

BIOMATERIALS BASED ON A NATURAL POLYSACCHARIDE: ALGINATE

Marguerite Rinaudo

Biomaterials Applications, 6, rue Lesdiguières, 38000 Grenoble (France).

E-mail: marguerite.rinaudo@sfr.fr

ABSTRACT

In this short review, our objective was to describe few new applications of a natural polysaccharide extracted from algae, the alginates. Firstly, the chemical composition is recalled and the main techniques used for characterization are cited. The role of guluronic acid blocks (GG blocks) is particularly important for gel mechanical properties in presence of calcium counterions. Then, the main applications in food and biomedicine are briefly mentioned followed by tentative applications in packaging, paper, textil and wound dressing which are described. Especially, fine fibers are produced now industrially under mixed sodium/calcium ionic form.

Key Words: Alginate applications, alginate composition, alginate fibers, alginate properties, Ca-gelation.

RESUMEN

En esta corta revisión, nuestro objetivo fue describir algunas nuevas aplicaciones de un polisacárido natural extraído de algas: el alginato. Primeramente, la composición química es revisada, además de citar las principales técnicas utilizadas para su caracterización. El papel de los bloques de ácido gulurónico (bloques GG) es particularmente importante para las propiedades mecánicas del gel en presencia de Ca como contraión. Después, se mencionan brevemente las principales aplicaciones en el área de alimentos y biomedicina, seguida de aplicaciones experimentales en embalaje, papel, textiles, y vendajes de heridas, las cuales son descritas. Especialmente, fibras finas de alginato son ahora producidas industrialmente en una forma iónica mixta de sodio/calcio.

Palabras Clave: Aplicaciones del alginato, composición del alginato, fibras de alginato, propiedades del alginato, gelato de calcio.

INTRODUCTION



Marine algae constitute a large source of natural polysaccharides having original physical properties. Algae also contain a large variety of nutriments such as vitamins, salts, iodine, sterols...¹ There is a large variety of such organisms which are exploited for a long time mainly for food applications. The brown algae (Phaeophyceae such as *Fucus*, *Laminaria*, *Ascophyllum*) contain large amounts of alginate in their cell walls^{1,2}. The quantity (between 25 and 45% dried weight of crude algae) and quality of the alginates depend on the algae species, the type and age of the tissues and methods used for extraction. They are linear polymers composed of (1→4)- α -L-guluronic acid blocks (GG) (Figure 1a), (1→4)- β -D-mannuronic acid blocks (MM) (Figure 1b), and

additionally, of heteropolymeric sequences of M and G (MG blocks) (Figure 1c).

Alginates are mainly used in the food and biomedical domains but in this paper we will focus on bioplastic applications, a less common field developed in the literature, i.e. applications of alginates in the domains of packaging, textiles, paper and wound dressing.

MAIN CHARACTERISTICS

The biological and physical properties of alginates in aqueous media depend not only on the M/G ratio (obtained by proton NMR) but also on the distribution of M and G units along the chain³⁻⁶. Purified alginates have widespread industrial uses especially due to their ability to form hydrogels, beads, fibers or films mainly in presence of calcium attributed to the presence of zones rich in GG blocks following the model of

