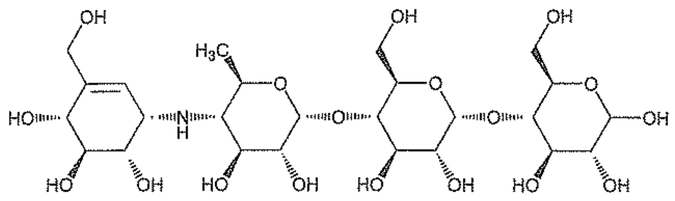
Acarbose



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

D-Glucose, *O*-4,6-dideoxy-4-[[[1*S*-(1α,4α,5β,6α)]-4,5,6-trihydroxy-3-(hydroxymethyl)-2-cyclohexen-1-yl]amino]-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-;
O-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)-2-cyclohexen-1-yl]amino}-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucose [56180-94-0].

DEFINITION

Acarbose is produced by certain strains of *Actinoplanes utahensis*. It contains NLT 95.0% and NMT 102.0% of acarbose ($C_{25}H_{43}NO_{18}$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 0.6 mg/mL of monobasic potassium phosphate and 0.35 mg/mL of dibasic sodium phosphate in water
Mobile phase: Acetonitrile and *Solution A* (3:1)
System suitability solution: 20 mg/mL of USP Acarbose System Suitability Mixture RS in water
Standard solution: 20 mg/mL of USP Acarbose RS in water
Sample solution: 20 mg/mL of Acarbose in water
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 210 nm
Column: 4-mm × 25-cm; packing L8
Column temperature: 35°
Flow rate: 2 mL/min
Injection volume: 10 µL
System suitability
Sample: *System suitability solution*
Identify the acarbose peak and the peaks due to the impurities listed in *Table 1*.
Suitability requirements
Peak-to-valley ratio: The ratio of the height of the impurity A peak to the height of the valley between the impurity A peak and the acarbose peak is NLT 1.2.
Chromatogram comparability: The chromatogram obtained is similar to the chromatogram provided with USP Acarbose System Suitability Mixture RS for the known impurities found.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of acarbose ($C_{25}H_{43}NO_{18}$) in the portion of Acarbose taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Acarbose RS in the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition** ⟨281⟩
Sample: 1.0 g
Acceptance criteria: NMT 0.2%

Delete the following:

- **Heavy Metals,** *Method II* ⟨231⟩**:** NMT 20 ppm (Official 1-Jan-2018)

- **Chromatographic Purity**
Mobile phase, System suitability solution, Sample solution, and Chromatographic system: Proceed as directed in the *Assay*.
Diluted sample solution: Dilute 1.0 mL of the *Sample solution* with water to 100.0 mL.
Analysis
Samples: *Sample solution* and *Diluted sample solution*
Calculate the percentage of each impurity in the portion of Acarbose taken:

$$\text{Result} = (r_U/r_A) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_A = peak response of the main acarbose peak from the *Diluted sample solution*
F = relative response factor for each impurity (see *Table 1*)
Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Impurity A[a]	0.9	1	0.6
Impurity B[b]	0.8	1.6	0.5
Impurity C[c]	1.2	1	1.5
Impurity D[d]	0.5	1.33	1.0
Impurity E[e]	1.7	0.8	0.2
Impurity F[f]	1.9	0.8	0.3
Impurity G[g]	2.2	0.8	0.3
Impurity H[h]	0.6	1	0.2

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

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

[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-enyl]amino}-α-D-glucopyranosyl]-α-D-glucopyranoside.

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

[e] *O*-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-enyl]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).

[f] *O*-4,6-Dideoxy-4-{[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-enyl]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).

[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-enyl]amino}-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-*O*-α-D-glucopyranoside (α-D-glucopyranosyl α-acarboside).

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