

Carboxymethylcellulose Sodium

1 Nonproprietary Names

BP: Carmellose sodium
JP: Carmellose sodium
PhEur: Carmellosum natricum
USP: Carboxymethylcellulose sodium

2 Synonyms

Akucell; *Aquasorb*; *Blanose*; cellulose gum; CMC sodium; E466; *Finnfix*; *Nymcel*; SCMC; sodium carboxymethylcellulose; sodium cellulose glycolate; sodium CMC; *Tylose CB*.

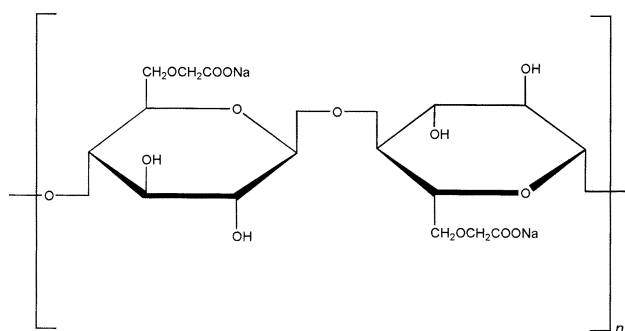
3 Chemical Name and CAS Registry Number

Cellulose, carboxymethyl ether, sodium salt [9004-32-4]

4 Empirical Formula Molecular Weight

The USP 25 describes carboxymethylcellulose sodium as the sodium salt of a polycarboxymethyl ether of cellulose. Typical molecular weight is 90 000–700 000.

5 Structural Formula



Structure shown with a degree of substitution (DS) of 1.0.

6 Functional Category

Coating agent; tablet and capsule disintegrant; tablet binder; stabilizing agent; suspending agent; viscosity-increasing agent; water-absorbing agent.

7 Applications in Pharmaceutical Formulation or Technology

Carboxymethylcellulose sodium is widely used in oral and topical pharmaceutical formulations, primarily for its viscosity-increasing properties. Viscous aqueous solutions are used to suspend powders intended for either topical application or oral and parenteral administration.⁽¹⁾ Carboxymethylcellulose sodium may also be used as a tablet binder and disintegrant,^(2–4) and to stabilize emulsions.⁽⁵⁾

Higher concentrations, usually 3–6%, of the medium-viscosity grade are used to produce gels that can be used as

the base for applications and pastes; glycols are often included in such gels to prevent them drying out. Carboxymethylcellulose sodium is additionally one of the main ingredients of self-adhesive ostomy, wound care, and dermatological patches, where it is used to absorb wound exudate or transepidermal water and sweat.

Carboxymethylcellulose sodium is also used in cosmetics, toiletries,⁽⁶⁾ and incontinence, personal hygiene, and food products.

See Table I.

Table I: Uses of carboxymethylcellulose sodium.

Use	Concentration (%)
Emulsifying agent	0.25–1.0
Gel-forming agent	3.0–6.0
Injections	0.05–0.75
Oral solutions	0.1–1.0
Tablet binder	1.0–6.0

8 Description

Carboxymethylcellulose sodium occurs as a white to almost white, odorless, granular powder. See also Section 18.

9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for carboxymethylcellulose sodium.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Characters	—	+	—
pH (1% w/v solution)	6.0–8.0	6.0–8.0	6.5–8.5
Appearance of solution	+	+	—
Viscosity	+	+	+
Loss on drying	≤ 10.0%	≤ 10.0%	≤ 10.0%
Heavy metals	≤ 20 ppm	≤ 20 ppm	≤ 20 ppm
Chloride	≤ 0.64%	≤ 0.25%	—
Arsenic	≤ 10 ppm	—	—
Sulfate	≤ 0.96%	—	—
Silicate	≤ 0.5%	—	—
Sodium glycolate	—	≤ 0.4%	—
Starch	+	—	—
Sulfated ash	—	20.0–33.3%	—
Organic volatile impurities	—	—	+
Assay (of sodium)	6.5–8.5%	6.5–10.8%	6.5–9.5%

10 Typical Properties

Density (bulk): 0.52 g/cm³

Density (tapped): 0.78 g/cm³

Dissociation constant: pK_a = 4.30

Melting point: browns at approximately 227°C, and chars at approximately 252°C.

Moisture content: typically contains less than 10% water. However, carboxymethylcellulose sodium is hygroscopic and absorbs significant amounts of water at temperatures up to 37°C at relative humidities of about 80%. See Section 11. See also Figure 1.

