rapidly changes through purple and blue to green.

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

Absorbance $E^{1\%}_{1\,cm}$ (265 nm): 450 - 490 (0.01 g, ethanol (95), 1000 mL).

Optical rotation $[\alpha]_D^{20}$ +103 - +112° (0.05 g, ethanol (95), 10 mL, 100 mm). Prepare the solution without delay, using Cholecalciferol from a container opened not longer than 30 minutes, previously, and determine the rotation within 30 minutes after the solution has been prepared.

Purity 7-Dehydrocholesterol—Dissolve 0.010 g of Cholecalciferol in 2.0 mL of diluted ethanol (95) (9 in 10), add a solution prepared by dissolving 0.020 g of digitonin in 2.0 mL of diluted ethanol (95) (9 in 10), and allow the mixture to stand for 18 hours: no precipitate is formed.

Assay Dissolve separately about 0.03 g each of Cholecalciferol and Cholecalciferol Reference Standard, accurately weighed, in isooctane to make exactly 50 mL. Pipet 10 mL each of these solutions, add 3 mL each of the internal standard solution, then add the mobile phase to make 50 mL, and use these solutions as the sample solution and 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 conditions, and calculate the ratios, Q_T and Q_S, of the peak area of cholecalciferol to that of the internal standard. Proceed with the operation avoiding contact with air or other oxidizing agents and using light-resistant containers.

Amount (mg) of $C_{27}H_{44}O$
= amount (mg) of Cholecalciferol Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of dimethyl phthalate in isooctane (1 in 100).

Operating conditions—

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

Column: A stainless steel column about 4 mm in inside diameter and 10 to 30 cm in length, packed with silica gel for liquid chromatography (5 to 10 μm in particle diameter).

Column temperature: Ordinary temperature.

Mobile phase: A mixture of hexane and *n*-amylalcohol (997:3).

Flow rate: Adjust the flow rate so that the retention time of cholecalciferol is about 25 minutes.

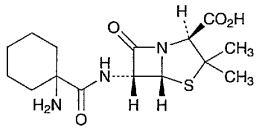
Selection of column: Dissolve 0.015 g of Cholecalciferol Reference Standard in 25 mL of isooctane. Transfer this solution to a flask, heat under a reflux condenser in an oil bath for 2 hours, and cool to room temperature rapidly. Transfer this solution to a quartz test tube, and irradiate under a short-wave lamp (main wavelength: 254 nm) and a long-wave lamp (main wavelength: 365 nm) for 3 hours. To this solution add the mobile phase to make 50 mL. Proceed with 10 μL of this solution under the above operating conditions. Use a column with the ratios of the retention time of previtamin D_3, trans-vitamin D_3 and tachysterol$_3$ to that of cholecalciferol being about 0.5, about 0.6 and about 1.1, respectively, and with resolution between previtamin D_3 and trans-vitamin D_3, and that between cholecalciferol and tachysterol$_3$ being not less than 1.0.

Containers and storage Containers—Hermetic containers.

Storage—Light-resistant, under nitrogen atmosphere, and in a cold place.

Ciclacillin

シクラシリン



$C_{15}H_{23}N_3O_4S$: 341.43
(2*S*,5*R*,6*R*)-6-[(1-Aminocyclohexanecarbonyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid [*3485-14-1*]

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

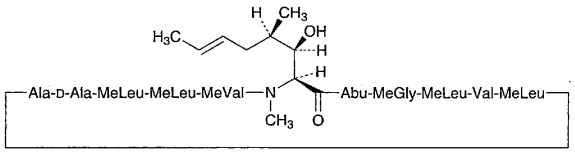
Description Ciclacillin occurs as a white to light yellowish white, crystalline powder.

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

Ciclosporin

Ciclosporin A

シクロスポリン



Abu = (2*S*)-2- Abu=(2*S*)-2-Aminobutyric acid
MeGly = *N*- MeGly=*N*-Methylglycine
MeLeu = *N*- MeLeu=*N*-Methylleucine
MeVal = *N*- MeVal=*N*-Methylvaline

$C_{62}H_{111}N_{11}O_{12}$: 1202.61
cyclo{-[(2*S*,3*R*,4*R*,6*E*)-3-Hydroxy-4-methyl-2-methylaminooct-6-enoyl]-L-2-aminobutanoyl-*N*-methylglycyl-*N*-methyl-L-leucyl-L-valyl-*N*-methyl-L-leucyl-L-alanyl-D-alanyl-*N*-methyl-L-leucyl-*N*-methyl-L-leucyl-*N*-methyl-L-valyl-} [*59865-13-3*]

Ciclosporin contains not less than 98.5% and not more than 101.5% of $C_{62}H_{111}N_{11}O_{12}$, calculated on

the dried basis.

