Pipet 1 mL of the sample solution, add diluted ethanol (99.5) (1 in 2) to make exactly 100 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 acetone, toluene, ethanol (99.5) and ammonia water (28) (20:20:3:1) to a distance of about 15 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 365 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 7.0% (1 g, 105°C, 3 hours).

Residue on ignition Not more than 0.20% (1 g).

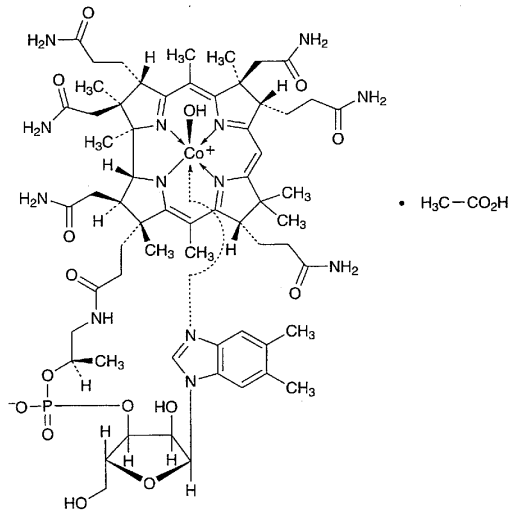
Assay Weigh accurately about 0.5 g of Hydrocotarnine Hydrochloride, previously dried. Dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3) by warming. Cool, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination.

Each mL of 0.1 mol/L perchloric acid VS
= 25.772 mg of $C_{12}H_{15}NO_3.HCl$

Containers and storage Containers—Tight containers.

Hydroxocobalamin Acetate

酢酸ヒドロキソコバラミン



$C_{62}H_{89}CoN_{13}O_{15}P.C_2H_4O_2$: 1406.41
Coα-[α-(5,6-Dimethylbenz-1*H*-imidazol-1-yl)]-*Coβ*-hydroxocobamide monoacetate
[*13422-51-0*, Hydroxocobalamin]

Hydroxocobalamin Acetate contains not less than 95.0% of $C_{62}H_{89}CoN_{13}O_{15}P.C_2H_4O_2$, calculated on the dried basis.

Description Hydroxocobalamin Acetate occurs as dark red crystals or powder. It is odorless.

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

It is hygroscopic.

Identification (1) Determine the absorption spectrum of a solution of Hydroxocobalamin Acetate in acetic acid-sodium acetate buffer solution, pH 4.5 (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.

(2) Mix 1 mg of Hydroxocobalamin Acetate with 0.05 g of potassium hydrogen sulfate, and fuse by igniting. Cool, break up the mass with a glass rod, add 3 mL of water, and dissolve by boiling. Add 1 drop of phenolphthalein TS, and add dropwise sodium hydroxide TS until the solution develops a light red. Then add 0.5 g of sodium acetate trihydrate, 0.5 mL of dilute acetic acid and 0.5 mL of a solution of disodium 1-nitroso-2-naphthol-3,6-disulfonate (1 in 500): a red to orange-red color develops immediately. Then add 0.5 mL of hydrochloric acid, and boil for 1 minute: the red color does not disappear.

(3) Add 0.5 mL of ethanol (99.5) and 1 mL of sulfuric acid to 0.02 g of Hydroxocobalamin Acetate, and heat the mixture: the odor of ethyl acetate is perceptible.

Purity Cyanocobalamin and colored impurities—Dissolve 0.050 g of Hydroxocobalamin Acetate in exactly 5 mL each of acetic acid-sodium acetate buffer solution, pH 5.0, in two tubes. To one tube add 0.15 mL of potassium thiocyanate TS, allow to stand for 30 minutes, and use this solution as the sample solution (1). To the other tube add 0.10 mL of potassium cyanide TS, allow to stand for 30 minutes, and use this solution as the sample solution (2). Separately, dissolve 3.0 mg of Cyanocobalamin Reference Standard in exactly 10 mL of acetic acid-sodium acetate buffer solution, pH 5.0, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Apply 20 μL each of the sample solution and the standard solution 25 mm in length along the starting line, 10 mm apart from each other, on a plate of silica gel for thin-layer chromatography. Develop the plate for 18 hours with 2-butanol saturated with water, while supporting the plate at an angle of about 15° to a horizontal plane, and air-dry the plate: the spot from the sample solution (1) corresponding to that from the standard solution is not more intense than the spot from the standard solution, and the spots other than the principal spot from the sample solution (2) are not more intense than the spot from the standard solution.

Loss on drying Not more than 12% (0.05 g, in vacuum at a pressure not exceeding 0.67 kP, phosphorus (V) oxide, 100°C, 6 hours).