SEM: 1

Excipient: Carboxymethylcellulose sodium

Manufacturer: Buckeye Cellulose Corp.

Lot No.: 9247 AP

Magnification: 120 ×

Voltage: 10 kV



SEM: 2

Excipient: Carboxymethylcellulose sodium

Manufacturer: Hercules Ltd.

Lot No.: 21 A-1 (44390)

Magnification: 600 ×

Voltage: 10 kV

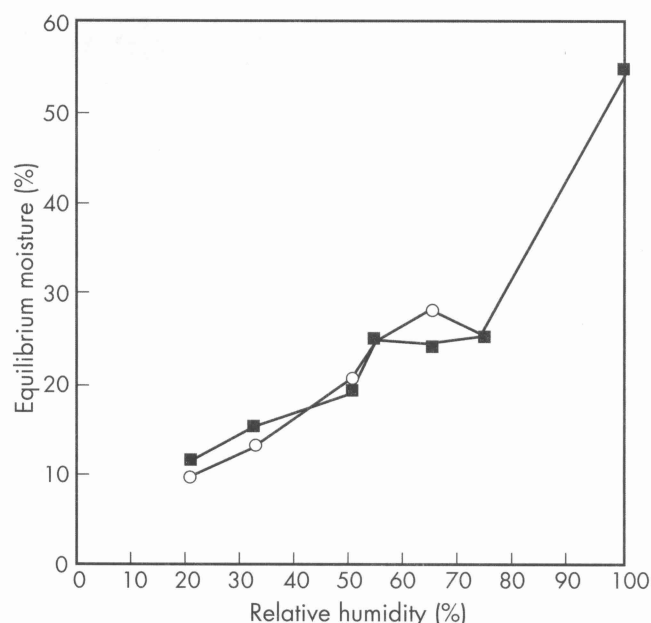
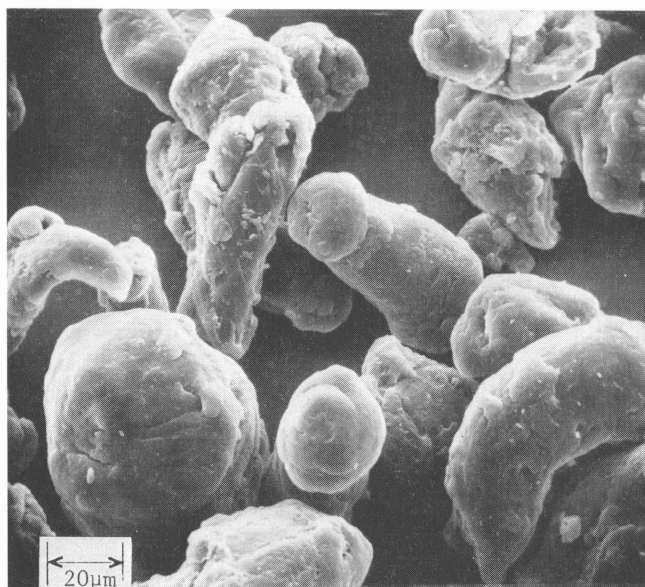


Figure 1: Sorption-desorption isotherm of carboxymethylcellulose sodium.

○: Sorption

■: Desorption

Solubility: practically insoluble in acetone, ethanol, ether, and toluene. Easily dispersed in water at all temperatures, forming clear, colloidal solutions. The aqueous solubility varies with the degree of substitution (DS). See Section 18.

Viscosity: various grades of carboxymethylcellulose sodium are commercially available that have differing aqueous viscosities; see Table III. Aqueous 1% w/v solutions with viscosities of 5–13 000 mPa s (5–13 000 cP) may be obtained. An increase in concentration results in an increase in aqueous solution viscosity.⁽⁶⁾ Prolonged heating at high temperatures will depolymerize the gum and permanently decrease the viscosity. The viscosity of sodium carboxymethylcellulose solutions is fairly stable over a pH range of 4–10. The optimum pH range is neutral. See Section 11.

Table III: Viscosity of aqueous carboxymethylcellulose sodium solutions. (Measurements made with a Brookfield LVT viscometer at 25°C.)

