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Ethylcellulose

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

Cellulose, ethyl ether;

Cellulose ethyl ether

CAS RN®: 9004-57-3.

DEFINITION

Ethylcellulose is a partly *O*-ethylated cellulose. It contains NLT 44.0% and NMT 51.0% of ethoxy ($-OC_2H_5$) groups, calculated on the dried basis. It may contain a suitable antioxidant.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197F**▲ (CN 1-May-2020)

Sample: Dissolve 40 mg in 1 mL of methylene chloride, spread 2 drops of this solution between two sodium chloride plates, then remove one of the plates to evaporate the solvent.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

[**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.]

[Note—Prepare the solutions immediately before use.]

Internal standard solution: To 10 mL of *o*-xylene add 0.5 mL of *n*-octane and dilute to 100.0 mL with *o*-xylene.

Sample solution: To 30.0 mg of the substance to be examined, previously dried, add 60 mg of adipic acid in a 5-mL pressure-tight reaction vial equipped with a pressure-tight membrane stopper coated with polytetrafluoroethylene and secured with an aluminum crimped cap or any other sealing system providing a sufficient air-tightness. Add 2.00 mL of *Internal standard solution* and 1.0 mL of hydriodic acid and close immediately. Accurately weigh the vial (total mass before heating). Do not mix the contents of the vial by hand before heating. Place the vial in an oven or heat in a suitable heater, with continuous mechanical agitation, maintaining the internal temperature of the vial at 115 ± 2° for 70 min. Allow to cool and weigh accurately the 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 test 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 test solution.

Standard solution: Place 60 mg of adipic acid and 2.00 mL of *Internal standard solution* in another 5-mL reaction vial, add 1.0 mL of hydriodic acid and close immediately. Accurately weigh the vial, then inject 25 µL of iodoethane through the septum in the vial. Weigh again accurately and mix. 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*.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

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

Temperatures

Injection port: 250°

Detector: 280°

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	0
100	34.9	250	8

Flow rate: 4.2 mL/min

Carrier gas: Helium

Split ratio: 40:1

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention time is about 0.6 for iodoethane with reference to *n*-octane (retention time about 10 min).]

Suitability requirements

Resolution: NLT 5.0 between *n*-octane and iodoethane

Relative standard deviation: NMT 2.0%, using the response factor of the principal peak for six injections of the *Standard solution*

Analysis

Sample: *Sample solution*

[NOTE—Measure all of the peak areas, excluding the solvent peak.]

Calculate the response factor (*F*):

$$\text{Result} = (A_1 \times W_1 \times C)/(A_2 \times 100)$$

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

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

C = content of iodoethane from the certificate of the manufacturer (%)

A_2 = peak area of the iodoethane peak from the *Standard solution*

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

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

A_4 = peak area of iodoethane from the *Sample solution*

F = response factor calculated from above

M_1 = molar mass of ethoxy group, 45.1

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 iodoethane, 156.0

Acceptance criteria: NLT 44.0% and NMT 51.0% of ethoxy groups on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩**

Sample: 1.0 g

Acceptance criteria: NMT 0.5%

- **CHLORIDES**

Standard stock solution: 0.824 mg/mL of sodium chloride

Standard solution: 8.24 µg/mL of sodium chloride, prepared from the *Standard stock solution*.[NOTE—Prepare immediately before use.]

Sample solution: Disperse 250 mg in 50 mL of water, heat to boiling, and allow to cool, shaking occasionally. Filter, and discard the first 10 mL of the filtrate.

Analysis

Samples: *Standard solution* and *Sample solution*

Separately dilute 10 mL of the *Sample solution* and *Standard solution* with water to 15 mL, add 1 mL of diluted nitric acid (125 g/L), and pour the mixtures as a single addition into test tubes containing 1 mL of 0.1 N silver nitrate VS. Examine the tubes laterally against a

black background.

Acceptance criteria: After standing for 5 min protected from light, any opalescence in the *Sample solution* is not more intense than that in the *Standard solution* (0.1%).

• **Acetaldehyde**

Solution A: 0.5 mg/mL of methylbenzothiazolone hydrazone hydrochloride

Solution B: 10 mg/mL of ferric chloride and 16 mg/mL of sulfamic acid

Standard stock solution: 10 mg/mL of acetaldehyde in water. [Note—Use immediately. Prepare the *Standard solution* and *Sample solution* at the same time.]

Standard solution: 3 µg/mL of acetaldehyde from the *Standard stock solution* in water. [Note—Use immediately.]

Sample solution: Dissolve 3.0 g of Ethylcellulose in 10 mL of water, stir by mechanical means for 1 h, allow to stand for 24 h, filter, and dilute the filtrate with water to 100.0 mL.

Analysis

Samples: *Standard solution* and *Sample solution*

Transfer 5.0 mL of the *Sample solution* and *Standard solution* to separate flasks. To each flask add 5 mL of *Solution A*, and heat in a water bath at 60° for 5 min. Add 2 mL of *Solution B*, and heat again at 60° for 5 min. Cool, and dilute with water to 25.0 mL.

Acceptance criteria: The *Sample solution* is not more intensely colored than the *Standard solution*.

SPECIFIC TESTS

• **Viscosity—Capillary Methods ⟨911⟩**

Solution A: Alcohol and toluene (1:4 w/w)

Sample solution: Shake a quantity of Ethylcellulose, equivalent to 5.00 g of the dried substance, with 95 g of *Solution A* until the substance is dissolved.

Analysis: Determine the viscosity using a capillary viscometer.

Acceptance criteria: The viscosity (mPa · s) determined at 25° is NLT 80.0% and NMT 120.0% of that stated on the label for a nominal viscosity greater than 6 mPa · s; and NLT 75.0% and NMT 140.0% of that stated on the label for a nominal viscosity of NMT 6 mPa · s.

• **Acidity or Alkalinity**

Solution A: Dissolve 100 mg of phenolphthalein in 80 mL of alcohol, and dilute with water to 100 mL.

Solution B: Dilute 50 mg of methyl red with 1.86 mL of 0.1 N sodium hydroxide and 50 mL of alcohol, and dilute with water to 100 mL.

Sample solution: To 0.5 g of Ethylcellulose add 25 mL of carbon dioxide-free water, and shake for 15 min. Pass through a sintered-glass filter with a maximum diameter of pores between 16 and 40 µm.

Analysis: To 10 mL of *Sample solution* add 0.1 mL of *Solution A* and 0.5 mL of 0.01 N sodium hydroxide (*Solution C*). To 10 mL of *Sample solution* add 0.1 mL of *Solution B* and 0.5 mL of 0.01 N hydrochloric acid (*Solution D*).

Acceptance criteria: *Solution C* is pink; *Solution D* is red.

• **Loss on Drying ⟨731⟩**

Sample: 1 g

Analysis: Dry at 105° for 2 h.

Acceptance criteria: It loses NMT 3.0% of its weight.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** Label to indicate its nominal viscosity in mPa · s for a 5% m/m solution. The label states the name and amount of any added antioxidant.

• **USP Reference Standards ⟨11⟩**

♦USP Ethylcellulose RS♦

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

Topic/Question	Contact	Expert Committee
ETHYLCELLULOSE	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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