

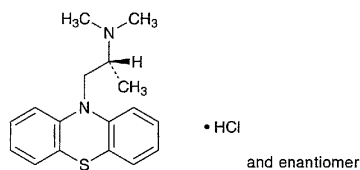
and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS
= 33.442 mg of $C_{18}H_{26}N_2O_4$

Containers and storage Containers—Well-closed containers.

Promethazine Hydrochloride

塩酸プロメタジン



$C_{17}H_{20}N_2S \cdot HCl$: 320.88

N,N-Dimethyl-*N*-[(*RS*)-1-methyl-2-(phenothiazin-10-yl)-ethyl]amine monohydrochloride [58-33-3]

Promethazine Hydrochloride, when dried, contains not less than 98.0% of $C_{17}H_{20}N_2S \cdot HCl$.

Description Promethazine Hydrochloride occurs as a white to light yellow powder.

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

It is gradually colored by light.

A solution of Promethazine Hydrochloride (1 in 25) shows optical rotation.

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

Identification (1) Determine the absorption spectrum of a solution of Promethazine 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 Promethazine 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 0.5 g of Promethazine Hydrochloride in 5 mL of water, add 2 mL of ammonia TS, and filter. To 5 mL of the filtrate add dilute nitric acid to make acidic: the solution responds to the Qualitative Tests (2) for chloride.

pH The pH of a solution of Promethazine Hydrochloride (1 in 10) is between 4.0 and 5.5.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Promethazine Hydrochloride in 10 mL of water, protecting from direct sunlight: the solution is clear and colorless.

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

(3) Related substances—Perform the test under the pro-

tection from sunlight. Dissolve 0.10 g of Promethazine Hydrochloride in exactly 5 mL of ethanol (95), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add ethanol (95) to make exactly 200 mL, and use this solution as the standard solution (1). Separately, dissolve 0.020 g of isopromethazine hydrochloride for thin-layer chromatography in ethanol (95) to make exactly 100 mL, and use this solution as the standard solution (2). 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 solutions (1) and (2) on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of methanol and diethylamine (19:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots from the sample solution corresponding to the spots from the standard solution (2) are not more intense than the spot from the standard solution (2), and any spot other than the principal spot from the sample solution is not more intense than the spot from the standard solution (1).

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

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

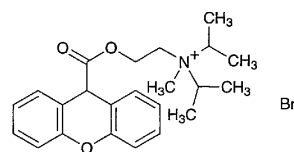
Assay Weigh accurately about 0.5 g of Promethazine Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 32.089 mg of $C_{17}H_{20}N_2S \cdot HCl$

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

Propranolol Bromide

臭化プロパンテリン



$C_{23}H_{30}BrNO_3$: 448.39

N,N-Diisopropyl-*N*-methyl-*N*-[2-(xanthen-9-yl)carbonyloxy]ethyl]ammonium bromide [50-34-0]

Propranolol Bromide, when dried, contains not less than 98.0% and not more than 102.0% of $C_{23}H_{30}BrNO_3$.

Description Propranolol Bromide occurs as a white to yellowish white, crystalline powder. It is odorless and has a very bitter taste.

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

The pH of a solution of Propranolol Hydrochloride (1 in 50) is between 5.0 and 6.0.

Melting point: about 161°C (with decomposition, after drying).

Identification (1) To 5 mL of a solution of Propranolol Hydrochloride (1 in 20) add 10 mL of sodium hydroxide TS, heat to boil for 2 minutes. Cool to 60°C, and add 5 mL of dilute hydrochloric acid. After cooling, collect the precipitates, and wash with water. Recrystallize from dilute ethanol, and dry at 105°C for 1 hour: the crystals melt between 217°C and 222°C.

(2) Dissolve 0.01 g of the crystals obtained in (1) in 5 mL of sulfuric acid: a vivid yellow to yellow-red color develops.

(3) To 5 mL of a solution of Propranolol Hydrochloride (1 in 10) add 2 mL of dilute nitric acid: this solution responds to the Qualitative Tests (1) for bromide.

Purity Xanthene-9-carboxylic acid and xanthone—Dissolve 0.010 g of Propranolol Hydrochloride in exactly 2 mL of chloroform, and use this solution as the sample solution. Separately, dissolve 1.0 mg of xanthene-9-carboxylic acid and 1.0 mg of xanthone in exactly 40 mL of chloroform, and use this solution as the standard solution. Perform the test immediately with these solutions as directed under the Thin-layer Chromatography. Spot 25 µL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography, and air-dry the plate for 10 minutes. Develop the plate with a mixture of 1,2-dichloroethane, methanol, water and formic acid (56:24:1:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light: the spots from the sample solution corresponding to the spots from the standard solution are not more intense than those from the standard solution.

Loss on drying Not more than 0.5% (2 g, 105°C, 4 hours).

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

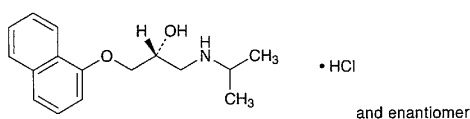
Assay Weigh accurately about 1 g of Propranolol Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 44.84 g of C₂₃H₃₀BrNO₃

Containers and storage Containers—Well-closed containers.

Propranolol Hydrochloride

塩酸プロプラノロール



C₁₆H₂₁NO₂.HCl: 295.80

(*RS*)-1-Isopropylamino-3-(naphthalen-1-yloxy)propan-2-ol monohydrochloride [318-98-9]

Propranolol Hydrochloride, when dried, contains not less than 99.0% of C₁₆H₂₁NO₂.HCl.

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

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

The pH of a solution of Propranolol Hydrochloride (1 in 10) is between 5.0 and 6.0.

It is colored by light.

Identification (1) Dissolve 0.1 g of Propranolol Hydrochloride in 5 mL of water, and add 5 drops of Reinecke salt TS: a light red precipitate is produced.

(2) Dissolve 1 g of Propranolol Hydrochloride in 30 mL of water. Add 5 mL of sodium hydroxide TS, and extract with two 25-mL portions of diethyl ether. Evaporate the combined diethyl ether extract on a water bath, and dry the residue at 50°C in vacuum for 1 hour: the residue melts between 91°C and 95°C.

(3) Determine the absorption spectrum of a solution of Propranolol Hydrochloride in methanol (1 in 50,000) 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.

(4) A solution of Propranolol Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

Melting point 163 – 166°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Propranolol Hydrochloride in 20 mL of water: the solution is clear and colorless.

(2) Sulfate—Perform the test using 2.0 g of Propranolol Hydrochloride. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.010%).

(3) Heavy metals—Proceed with 1.0 g of Propranolol 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).

(4) Arsenic—Prepare the test solution with 1.0 g of Propranolol Hydrochloride according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—To 0.10 g of Propranolol Hydrochloride add 10 mL of chloroform, dissolve by warming, if necessary, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add chloroform to make exactly 100 mL. Pipet 5 mL of this solution, add chloroform 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 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 a mixture of 1,2-dichloroethane, methanol, water and formic acid (56:24:1:1) 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 0.5% (1 g, 105°C, 4 hours).

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