

and 50 cm in length, packed with gel type strong acid ion-exchange resin for liquid chromatography (degree of crosslinkage: 6%) (11 μ m in particle diameter).

Column temperature: A constant temperature of about 75°C.

Mobile phase: Water.

Flow rate: Adjust the flow rate so that the retention time of lactulose is about 18 minutes.

System suitability—

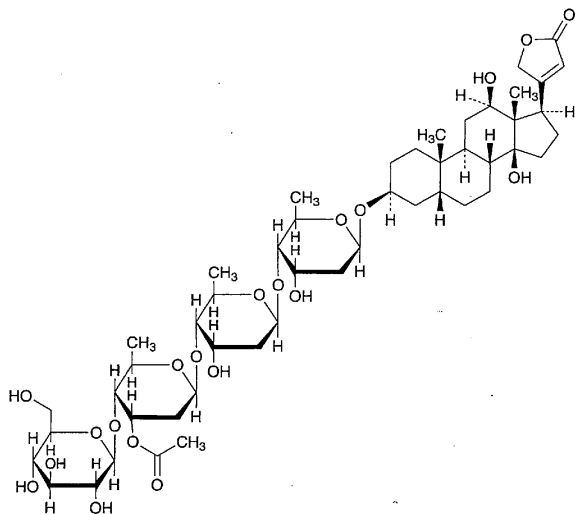
System performance: When the procedure is run with 10 μ L of the standard solution under the above operating conditions, lactulose and the internal standard are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 20 μ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak heights of lactulose, galactose and lactose to the height of the internal standard are not more than 2.0%, respectively.

Containers and storage Containers—Tight containers.

Lanatoside C

ラナトシド C



$C_{49}H_{76}O_{20}$: 985.12

3 β -[O- β -D-Glucopyranosyl-(1 \rightarrow 4)-O-3-acetyl-2,6-dideoxy- β -D-ribohexopyranosyl-(1 \rightarrow 4)-O-2,6-dideoxy- β -D-ribohexopyranosyloxy]-12 β ,14-dihydroxy-5 β ,14 β -card-20(22)-enolide [17575-22-3]

Lanatoside C, when dried, contains not less than 90.0% and not more than 102.0% of $C_{49}H_{76}O_{20}$.

Description Lanatoside C occurs as colorless or white crystals or a white, crystalline powder. It is odorless.

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

It is hygroscopic.

Identification Place 1 mg of Lanatoside C to a small test tube having an internal diameter of about 10 mm, dissolve in 1 mL of a solution of iron (III) chloride hexahydrate in acetic acid (100) (1 in 10,000), and underlay gently with 1 mL of sulfuric acid: at the zone of contact of the two liquids, a brown ring is produced, and the color of the upper layer near the contact zone gradually changes to blue through purple. Finally the color of the entire acetic acid layer changes to blue-green through deep blue.

Purity Related substances—Dissolve 0.010 g of Lanatoside C in exactly 5 mL of methanol, and use this solution as the sample solution. Separately, dissolve 1.0 mg of Lanatoside C Reference Standard in exactly 5 mL of methanol, and use this solution as the standard solution. Perform the test as directed under the Thin-layer Chromatography with the sample solution and the standard solution. Spot 20 μ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of dichloromethane, methanol and water (84:15:1) to a distance of about 13 cm, and air-dry the plate. Spray evenly dilute sulfuric acid on the plate, and heat the plate at 110°C for 10 minutes: any spots other than the principal spot from the sample solution are neither larger nor darker than the spot from the standard solution.

Optical rotation $[\alpha]_D^{20}$: +32 – +35° (after drying, 0.5 g, methanol, 25 mL, 100 mm).

Loss on drying Not more than 7.5% (0.5 g, in vacuum, phosphorus (V) oxide, 60°C, 4 hours).

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

Assay Weigh accurately about 0.05 g each of Lanatoside C and Lanatoside C Reference Standard, previously dried, and dissolve in methanol to make exactly 25 mL. Pipet 5 mL each of these solutions, add methanol to make exactly 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Pipet 5 mL each of the sample solution and the standard solution into 25-mL light-resistant, volumetric flasks, and add 5 mL of 2,4,6-trinitrophenol TS and 0.5 mL of a solution of sodium hydroxide (1 in 10), shake well, and add methanol to make 25 mL. Allow these solutions to stand between 18°C and 22°C for 25 minutes, and determine the absorbances, A_T and A_S , of the solutions at 485 nm as directed under the Ultraviolet-visible Spectrophotometry, using a solution prepared with 5 mL of methanol in the same manner as the blank solution.

$$\begin{aligned} & \text{Amount (mg) of } C_{49}H_{76}O_{20} \\ &= \text{amount (mg) of Lanatoside C Reference Standard} \\ & \quad \times \frac{A_T}{A_S} \end{aligned}$$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Lanatoside C Tablets

ラナトシド C 錠

Lanatoside C Tablets contain not less than 90%

and not more than 110% of the labeled amount of lanatoside C ($C_{49}H_{76}O_{20}$: 985.12).

