

(vi) Procedure: In 4 clean 13 × 150 mm glass-stoppered test tubes, place 1 mL each of S_H , S_L , T_H and T_L separately. To each tube add 0.20 mL of the thrombokinase extract: the amount of the thrombokinase extract should be controlled so that the longest coagulation time is 9 to 12 minutes. Then, to each tube add 1 mL of the sulfated whole blood, stopper each tube, mix by inverting the tubes gently, and observe each tube by gentle tilting at 15-second intervals. The coagulation time is the time required for the formation of a solid clot on the bottom of the tube which does not come down when inverting the tube. If a tube has been inverted before the coagulation is completed, stop the test, and try the test again. Repeat the complete test more than four times.

(vii) Method of calculation: Designate the logarithms of the coagulation time for each dose groups of S_H , S_L , T_H and T_L as y_1 , y_2 , y_3 and y_4 , respectively. Sum up y_1 , y_2 , y_3 and y_4 for each test and designate them as Y_1 , Y_2 , Y_3 and Y_4 , respectively.

$$\begin{aligned} & \text{Units per mg of Heparin Sodium} \\ &= \text{antilog } M \times (\text{units per mL of the high-dose} \\ & \quad \text{standard solution}) \\ & \quad \times \frac{b}{a} \end{aligned}$$

$$M = \frac{IY_a}{Y_b}$$

$$I = \log \frac{S_H}{S_L} = \log \frac{T_H}{T_L}$$

$$Y_a = -Y_1 - Y_2 + Y_3 + Y_4$$

$$Y_b = Y_1 - Y_2 + Y_3 - Y_4$$

a : Mass (mg) of Heparin Sodium sample.

b : Total volume (mL) of the high-dose sample solution prepared by dissolving Heparin Sodium in water.

Compute L ($P = 0.95$) by using the following equation: L is not more than 0.15. If L exceeds 0.15, increase the number of the tests until L reaches 0.15 or less.

$$L = 2\sqrt{(C-1)(CM^2 + P)}$$

$$C = \frac{Y_b^2}{Y_b^2 - 4fs^2t^2}$$

f : The number of the runs.

$$s^2 = \frac{\Sigma y^2 - \frac{Y}{f} - \frac{Y'}{4} + \frac{Y''}{4f}}{n}$$

Σy^2 : The sum of the squares of each y_1 , y_2 , y_3 and y_4 in each test.

$$Y = Y_1^2 + Y_2^2 + Y_3^2 + Y_4^2$$

Y' : The sum of the squares of the sum of y_1 , y_2 , y_3 and y_4 in each test, for the whole run.

$$Y'' = (Y_1 + Y_2 + Y_3 + Y_4)^2$$

$$n = 3(f-1)$$

t^2 : Value shown in the table in the Assay under Insulin Injection against n for which s^2 is calculated.

Containers and storage Containers—Tight containers.

Heparin Sodium Injection

ヘパリンナトリウム注射液

Heparin Sodium Injection is an aqueous solution for injection. It contains not less than 90% and not more than 110% of the labeled heparin Units.

Label the name of organ used as the starting material of Heparin Sodium supplied for preparing Heparin Sodium Injection.

Method of preparation Dissolve Heparin Sodium in Isotonic Sodium Chloride Solution and prepare as directed under Injections.

Description Heparin Sodium Injection is a clear, colorless to light yellow liquid.

pH 5.5 – 8.0

Purity (1) Barium—Measure exactly a portion of Heparin Sodium Injection, equivalent to 3000 Units of Heparin Sodium according to the labeled Unit. Add water to make 3.0 mL and use this solution as the sample solution. To 1.0 mL of the sample solution add 3 drops of dilute sulfuric acid, and allow to stand for 10 minutes: no turbidity is produced.

(2) Protein—Proceed as directed in the Purity (4) under Heparin Sodium.

Bacterial endotoxins Less than 0.0030 EU/unit.

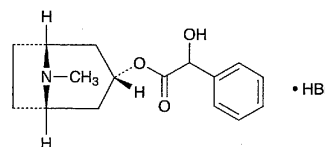
Assay Proceed as directed in the Assay under Heparin Sodium. However, the sample solutions indicated in (ii) are as follows.

Sample solution: Measure exactly adequate portions of Heparin Sodium Injection according to the labeled Units, dilute them with water so as to obtain two solutions containing exactly 2.00 and 1.60 Units per ml, and use them as high-dose (T_H) and low-dose (T_L) sample solutions, respectively.

