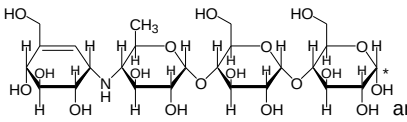
Acarbose

アカルボース



$C_{25}H_{43}NO_{18}$: 645.60

O-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose

[*56180-94-0*]

Acarbose is an olygosaccharide having α-amylase and β-amylase inhibiting activity produced by the growth of *Actinoplanes utahensis*.

Acarbose contains not less than 95.0% and not more than 101.0% of acarbose ($C_{25}H_{43}NO_{18}$), calculated on the anhydrous basis.

Description Acarbose occurs as a white to light yellow powder.

It is very soluble in water, soluble in methanol, and slightly soluble in ethanol (99.5).

It is hygroscopic.

Identification Determine the infrared absorption spectrum of Acarbose as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>, and compare the spectrum with the Reference Spectrum or the spectrum of Acarbose RS: both spectra exhibit similar intensities of absorption at the same wave numbers.

Optical rotation <*2.49*> $[\alpha]_D^{20}$: + 171 – + 181° (0.5 g calculated on the anhydrous basis, water, 50 mL, 100 mm).

pH <*2.54*> Dissolve 1.0 g of Acarbose in freshly boiled and cooled water to make 20 mL: the pH of this solution is between 5.5 and 7.5.

Purity **(1)** Chloride <*1.03*>－Perform the test with 0.10 g of Acarbose. Prepare the control solution with 1.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.496%).

(2) Heavy metals <*1.07*>－Proceed with 2.0 g of Acarbose according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Related substances－Use the sample solution obtained in the Assay as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine each peak area by the automatic integration method: the peak area of the related substance D having the relative retention time of about 0.5 to acarbose from the sample solution is not larger than the peak area of acarbose from the standard solution, the peak areas of the related substance B having the relative retention time of about 0.8 to acarbose, the related substance A having the relative retention time of about 0.9, the related substance C having the relative retention time of about 1.2, the related substance E having the relative retention time of about 1.7, the related substance F having the relative retention time of about 1.9 and the related substance G having the relative retention time of about 2.2 from the sample solution are not larger than 1/2, 3/5, 1.5, 1/5, 3/10 and 3/10 times the peak area of acarbose from the standard solution, respectively, and the area of the peak other than acarbose and the peaks mentioned above from the sample solution is not larger than 1/5 times the peak area of acarbose from the standard solution. Furthermore, the total area of the peaks of the related substance D, B, A, C, E, F and G from the sample solution is not larger than 3 times the peak area of acarbose from the standard solution. For the peak areas of the related substance D, B, E, F and G, multiply their relative response factors, 0.75, 0.63, 1.25, 1.25 and 1.25, respectively.

Operating conditions－

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

Time span of measurement: About 2.5 times as long as the retention time of acarbose.

System suitability－

System performance: Proceed as directed in the system suitability in the Assay.

Test for required detectability: To 5 mL of the standard solution add water to make 100 mL. When the procedure is run with this solution under the above operating conditions, the SN ratio of the peak of acarbose is more than 10.

System repeatability: Pipet 1 mL of the standard solution obtained in the Assay, and add water to make exactly 100 mL. When the test is repeated 6 times with 10 μL of this solution under the above operating conditions, the relative standard deviation of the peak area of acarbose is not more than 2.0%.

Water <*2.48*> Not more than 4.0% (0.3 g, volumetric titration, direct titration).

Residue on ignition <*2.44*> Not more than 0.2% (1 g).

Assay Weigh accurately about 0.1 g of Acarbose, dissolve in water to make exactly 5 mL, and use this solution as the sample solution. Separately, weigh about 0.1 g of Acarbose RS (separately determine the water <*2.48*> in the same manner as Acarbose), add exactly 5 mL of water, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak areas, A_T and A_S, of acarbose in each solution.

$$\text{Amount (mg) of acarbose } (C_{25}H_{43}NO_{18}) = M_S \times A_T / A_S$$

M_S: Amount (mg) of Acarbose RS taken, calculated on the anhydrous basis

Operating conditions —

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

Column: A stainless steel column 4 mm in inside diameter and 25 cm in length, packed with aminopropylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 35℃.

