Hydroxyethyl Cellulose

**Change to read:**

▲ 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. ▲ NF 1-Aug-2020

Cellulose, 2-hydroxyethyl ether [9004-62-0].

**DEFINITION**

**Change to read:**

▲ Partly O-(2-hydroxyethylated) cellulose. It may contain suitable pH-stabilizers such as phosphates. It contains 30.0%–70.0% of hydroxyethoxy (–OC₂H₄OH) groups (dried substance). ▲ NF 1-Aug-2020

**IDENTIFICATION**

**Add the following:**

▲ A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197A ▲ NF 1-Aug-2020

**Change to read:**

▲ B. ▲ NF 1-Aug-2020

Sample solution: ▲ Disperse 1.0 g of the dried substance in 50 mL of carbon dioxide-free water. After 10 min, dilute with carbon dioxide-free water to 100 mL, and stir until dissolution is complete. ▲ NF 1-Aug-2020

Analysis: ▲ Heat 10 mL of the Sample solution to boiling. ▲ NF 1-Aug-2020

Acceptance criteria: ▲ The solution remains clear. ▲ NF 1-Aug-2020

**Delete the following:**

▲ B.

Sample: 1 mL of the solution from Identification test A

Analysis: Place the Sample on a glass plate, and allow to evaporate.

Acceptance criteria: A thin, self-sustaining film is formed. ▲ NF 1-Aug-2020

**Delete the following:**

▲ C.

Sample solution: 1 in 2000

Analysis: To 1 mL of the Sample solution add 1 mL of phenol solution (50 mg/mL), then add 5 mL of sulfuric acid, shake, and allow to cool.

Acceptance criteria: The color of the solution becomes orange. ▲ NF 1-Aug-2020

**ASSAY**

**Add the following:**

▲ A. PROEDURE

[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.]

**APPARATUS:** For the reaction vial, use a 5-mL pressure-tight serum vial, 50 mm in height, 20 mm in outside diameter, and 13 mm in inside diameter at the mouth. The vial is 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 heating module that has a square-shape aluminum block with holes 20 mm in diameter and 32 mm in depth, 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 per minute.

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

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

**Standard solution:** Transfer 60 mg of adipic acid and 2.00 mL of Internal standard solution to a 5-mL reaction vial, then add 1.0 mL of Hydriodic acid, and close immediately with a septum. Accurately weigh the vial, then inject 55 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 layer as the Standard solution.

**Sample solution:** To 30.0 mg of the substance to be examined (dried substance), 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 reaction vial (total mass before heating). Do not mix the contents of the vial by hand before placing in the oven or the heater. Place the vial in an oven or heat in a suitable heater with continuous mechanical agitation, maintaining an internal temperature of the vial at 165 ± 2° for 2.5 h. Allow to cool and accurately weigh 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 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 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

**Carrier gas:** Helium

**Temperatures**

<table>
<thead>
<tr>
<th>Injection port (°)</th>
<th>Temperature Ramp (°/min)</th>
<th>Final Temperature (°)</th>
<th>Hold Time at Final Temperature (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>0</td>
<td>50</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 1

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Add the following:

**NITRATES**

Add the following:

**Aldehydes**

Add the following:

**Chlorides**

Chloride standard solution (5 ppm chloride): Dissolve 0.824 g of USP Sodium Chloride RS in water to make 1000.0 mL. Immediately before use, dilute 1.0 mL of the solution so obtained with water to 100.0 mL.

**Standard solution:** Mix 10 mL of the Chloride standard solution and 5 mL of water immediately before use.

**Sample solution:** Dilute 1 mL of the Sample solution prepared in Identification 8 with water to 30 mL.

**Analysis:** Add 1 mL of a dilute nitric acid solution (200 g/L) to 15 mL of the Sample solution, and pour the mixture as a single addition into a test tube containing 1 mL of silver nitrate solution (17 g/L). Prepare a standard in the same manner. 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 (NMT 1.0%).

**Add the following:**

**Nitrate standard solution** (500 ppm nitrate): Dissolve 0.8154 g of potassium nitrate in 500 mL of Buffered water, and dilute with the same solvent to 1000.0 mL.

**Sample solution:** Dissolve 0.5 g of the substance to be examined in Buffered water, and dilute with the same solvent to 100.0 mL.

**Reference solutions:** If hydroxyethyl cellulose has a viscosity of more than 1000 mPa · s, dilute 1.0, 2.0, and 4.0 mL of Nitrate standard solution with Buffered water to 100.0 mL, and mix. To determine the applicable limit, determine the viscosity using the method described in the Note in the test for Viscosity—Rotational Methods (912).

**Analysis:** Carry out the measurements for each solution, potentiometrically (see Titrimetry (541)), using a nitrate selective electrode as an indicator and a silver–silver chloride electrode with 0.1 M ammonium sulfate as a reference electrolyte. Calculate the concentration of nitrates using a calibration curve.

**Acceptance criteria:** NMT 3.0% (dried substance), if hydroxyethyl cellulose has a viscosity of more than 1000 mPa · s or less; and NMT 0.2% (dried substance), if hydroxyethyl cellulose has a viscosity of more than 1000 mPa · s.

