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Low-Substituted Carboxymethylcellulose Sodium

Cellulose, carboxymethyl ether, sodium salt, low-substituted;
Carmellose sodium, low-substituted
CAS RN®: 9004-32-4.

DEFINITION

Low-Substituted Carboxymethylcellulose Sodium is the sodium salt of a partly *O*-(carboxymethylated) cellulose. It contains NLT 2.0% and NMT 4.5% of sodium (Na), calculated on the dried basis.

IDENTIFICATION

Add the following:

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

Change to read:

• ▲**B.**▲ (NF 1-May-2020)

Solution A: 100 mg/mL of sodium hydroxide

Sample: 1 g

Analysis: Shake the *Sample* with 100 mL of *Solution A*.

Acceptance criteria: A suspension is produced.

Change to read:

• ▲**C.**▲ (NF 1-May-2020)

Sample: 1 g

Analysis: Shake the *Sample* with 50 mL of water. Transfer 1 mL to a test tube, and add 1 mL of water and 1 mL of 1-naphthol TS. Incline the test tube, and add carefully 2 mL of sulfuric acid down the side so that it forms a lower layer.

Acceptance criteria: A reddish-purple color develops at the interface.

Delete the following:

▲• **C.** It meets the requirements in *Impurities* for *Residue on Ignition*.▲ (NF 1-May-2020)

• **D.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium, A***

Sample solution: To the residue obtained in the test for *Residue on Ignition* add 1 mL of hydrochloric acid, evaporate on a water bath, and dissolve in 20 mL of water.

Acceptance criteria: Meets the requirements

ASSAY

• **Content of Sodium**

Analysis: Calculate the percentage of sodium in the portion of Low-Substituted Carboxymethylcellulose Sodium taken:

$$\text{Result} = a \times (M \times A_r / M_r)$$

a = percentage obtained from the test for *Residue on Ignition*, determined separately

M = number of moles of sodium per mole of sodium sulfate, 2

A_r = atomic weight of sodium, 22.99

M_r = molecular weight of sodium sulfate, 142.04

Acceptance criteria: 2.0%–4.5% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩**

Sample: 1.0 g

Analysis: Determine using a mixture of sulfuric acid and water (1:1) and an ignition temperature of 600 ± 50°.

Acceptance criteria: 6.5%–13.5%

- **Limit of Sodium Chloride and Sodium Glycolate**

Sodium chloride

Sample: 5 g

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.05 N silver nitrate VS

Electrode system: Silver electrode and mercurous sulfate electrode with a potassium sulfate bridge

Endpoint detection: Potentiometric

Analysis: Transfer the *Sample* to a 250-mL conical flask. Add 50 mL of water and 5 mL of 30% hydrogen peroxide, and heat on a water bath for 20 min, stirring occasionally to ensure hydration. Cool, and add 100 mL of water and 10 mL of nitric acid. Titrate with *Titrant*. Calculate the percentage of sodium chloride in the *Sample*:

$$\text{Result} = \{[(V \times N \times F)/W] \times [100/(100 - b)]\} \times 100$$

V = volume of *Titrant* (mL)

N = normality of the *Titrant* (mEq/mL)

F = equivalency factor for sodium chloride, 0.05844 g/mEq

W = weight of the *Sample* (g)

b = percentage obtained from the test for *Loss on Drying*, determined separately

Sodium glycolate

Standard stock solution: Transfer 100 mg of glycolic acid, previously dried overnight in a vacuum desiccator over phosphorus pentoxide, to a 100-mL volumetric flask, and dissolve in and dilute with water to volume.

Standard solution A: Transfer 0.5 mL of the *Standard stock solution* to a 100-mL volumetric flask. Add water to make 5 mL, add 5 mL of glacial acetic acid, then dilute with acetone to volume.

Standard solution B: Transfer 1.0 mL of the *Standard stock solution* to a 100-mL volumetric flask. Add water to make 5 mL, add 5 mL of glacial acetic acid, then dilute with acetone to volume.

Standard solution C: Transfer 1.5 mL of the *Standard stock solution* to a 100-mL volumetric flask. Add water to make 5 mL, add 5 mL of glacial acetic acid, then dilute with acetone to volume.

Standard solution D: Transfer 2.0 mL of the *Standard stock solution* to a 100-mL volumetric flask. Add water to make 5 mL, add 5 mL of glacial acetic acid, then dilute with acetone to volume.

