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Alginates - A Seaweed Product: Its Properties and Applications

S. Giridhar Reddy

Abstract

Alginates are natural polysaccharides available as seaweed products. They possess several properties due to their molecular structure made of bipolymeric α -L-Guluronic acid and β -D-Mannuronic acid polymers. Alginates have several properties such as film-forming ability, pH responsiveness, and gelling, hydrophilicity, biocompatibility, biodegradability, non-toxic, processability and ionic crosslinking. They're commonly used in several industries, including food, pharmaceuticals, dental applications, welding rods and scaffolding. Due to their gelling and non-toxic properties, as well as their abundance in nature, the cosmetics and healthcare industries have shown a great deal of interest in biodegradable polymers in general and alginates particularly over the last few decades.

Keywords: Alginates, hydrogels, biodegradable polymers, controlled drug delivery, seaweeds

1. Introduction

Polymers are the chemical compounds that play a significant role in the development of medicine and engineering with day-to-day life. Polymers are made of several repeating units of monomers, which decide the structure and properties. In the field of medicine, a range of polymeric materials is being used, however, biodegradable polymers gaining more attention.

Brown algae are composed primarily of alginates, a carbohydrate polymer found in the form of an insoluble combination of potassium, sodium, magnesium, and calcium salts of alginic acid that are structural components of brown seaweed cell walls. They are unbranched binary polymers made up of 1, 4 linkages between β -d-Mannuronic (M) and α -l-Guluronic (G) acids [1]. The composition of alginates i.e. G: M ratio varies based on the source [2]. They can also be tailored or resized in many varieties by varying molecular weight, cation content, particle form, volume fraction and, G: M ratio.

Alginates were first used in 1883 by a researcher named Edward Stanford, and commercial development commenced in 1927. The global production of alginates has now risen to about 40,000 tonnes per year. Alginates are used extensively in the food, pharmaceutical, cosmetic, and dental industries [3]. Perhaps, in recent years, the medical and pharmaceutical industries have become incredibly influential in biopolymers, specifically alginates.

Alginates are particularly known for their applications in pharmaceutical industries for controlled drug delivery [4], wound healing [5], dermatology [6],



Figure 1.
Alginates – Brown algae and seaweeds.

and scaffolds [7] because of their properties such as natural disintegration, gel formation, biocompatibility, and non-toxicity. Alginates are a natural gum that has an advantage over synthetic polymers because they form hydrogels, are less expensive, and are readily accessible. Alginate gels may also be orally administered into the body in a minimally invasive manner, enabling a wide range of pharmaceutical applications. Alginate gels are promising biomaterials for tissue engineering and cell transplantation, to replace organs in patients that have lost or failed organs or tissues (**Figure 1**) [8, 9].

2. Properties of alginates

Brown algae obtained from seaweeds such as *Laminaria hyperborea*, *Laminaria digitata*, *Laminaria japonica*, *Ascophyllum nodosum*, and *Macrocystis pyrifera* are used to make commercially available alginates [10]. In general, alginates are insoluble compounds; they are washed, crushed, dried, powdered, and treated with a basic solution especially NaOH or KOH to form sodium/potassium salt of alginic acid which is water-soluble (**Figure 2**).

Alginates are generally available in the market as Alginic acid of sodium salt or Sodium alginate [12]. Alginates due to their acidic nature make them a favorable biopolymeric biodegradable product in biomedical applications. Because of high acid content, alginates form gels due to the presence of Guluronic acid (G) monomer in alginates within a short period especially in the presence of Ca^{2+} ions. This property of gelling allows the alginate to possess multiple applications such as encapsulation of varied fragments or even cells interior of the alginate matrix with very low side effects [13]. The carboxylic group in alginates are very effective i.e. reason find many applications and can be modified based on the need [14].

Bacteria such as *Pseudomonas* and *Azotobacter* can develop bacterial alginate as an exopolysaccharide. These bacterial alginate producers may be able to produce alginates with particular monomer formulations and might be capable of producing 'tailor made' bacterial alginates using genetic and protein engineering [15].

