adjust to pH 5.3 with 2 mol/L sodium hydroxide TS. To this solution add 315 mL of acetonitrile.

Mobile phase B: A mixture of acetonitrole and water (7:3).

Flowing of the mobile phase: Control the gradient by mixing the mobile phases A and B as directed in the following table.

Time after injection of sample (min)	Mobile phase A (%)	Mobile phase B (%)
0 - 38	100	0
38 - 39	100→90	0→10
39 - 80	90	10

Flow rate: Adjust the flow rate so that the retention time of roxithromycin is about 21 minutes.

System suitability—

Test for required detection: To exactly 2 mL of the standard solution add the mobile phase A to make exactly 10 mL. Confirm that the peak area of roxithromycin obtained from 20 μL of this solution is equivalent to 15 to 25% of that of roxithromycin obtained from 20 μL of the standard solution.

System performance: Dissolve 5 mg each of Roxithromycin Reference Standard and *N*-demethylroxithromycin in the mobile phase A to make 100 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, *N*-demethylroxithromycin and roxithromycin are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 5 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of roxithromycin is not more than 2.0%.

Water Not more than 3.0% (0.3 g, volumetric titration, direct titration).

Residue on ignition Not more than 0.1% (1 g).

Assay Weigh accurately an amount of Roxithromycin and Roxithromycin Reference Standard, equivalent to about 0.02 g (potency), and dissolve separately in the mobile phase to make exactly 10 mL, and use these solutions as the sample solution and the standard solution. Perform the test with exactly 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the peak areas, A_T and A_S, of roxithromycin.

Amount [μg (potency)] of $C_{41}H_{76}N_2O_{15}$
= amount [mg (potency)] of Roxithromycin Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 205 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: To 200 mL of a solution of ammonium dihydrogenphosphate (17 in 100) add 510 mL of water, and adjust to pH 5.3 with 2 mol/L sodium hydroxide TS. To this solution add 315 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of roxithromycin is about 11 minutes.

System suitability—

System performance: Dissolve 5 mg each of Roxithromycin Reference Standard and *N*-demethylroxithromycin in the mobile phase to make 100 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, *N*-demethylroxithromycin and roxithromycin are eluted in this order with the resolution between these peaks being not less than 6 and the symmetry coefficient of the peak of roxithromycin is not more than 1.5.

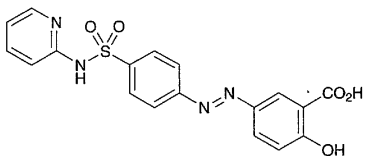
System repeatability: When, the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of roxithromycin is not more than 1.0%.

Containers and storage Containers—Tight containers.

Salazosulfapyridine

Sulfasalazine

サラゾスルファピリジン



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

2-Hydroxy-5-[4-(pyridin-2-ylsulfamoyl)phenylazo]benzoic acid [*599-79-1*]

Salazosulfapyridine, when dried, contains not less than 96.0% of $C_{18}H_{14}N_4O_5S$.

Description Salazosulfapyridine occurs as a yellow to yellow-brown, fine powder. It is odorless and tasteless.

It is sparingly soluble in pyridine, slightly soluble in ethanol (95), practically insoluble in water, in chloroform and in diethyl ether.

It dissolves in sodium hydroxide TS.

Melting point: 240 - 249°C (with decomposition).

Identification (1) Dissolve 0.1 g of Salazosulfapyridine in 20 mL of dilute sodium hydroxide TS: a red-brown color develops. This color gradually fades upon gradual addition of 0.5 g of sodium hydrosulfite with shaking. Use this solution in the following tests (2) to (4).

(2) To 1 mL of the solution obtained in (1) add 40 mL of water, neutralize with 0.1 mol/L hydrochloric acid TS, and add water to make 50 mL. To 5 mL of this solution add 2 to 3 drops of dilute iron (III) chloride TS: a red color develops and changes to purple, then fades when dilute hydrochloric acid is added dropwise.

(3) The solution obtained in (1) responds to the Qualitative Tests for primary aromatic amines.

(4) To 1 mL of the solution obtained in (1) add 1 mL of

pyridine and 2 drops of copper (II) sulfate TS, and shake. Add 3 mL of water and 5 mL of chloroform, shake, and allow to stand: a green color develops in the chloroform layer.

