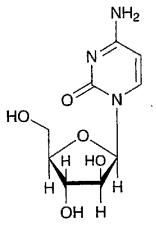
Cytarabine

シタラビン



$C_9H_{13}N_3O_5$: 243.22
4-Amino-1-β-D-arabinofuranosylpyrimidin-2(1*H*)-one
[*147-94-4*]

Cytarabine, when dried, contains not less than 98.5% of $C_9H_{13}N_3O_5$.

Description Cytarabine occurs as white crystals or crystalline powder.

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

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

Identification (1) To 1 mL of a solution of Cytarabine (1 in 1000) add 1 drop of bromine TS, allow to stand for 10 minutes, and expel the excess bromine under a current of air. To this solution add 1 mL of a solution of L-ascorbic acid (1 in 5000) and 1 mL of ninhydrin TS, and heat in a water bath for 30 minutes: a purple color develops.

(2) To 1 mL of a solution of Cytarabine (1 in 100) add 1 mL of orcin-ferric chloride TS, and heat in a water bath for 30 minutes: a green color develops.

Absorbance $E^{1\%}_{1cm}$ (282 nm): 530 – 570 (after drying, 2 mg, 0.1 mol/L hydrochloric acid TS, 200 mL).

Optical rotation $[\alpha]^{20}_D$: +154 – +160° (after drying, 0.1 g, water, 10 mL, 100 mm).

pH Dissolve 0.20 g of Cytarabine in 20 mL of water: the pH of this solution is between 6.5 and 8.0.

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

(2) Chloride—Perform the test with 1.0 g of Cytarabine. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.009%).

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

(5) Related substances—Dissolve 0.10 g of Cytarabine in 10 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water 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 silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with 1-butanol saturated with water to a distance of about 12 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 acidic potassium permanganate TS on the plate: any spot other than the principal spot does not appear.

Loss on drying Not more than 1.0% (1 g, in vacuum, silica gel, 4 hours).

Residue on ignition Not more than 0.5% (1 g).

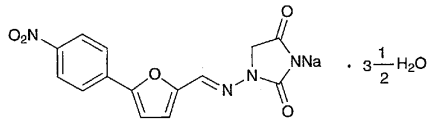
Assay Weigh accurately about 0.2 g of Cytarabine, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.05 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L perchloric acid VS
= 12.161 mg of $C_9H_{13}N_3O_5$

Containers and storage Containers—Tight containers.

Dantrolene Sodium

ダントロレンナトリウム



$C_{14}H_9N_4NaO_5.3\frac{1}{2}H_2O$: 399.29
Monosodium 3-[5-(4-nitrophenyl)furan-2-ylmethylene]amino-2,5-dioxo-1,3-imidazolidinate hemiheptahydrate
[*14663-23-1*, anhydride]

Dantrolene Sodium contains not less than 98.0% of $C_{14}H_9N_4NaO_5$, calculated on the anhydrous basis.

Description Dantrolene Sodium occurs as a yellowish orange to deep orange, crystalline powder.

It is soluble in propylene glycol, sparingly soluble in methanol, slightly soluble in ethanol (95), very slightly soluble in water and in acetic acid (100), and practically insoluble in acetone, in tetrahydrofuran and in diethyl ether.

Identification (1) Determine the absorption spectrum of a solution of Dantrolene Sodium 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.

(2) Determine the infrared absorption spectrum of Dantrolene Sodium 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 0.1 g of Dantrolene Sodium add 20 mL of water and 2 drops of acetic acid (100), shake well, and filter: the filtrate responds to the Qualitative Tests (1) for sodium salt.

Purity (1) Alkali—To 0.7 g of Dantrolene Sodium add 10 mL of water, shake well, and centrifuge or filter through a membrane filter. To 5 mL of the supernatant or the filtrate add 45 mL of water, 3 drops of phenolphthalein TS and 0.10 mL of 0.1 mol/L hydrochloric acid VS: a red color is not produced.