2.1 Molecular weight

Alginates obtained from different locations in a sea bed have different molecular weights ranges between 50,000 to 5lakhs [16]. The viscosity of the alginate solution

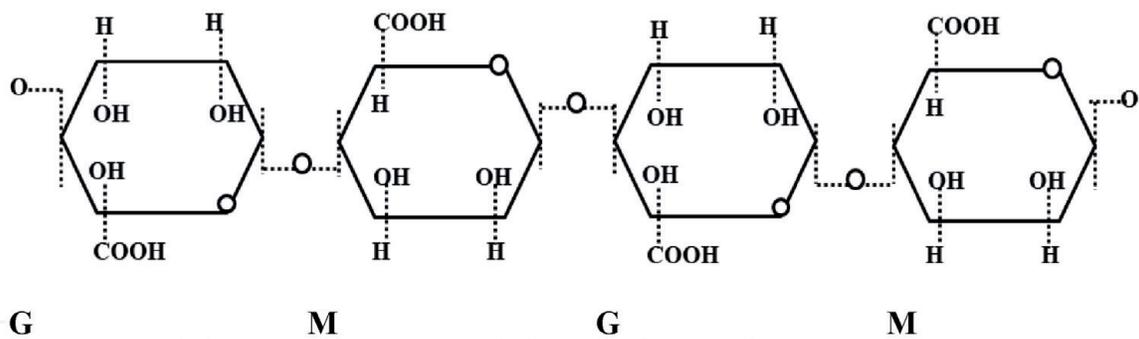


Figure 2.
Structure of Alginic acids with 1, 4 linkages between L-Guluronic acid (G) and D-Mannuronic acid (M) [11].

is pH-responsive and increase viscosity is reported with the decrease in pH and reaches a pH ~ 3.5 because carboxylate groups in Guluronic acid present in the alginate structure protonated and form hydrogen bonds [17]. Alginates may have different molecular weights depending on whether they need to monitor pre-gel solution viscosity or post-gelling strength distribution separately. To adjust the viscosity of the solution, a mixture of high and low molecular weight alginate polymers is used [18].

2.2 Biocompatibility

The biocompatibility of alginate has been extensively evaluated *in-vitro* as well as *in-vivo* at varying levels of purity. It has been reported that alginate containing high M monomers are more immunogenic and 10 times more effective in promoting cytokine synthesis compared to G monomer in alginates [19], but others reported very little response or no immune response across alginate implants [20]. Impurities in the alginates, such as heavy metals, endotoxins, proteins, and polyphenolic compounds, may be causing the variable reaction at the injection or implantation sites. However, not many serious inflammatory results were reported in commercially available or certified or alginates obtained from branded companies [21].

2.3 Alginate derivatives

Alginates are exploited or synthesized for various biomedical applications by introducing different hydrophilic moieties such as alkyl groups or hydrophilic polymers in the alginate matrix. Long-chain alkyl groups such as dodecyl or octadecyl are bonded with alginates matrix *via* esterification. The various properties such as rheology, gelling and crosslinking characteristics are very useful in bone regeneration and cartilage repair [22]. Sustained or controlled drug delivery vehicles are achieved from alginate derived from Poly (butyl methacrylate) [23].

Alginates are also investigated for their derivatives with cell-adhesive peptides are prepared by adding peptides as side chains and coupled through the carboxylic groups of the sugar residues [24, 25].

2.4 Gelling properties

The ability of aqueous alginate solutions to form gels when treated with divalent ions (Ca^{2+} , Sr^{2+} , and Ba^{2+}) or trivalent ions (Fe^{3+} and Al^{3+}) ions has been extensively explored for the fabrication of carriers for sustained or controlled delivery of therapeutic agents. This is due to intramolecular bonding and ionic interactions that exist

within the carboxylic acid groups on the polymer matrix and the cations present as shown in **Figure 2** [26, 27].

The calcium or any other divalent or trivalent ions will interact with the G monomer present in the alginate structure to crosslink with another molecule, and the structure is identical to the egg box model (**Figure 3**) [28].

The complexing forming agents such as EDTA-sodium citrate [29] or monovalent cations, complex anions (phosphate, and citrate) which have a high affinity for Ca^{2+} ions, which can disrupt calcium alginate gels easily. The presence of high concentrations of non-gelling ions (Na^+ and Mg^{2+}) also contributes to the instability. It was reported that the strength and uniformity of gelling largely depend on the type of crosslinking and temperature [30].

