

Sodium Alginate

1 Nonproprietary Names

BP: Sodium alginate
PhEur: Natrii alginas
USPNF: Sodium alginate

2 Synonyms

Algin; alginic acid, sodium salt; E401; *Kelcosol*; *Keltone*; *Protanal*; sodium polymannuronate.

3 Chemical Name and CAS Registry Number

Sodium alginate [9005-38-3]

4 Empirical Formula Molecular Weight

Sodium alginate consists chiefly of the sodium salt of alginic acid, which is a mixture of polyuronic acids composed of residues of D-mannuronic acid and L-guluronic acid.

The block structure and molecular weight of sodium alginate samples has been investigated.⁽¹⁾

5 Structural Formula

See Section 4.

6 Functional Category

Stabilizing agent; suspending agent; tablet and capsule disintegrant; tablet binder; viscosity-increasing agent.

7 Applications in Pharmaceutical Formulation or Technology

Sodium alginate is used in a variety of oral and topical pharmaceutical formulations. In tablet formulations, sodium alginate may be used as both a binder and disintegrant;⁽²⁾ it has been used as a diluent in capsule formulations.⁽³⁾ Sodium alginate has also been used in the preparation of sustained-release oral formulations since it can delay the dissolution of a drug from tablets,⁽⁴⁾ capsules,⁽⁵⁾ and aqueous suspensions.⁽⁶⁾

In topical formulations, sodium alginate is widely used as a thickening and suspending agent in a variety of pastes, creams, and gels, and as a stabilizing agent for oil-in-water emulsions.

Recently, sodium alginate has been used for the aqueous microencapsulation of drugs,⁽⁷⁾ in contrast with the more conventional microencapsulation techniques which use organic-solvent systems. It has also been used in the formation of nanoparticles.⁽⁸⁾

The adhesiveness of hydrogels prepared from sodium alginate has been investigated⁽⁹⁾ and drug release from oral mucosal adhesive tablets based on sodium alginate has been reported.⁽¹⁰⁾ Other novel delivery systems containing sodium alginate include an ophthalmic solution that forms a gel *in situ* when administered to the eye⁽¹¹⁾ and a freeze-dried device intended for the delivery of bone-growth factors.⁽¹²⁾

Hydrogel systems containing alginates have also been investigated for delivery of proteins and peptides.⁽¹³⁾

Therapeutically, sodium alginate has been used in combination with an H₂-receptor antagonist in the management of gastroesophageal reflux,⁽¹⁴⁾ and as a hemostatic agent in surgical dressings.^(15,16) Alginate dressings, used to treat exuding wounds, often contain significant amounts of sodium alginate as this improves the gelling properties.⁽¹⁷⁾

Sodium alginate is also used in cosmetics and food products; see Table I.

Table I: Uses of sodium alginate.

Use	Concentration (%)
Pastes and creams	5–10
Stabilizer in emulsions	1–3
Suspending agent	1–5
Tablet binder	1–3
Tablet disintegrant	2.5–10

8 Description

Sodium alginate occurs as an odorless and tasteless, white to pale yellowish-brown colored powder.

9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for sodium alginate.

Test	PhEur 2002	USPNF 20
Identification	+	+
Appearance of solution	+	—
Microbial limits	≤ 1000/g	≤ 200/g
Loss on drying	≤ 15.0%	≤ 15.0%
Ash	—	18.0–27.0%
Sulfated ash	30.0–36.0%	—
Arsenic	—	≤ 1.5 ppm
Calcium	≤ 1.5%	—
Chlorides	≤ 1.0%	—
Lead	—	≤ 0.001%
Heavy metals	≤ 20 ppm	≤ 0.004%
Assay (dried basis)	—	90.8–106.0%

10 Typical Properties

Acidity/alkalinity: pH ≈ 7.2 for a 1% w/v aqueous solution.

Solubility: practically insoluble in ethanol, ether, chloroform, and ethanol/water mixtures in which the ethanol content is greater than 30%. Also, practically insoluble in other organic solvents and aqueous acidic solutions in which the pH is less than 3. Slowly soluble in water, forming a viscous colloidal solution.

Viscosity (dynamic): various grades of sodium alginate are commercially available that yield aqueous solutions of varying viscosity. Typically, a 1% w/v aqueous solution, at 20 °C, will have a viscosity of 20–400 mPa s (20–400 cP).

Viscosity may vary depending upon concentration, pH, temperature, or the presence of metal ions.⁽¹⁸⁻²⁰⁾ Above pH 10, viscosity decreases, *see also* Alginic Acid and Section 11.

