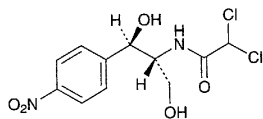


Chloramphenicol

クロラムフェニコール



$C_{11}H_{12}Cl_2N_2O_5$: 323.13

2,2-Dichloro-*N*-[(1*R*,2*R*)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl]acetamide [56-75-7]

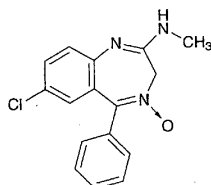
Chloramphenicol conforms to the requirements of Chloramphenicol in the Requirements for Antibiotic Products of Japan.

Description Chloramphenicol occurs as white to yellowish white crystals or crystalline powder. It has a bitter taste.

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

Chlordiazepoxide

クロルジアゼポキシド



$C_{16}H_{14}ClN_3O$: 299.75

7-Chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepin-4-oxide [58-25-3]

Chlordiazepoxide, when dried, contains not less than 98.5% of $C_{16}H_{14}ClN_3O$.

Description Chlordiazepoxide occurs as white to light yellow crystals or crystalline powder.

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

It dissolves in dilute hydrochloric acid.

It is gradually affected by light.

Melting point: about 240°C (with decomposition).

Identification (1) Determine the absorption spectrum of a solution of Chlordiazepoxide in 0.1 mol/L hydrochloric acid TS (1 in 200,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Chlordiazepoxide Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectra of Chlordiazepoxide, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotomet-

ry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Chlordiazepoxide Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Proceed with Chlordiazepoxide as directed under the Flame Coloration Test (2), and perform the test: a green color develops.

Purity (1) Heavy metals—Proceed with 1.0 g of Chlordiazepoxide 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).

(2) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.20 g of Chlordiazepoxide in exactly 10 mL of a mixture of methanol and ammonia TS (97:3), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of methanol and ammonia TS (97:3) to make exactly 200 mL, and use this solution as the standard solution (1). Separately, dissolve 0.010 g of 2-amino-5-chlorobenzophenone for thin-layer chromatography in methanol to make exactly 200 mL, and use this solution as the standard solution (2). Perform the test with the these solutions as directed under the Thin-layer Chromatography. Spot 25 μ L of the sample solution and 5 μ L each of the standard solutions (1) and (2) on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate and ethanol (99.5:0.5) 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 (1). Spray evenly a solution of sodium nitrite in 1 mol/L hydrochloric acid TS (1 in 100) on the plate, allow to stand for 1 minute, and spray evenly *N*-(1-naphthyl)-*N'*-diethylethylenediamine oxalate-acetone TS on the plate: the spots from the sample solution are not more intense than the spots from the standard solution (2).

Loss on drying Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 60°C, 4 hours).

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

Assay Weigh accurately about 0.6 g of Chlordiazepoxide, previously dried, and dissolve in 50 mL of acetic acid (100). Titrate with 0.1 mol/L perchloric acid VS until the color of the supernatant liquid changes from purple through blue-purple to blue (indicator: 3 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 29.976 mg of $C_{16}H_{14}ClN_3O$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Chlordiazepoxide Powder

クロルジアゼポキシド散

Chlordiazepoxide Powder contains not less than 93% and not more than 107% of the labeled amount

of chlordiazepoxide ($C_{16}H_{14}ClN_3O$: 299.75).

Method of preparation Prepare as directed under Powder, with Chlordiazepoxide.

Identification (1) Weigh a portion of Chlordiazepoxide Powder, equivalent to 0.01 g of Chlordiazepoxide according to the labeled amount, add 100 mL of 0.1 mol/L hydrochloric acid TS, shake, and filter. To 5 mL of the filtrate add 0.1 mol/L hydrochloric acid TS to make 100 mL, and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 244 nm and 248 nm and between 306 nm and 310 nm, and a minimum between 288 nm and 292 nm.

(2) Weigh a portion of Chlordiazepoxide Powder, equivalent to 0.02 g of Chlordiazepoxide according to the labeled amount, add 10 mL of methanol, shake for 5 minutes, then filter by suction through a glass filter (G4), evaporate the filtrate with the aid of a current of air to dryness, and dry the residue in vacuum at 60°C for 1 hour. Determine the infrared absorption spectrum of the residue as directed in the potassium bromide disk method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 1625 cm^{-1} , 1465 cm^{-1} , 1265 cm^{-1} , 850 cm^{-1} and 765 cm^{-1} .