It is also reported that the strength of alginate film with Al^{3+} ion is very low compared to other divalent ions (Ca^{2+} and Ba^{2+}) crosslinking because in the case of Al^{3+} ions the crosslinking occurs in two different planes of the alginate structure and at the same time it makes the alginate framework more compact [31]. The small size of the Al^{3+} ion (0.58 Å) facilitates its diffusion into the matrix of the film without crosslinking on the surface and thus results in poor crosslinking [32].

For a variety of uses, including tissue engineering, alginates are being investigated for covalent bonding to enhance the physical properties of gels. In the case of alginates with covalent bonding degradation of chain occurs even with a slight increase in temperature due to breaking of crosslinks ultimately leading to stress relaxation due to water migration. It was reported that covalently bonded alginates are found to be toxic [33]. Furthermore, the Ca^{2+} ions released out of the gel can boost hemostasis, while the gel acts as a matrix for platelet and erythrocyte aggregation [34].

To prepare gels with a wide spectrum of mechanical properties, covalent crosslinking of alginate with Poly (ethylene glycol)-diamines of different molecular weights was first investigated. The elastic modulus showed improvement in gel with crosslinking density or weight fraction of Polyethylene glycol (PEG), but then decreased as the molecular weight between cross-links increased became less compared to the original PEG [35]. Using various types of cross-linking molecules and regulating cross-linking densities, it was later investigated that the mechanical properties, as well as swelling of alginate strength, are tightly regulated. As most would imagine, the chemistry of the cross-linking molecules has a major impact on hydrogel swelling. While shaping hydrogels, multi-functional

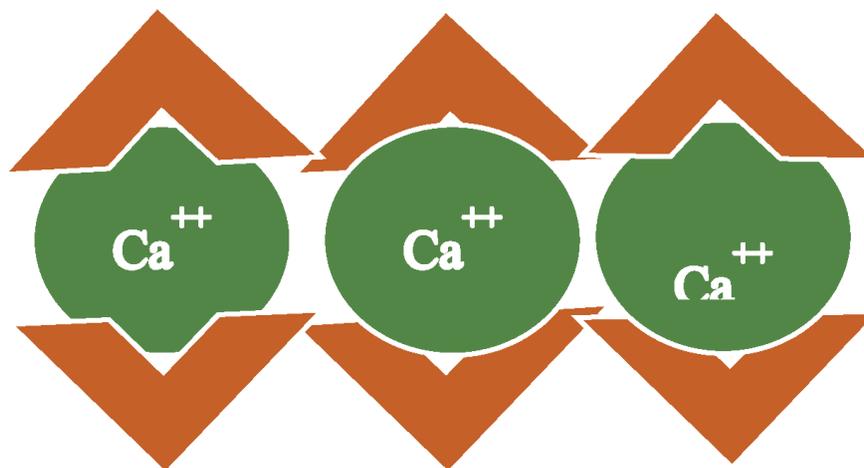


Figure 3.
The divalent calcium cation binds in the cavities of alginates like eggs in an egg box.

cross-linking entities have a greater scope of degradation efficiency and mechanical strength performance than bi-functional cross-linking molecules. Physical properties and degradation behavior of Poly-aldehyde guluronate (PAG) gels are prepared with either Poly-acrylamide-co-hydrazide (PAH) or Adipic acid dihydrazide (AAD) as a cross-linking agent were investigated *in-vitro*. PAG/PAH gels had higher mechanical stiffness and very low degradation is observed compared to PAG/AAD gels [36].

Photo crosslinking is used for crosslinking in alginates structures under mild conditions either direct or indirect sunlight or in the presence of suitable initiators. For example, the mechanical properties of Polyallylamine and alginate were significantly improved from this technique [37].

2.5 Solubility

The alginates with divalent or trivalent cations are not soluble in water because the alginates contain a terminal carboxylic ion ($-\text{COO}^-$), so these cations bond to this and yield an insoluble product. As a consequence, the alternative is the absorption of as much as 200–300 times their weight in water, thus swelling to a hydrogel of paste-like consistency. However, alginates with monovalent cations (Na^+ , K^+ , and NH_4^+) are soluble in hot and cold water. Alginates have a wide range of solubilities due to their different molecular weights.

