

tion between these peaks being not less than 1.2.

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

**Containers and storage** Containers—Tight containers.

Storage—Preserve at  $-20^{\circ}\text{C}$  or lower.

## Silver Nitrate

硝酸銀

$\text{AgNO}_3$ : 169.87

Silver Nitrate, when dried, contains not less than 99.8% of  $\text{AgNO}_3$ .

**Description** Silver Nitrate occurs as lustrous, colorless or white crystals.

It is very soluble in water, soluble in ethanol (95), and practically insoluble in diethyl ether.

It gradually turns grayish black by light.

**Identification** A solution of Silver Nitrate (1 in 50) responds to the Qualitative Tests for silver salt and for nitrate.

**Purity** (1) Clarity and color of solution, and acidity or alkalinity—Dissolve 1.0 g of Silver Nitrate in 10 mL of freshly boiled and cooled water: the solution is clear and colorless. It is neutral.

(2) Bismuth, copper and lead—To 5 mL of a solution of Silver Nitrate (1 in 10) add 3 mL of ammonia TS: the solution is clear and colorless.

**Loss on drying** Not more than 0.20% (2 g, silica gel, light resistant, 4 hours).

**Assay** Weigh accurately about 0.7 g of Silver Nitrate, previously powdered and dried, dissolve in 50 mL of water, add 2 mL of nitric acid, and titrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS).

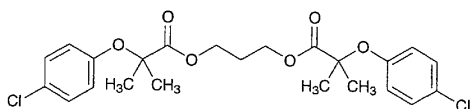
Each mL of 0.1 mol/L ammonium thiocyanate VS  
= 16.987 mg of  $\text{AgNO}_3$

**Containers and storage** Containers—Tight containers.

Storage—Light-resistant.

## Simfibrate

シンフィブラート



$\text{C}_{23}\text{H}_{26}\text{Cl}_2\text{O}_6$ : 469.53

Trimethylene bis[2-(4-chlorophenoxy)-2-methylpropanoate]  
[14929-11-4]

Simfibrate, when dried, contains not less than 98.5% of  $\text{C}_{23}\text{H}_{26}\text{Cl}_2\text{O}_6$ .

**Description** Simfibrate occurs as white to light yellow crystals or crystalline powder. It is odorless and tasteless.

It is very soluble in acetonitrile and in diethyl ether, soluble in ethanol (95) and in hexane, and practically insoluble in water.

**Identification** (1) To 0.05 g of Simfibrate add 0.5 mL of ethanol (95), and dissolve by warming on a water bath. After cooling, add 0.3 mL of a saturated solution of hydroxylammonium chloride in ethanol (95) and 0.3 mL of potassium hydroxide-ethanol TS, heat gently to boiling, and cool. To this solution add 1 mL of 1 mol/L hydrochloric acid TS and 2 mL of ethanol (95), and then add 1 drop of iron (III) chloride TS: a red-purple color develops.

(2) Determine the absorption spectrum of a solution of Simfibrate in hexane for ultraviolet-visible spectrophotometry (3 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Simfibrate in hexane for ultraviolet-visible spectrophotometry (3 in 200,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Perform the test with Simfibrate as directed under the Flame Coloration Test (2): a green color appears.

**Melting point**  $49 - 53^{\circ}\text{C}$

**Purity** (1) Clarity and color of solution—Dissolve 1.0 g of Simfibrate in 10 mL of ethanol (95) by warming on a water bath: the solution is clear and colorless to light yellow.

(2) Acid—To 4.0 g of Simfibrate add 40 mL of neutralized ethanol, dissolve by warming on a water bath, cool, and add 2 drops of phenolphthalein TS and 0.20 mL of 0.1 mol/L sodium hydroxide VS: a red color develops.

(3) Heavy metals—Proceed with 1.0 g of Simfibrate 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—Prepare the test solution with 1.0 g of Simfibrate according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) *p*-Chlorophenol—To 2.0 g of Simfibrate add exactly 1 mL of the internal standard solution, dissolve in acetonitrile to make 10 mL, and use this solution as the sample solution. Separately, dissolve 0.10 g of 4-chlorophenol in acetonitrile to make exactly 100 mL. Pipet 2 mL of this solution, and add acetonitrile to make exactly 100 mL. Pipet 1 mL of this solution, add exactly 1 mL of the internal standard solution and acetonitrile to make 10 mL, and use this solution as the standard solution. Perform the test with 20  $\mu\text{L}$  each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Calculate the ratios,  $Q_T$  and  $Q_S$ , of the peak height of 4-chlorophenol to that of the internal standard from each solution:  $Q_T$  is not larger than  $Q_S$ .

**Internal standard solution**—A solution of 4-ethoxyphenol in acetonitrile (1 in 50,000).

**Operating conditions—**

**Detector:** An ultraviolet absorption photometer (wavelength: 281 nm).

**Column:** A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5  $\mu$ m in particle diameter).

**Column temperature:** Room temperature.

**Mobile phase:** A mixture of water and acetonitrile (1:1).

**Flow rate:** Adjust the flow rate so that the retention time of 4-chlorophenol is about 7 minutes.

**Selection of column:** Proceed with 20  $\mu$ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of the internal standard and 4-chlorophenol in this order, and showing complete separation between these peaks.

