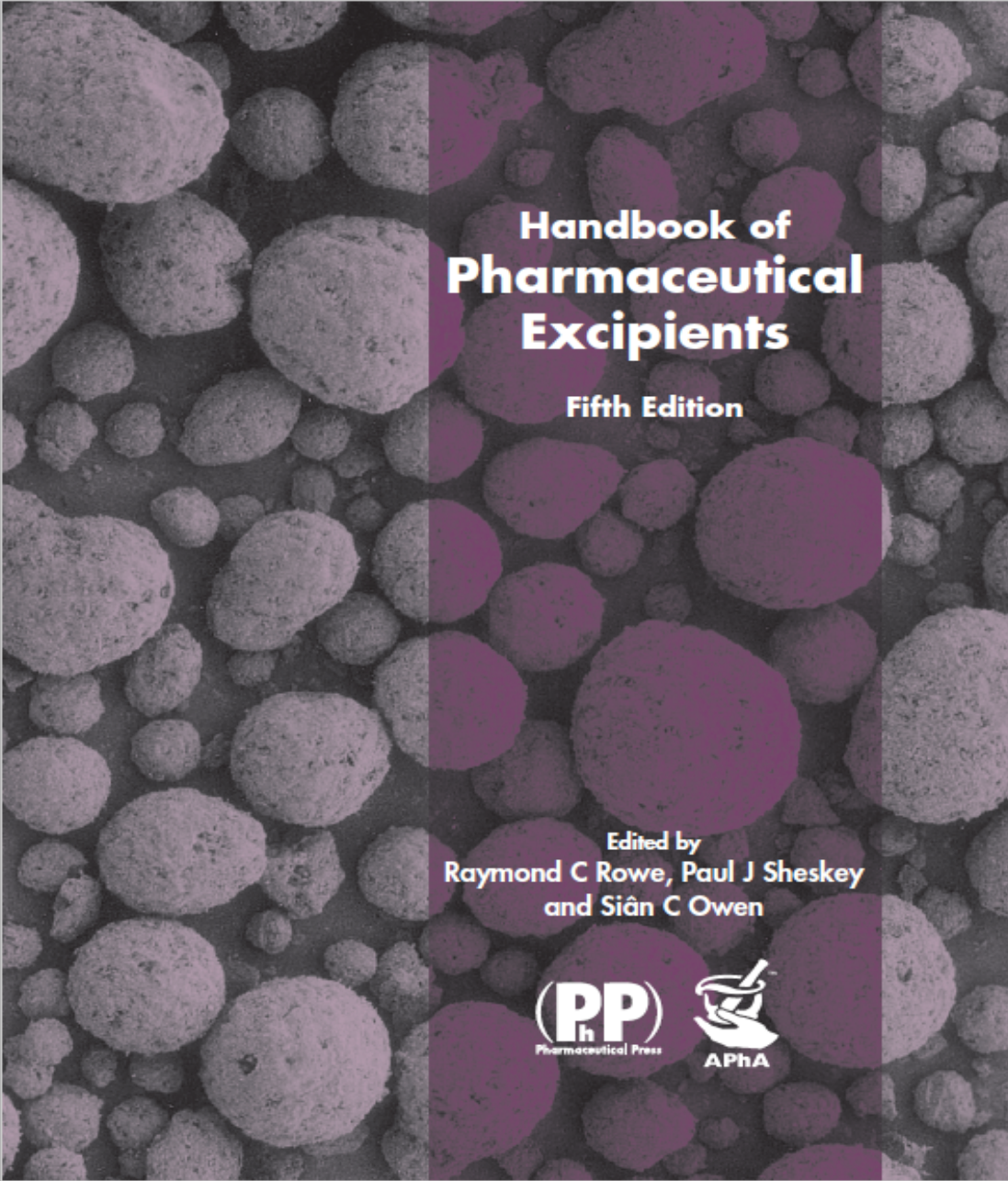




Handbook of Pharmaceutical Excipients

Fifth Edition

Edited by
Raymond C Rowe, Paul J Sheskey
and Siân C Owen



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Pharmaceutical Excipients**

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FIFTH EDITION

Edited by

Raymond C Rowe

BPharm, PhD, D.Sc, FRPharmS, CChem,
FRSC, CPhys, MInstP

Chief Scientist

Intelligence Ltd
Billingham, UK

Paul J Sheskey

B.Sc, R.Ph

Technical Services Leader

The Dow Chemical Company
Midland
MI, USA

Siân C Owen

B.Sc, MA

Development Editor

Royal Pharmaceutical Society of Great Britain
London, UK



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Croscarmellose Sodium

1 Nonproprietary Names

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

2 Synonyms

Ac-Di-So[®]; crosslinked carboxymethylcellulose sodium; Explo-
cel[®]; modified cellulose gum; Nymcol 25X; Pharmacol XI;
Primellose; Solubul; Viscoel.

3 Chemical Name and CAS Registry Number

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

4 Empirical Formula and Molecular Weight

Croscarmellose sodium is a crosslinked polymer of carboxy-
methylcellulose 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 for-
mulations as a disintegrant for capsules,^(1,2) tablets,⁽³⁻¹⁵⁾ 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.