Method of preparation Prepare as directed under Tablets, with Lanatoside C.

Identification (1) Shake a quantity of powdered Lanatoside C Tablets, equivalent to 1 mg of Lanatoside C according to the labeled amount, with 3 mL of diethyl ether, and filter. Wash the residue with two 3-mL portions of diethyl ether, and air-dry. To the remaining residue add 10 mL of a mixture of chloroform and methanol (9:1), shake, and filter. Wash the residue with two 5-mL portions of a mixture of chloroform and methanol (9:1), combine the filtrate and washings, and evaporate on a water bath to a smaller volume. Transfer the solution to a small test tube having an internal diameter of about 10 mm, further evaporate on a water bath to dryness, and proceed as directed in the Identification under Lanatoside C.

(2) Perform the test with the sample solution and the standard solution obtained in the Assay as directed under the Thin-layer Chromatography. Spot 25 μ L each of these solutions on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of dichloromethane, methanol and water (84:15:1) to a distance of about 13 cm, and air-dry the plate. Spray evenly dilute sulfuric acid on the plate, and heat the plate at 110°C for 10 minutes: the spots obtained from the sample solution and the standard solution show a black color, and have the same *R_f* values.

Dissolution test Take 1 tablet of Lanatoside C Tablets, and perform the test with 500 mL of diluted hydrochloric acid (3 in 500) deaired by a suitable method as the test solution at 100 revolutions per minute as directed in Method 2 under the Dissolution Test. Take 20 mL of the dissolved solution at 60 minutes after starting the test, and filter through a membrane filter (not more than 0.8 μ m). Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, dry Lanatoside C Reference Standard in vacuum over phosphorus (V) oxide at 60°C for 4 hours, weigh accurately a portion of it, equivalent to 100 times an amount of the labeled amount of lanatoside C ($C_{49}H_{76}O_{20}$), dissolve in ethanol (95) to make exactly 100 mL. Pipet 1 mL of this solution, add the test solution to make exactly 500 mL, warm at 37 \pm 0.5°C for 60 minutes, and use this solution as the standard solution. Pipet 3 mL each of the sample solution, the standard solution and the test solution, and transfer to glass-stoppered brown test tubes T, S and B, respectively. To these solutions add exactly 10 mL each of 0.012 w/v% L-ascorbic acid-hydrochloric acid TS, and shake. Immediately add exactly 0.2 mL each of diluted hydrogen peroxide TS (1 in 100), shake well, and allow to stand at a constant temperature between 30°C and 37°C for 45 minutes. Determine immediately the fluorescence intensities, *F_T*, *F_S* and *F_B*, of the sample solution and the standard solution at 355 nm of the excitation wavelength and at 490 nm of the fluorescence wavelength as directed under the Fluorometry.

Dissolution rate of each of six Lanatoside C Tablets after 60 minutes should be not less than 65%.

Requirement of retest is not applied to Lanatoside C Tablets.

Dissolution rate (%) to labeled amount of lanatoside C ($C_{49}H_{76}O_{20}$)

$$= W_S \times \frac{F_T - F_B}{F_S - F_B} \times \frac{1}{C}$$

W_S: Amount (mg) of Lanatoside C Reference Standard.
C: Labeled amount (mg) of lanatoside C ($C_{49}H_{76}O_{20}$) in each tablet.

Content uniformity Warm 1 tablet of Lanatoside C Tablets with 5 mL of water until the tablet is disintegrated, add 30 mL of ethanol (95), disperse finely the particles with the aid of ultrasonic radiation, add ethanol (95) to make exactly *V* mL of a solution containing about 5 μ g of lanatoside C ($C_{49}H_{76}O_{20}$) in each mL, and filter. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.025 g of Lanatoside C Reference Standard, previously dried in vacuum over phosphorus (V) oxide at 60°C for 4 hours, and dissolve in ethanol (95) to make exactly 100 mL. Pipet 2 mL of this solution, add 10 mL of water, add ethanol (95) to make exactly 100 mL, and use this solution as the standard solution. Pipet 2 mL each of the sample solution, the standard solution and diluted ethanol (95) (17 in 20) into three brown glass-stoppered test tubes T, S and B, previously containing exactly 10 mL of 0.012 w/v% L-ascorbic acid-hydrochloric acid TS, add exactly 1 mL each of dilute hydrogen peroxide TS immediately, shake vigorously, and allow to stand at a constant temperature between 25°C and 30°C for 40 minutes. Determine the fluorescence intensities, *F_T*, *F_S* and *F_B*, of the subsequent solutions from the sample solution and the standard solution and the diluted ethanol (95) (17 in 20) at 355 nm of the excitation wavelength and at 490 nm of the fluorescence wavelength as directed under the Fluorometry, respectively.

