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Carboxymethylcellulose Sodium 12

DEFINITION

Carboxymethylcellulose Sodium 12 is the sodium salt of a polycarboxymethyl ether of cellulose. Its degree of substitution is NLT 1.15 and NMT 1.45, corresponding to a sodium (Na) content of NLT 10.4% and NMT 12.0%, calculated on the dried basis.

IDENTIFICATION

- **A.**

Sample solution: Add 1 g of powdered Carboxymethylcellulose Sodium 12 to 50 mL of water, while stirring to produce a uniform dispersion. Continue the stirring until a clear solution is produced. [NOTE—Save the unused portion of this solution for use in *Identification* tests *B* and *C*.]

Analysis: To 1 mL of the *Sample solution*, diluted with an equal volume of water, in a small test tube, add 5 drops of 1-naphthol TS. Incline the test tube, and carefully introduce down the side of the tube 2 mL of sulfuric acid so that it forms a lower layer.

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

- **B.**

Analysis: To 5 mL of the *Sample solution* prepared for *Identification* test *A* add an equal volume of barium chloride TS.

Acceptance criteria: A fine, white precipitate is formed.

- **C. IDENTIFICATION TESTS—GENERAL, *Sodium*⟨191⟩:** A portion of the *Sample solution* prepared for *Identification* test *A* meets the requirements.

ASSAY

- **DEGREE OF SUBSTITUTION**

Sample: 200 mg, previously dried at 105° for 3 h

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.1 N perchloric acid in dioxane VS

Endpoint detection: Potentiometric

Electrode system: A pH meter equipped with a standard glass electrode and a calomel electrode modified as follows. Discard the aqueous potassium chloride solution contained in the electrode, rinse, and fill with the supernatant obtained by shaking thoroughly 2 g each of potassium chloride and silver chloride (or silver oxide) with 100 mL of methanol, then add a few crystals of potassium chloride and silver chloride (or silver oxide) to the electrode.

Analysis: Weigh the *Sample*, and transfer to a glass-stoppered, 250-mL conical flask. Add 75 mL of glacial acetic acid, connect the flask to a water-cooled condenser, and reflux gently on a hot plate for 2 h. Cool, and transfer the solution to a 250-mL beaker with the aid of 50 mL of glacial acetic acid. Titrate with *Titrant* while stirring with a magnetic stirrer. Record the amount, in mL, of *Titrant* versus mV (0- to 700-mV range), and continue the titration to a few mL beyond the endpoint. Plot the titration curve, and read the volume of *Titrant* at the inflection point.

Calculate the degree of substitution in the Carboxymethylcellulose Sodium 12 taken:

$$\text{Result} = (M_{r1} \times N \times V)/(G - \Delta M_{r2} \times N \times V)$$

M_{r1} = molecular weight of 1 anhydroglucose unit, 162

N = *Titrant* normality

V = volume of *Titrant* (mL)

G = weight of Carboxymethylcellulose Sodium 12 taken (mg)

ΔM_{r2} = increase in molecular mass of 1 anhydroglucose unit for each sodium carboxymethyl group added, 80

Acceptance criteria: 1.15–1.45, corresponding to 10.4%–12.0% sodium content, on the dried basis

IMPURITIES

- **LIMIT OF SODIUM CHLORIDE**

Sample: 5 g

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.05 N silver nitrate VS

Endpoint detection: Potentiometric

Electrode system: A silver electrode and a mercurous sulfate electrode having a potassium sulfate bridge

Analysis: Transfer the *Sample* to a 250-mL beaker, 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, add 100 mL of water and 10 mL of nitric acid, and titrate with *Titrant*, determining the endpoint while stirring constantly.

Calculate the percentage of NaCl in the sample taken:

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

M_r = molecular weight of sodium chloride, 58.44

V = volume of *Titrant* (mL)

N = normality of *Titrant*

F = conversion factor, 10^{-3} g/mg

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

W = *Sample* weight (g)

Acceptance criteria: See *Limit of Sodium Glycolate*.