**Add the following:**

**Aldehydes**

**Standard stock solution** (20 ppm glyoxal): In a 100-mL graduated flask, weigh a quantity of glyoxal solution [40% (w/w)] corresponding to 0.200 g of glyoxal (C₂H₃O₂), and dilute with anhydrous ethanol to volume. Immediately before use dilute the solution with the same solvent to 100 times its volume.

**Standard solution** (2 ppm glyoxal): Immediately before use, dilute the Standard stock solution with anhydrous ethanol to 10 times its volume.

**Sample solution:** Transfer 1.0 g of Hydroxyethyl Cellulose to a test tube with a ground-glass stopper, and add 10.0 mL of water.

**IMPURITIES**

Add the following:

<table>
<thead>
<tr>
<th>Initial Temperature (°C)</th>
<th>Temperature Ramp (°C/min)</th>
<th>Final Temperature (°C)</th>
<th>Hold Time at Final Temperature (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>10</td>
<td>100</td>
<td>20.3 min</td>
</tr>
<tr>
<td>100</td>
<td>34.9</td>
<td>250</td>
<td>8</td>
</tr>
</tbody>
</table>

**Flow rate:** 4.2 mL/min

**Injection volume:** 1 µL

**Injection type:** Split; split ratio, 40:1

**Run time:** 20.3 min

**System suitability**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Standard solution</th>
</tr>
</thead>
</table>

**Suitability requirements**

**Analysis**

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

Calculate the response factor ($F$):

\[
F = \frac{r_{51} \times W \times C}{r_{52} \times 100}
\]

where:

- $r_{51}$ is the peak area of the internal standard from the Standard solution
- $W$ is the weight of iodoethane in the Standard solution (mg)
- $C$ is the percentage content of iodoethane from the certificate of the manufacturer
- $r_{52}$ is the peak area of iodoethane from the Standard solution

Calculate the percentage content (m/m) of the hydroxyethoxy groups (−OC₂H₃OH) on the dried basis.

**Acceptance criteria:** 30.0%–70.0% of hydroxyethoxy groups (−OC₂H₃OH) on the dried basis.

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mL of anhydrous ethanol. Stopper the tube, and stir by mechanical means for 30 min. Centrifuge, and retain the supernatant.

Analysis: To 2.0 mL of the Sample solution, add 5.0 mL of a 4-g/L solution of methylbenzothiazolone hydrazone hydrochloride to an 80% (v/v) solution of glacial acetic acid in water. Shake to homogenize. After 2 h, the solution is not more intensely colored than a standard prepared at the same time and in the same manner using 2.0 mL of the Standard solution instead of 2.0 mL of the Sample solution.

Acceptance criteria: NMT 20 ppm, expressed as glyoxal.

Change to read:

- **Residue on Ignition** (281): NMT 4.0% if hydroxyethyl cellulose has a viscosity of 1000 mPa·s or less and NMT 1.0% if hydroxyethyl cellulose has a viscosity of more than 1000 mPa·s, determined on 1.0 g. In order to determine the applicable limit, determine the viscosity using the method described in the Note in the test for Viscosity—Rotational Methods (912).

**SPECIFIC TESTS**

- **pH** (791)
  Sample solution: Use the Sample solution prepared in Identification B (10 mg/mL).
  Acceptance criteria: 5.5–8.5

**Change to read:**

- **Loss on Drying** (731)
  Sample: 1.000 g
  Analysis: Dry the Sample at 105° for 3 h.
  Acceptance criteria: NMT 10.0%

**Change to read:**

- **Viscosity—Rotational Methods** (912): When determined at the concentration and under the conditions specified in the labeling, its viscosity is 50%–150% of the labeled viscosity, where stated as a single value, or it is between the maximum and minimum values, where stated as a range of viscosities.

- **[Note—To determine the applicable limit for the tests for Nitrates and Residue on Ignition (281), determine the viscosity using the following procedure.**

  While stirring transfer a quantity of the substance to be examined, equivalent to 2.00 g of the dried substance, to 50 g of water. Dilute with water to 100.0 g, and stir until dissolution is complete. Determine the viscosity using a rotating viscometer at 25° and at a shear rate of 100 s⁻¹ for substances with an expected viscosity up to 100 mPa·s, at a shear rate of 10 s⁻¹ for substances with an expected viscosity between 100 mPa·s and 20,000 mPa·s and at a shear rate of 1 s⁻¹ for substances with an expected viscosity above 20,000 mPa·s. If it is impossible to obtain a shear rate of exactly 10 s⁻¹ or 100 s⁻¹, respectively, use a rate slightly higher and a rate slightly lower and interpolate.

**ADDITIONAL REQUIREMENTS**

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

**Change to read:**

- **Labeling:** The labeling indicates its viscosity, under specified conditions, in aqueous solution. The indicated viscosity may be in the form of a range encompassing 50%–150% of the labeled value. The label states the name and concentration of any added pH-stabilizer.

**Add the following:**

- **USP Reference Standards (11)**
  - USP Hydroxyethyl Cellulose RS
  - USP Sodium Chloride RS