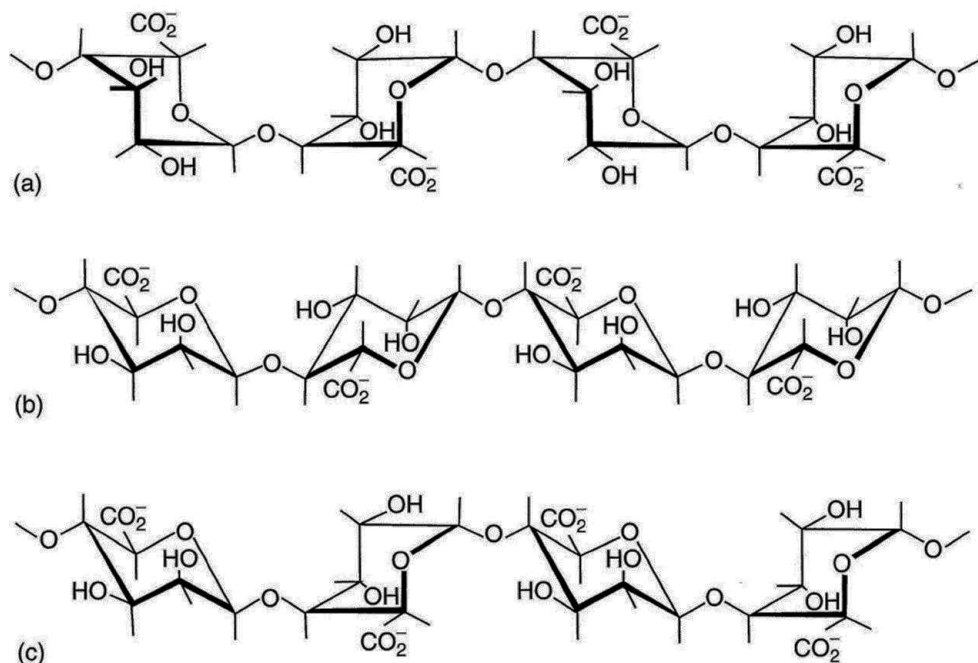


Figure 1. Chemical structures of uronic acid blocks involved in alginate composition.

an egg-box⁷. Nevertheless, it must be mentioned that MM and MG blocks also interact with calcium counterions. A schematic representation of gelation for progressive and cooperative fixation of calcium is given in Figure 2.

The stiffness of alginates gels is directly related to the GG block content⁸. Under their monovalent salt form (especially sodium form), alginates are perfectly water soluble and increase of solvent viscosity upon dissolution causing an interesting thickening character (in relation with the semi-rigid conformation of this copolymer) which found valuable applications. In addition, the ion-exchange properties of alginates are important due to specific strong interactions with counterions such as Ba, Sr and Ca giving a gel which is reversible in presence of large excess of monovalent salts or complexing agent (EDTA, sodium oxalate, sodium citrate). Alginic acid or alginate in acidic medium gives also specific gels based on H-bond network⁹. Another important parameter is the distribution of the molar masses and the average molar mass (obtained by steric exclusion chromatography) which also control the viscosity of solution and stiffness of the gels. It is important to mention that specific low molar mass oligomers may be obtained by partial hydrolysis in acidic conditions followed by fractionation at controlled pH to isolate GG and MM blocks^{10,11}.

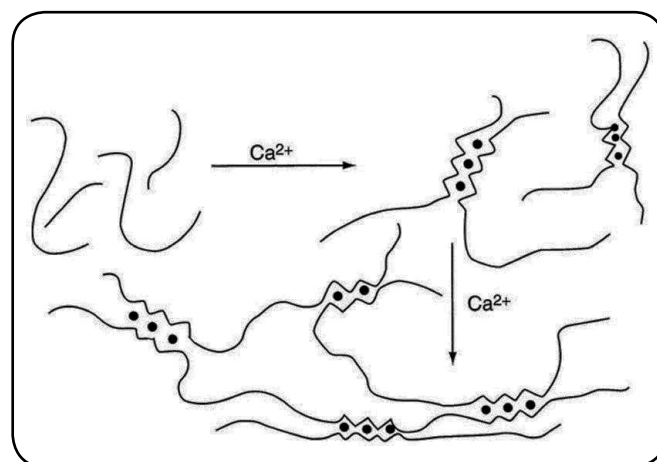


Figure 2. Schematic crosslinking of alginate in the presence of calcium counterions (•) complexed with L-guluronic blocks.

ALGINATES APPLICATIONS

Alginates in Foods

Up to now, the main applications of alginates were based mainly on their gel-forming ability and used as food additives in jams, jellies.... to improve and stabilize the structure of food. In this domain, alginates are also widely used as additives capable of viscosifying, stabilizing, emulsifying solutions¹².

Alginates in biomedical applications

Pharmaceutical industries use purified alginates as stabilizer in solution and dispersion of solid substances. In the biomedical domain, alginates are used for controlled drug release¹³, cells encapsulation¹⁴, scaffolds in ligament and tendon tissue engineering or to prepare moulds in dentistry (in presence of slow release calcium salt)¹⁵⁻¹⁷.