Purity Conduct this procedure without exposure to daylight, using light-resistant vessels. To a portion of Chlordiazepoxide Powder, equivalent to 0.050 g of Chlordiazepoxide according to the labeled amount, add exactly 5 mL of a mixture of methanol and ammonia TS (97:3), shake, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 0.050 g of Chlordiazepoxide Reference Standard in a mixture of methanol and ammonia TS (97:3) to make exactly 50 mL, and use this solution as the standard solution (1). Dissolve 5.0 mg of 2-amino-5-chlorobenzophenone for thin-layer chromatography in methanol to make exactly 200 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 25 μL of the sample solution and 10 μL each of the standard solutions (1) and (2) on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Proceed as directed in the Purity (2) under Chlordiazepoxide.

Assay Conduct this procedure without exposure to daylight, using light-resistant vessels. Weigh accurately a quantity of Chlordiazepoxide Powder, equivalent to about 0.1 g of Chlordiazepoxide ($C_{16}H_{14}ClN_3O$), transfer to a glass-stoppered flask, add exactly 100 mL of methanol, stopper, shake vigorously for 15 minutes, and centrifuge. Pipet 10 mL of the supernatant liquid, add exactly 5 mL of the internal standard solution, add methanol to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of Chlordiazepoxide Reference Standard, previously dried in a desiccator (in vacuum, phosphorus (V) oxide, 60°C) for 4 hours, dissolve in methanol, add exactly 5 mL of the internal standard solution, add methanol to make exactly 100 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 operating conditions, and calculate the ratios, Q_T and Q_S , of the peak area of chlordiazepoxide to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of chlordiazepoxide (C}_{16}\text{H}_{14}\text{ClN}_3\text{O)} \\ & = \text{amount (mg) of Chlordiazepoxide} \\ & \quad \text{Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \times 10 \end{aligned}$$

Internal standard solution—A solution of isobutyl salicylate in methanol (1 in 20).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 4 mm in inside diameter and 25 to 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

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

Mobile phase: A mixture of methanol and 0.02 mol/L ammonium dihydrogenphosphate TS (7:3).

Flow rate: Adjust the flow rate so that the retention time of chlordiazepoxide is about 5 minutes.

Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions. Use a column giving elution of chlordiazepoxide and the internal standard in this order with the resolution between these peaks being not less than 9.

Containers and storage Containers—Tight containers.

Chlordiazepoxide Tablets

クロルジアゼポキシド錠

Chlordiazepoxide Tablets contain not less than 93% and not more than 107% of the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$: 299.75).

Method of preparation Prepare as directed under Tablets, with Chlordiazepoxide.

Identification (1) Weigh a portion of powdered Chlordiazepoxide Tablets, equivalent to 0.01 g of Chlordiazepoxide according to the labeled amount, add 100 mL of 0.1 mol/L hydrochloric acid TS, shake, and filter. To 5 mL of the filtrate add 0.1 mol/L hydrochloric acid TS to make 100 mL, and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 244 nm and 248 nm and between 306 nm and 310 nm, and a minimum between 288 nm and 292 nm.

(2) Weigh a portion of powdered Chlordiazepoxide Tablets, equivalent to 0.01 g of Chlordiazepoxide according to the labeled amount, add 10 mL of diethyl ether, shake vigorously, and centrifuge. Evaporate 5 mL of the supernatant liquid by warming on a water bath to dryness. Determine the infrared absorption spectrum of the residue as directed in the potassium bromide disk method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 1625 cm^{-1} , 1465 cm^{-1} , 1265 cm^{-1} , 850 cm^{-1} and 765 cm^{-1} .

Purity Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. To a portion of powdered Chlordiazepoxide Tablets, equivalent to 0.01 g of Chlordiazepoxide according to the labeled amount, add 10 mL of diethyl ether, shake vigorously, and centrifuge. Evaporate 5 mL of the supernatant liquid by warming on a water bath to dryness. Determine the infrared absorption spectrum of the residue as directed in the potassium bromide disk method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 1625 cm^{-1} , 1465 cm^{-1} , 1265 cm^{-1} , 850 cm^{-1} and 765 cm^{-1} .