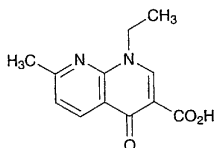


Nalidixic Acid

ナリジクス酸



$C_{12}H_{12}N_2O_3$: 232.24

1-Ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid [389-08-2]

Nalidixic Acid, when dried, contains not less than 98.5% of $C_{12}H_{12}N_2O_3$.

Description Nalidixic Acid occurs as white to light yellow crystals or crystalline powder. It is odorless.

It is sparingly soluble in chloroform and in *N,N*-dimethylformamide, very slightly soluble in ethanol (95) and in diethyl ether, and practically insoluble in water.

It dissolves in sodium hydroxide TS.

Identification (1) Dissolve 0.10 g of Nalidixic Acid in 0.01 mol/L sodium hydroxide TS to make 100 mL. To 1 mL of the solution add 0.01 mol/L sodium hydroxide TS to make 200 mL. Determine the absorption spectrum of the solution 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) Dissolve 0.02 g of Nalidixic Acid in 2.0 mL of water and 1.0 mL of sulfuric acid, add 0.02 g of vanillin, and boil gently for 2 minutes: the color of the solution changes from yellow to orange-red. Shake this solution vigorously while cooling, and allow to stand for 30 minutes: an orange-yellow precipitate is formed.

Melting point 225 – 231°C

Purity (1) Clarity and color of solution—Dissolve 0.5 g of Nalidixic Acid in 3 mL of sodium hydroxide TS and 7 mL of water: the solution is clear and colorless to pale yellow.

(2) Chloride—To 2.0 g of Nalidixic Acid add 50 mL of water, warm at 70°C for 5 minutes, cool quickly, 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 0.35 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.012%).

(3) Heavy metals—Proceed with 1.0 g of Nalidixic Acid 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 0.40 g of Nalidixic Acid, according to Method 3, and perform the test using Apparatus B (not more than 5 ppm).

(5) Related substances—Dissolve 0.50 g of Nalidixic Acid in 25 mL of chloroform, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add chloroform to make exactly 200 mL, and use this solution as

the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μ L 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 a mixture of ethanol (95), chloroform and ammonia TS (7:2:1) to a distance of about 10 cm, and air-dry the plate. Examine 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.

Loss on drying Not more than 0.20% (1 g, 105°C, 3 hours).

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

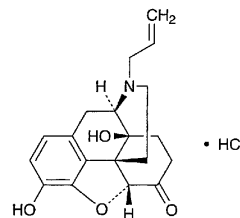
Assay Weigh accurately about 0.3 g of Nalidixic Acid, previously dried, dissolve in 50 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L sodium methoxide-dioxane VS, until the color of the solution changes from pale yellow to blue (indicator: 2 drops of thymolphthalein TS). To 50 mL of *N,N*-dimethylformamide add 13 mL of a mixture of 1,4-dioxane and methanol (17:3), perform a blank determination with the solution, and make any necessary correction.

Each mL of 0.1 mol/L sodium methoxide-dioxane VS = 23.224 mg of $C_{12}H_{12}N_2O_3$

Containers and storage Containers—Tight containers.

Naloxone Hydrochloride

塩酸ナロキソン



$C_{19}H_{21}NO_4 \cdot HCl$: 363.84

(5*R*,14*S*)-17-Allyl-4,5-epoxy-3,14-dihydroxymorphinan-6-one monohydrochloride [357-08-4]

Naloxone Hydrochloride contains not less than 98.5% of $C_{19}H_{21}NO_4 \cdot HCl$, calculated on the dried basis.

Description Naloxone Hydrochloride occurs as white to yellowish white, crystals or crystalline powder.

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

It is hygroscopic.

It is gradually colored by light.

Identification (1) Determine the absorption spectrum of a solution of Naloxone Hydrochloride (1 in 10,000) 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

wavelength.

(2) Determine the infrared absorption spectrum of Naloxone Hydrochloride, previously dried, as directed in the potassium chloride 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) A solution of Naloxone Hydrochloride (1 in 50) responds to the Qualitative Test (2) for chloride.

Optical rotation $[\alpha]_D^{25}$: $-170 - -181^\circ$ (0.25 g calculated on the dried basis, water, 10 mL, 100 mm).

pH Dissolve 0.10 g of Naloxone Hydrochloride in 10 mL of freshly boiled and cooled water: the pH of the solution is between 4.5 and 5.5.

Purity Related substances—Conduct this procedure as rapidly as possible without exposure to light, using light-resistant containers. Dissolve 0.08 g of Naloxone Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop with a mixture of ammonia-saturated 1-butanol TS and methanol (20:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly iron (III) chloride-potassium hexacyanoferrate (III) TS on the plate: the number of the spot other than the principal spot from the sample solution is not more than 1 and it is not more intense than the spot from the standard solution.

Loss on drying Not more than 2.0% [0.1 g, 105°C, 5 hours. Use a desiccator (phosphorus (V) oxide) for cooling].

Residue on ignition Not more than 0.2% (0.1 g).

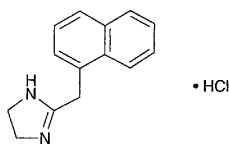
Assay Weigh accurately about 0.3 g of Naloxone Hydrochloride, dissolve in 80 mL of acetic acid (100) by warming. After cooling, add 80 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 36.384 mg of $C_{19}H_{21}NO_4 \cdot HCl$

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

Naphazoline Hydrochloride

塩酸ナファゾリン



$C_{14}H_{14}N_2 \cdot HCl$: 246.74
2-(Naphthalen-1-ylmethyl)-4,5-dihydro-1H-imidazole

monohydrochloride [550-99-2]

Naphazoline Hydrochloride, when dried, contains not less than 98.5% of $C_{14}H_{14}N_2 \cdot HCl$.

Description Naphazoline Hydrochloride occurs as a white, crystalline powder. It is odorless, and has a bitter taste.

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

Melting point: 255 – 260°C (with decomposition).

Identification (1) To 10 mL of a solution of Naphazoline Hydrochloride (1 in 100) add 5 mL of bromine TS, and boil: a deep purple color develops.

(2) To 30 mL of a solution of Naphazoline Hydrochloride (1 in 100) add 2 mL of sodium hydroxide TS, and extract with two 25-mL portions of diethyl ether. Evaporate the combined diethyl ether extracts to dryness with the aid of a current of air. Dry the residue at 80°C for 1 hour: the residue melts between 117°C and 120°C.

(3) Dissolve 0.02 g of the residue obtained in (2) in 2 to 3 drops of dilute hydrochloric acid and 5 mL of water, and add 2 mL of Reinecke salt TS: a red-purple, crystalline precipitate is formed.

(4) A solution of Naphazoline Hydrochloride (1 in 10) responds to the Qualitative Tests for chloride.

pH Dissolve 0.10 g of Naphazoline Hydrochloride in 10 mL of freshly boiled and cooled water: the pH of the solution is between 5.0 and 7.0.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Naphazoline Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Naphazoline Hydrochloride 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).

Loss on drying Not more than 0.5% (1 g, 105°C, 2 hours).

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

Assay Weigh accurately about 0.4 g of Naphazoline Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 24.674 mg of $C_{14}H_{14}N_2 \cdot HCl$

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