Alginates in packaging

Cooking or warming breaded foods in a microwave oven causes a lack of crunchiness. New products are now proposed for microwave heating by using active packaging (with susceptors). In that view, a film of alginate gel with high salt concentration was used as an edible susceptor. Better heating and shorter cooking times were demonstrated¹⁸. Edible films were also prepared as emulsifiable alginate with new barrier properties and good mechanical properties also allowing protecting encapsulated active substances¹⁹. Incorporation of garlic oil, a natural antibacterial agent gives good edible film²⁰.

Vegetable and fruit preservation was favoured by incorporation of stable silver nanoparticles in alginate film²¹. Antibacterial films were obtained by incorporation of extruded white ginseng to ensure healthy foods²². Antimicrobial packaging with lactic acid bacteria incorporated in alginate film matrix allows to control the growth of food-borne pathogens in ready-to-eat food²³. Antiradical properties were obtained with oregano-based film made of polycaprolactone/alginate-calcium film²⁴.

Alginates in paper industry

Alginate partially complexed with calcium (such as forming a loose gel) mixed with starch was proposed to get high water retention in paper coating. Such advantage is important for size press coating formulation to improve coating rheology, control migration and get coat weight uniformity²⁵.

Alginates in textiles and medical textiles

A review was recently available which is devoted to processing of alginate fibers for their use as a wound management material²⁶⁻²⁷. Wet-spinning is the usual way to produce fibers which may be highly absorbent wound dressing materials; especially, mixed sodium and calcium fibers may be produced, calcium giving the wet integrity and sodium the large absorbency. Alginic acid fibers or silver fibers may also be prepared to enhance antimicrobial properties, zinc fibers to generate immune-modulatory and anti-microbial effects. Due to the process in aqueous and mild conditions, it is also easy to prepare fibers for enzyme immobilization or as support for bioactive molecules²⁸.

Alginate calcium fibers were prepared through wet spinning with good tensile strength which can be used for cloth materials. Blending yarns and textile of alginate calcium fibers give good hand feeling and strength. Alginate calcium fibers is an inherent flame-retardant fiber.

Nanoparticles of sodium alginate and 3-(trimethoxysilyl) propyl-octadecyl-dimethylammonium chloride (TSA) with an average size 99nm were loaded onto cotton fabrics by pad-dry-cure method. Fibers have an efficient antimicrobial activity maintained after 30 laundry cycles (non-leaching antimicrobial agent)²⁹.

Alginates in hemostatic material and wound dressing

New generation of medical textiles are an important growing field, showing great expansion, in wound management products³⁰. The main qualities of fibers and dressings as wound care products include that they are bacteriostatic, anti-viral, fungistatic, non-toxic, high absorbent, non-allergic, breathable, haemostatic, biocompatible, and manipulatable to incorporate medications, with good mechanical properties. Textile structures used for modern wound dressings are of large variety: sliver, yarn, woven, non-woven, knitted, crochet, braided, composite materials. Specialized additives with special functions can be introduced in advanced wound dressings with the aim to absorb odors, provide strong antibacterial properties, smooth pain and relieve irritation. Because of unique properties as high surface area to volume ratio, nanoscale fiber diameter, porosity, light weight, nanofibers are used in wound care. Nanofibers of alginates were produced by electrospinning technique in presence of various synthetic polymers and/or surfactants to improve processability³¹. Calcium alginate fibers have a novel gel-forming capability in that, upon the ion exchange between sodium ions in the contact solution and calcium ions in the fiber, the fiber slowly transforms into a fibrous gel. The gel-forming process for alginate fibers and the gelling behavior of various types of alginate fibers were described.



Figure 3. Fibers of alginate stabilized with calcium (personal document).

The absorption characteristics of alginate wound dressings were analyzed and it was found that alginate wound dressings absorb a large quantity of liquid into the fiber structure, in addition to those held between the fibers in the textile structure. This gives rise to the unique gel blocking properties of alginate wound dressings. In addition, alginate wound dressings also have novel hemostatic and antimicrobial properties as well as the ability to promote wound healing. They are now widely used in the management of highly exuding wounds such as leg ulcers, pressure sores, and surgical wounds²⁸.