Alginates derived from *Ascophyllum*, for example, have aqueous solubility in the range of 22–30% weight percent, whereas those of two *Laminaria* groups are 17–33% weight percent and 25–44% weight percent, respectively [38, 39].

2.6 Effect of pH on alginates

The solubility of alginates was influenced by parameters such as pH and ionic strength. Alginates have very low solubility in lower pH values due to the deprotonation of carboxylic groups ($-\text{COO}^-$). The viscosity of alginates is unaffected above $\text{pH} > 5$, whereas solution having $\text{pH} < 5$, the COO^- group present in alginates gets protonated to $-\text{COOH}$, and the electrostatic repulsion between chains decreases, they can move closer together to form hydrogen bonds, whereby the viscosity decreases [40]. It has been reported $\text{pH} > 11$ alginates viscosity is reduced due to de-polymerization [41].

The concentration of ionic solution influences the crosslinking, which increases the viscosity and molecular weight of alginates [39, 42]. Furthermore, the cross-linking depends on the confirmation of monomers G and M groups present in the alginate matrix.

2.7 Sterilization

It is reported that the viscosity of alginates decreases with autoclave sterilization because the heating randomly breaks alginate chains. The degree to which this loss occurs is determined by the presence of other kinds of stuff in the solution. Alginate solutions have also been sterilized using γ -radiation and ethylene oxide [43].

2.8 Immunogenicity

Control drug delivery is the latest trend in the presence of pharmaceutical dosage requirements for successful application in drug carriers; alginates play an important role because of their biocompatibility and immunogenicity [44].

The two key factors responsible for alginate immunogenicity are its chemical composition and the mitogenic pollutants present in alginates [45]. When alginate comes into contact with blood, it is believed to have mild cytotoxic effects and decreased hemolysis.

2.9 Biocompatibility

The biocompatibility and strength of alginic acid are determined by the quantity and quality of the acid. Furthermore, the impacts of the quantity of G monomer on alginate biocompatibility are still under investigation. Experts find different opinions on the G content of extremely purified alginate rich in G monomer residues, while others have emphasized the importance of high purity while ignoring the effects of chemical composition [46]. Animals such as rats are injected in their kidney parts with calcium alginate for biocompatibility studies and the results obtained are very promising [45].

Alginates are also experimented on in mammals and observed that they could not digest because they lack the enzyme '*Alginase*' that can break the polymer chains. Whereas ionically cross-linked alginate gels undergo dissolution by replacing the divalent crosslinked gel with monovalent cations into the surrounding media. Even alginates dissolve in the body they cannot be expelled from the body because of its high molecular weight are higher than renal clearance [47]. It is reported, alginates were obtained from *Undaria pinnatifida*, a brown seaweed invasive in the Argentinian coast are found to be toxic, but its purification using commercial techniques improves its biocompatibility and eliminates cytotoxicity in an alginate matrix for bone tissue engineering [48].

2.10 Bioadhesion

The binding or contact between two surfaces, one among being a biological substrate, is known as bioadhesion [49]. Mucoadhesion is an example in which the mucosal layer used. The carboxyl group in alginates represents a mucoadhesive anionic polymeric layer. It was reported polyanion polymers are more efficient bioadhesives compared to polycation or non-ionic polymers [50]. Alginate has better mucoadhesive strength as compared to polymers like Polystyrene, Chitosan, Carboxymethyl cellulose, and Poly (lactic acid). The bioadhesive properties of alginate would be advantageous as a mucosal drug delivery vehicle to the GI tract and nasopharynx by extending drug residence time at the site of action making them more effective [44, 51, 52].

2.11 Toxicity

Plenty of studies are reported that alginates especially crosslinked sodium/calcium alginates are non-toxic to cells, even not shown any irritation to eyes and skin [53]. Because of the nontoxicity, they found various applications in drug delivery, cosmetics, and food industries.

3. Applications of Alginates

Alginates are available in plenty in oceans and because of their diverse properties such as biodegradation, biodegradable, non-toxic, etc., as mentioned above; they have plenty of applications in the food industry, pharmaceuticals, cosmetics, textile industry, welding, and animal feeds, etc.

3.1 Food industry

FAO/WHO approves that alginates are the safest food additives because of its unique properties in food applications [54]. Over decades, alginates are used in a variety of food items, such as ice cream toppings, fruit jams, jelly, milk products, food packing, instant noodles, beer, etc., because of their unique properties such as thickening, gelling, emulsification, stabilization, texture functionality.

