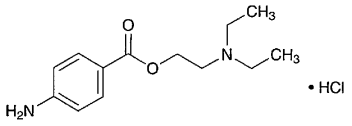
Procaine Hydrochloride

塩酸プロカイン



$C_{13}H_{20}N_2O_2.HCl$: 272.77
2-(Diethylamino)ethyl 4-aminobenzoate monohydrochloride [*51-05-8*]

Procaine Hydrochloride, when dried, contains not less than 99.0% of $C_{13}H_{20}N_2O_2.HCl$.

Description Procaine Hydrochloride occurs as white crystals or crystalline powder.

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

Identification (1) Determine the absorption spectrum of a solution of Procaine Hydrochloride (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 Procaine 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 Procaine Hydrochloride (1 in 10) responds to the Qualitative Tests for chloride.

pH The pH of a solution of Procaine Hydrochloride (1 in 20) is between 5.0 and 6.0.

Melting point 155 - 158°C

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

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

(3) Related substances—To 1.0 g of Procaine Hydrochloride add 5 mL of ethanol (95), dissolve by mixing well, add water to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 0.010 g of 4-aminobenzoic acid in ethanol (95) to make exactly 20 mL, then pipet 1 mL of this solution, add 4 mL of ethanol (95) and water to make exactly 10 mL, and use this solution as 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 with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of dibutyl ether, *n*-hexane and acetic acid (100) (20:4:1) to a distance of about 10 cm, and air-dry the plate. After drying the plate more at 105°C for 10 minutes, 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. The principal spot from the sample solution stays at the origin.

Loss on drying Not more than 0.5% (1 g, silica gel, 4 hours).

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

Assay Weigh accurately about 0.4 g of Procaine Hydrochloride, previously dried, dissolve in 5 mL of hydrochloric acid and 60 mL of water, add 10 mL of a solution of potassium bromide (3 in 10), cool to below 15°C, and titrate with 0.1 mol/L sodium nitrite VS according to the potentiometric titration method or the amperometric titration method under the Electrometric Titration.

Each mL of 0.1 mol/L sodium nitrite VS
= 27.277 mg of $C_{13}H_{20}N_2O_2.HCl$

Containers and storage Containers—Well-closed containers.

Procaine Hydrochloride Injection

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Procaine Hydrochloride Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of procaine hydrochloride ($C_{13}H_{20}N_2O_2.HCl$: 272.77).

Method of preparation Prepare as directed under Injections, with Procaine Hydrochloride.

Description Procaine Hydrochloride Injection is a clear, colorless liquid.

Identification (1) To a volume of Procaine Hydrochloride Injection, equivalent to 0.01 g of Procaine Hydrochloride according to the labeled amount, add water to make 1000 mL. Determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 219 nm and 223 nm, and between 289 nm and 293 nm.

(2) Procaine Hydrochloride Injection responds to the Qualitative Tests (2) for chloride.

pH 3.3 - 6.0

Assay To an exactly measured volume of Procaine Hydrochloride Injection, equivalent to about 0.02 g of procaine hydrochloride ($C_{13}H_{20}N_2O_2.HCl$), add the mobile phase to make exactly 20 mL. Pipet 5 mL of this solution, add exactly 5 mL of the internal standard solution and the mobile phase to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of procaine hydrochloride for assay, previously dried in a desiccator (silica gel) for 4 hours, dissolve in the mobile phase to make exactly 50 mL. Pipet 5 mL of this solution, add exactly 5 mL of the internal standard solution and the mobile phase to make 20 mL, and use this solution as the standard solution. Perform the test with 5 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak

area of procaine hydrochloride to that of the internal standard.

Amount (mg) of $C_{13}H_{20}N_2O_2.HCl$
= amount (mg) of procaine hydrochloride for assay
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of caffeine in the mobile phase (1 in 1000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 6 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Adjust the pH of 0.05 mol/L potassium dihydrogenphosphate to 3.0 with phosphoric acid, and add an amount of sodium 1-pentane sulfonate to make a solution of 0.1%. Prepare a mixture of this solution and methanol (4:1).

Flow rate: Adjust the flow rate so that the retention time of procaine hydrochloride is about 10 minutes.

Selection of column: Proceed with 5 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of procaine and the internal standard in this order with the resolution between these peaks being not less than 8.

Containers and storage Containers—Hermetic containers.

Procarbazine Hydrochloride

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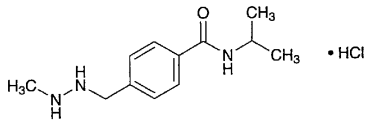

$C_{12}H_{19}N_3O.HCl$: 257.76
N-Isopropyl-4-(*N'*-methylhydrazinomethyl)benzamide monohydrochloride [*366-70-1*]

Procarbazine Hydrochloride, when dried, contains not less than 98.5% of $C_{12}H_{19}N_3O.HCl$.

Description Procarbazine Hydrochloride occurs as white to light yellowish white crystals or crystalline powder.

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

Melting point: about 223°C (with decomposition).

Identification (1) Dissolve 0.01 g of Procarbazine Hydrochloride in 1 mL of diluted copper (II) sulfate TS (1 in 10), and add 4 drops of sodium hydroxide TS: a green precipitate is formed immediately, and the color changes from green through yellow to orange.

(2) Determine the absorption spectrum of a solution of Procarbazine Hydrochloride in 0.1 mol/L hydrochloric acid 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.

(3) Determine the infrared absorption spectrum of Procarbazine 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.

(4) A solution of Procarbazine Hydrochloride (1 in 20) responds to the Qualitative Tests for chloride.

pH Dissolve 0.10 g of Procarbazine Hydrochloride in 10 mL of water: the pH of this solution is between 3.0 and 5.0.

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

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

(3) Arsenic—Dissolve 1.0 g of Procarbazine Hydrochloride in 6 mL of 0.1 mol/L hydrochloric acid TS and 4 mL of ethanol (95), use this solution as the test solution, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.050 g of Procarbazine Hydrochloride in 5 mL of a solution of L-cysteine hydrochloride in diluted methanol (7 in 10) (1 in 200), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a solution of L-cysteine hydrochloride in diluted methanol (7 in 10) (1 in 200) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Immerse slowly, by inclining, a plate of silica gel with fluorescent indicator for thin-layer chromatography in a solution of L-cysteine hydrochloride in diluted methanol (7 in 10) (1 in 200), allow to stand for 1 minute, lift the plate from the solution, dry it in cold wind for 10 minutes, then in warm wind for 5 minutes, and then dry at 60°C for 5 minutes. After cooling, spot 5 μL each of the sample solution and the standard solution on the plate. Develop the plate with a mixture of methanol and ethyl acetate (1:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): not more than 1 spot other than the principal spot and the spot of the starting point from the sample solution appears, and is not more intense than the spot from the standard solution.

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 0.15 g of Procarbazine Hydrochloride, previously dried, place in a glass-stoppered flask, dissolve in 25 mL of water, add 25 mL of hydrochloric acid, and cool to room temperature. To this solution add 5 mL of chloroform, and titrate, while shaking, with 0.05 mol/L potassium iodate VS until the purple color of the chloroform layer disappears. The end point is reached when the red-purple color of the chloroform layer no more reappears within 5 minutes after the purple color disappeared.