(2) Heavy metals—Proceed with 1.0 g of Dantrolene Sodium 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 0.050 g of Dantrolene Sodium in 20 mL of tetrahydrofuran and 2 mL of acetic acid (100), add ethanol (99.5) to make 100 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add ethanol (99.5) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with 10 μL of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area from these solutions by the automatic integration method: the total area of all peaks other than the peak of dantrolene from the sample solution is not larger than the peak area of dantrolene from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 300 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 30°C.

Mobile phase: A mixture of hexane, acetic acid (100) and ethanol (99.5) (90:10:9).

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

Selection of column: Dissolve 5 mg of Dantrolene Sodium and 0.1 g of theophylline in 20 mL of tetrahydrofuran and 2 mL of acetic acid (100), and add ethanol (99.5) to make 100 mL. To 10 mL of this solution add ethanol (99.5) to make 100 mL. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of theophylline and dantrolene in this order with the resolution between these peaks being not less than 6.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of dantrolene from 10 μL of the standard solution is 10% to 40% of the full scale.

Time span of measurement: About twice as long as the retention time of dantrolene, after the solvent peak.

Water 14.5 - 17.0% (0.2 g, direct titration).

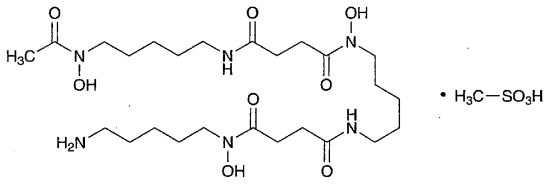
Assay Weigh accurately about 0.7 g of Dantrolene Sodium, dissolve in 180 mL of a mixture of propylene glycol and acetone (1:1), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 33.624 mg of $C_{14}H_9N_4NaO_5$

Containers and storage Containers—Tight containers.

Deferoxamine Mesilate

メシル酸デフェロキサミン



$C_{25}H_{48}N_6O_8.CH_4O_3S$: 656.79

N-[5-(Acetylhydroxyamino)pentyl]-*N'*-(5-{3-[(5-aminopentyl)hydroxycarbamoyl]propanoylamino}pentyl)-*N'*-hydroxysuccinamide monomethanesulfonate

[*138-14-7*]

Deferoxamine Mesilate contains not less than 98.0% and not more than 102.0% of $C_{25}H_{48}N_6O_8.CH_4O_3S$, calculated on the anhydrous basis.

Description Deferoxamine Mesilate occurs as a white to pale yellowish white, crystalline powder.

It is freely soluble in water, and practically insoluble in ethanol (99.5), in 2-propanol and in diethyl ether.

Melting point: about 147°C (with decomposition).

Identification (1) To 5 mL of a solution of Deferoxamine Mesilate (1 in 500) add 1 drop of iron (III) chloride TS: a deep red color develops.

(2) To 0.05 g of Deferoxamine Mesilate add 0.2 g of sodium hydroxide, melt by heating over a small flame, and heat further for 2 to 3 seconds. To the residue add 0.5 mL of water, acidify with dilute hydrochloric acid, and warm: the gas evolved changes moistened potassium iodate-starch paper to blue.

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

pH Dissolve 1.0 g of Deferoxamine Mesilate in 10 mL of water: the pH of this solution is between 3.5 and 5.5.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Deferoxamine Mesilate in 10 mL of water: the solution is clear and colorless to pale yellow.

(2) Chloride—Perform the test with 1.0 g of Deferoxamine Mesilate. Prepare the control solution with 0.90 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.032%).

(3) Sulfate—Perform the test with 0.6 g of Deferoxamine Mesilate. Prepare the control solution with 0.50 mL of 0.005 mol/L sulfuric acid VS (not more than 0.040%).

(4) Heavy metals—Proceed with 2.0 g of Deferoxamine Mesilate according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(5) Arsenic—Prepare the test solution with 1.0 g of Deferoxamine Mesilate according to Method 3, and perform the test using Apparatus B. Use a solution of magnesi-