CROSS-LINKED SODIUM CARBOXYMETHYL CELLULOSE

New specifications prepared at the 59th JECFA (2002), published in FNP 52 Add 10 (2002), re-published with editorial corrections in FNP 52 Add 11(2003). This substance was included at the 59th meeting in the group ADI "not specified" for modified celluloses, established at the 35th JECFA in 1989.

SYNONYMS

Cross-linked carboxymethyl cellulose, cross-linked sodium CMC, cross-linked CMC, croscarmellose sodium, cross-linked cellulose gum; INS No. 468

DEFINITION

Cross-linked sodium carboxymethyl cellulose is the sodium salt of thermally cross-linked partly O-carboxymethylated cellulose. It is manufactured by acidifying an aqueous suspension of sodium carboxymethyl cellulose and heating the suspension to achieve cross-linking. The product is then washed and dried. It is also produced during the manufacture of sodium carboxymethyl cellulose by lowering the pH and heating to achieve cross-linking.

C.A.S. number

74811-65-7

Chemical formula

The polymers contain substituted anhydroglucose units with the general formula: $C_6H_7O_2(OR_1)(OR_2)(OR_3)$
where R_1, R_2, and R_3 represent the following groups, present in varying proportions

$-H$
$-CH_2COONa$
$-CH_2COOH$

DESCRIPTION

A slightly hygroscopic, white to greyish-white, odourless powder

FUNCTIONAL USES

Tabletting agent

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4)

Practically insoluble in acetone, in ethanol and in toluene

Colour reaction

Add 1 g of the powdered sample to 50 ml water, while stirring to produce a uniform dispersion. Dilute 1 ml of this mixture with 1 ml of water in a small test tube and 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. A red-purple colour develops at the interface.

Precipitate formation

Mix 1 g of the powdered sample with 100 ml of solution containing 4 mg/kg of methylene blue in water and allow to settle. The substance absorbs methylene blue and settles as a blue, fibrous mass.

Test for sodium (Vol. 4)

Passes test

PURITY

pH (vol.4)	Not less than 5.0 and not more than 7.0 (1 in 100 suspension in water)
Loss on drying (Vol. 4)	Not more than 6% (105^o, 3h)
Sulfated ash (Vol. 4)	Not less than 14.0 % and not more than 28.0 % on the dried basis (2 g of sample)
Water-soluble substances	Not more than 10% See description under TESTS
Degree of substitution	Not less than 0.2 and not more than 1.5 carboxymethyl groups (-CH_2COOH) per anhydroglucose unit on the dried basis. See description under TESTS
Sodium chloride and sodium glycolate	Not more than 0.5% (sum of sodium chloride and sodium glycolate) on the dried basis See description under TESTS
Lead (Vol. 4)	Not more than 2 mg/kg Determine using an atomic absorption technique appropriate to the specified level. The selection of sample size and method of sample preparation may be based on the principles of the methods described in Volume 4, "Instrumental Methods."

TESTS

PURITY TESTS

Water soluble substances

Weigh accurately about 10 g of sample and disperse in 800 ml of water. Stir for 1 min at the beginning, at 10 min, 20 min and 30 min. Allow to stand for 1 h and centrifuge, if necessary. Filter under vacuum using a fast filter paper and collect 150 ml of the filtrate. Evaporate 100 ml to dryness and dry the residue at 100 – 105^o for 4 h. Weigh the residue and calculate percentage of water soluble substances using the formula:

$$\% \text{ water soluble substances} = \frac{M \text{ x } 800}{W}$$

where:
M = weight of residue, in g
W = weight of sample, in g

Degree of substitution

Degree of substitution is the sum of the degree of acid carboxymethyl substitution and degree of sodium carboxymethyl substitution.

Weigh accurately about 1 g of sample into a 500 ml Erlenmeyer flask and add 300 ml sodium chloride solution (10 % in water). Pipette 25.0 ml of 0.1M sodium hydroxide into the flask, stopper flask and allow to stand for 5 min shaking occasionally. Add 5 drops of m-cresol purple solution (dissolve 0.1g in minimum volume of alcohol and dilute to 100 ml with water), 15 ml of 0.1M hydrochloric acid from a burette, stopper the flask and shake. If the solution is violet, add 0.1M hydrochloric acid in 1 ml portions until the solution becomes yellow, shaking after each addition. Titrate with 0.1M sodium hydroxide until the colour turns to violet.

