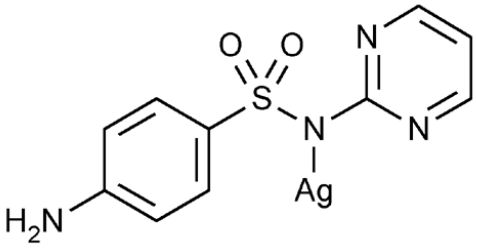
**Silver Sulfadiazine**




$C_{10}H_9AgN_4O_2S$ 357.14

Benzenesulfonamide, 4-amino-*N*-2-pyrimidinyl-, monosilver(1+) salt.
*N* [1] -2-Pyrimidinylsulfanilamide monosilver(1+) salt [*22199-08-2*].

» Silver Sulfadiazine contains not less than 98.0 percent and not more than 102.0 percent of $C_{10}H_9AgN_4O_2S$, calculated on the dried basis.

**Packaging and storage—** Preserve in well-closed, light-resistant containers.

**USP Reference standards** ⟨ 11 ⟩ —
*USP Silver Sulfadiazine RS* .

**Identification—**

**A:** *Infrared Absorption* ⟨ 197K ⟩ .

**B:** The $R_F$ value of the principal spot in the thin-layer chromatogram of the *Test solution* as obtained in the test for *Chromatographic purity* corresponds to that obtained from *Standard solution A*.

**C:** Dissolve about 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: the solution so obtained responds to the tests for *Silver* ⟨ 191 ⟩ .

**Particle size—** [ NOTE— Perform in subdued light. ] Wrap a 1-L flask in aluminum foil, add 0.5 g of Silver Sulfadiazine, add 1000 mL of a suitable isotonic solution, and mix for 2 hours. Add 5 or 6 drops of a suitable dispersant. Place the container in an ultrasonic bath, sonicate for 15 seconds, and immediately analyze, using a suitable electronic particle counter equipped with a population counter and 140- and 30-µm apertures. The average particle size is not greater than 10 µm and the size of not more than 10% of the particles is greater than 40 µm.

**Loss on drying** ⟨ 731 ⟩ — Dry it at 105° for 1 hour: it loses not more than 0.5% of its weight.

**Limit of nitrate—**

*Standard solution*— Prepare a solution of potassium nitrate in water having a known concentration of about 200 µg of nitrate per mL.

*Test solution*— Transfer about 2 g of Silver Sulfadiazine, accurately weighed, to a beaker, add 30.0 mL of water, stir for 20 minutes, and filter through a suitable, nitrate-free filter.

*Procedure*— Pipet 3 mL of the *Test solution* and of deionized water to provide the 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 minutes after the addition of the chromotropic acid solution. Remove the test

tubes from the ice bath, and allow to stand for 30 minutes. Concomitantly determine the absorbances of the *Test solution* and the *Standard solution* at the wavelength of maximum absorbance at about 408 nm, with a suitable spectrophotometer, against the blank. Calculate the nitrate content, in mg, in the portion of Silver Sulfadiazine taken by the formula:

$$0.01C\,(A_U / A_S)$$

in which $C$ is the concentration, in µg per mL, of nitrate in the *Standard solution;* and $A_U$ and $A_S$ are the absorbances obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.1% is found.

**Chromatographic purity—**

*Standard solution A*— Transfer about 50 mg of *USP Silver Sulfadiazine RS* to a 10-mL volumetric flask, and dissolve in 3.0 mL of ammonium hydroxide. Dilute with methanol to volume, and mix to obtain a solution having a known concentration of about 5 mg per mL.

*Standard solution B*— Dilute a volume of *Standard solution A* quantitatively, and stepwise if necessary, with a mixture of methanol and ammonium hydroxide (4:1) to obtain a solution having a known concentration of about 0.05 mg per mL.

*Test solution*— Transfer about 50 mg of Silver Sulfadiazine to a 10-mL volumetric flask, and dissolve in 3.0 mL of ammonium hydroxide. Dilute with methanol to volume, and mix to obtain a solution having a known concentration of about 5 mg per mL.

