Identification (1) Determine the absorption spectrum of a solution of Distigmine Bromide (1 in 25,000) 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) Determine the infrared absorption spectrum of Distigmine Bromide as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) To 5 mL of a solution of Distigmine Bromide (1 in 10) add 2 mL of dilute nitric acid: the solution responds to the Qualitative Tests (1) for bromide.

Purity (1) Clarity and color of solution—Dissolve 0.25 g of Distigmine Bromide in 5 mL of water: the solution is clear and colorless.

(2) Sulfate—Perform the test with 0.40 g of Distigmine Bromide. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(3) Heavy metals—Proceed with 2.0 g of Distigmine Bromide according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Related substances—Dissolve 0.040 g of Distigmine Bromide in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of this 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 10 μL each of the sample solution and the standard solution on a plate of cellulose with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water, ethanol (99.5) and acetic acid (100) (8:3:2:1) to a distance of about 13 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. 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.

Water Not more than 1.0% (1 g, direct titration).

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

Assay Weigh accurately about 0.4 g of Distigmine Bromide, dissolve in 60 mL of a mixture of acetic anhydride and acetic acid (100) (8:1), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration with platinum electrode). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 28.816 mg of $C_{22}H_{32}Br_2N_4O_4$

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

Distigmine Bromide Tablets

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Distigmine Bromide Tablets contain not less than 95% and not more than 105% of the labeled amount of distigmine bromide ($C_{22}H_{32}Br_2N_4O_4$: 576.32).

Method of preparation Prepare as directed under Tablets, with Distigmine Bromide.

Identification Determine the absorption spectrum of the solution obtained in the Assay, as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 268 nm and 272 nm, and a minimum between 239 nm and 243 nm.

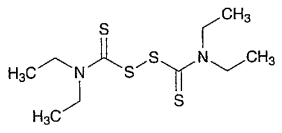
Assay Weigh accurately and powder not less than 20 tablets of Distigmine Bromide Tablets. Weigh accurately a portion of the powder, equivalent to about 0.015 g of Distigmine Bromide ($C_{22}H_{32}Br_2N_4O_4$), add 30 mL of 0.1 mol/L hydrochloric acid TS, shake for 1 hour, add 0.1 mol/L hydrochloric acid TS to make exactly 50 mL, and filter. Discard the first 20 mL of the filtrate, pipet 10 mL of the subsequent filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.03 g of distigmine bromide for assay (previously determine the water), and dissolve in 0.1 mol/L hydrochloric acid TS to make exactly 100 mL. Pipet 10 mL of this solution, add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances of the sample solution and the standard solution, A_{T2} and A_{S2}, at 270 nm and, A_{T1} and A_{S1}, at 241 nm as directed under the Ultraviolet-visible Spectrophotometry, respectively.

Amount (mg) of distigmine bromide ($C_{22}H_{32}Br_2N_4O_4$)
= amount (mg) of distigmine bromide for assay, calculated on the anhydrous basis
$\times \frac{A_{T2} - A_{T1}}{A_{S2} - A_{S1}} \times \frac{1}{2}$

Containers and storage Containers—Tight containers.

Disulfiram

ジスルフィラム



$C_{10}H_{20}N_2S_4$: 296.54
Tetraethylthiuram disulfide [*97-77-8*]

Disulfiram, when dried, contains not less than 99.0% of $C_{10}H_{20}N_2S_4$.

Description Disulfiram occurs as white to yellowish white

crystals or crystalline powder.

It is freely soluble in acetone and in toluene, sparingly soluble in methanol and in ethanol (95), and practically insoluble in water.

Identification (1) Determine the absorption spectrum of a solution of Disulfiram in ethanol (95) (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.

(2) Determine the infrared absorption spectrum of Disulfiram, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

Melting point 70 - 73°C

Purity (1) Heavy metals—Proceed with 2.0 g of Disulfiram according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Disulfiram according to Method 4, and perform the test using Apparatus B (not more than 2 ppm).

(3) Diethyldithiocarbamic acid—Dissolve 0.10 g of Disulfiram in 10 mL of toluene, and shake with 10 mL of diluted sodium carbonate TS (1 in 20). Discard the toluene layer, wash the water layer with 10 mL of toluene, shake with 5 drops of a solution of cupric sulfate (1 in 250) and 2 mL of toluene, and allow to stand: no light yellow color develops in the toluene layer.

(4) Related substances—Dissolve 0.050 g of Disulfiram in 40 mL of methanol, add water to make 50 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: the total area of the peaks other than the peak of disulfiram from the sample solution is not larger than the peak area of disulfiram from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 210 nm).

Column: A stainless steel column about 5 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of methanol and water (7:3).

Flow rate: Adjust the flow rate so that the retention time of disulfiram is about 8 minutes.

Selection of column: Dissolve 0.050 g of Disulfiram and 0.050 g of benzophenone in 40 mL of methanol, and add water to make 50 mL. To 1 mL of this solution add the mobile phase to make 200 mL. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of benzophenone and disulfiram in this order with the resolution between these peaks being not less than 4.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of disulfiram obtained from 10 μL of the standard solution is 15 - 30 mm.

Time span of measurement: About 3.5 times of the retention time of disulfiram.

Loss on drying Not more than 0.20% (2 g, silica gel, 24 hours).

Residue on ignition Not more than 0.10% (2 g).

Assay Weigh accurately about 0.2 g of Disulfiram, previously dried, in an iodine bottle, dissolve in 20 mL of acetone, add 1.5 mL of water and 1.0 g of potassium iodide, and dissolve by shaking thoroughly. To this solution add 3.0 mL of hydrochloric acid, stopper the bottle tightly, shake, and allow to stand in a dark place for 3 minutes. Add 70 mL of water, and titrate with 0.1 mol/L sodium thiosulfate VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L sodium thiosulfate VS
= 14.827 mg of $C_{10}H_{20}N_2S_4$

Containers and storage Containers—Tight containers.

Dobutamine Hydrochloride

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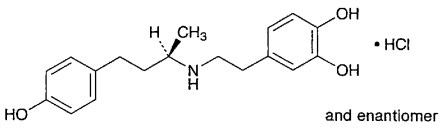

$C_{18}H_{23}NO_3.HCl$: 337.84

4-{2-[(*RS*)-3-(4-Hydroxyphenyl)-1-methylpropylamino]-ethyl}benzene-1,2-diol monohydrochloride [*49745-95-1*]

Dobutamine Hydrochloride, when dried, contains not less than 98.0% of $C_{18}H_{23}NO_3.HCl$.

Description Dobutamine Hydrochloride occurs as white to very pale orange crystalline powder or grains.

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

A solution of Dobutamine Hydrochloride (1 in 100) shows no optical rotation.

Identification (1) Determine the infrared absorption spectra of Dobutamine Hydrochloride, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Dobutamine Hydrochloride Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(2) A solution of Dobutamine Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

pH Dissolve 1.0 g of Dobutamine Hydrochloride in 100 mL of water: the pH of this solution is between 4.5 and 5.5.

Melting point 188 - 191°C