

The pH of a solution of Propantheline Bromide (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 Propantheline Bromide (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 Propantheline Bromide (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 Propantheline Bromide 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).

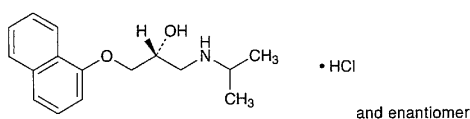
**Assay** Weigh accurately about 1 g of Propantheline Bromide, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 44.84 g of C<sub>23</sub>H<sub>30</sub>BrNO<sub>3</sub>

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

## Propranolol Hydrochloride

塩酸プロプラノロール



C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub>.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 C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub>.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).

**Assay** Weigh accurately about 0.5 g of Propranolol Hydrochloride, previously dried, dissolve in 20 mL of acetic acid (100), add 30 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.

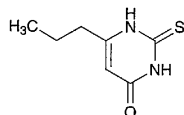
Each mL of 0.1 mol/L perchloric acid VS  
= 29.581 mg of  $C_{16}H_{21}NO_2 \cdot HCl$

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

Storage—Light-resistant.

## Propylthiouracil

プロピルチオウラシル



$C_7H_{10}N_2OS$ : 170.23  
2,3-Dihydro-6-propyl-2-thioxopyrimidin-4(1*H*)-one  
[51-52-5]

Propylthiouracil, when dried, contains not less than 98.0% of  $C_7H_{10}N_2OS$ .

**Description** Propylthiouracil occurs as a white powder. It is odorless, and has a bitter taste.

It is sparingly soluble in ethanol (95), and very slightly soluble in water and in diethyl ether.

It dissolves in sodium hydroxide TS and in ammonia TS.

**Identification (1)** Shake well 0.02 g of Propylthiouracil with 7 mL of bromine TS for 1 minute, and heat until the color of bromine TS disappears. Cool, filter, and add 10 mL of barium hydroxide TS to the filtrate: a white precipitate is produced. The color of the precipitate does not turn purple within 1 minute.

**(2)** To 5 mL of a hot saturated solution of Propylthiouracil add 2 mL of a solution of sodium pentacyanoammine ferroate (II) *n*-hydrate (1 in 100): a green color develops.

**Melting point** 218 – 221°C

**Purity (1)** Sulfate—Triturate Propylthiouracil finely in a mortar. To 0.75 g of the powder add 25 mL of water, heat for 10 minutes on a water bath, cool, filter, and wash the residue with water until the volume of the filtrate becomes 30 mL. To 10 mL of the filtrate add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.077%).

**(2)** Thiourea—Dissolve 0.30 g of Propylthiouracil in 50 mL of water by heating under a reflux condenser for 5 minutes, cool, and filter. To 10 mL of the filtrate add 3 mL of ammonia TS, shake well, and add 2 mL of silver nitrate TS: the solution has no more color than the following control solution.

Control solution: Weigh exactly 0.060 g of thiourea, and dissolve in water to make exactly 100 mL. Pipet 1 mL of this solution, add water to make exactly 100 mL, and proceed with 10 mL of this solution in the same manner.

**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 0.3 g of Propylthiouracil, previously dried, and add 30 mL of water. Add 30 mL of 0.1 mol/L sodium hydroxide VS from a burette, heat to boil, and dissolve by stirring. Wash down the solid adhering to the wall of the flask with a small amount of water, and add 50 mL of 0.1 mol/L silver nitrate VS with stirring. Boil gently for 5 minutes, add 1 to 2 mL of bromothymol blue TS, and titrate with 0.1 mol/L sodium hydroxide VS until a persistent blue-green color develops. Determine the total volume of 0.1 mol/L sodium hydroxide VS consumed.

Each mL of 0.1 mol/L sodium hydroxide VS  
= 8.512 mg of  $C_7H_{10}N_2OS$

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

Storage—Light-resistant.

## Propylthiouracil Tablets

プロピルチオウラシル錠

Propylthiouracil Tablets contain not less than 93% and not more than 107% of the labeled amount of propylthiouracil ( $C_7H_{10}N_2OS$ : 170.23).

**Method of preparation** Prepare as directed under Tablets, with Propylthiouracil.

**Identification** To a quantity of powdered Propylthiouracil Tablets, equivalent to 0.3 g of Propylthiouracil according to the labeled amount, add 5 mL of ammonia TS, allow to stand for 5 minutes with occasional shaking, add 10 mL of water, and centrifuge. To the supernatant liquid add acetic acid (31), collect the precipitate produced, recrystallize from water, and dry at 105°C for 1 hour: it melts between 218°C and 221°C. Proceed with the residue as directed in the Identification under Propylthiouracil.

**Dissolution test** Perform the test with 1 tablet of Propylthiouracil Tablets at 75 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of diluted phosphate buffer solution, pH 6.8, (1 in 2) as the test solution. Take 20 mL or more of the dissolved solution 30 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.8 μm. Discard the first 10 mL of the filtrate, and use the subsequent as the sample solution. Separately, weigh accurately about 0.05 g of propylthiouracil for assay, previously dried at 105°C for 3 hours, dissolve in diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 1000 mL, and use this solution as the standard solution. Determine the absorbances,  $A_T$  and  $A_S$ , of the sample solution and the standard solution at 274 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Propylthiouracil Tablets in 30