Dextran Sulfate Sodium Sulfur 18

デキストラン硫酸ナトリウム イオウ 18

Dextran Sulfate Sodium Sulfur 18 is a sodium salt of sulfate ester obtained by sulfation of partial decomposition products of dextran, which is produced by fermentation of sucrose with *Leuconostoc mesenteroides* Van Tieghem (*Lactobacillaceae*).

Description Dextran Sulfate Sodium Sulfur 18 occurs as a white to light yellowish white powder. It is odorless, and has a saline taste.

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

It is hygroscopic.

Identification **(1)** To 10 mL of a solution of toluidine blue (1 in 100,000) add 0.05 mL of a solution of Dextran Sulfate Sodium Sulfur 18 (3 in 50) dropwise: a color of the solution changes from blue to red-purple.

(2) To 1 mL of a solution of Dextran Sulfate Sodium Sulfur 18 (1 in 1500) add 2 mL of anthrone TS: a blue-green color develops, which turns dark blue-green gradually. Then, add 1 mL of diluted sulfuric acid (1 in 2) or 1 mL of acetic acid (100) to this solution: the solution remains dark blue-green.

(3) A solution of Dextran Sulfate Sodium Sulfur 18 (1 in 100) responds to the Qualitative Tests **(1)** for sodium salt.

Optical rotation $[\alpha]_D^{20}$: +90.0 – +110.0° (calculated on the dried basis, 1.5 g, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Dextran Sulfate Sodium Sulfur 18 in 20 mL of water: the pH of this solution is between 5.5 and 7.5.

Purity **(1)** Chloride—Perform the test with 0.10 g of Dextran Sulfate Sodium Sulfer 18. Prepare the control solution with 0.30 mL of 0.01 mol/L hydrochloric acid (not more than 0.106%).

(2) Sulfate—Dissolve 0.10 g of Dextran Sulfate Sodium Sulfur 18 in 6 mL of water, add 0.6 mL of barium chloride TS, and heat in a water bath for 4 minutes. After cooling, add 1 mL of dilute hydrochloric acid and water to make 50 mL, allow to stand for 10 minutes, and observe: the turbidity of the solution is not more intense than that of the control solution. Prepare the control solution as follows: to 1.0 mL of 0.005 mol/L sulfuric acid add 6 mL of water, and proceed in the same manner (not more than 0.480%).

(3) Heavy metals—Proceed with 1.0 g of Dextran Sulfate Sodium Sulfur 18 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).

(4) Arsenic—Prepare the test solution with 1.0 g of Dextran Sulfate Sodium Sulfur 18 according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

Sulfur content Weigh accurately about 0.5 g of Dextran Sulfate Sodium Sulfur 18, dissolve in 5 mL of water, add 1.5 mL of hydrochloric acid, and heat in a water bath for 1 hour. After cooling, add water to make exactly 100 mL, and use this solution as the sample solution. To exactly 10 mL of the sample solution add exactly 20 mL of 0.02 mol/L barium chloride VS, add 5 mL of methanol, and heat in a water bath for 30 minutes. After cooling, neutralize with sodium hydroxide TS, and add 70 mL of water, 10 mL of a solution of zinc disodium ethylenediamine tetraacetate tetrahydrate (1 in 20), 3 mL of ammonium chloride TS and 7 mL of strong ammonium water, and titrate with 0.02 mol/L disodium dihydrogen ethylenediamine tetraacetate VS until the color of the solution changes from red to light blue (indicator: 5 drops of eriochrome black T TS). Perform a blank determination. Amount of sulfur (S: 32.07), calculated on the dried basis, is between 15.0 and 20.0%.

Each mL of 0.02 mol/L barium chloride VS
= 0.6413 mg of S

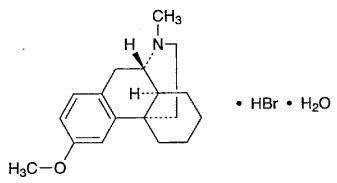
Loss on drying Not more than 10.0% (0.5 g, in vacuum, phosphorus (V) oxide, 60°C, 4 hours).

Intrinsic viscosity Weigh accurately about 1.5 g of Dextran Sulfate Sodium Sulfur 18, calculated on the dried basis, dissolve in a solution of sodium chloride (29 in 500) to make exactly 100 mL, and use this solution as the sample solution. Perform the test with the sample solution and a solution of sodium chloride (29 in 500) at 25 ± 0.02°C as directed under the Viscosity Determination: the intrinsic viscosity is between 0.020 and 0.032.

Containers and storage Containers—Tight containers.

Dextromethorphan Hydrobromide

臭化水素酸デキストロメトルファン



$C_{18}H_{25}NO.HBr.H_2O$: 370.32
(9*S*,13*S*,14*S*)-3-Methoxy-17-methylmorphinan monohydrobromide monohydrate [*6700-34-1*]

Dextromethorphan Hydrobromide contains not less than 98.0% of $C_{18}H_{25}NO.HBr$ (mol. wt.: 352.31), calculated on the anhydrous basis.

