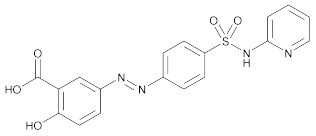
Sulfasalazine



$C_{18}H_{14}N_4O_5S$ 398.39

Benzoic acid, 2-hydroxy-5-[[4-[(2-pyridinylamino)sulfonyl] phenyl]azo]-;
5-[[*p*-(2-Pyridylsulfamoyl)phenyl]azo]salicylic acid [599-79-1].

DEFINITION

Sulfasalazine contains NLT 97.0% and NMT 101.5% of $C_{18}H_{14}N_4O_5S$, calculated on the dried basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B. PROCEDURE**

Standard solution: Use the *Standard solution*, prepared as directed in the *Assay*.

Sample solution: Use the *Sample solution*, prepared as directed in the *Assay*.

Acceptance criteria: The visible absorption spectrum of the *Sample solution* corresponds to that of the *Standard solution*, as obtained from the *Assay*.

ASSAY

- **PROCEDURE**

Sample stock solution: 1.5 mg/mL of Sulfasalazine in 0.1 N sodium hydroxide

Sample solution: Transfer 5.0 mL of the *Sample stock solution* to a 1000-mL volumetric flask containing 750 mL of water, mix, add 20.0 mL of 0.1 N acetic acid, and dilute with water to volume.

Standard solution: 7.5 µg/mL of USP Sulfasalazine RS in the same medium as the *Sample solution*

Spectrometric conditions

(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)

Mode: UV-Vis

Analytical wavelength: Maximum at about 359 nm

Blank: Water

Analysis

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

Concomitantly determine the absorbances of the *Samples*. Calculate the percentage of $C_{18}H_{14}N_4O_5S$ in the portion of Sulfasalazine 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 USP Sulfasalazine RS in the *Standard solution* (µg/mL)
C_U = concentration of Sulfasalazine in the *Sample solution* (µg/mL)

Acceptance criteria: 97.0%–101.5% on the dried basis

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.5%
- **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩

Analysis: Digest 2.0 g of Sulfasalazine with 100 mL of water at 70° for 5 min. Cool immediately to room temperature, and filter. Transfer a 25-mL portion of the filtrate to a 50-mL beaker (retain the remainder of this filtrate for the *Sulfate* test). Add 1 mL of nitric acid, mix, and allow to stand for 5 min. Pass through a fine texture, retentive filter paper (Whatman No. 42, or equivalent).

Acceptance criteria: The filtrate shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (0.014%).

- **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩

Analysis: Transfer a 25-mL portion of the filtrate from the *Chloride* test to a 50-mL beaker. Add 1 mL of 3 N hydrochloric acid, mix, and allow to stand for 5 min. Pass through a fine texture, retentive filter paper (Whatman No. 42, or equivalent).

Acceptance criteria: The filtrate shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (0.04%).

- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm

Organic Impurities

- **PROCEDURE**

Standard stock solution: 10 mg/mL of USP Sulfasalazine RS in a mixture of alcohol and 2 M ammonium hydroxide (4:1)

Standard solutions: Dilute aliquots of the *Standard stock solution* stepwise with the same medium to obtain solutions having concentrations of 200, 150, 100, and 20 µg/mL, corresponding to 2.0%, 1.5%, 1.0%, and 0.2%, respectively (*Standard solutions A, B, C,* and *D*).

Sample solution: 10 mg/mL of Sulfasalazine in a mixture of alcohol and 2 M ammonium hydroxide (4:1)

Chromatographic system

(See *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Chloroform, acetone, and formic acid (12:6:1)

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in the chapter. Allow the spots to dry, and develop the chromatogram in an unequilibrated chamber until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, dry with the aid of a current of hot air, and examine the plate under short-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*. No spots, other than the principal spot, in the chromatogram of the *Sample solution* are larger or more intense than the principal spot of *Standard solution A* (2%), and the sum of the intensities of any secondary spots detected does not exceed 4%.

SPECIFIC TESTS

- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample at 105° for 2 h: it loses NMT 1.0% of its weight.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Sulfasalazine RS

Sulfasalazine Tablets

DEFINITION

Sulfasalazine Tablets contain NLT 95.0% and NMT 105.0% of the labeled quantity of sulfasalazine ($C_{18}H_{14}N_4O_5S$).

IDENTIFICATION

- **PROCEDURE**

Standard solution: Use the *Standard solution*, prepared as directed in the *Assay.*

Sample solution: Use the *Sample solution*, prepared as directed in the *Assay.*

Acceptance criteria: The visible absorption spectrum of the *Sample solution* corresponds to that of the *Standard solution*, as prepared in the *Assay*.