Sample solution: Transfer 500 mg of Low-Substituted Carboxymethylcellulose Sodium to a beaker, moisten thoroughly with 5 mL of glacial acetic acid, add 5 mL of water, and stir with a glass rod to ensure proper hydration (about 30 min). Add 80 mL of acetone while stirring, add 2 g of sodium chloride, and stir for several minutes to ensure the complete precipitation of carboxymethylcellulose. Pass through a fast filter paper, previously wetted with a small amount of acetone, and collect the filtrate in a 100-mL volumetric flask. Rinse the beaker and filter with acetone, and add the washings to the flask. Dilute the filtrate with acetone to volume, and mix. Allow to stand for 24 h without shaking, and use the clear supernatant.

Instrumental conditions

Mode: Vis

Analytical wavelength: 540 nm

Blank: Use acetone solution containing 5% of glacial acetic acid and 5% of water.

Analysis: Transfer 2.0 mL of the *Sample solution* and 2.0 mL of each *Standard solution* to separate 25-mL volumetric flasks. Place the uncovered flasks in a boiling water bath for 20 min, accurately timed, to remove the acetone, then remove from the bath, and cool. Add to each flask 5.0 mL of 2,7-dihydroxynaphthalene TS, mix, add an additional 15 mL, and again mix. Cover the mouth of each flask with a small piece of aluminum foil. Place the flasks upright in a boiling water bath for 20 min, then remove from the bath, cool, and dilute with sulfuric acid to volume.

Determine the absorbances of the solutions against the *Blank*, and prepare a standard curve using the absorbances obtained from the solutions prepared from the *Standard solutions*. From the standard curve and the absorbance of the *Sample solution*, determine the concentration, in mg/mL, of glycolic acid in the *Sample solution*, and calculate the percentage of sodium glycolate in the sample taken:

$$\text{Result} = \{[(C \times V)/(W \times F)] \times (M_{r1}/M_{r2}) \times [100/(100 - b)]\} \times 100$$

C = concentration of glycolic acid in the sample, determined from the standard curve (mg/mL)

V = volume of *Sample solution* (mL)

W = weight of sample (g)

F = unit conversion factor, 1000 mg/g

M_{r1} = molecular weight of sodium glycolate, 98.03

M_{r2} = molecular weight of glycolic acid, 76.05

b = percentage obtained from the test for *Loss on Drying*, determined separately

Acceptance criteria: The sum of the percentages obtained from the tests for *Sodium chloride* and *Sodium glycolate* is NMT 0.5%.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample: 1 g

Analysis: Shake the *Sample* with 100 mL of carbon dioxide-free water, centrifuge, and test the suspension.

Acceptance criteria: 6.0–8.5

• **Loss on Drying** ⟨731⟩

Sample: 1.0 g

Analysis: Dry the *Sample* at 105° for 3 h.

Acceptance criteria: NMT 10.0%

• **Water-Soluble Substances**

Sample: 5.0 g

Analysis: Disperse the *Sample* in 400 mL of water, and during the first 30 min, stir for 1 min every 10 min. Allow to stand for 1 h, and centrifuge, if necessary. Decant 100.0 mL of the supernatant onto a fast filter paper in a vacuum filtration funnel, apply a vacuum, and collect 75.0 mL of the filtrate. Evaporate in a tared platinum or porcelain dish, and dry at 105° for 4 h.

Acceptance criteria: NMT 70%

• **Settling Volume**

[Note—The following test, which can relate to excipient function, may be carried out depending on the intended use in the formulation. In cases where there are no concerns regarding the settling volume of this article, this test may be omitted. Where the labeling states the settling volume, determine the settling volume as follows.]

Sample: 5.0 g

Analysis: In a 100-mL graduated cylinder, transfer 20 mL of isopropyl alcohol, add the *Sample*, and shake vigorously. Dilute with isopropyl alcohol to 30 mL, then with water to 50 mL, and shake vigorously. Within 15 min, repeat the shaking three times. Allow to stand for 4 h, and determine the volume of the settled mass.

Acceptance criteria: 15.0–35.0 mL

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. No storage requirements specified.

• **Labeling:** When the settling volume is determined, label it to indicate the settling volume value.

Add the following:

▲• **USP Reference Standards** ⟨11⟩

USP Low-Substituted Carboxymethylcellulose Sodium RS▲ (NF 1-May-2020)

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

Topic/Question	Contact	Expert Committee
LOW-SUBSTITUTED CARBOXYMETHYLCELLULOSE SODIUM	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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