**Loss on drying** Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

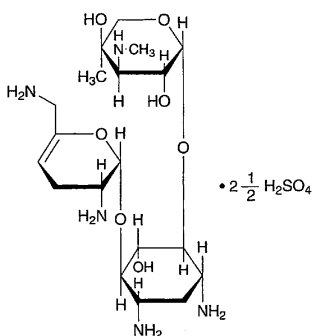
**Assay** Weigh accurately about 0.8 g of Simfibrate, previously dried, add exactly 50 mL of 0.1 mol/L potassium hydroxide-ethanol VS, and boil gently under a reflux condenser with a carbon dioxide absorption tube (soda lime) on a water bath for 60 minutes. After cooling, titrate the excess potassium hydroxide immediately with 0.1 mol/L hydrochloric acid VS (indicator: 3 drops of phenolphthalein TS). Perform a blank determination.

Each mL of 0.1 mol/L potassium hydroxide-ethanol VS = 23.468 mg of  $C_{23}H_{26}Cl_2O_6$

**Containers and storage** Containers—Well-closed containers.

## Sisomicin Sulfate

硫酸シソマイシン



$C_{19}H_{37}N_5O_7 \cdot 2\frac{1}{2}H_2SO_4$ : 692.72

*O*-3-Deoxy-4-*C*-methyl-3-methylamino- $\beta$ -L-arabinopyranosyl-(1 $\rightarrow$ 6)-*O*-[2,6-diamino-4,5-dehydro-2,3,4,6-tetra-deoxy- $\alpha$ -D-glycero-hexopyranosyl-(1 $\rightarrow$ 4)]-2-deoxy-D-streptamine hemiheptasulfate [53179-09-2]

Sisomicin Sulfate contains not less than 590  $\mu$ g (potency) per mg, calculated on the dried basis. The potency of Sisomicin Sulfate is expressed as mass (potency) of sisomicin ( $C_{19}H_{37}N_5O_7$ : 447.53).

**Description** Sisomicin Sulfate occurs as a white to light yellowish white powder.

It is very soluble in water, and practically insoluble in ethanol (95).

It is hygroscopic.

**Identification (1)** Dissolve 0.05 g of Sisomicin Sulfate in 5 mL of water, and add 0.3 mL of bromine TS: the solution is immediately decolorized.

**(2)** Dissolve 0.015 g each of Sisomicin Sulfate and Sisomicin Sulfate Reference Standard in 5 mL of water, and use these solutions as the sample solution and the standard solution. Perform the test with these solutions as directed under the Thin-layer chromatography. Spot 5  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of methanol, chloroform, ammonia water (28) and acetone (2:2:1:1) to a distance of about 15 cm, and air-dry the plate. Spray evenly 0.2% ninhydrin-water saturated 1-butanol TS on the plate, and heat at 100°C for 5 minutes: the principal spots from the sample solution and the standard solution exhibit a red-purple to red-brown color and show the same *R<sub>f</sub>* value.

**(3)** A solution of Sisomicin Sulfate (1 in 100) responds to the Qualitative Test (1) for sulfate.

**Optical rotation**  $[\alpha]_D^{20}$ : +100 – +110° (0.25 g calculated on the dried basis, water, 25 mL, 100 mm).

**pH** Dissolve 0.5 g of Sisomicin Sulfate in 5 mL of water: the pH of the solution is between 3.5 and 5.5.

**Purity (1)** Clarity and color of solution—Dissolve 0.5 g of Sisomicin Sulfate in 5 mL of water: the solution is clear and colorless to light yellow.

**(2)** Heavy metals—Proceed with 1.0 g of Sisomicin Sulfate 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).

**(3)** Related substances—Dissolve 0.05 g of Sisomicin Sulfate, calculated on the dried basis, in water to make 10 mL, and use this solution as the sample solution. Separately, weigh accurately an amount of Sisomicin Sulfate Reference Standard, equivalent to 0.025 g (potency), dissolve in water to make exactly 50 mL. Pipet 1 mL, 2 mL and 3 mL of this solution, add water to each to make exactly 10 mL, and use these solutions as the standard solution (1), the standard solution (2) and the standard solution (3), respectively. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10  $\mu$ L each of the sample solution and the standard solutions (1), (2), and (3) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of methanol, chloroform, ammonia water (28) and acetone (2:2:1:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly 0.2% ninhydrin-water saturated 1-butanol TS on the plate, and heat at 100°C for 5 minutes. The spots corresponding to *R<sub>f</sub>* about 0.35 and *R<sub>f</sub>* about 0.30 are not more intense than that of the spot from the standard solution (3), and the spot of gallamine corresponding to *R<sub>f</sub>* about 0.25 is not more intense than the spot from the standard solution (1). The total amount of the intensity of the spots other than the principal spot from the sample solution is not more than 6%.

**Loss on drying** Not more than 15.0% (0.15 g, in vacuum not exceeding 0.67 kPa, 110°C, 3 hours). Sampling should