11 Stability and Storage Conditions

Sodium alginate is a hygroscopic material, although it is stable if stored at low relative humidities and a cool temperature.

Aqueous solutions of sodium alginate are most stable at pH 4-10. Below pH 3, alginic acid is precipitated. A 1% w/v aqueous solution of sodium alginate exposed to differing temperatures had a viscosity 60-80% of its original value after storage for 2 years.⁽²¹⁾ Solutions should not be stored in metal containers.

Sodium alginate solutions are susceptible on storage to microbial spoilage, which may affect solution viscosity. Solutions are ideally sterilized using ethylene oxide, although filtration using a 0.45- μ m filter also has only a slight adverse effect on solution viscosity.⁽²²⁾ Heating sodium alginate solutions to temperatures above 70°C causes depolymerization with a subsequent loss of viscosity. Autoclaving of solutions can cause a decrease in viscosity, which may vary depending upon the nature of any other substances present.^(22,23) Gamma irradiation should not be used to sterilize sodium alginate solutions since this process severely reduces solution viscosity.^(22,24)

Preparations for external use may be preserved by the addition of 0.1% chlorocresol, 0.1% chloroxylenol, or parabens. If the medium is acidic, benzoic acid may also be used.

The bulk material should be stored in an airtight container in a cool, dry place.

12 Incompatibilities

Sodium alginate is incompatible with acridine derivatives, crystal violet, phenylmercuric acetate and nitrate, calcium salts, heavy metals, and ethanol in concentrations greater than 5%. Low concentrations of electrolytes cause an increase in viscosity but high electrolyte concentrations cause salting-out of sodium alginate; salting-out occurs if more than 4% of sodium chloride is present.

13 Method of Manufacture

Alginic acid is extracted from brown seaweed and is neutralized with sodium bicarbonate to form sodium alginate.

14 Safety

Sodium alginate is widely used in cosmetics, food products, and pharmaceutical formulations, such as tablets and topical products, including wound dressings. It is generally regarded as a nontoxic and nonirritant material, although excessive oral consumption may be harmful. A study in five healthy male volunteers fed a daily intake of 175 mg/kg body-weight of sodium alginate for 7 days, followed by a daily intake of 200 mg/kg body-weight of sodium alginate for a further 16 days, showed no significant adverse effects.⁽²⁵⁾

The WHO has not specified an acceptable daily intake for alginic acid and alginate salts as the levels used in food do not represent a hazard to health.⁽²⁶⁾

Inhalation of alginate dust may be irritant and has been associated with industrial-related asthma in workers involved in alginate production. However, it appears that the cases of asthma were linked to exposure to seaweed dust rather than pure alginate dust.⁽²⁷⁾

LD₅₀ (cat, IP): 0.25 g/kg⁽²⁸⁾
 LD₅₀ (mouse, IV): 0.2 g/kg
 LD₅₀ (rabbit, IV): 0.1 g/kg
 LD₅₀ (rat, IV): 1 g/kg
 LD₅₀ (rat, oral): >5 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Sodium alginate may be irritant to the eyes or respiratory system if inhaled as dust; *see* Section 14. Eye protection, gloves, and a dust respirator are recommended. Sodium alginate should be handled in a well-ventilated environment.

16 Regulatory Status

GRAS listed. Accepted in Europe for use as a food additive. Included in the FDA Inactive Ingredients Guide (oral suspensions and tablets). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Alginic acid; calcium alginate; potassium alginate; propylene glycol alginate.

Calcium alginate

CAS number: [9005-35-0]

Synonyms: alginic acid, calcium salt; calcium polymannuronate; calginat; E404.

Comments: calcium alginate is used in applications similarly to sodium alginate, such as in sustained-release formulations,^(29,30) and the preparation of beads,⁽³¹⁾ hydrogels,⁽³²⁾ and hemostatic wound dressings that can be washed off with sterile sodium chloride solution.⁽¹⁵⁾

The microencapsulation of live attenuated *Bacillus Calmette-Guérin* (BCG) cells within a calcium alginate matrix has also been reported.⁽³³⁾

Potassium alginate

CAS number: [9005-36-1]

Synonyms: alginic acid, potassium salt; E402; potassium polymannuronate.

18 Comments

A number of different grades of sodium alginate, which have different solution viscosities, are commercially available. Many different alginate salts and derivatives are also commercially available including ammonium alginate; calcium alginate; magnesium alginate, and potassium alginate.

To assist in the preparation of dispersions of sodium alginate, the material may be mixed with a dispersing agent such as sucrose, ethanol, glycerol, or propylene glycol.

See also Alginic Acid for further information.

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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