3.2 Pharmaceuticals

In the present medical field, many medicines or drugs administered to patients are causing a lot of side effects. Hence, there's a lot of demand created in the world for drug loading carriers which increase drug resident time *in-vitro* or *in-vivo*, especially in the gastrointestinal tract and on the exterior part of the human body should be safe and non-toxic. The developments of alginates and alginate derivatives are discussed about controlled drug delivery, sustained drug delivery, and targeted drug delivery, etc.

3.2.1 Controlled drug delivery

In general, the structure of alginates gels shows it possesses porous size (~5 nm) helps to fill this gap with small molecular weight drugs through either physical or chemical bonding. When a drug-loaded/embedded drug comes in contact with an aqueous medium, the drug release is controlled. Furthermore, the drug-loaded carriers are water-soluble and may undergo degradation in an aqueous medium, hence crosslinking the alginates with bivalent or trivalent cation will enhance the stability of the gels or films. These properties help us to study the kinetics of drug release. The Sodium salt of alginic acid (SA) and Polyethylene oxide blends are investigated for controlled release of Valganciclovir hydrochloride *in-vitro*, as an anti-HIV drug [55]. Floating microbeads made of SA and modified Chinese yam starch investigated for controlled delivery of Metformin hydrochloride drug [56]. SA and Chitosan blend with different wt% of Montmorillonite (Cloisite 30B) solution studied for controlled release [57]. An anti-cancer drug such as Paclitaxel was loaded and investigated for release *in-vitro* in variable pH medium, time, and drug concentrations. SA and Xanthum gum blends crosslinked with zinc acetate loading Ranitidine hydrochloric acid drug *in vitro* release investigated in simulated intestinal fluid (pH 7.5) and simulated gastric fluid (pH 1.2) [58]. Oral delivery of protein drug is explored for Bovine serum albumin (BSA) using composite microparticles made of Chitosan, SA, and Pectin crosslinked by tripolyphosphate [59]. A pH-responsive Tamarind seed polysaccharide and alginate blends are studied for controlled release of Diclofenac sodium. Swelling and degradation studies were also investigated in different pH mediums [60].

An anti-inflammatory drug such as Nifedipine is investigated for microspheres made of SA and Methylcellulose using Glutaraldehyde as crosslinking agent [61].

The Acrylamide and Poly(vinyl alcohol) beads with SA are grafted on exposure to UV radiation and further crosslinked with glutaraldehyde. The crosslinked beads are used to study the controlled release of Diclofenac sodium drug [62].

The transdermal films are synthesized using SA and Xanthum gum. The films loaded with Ketoprofen drug is studied *in vitro* for skin permeation [63].

SA mixture with Sodium Carboxymethylcellulose, Carbopol-934, and Polyvinyl pyrrolidone and backing membrane (Ethylcellulose), and Glycerol as plasticizer give promising results for control of drugs [64].

Hypertension drugs such as Felodipine were investigated for control release from alginate microspheres in combination with a mixture of Hydroxypropyl methylcellulose, Eudragit RS 30D, and Chitosan in simulated intestinal media [65].

Bioadhesive ocular insert of Ciprofloxacin hydrochloride using SA as gel and Chitosan as bioadhesive agent, Glycerin as a plasticizing agent are used *in-vitro* release studies were carried [66].

3.2.2 Protein delivery

The proteins drugs are in high demand and thanks to advances in recombinant DNA technology, a diverse variety of protein drugs are now available. Alginates are an ideal candidate for protein drug delivery because they can load into the alginate matrix at different formulations at relatively mild conditions which can avoid denaturation as well as degradation. A variety of techniques are explored for the controlled release of protein from alginate gels. Alginates are known for minute pores due to the presence of G and M blocks because of their bi-polymeric structural arrangements. The vascular endothelial growth factor binding to alginate hydrogels is successful in sustained and localized release [67, 68]. It is reported that alginate microspheres are efficiently loaded with lysozyme and chymotrypsin for sustained release [69]. Oral delivery of proteins such as Amino group-terminated Poly((2-dimethylamino) ethyl methacrylate with alginate gel beads was prepared [70]. Alginates are explored for stimuli-responsive gels in the synthesis of tetra-functional acetal-linked polymer networks with adjustable pore sizes.