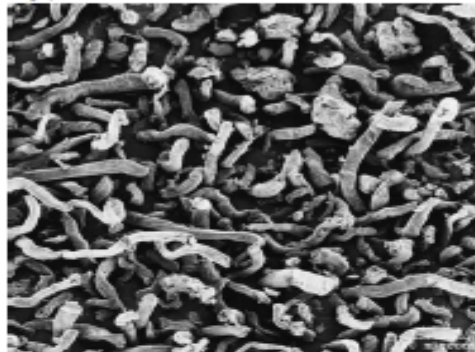
Use	Concentration (%)
Disintegrant in capsules	1.0–2.5
Disintegrant in tablets	0.5–5.0

SEM: 1

Excipient: Croscarmellose sodium (Ac-Di-So[®])

Manufacturer: FMC Biopolymer

Magnification: 1000x



SEM: 2

Excipient: Croscarmellose sodium (Ac-Di-So[®])

Manufacturer: FMC Biopolymer

Magnification: 1000x



Colloidal Silicon Dioxide

1 Nonproprietary Names

BP: Colloidal anhydrous silica
PhEur: Silica colloidalis anhydrica
USP/NF: Colloidal silicon dioxide

2 Synonyms

Aerocel, *Cab-O-Sil*, *Cab-O-Sil M-5P*; colloidal silica; fumed silica; light anhydrous silicic acid; silicic anhydride; silicon dioxide fumed; *Wücker HDK*

3 Chemical Name and CAS Registry Number

Silica [7631-86-9]

4 Empirical Formula and Molecular Weight

SiO₂ 60.08

5 Structural Formula

SiO₂

6 Functional Category

Adsorbent; anticaking agent; emulsion stabilizer; gellant; suspending agent; tablet disintegrant; thermal stabilizer; viscosity-increasing agent.

7 Applications in Pharmaceutical Formulation or Technology

Colloidal silicon dioxide is widely used in pharmaceuticals, cosmetics, and food products; see Table I. Its small particle size and large specific surface area give it desirable flow characteristics that are exploited to improve the flow properties of dry powders in a number of processes such as tableting.¹⁰⁻¹⁸

Colloidal silicon dioxide is also used to stabilize emulsions and as a thixotropic thickening and suspending agent in gels and semisolid preparations.¹⁹ With other ingredients of similar refractive index, transparent gels may be formed. The degree of viscosity increase depends on the polarity of the liquid (polar liquids generally require a greater concentration of colloidal silicon dioxide than nonpolar liquids). Viscosity is largely independent of temperature. However, changes to the pH of a system may affect the viscosity; see Section 11.

In aerosols, other than those for inhalation, colloidal silicon dioxide is used to promote particulate suspension, eliminate hard settling, and minimize the clogging of spray nozzles. Colloidal silicon dioxide is also used as a tablet disintegrant and as an adsorbent/dispersing agent for liquids in powders.¹³ Colloidal silicon dioxide is frequently added to suppository formulations containing lipophilic excipients to increase

viscosity, prevent sedimentation during molding, and decrease the release rate.^{16,20} Colloidal silicon dioxide is also used as an adsorbent during the preparation of wax microspheres,¹⁶ as a thickening agent for topical preparations,¹⁹ and has been used to aid the freeze-drying of nanocapsules and nanosphere suspensions.¹¹⁰

Table I: Uses of colloidal silicon dioxide.

Use	Concentration (%)
Aerosols	0.5-2.0
Emulsion stabilizer	1.0-5.0
Gellant	0.1-0.5
Suspending and thickening agent	2.0-10.0

8 Description

Colloidal silicon dioxide is a submicroscopic fumed silica with a particle size of about 15 nm. It is a light, loose, bluish-white-colored, odorless, tasteless, nongritty amorphous powder.

9 Pharmacopoeial Specifications

See Table II.

Table II: Pharmacopoeial specifications for colloidal silicon dioxide.

Test	PhEur 2005	USP/NF 23
Identification	+	+
Character	+	—
pH (1% w/v dispersion)	3.5-5.5	3.5-5.5
Arsenic	—	≤8 µg/g
Chloride	≤250 ppm	—
Heavy metals	≤25 ppm	—
Loss on drying	—	≤2.5%
Loss on ignition	≤5.0%	≤2.0%
Organic volatile impurities	—	+
Assay (on ignited sample)	99.0-100.5%	99.0-100.5%

10 Typical Properties

Acidity/alkalinity: pH = 3.5-4.4 (4% w/v aqueous dispersion)
Density (bulk): 0.029-0.042 g/cm³
Density (tapped): See Tables III, IV and V.
Flowability: 3.5-52% (Carr compressibility index)
Moisture content: See Figure 1.^{11,13,14}
Particle size distribution: 7-16 nm. See also Figure 2.
Refractive index: 1.46
Solubility: practically insoluble in organic solvents, water, and acids, except hydrofluoric acid; soluble in hot solutions of alkali hydroxide. Forms a colloidal dispersion with water.
Specific gravity: 2.2

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- [illegible]