HYDROXYPROPYL CELLULOSE

Revised specification prepared at the 63rd JECFA (2004) and published in FNP52 Add 12 (2004) superseding specifications prepared at the 29th JECFA (1985) and published in FNP 52. An ADI 'not specified' was established for modified celluloses at the 35th JECFA (1989).

SYNONYMS Cellulose hydroxypropyl ether; modified cellulose; INS No. 463

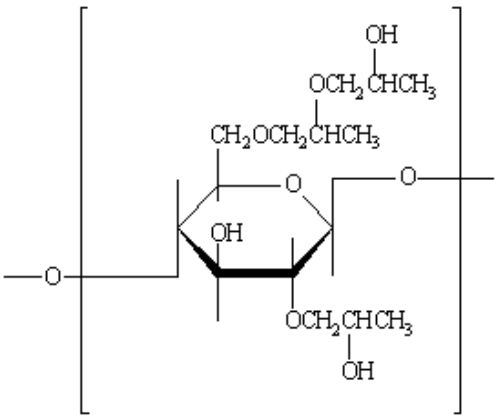
DEFINITION An ether of cellulose containing hydroxypropyl substitution prepared from cellulose by treatment with alkali and propylene oxide. The article of commerce can be specified further by viscosity.

Chemical names: Hydroxypropyl ether of cellulose, cellulose hydroxypropyl ether

C.A.S. number: 9004-64-2

Chemical formula: $[C_6H_7O_2(OH)_X(OCH_2CHOHCH_3)_y(OCH_2CH[R_w]CH_3)_z]_n$
where
x + y + z = 3
y + z (1+w) = not greater than 4.6
R = A substituent comprising "w" hydroxypropoxy groups

Structural formula



One of many possible structural formulae for the repeating unit of a hydroxypropyl cellulose with molar substitution of 3.0 and a degree of polymerization of n, showing a monomeric hydroxypropyl substitution at C_2 and a dimeric hydroxypropyl substitution at C_6.

Formula weight: Unsubstituted structural unit: 162.14
Trisubstituted structural unit: 336.37
Macromolecules: from about 30 000 (n about 100) up to about 1 million (n about 2500)

Assay: Not more than 80.5% of hydroxypropoxy groups equivalent to not more than 4.6 hydroxypropyl groups per anhydroglucose unit on the dried basis

DESCRIPTION Slightly hygroscopic, white or off-white, almost odourless, granular or fibrous powder

FUNCTIONAL USES Emulsifier, thickener, stabiliser, binder, suspension agent, film coating

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4)	Swells in water, producing a clear to opalescent, viscous colloidal solution; insoluble in ethanol; insoluble in ether
Foam formation	A 0.1% solution of the sample is shaken vigorously. A layer of foam appears. This test permits the distinction of sodium carboxymethyl cellulose from other cellulose ethers.
Precipitate formation	To 5 ml of a 0.5% solution of the sample, add 5 ml of a 5% solution of copper sulfate or of aluminium sulfate. No precipitate appears. This test permits the distinction of sodium carboxymethyl cellulose from other cellulose ethers.
Substituents	See description under METHOD OF ASSAY

PURITY

Loss on drying (Vol. 4)	Not more than 10.0% (105° to constant weight)
pH (Vol. 4)	Not less than 5.0 and not more than 8.0 (1 in 100 soln)
Sulfated ash (Vol. 4)	Not more than 0.5%. Test 1 g of the sample
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"
Propylene chlorohydrins	Not more than 0.1 mg/kg See description under TESTS

TESTS

PURITY TESTS

Propylene chlorohydrins — Determine by gas liquid chromatography (see Volume 4) using the following procedure:

Preparation of Standards

Stock Standard Solution: Weigh 0.1 g propylene chlorohydrin (C.A.S. No. 127-00-4, mixture of 1-Chloro-2-propanol-70% and 2-Chloro-1-propanol-30%) to the nearest 0.0001g and bring to a final volume of 100 ml with diethyl ether.

Working Standard Solution: Perform serial dilutions (in diethyl ether) of stock standard to achieve a working calibration range of 6-25 ng/ml.

Note**:** All standard solutions should be prepared with diethyl ether of the highest purity

Gas Chromatography

Gas Chromatograph with a Halogen Specific Detector, on-column injector, and linear column temperature programming.

Column: 30 m x 0.53 mm x 1 μm DB-WAX or equivalent.

Temperature programming:

Initial Temperature	35^{o}
Initial Hold Time	7.0 min
Ramp Rate	8.0^{o}/min
Final Temperature	200^{o}
Final Hold Time	5.0 min
Inlet	200^{o}
Detector (XSD)	1000^{o}

Flow rates:

Helium (carrier gas) 5 psi (column head pressure at 35^{o})
Detector Make-up Gas (air) 40 psi
Retention times (min):

1-Chloro-2-propanol	~11.7
2-Chloro-1-propanol	~12.5

Procedure:
Weigh ~1 g of sample into a centrifuge tube and record weight to the nearest 0.01 g. Quantitatively add 5.0 ml diethyl ether to the sample and sonicate for 10 minutes. Centrifuge the sample to separate the mixture. Remove a portion of the diethyl ether extract for GC analysis.