Calculate the number of milliequivalents of the base required for the neutralisation equivalent to 1 g of dried substance.
Calculate the degree of acid carboxymethyl substitution from the expression:

$$\frac{1150M}{(7102 - 412M - 80C)}$$

where:
M = milliequivalents of sodium hydroxide required for neutralisation of 1 g of dried substance
C = percentage of sulfated ash

Calculate the sodium carboxymethyl substitution from the expression:

$$\frac{(162 + 58A)C}{(7102) - (80xC)}$$

where:
A = acid carboxymethyl substitution
C = percentage of sulfated ash

Sodium chloride and sodium glycolate

Determine sodium chloride and sodium glycolate separately and calculate their sum.

Sodium chloride

Weigh accurately about 5 g of sample (previously dried to constant weight) to a 250 ml conical flask, add 50 ml of water and 5 ml of hydrogen peroxide solution (30%) and heat on a water-bath for 20 min, stirring occasionally to ensure total hydration. Cool, add 100 ml of water and 10 ml of nitric acid. Titrate with 0.05 M silver nitrate determining the end point potentiometrically using a silver electrode and a double-junction reference electrode containing a 100 g/l solution of potassium nitrate in the outer jacket and a standard filling solution in the inner jacket, and stirring constantly. 1 ml of 0.05 M silver nitrate is equivalent to 2.922 mg of NaCl.

Sodium glycolate

Weigh 0.5 g of the sample to the nearest 0.1 mg and transfer to a 100 ml beaker. Moisten the sample thoroughly with 5 ml of glacial acetic acid, 5 ml of water and stir for about 15 min to ensure total hydration. Slowly add 50 ml of acetone and 1 g of sodium chloride. Continue the stirring for several minutes to ensure complete precipitation of the carboxymethyl cellulose. Filter through a fast filter paper previously washed with acetone into a 100 ml volumetric flask, rinse the beaker and filter with 30 ml of acetone and make up to volume with acetone. Allow to stand for 24 h without shaking. Use the clear supernatant to prepare the test solution.
Prepare a blank solution containing 5 ml water, 5 ml of glacial acetic acid and acetone in 100 ml volumetric flask. Pipette 2 ml each of the test and blank solutions into separate 25 ml volumetric flasks. Remove the acetone by heating the uncovered flasks upright in a boiling water bath for exactly 20 min. Cool to room temperature and add 5 ml of 2,7-dihydroxynaphthalene TS and mix thoroughly, then add 15 ml more of the 2,7-dihydroxynaphthalene TS and mix. Cover the mouth of the flask with a small piece of aluminium foil and heat on a water-bath for 20 min. Cool to room temperature and make up to volume with 2,7-dihydroxynaphthalene TS. Measure the absorbance of the test solution against blank solution at 540 nm using 1 cm cells. Read the corresponding mg of glycolic acid from

the calibration curve obtained as follows.

Weigh accurately 0.100 g of glycolic acid standard (previously dried in vacuum over phosphorus pentoxide), dissolve in water in a 100 ml volumetric flask and make up to volume with water (use the solution within 30 days). Pipette 0.0, 1.0, 2.0, 3.0 and 4.0 ml aliquots of standard glycolic acid solution into a series of 100 ml volumetric flasks, add water to each flask to a volume of 5 ml, then add 5 ml of glacial acetic acid, dilute to volume with acetone and mix. Pipette 2 ml of each solution (containing, respectively, 0, 1, 2, 3 and 4 mg of glycolic acid per 100 ml) into a series of 25 ml volumetric flasks and proceed in the same manner as described for the test solution. Plot the mg of glycolic acid in the original 100 ml solution against absorbance to give a calibration curve.
Calculate the sodium glycolate content from the following formula:

$$\%\,\text{sodium glycolate} = \frac{\text{a x } 1.29}{\text{b}}$$

where
1.29 = Factor for converting glycolic acid into sodium glycolate
a = mg of glycolic acid read from the calibration curve
b = dry weight of sample, in g