Purity Heavy metals—Proceed with 2.0 g of Diethylcarbamazine Citrate according to Method 4, and perform the test. Prepare the control solution with 4.0 mL of Standard Lead Solution (not more than 20 ppm).

Loss on drying Not more than 1.0% (2 g, 105°C, 4 hours).

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

Assay Weigh accurately about 0.75 g of Diethylcarbamazine Citrate, previously dried, dissolve in 50 mL of acetic acid (100) by warming, cool, 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
= 39.142 mg of $C_{10}H_{21}N_3O.C_6H_8O_7$

Containers and storage Containers—Tight containers.

Diethylcarbamazine Citrate Tablets

クエン酸ジエチルカルバマジン錠

Diethylcarbamazine Citrate Tablets contain not less than 95% and not more than 105% of the labeled amount of diethylcarbamazine citrate ($C_{10}H_{21}N_3O.C_6H_8O_7$: 391.42).

Method of preparation Prepare as directed under Tablets, with Diethylcarbamazine Citrate.

Identification **(1)** To a quantity of powdered Diethylcarbamazine Citrate Tablets, equivalent to 0.5 g of Diethylcarbamazine Citrate according to the labeled amount, add 10 mL of water, shake, and filter. Add 10 mL of sodium hydroxide TS to the filtrate, and proceed as directed in the Identification (1) under Diethylcarbamazine Citrate.

(2) To a quantity of powdered Diethylcarbamazine Citrate Tablets, equivalent to 0.8 g of diethycarbamazine citrate according to the labeled amount, add 10 mL of water, shake, centrifuge, and filter the supernatant liquid. To 5 mL of the filtrate add 5 mL of sodium hydroxide TS, and extract with two 20-mL portions of chloroform. Separate the aqueous layer, and neutralize with dilute hydrochloric acid: the solution responds to the Qualitative Tests (2) and (3) for citrate.

Assay Weigh accurately and powder not less than 20 Diethylcarbamazine Citrate Tablets. Weigh accurately a portion of the powder, equivalent to about 0.05 g of diethylcarbamazine citrate ($C_{10}H_{21}N_3O.C_6H_8O_7$), add 10 mL of water, shake well, add 5 mL of sodium hydroxide TS, then add exactly 20 mL of the internal standard solution, and shake vigorously for 10 minutes. Centrifuge, discard the aqueous layer, and use the chloroform layer as the sample solution. Separately, weigh accurately about 0.05 g of Diethylcarbamazine Citrate Reference Standard, previously dried at 105°C for 4 hours, dissolve in 10 mL of water, add 5 mL of sodium hydroxide TS, proceed in the same manner as the preparation of the sample solution, and use the chloroform layer as the standard solution. Perform the test with 2 μL of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of diethycarbamazine to that of the internal standard, respectively.

Amount (mg) of diethylcarbamazine citrate ($C_{10}H_{21}N_3O.C_6H_8O_7$)
= amount (mg) of Diethycarbamazine Citrate Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of *n*-octadecane in chloroform (1 in 1250).

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A glass tube 3 mm in inside diameter and 1 to 2 m in length, having methylphenyldimethyl silicone polymer coated at the ratio of 3% on silanized siliceous earth for gas chromatography (180 to 250 μm in particle diameter).

Column temperature: A constant temperature of about 145°C.

Carrier gas: Nitrogen.

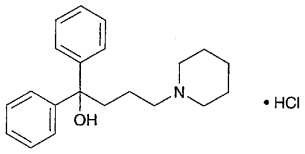
Flow rate: Adjust the flow rate so that the retention time of the internal standard is 8 to 11 minutes.

Selection of column: Proceed with 2 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of diethylcarbamazine and the internal standard in this order with the resolution between these peaks being not less than 5.

Containers and storage Containers—Well-closed containers.

Difenidol Hydrochloride

塩酸ジフェニドール



$C_{21}H_{27}NO.HCl$: 345.91
1,1-Diphenyl-4-piperidin-1-ylbutan-1-ol monohydrochloride [*3254-89-5*]

Difenidol Hydrochloride, when dried, contains not less than 98.5% of $C_{21}H_{27}NO.HCl$.

Description Difenidol Hydrochloride occurs as white crystals or crystalline powder. It is odorless.

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

Melting point: about 217°C (with decomposition).