Mobile phase: Dissolve 0.60 g of potassium dihydrogenphosphate and 0.35 g of disodium hydrogenphosphate dihydrate in 1000 mL of water. To 250 mL of this solution add 750 mL of acetonitrile for liquid chromatography.

Flow rate: 2.0 mL per minute.

System suitability —

System performance: Dissolve Acarbose RS for System Suitability in water to make a solution so that each mL contains 20 mg/mL. When the procedure is run with 10 μL of this solution under the above operating conditions, the peaks of the related substance D having the relative retention time of about 0.5 to acarbose, the related substance B having the relative retention time of about 0.8, the related substance A having the relative retention time of about 0.9, the related substance C having the relative retention time of about 1.2, the related substance E having the relative retention time of about 1.7, the related substance F having the relative retention time of about 1.9 and the related substance G having the relative retention time of about 2.2 are observed, and the peak-valley ratio between the peaks of the related substance A and acarbose is not less than 1.2.

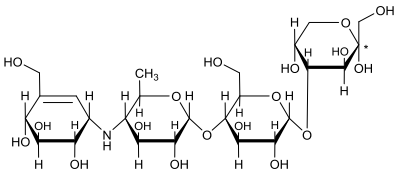
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of acarbose is not more than 1.0%.

Containers and storage Containers — Tight containers.

Others

Related substance A:

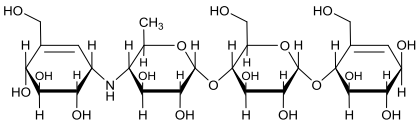
O-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-*arabino*-hex-2-ulopyranose



and epimer at C*

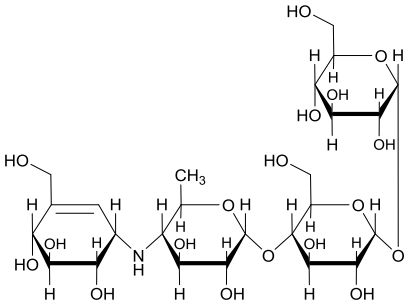
Related substance B:

(1*R*,4*R*,5*S*,6*R*)-4,5,6-Trihydroxy-2-(hydroxymethyl)cyclohex-2-en-1-yl 4-*O*-(4,6-dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl)-α-D-glucopyranoside



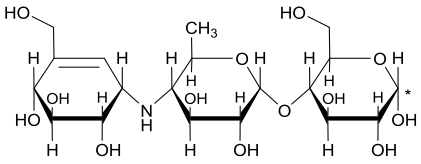
Related substance C:

α-D-Glucopyranosyl 4-*O*-(4,6-dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl)-α-D-glucopyranoside



Related substance D:

4-*O*-(4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl)-D-glucopyranose



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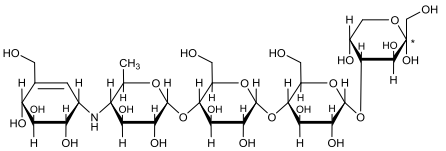
Related substance E:

O-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-*arabino*-hex-2-ulopyranose (4-*O*-α-Acarbosyl-D-fructopyranose)

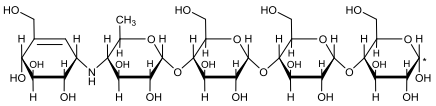


and epimer at C*

Related substance F:

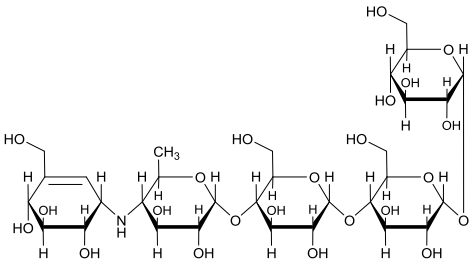
O-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-

glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose (4-*O*-α-Acarbosyl-D-glucopyranose)


and epimer at C*

Related substance G:

α-D-Glucopyranosyl *O*-4,6-dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl]amino}-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranoside (α-D-Glucopyranosyl α-acarboside)



Add the following to 9.01 Reference Standards (1):

Acarbose RS

Acarbose RS for System Suitability

Add the following to 9.41 Reagents, Test Solutions:

Disodium hydrogenphosphate dihydrate $Na_2HPO_4.2H_2O$ Colorless crystals or white crystalline powder. Soluble in water, and practically insoluble in ethanol (95).