	Grade	Concentration (% w/v)	Viscosity (mPa s)	Spindle	Speed
Low viscosity	Akucell AF 0305	1	10–15	#1	60 rpm
Medium viscosity	Akucell AF 2785	1	1500–2500	#3	30 rpm
High viscosity	Akucell AF 3085	1	8000–12000	#4	30 rpm

11 Stability and Storage Conditions

Carboxymethylcellulose sodium is a stable, though hygroscopic material. Under high-humidity conditions, carboxymethylcellulose sodium can absorb a large quantity (>50%) of water. In tablets, this has been associated with a decrease in tablet hardness and an increase in disintegration time.⁽⁷⁾

Aqueous solutions are stable at pH 2–10; precipitation can occur below pH 2, and solution viscosity decreases rapidly

above pH 10. Generally, solutions exhibit maximum viscosity and stability at pH 7–9.

Carboxymethylcellulose sodium may be sterilized in the dry state by maintaining it at a temperature of 160°C for 1 hour. However, this process results in a significant decrease in viscosity and some deterioration in the properties of solutions prepared from the sterilized material.

Aqueous solutions may similarly be sterilized by heating, although this also results in some reduction in viscosity. After autoclaving, viscosity is reduced by about 25%, but this reduction is less marked than for solutions prepared from material sterilized in the dry state. The extent of the reduction is dependent on the molecular weight and degree of substitution; higher molecular weight grades generally undergo a greater percentage reduction in viscosity. Sterilization of solutions by gamma irradiation also results in a reduction in viscosity.

Aqueous solutions stored for prolonged periods should contain an antimicrobial preservative.⁽⁸⁾

The bulk material should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

Carboxymethylcellulose sodium is incompatible with strongly acidic solutions and with the soluble salts of iron and some other metals, such as aluminum, mercury, and zinc. Precipitation may occur at pH <2, and also when it is mixed with ethanol (95%).

Carboxymethylcellulose sodium forms complex coacervates with gelatin and pectin. It also forms a complex with collagen and is capable of precipitating certain positively charged proteins.

13 Method of Manufacture

Alkali cellulose is prepared by steeping cellulose obtained from wood pulp or cotton fibers in sodium hydroxide solution. The alkaline cellulose is then reacted with sodium monochloroacetate to produce carboxymethylcellulose sodium. Sodium chloride and sodium glycolate are obtained as by-products of this etherification.

14 Safety

Carboxymethylcellulose sodium is used in oral, topical, and some parenteral formulations. It is also widely used in cosmetics, toiletries, and food products, and is generally regarded as a nontoxic and nonirritant material. However, oral consumption of large amounts of carboxymethylcellulose sodium can have a laxative effect; therapeutically, 4–10 g in daily divided doses of the medium- and high-viscosity grades of carboxymethylcellulose sodium have been used as bulk laxatives.

The WHO has not specified an acceptable daily intake for carboxymethylcellulose sodium as a food additive since the levels necessary to achieve a desired effect were not considered to be a hazard to health.⁽⁹⁾ However, in animal studies, subcutaneous administration of carboxymethylcellulose sodium has been found to cause inflammation, and in some cases of repeated injection fibrosarcomas have been found at the site of injection.⁽¹⁰⁾

Hypersensitivity and anaphylactic reactions have occurred in cattle and horses, which have been attributed to carboxymethylcellulose sodium in parenteral formulations such as vaccines and penicillins.^(11,12)

LD₅₀ (guinea pig, oral): 16 g/kg⁽¹³⁾
LD₅₀ (rat, oral): 27 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Carboxymethylcellulose sodium may be irritant to the eyes. Eye protection is recommended.

16 Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (dental preparations; inhalations; intra-articular, intrabursal, intradermal, intralesional, IM, intrasynovial and SC injections; oral capsules, drops, solutions, suspensions, syrups and tablets; topical and vaginal preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Carboxymethylcellulose calcium.

18 Comments

A number of grades of carboxymethylcellulose sodium are commercially available, such as *Accelerate*. These have a degree of substitution (DS) in the range 0.7–1.2. The DS is defined as the average number of hydroxyl groups substituted per anhydroglucose unit and it is this that determines the aqueous solubility of the polymer. Thermal crosslinking reduces solubility while retaining water absorption, therefore producing materials suitable for water absorption.

Grades are typically classified as being of low, medium, or high viscosity. The degree of substitution and the maximum viscosity of an aqueous solution of stated concentration should be indicated on any carboxymethylcellulose sodium labeling.

Carboxymethylcellulose sodium has been reported to give false positive results in the LAL test for endotoxins.⁽¹⁴⁾

19 Specific References

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20 General References

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21 Author

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22 Date of Revision

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