Description Ciclosporin occurs as a white powder.

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

Identification Determine the infrared absorption spectrum of Ciclosporin 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.

Optical rotation $[\alpha]_D^{20}$: -185 – $-193°$ (0.1 g calculated on the dried basis, methanol, 20 mL, 100 mm).

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Ciclosporin in 10 mL of ethanol (95): the solution is clear, and has no more color than the following control solution (1), (2) or (3).

Control solution (1): To exactly 3.0 mL of Ferric Chloride Stock CS and exactly 0.8 mL of Cobaltous Chloride Stock CS add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

Control solution (2): To exactly 3.0 mL of Ferric Chloride Stock CS, exactly 1.3 mL of Cobaltous Chloride Stock CS and exactly 0.5 mL of Cupric Sulfate Stock CS add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

Control solution (3): To exactly 0.5 mL of Iron (III) chloride Stock CS and exactly 1.0 mL of Cobaltous Chloride Stock CS add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

(2) Heavy metals—Proceed with 1.0 g of Ciclosporin 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—Use the sample solution obtained in the Assay as the sample solution. Pipet 2 mL of the sample solution, add a mixture of water and acetonitrile (1:1) to make exactly 200 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 conditions. Determine each peak area of both solutions by the automatic integration method: the total area of all peaks other than the ciclosporin peak from the sample solution is not more than 1.5 times of the peak area of ciclosporin from the standard solution, and the each peak area other than the ciclosporin peak from the sample solution is not more than 0.7 times of the peak area of ciclosporin from the standard solution.

Operating conditions—

Detector, column, column temperature, mobile phase, flow rate, and selection of column: Proceed as directed in the operating conditions in the Assay.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of ciclosporin from 20 μL of the standard solution is about 10 mm.

Time span of measurement: About 2 times as long as the retention time of ciclosporin after the solvent peak.

Loss on drying Not more than 2.0% (1 g, in vacuum at a pressure not exceeding 0.67 kPa, 60°C, 3 hours).

Residue on ignition Not more than 0.1% (0.5 g).

Assay Weigh accurately about 0.03 g each of Ciclosporin and Ciclosporin Reference Standard, previously determined the loss on drying as the same manner as above, and dissolve each in a mixture of water and acetonitrile (1:1) to make exactly 25 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine the peak areas, A_T and A_S, of ciclosporin in each solution.

Amount (mg) of $C_{62}H_{111}N_{11}O_{12}$
= amount (mg) of Ciclosporin Reference Standard, calculated on the dried basis

$$\times \frac{A_S}{A_T}$$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 210 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (3 to 5 μm in particle diameter). Connect the sample injection port to the column with a stainless steel tube about 0.3 mm in inside diameter and about 1 m in length.

Column temperature: A constant temperature of about 80°C (including the sample injection port and the connecting tube).

Mobile phase: A mixture of water, acetonitrile, *tert*-butyl methyl ether and phosphoric acid (520:430:50:1).

Flow rate: Adjust the flow rate so that the retention time of ciclosporin is about 27 minutes.

Selection of column: Dissolve 3 mg of Ciclosporin U Reference Standard in 2.5 mL of a mixture of water and acetonitrile (1:1), and add 2.5 mL of the standard solution. Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use the column giving elution of ciclosporin U and ciclosporin in this order with the resolution between these peaks being not less than 1.2.

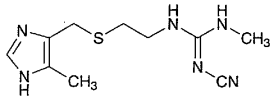
System repeatability: When the test is repeated 6 times with the standard solution under the above operating conditions, the relative standard deviation of the peak area of ciclosporin is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cimetidine

シメチジン



$C_{10}H_{16}N_6S$: 252.34

2-Cyano-1-methyl-3-{2-[(5-methyl-1*H*-imidazol-4-yl)methylsulfanyl]ethyl}guanidine [*51481-61-9*]

Cimetidine, when dried, contains not less than 99.0% of $C_{10}H_{16}N_6S$.