Assay Weigh accurately about 0.02 g of Hydroxocobalamin Acetate, and dissolve in acetic acid-sodium acetate buffer solution, pH 5.0, to make exactly 50 mL. Pipet 2 mL of this solution into a 50-mL volumetric flask, add 1 mL of a solution of potassium cyanide (1 in 1000), and allow to stand for 30 minutes at ordinary temperature. Add acetic acid-sodium acetate buffer solution, pH 5.0, to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.02 g of Cyanocobalamin Reference Standard after determining the loss on drying in the same manner as for Cyanocobalamin, and dissolve in

water to make exactly 50 mL. To 2 mL of this solution, exactly measured, add acetic acid-sodium acetate buffer solution, pH 5.0, to make exactly 50 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 361 nm as directed under the Ultraviolet-visible Spectrophotometry.

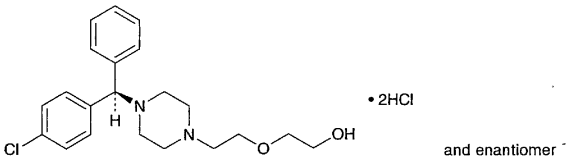
Amount (mg) of $C_{62}H_{89}CoN_{13}O_{15}P.C_2H_4O_2$
= amount (mg) of Cyanocobalamin Reference Standard, calculated on the dried basis

$$\times \frac{A_T}{A_S} \times 1.0377$$

Containers and storage Containers—Tight containers.
Storage—Light-resistant, and in a cold place.

Hydroxyzine Hydrochloride

塩酸ヒドロキシジン



and enantiomer

$C_{21}H_{27}ClN_2O_2.2HCl$: 447.83
2-(2-{4-[(*RS*)-(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)ethanol dihydrochloride [*2192-20-3*]

Hydroxyzine Hydrochloride, when dried, contains not less than 98.5% of $C_{21}H_{27}ClN_2O_2.2HCl$.

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

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

Melting point: about 200°C (with decomposition).

Identification **(1)** To 5 mL of a solution of Hydroxyzine Hydrochloride (1 in 100) add 2 to 3 drops of ammonium thiocyanate-cobaltous nitrate TS: a blue precipitate is formed.

(2) Determine the absorption spectrum of a solution of Hydroxyzine Hydrochloride in methanol (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) A solution of Hydroxyzine Hydrochloride (1 in 10) responds to the Qualitative Tests for chloride.

pH Dissolve 1.0 g of Hydroxyzine Hydrochloride in 20 mL of water: the pH of this solution is between 1.3 and 2.5.

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

(2) Heavy metals—Proceed with 1.0 g of Hydroxyzine 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—Dissolve 0.20 g of Hydroxyzine Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 200 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 for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, ethanol (95) and ammonia solution (28) (150:95:1) to a distance of about 10 cm, and air-dry the plate. Allow the plate to stand in iodine vapor: 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 3.0% (1 g, 105°C, 2 hours).

Residue on ignition Not more than 0.20% (1 g).

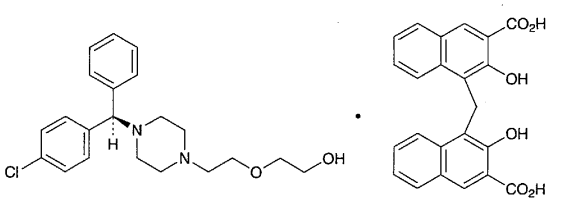
Assay Weigh accurately about 0.1 g of Hydroxyzine Hydrochloride, previously dried, dissolve in 60 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 22.392 mg of $C_{21}H_{27}ClN_2O_2.2HCl$

Containers and storage Containers—Tight containers.

Hydroxyzine Pamoate

パモ酸ヒドロキシジン



and enantiomer

$C_{21}H_{27}ClN_2O_2.C_{23}H_{16}O_6$: 763.27
2-(2-{4-[(*RS*)-(4-Chlorophenyl)phenylmethyl]piperazin-1-yl}ethoxy)ethanol mono[4,4′-methylenebis(3-hydroxy-2-naphthoate)] (1/1) [*10246-75-0*]

Hydroxyzine Pamoate contains not less than 98.0% of $C_{21}H_{27}ClN_2O_2.C_{23}H_{16}O_6$, calculated on the anhydrous basis.

Description Hydroxyzine Pamoate occurs as a light yellow, crystalline powder. It is odorless, and has a slightly bitter taste.

It is freely soluble in *N,N*-dimethylformamide, slightly soluble in acetone, and practically insoluble in water, in methanol, in ethanol (95) and in diethyl ether.

Identification **(1)** To 0.1 g of Hydroxyzine Pamoate add 25 mL of sodium hydroxide TS, and shake well. Extract