Cellulose Acetate

1 Nonproprietary Names

BP: Cellulose acetate
PhEur: Cellulosi acetas
USPNF: Cellulose acetate

2 Synonyms

Acetyl cellulose; cellulose diacetate; cellulose triacetate.

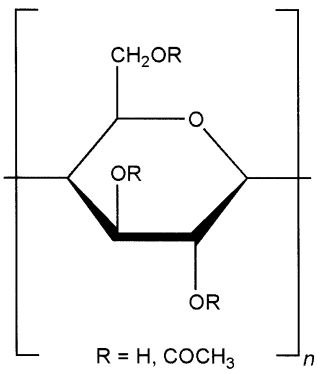
3 Chemical Name and CAS Registry Number

Cellulose acetate [9004-35-7]
Cellulose diacetate [9035-69-2]
Cellulose triacetate [9012-09-3]

4 Empirical Formula Molecular Weight

Cellulose acetate is cellulose in which a portion or all of the hydroxyl groups are acetylated. Cellulose acetate is available in a wide range of acetyl levels and chain lengths and thus molecular weights; *see* Table I

5 Structural Formula



6 Functional Category

Coating agent; extended release agent; tablet and capsule diluent.

7 Applications in Pharmaceutical Formulation or Technology

Cellulose acetate is widely used in pharmaceutical formulations both in sustained-release applications and for taste masking.

Cellulose acetate is used as a semipermeable coating on tablets, especially on osmotic pump-type tablets and implants. This allows for controlled, extended release of actives.[1–4] Cellulose acetate films, in conjunction with other materials, also offer sustained release without the necessity of drilling a hole in the coating as is typical with osmotic pump systems. Cellulose acetate and other cellulose esters have also been used to form drug-loaded microparticles with controlled-release characteristics.[5,6]

Cellulose acetate films are used in transdermal drug delivery systems[7,8] and also as film coatings on tablets or granules for taste masking. For example, acetaminophen granules have been coated with a cellulose acetate-based coating before being processed to provide chewable tablets. Extended-release tablets can also be formulated with cellulose acetate as a directly compressible matrix former.[9] The release profile can be modified by changing the ratio of active to cellulose acetate and by incorporation of plasticizer, but was shown to be insensitive to cellulose acetate molecular weight and particle size distribution.

Therapeutically, cellulose acetate has been used to treat cerebral aneurysms, and also for spinal perimedullary arteriovenous fistulas.[10]

8 Description

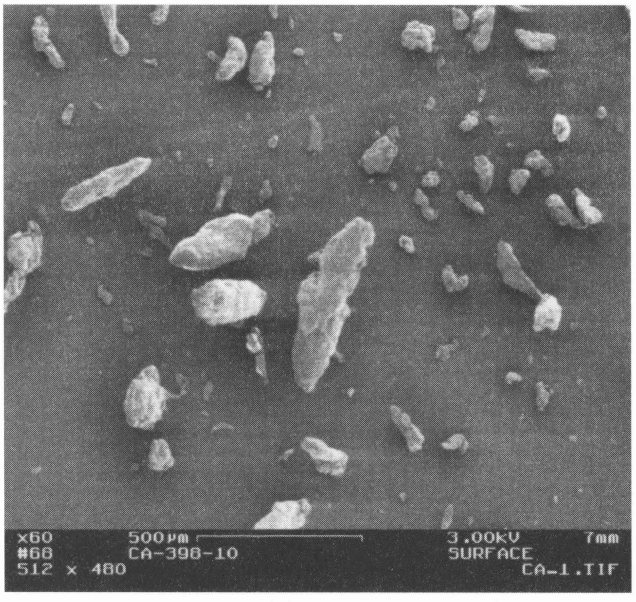
Cellulose acetate occurs as a white to off-white powder, free-flowing pellets, or flakes. It is tasteless and odorless, or may have a slight odor of acetic acid.

Table I: Comparison of different types of cellulose acetate.[1]

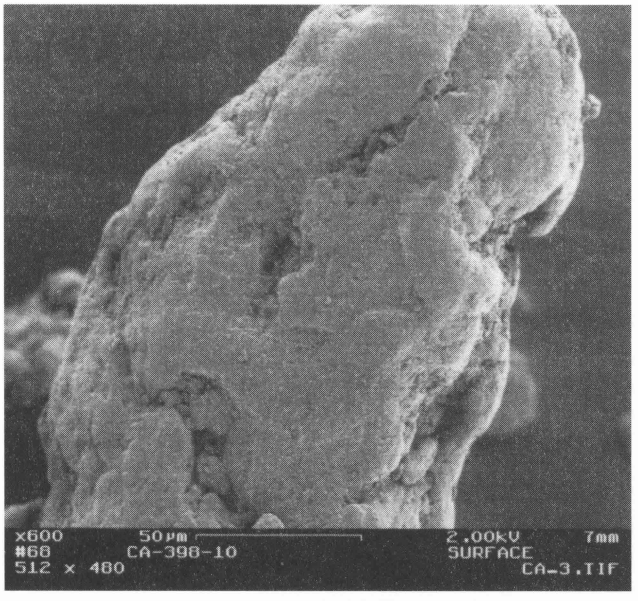
Type	Acetyl (%)	Viscosity (mPa s)	Hydroxyl (%)	Melting range (°C)	T_g[a] (°C)	Density[b] (g/cm^3)	MWn[c]
CA-320S	32.0	210.0	8.7	230–250	180	0.4	38 000
CA-398-3	39.8	11.4	3.5	230–250	180	0.4	30 000
CA-398-6	39.8	22.8	3.5	230–250	182	0.4	35 000
CA-398-10NF	39.8	38.0	3.5	230–250	185	0.4	40 000
CA-398-30	39.7	114.0	3.5	230–250	189	0.4	50 000
CA-394-60S	39.5	228.0	4.0	240–260	186	—	60 000
CA-435-75	43.5	—	0.9	280–300	185	0.7	122 000

[a] Glass transition temperature.
[b] Tapped.
[c] Number average molecular weight in polystyrene equivalents.
Supplier: Eastman Chemical Company.