$$\begin{aligned} &\text{Amount (mg) of lanatoside C (} C_{49}H_{76}O_{20} \text{)} \\ &= \text{amount (mg) of Lanatoside C Reference Standard} \\ &\quad \times \frac{F_T - F_B}{F_S - F_B} \times \frac{V}{5000} \end{aligned}$$

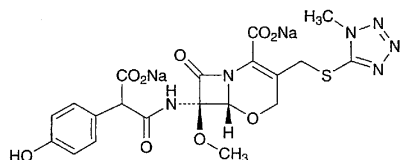
Assay Weigh accurately and powder not less than 20 Lanatoside C Tablets. Weigh accurately a portion of the powder, equivalent to about 5 mg of lanatoside C ($C_{49}H_{76}O_{20}$), into a 100-mL light-resistant volumetric flask, add 50 mL of ethanol (95), and shake for 15 minutes. Then dilute with ethanol (95) to make exactly 100 mL. Filter this solution, discard the first 20 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 5 mg of Lanatoside C Reference Standard, previously dried in vacuum over phosphorus (V) oxide at 60°C for 4 hours, dissolve in ethanol (95) to make exactly 100 mL, and use this solution as the standard solution. Pipet 5 mL each of the sample solution and the standard solution into light-resistant, glass-stoppered test tubes, add 3 mL each of alkaline 2,4,6-trinitrophenol TS, shake well and allow these solutions to stand between 22°C and 28°C for 25 minutes. Determine the absorbances, *A_T* and *A_S*, of the subsequent sample solution and the subsequent standard solution at 490 nm as directed under the Ultraviolet-visible Spectrophotometry, using a solution, prepared by the same manner with 5 mL of ethanol (95), as the blank.

$$\begin{aligned} &\text{Amount (mg) of lanatoside C (} C_{49}H_{76}O_{20} \text{)} \\ &= \text{amount (mg) of Lanatoside C Reference Standard} \\ &\quad \times \frac{A_T}{A_S} \end{aligned}$$

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

Latamoxef Sodium

ラタモキセフナトリウム



$C_{20}H_{18}N_6Na_2O_9S$: 564.44

Disodium (6*R*,7*R*)-7-[2-carboxylato-2-(4-hydroxyphenyl)acetamino]-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-oxa-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [64953-12-4]

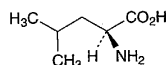
Latamoxef Sodium conforms to the requirements of Latamoxef Sodium in the Requirements for Antibiotic Products of Japan.

Description Latamoxef Sodium occurs as white to light yellowish white powder or masses.

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

L-Leucine

L-ロイシン



$C_6H_{13}NO_2$: 131.17

(2*S*)-2-Amino-4-methylpentanoic acid [61-90-5]

L-Leucine, when dried, contains not less than 98.5% of $C_6H_{13}NO_2$.

Description L-Leucine occurs as white crystals or crystalline powder. It is odorless or has a faint characteristic odor, and has a slightly bitter taste.

It is freely soluble in formic acid, sparingly soluble in water, and practically insoluble in ethanol (95).

It dissolves in dilute hydrochloric acid.

Identification Determine the infrared absorption spectrum of L-Leucine, 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.

Optical rotation $[\alpha]_D^{20}$: +14.5 – +16.0° (after drying, 1 g, 6 mol/L hydrochloric acid TS, 25 mL, 100 mm).

pH Dissolve 1.0 g of L-Leucine in 100 mL of water: the pH of this solution is between 5.5 and 6.5.

Purity (1) Clarity and color of solution—Dissolve 0.5 g of L-Leucine in 10 mL of 1 mol/L hydrochloric acid TS: the solution is clear and colorless.

(2) Chloride—Dissolve 0.5 g of L-Leucine in 40 mL of water and 6 mL of dilute nitric acid, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.30 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.021%).

(3) Sulfate—Dissolve 0.6 g of L-Leucine in 40 mL of water and 1 mL of dilute hydrochloric acid, and add 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 0.028%).

(4) Ammonium—Perform the test with 0.25 g of L-Leucine. Prepare the control solution with 5.0 mL of Standard Ammonium Solution (not more than 0.02%).

(5) Heavy metals—Proceed with 1.0 g of L-Leucine according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(6) Arsenic—Prepare the test solution with 1.0 g of L-Leucine according to Method 2, and perform the test using Apparatus B (not more than 2 ppm).

(7) Other amino acids—Dissolve 0.10 g of L-Leucine by warming, after cooling, add water to make 25 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add water to make exactly 50 mL. Pipet 5 mL of this solution, add water to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water and acetic acid (100) (3:1:1) to a distance of about 10 cm, and dry the plate at 80°C for 30 minutes. Spray evenly a solution of ninhydrin in acetone (1 in 50) on the plate, and heat at 80°C for 5 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 0.30% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.13 g of L-Leucine, previously dried, and dissolve in 3 mL of formic acid, add 50 mL of acetic acid (100), 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
= 13.117 mg of $C_6H_{13}NO_2$

Containers and storage Containers—Well-closed containers.