenium ⟨291⟩:** NMT 0.003%▲ (USP 1-May-2022)

- **Ordinary Impurities ⟨466⟩**

  Standard solution: Methanol

  Sample solution: Methanol

  Eluant: Acetone

  Visualization: 1

  Acceptance criteria: Meets the requirements

SPECIFIC TESTS

- **Melting Range or Temperature ⟨741⟩:** 208°–212°
- **Acidity**

  Sample: 2.0 g

  Analysis: Digest the *Sample* with 100 mL of water at 70° for 5 min, cool immediately to about 20°, and filter. To 25.0 mL of the filtrate add 2 drops of phenolphthalein TS, and titrate with 0.10 N sodium hydroxide. Save the remainder of the filtrate for the tests for *Chloride* and *Sulfate*.

  Acceptance criteria: NMT 0.50 mL is required for neutralization.
- **Loss on Drying ⟨731⟩**

  Analysis: Dry at 105° for 2 h.

  Acceptance criteria: NMT 0.5%
- **Clarity and Color of Solution**

  Sample: 1.0 g

  Analysis: Dissolve the *Sample* in 20 mL of water and 5 mL of 1 N sodium hydroxide.

  Acceptance criteria: The solution is clear and not more than pale yellow.

ADDITIONAL REQUIREMENTS

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

  USP Sulfamethizole RS

Topic/Question	Contact	Expert Committee
SULFAMETHIZOLE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(6)

Current DocID: GUID-40B5E90B-09DC-48E8-914C-0BDDB1183B56_5_en-US

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