(5) Determine the absorption spectrum of a solution of Salazosulfapyridine in dilute sodium hydroxide TS (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

Purity (1) Chloride—Dissolve 2.0 g of Salazosulfapyridine in 12 mL of sodium hydroxide TS and 36 mL of water, add 2 mL of nitric acid, shake, and filter. To 25 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(2) Sulfate—Dissolve 2.0 g of Salazosulfapyridine in 12 mL of sodium hydroxide TS and 36 mL of water, add 2 mL of hydrochloric acid, shake, and filter. To 25 mL of the filtrate add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(3) Heavy metals—Proceed with 1.0 g of Salazosulfapyridine according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Arsenic—Take 1.0 g of Salazosulfapyridine in a decomposition flask, add 20 mL of nitric acid, and heat gently until it becomes fluid. After cooling, add 5 mL of sulfuric acid, and heat until white fumes are evolved. Add, if necessary, 5 mL of nitric acid after cooling, and heat again. Repeat this operation until the solution becomes colorless to slightly yellow. After cooling, add 15 mL of a saturated solution of ammonium oxalate monohydrate, and heat until white fumes are evolved again. After cooling, add water to make 25 mL. Perform the test using Apparatus B with 5 mL of this solution as the test solution: the color of the test solution is not deeper than that of the following standard stain.

Standard stain: Proceed in the same manner without Salazosulfapyridine, transfer 5 mL of the obtained solution to a generator bottle, add exactly 2 mL of Standard Arsenic Solution, and proceed in the same manner as the test with the test solution (not more than 10 ppm).

(5) Related substances—Dissolve 0.20 g of Salazosulfapyridine in 20 mL of pyridine, and use this solution as the sample solution. Pipet 1 mL of this solution, add pyridine to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with diluted methanol (9 in 10) to a distance of about 10 cm, and air-dry the plate. Examine the plate under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

(6) Salicylic acid—To 0.10 g of Salazosulfapyridine add 15 mL of diethyl ether, and shake vigorously. Add 5 mL of dilute hydrochloric acid, shake vigorously for 3 minutes, collect the diethyl ether layer, and filter. To the water layer add 15 mL of diethyl ether, shake vigorously for 3 minutes, collect the diethyl ether layer, filter, and combine the filtrates. Wash the residue on the filter paper with a small quantity of diethyl ether, and combine the washings and the filtrate. Evaporate the diethyl ether with the aid of air-stream at room temperature. To the residue add dilute ammonium iron (III) sulfate TS, shake, and filter, if necessary. Wash the residue on the filter paper with a small quantity of dilute ammonium iron (III) sulfate TS, combine the washings and the filtrate, add dilute ammonium iron (III) sulfate TS to make exactly 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of salicylic acid for assay, previously dried in a desiccator (silica gel) for 3 hours, dissolve in dilute ammonium iron (III) sulfate TS to make exactly 400 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, at 535 nm of the sample solution and the standard solution as directed under the Ultraviolet-visible Spectrophotometry: salicylic acid content is not more than 0.5%.

$$\text{Content (\%) of salicylic acid } (C_7H_6O_3) = \text{amount (mg) of salicylic acid for assay} \times \frac{A_T}{A_S} \times 0.05$$

Loss on drying Not more than 2.0% (1 g, 105°C, 4 hours).

Residue on ignition Not more than 0.20% (1 g).

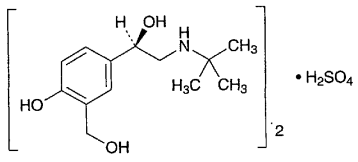
Assay Weigh accurately about 0.02 g of Salazosulfapyridine, previously dried, and perform the test as directed in the procedure of determination for sulfur under the Oxygen Flask Combustion Method, using 10 mL of diluted hydrogen peroxide (30) (1 in 40) as an absorbing liquid.

Each mL of 0.005 mol/L barium perchlorate VS
= 1.9920 mg of $C_{18}H_{14}N_4O_5S$

Containers and storage Containers—Tight containers.
Storage—Light-resistant.

Salbutamol Sulfate

硫酸サルブタモール



and enantiomer

$(C_{13}H_{21}NO_3)_2.H_2SO_4$: 576.70
(*RS*)-2-*tert*-Butylamino-1-(4-hydroxy-3-hydroxymethylphenyl)ethanol hemisulfate [*51022-70-9*]

Salbutamol Sulfate, when dried, contains not less than 98.0% of $(C_{13}H_{21}NO_3)_2.H_2SO_4$.

Description Salbutamol Sulfate occurs as a white powder.

It is freely soluble in water, slightly soluble in ethanol (95), and in acetic acid (100) and practically insoluble in diethyl ether.

A solution of Salbutamol Sulfate (1 in 20) shows no optical rotation.