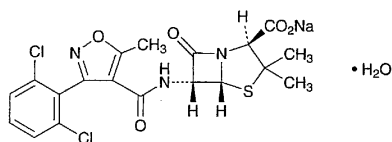


Dicloxacillin Sodium

Methyldichlorophenylisoxazolympenicillin Sodium

ジクロキサシリンナトリウム



$C_{19}H_{16}Cl_2N_3NaO_5S \cdot H_2O$: 510.32
 Monosodium (2*S*,5*R*,6*R*)-6-[[3-(2,6-dichlorophenyl)-5-methylisoxazole-4-carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate [13412-64-1]

Dicloxacillin Sodium contains not less than 850 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Dicloxacillin Sodium is expressed as mass (potency) of dicloxacillin ($C_{19}H_{17}Cl_2N_3O_5S$: 470.33).

Description Dicloxacillin Sodium occurs as a white to light yellowish white crystalline powder.

It is freely soluble in water and in methanol, and soluble in ethanol (95).

Identification (1) Determine the absorption spectrum of a solution of Dicloxacillin Sodium (1 in 2500) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Dicloxacillin Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

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

(3) Dicloxacillin Sodium responds to the Quantitative Test (1) for sodium salt.

Water Not less than 3.0% and not more than 4.5% (0.1 g, volumetric titration, direct titration).

Assay Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Bacillus subtilis* ATCC 6633

(2) Culture medium—Use the medium i in 1) Medium for test organism [5] under (1) Agar media for seed and base layer. Adjust the pH of the medium so that it will be 6.5 to 6.6 after sterilization.

(3) Standard solution—Weigh accurately an amount of Dicloxacillin Sodium Reference Standard equivalent to about 0.05 g (potency), dissolve in phosphate buffer solution, pH 6.0 to make exactly 50 mL, and use this solution as the standard stock solution. Keep the standard stock solution at 5°C or below and use within 24 hours. Take exactly a suitable amount of the standard stock solution before use,

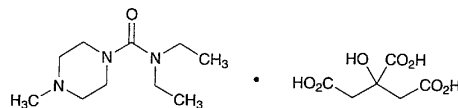
add phosphate buffer solution, pH 6.0 to make solutions so that each mL contains 10 μ g (potency) and 2.5 μ g (potency), and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

(4) Sample solution—Weigh accurately an amount of Dicloxacillin Sodium equivalent to about 0.05 g (potency), dissolve in phosphate buffer solution, pH 6.0 to make exactly 50 mL. Take exactly a suitable amount of the solution, add phosphate buffer solution, pH 6.0 to make solutions so that each mL contains 10 μ g (potency) and 2.5 μ g (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

Containers and storage Containers—Tight containers.

Diethylcarbamazine Citrate

クエン酸ジエチルカルバマジン



$C_{10}H_{21}N_3O \cdot C_6H_8O_7$: 391.42
N,N-Diethyl-4-methylpiperazine-1-carboxamide monocitrate [1642-54-2]

Diethylcarbamazine Citrate, when dried, contains not less than 98.0% of $C_{10}H_{21}N_3O \cdot C_6H_8O_7$.

Description Diethylcarbamazine Citrate occurs as a white, crystalline powder. It is odorless, and has an acid and bitter taste.

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

A solution of Diethylcarbamazine Citrate (1 in 20) is acid. It is hygroscopic.

Identification (1) Dissolve 0.5 g of Diethylcarbamazine Citrate in 2 mL of water, add 10 mL of sodium hydroxide TS, and extract with four 5-mL portions of chloroform. Wash the combined chloroform extracts with 10 mL of water, and evaporate the chloroform on a water bath. Add 1 mL of iodoethane to the residue, and boil gently under a reflux condenser for 5 minutes. Evaporate the excess iodoethane with the aid of a current of air, and dissolve the residue in 4 mL of ethanol (95). Cool the ethanol solution in an ice bath, with continuous stirring, add diethyl ether until precipitates are formed, and stir until crystallization is evident. Allow to stand in the ice bath for 30 minutes, and collect the precipitate. Dissolve the precipitate in 4 mL of ethanol (95), repeat the recrystallization in the same manner, then dry at 105°C for 4 hours: the crystals so obtained melt between 151°C and 155°C.

(2) Neutralize the remaining aqueous layer obtained in (1) with dilute sulfuric acid: the solution responds to the Qualitative Tests (2) and (3) for citrate.

Melting point 135.5 – 138.5°C

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 $C_{10}H_{21}N_3O \cdot C_6H_8O_7$

Containers and storage Containers—Tight containers.

Diethylcarbamazine Citrate Tablets

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Diethylcarbamazine Citrate Tablets contain not less than 95% and not more than 105% of the labeled amount of diethylcarbamazine citrate ($C_{10}H_{21}N_3O \cdot C_6H_8O_7$; 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 diethylcarbamazine 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 ($C_{10}H_{21}N_3O \cdot C_6H_8O_7$), 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 μ L 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 diethylcarbamazine to that of the internal standard, respectively.

$$\begin{aligned} & \text{Amount (mg) of diethylcarbamazine citrate} \\ & (C_{10}H_{21}N_3O \cdot C_6H_8O_7) \\ & = \text{amount (mg) of Diethylcarbamazine Citrate} \\ & \quad \text{Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

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 μ m in particle diameter).

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

Carrier gas: Nitrogen.

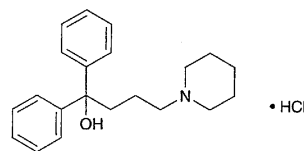
Flow rate: Adjust the flow rate so that the retention time of the internal standard is 8 to 11 minutes.

Selection of column: Proceed with 2 μ L 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



$C_{21}H_{27}NO \cdot HCl$: 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 $C_{21}H_{27}NO \cdot HCl$.

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