Identification **(1)** Dissolve 0.01 g of Difenidol Hydrochloride in 1 mL of sulfuric acid: an orange-red color develops. To this solution add carefully 3 drops of water: the solution becomes yellowish brown, and colorless on the addition of 10 mL of water.

(2) To 5 mL of a solution of Difenidol Hydrochloride (1 in 100) add 2 mL of Reinecke salt TS: a light red precipitate

is formed.

(3) To 10 mL of a solution of Difenidol Hydrochloride (1 in 100) add 2 mL of sodium hydroxide TS, and extract with two 15-mL portions of chloroform. Combine the extracts, wash with three 10-mL portions of water, evaporate the chloroform on a water bath, and dry the residue in a desiccator (in vacuum, silica gel, 55°C) for 5 hours: the residue melts between 103°C and 106°C.

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

pH Dissolve 1.0 g of Difenidol Hydrochloride in 100 mL of freshly boiled and cooled water: the pH of this solution is between 4.7 and 6.5.

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

(2) Heavy metals—Proceed with 1.0 g of Difenidol 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) Arsenic—Prepare the test solution with 2.0 g of Difenidol Hydrochloride according to Method 3, and perform the test using Apparatus B (not more than 1 ppm).

(4) Related substances—Dissolve 0.10 g of Difenidol Hydrochloride in methanol to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 0.010 g of 1,1-diphenyl-4-piperidino-1-butene hydrochloride for thin-layer chromatography in methanol to make exactly 20 mL, pipet 1 mL of this solution, add methanol 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 5 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 toluene, methanol and acetic acid (100) (10:2:1) to a distance of about 15 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, in vacuum, silica gel, 5 hours).

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

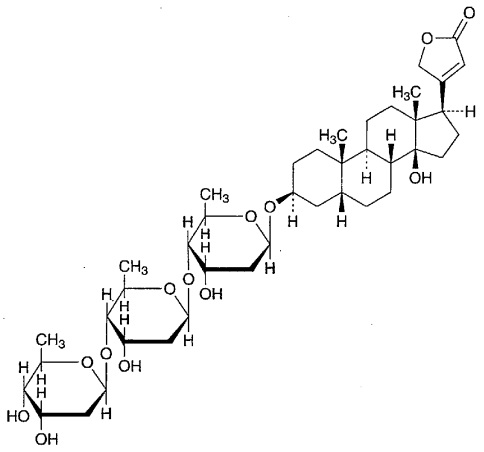
Assay Weigh accurately about 0.35 g of Difenidol Hydrochloride, previously dried, dissolve in 30 mL of acetic acid (100) by warming if necessary, cool, add 30 mL of acetic anhydride, and titrate with 0.05 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L perchloric acid VS
= 17.296 mg of $C_{21}H_{27}NO.HCl$

Containers and storage Containers—Well-closed containers.

Digitoxin

ジギトキシン



$C_{41}H_{64}O_{13}$: 764.94
3β-[*O*-2,6-Dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyloxy]-14-hydroxy-5β,14β-card-20(22)-enolide [*71-63-6*]

Digitoxin, when dried, contains not less than 90.0% of $C_{41}H_{64}O_{13}$.

Description Digitoxin occurs as a white to light yellowish white, crystalline powder. It is odorless.

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

Identification **(1)** Transfer 1 mg of Digitoxin to a small test tube about 10 mm in inside diameter, dissolve in 1 mL of a solution of iron (III) chloride hexahydrate in acetic acid (100) (1 in 10,000), and underlay gently with 1 mL of sulfuric acid: at the zone of contact of the two liquids a brown ring free from a reddish color is produced, and the color of the upper layer near the contact zone changes to green through purple. Finally the color of the entire acetic acid layer changes to green through deep blue.

(2) To 2 mg of Digitoxin add 25 mL of a freshly prepared solution of 1,3-dinitrobenzene in ethanol (95) (1 in 100), and dissolve by shaking. Take 2 mL of this solution, add 2 mL of a solution of tetramethylammonium hydroxide in ethanol (95) (1 in 200), and mix: a red-purple color develops slowly, and then fades.

(3) Dissolve 1 mg each of Digitoxin and Digitoxin Reference Standard in a mixture of chloroform and ethanol (95) (1:1) to make 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 20 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 dichloromethane, methanol and water (84:15:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly dilute sulfuric acid upon the plate, and heat at 110°C for 10 minutes: the spot from the sample solution shows the same *Rf* value as the spot from the standard solution.