of neostigmine methylsulfate is about 9 minutes.

System suitability—

System performance: Dissolve 0.025 g of Neostigmine Methylsulfate and 4 mg of dimethylaminophenol in 50 mL of the mobile phase. When the procedure is run with 10 μL of this solution under the above operating conditions, dimethylaminophenol and neostigmine methylsulfate are eluted in this order with the resolution between these peaks being not less than 6.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of neostigmine methylsulfate is not more than 1.0%.

Containers and storage Containers—Tight containers.

Neostigmine Methylsulfate Injection

メチル硫酸ネオスチグミン注射液

Neostigmine Methylsulfate Injection is an aqueous solution for injection. It contains not less than 93% and not more than 107% of the labeled amount of neostigmine methylsulfate ($C_{13}H_{22}N_2O_6S$: 334.39).

Method of preparation Prepare as directed under Injections, with Neostigmine Methylsulfate.

Description Neostigmine Methylsulfate Injection is a clear, colorless liquid.

It is slowly affected by light.

pH: 5.0 - 6.5

Identification Take a volume of Neostigmine Methylsulfate Injection equivalent to 5 mg of neostigmine methylsulfate according to the labeled amount, add water to make 10 mL if necessary, and determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 257 nm and 261 nm.

Bacterial endotoxins Less than 5 EU/mg.

Assay Use Neostigmine Methylsulfate Injection as the sample solution. Separately, weigh accurately about 0.025 g of Neostigmine Methylsulfate Reference Standard, previously dried at 105°C for 3 hours, dissolve in the mobile phase to make exactly 50 mL, and use this solution as the standard solution. Proceed as directed in the Assay under Neostigmine Methylsulfate.

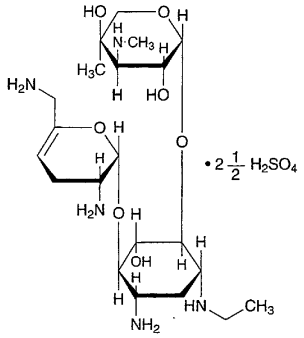
Amount (mg) of neostigmine methylsulfate ($C_{13}H_{22}N_2O_6S$) = amount (mg) of Neostigmine Methylsulfate Reference Standard $\times \frac{A_T}{A_S}$

Containers and storage Containers—Hermetic containers.

Storage—Light-resistant.

Netilmicin Sulfate

硫酸ネチルマイシン



$C_{21}H_{41}N_5O_7.2½H_2SO_4$: 720.78

O-3-Deoxy-4-*C*-methyl-3-methylamino-*β*-L-arabinopyranosyl-(1→6)-*O*-[2,6-diamino-4,5-dehydro-2,3,4,6-tetradeoxy-*α*-D-*glycero*-hexopyranosyl-(1→4)]-2-deoxy-1-*N*-ethyl-D-streptamine hemiheptasulfate

[*56391-57-2*]

Netilmicin Sulfate contains not less than 595 μg (potency) per mg, calculated on the dried basis. The potency of Netilmicin Sulfate is expressed as mass (potency) of netilmicin ($C_{21}H_{41}N_5O_7$: 475.58).

Description Netilmicin 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 0.03 g of Netilmicin Sulfate in 3 mL of water, and add 0.2 mL of bromine TS: the solution is immediately decolorized.

(2) Dissolve 0.015 g each of Netilmicin Sulfate and Netilmicin 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 μL 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-butabol 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*f value.

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

Optical rotation $[\alpha]_D^{20}$: +88 - +96° (0.1 g calculated on the dried basis, water, 10 mL, 100 mm).

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

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

(2) Heavy metals—Proceed with 1.0 g of Netilmicin 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 Netilmicin Sulfate, calculated on the dried basis, in water to make 5 mL, and use this solution as the sample solution. Pipet 0.5 mL, 1 mL, and 1.5 mL of the sample solution, add water to each to make exactly 50 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 5 μL each of the sample solution and the standard solution (1), the standard solution (2), the standard solution (3) on a plate of silica gel for thin-layer chromatography. Develop 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-butabol TS on the plate, and heat at 100°C for 5 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution (3), and 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 be carried out in a manner to avoid moisture absorption.

Residue on ignition Not more than 1.0% (1 g).

Assay Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Staphylococcus aureus* ATCC 6538 P

(2) Culture medium—Use the medium ii in 3) Medium for other organisms under (1) Agar media for seed and base layer. Adjust the pH of the medium so that it will be 7.8 to 8.0 after sterilization.

(3) Standard solution—Weigh accurately an amount of Netilmicin Sulfate Reference Standard equivalent to about 0.025 g (potency), dissolve in 0.1 mol/L phosphate buffer solution, pH 8.0 to make exactly 25 mL, and use this solution as the standard stock solution. Keep the standard stock solution at 5°C or below and use within 7 days. Take exactly a suitable amount of the standard stock solution before use, add 0.1 mol/L phosphate buffer solution, pH 8.0 to make solutions so that each mL contains 4 μg (potency) and 1 μg (potency), and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

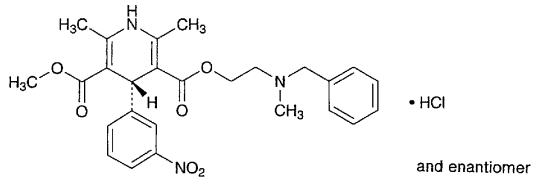
(4) Sample solution—Weigh accurately an amount of Netilmicin Sulfate equivalent to about 0.025 g (potency), dissolve in 0.1 mol/L phosphate buffer solution, pH 8.0 to make exactly 25 mL. Take exactly a suitable amount of the solution, add 0.1 mol/L phosphate buffer solution, pH 8.0 to make solutions so that each mL contains 4 μg (potency) and 1 μg (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

Containers and storage Containers—Tight containers.

Storage—Light-resistant, not exceeding 5°C, under nitrogen or argon atmosphere.

Nicardipine Hydrochloride

塩酸ニカルジピン



$C_{26}H_{29}N_3O_6.HCl$: 515.99

2-(*N*-Benzyl-*N*-methylamino)ethyl methyl (*RS*)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate monohydrochloride [*54527-84-3*]

Nicardipine hydrochloride, when dried, contains not less than 98.5% of $C_{26}H_{29}N_3O_6.HCl$.

Description Nicardipine Hydrochloride occurs as a pale greenish yellow crystalline powder.

It is freely soluble in methanol and in acetic acid (100), sparingly soluble in ethanol (99.5), and slightly soluble in water, in acetonitrile and in acetic anhydride.

A solution of Nicardipine Hydrochloride in methanol (1 in 20) shows no optical rotation.

It is gradually affected by light.

Identification (1) Determine the absorption spectrum of a solution of Nicardipine Hydrochloride in ethanol (99.5) (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.

(2) Determine the infrared absorption spectrum of Nicardipine Hydrochloride, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Dissolve 0.02 g of Nicardipine Hydrochloride in 10 mL of water and 3 mL of nitric acid: the solution responds to the Qualitative Tests for chloride.

Melting point 167 - 171°C

Purity (1) Heavy metals—Proceed with 1.0 g of Nicardipine Hydrochloride according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(2) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.10 g of Nicardipine Hydrochloride in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 50 mL, then take exactly 1 mL of this solution, add the mobile phase to make exactly 10 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: the area of each peak other than the peak of nicardipine from