Bovine serum albumin is used as a model protein using blends made of alginate, chitosan, and pectin composite mixture [71]. In another work, hemoglobin as a model protein loaded in poly (L-histidine)-chitosan/alginate microcapsules are reported [72, 73].

3.2.3 Wound dressing

Any injury, burns, torn, muscle pains, cuts occurring on the human body may take a longer duration for curing for even applying any ointments such as antiseptic, antimicrobial, anti-inflammatory, antipruritic, pain-relieving gels, anti-mycotic with fungal action may cause skin irritation or side effects. Hence alginates due to their appreciable properties and due to their non-toxic are extensively used in wound healing to load appropriate drugs in alginate gels and which increases the retention time of the drug, so that the drug release in small dosages on the specific site. Alginates also have hemostatic properties, making them useful in the treatment of bleeding wounds. Several investigations are reported which initially experimented on animals such as mice, pigs, and rabbits. Alginates are employed to make hydrogels, films, wafers, foams, nanofibers, including therapeutic formulations for wound dressings. Alginate wound dressings readily absorb wound fluid, maintain a physiologically moist atmosphere, and protect against bacterial infections at the wound site. Since alginates are poor in mechanical strength are blended with other polymers or composites to improve film strength. The amount of M-block presents in alginate influences the immunogenic effect and M-block induces cytokine production (**Table 1; Figure 4**) [81].

3.3 Alginates in cosmetics

Scientists have been researching alginates for decades to create high-quality cosmetic products that provide all benefits to the skin. Alginates, being marine

Applications	Alginate based dressings for wound healing	Refs.
Ulcer	1. Algicell™ 2. AlgiSite M™ 3. Comfeel Plus™ 4. Kaltostat™ Sorbsan™ 5. SeaSorb	[74–77]
Diabetic wounds	1. Tegagen™ 2. Hyalogran®	[78]
Thyroid and spine surgeries.	1. Guardix-SG	[81]
Necrotic wounds	1. Algivon	[79]
Burns	1. Fibracol™ Plus	[80]

Table 1.
Some of the commercially available alginate-based dressings.



Figure 4.
Application of Alginate in wound dressings [82].

plants known to absorb UV rays, repair the sun's harmful effects, moisturize the epidermis, skin smoothing, and ensure the small cells renewal [83]. Alginates, in general, are known for gel formation can thicken and maintain moisture, are used in a variety of cosmetics. By forming a gel network, alginate assists in the retention of lipstick color on the lips and face creams as well as body lotion moisturizers. To make stable all-around lotions, alginate a natural thickener is incorporated in sunflower wax. Polysorbate-20 is the best commercial product is manufactured which is a smooth lotion in which instant cold emission products are combined with an emulsifier [84]. Alginates are a natural polysaccharide that possesses a very high viscosity and has a strong potential for water absorption. Perhaps, alginate's viscosity can be optimized to ensure maximum viscosity. Alginates are explored for anti-aging masks and face masks which slow down the aging process, even wrinkles and lift the skin. Also, alginates are explored in Dentures which removable set of replacement teeth and gum tissue that can provide you with the complete backing and attractive appearance you need, even as you age.

Alginates application indentures are a removable set of restorative dentistry and gum tissues that can provide us with both the complete backing and beautiful appearance even at older age (**Figures 5 and 6**) [87].



Figure 5.
Cosmetics made of alginates [85].

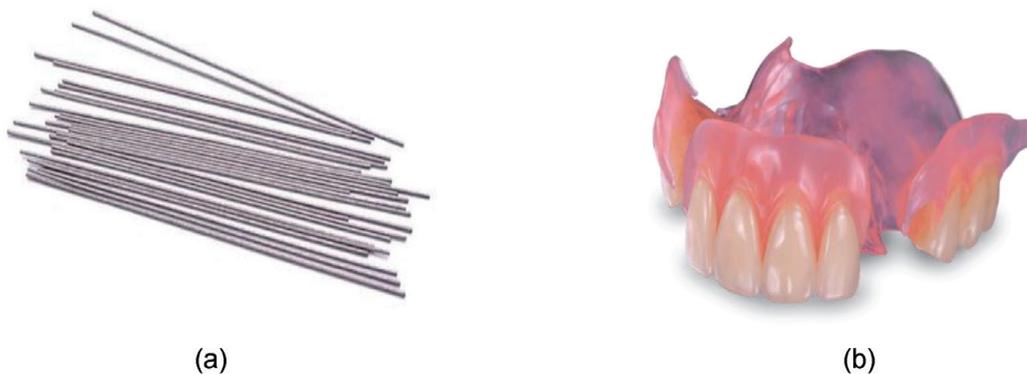


Figure 6.
Application of alginates in a) dental solders [85] and b) flexible dentures [86].