SEM: 1
Excipient: Cellulose acetate, CA-398-10NF
Manufacturer: Eastman Chemical Co.
Lot No.: AC65280NF
Magnification: 60×
Voltage: 3 kV



SEM 2
Excipient: Cellulose acetate, CA-398-10NF
Manufacturer: Eastman Chemical Co.
Lot No.: AC65280NF
Magnification: 600×
Voltage: 2 kV



9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for cellulose acetate.

Test	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
Loss on drying	≤5.0%	≤5.0%
Residue on ignition	≤0.1%	≤0.1%
Free acid	+	≤0.1%
Heavy metals	≤10 ppm	≤0.001%
Microbial contamination	1000/g	—
Organic volatile impurities	—	+
Assay (of acetyl groups)	29.0–44.8%	29.0–44.8%

10 Typical Properties

Density (bulk): typically 0.4 g/cm^3 for powders
Glass transition temperature: 170–190°C
Melting point: melting range 230–300°C
Solubility: the solubility of cellulose acetate is greatly influenced by the level of acetyl groups present. In general, cellulose acetates are soluble in acetone–water blends of varying ratios, dichloromethane–ethanol blends, dimethyl formamide, and dioxane. The cellulose acetates of higher acetyl level are generally more limited in solvent choice than are the lower-acetyl materials.
Viscosity (dynamic): various grades of cellulose acetate are commercially available that differ in their acetyl content and degree of polymerization. They can be used to produce 10% w/v solutions in organic solvents with viscosities of 10–230 mPa s. Blends of cellulose acetates may also be prepared with intermediate viscosity values. *See also* Table I.

11 Stability and Storage Conditions

Cellulose acetate is stable if stored in a well-closed container in a cool, dry place. Cellulose acetate hydrolyzes slowly under prolonged adverse conditions such as high temperature and humidity, with a resultant increase in free acid content and odor of acetic acid.

12 Incompatibilities

Cellulose acetate is incompatible with strongly acidic or alkaline substances. Cellulose acetate is compatible with the following plasticizers: diethyl phthalate, polyethylene glycol, triacetin, and triethyl citrate.

13 Method of Manufacture

Cellulose acetate is prepared from highly purified cellulose by treatment with acid catalysis and acetic anhydride.

14 Safety

Cellulose acetate is widely used in oral pharmaceutical products and is generally regarded as a nontoxic and nonirritant material.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Dust may be irritant to the eyes and eye protection should be worn. Like most organic materials in powder form, these materials are capable of creating dust explosions. Cellulose acetate is combustible.

16 Regulatory Acceptance

Included in the FDA Inactive Ingredients Guide (oral tablets).

17 Related Substances

Cellulose acetate phthalate.

18 Comments

When solutions are being prepared, cellulose acetate should always be added to the solvent, not the reverse. Various grades of cellulose acetate are available with varying physical properties; *see* Table I.

19 Specific References

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2 Theeuwes F. Elementary osmotic pump. *J Pharm Sci* 1975; **64**(12): 1987–1991.
3 Santus G, Baker RW. Osmotic drug delivery: review of the patent literature. *J Control Release* 1995; **35**: 1–21.
4 Van Savage G, Rhodes CT. The sustained release coating of solid dosage forms: a historical review. *Drug Dev Ind Pharm* 1995; **21**(1): 93–118.
5 Soppimath KS, Kulkarni AR, Aminabhavi TM. Development of hollow microspheres as floating controlled-release systems for cardiovascular drugs: preparation and release characteristics. *Drug Dev Ind Pharm* 2001; **27**(6): 507–515.
6 Soppimath KS, Kulkarni AR, Aminabhavi TM, Bhaskar C. Cellulose acetate microspheres prepared by o/w emulsification and solvent evaporation method. *J Microencapsul* 2001; **18**(6): 811–817.
7 Rao PR, Diwan PV. Drug diffusion from cellulose acetate-polyvinyl pyrrolidine free films for transdermal administration. *Indian J Pharm Sci* 1996; **58**(6): 246–250.
8 Rao PR, Diwan PV. Permeability studies of cellulose acetate free films for transdermal use: influences of plasticizers. *Pharm Acta Helv* 1997; **72**: 47–51.
9 Yuan J, Wu SHW. Sustained-release tablets via direct compression: a feasibility study using cellulose acetate and cellulose acetate butyrate. *Pharm Technol* 2000; **24**(10): 92, 94, 96, 98, 100, 102, 104, 106.
10 Sugiu K, Meguro T, Nakashiama H, Ohmoto T. Successful embolization of a spinal perimedullary arteriovenous fistula with cellulose acetate polymer solution: technical case report. *Neurosurgery* 2001; **49**(5): 1257–1260.

20 General References

Doelker E. Cellulose derivatives. *Adv Polym Sci* 1993; **107**: 199–265.

21 Author

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22 Date of Revision

21 October 2002.