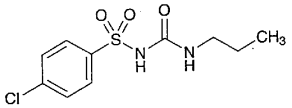
Soxhlet extractor, and extract with 100 mL of chloroform on a water bath for 3 hours. Distil the chloroform solution under reduced pressure on a water bath. Dissolve the residue in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.05 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L perchloric acid VS
= 17.767 mg of $C_{17}H_{19}ClN_2S.HCl$

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

Chlorpropamide

クロルプロパミド



$C_{10}H_{13}ClN_2O_3S$: 276.74
4-Chloro-*N*-(propylcarbamoyl)benzenesulfonamide
[*94-20-2*]

Chlorpropamide, when dried, contains not less than 98.0% of $C_{10}H_{13}ClN_2O_3S$.

Description Chlorpropamide occurs as white, crystals or crystalline powder.

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

Identification **(1)** Dissolve 0.08 g of Chlorpropamide in 50 mL of methanol. To 1 mL of the solution add 0.01 mol/L hydrochloric acid TS to make 200 mL. 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.

(2) Determine the infrared absorption spectrum of Chlorpropamide, 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.

(3) Perform the test with Chlorpropamide as directed under the Flame Coloration Test (2): a green color appears.

Melting point 127 - 131°C

Purity **(1)** Acid—To 3.0 g Chlorpropamide add 150 mL of water, and warm at 70°C for 5 minutes. Allow to stand in ice water for 1 hour, and filter. To 25 mL of the filtrate add 2 drops of methyl red TS and 0.30 mL of 0.1 mol/L sodium hydroxide VS: a yellow color develops.

(2) Chloride—To 40 mL of the filtrate obtained in (1) add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.011%).

(3) Sulfate—To 40 mL of the filtrate obtained in (1) add 1 mL of dilute hydrochloric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.35 mL of 0.005 mol/L sulfuric acid VS (not more than 0.021%).

(4) Heavy metals—Proceed with 2.0 g of Chlorpropamide 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).

(5) Related substances—Dissolve 0.6 g of Chlorpropamide in acetone to make exactly 10 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetone to make exactly 300 mL, and use this solution as the standard solution (1). Separately, dissolve 0.060 g of 4-chlorobenzene sulfonamide in acetone to make exactly 300 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution, the standard solution (1) and (2) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of cyclohexane, 3-methyl-1-butanol, methanol and ammonia solution (28) (15:10:5:1) to a distance of about 10 cm, and air-dry the plate. After drying the plate at 100°C for 1 hour, spray evenly sodium hypochlorite TS on the plate, and air-dry for 15 minutes. Then spray evenly potassium iodide-starch TS on the plate: the spot from the sample solution equivalent to the spot from the standard solution (2) is not more intense than the spot from the standard solution (2), and the spots other than the spot mentioned above and other than the principal spot from the sample solution is not more intense than the spot from the standard solution (1).

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

Residue on ignition Not more than 0.20% (1 g).

Assay Weigh accurately about 0.5 g of Chlorpropamide, previously dried, dissolve in 30 mL of neutralized ethanol, and add 20 mL of water. Titrate with 0.1 mol/L sodium hydroxide VS (indicator: 3 drops of phenolphthalein TS).

Each mL of 0.1 mol/L sodium hydroxide VS
= 27.674 mg of $C_{10}H_{13}ClN_2O_3S$

Containers and storage Containers—Well-closed containers.

Chlorpropamide Tablets

クロルプロパミド錠

Chlorpropamide Tablets contain not less than 95% and not more than 105% of the labeled amount of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$: 276.74).

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

Identification Take a quantity of powdered Chlorpropamide Tablets, equivalent to 0.08 g of Chlorpropamide according to the labeled amount, add 50 mL of methanol, shake, and filter. To 1 mL of the filtrate add 0.01 mol/L hydrochloric acid TS to make 200 mL, and determine the ab-

sorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 231 nm and 235 nm.

Dissolution test Perform the test with 1 tablet of Chlorpropamide Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of diluted phosphate buffer solution, pH 6.8, (1 in 2) as the test solution. Take 20 mL or more of the dissolved solution 45 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.8 μm. Discard the first 10 mL of the filtrate, pipet the subsequent V mL of the filtrate, add diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly V' mL so that each mL contains about 10 μg of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of chlorpropamide for assay, previously dried at 105°C for 3 hours, dissolve in 10 mL of methanol, and add water to make exactly 50 mL. Pipet 1 mL of this solution, add diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and the standard solution at 232 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Chlorpropamide Tablets in 45 minutes should be not less than 70%.

Dissolution rate (%) with respect to the labeled amount of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times 18$$

W_S: Amount (mg) of chlorpropamide for assay.
C: Labeled amount (mg) of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Chlorpropamide Tablets. Weigh accurately a quantity of the powder, equivalent to about 0.05 g of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$), add 75 mL of the mobile phase, shake for 10 minutes, and add the mobile phase to make exactly 100 mL. Centrifuge this solution, pipet 10 mL of the supernatant liquid, add the mobile phase to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of chlorpropamide for assay, previously dried at 105°C for 3 hours, dissolve in the mobile phase to make exactly 100 mL. Pipet 10 mL of this solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions. Determine the peak areas, A_T and A_S, of chlorpropamide of the sample solution and the standard solution.

Amount (mg) of $C_{10}H_{13}ClN_2O_3S$
= amount (mg) of chlorpropamide for assay
$\times \frac{A_T}{A_S}$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 240 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 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 diluted acetic acid (100) (1 in 100) and acetonitrile (1:1).

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

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry constant of the peak of chlorpropamide are not less than 1500 and not more than 1.5, respectively.

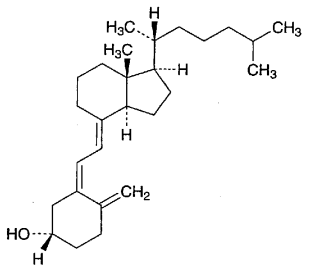
System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of chlorpropamide is not more than 1.5%.

Containers and storage Containers—Well-closed containers.

Cholecalciferol

Vitamin D_3

コレカルシフェロール



$C_{27}H_{44}O$: 384.64
(3*S*,5*Z*,7*E*)-9,10-Secocholesta-5,7,10(19)-trien-3-ol
[*67-97-0*]

Cholecalciferol contains not less than 97.0% and not more than 103.0% of $C_{27}H_{44}O$.

Description Cholecalciferol occurs as white crystals. It is odorless.

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

It is affected by air and by light.

Melting point: 84 - 88°C Transfer Cholecalciferol to a capillary tube, and dry for 3 hours in a desiccator (in vacuum at a pressure not exceeding 2.67 kPa). Immediately fireseal the capillary tube, put it in a bath fluid, previously heated to a temperature about 10°C below the expected melting point, and heat at a rate of rise of about 3°C per minute, and read the melting point.

Identification (1) Dissolve 0.5 mg of Cholecalciferol in 5 mL of chloroform, add 0.3 mL of acetic anhydride and 0.1 mL of sulfuric acid, and shake: a red color is produced, and