Croscarmellose Sodium

1 Nonproprietary Names

BP: Croscarmellose sodium
PhEur: Carmellosum natricum conexum
USPNF: Croscarmellose sodium

2 Synonyms

Ac-Di-Sol; crosslinked carboxymethylcellulose sodium; *Explocel*; modified cellulose gum; *Nymcel ZSX*; *Pharmacel XL*; *Primellose*; *Solutab*; *Vivasol.*

3 Chemical Name and CAS Registry Number

Cellulose, carboxymethyl ether, sodium salt, crosslinked [74811-65-7]

4 Empirical Formula Molecular Weight

Croscarmellose sodium is a crosslinked polymer of carboxymethylcellulose sodium.

See Carboxymethylcellulose sodium.

5 Structural Formula

See Carboxymethylcellulose sodium.

6 Functional Category

Tablet and capsule disintegrant.

7 Applications in Pharmaceutical Formulation or Technology

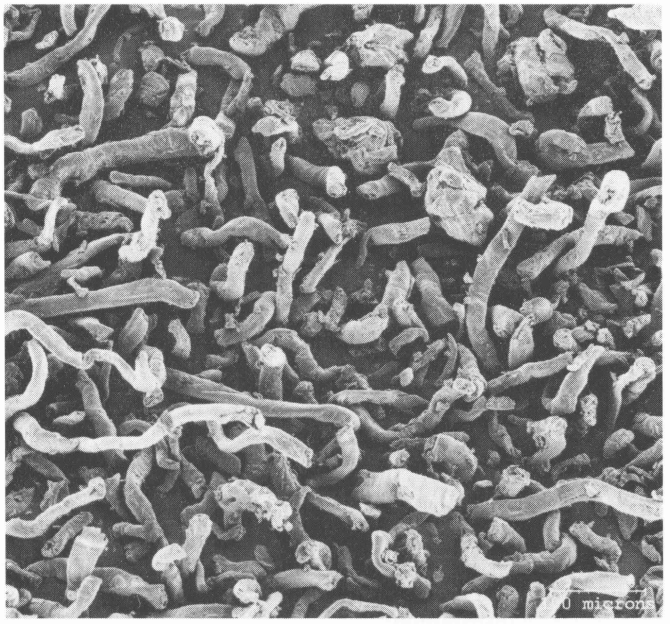
Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules,[1,2] tablets,[3–13] and granules.

In tablet formulations, croscarmellose sodium may be used in both direct-compression and wet-granulation processes. When used in wet granulations, the croscarmellose sodium should be added in both the wet and dry stages of the process (intra- and extragranularly) so that the wicking and swelling ability of the disintegrant is best utilized.[11,12] Croscarmellose sodium at concentrations up to 5% w/w may be used as a tablet disintegrant, although normally 2% w/w is used in tablets prepared by direct compression and 3% w/w in tablets prepared by a wet-granulation process. *See* Table I.

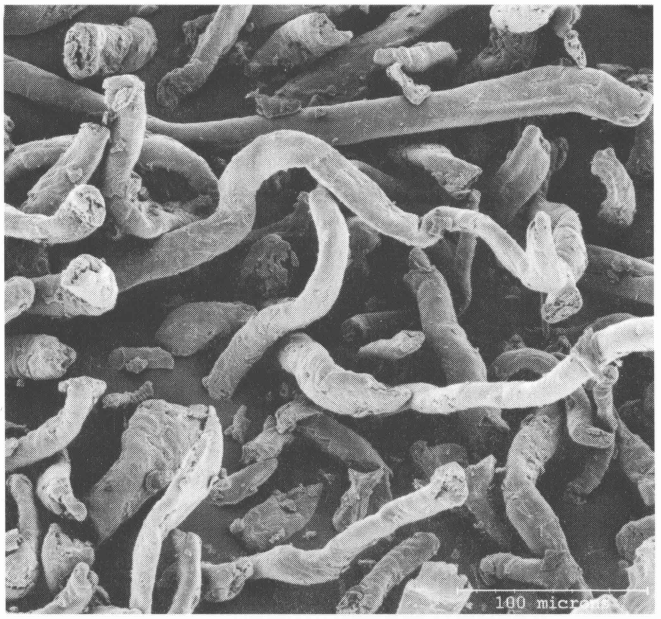
Table I: Uses of croscarmellose sodium.

