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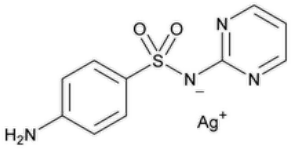
Silver Sulfadiazine



$C_{10}H_9AgN_4O_2S$ 357.14

Benzenesulfonamide, 4-amino-*N*-2-pyrimidinyl-, monosilver(1+) salt;

N^1-2-Pyrimidinylsulfanilamide monosilver(1+) salt CAS RN®: 22199-08-2; UNII: W46JY43EJR.

DEFINITION

Silver Sulfadiazine contains NLT 98.0% and NMT 102.0% of silver sulfadiazine ($C_{10}H_9AgN_4O_2S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A, 197D, or 197K▲ (CN 1-May-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Silver***

  Sample: 1 g in 15 mL of ammonium hydroxide and 15 mL of water in a 50-mL volumetric flask. Dilute with water to volume, and mix.

  Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

  Solution A: 0.77 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 5.2 ± 0.1.

  Solution B: Methanol

  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	98	2
4	98	2
16	40	60
20	40	60
22	20	80
32	20	80
34	98	2
40	98	2

Diluent: Acetonitrile, ammonium hydroxide, and water (5:6:90)

Standard solution: 0.05 mg/mL of USP Silver Sulfadiazine RS in *Diluent*. Sonicate, if necessary, to dissolve.

Sample solution: 0.05 mg/mL of Silver Sulfadiazine in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of silver sulfadiazine ($C_{10}H_9AgN_4O_2S$) in the portion of Silver Sulfadiazine 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 Silver Sulfadiazine RS in the *Standard solution* (mg/mL)

C_U = concentration of Silver Sulfadiazine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

OTHER COMPONENTS

• **Content of Silver**

Sample solution: Add 500 mg to 150 mL of water and 50 mL of nitric acid, and stir for 15 min.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N potassium thiocyanate VS or 0.1 N ammonium thiocyanate VS

Endpoint detection: Potentiometric

Analysis: Titrate the *Sample solution* with *Titrant* using a silver-based indicator electrode and a double-junction reference electrode. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N potassium thiocyanate VS or 0.1 N ammonium thiocyanate VS is equivalent to 10.79 mg of silver.

Acceptance criteria: 29.3%–30.5% of silver is found.

IMPURITIES

• **Limit of Nitrate**

Standard solution: 200 µg/mL of nitrate from potassium nitrate

Sample solution: Add 30.0 mL of water to 2 g of Silver Sulfadiazine, stir for 20 min, and pass through a suitable, nitrate-free filter.

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: 408 nm

Blank: Deionized water

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Pipet 3 mL of the *Sample solution* and *Blank* into separate test tubes. Pipet 1 mL of the *Standard solution* and 2 mL of water into a third test tube. Cool the three test tubes in an ice bath. Slowly add 7.0 mL of cold chromotropic acid solution, prepared by dissolving 50 mg of chromotropic acid in 100 mL of cold sulfuric acid, to each test tube, while swirling, and allow the test tubes to remain in the ice bath

for 3 min after the addition of the chromotropic acid solution. Remove the test tubes from the ice bath, and allow to stand for 30 min. Concomitantly determine the absorbances of the *Sample solution* and the *Standard solution* with a suitable spectrophotometer, against the *Blank*.

Calculate the percentage of nitrate content in the portion of Silver Sulfadiazine taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of nitrate in the *Standard solution* (µg/mL)

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

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 1.0 mg/mL of USP Silver Sulfadiazine RS and 0.001 mg/mL each of USP Sulfanilic Acid RS, USP Sulfanilamide RS, and sulfaguanidine in *Diluent*

Standard solution: 0.001 mg/mL of USP Silver Sulfadiazine RS in *Diluent*

Sample solution: 1.0 mg/mL of Silver Sulfadiazine in *Diluent*

System suitability

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

[Note—The relative retention times for sulfaguanidine and sulfanilamide are about 0.65 and 0.71, respectively.]

Suitability requirements

Resolution: NLT 2.0 between sulfaguanidine and sulfanilamide, *System suitability solution*

Relative standard deviation: NMT 5.0% for the sulfadiazine peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Silver Sulfadiazine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of silver sulfadiazine from the *Standard solution*

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

C_U = concentration of Silver Sulfadiazine in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any impurity peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Sulfanilic acid	0.27	0.27	0.3
Sulfaguanidine[a,b]	0.65	0.85	—
Sulfanilamide[b]	0.71	1.0	—
2-Aminopyrimidine[c]	0.82	0.48	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Sulfadiazine[d]	1.00	—	—
Acetylsulfadiazine[e]	1.14	1.0	0.2
Specified unidentified impurity[f]	1.28	1.0	0.15
Individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] 4-Amino-*N*-carbamimidoylbenzenesulfonamide.

[b] These are controlled using the limit for individual unspecified impurities.

[c] Pyrimidin-2-amine.

[d] 4-Amino-*N*-2-pyrimidinyl-benzenesulfonamide.

[e] *N*-{4-[*N*-(Pyrimidin-2-yl)sulfamoyl]phenyl}acetamide.

[f] This compound is a specified unknown impurity. No information is available about the chemical structure or chemical name for this impurity.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 1 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Silver Sulfadiazine RS

USP Sulfanilamide RS

4-Aminobenzenesulfonamide.

$C_6H_8N_2O_2S$ 172.20

USP Sulfanilic Acid RS

4-Aminobenzenesulfonic acid.

$C_6H_7NO_3S$ 173.19

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

Topic/Question	Contact	Expert Committee
SILVER SULFADIAZINE	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

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