Haemostasis and tissue repair is an important domain of development of alginate produced as thin filament in the calcium form. In contact with blood, Ca^{+2} ions are liberated activating platelet aggregation and reducing coagulation time. Materials are commercialised under different trademarks; as example are: Coalgan from Brothier Laboratories (France) soled as an haemostatic fibers pad for nosebleeds, Algosteril® or Sorban® are also non-woven dressing absorbing rapidly and retains wound fluid resulting in haemostasis and accelerates wound healing^{32,33}. Alginates fibers were reinforced by introduction of hydrolysed chitosans (which diffuse into the alginate fiber) allowing to introduce antibacterial properties³⁴.

CONCLUSION

From this short review, it seems clear that alginates are new industrial polysaccharides which may be used in many other applications than only food industry. Nevertheless, biomedical and pharmaceutical applications of purified alginates seem certainly the most promising development of alginates at present time. At end, it is important to mention the recent synthesis of well defined new biohybrid glycopolymers having guluronic oligomers grafted on a hydrophilic backbone giving also gels in the presence of calcium counterions. For many applications, these copolymers may compete directly with alginates³⁵.

REFERENCES

1. Rinaudo, M. Seaweed polysaccharides. In Comprehensive Glycoscience, Vol. 2: Polysaccharide Functional Properties (eds. Kamerling, J.P. *et al.*) **21**, 691-735 (Elsevier Science Technology, Oxford, UK, 2007).
2. Rinaudo, M. Main properties and current applications of some polysaccharides as biomaterials. *Polymer International* **57**, 397-430 (2008).
3. Smidsrod, O. & Haug, A. Properties of poly(1,4-hexuronates) in the gel state. II. Comparison of gels of different chemical composition. *Acta Chemica Scandinavica* **26**, 79-88 (1972).
4. Smidsrod, O. The relative extension of alginates having different chemical composition. *Carbohydrate Research* **27**, 107-118 (1973).
5. Haug, A., Larsen, B., Smidsrod, O. & Painter, T. Development of compositional heterogeneity in alginate degraded in homogeneous solution. *Acta Chemica Scandinavica* **23**, 2955-2962 (1969).
6. Aarstad, O.A., Tondervik, A., Sletta, H. & Skjak-Braek, G. Alginate sequencing: An analysis of block distribution in alginates using specific alginate degrading enzymes. *Biomacromolecules* **13**, 106-116 (2012).
7. Kohn, R. Ion binding on polyuronates-Alginate and pectin. *Pure and Applied Chemistry* **42**, 371-397 (1975).
8. Martinsen, A., Skjak-Braek, G. & Smidsrod, O. Alginate as immobilization material: I. Correlation between chemical and physical properties of alginate gel beads. *Biotechnology and Bioengineering* **33**, 79-89 (1989).
9. Andriamanantoanina, H. & Rinaudo, M. Relationship between the molecular structure of alginates and their gelation in acidic conditions. *Polymer International* **59(11)**, 1531-1541 (2010).
10. Haug, A., Larsen, B. & Smidsrod, O. A study of the constitution of alginic acid by partial acid hydrolysis. *Acta Chemica Scandinavica* **20**, 183-190 (1966).
11. Haug, A., Larsen, B. & Smidsrod, O. Studies on the sequence of uronic acid residues in alginic acid. *Acta Chemica Scandinavica* **21**, 691-704 (1967).
12. Sabra, W. & Deckwer, W-D. Alginate - A polysaccharide of industrial interest and diverse biological functions. In Polysaccharides. Structural diversity and functional versatility, 2^d edition (ed. Dumitriu, S.) 515-533 (Marcel Dekker, New York, 2005).
13. Fundueanu, G. *et al.* Preparation and characterization of Ca-alginate microspheres by a new emulsification method. *International Journal of Pharmaceutics* **170**, 11-21 (1998).
14. Yi, Y., Neufeld, R.J. & Poncelet, D. Immobilization of cells in Polysaccharide gels. In Polysaccharides. Structural diversity and functional versatility, 2^d edition (ed. Dumitriu, S.) 867-891 (Marcel Dekker, New York, 2005).
15. Lee, K.Y. & Mooney, D.J. Alginate: properties and biomedical applications. *Progress in Polymer Science* **7**, 106-126 (2012).
16. Draget, K.I. & Taylor, C. Chemical, physical and biological properties of alginates and their biomedical implications. *Food Hydrocolloids* **25**, 251-256 (2011).
17. Kong, H. & Mooney, D. Polysaccharide- based hydrogels in tissue engineering, in Polysaccharides. Structural diversity and functional versatility, 2^d edition (ed. Dumitriu, S.) 817-837 (Marcel Dekker, New York, 2005).
18. Albert, A., Salvador, A. & Fiszman, S.M. A film of alginate plus salt as an edible susceptor in microwaveable food. *Food Hydrocolloids* **27**, 421-426 (2012).
19. Hambleton, A., Debeaufort, F., Bonnote, A. & Voilley, A. Influence of alginate emulsion-based films structure on its barrier properties and on the protection of microencapsulated aroma compound. *Food Hydrocolloids* **23**, 2116-2124 (2009).
20. Pranoto, Y., Salokhe, V.M. & Rakshit, S.K. Physical and antibacterial properties of alginate-based film incorporated with garlic oil. *Food Res. Int.* **38**, 267-272 (2005).
21. Fayaz, A., Balaji, K., Girilal, M., Kalaichelvan, P.T. & Venkatesan, R. Mycobased synthesis of silver nanoparticles and their incorporation into sodium alginate films for vegetable and fruit preservation. *Journal of Agricultural and Food Chemistry* **57**, 6246-52 (2009).
22. Norajit, K. & Ryu, G.H. Preparation and properties of antibacterial alginate films incorporating extruded white ginseng extract. *Journal of Food Processing and Preservation* **35**, 387-393 (2011).