Calculations:
Prepare a calibration curve by plotting the concentration (ng/ml) versus detector response (in a linear range of 6-25 ng/ml). From the linear regression of this curve, calculate ng/g using the following equation:

$$ng/g = (V \times (R-b)/m)/W$$

where:

- R= detector response for the sample
- b = y-intercept of the linear regression curve
- m = slope of the linear regression curve
- V= final volume (5.0 ml)
- W= weight of the sample in grams

METHOD OF ASSAY

Determination of the hydroxypropoxy group content

Apparatus
The apparatus for hydroxypropoxy group determination is shown in the accompanying diagram. The boiling flask, D, is fitted with an aluminium foil-covered Vigreux column, E, on the sidearm and with a bleeder tube through the neck and to the bottom of the flask for the introduction of steam and nitrogen. A steam generator, B, is attached to the bleeder tube through Tube C, and a condenser, F, is attached to the Vigreux column. The boiling flask and steam generator are immersed in an oil bath, A, equipped with a thermo-regulator such that a temperature of 155^{o} and the desired heating rate may be maintained. The distillate is collected in a 150 ml beaker, G, or other suitable container.

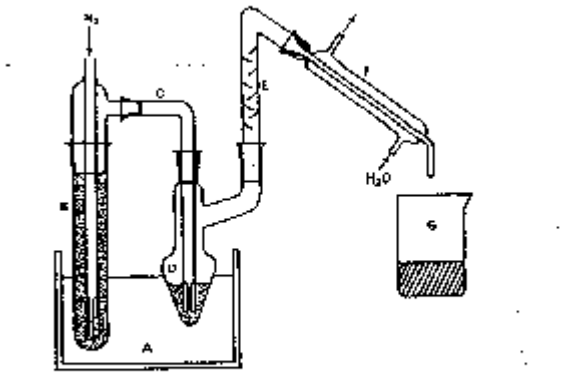


Figure Apparatus for Hydroxypropyl Determination

Procedure

Transfer about 100 mg of the sample, previously dried at 105° for 2 h and accurately weighed, into the boiling flash, and add 10 ml of chromium trioxide solution (60 g in 140 ml of water). Immerse the steam generator and the boiling flask in the oil bath (at room temperature) to the level of the top of the chromium trioxide solution. Start cooling water through the condenser and pass nitrogen gas through the boiling flask at the rate of one bubble per sec. Starting at room temperature, raise the temperature of the oil bath to 155° over a period of not less than 30 min, and maintain this temperature until the end of the determination. Distil until 50 ml of the distillate is collected. Detach the condenser from the Vigreux column, and wash it with water, collecting the washings in the distillate container. Titrate the combined washings and distillate with 0.02 N sodium hydroxide to a pH of 7.0, using a pH meter set at the expanded scale.
NOTE: Phenolphthalein TS may be used for this titration, if it is also used for all standards and blanks.

Record the volume, V_a of the 0.02 N sodium hydroxide used. Add 500 mg of sodium bicarbonate and 10 ml of dilute sulfuric acid TS, and then after evolution of carbon dioxide has ceased, add 1 g of potassium iodide. Stopper the flask, shake the mixture, and allow it to stand in the dark for 5 min. Titrate the liberated iodine with 0.02 N sodium thiosulfate to the sharp disappearance of the yellow colour, confirming the end-point by the addition of a few drops of starch TS. Record the volume of 0.02 N sodium thiosulfate required as Y_a.
Make several reagent blank determinations, using only the chromium trioxide solution in the above procedure. The ratio of the sodium hydroxide titration (V_b) to the sodium thiosulfate titration (Y_b), corrected for variation in normalities, will give the acidity-to-oxidizing ratio, $V_b/Y_b = K$, for the chromium trioxide carried over in the distillation. The factor K should be constant for all determinations.
Make a series of blank determinations using 100 mg of methyl cellulose (containing no foreign material) in place of the sample, recording the average volume of 0.02 N sodium hydroxide required as V_m and the average volume of 0.02 N sodium thiosulfate required as Y_m.

Calculate the hydroxypropoxy group content of the sample, in mg, by the formula:

$75.0 \times [N_1 (V_a - V_m) - k N_2 (Y_a - Y_m)]$
where
N_1 = the exact normality of the 0.02 N sodium hydroxide solution
N_2 = the exact normality of the 0.02 N sodium thiosulfate solution
$k = V_b N_1 / Y_b N_2$

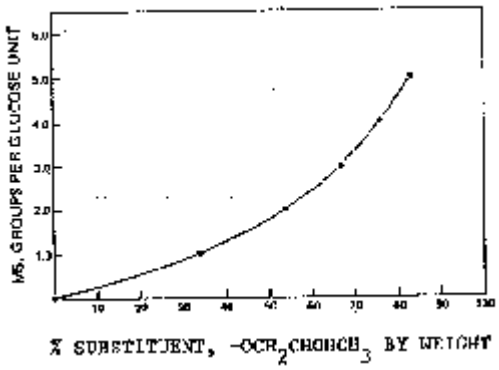


Chart for converting percentage of substitution, by weight, of hydroxypropoxy groups to molecular substitution per glucose unit.

Determination of the methoxy group
See Apparatus and Procedure in *Ethoxy and Methoxy Group Determination* and determine the content of methoxy group ($-OCH_3$).

Calculation
Calculate as percentage. Correct the % of methoxy groups thus determined by the formula:

$$A - (B \times 0.93 \times 31 / 75)$$

where

A = the total % of $-OCH_3$ groups determined
B = the % of $-OCH_2CHOHCH_3$ determined in the Method of Assay for Hydroxypropoxy group content
0.93 = an average obtained by determining, on a large number of samples, the propylene produced from the reaction of hydriodic acid with hydroxypropoxy groups during the Method of Assay for methoxy groups ($-OCH_3$).