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Low-Substituted Hydroxypropyl Cellulose

Portions of this monograph that are national *USP* text, and are not part of the harmonized text, are marked with symbols (◆ ◆) to specify this fact.

Change to read:

Cellulose, 2-hydroxypropyl ether

CAS RN®: 9004-64-2▲ ▲ (NF 1-Aug-2024) .

DEFINITION

Low-Substituted Hydroxypropyl Cellulose is a low-substituted *O*-(2-hydroxypropylated) cellulose. It contains NLT 5.0% and NMT 16.0% of hydroxypropoxy groups ($-OCH_2CHOHCH_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K▲ ▲ (NF 1-Aug-2024)
- **B.**

  Sample: 0.1 g

  Analysis: Shake the *Sample* thoroughly with 10 mL of water.

  Acceptance criteria: It does not dissolve.
- **C.**

  Sample solution: To the suspension obtained in *Identification B* add 1 g of sodium hydroxide and shake until it becomes homogeneous.

  Analysis: Transfer 5 mL of *Sample solution* to a suitable container, add 10 mL of a mixture of acetone and methanol (4:1), and shake.

  Acceptance criteria: A white, flocculent precipitate is formed.

ASSAY

Change to read:

- **Hydroxypropoxy Groups**

  [Caution—Hydriodic acid and its reaction byproducts are highly toxic. Perform all steps of the *Standard solution* and the *Sample solution* in a properly functioning hood. Specific safety practices to be followed are to be identified to the analyst performing this test.]

  Apparatus: For the reaction vial, use a 5-mL pressure-tight serum vial,▲ ▲ (NF 1-Aug-2024) equipped with a pressure-tight septum with a polytetrafluoroethylene-faced butyl rubber and an air-tight seal using an aluminum crimp or any sealing system that provides sufficient air-tightness. Use a heater with a heating module that has a square-shape aluminum block with holes▲ ▲ (NF 1-Aug-2024) , into which the reaction vial fits. The heating module is also equipped with a magnetic stirrer capable of mixing the contents of the vial, or use a reciprocal shaker that performs a reciprocating motion of approximately 100 times/min.

  Hydriodic acid**:** Use a reagent with a typical concentration of hydrogen iodide (HI) of about 57%.

  Internal standard solution: 30 mg/mL of *n*-octane in *o*-xylene

  Standard solution: Into a suitable serum vial, weigh between 60 and 100 mg of adipic acid, and add 2.0 mL of Hydriodic acid and 2.0 mL of *Internal standard solution* into the vial. Close the vial securely with a suitable septum stopper. Weigh the vial and contents, add 15–22 µL of isopropyl iodide through the septum with a syringe, weigh again, and calculate the weight of isopropyl iodide added, by difference. Shake the reaction vial well, and use the upper layer as the *Standard solution*.

  Sample solution: Transfer 0.065 g of Low-Substituted Hydroxypropyl Cellulose to a 5-mL, thick-walled reaction vial equipped with a pressure-tight septum-type closure, add between 60 and 100 mg of adipic acid, and pipet 2.0 mL of *Internal standard solution* into the vial. Cautiously pipet 2.0 mL of Hydriodic acid into the mixture, immediately cap the vial tightly, and weigh. Using the magnetic stirrer equipped in the heating module, or using a reciprocal shaker, mix the contents of the vial continuously, heating and maintaining the temperature of the contents at 130 ± 2° for 60 min. If a reciprocal shaker or magnetic stirrer cannot be used, shake the vial well by hand at 5-min intervals during the initial 30 min of the heating time. Allow the vial to cool, and weigh. If the weight loss is less than 26 mg and there is no evidence of a leak, use the upper layer of the mixture as the *Sample solution*.

  Chromatographic system

  (See *Chromatography ⟨621⟩,System Suitability*.)

Mode: GC

Detector: Thermal conductivity or hydrogen flame ionization

Column: 0.53-mm × 30-m fused silica capillary, coated with a 3-µm layer of phase G1. Use a guard column if necessary.

Temperatures

Detector: 280°

Injection port: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	0	50	3
50	10	100	—
100	34.9	250	8

Carrier gas: Helium

Flow rate: With the *Standard solution*, adjust the flow rate so that the retention time of the internal standard is about 10 min (about 4.3 mL/min). [NOTE—The relative retention time for isopropyl iodide (with reference to the *n*-octane) is about 0.8.]

Injection volume: 1–2 µL

Injection type: Split; split ratio 40:1

Run time: 20.3 min

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 5 between isopropyl iodide and *n*-octane

Relative standard deviation: NMT 2.0%, using the peak area ratio between isopropyl iodide and the internal standard for 6 injections

Analysis

Samples: Upper layer of the *Standard solution* and the *Sample solution*

Calculate the percentage of hydroxypropoxy in the sample taken:

$$\text{Result} = (Q_{Tb}/Q_{Sb}) \times (W_{Sb}/W_U) \times 44.17$$

Q_{Tb} = ratio of the peak area of isopropyl iodide to *n*-octane in the *Sample solution*

Q_{Sb} = ratio of the peak area of isopropyl iodide to *n*-octane in the *Standard solution*

W_{Sb} = weight of isopropyl iodide in the *Standard solution* (mg)

W_U = weight of Low-Substituted Hydroxypropyl Cellulose calculated on the dried basis, taken for the *Sample solution* (mg)

44.17 = molar mass of hydroxypropoxy group/molar mass of isopropyl iodide × 100

Acceptance criteria: 5.0%–16.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩**

Sample: 1.0 g

Acceptance criteria: NMT 0.8%

- ◆**CHLORIDE AND SULFATE ⟨221⟩, *Chloride***

Sample solution: Shake 0.50 g of Low-Substituted Hydroxypropyl Cellulose thoroughly with 30 mL of boiling water, heat on a water bath for 10 min, and filter the supernatant by decantation while hot. Wash the residue thoroughly with 50 mL of boiling water, combine the washings with the filtrate, and add water to make 100 mL after cooling.

Control solution: 0.25 mL of 0.02 N hydrochloric acid

Analysis: Using 10 mL of the *Sample solution* and the *Control solution*, proceed as directed in the chapter, starting with the addition of the nitric acid.

Acceptance criteria: NMT 0.36%; the *Sample solution* shows no more chloride than the *Control solution*.◆

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 10 mg/mL suspension, prepared by evenly distributing 1.0 g of the powder with 100 mL of carbon dioxide-free water and stirring the mixture with a magnetic stirrer

  Acceptance criteria: 5.0–7.5

- **Loss on Drying** ⟨731⟩

  Sample: 1 g

  Analysis: Dry the *Sample* at 105° for 1 h.

  Acceptance criteria: NMT 5.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.

Change to read:

- **USP Reference Standards** ▲⟨11⟩▲ (NF 1-Aug-2024)

  USP Low-Substituted Hydroxypropyl Cellulose RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LOW-SUBSTITUTED HYDROXYPROPYL CELLULOSE	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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