

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.

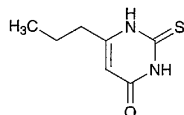
Each mL of 0.1 mol/L perchloric acid VS
= 29.581 mg of $C_{16}H_{21}NO_2 \cdot HCl$

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

minutes should be not less than 80%.

Dissolution rate (%) with respect to the labeled amount of propylthiouracil ($C_7H_{10}N_2OS$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{1}{C} \times 90$$

W_S : Amount (mg) of propylthiouracil for assay.

C : Labeled amount (mg) of propylthiouracil ($C_7H_{10}N_2OS$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Propylthiouracil Tablets. Weigh accurately a portion of the powder, equivalent to about 0.3 g of propylthiouracil ($C_7H_{10}N_2OS$), transfer to a Soxhlet extractor, and extract with 100 mL of acetone for 4 hours. Evaporate the acetone extract by warming on a water bath to dryness. To the residue add 30 mL of water, and proceed as directed in the Assay under Propylthiouracil.

$$\begin{aligned} \text{Each mL of 0.1 mol/L sodium hydroxide VS} \\ = 8.512 \text{ mg of } C_7H_{10}N_2OS \end{aligned}$$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Protamine Sulfate

硫酸プロタミン

Protamine Sulfate is the sulfate of protamine prepared from the mature spermary of fish belonging to the family *Salmonidae* and others.

Description Protamine Sulfate occurs as a white to light grayish yellow powder.

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

The pH of a solution of Protamine Sulfate (1 in 100) is between 4.0 and 7.0.

Identification (1) Dissolve 1 mg of Protamine Sulfate in 2 mL of water, add 5 drops of a solution prepared by dissolving 0.1 g of 1-naphthol in 100 mL of diluted ethanol (99.5) (7 in 10) and 5 drops of sodium hypochlorite TS, then add sodium hydroxide TS until the solution becomes alkaline: a vivid red color develops.

(2) Dissolve 5 mg of Protamine Sulfate in 1 mL of water by warming, add 1 drop of a solution of sodium hydroxide (1 in 10) and 2 drops of copper (II) sulfate TS: a red-purple color develops.

(3) An aqueous solution of Protamine Sulfate (1 in 20) responds to the Qualitative Tests for sulfate.

Purity (1) Clarity and color of solution—Dissolve 0.10 g of Protamine Sulfate in 10 mL of water: the solution is clear and colorless.

(2) Nitrogen—Weigh accurately about 0.01 g of Protamine Sulfate, previously dried at 105°C to constant mass, and perform the test as directed under the Nitrogen Determination: not more than 0.255 mg of nitrogen (N: 14.01) is found for each mg of Protamine Sulfate.

Potency as antiheparin (i) Sample solution—Dissolve

20.0 mg of Protamine Sulfate in isotonic sodium chloride solution to make exactly 20 mL.

(ii) Heparin sodium standard solution—Dissolve 10.0 mg of Heparin Sodium Reference Standard in isotonic sodium chloride solution to make a standard solution containing exactly 0.7 mg per ml.

(iii) Sulfated whole blood—Place 250 mL of fresh bovine blood in a wide-mouthed stoppered polyethylene bottle containing 50 mL of a solution of sodium sulfate decahydrate (9 in 50), and store between 1°C and 4°C. Remove any clotted substance before use.

(iv) Thrombokinase extract—To 1.5 g of acetone-dried cattle brain add 60 mL of water, extract at 50°C for 10 to 15 minutes, and centrifuge for 2 minutes at 1500 revolutions per minute. To the supernatant add cresol to make 0.3% as a preservative, and store between 1°C and 4°C. The potency of this solution will be maintained for several days.

(v) Procedure—To one of 10 clean, glass-stoppered test tubes, 13 mm in inside diameter and 150 mm in length, transfer 1.30 mL of isotonic sodium chloride solution and 0.20 mL of thrombokinase extract, then add exactly 1 mL of sulfated whole blood, stopper the tube, mix the contents by inverting once, and note the time on a stop watch. When the solid clot which is formed at the bottom of the tube does not fall on inverting the tube, designate this time as the control clotting time. Adjust appropriately the volume of thrombokinase extract so that the control clotting time is between 2 and 3 minutes. To the nine remaining tubes add 0.50 mL of the sample solution and the same volume of thrombokinase extract as was used in the previous measurement of the control clotting time, pipet into the tubes 0.43 mL, 0.45 mL, 0.47 mL, 0.49 mL, 0.50 mL, 0.51 mL, 0.53 mL, 0.55 mL and 0.57 mL of the heparin sodium standard solution, respectively, and make the volume in each tube up to 1.50 mL by adding isotonic sodium chloride solution. Add finally 1.0 mL of sulfated whole blood, stopper, mix the contents by inverting once, and determine the clotting times with a stop watch. The estimated ratio, v/V , is between 0.85 and 1.15, where v is the volume of the heparin sodium standard solution and V is the volume of the sample solution in that tube in which the clotting time is most nearly the same as the control clotting time.

Containers and storage Containers—Tight containers.

Protamine Sulfate Injection

硫酸プロタミン注射液

Protamine Sulfate Injection is an aqueous solution for injection.

The amount of Protamine Sulfate should be labeled.

Method of preparation Prepare as directed under Injections, with Protamine Sulfate.

Description Protamine Sulfate Injection is a colorless liquid. It is odorless or has the odor of preservatives.

Identification (1) Dilute a volume of Protamine Sulfate Injection, equivalent to 1 mg of Protamine Sulfate according to the labeled amount, with water to make 2 mL, and