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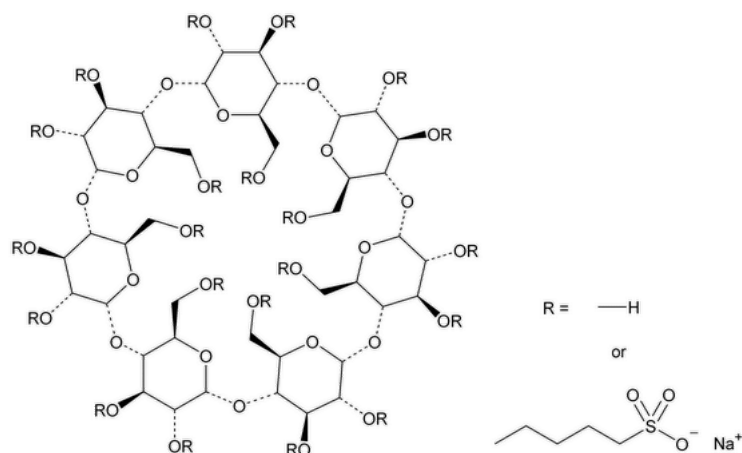
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Betadex Sulfobutyl Ether Sodium


 $\text{C}_{42}\text{H}_{70-n}\text{O}_{35} \cdot (\text{C}_4\text{H}_8\text{SO}_3\text{Na})_n$ 2163 when $n = 6.5$

Beta cyclodextrin sulfobutyl ethers, sodium salts;

Beta cyclodextrin sulfobutyl ether sodium CAS RN®: 182410-00-0.

DEFINITION

Betadex Sulfobutyl Ether Sodium is prepared by alkylation of betadex using 1,4-butane sultone under basic conditions. The average degree of substitution in betadex is NLT 6.2 and NMT 6.9. It contains NLT 95.0% and NMT 105.0% of $\text{C}_{42}\text{H}_{70-n}\text{O}_{35} \cdot (\text{C}_4\text{H}_8\text{SO}_3\text{Na})_n$ ($n = 6.2\text{--}6.9$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K ▲](#) (CN 1-MAY-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **C.** It meets the requirements of the test for *Average Degree of Substitution*.
- **D.** [IDENTIFICATION TESTS—GENERAL, Sodium \(191\).](#)

ASSAY

PROCEDURE

Mobile phase: 0.1 M potassium nitrate in a mixture of acetonitrile and water (1:4)

Standard solution: 10 mg/mL of [USP Betadex Sulfobutyl Ether Sodium RS](#) in *Mobile phase*

Sample solution: 10 mg/mL of Betadex Sulfobutyl Ether Sodium in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: Refractive index

Detector temperature: $35 \pm 2^\circ$

Column: 7.8-mm $\times$ 30-cm analytical column; packing L37. [NOTE—Rinse the column with a solution of acetonitrile and water (1:9) at the completion of the run series.]

Flow rate: 1.0 mL/min

Injection size: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of betadex sulfobutyl ether sodium $[C_{42}H_{70-n}O_{35} \cdot (C_4H_8SO_3Na)_n]$ in the portion of Betadex Sulfobutyl Ether Sodium taken:

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

r_U = peak response for betadex sulfobutyl ether sodium from the *Sample solution*

r_S = peak response for betadex sulfobutyl ether sodium from the *Standard solution*

C_S = concentration of [USP Betadex Sulfobutyl Ether Sodium RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Betadex Sulfobutyl Ether Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0% on the anhydrous basis

IMPURITIES• **LIMIT OF BETA CYCLODEXTRIN (BETADEX)**

Solution A: 25 mM sodium hydroxide

Solution B: 250 mM sodium hydroxide and 1 M potassium nitrate

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4	100	0
5	0	100
10	0	100
11	100	0
20	100	0

Standard solution: 2 µg/mL of [USP Beta Cyclodextrin RS](#)

Sample solution: 2 mg/mL of Betadex Sulfobutyl Ether Sodium

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#) and [Ion Chromatography \(1065\)](#).)

Mode: IC

Detector: Pulsed amperometry (amperometric cell with gold working electrode and silver reference electrode)

Column

Guard: 4.0-mm × 5-cm anion-exchange; packing L61

Analytical: 4.0-mm × 25-cm anion-exchange; packing L61

Column temperature: 50 ± 2°

Flow rate: 1.0 mL/min

Injection size: 20 µL

Waveform for pulsed amperometric detector: See [Table 2](#).

Table 2

Time (s)	Voltage (V)
0.00	0.10
0.30	Start integration
0.50	0.10
0.50	Stop integration

Time (s)	Voltage (V)
0.51	0.60
0.59	0.60
0.60	-0.60
0.65	-0.60

System suitability**Sample:** *Standard solution***Suitability requirements****Relative standard deviation:** NMT 5.0%**Analysis****Samples:** *Standard solution and Sample solution*

Calculate the percentage of beta cyclodextrin (betadex) in the portion of Betadex Sulfobutyl Ether Sodium taken:

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

 r_U = peak response for beta cyclodextrin from the *Sample solution* r_S = peak response for beta cyclodextrin from the *Standard solution* C_S = concentration of [USP Beta Cyclodextrin RS](#) in the *Standard solution* (µg/mL) C_U = concentration of Betadex Sulfobutyl Ether Sodium in the *Sample solution* (mg/mL) F = conversion factor (10^{-3} mg/µg)**Acceptance criteria:** NMT 0.1%**• LIMIT OF 1,4-BUTANE SULTONE****Internal standard solution:** 0.25 µg/mL of diethyl sulfone**Standard stock solution A:** 0.5 µg/mL of 1,4-butane sultone**Standard stock solution B:** 1.0 µg/mL of 1,4-butane sultone**Standard stock solution C:** 2.0 µg/mL of 1,4-butane sultone**Sample stock solution:** 250 mg/mL of Betadex Sulfobutyl Ether Sodium in the *Internal standard solution*

Blank solution, and Sample solutions A, B, C, and D: Follow [Table 3](#) to place the quantities of *Internal standard solution*, each *Standard stock solution*, *Sample stock solution*, water, or methylene chloride in each glass test tube with a stopper. [NOTE—A screw-capped, 10-mL test tube is suitable.] Mix on a vortex mixer each test tube for 30 s, and allow it stand for at least 5 min or until complete separation of the phase. Extract the organic phase into a GC vial and seal. [NOTE—With great care take the minimum possible amount of aqueous phase.] Added quantities of 1,4-butane sultone in *Sample solutions A, B, C, and D* are 0.5, 1.0, 2.0, and 0 µg, respectively.

Table 3

Sample Name	Solution 1 Added (mL)	Solution 2 Added (mL)	Methylene Chloride Added (mL)
Blank solution	Internal standard solution, 4.0	Water, 1.0	1.0
Sample solution A	Sample stock solution, 4.0	Standard stock solution A, 1.0	1.0
Sample solution B	Sample stock solution, 4.0	Standard stock solution B, 1.0	1.0
Sample solution C	Sample stock solution, 4.0	Standard stock solution C, 1.0	1.0
Sample solution D	Sample stock solution, 4.0	Water, 1.0	1.0

[NOTE—Prepare immediately before use.]