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

Homatropine Hydrobromide

臭化水素酸ホマトロピン



$C_{16}H_{21}NO_3 \cdot HBr$: 356.25

(1*R*,3*r*,5*S*)-8-Methyl-8-azabicyclo[3.2.1]oct-3-yl [(*RS*)-2-hydroxy-2-phenyl]acetate monohydrobromide [51-56-9]

Homatropine Hydrobromide contains not less than 99.0% of $C_{16}H_{21}NO_3 \cdot HBr$, calculated on the dried basis.

Description Homatropine Hydrobromide occurs as white

crystals or crystalline powder. It is odorless.

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

It is affected by light.

Melting point: about 214°C (with decomposition).

Identification (1) To 5 mL of a solution of Homatropine Hydrobromide (1 in 20) add 2 to 3 drops of iodine TS: a brown precipitate is produced.

(2) Dissolve 0.05 g of Homatropine Hydrobromide in 5 mL of water, and add 3 mL of 2,4,6-trinitrophenol TS: a yellow precipitate is produced. Filter the precipitate, wash with five 10-mL portions of water, and dry at 105°C for 2 hours: it melts between 184°C and 187°C.

(3) A solution of Homatropine Hydrobromide (1 in 20) responds to the Qualitative Tests for bromide.

Purity (1) Acid—Dissolve 1.0 g of Homatropine Hydrobromide in 20 mL of water, and add 0.40 mL of 0.01 mol/L sodium hydroxide VS and 1 drop of methyl red-methylene blue TS: a green color develops.

(2) Atropine, hyoscyamine and scopolamine—To 0.010 g of Homatropine Hydrobromide add 5 drops of nitric acid, evaporate on a water bath to dryness, and cool. Dissolve the residue in 1 mL of *N,N*-dimethylformamide, and add 5 to 6 drops of tetraethylammonium hydroxide TS: no red-purple color is produced.

(3) Other alkaloids—Dissolve 0.15 g of Homatropine Hydrobromide in 3 mL of water, and use this solution as the sample solution.

(i) To 1 mL of the sample solution add 2 to 3 drops of tannic acid TS: no precipitate is produced.

(ii) To 1 mL of the sample solution add 2 to 3 drops each of dilute hydrochloric acid and platinum chloride TS: no precipitate is produced.

Loss on drying Not more than 1.5% (0.5 g, 105°C, 2 hours).

Residue on ignition Not more than 0.25% (0.2 g).

Assay Dissolve by warming about 0.4 g of Homatropine Hydrobromide in 60 mL of a mixture of acetic anhydride and acetic acid (100) (7:3). Cool, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination.

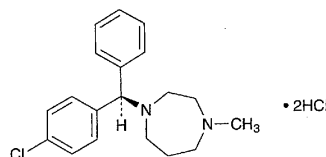
Each mL of 0.1 mol/L perchloric acid VS
= 35.626 mg of $C_{16}H_{21}NO_3 \cdot HBr$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Homochlorcyclizine Hydrochloride

塩酸ホモクロルシクリジン



and enantiomer

$C_{19}H_{23}ClN_2 \cdot 2HCl$: 387.77

1-[(*RS*)-(4-Chlorophenyl)(phenyl)methyl]-4-methyl-1,4-diazepine dihydrochloride [1982-36-1]

Homochlorcyclizine Hydrochloride, when dried, contains not less than 98.0% of $C_{19}H_{23}ClN_2 \cdot 2HCl$.

Description Homochlorcyclizine Hydrochloride occurs as white to pale brown crystals or powder. It is odorless.

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

It is hygroscopic.

Melting point: about 227°C (with decomposition).

Identification (1) To 5 mL of a solution of Homochlorcyclizine Hydrochloride (1 in 100) add 5 drops of Reinecke salt TS: a light red precipitate is produced.

(2) Determine the absorption spectrum of a solution of Homochlorcyclizine Hydrochloride in 0.1 mol/L hydrochloric acid TS (1 in 4000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Homochlorcyclizine 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 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) A solution of Homochlorcyclizine Hydrochloride (1 in 100) responds to the Qualitative Tests for chloride.

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

(2) Arsenic—Take 1.0 g of Homochlorcyclizine Hydrochloride, add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10), ignite the ethanol, and heat gradually to incinerate at 800°C. After cooling, add 3 mL of hydrochloric acid, heat on a water bath to dissolve the residue, use this solution as the test solution, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.20 g of Homochlorcyclizine Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Measure exactly 5 mL of the sample solution, and add methanol to make exactly 100 mL. Measure exactly 5 mL of this solution, add methanol 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. Spot 10 μ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of chloroform, methanol and formic acid (13:5:2) to a distance of about 15 cm, and air-dry the plate. Spray evenly Dragendorff's TS for spraying on the plate: 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 2.0% (1 g, 110°C, 4 hours).