Description Dextromethorphan Hydrobromide occurs as white crystals or crystalline powder.

It is very soluble in methanol, freely soluble in ethanol (95) and in acetic acid (100), and sparingly soluble in water.

Melting point: about 126°C (Insert the capillary tube into the bath preheated to 116°C, and continue the heating so that the temperature rises at a rate of about 3°C per minute.)

Identification **(1)** Determine the absorption spectrum of a solution of Dextromethorphan Hydrobromide (1 in 10,000) 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 Dex-

tromethorphan Hydrobromide 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 50 mL of a solution of Dextromethorphan Hydrobromide (1 in 100) add 2 drops of phenolphalein TS and sodium hydroxide TS until a red color develops. Add 50 mL of chloroform, shake, and add 5 mL of dilute nitric acid to 40 mL of the water layer. This solution responds to the Qualitative Tests for bromide.

Optical rotation $[\alpha]_D^{20}$: +26 - +30° (0.34 g, calculated on the anhydrous basis, water, 20 mL, 100 mm).

pH Dissolve 1.0 g of Dextromethorphan Hydrobromide in 100 mL of water: the pH of this solution is between 5.2 and 6.5.

Purity (1) Clarity and color of solution—Dissolve 0.20 g of Dextromethorphan Hydrobromide in 20 mL of water: the solution is clear and colorless.

(2) *N,N*-dimethylaniline—To 0.50 g of Dextromethorphan Hydrobromide add 20 mL of water, and dissolve by heating on a water bath. After cooling, add 2 mL of dilute acetic acid, 1 mL of sodium nitrite TS and water to make 25 mL: the solution has no more color than the following control solution.

Control solution: Dissolve 0.10 g of *N,N*-dimethylaniline in 400 mL of water by warming on a water bath, cool, and add water to make 500 mL. Pipet 5 mL of this solution, and add water to make 200 mL. To 1.0 mL of this solution add 2 mL of dilute acetic acid, 1 mL of sodium nitrite TS and water to make 25 mL.

(3) Heavy metals—Proceed with 1.0 g of Dextromethorphan Hydrobromide according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Phenolic compounds—Dissolve 5 mg of Dextromethorphan Hydrobromide in 1 drop of dilute hydrochloric acid and 1 mL of water, add 2 drops of iron (III) chloride TS and 2 drops of potassium hexacyanoferrate (III) TS, shake, and allow to stand for 15 minutes: no blue-green color develops.

(5) Related substances—Dissolve 0.25 g of Dextromethorphan Hydrobromide 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 toluene, ethyl acetate, methanol, dichloromethane and 13.5 mol/L ammonia TS (55:20:13:10:2) to a distance of about 15 cm, and air-dry the plate. Spray evenly bismuth potassium iodide TS on the plate, and then spray evenly hydrogen peroxide TS 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 4.0 - 5.5% (0.2 g, back titration).

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

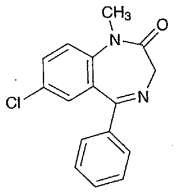
Assay Weigh accurately about 0.5 g of Dextromethorphan Hydrobromide, dissolve in 10 mL of acetic acid (100) and add 40 mL of acetic anhydride. Titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 35.231 mg of $C_{18}H_{25}NO.HBr$

Containers and storage Containers—Well-closed containers.

Diazepam

ジアゼパム



$C_{16}H_{13}ClN_2O$: 284.74
7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one [*439-14-5*]

Diazepam, when dried, contains not less than 98.0% of $C_{16}H_{13}ClN_2O$.

Description Diazepam occurs as a white to light yellow, crystalline powder. It is odorless, and has a slightly bitter taste.

It is freely soluble in acetone, soluble in acetic anhydride and in ethanol (95), sparingly soluble in diethyl ether, slightly soluble in ethanol (99.5), and practically insoluble in water.

Identification (1) Dissolve 0.01 g of Diazepam in 3 mL of sulfuric acid, and observe under ultraviolet light (main wavelength: 365 nm): the solution shows a yellow-green fluorescence.

(2) Dissolve 2 mg of Diazepam in 200 mL of a solution of sulfuric acid in ethanol (99.5) (3 in 1000). Determine the absorption spectrum of the solution 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) Perform the test with Diazepam as directed under the Flame Coloration Test (2): a blue to blue-green color appears.

Absorbance $E_{1\,cm}^{1\%}$ (285 nm): 425 - 445 [after drying, 2 mg, a solution of sulfuric acid in ethanol (99.5) (3 in 1000), 200 mL].

Melting point 130 - 134°C

Purity (1) Clarity of solution—Dissolve 0.10 g of Diazepam in 20 mL of ethanol (95): the solution is clear.

(2) Chloride—To 1.0 g of Diazepam add 50 mL of water, allow to stand for 1 hour, with occasional shaking, and filter. To 25 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this