Use	Concentration (%)
Disintegrant in capsules	10–25
Disintegrant in tablets	0.5–5.0

SEM: 1
Excipient: Croscarmellose sodium (*Ac-Di-Sol*)
Manufacturer: FMC Biopolymer
Magnification: 100 ×



SEM: 2
Excipient: Croscarmellose sodium (*Ac-Di-Sol*)
Manufacturer: FMC Biopolymer
Magnification: 1000 ×



8 Description

Croscarmellose sodium occurs as an odorless, white or greyish-white powder.

9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for croscarmellose sodium.

Test	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
pH (1% w/v dispersion)	5.0–7.0	5.0–7.0
Loss on drying	≤10.0%	≤10.0%
Heavy metals	≤10 ppm	≤0.001%
Sodium chloride and sodium glycolate	≤0.5%	≤0.5%
Sulfated ash	14.0–28.0%	—
Degree of substitution	0.60–0.85	0.60–0.85
Content of water-soluble material	≤10.0%	1.0–10.0%
Settling volume	+	+
Microbial contamination	+	—
Organic volatile impurities	—	+

10 Typical Properties

Bonding index: 0.0456
Brittle fracture index: 0.1000
Density (bulk): 0.529 g/cm^3 for *Ac-Di-Sol*[7]
Density (tapped): 0.819 g/cm^3 for *Ac-Di-Sol*[7]
Density (true): 1.543 g/cm^3 for *Ac-Di-Sol*[7]
Particle size distribution:
Ac-Di-Sol: not more than 2% retained on a #200 (73.7 μm) mesh and not more than 10% retained on a #325 (44.5 μm) mesh
Pharmacel XL: more than 90% less than 45 μm, and more than 98% less than 100 μm in size
Solubility: insoluble in water, although croscarmellose sodium rapidly swells to 4–8 times its original volume on contact with water.
Specific surface area: 0.81–0.83 m^2/g

11 Stability and Storage Conditions

Croscarmellose sodium is a stable though hygroscopic material.

A model tablet formulation prepared by direct compression, with croscarmellose sodium as a disintegrant, showed no significant difference in drug dissolution after storage at 30°C for 14 months.[9]

Croscarmellose sodium should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

The efficacy of disintegrants, such as croscarmellose sodium, may be slightly reduced in tablet formulations prepared by either the wet-granulation or direct-compression process that contain hygroscopic excipients such as sorbitol.[10]

Croscarmellose sodium is not compatible with strong acids or with soluble salts of iron and some other metals such as aluminum, mercury, and zinc.

13 Method of Manufacture

Alkali cellulose is prepared by steeping cellulose, obtained from wood pulp or cotton fibers, in sodium hydroxide solution. The alkali cellulose is then reacted with sodium monochloroacetate to obtain carboxymethylcellulose sodium. After the substitution reaction is completed and all of the sodium hydroxide has been used, the excess sodium monochloroacetate slowly hydrolyzes to glycolic acid. The glycolic acid changes a few of the sodium carboxymethyl groups to the free acid and catalyzes the formation of crosslinks to produce croscarmellose sodium. The croscarmellose sodium is then extracted with aqueous alcohol and any remaining sodium chloride or sodium glycolate is removed. After purification, croscarmellose sodium of purity greater than 99.5% is obtained.[4] The croscarmellose sodium may be milled to break the polymer fibers into shorter lengths and hence improve its flow properties.

14 Safety

Croscarmellose sodium is mainly used as a disintegrant in oral pharmaceutical formulations and is generally regarded as an essentially nontoxic and nonirritant material. However, oral consumption of large amounts of croscarmellose sodium may have a laxative effect, although the quantities used in solid dosage formulations are unlikely to cause such problems.

In the UK, croscarmellose sodium is accepted for use in dietary supplements.

The WHO has not specified an acceptable daily intake for the related substance carboxymethylcellulose sodium, used as a food additive, since the levels necessary to achieve a desired effect were not considered sufficient to be a hazard to health.[14]

See also Carboxymethylcellulose sodium.

15 Handling Precautions

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

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (oral capsules and tablets). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Carboxymethylcellulose calcium; carboxymethylcellulose sodium.

18 Comments

Typically, the degree of substitution (DS) for croscarmellose sodium is 0.7.

19 Specific References

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20 General References

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22 Date of Revision

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