3.4 Alginates in the textile industry

Color paste substrates are prepared using textile-grade alginates in the application of patterns in print fabrics, shawls, towels, and other products. Alginates are cleaner and easier to decompose substrate for textile printing than other substrates. Alginates application in printing cotton, jute, and rayon allows for easier disposal of wastewater. Sodium alginates are thickeners used in textile printing to thicken the dye paste.

Screen or roller printing devices may be used to apply the pastes to the cloth. Alginates became common thickeners with the discovery of reactive dyes. The cellulose in the cloth reacts chemically with these substances. Many popular thickeners, such as starch, react with reactive dyes, resulting in lower color yields and sometimes difficult-to-wash-out by-products. Alginates are the strongest thickeners for reactive dyes because they non-reactive with the dyes and quickly washout from the finished textile.

In older screen printing the alginate of medium to high viscosity is used, whereas in modern high-speed roller printers even low viscosity alginates are giving very attractive printing.

3.5 Welding rods

Welding is the technique finds application building all kind of structures with metals. In the welding, process coating is used as a flux and to monitor conditions

near the weld, such as temperature, and oxygen, and hydrogen. In this case, sodium silicate (water glass) is mixed with the dry coating ingredients to provide some of the plasticity needed for coating extrusion into the rod and to tie the dried coating to the rod. The silicate, on the other hand, neither binds nor provides enough lubrication to allow for successful and smooth extrusion. A lubricant and a binder are needed to keep the damp mass together before extrusion and to keep the coating on the rod in form throughout drying and baking [88]. To achieve these standards, alginates are used.

3.6 Alginates used in animal feeds

Alginate salts of sodium and potassium are meant to be used as industrial substances as emulsifiers, stabilizers, thickeners, gelling agents, and binders. There is no competent authority that has recommended the usage of sodium alginate in feeding stuffs for dogs, other non-food-producing animals, and fish. Whereas potassium alginate is used in cat and dog food at a speck of 40 g/kg feed [89]. The use of alginates in fish feed has no harmful effect on the consumer. Alginates are said to be slightly irritating to the eyes but not to the skin. The use of these ingredients in fish feed poses no threat to the aquatic environment.

A gel-type livestock feed mixture is formed by mixing feed nutrients, water, alginate, and a water-insoluble calcium component to resist the calcium content from reacting with the alginate. The calcium component is solubilized or the sequester affecting the reactivity between the alginate and the calcium component is extracted after the feed mixture is formed, resulting in a gel feed containing a gel matrix containing the feed nutrient ingredients. The livestock can then be fed the gel meal [90].

4. Conclusions

Alginate is a seaweed product which is a polysaccharide or carbohydrate polymer has plenty of applications in day-to-day life due to its potential characters. The Alginate properties such as biocompatibility, biodegradability, hydrogel formations, nontoxic, pH-responsive, and its ability to form a gel with crosslinking agents find their application in controlled, sustained, and targeted drug delivery carriers for a wide range of drugs or any other bioactive agents. Alginates films like any other hydrogels lack physical strength, which can be overcome by crosslinking with different divalent or trivalent cations. A continuous challenge was on researchers to explore the possibility of modification of alginate structure by grafting with other low or high molecular weight polymers to improve its strength based on the need of the application. Biomedical applications, specifically in wound healing *in vitro* cell culture, and tissue engineering, look interesting as a potential biomaterial. Acid-responsive drugs and drugs that irritate the gastric mucosa can also be released with alginate. Alginates in combination with other polymer additives or nanoparticles are used in wound healing in diabetic wounds, ulcers, and burns. Alginates are used in an increasing number of food-related applications and have the potential to be used in a growing number of food-related applications. The gelling property of alginates makes them ideal for use as thickeners, stabilizers. Alginate consumption has several physiological effects in the gastrointestinal tract and in the body that are similar to a variety of other viscous polysaccharides. Dentures made of alginates composites are found to be very flexible, removable, and compact with the gum tissues. The high viscosity of alginates finds suitable thickeners in the textile industry as a paste containing a dye that can be applied to the fabric by either screen or roller printing. Potassium alginates and gel-type animal feeds are found to be highly nutritious for cats, fishes, and piglets.

