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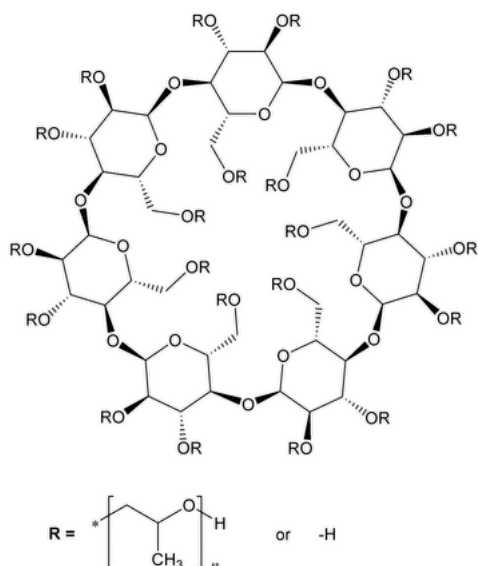
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Hydroxypropyl Betadex



$$\text{C}_{42}\text{H}_{70}\text{O}_{35}(\text{C}_3\text{H}_6\text{O})_x \text{ where } x = 7 \times \text{MS, MS being molar substitution}$$

Beta cyclodextrin, 2-hydroxypropyl ether

CAS RN®: 128446-35-5.

DEFINITION

Hydroxypropyl Betadex is a partially substituted poly(hydroxypropyl) ether of Betadex. The number of hydroxypropyl groups per anhydroglucose unit expressed as molar substitution (MS) is NLT 0.40 and NMT 1.50 and is within 10% of the value stated on the label.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K.** The spectrum obtained with Hydroxypropyl Betadex shows the same absorption bands as the spectrum acquired with [USP Hydroxypropyl Betadex RS](#). Due to the difference in the substitution of the substance, the intensity of some absorption bands may vary.
- **B.** It meets the requirements of the test for *Clarity of Solution*.

ASSAY

• MOLAR SUBSTITUTION

(See [Nuclear Magnetic Resonance Spectroscopy \(761\)](#).)

The molar substitution (MS) is calculated from the ratio between the signal from the three protons of the methyl group, contained in the hydroxypropyl functional group, and the signal from the proton attached to the carbon C₁ (glycosidic proton) of the anhydroglucose units.

Use a Fourier-transform nuclear magnetic resonance (NMR) spectrometer having a magnetic field strength of at least 6 Tesla and that is capable of performing quantitative analysis using proton NMR spectroscopy at a temperature of at least 25°.

Sample solution: Mix NLT the equivalent of 10.0 mg of dried Hydroxypropyl Betadex with 0.75 mL of deuterium oxide thoroughly in an NMR tube. Place the tube into an NMR probe.

Analysis: Adjust the spectrometer settings so that a high-resolution proton NMR spectrum can be acquired that will provide quantitative data.

Acquire a free induction decay (FID) with at least 8 transients using a spectral window from at least 0–6.2 ppm, with the solvent peak located at 4.8 ppm at 25°. Zero fill the spectrum at least three times, and Fourier transform the FID with no Gaussian line broadening and no more than 0.2 Hz of Lorentzian line broadening.

Determine the peak areas of the doublet from the methyl protons of the hydroxypropyl functional group at 1.2 ppm (A₁) and the peak areas from the glycosidic protons, which are located between 5 and 5.4 ppm (A₂).

Calculate the MS:

$$\text{Result} = A_1 / (3A_2)$$

A_1 = area of the methyl group of hydroxypropyl

A_2 = area of the glycosidic proton

The degree of substitution is the number of hydroxypropyl groups per molecule of betadex and is obtained by multiplying the MS by 7.

Acceptance criteria: 0.40–1.50 and within 10% of the value stated on the label

IMPURITIES

Change to read:

• LIMIT OF BETADEX, PROPYLENE GLYCOL, AND OTHER RELATED SUBSTANCES

Mobile phase: Water

Standard solution A: 15 mg/mL of [USP Beta Cyclodextrin RS](#) and 25 mg/mL of [USP Propylene Glycol RS](#)

Standard solution B: 1.0 mL of *Standard solution A* diluted with water to 10.0 mL

Sample solution: Dissolve 2.50 g of Hydroxypropyl Betadex, accurately weighed and calculated on the dried basis, in water with the aid of heat. Cool, and dilute with water to 25.0 mL. The resulting solution is 100 mg/mL of Hydroxypropyl Betadex, calculated on the dried basis, in water.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: Differential refractometer

Columns

Guard: Packing L11

Analytical: 3.9-mm × 30-cm; packing L11

▲Temperatures

Detector: 40°

Columns: 40° ▲ (ERR 1-Feb-2025)

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solution A* and *Standard solution B*

[NOTE—The retention time of propylene glycol is about 2.5 min, and the relative retention times with reference to that of propylene glycol for betadex and hydroxypropyl betadex are about 4.2 and about 6, respectively; Hydroxypropyl Betadex elutes as a very wide peak or several peaks.]

Suitability requirements

Resolution: NLT 4 between betadex and propylene glycol, *Standard solution A*

Relative standard deviation: NMT 2.0%, *Standard solution B*

Analysis

Samples: *Standard solution B* and *Sample solution*

Acceptance criteria: Disregard any peaks eluting before propylene glycol and after the hydroxypropyl betadex peak.

Betadex: NMT 1.5%; the area of the betadex peak in the *Sample solution* is NMT the area of the corresponding peak from *Standard solution B*.

Propylene glycol: NMT 2.5%; the area of the propylene glycol peak in the *Sample solution* is NMT the area of the corresponding peak from *Standard solution B*.

Any other single impurity: NMT 0.25%; the area from any other single impurity peak is NMT 0.1 times the area of propylene glycol in the chromatogram of *Standard solution B*.

Total impurities excluding betadex and propylene glycol: NMT 1%; the total area from all impurity peaks, excluding betadex and propylene glycol, is NMT 0.4 times the area of propylene glycol from *Standard solution B*.

Disregard limit: 0.1%; disregard any peaks that are less than 0.04 times the area of propylene glycol from *Standard solution B*.

• LIMIT OF PROPYLENE OXIDE

Ether stock solution: Add 75 µL of ether to 30 mL of dimethylacetamide in a 50-mL volumetric flask, dilute with dimethylacetamide to volume, and mix. This solution contains 1.0 mg/mL of ether.

Internal standard solution: Add 30 µL of *Ether stock solution* to 70 mL of dimethylacetamide in a 100-mL volumetric flask, dilute with dimethylacetamide to volume, and mix.

Propylene oxide stock solution

[CAUTION—Propylene oxide is toxic and flammable. Prepare this solution in a well-ventilated fume hood.]

Add 30 mL of dimethylacetamide into a 50-mL volumetric flask. Weigh the flask and contents accurately, add 60 µL of propylene oxide (cooled in a refrigerator) into the flask with a 100-µL cooled microsyringe, weigh again, and calculate the weight of propylene oxide added, by difference. Dilute with dimethylacetamide to volume, and mix. This solution contains 1.0 mg/mL of propylene oxide.