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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.

Cellulose, 2-hydroxypropyl ether

CAS RN®: 9004-64-2.

DEFINITION

Hydroxypropyl Cellulose is partly *O*-(2-hydroxypropylated) cellulose. It contains NLT 53.4% and NMT 80.5% of hydroxypropoxy groups, calculated on the dried basis. It may contain suitable anti-caking agents, such as silica.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K.** [Note—Disregard any peak at about 1719 cm^{-1}.]
- **B.**

Sample: 1 g of Hydroxypropyl Cellulose

Analysis: Dissolve the *Sample* in 100 mL of water. Transfer 1 mL of this solution to a glass plate, and allow the water to evaporate.

Acceptance criteria: A thin film is formed.

ASSAY

- **Hydroxypropoxy Groups**

Internal standard solution: Methylcyclohexane in *o*-xylene (1 in 50)

Standard solution: Weigh accurately 60 mg of adipic acid in a reaction vial, add 2.00 mL of *Internal standard solution*, and 1.0 mL of hydriodic acid. Stopper the vial tightly, and weigh accurately. Inject 25 µL of isopropyl iodide through the septum, and again weigh accurately. Mix well. After phase separation, pierce through the septum of the vial with a cooled syringe, and withdraw a sufficient volume of the upper phase as the *Standard solution*.

Sample solution: Weigh accurately 30 mg of hydroxypropylcellulose (dried substance), and transfer to a reaction vial. Add 60 mg of adipic acid, 2.00 mL of *Internal standard solution*, and 1.0 mL of hydriodic acid. Stopper the vial tightly with the valve, and weigh accurately the reaction vial (total mass before heating). Place the vial in an oven or heat in a suitable heater with continuous stirring, maintaining an internal temperature of 115 ± 2° for 70 min. Allow the vial to cool, and weigh accurately the reaction vial (total mass after heating). If the difference of the total mass before heating to the total mass after heating is more than 10 mg, prepare a new *Sample solution*. After phase separation, pierce through the septum of the vial with a cooled syringe, and withdraw a sufficient volume of the upper phase as the *Sample solution*.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused silica capillary, coated with a 3-µm layer of phase G1

Temperatures

Detector: 280°

Injection port: 180°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	3
40	10	100	—

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	50	250	3

Carrier gas: Helium

Linear velocity: 52 cm/s

Injection volume: 2 µL

Injection type: Split; split ratio, 50:1

Run time: 15 min

System suitability

Sample: *Standard solution*

[NOTE—The relative retention time for isopropyliodide is about 0.8 with reference to methylcyclohexane (retention time about 8 min).]

Suitability requirements

Resolution: NLT 2 between isopropyl iodide and methylcyclohexane

Relative standard deviation: NMT 2.0%, using the response factor calculation (*F*) for six injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the response factor (*F*):

$$F = (A_1 \times W_1 \times C)/(A_2 \times 100)$$

A_1 = peak area of the internal standard from the *Standard solution*

W_1 = weight of isopropyl iodide in the *Standard solution* (mg)

C = content of isopropyl iodide (%)

A_2 = peak area of isopropyl iodide from the *Standard solution*

Calculate the percentage content (m/m) of the hydroxypropoxy group:

$$\text{Result} = (A_4 \times F \times M_1 \times 1.15 \times 100)/(A_3 \times W_2 \times M_2)$$

A_4 = peak area of isopropyl iodide from the *Sample solution*

F = response factor calculated from above

M_1 = molar mass of hydroxypropoxy group, 75.1

1.15 = correction factor to correlate results to previous assay method replaced by this method

A_3 = peak area of the internal standard from the *Sample solution*

W_2 = weight of the sample (dried substance) in the *Sample solution* (mg)

M_2 = molar mass of isopropyl iodide, 170.0

Acceptance criteria: 53.4%–80.5% of hydroxypropoxy groups

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩**

Sample: 1.0 g

Analysis: Proceed as directed in the chapter, using a platinum crucible.

Acceptance criteria: NMT 0.8%

• **SILICA**

[**CAUTION—**Perform the mixing and heating of the mixtures containing hydrofluoric acid in a well-ventilated hood.]

Analysis: If the addition of silica is stated on the label, and if more than 0.2% residue is found from the *Residue on Ignition* test, moisten the residue with water, and add 5 mL of hydrofluoric acid in small portions. Evaporate on a steam bath to dryness, and cool. Add 5 mL of hydrofluoric acid and 0.5 mL of sulfuric acid, and evaporate to dryness. Slowly increase the temperature until all of the acids have been volatilized, and ignite at 1000 ± 25°. Cool in a desiccator, and weigh. The difference between the final weight and the weight of the initially ignited portion represents the weight of silica.

Acceptance criteria: The weight of silica is NMT 0.6%.

Change to read:

• ♦▲Lead ⟨251⟩, *Procedures, Procedure 1*▲ (CN 1-Jun-2023) : NMT 10 ppm♦

SPECIFIC TESTS

• pH ⟨791⟩: 5.0–8.0, in a solution (1 in 100), prepared by evenly distributing the powder into boiling carbon dioxide-free water and stirring the mixture with a magnetic stirrer

• Loss on Drying ⟨731⟩
Analysis: Dry at 105° for 4 h.
Acceptance criteria: NMT 5.0%

• ♦Viscosity—Rotational Methods ⟨912⟩: Determine the apparent viscosity at the concentration and temperature specified on the label with a suitable rotational viscometer (see *Labeling*).♦

ADDITIONAL REQUIREMENTS

• ♦**Packaging and Storage:** Store in well-closed containers.♦

• ♦**Labeling:** Label it to indicate the viscosity in an aqueous solution of stated concentration and temperature. The indicated viscosity may be in the form of a range encompassing 50%–150% of the average value. Suitable anti-caking agents, such as silica, should be stated on the label.♦

• **USP Reference Standards** ⟨11⟩
USP Hydroxypropyl Cellulose RS

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

Topic/Question	Contact	Expert Committee
HYDROXYPROPYL CELLULOSE	Documentary Standards Support	CE2020 Complex Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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