23. Concha-Meyer, A., Schoebitz, R., Brito, C. & Fuentes, R. Lactic acid bacteria in an alginate film inhibit *Listeria monocytogenes* growth on smoked salmon. *Food Control* **22**, 485-489 (2011).
24. Salmieri, S. & Lacroix, M. Physicochemical properties of alginate/polycaprolactone-based films containing essential oils. *Journal of Agricultural and Food Chemistry* **54**, 10205-10214 (2006).
25. Joyce, M. & Gilbert, S.A. Effect of Ca^{+2} on the water retention of alginate in paper coatings. *Journal of Pulp and Paper Science* **22**, J126-J130 (1996).
26. Qin, Y. The characterization of alginate wound dressing with different fiber and textile structures. *Journal of Applied Polymer Science* **100**, 2516-2520 (2006).
27. Qin, Y. Alginate fibres: an overview of the production processes and applications in wound management. *Polymer International* **57**, 171-108 (2008).
28. Qin, Y. The gel swelling properties of alginate fibers and their applications in wound management. *Polymer for Advanced Technologies* **19**, 6-14 (2008).
29. Kim, H.W., Kim, B.R. & Rhee, H. Imparting durable antimicrobial properties to cotton fabrics using alginate quaternary ammonium complex nanoparticles. *Carbohydrate Polymer* **79**, 1057-1062 (2010).
30. Petrulyte, S. Advanced textile materials and biopolymers in wound management. *Danish Medical Bulletin* **55**(1), 72-77 (2008).
31. Kim, G.H. & Park, K. Alginate-nanofibers by an electrohydrodynamic process. *Polymer Engineering and Science* **49**, 2242-2248 (2009).
32. Gilchrist, T. & Martin, A.M. Wound treatment with Sorban-an alginate fibre dressing. *Biomaterials* **4**, 317-320 (1983).
33. Fraser, R. & Gilchrist, T. Sorban calcium alginate fibre dressings in footcare. *Biomaterials* **4**, 222-224 (1983).
34. Knill, C.J. *et al.* Alginate fibres modified with unhydrolysed and hydrolysed chitosans for wound dressings. *Carbohydrate Polymer* **55**, 65-76 (2004).
35. Ghadban, A., Albertin, L., Rinaudo, M. & Heyraud, A. Biohybrid glycopolymer capable of ionotropic gelation. *Biomacromolecules* **13**, 3108-3119 (2012).