*Procedure*— Prepare a chromatographic chamber containing a mixture of chloroform, methanol, and ammonium hydroxide (7:4:1) as the developing solvent. [ NOTE— Mix the chloroform and methanol, then add the ammonium hydroxide. ] Separately apply 10-µL portions of *Standard solution A*, *Standard solution B*, and the *Test solution* to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨ 621 ⟩ ) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and place the plate in the chromatographic chamber. When the solvent front has moved about three-fourths of the length of the plate, remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Examine the plate under short-wavelength UV light: no secondary spot in the chromatogram of the *Test solution* is larger or more intense than the principal spot obtained from *Standard solution B* (1.0%), and the sum of all secondary spots observed is not greater than 2.0%.

**Silver content—** Transfer about 500 mg, accurately weighed, to a beaker, add 150 mL of water and 50 mL of nitric acid, and stir for 15 minutes. Titrate with 0.1 N potassium thiocyanate VS to a potentiometric endpoint, using a silver-based indicator electrode and a double-junction reference electrode. Perform a blank determination (see *Titrimetry* ⟨ 541 ⟩ ), and make any necessary correction. Each mL of 0.1 N potassium thiocyanate is equivalent to 10.79 mg of silver: not less than 29.3% and not more than 30.5% of silver is found.

**Assay—**

*Mobile phase*— Prepare a degassed solution consisting of water, acetonitrile, and phosphoric acid (900:99:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨ 621 ⟩ ).

*Diluting solution*— Transfer 100 mL of ammonium hydroxide to a 1-liter volumetric flask, dilute with water to volume, and mix.

*Internal standard solution*— Dissolve an accurately weighed quantity of sulfamerazine in *Diluting solution*, and dilute quantitatively, and stepwise if necessary, with *Diluting solution* to obtain a solution having a known concentration of about 10 mg per mL.

*Standard stock solution*— Dissolve about 250 mg of *USP Silver Sulfadiazine RS*, accurately weighed, in 100 mL of *Diluting solution* in a 200-mL volumetric flask, and sonicate for five minutes. Add 25.0 mL of *Internal standard solution*, dilute with *Diluting solution* to volume, and mix.

*Standard preparation*— Pipet 2.0 mL of *Standard* into a 50-mL volumetric flask. Dilute with *Mobile phase* to volume, and mix.

*Assay preparation*— Transfer about 250 mg of Silver Sulfadiazine, accurately weighed, to a 50-mL round-bottom centrifuge tube. Add about 35 mL of methanol, tightly seal the tube with a cap containing an inert liner, and mix, using a vortex mixer, for about 15 seconds. Centrifuge for 15 minutes to separate the phases. Aspirate, and discard the methanol supernatant layer. [ NOTE— Care should be taken to avoid aspirating any of the residue. ] Pipet 25.0 mL of *Internal standard solution* into a 200-mL volumetric flask. Add about 30 mL of *Diluting solution* to the centrifuge tube, replace the cap, and mix, using a vortex mixer, for about 15 seconds. Quantitatively transfer the contents to the 200-mL volumetric flask, using the *Diluting solution* to rinse the tube. Repeat the addition of 30 mL of *Diluting solution*, mixing and quantitatively transferring three more times. Dilute with the *Diluting solution* to volume, and mix. Sonicate if necessary to obtain dissolution of the residue. Pipet 2.0 mL into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, mix, and filter.

*Chromatographic system* (see *Chromatography* 〈 621 〉 )—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2.0 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure:* the resolution, *R,* between sulfadiazine and sulfamerazine is not less than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*— Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{10}H_9AgN_4O_2S$ in the portion of Silver Sulfadiazine taken by the formula:

$$200C\,(R_U / R_S)$$

in which $C$ is the concentration, in mg per mL, of Silver Sulfadiazine in the *Standard stock preparation;* and $R_U$ and $R_S$ are the relative peak ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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