- **Limit of Sodium Glycolate**

Standard stock solution: Transfer 100 mg of glycolic acid, previously dried in a desiccator at room temperature overnight, to a 100-mL volumetric flask. Dissolve in and dilute with water to volume, and mix. [Note—Use this solution within 30 days.]

Standard solutions: Into four separate 100-mL volumetric flasks, transfer 1.0-, 2.0-, 3.0-, and 4.0-mL portions of the *Standard stock solution*, respectively. To each flask, add water to make 5 mL, add 5 mL of glacial acetic acid, dilute with acetone to volume, and mix.

Sample solution: Transfer 500 mg to a 100-mL beaker, moisten thoroughly with 5 mL of glacial acetic acid, followed by 5 mL of water, and stir with a glass rod to ensure proper hydration (usually about 15 min). Slowly add 50 mL of acetone, with stirring, then add 1 g of sodium chloride, and stir for several min to ensure complete precipitation of the carboxymethylcellulose. Filter through a soft, open-textured paper, previously wetted with a small amount of acetone, and collect the filtrate in a 100-mL volumetric flask. Use an additional 30 mL of acetone to facilitate the transfer of the solids and to wash the filter cake, then dilute with acetone to volume.

Blank: Prepare a 25-mL blank flask containing 2.0 mL of a solution containing 5% each of glacial acetic acid and water in acetone.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: Spectrophotometry

Analytical wavelength: 540 nm

Analysis: Transfer 2.0 mL of the *Sample solution* and 2.0 mL of each *Standard solution* to separate 25-mL volumetric flasks. The 25-mL volumetric flask containing the *Blank* is included in the following tests. Place the uncovered flasks in a boiling water bath for 20 min, accurately timed, to remove the acetone, 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, dilute with sulfuric acid to volume, and mix.

Determine the absorbances of each solution 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 weight (w), in mg, of glycolic acid in the *Sample solution*.

Calculate the percentage of sodium glycolate in the specimen taken:

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

w = weight of glycolic acid in the sample determined from the standard curve (mg)

F = factor converting glycolic acid to sodium glycolate, 1.29

b = percentage of *Loss on Drying*, determined separately

W = weight of the sample taken (mg)

Acceptance criteria: The sum of the percentages from the tests for *Limit of Sodium Chloride* and *Limit of Sodium Glycolate* is NMT 0.5%.

SPECIFIC TESTS

- **pH ⟨791⟩:** 6.5–8.5, in a 10-mg/mL solution
- **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 3 h: it loses NMT 10.0% of its weight.
- **Viscosity–Rotational Methods ⟨912⟩**

Analysis: Determine the viscosity in a water solution at the concentration stated on the label. Using undried Carboxymethylcellulose Sodium 12, weigh the amount which, on the dried basis, will provide 200 g of solution of the stated concentration. Add the substance in small amounts to 180 mL of stirred water contained in a tared, wide-mouth bottle, continue stirring rapidly until the powder is well wetted, add sufficient water to make the mixture weigh 200 g, and allow to stand, with occasional stirring, until solution is complete. Adjust the temperature to 25 ± 0.2°, and determine the viscosity, using a rotational type of viscometer, making certain that the system reaches equilibrium before taking the final reading.

Acceptance criteria: The viscosity of solutions of 2% concentration is NLT 80.0% and NMT 120.0% of that stated on the label; the viscosity of solutions of 1% concentration is NLT 75.0% and NMT 140.0% of that stated on the label or it is between the maximum and minimum values, where stated as a range of viscosities.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** Label it to indicate the nominal viscosity in solutions of stated concentrations of either 1% (w/w) or 2% (w/w). The indicated viscosity may be in the form of a range encompassing 80.0%–120.0% of the nominal viscosity, where the solution concentration is 2% (w/w); or 75.0%–140.0% of the nominal viscosity, where the solution concentration is 1% (w/w).

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

Topic/Question	Contact	Expert Committee
CARBOXYMETHYLCELLULOSE SODIUM 12	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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