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References

- [1] Ott C.M, Day D.F., Marcel Dekker, J.J. Inc. New York, Chap. 5.2000.
- [2] Domb AJ, Wiseman DM. Handbook of Biodegradable Polymers. Boca Raton, CRC Press.1998.
- [3] Ertesvag H, Valla S. (1998): Biosynthesis and applications of alginates. *Polymer Degradation and Stability*, 5, 985.
- [4] Hanne Hjorth Tønnesen , Jan Karlsen. *Drug Development and Industrial Pharmacy* , Volume 28, 2002 - Issue 6, doi.org/10.1081/DDC-120003853
- [5] Alginate dressings, Hand book of medical textiles. 2011
- [6] Maedeh Bahadoran, Amir Shamloo, Yeganeh Dorri Nokoorani , *Scientific Reports* . 2020; 10: 7342.
- [7] Maryam Farokhi, Farinaz Jonidi Shariatzadeh, Atefeh Solouk , Hamid Mirzadeh, *International Journal of Polymeric Materials and Polymeric Biomaterials*. Alginate Based Scaffolds for Cartilage Tissue Engineering: A Review, 2020 69(4): 230-247. doi.org/10.1080/00914037.2018.1562924.
- [8] Langer R, Vacanti JP. *Tissue engineering*. Science. 1993;260:920-926.
- [9] Lee KY, Mooney DJ. *Hydrogels for tissue engineering*. Chem Rev. 2001;101:1869-1879
- [10] Smidsrod O, Skjak-Bræk G. Alginate as immobilization matrix for cells. *Trend Biotechnol*. 1990;8:71-78. doi.org/10.1016/0167-7799(90)90139-O.
- [11] Soares PJ, Santos JE, Chierice GO, Cavalheiro ETG. Thermal behavior of alginic acid and its sodium salt, *Eclet. Química*. 2004, .29 (2): 57-64. Doi.org/10.1590/S0100-46702004000200009.
- [12] Kuen Yong Lee, David J. Mooney. Alginate: Properties and biomedical applications. *Prog Polym Sci*. 2012, 37(1): 106-126. doi:10.1016/j.progpolymsci.2011.06.003.
- [13] Klock G, Pfeffermann A, Ryser C, Grohn P, Kuttler B, Hahn HJ, et al. Biocompatibility of mannuronic acid-rich alginates. *Biomaterials*. 1997, 18:707-713. DOI: 10.1016/S0142-9612(96)00204-9
- [14] Luca Szabó, Sandrine Gerber-Lemaire, * Christine Wandrey, Strategies to functionalize the anionic biopolymer Na-Alginate without restricting its polyelectrolyte properties, *Polymers (Basel)*. 2020; 12(4): 919. doi: 10.3390/polym12040919.
- [15] Lain Hay D, Zahid Ur Rehman , Aamir Ghafoor , Bernd H. A. Rehm, Bacterial biosynthesis of alginates, *Journal of chemical tech and Biotech*. 2010;85(6): 752-759. doi.org/10.1002/jctb.2372.
- [16] Lakshmi S. Nair, Cato T. Laurencin. Biodegradable polymers as biomaterials. *Prog. Polym. Sci*. 32 (2007) 762-798. doi:10.1016/j.progpolymsci.2007.05.017.
- [17] Rinaudo M. On the abnormal exponents' α_n and α_D in mark-Houwink type equations for wormlike chain polysaccharides. *Polym Bull*. 1992; 27:585-589. doi.org/10.1007/BF00300608.
- [18] Kong HJ, Lee KY, Mooney DJ. Decoupling the dependence of rheological/mechanical properties of hydrogels from solids concentration. *Polymer*. 2002; 43:6239-6246. doi.org/10.1016/S0032-3861(02)00559-1.

- [19] Otterlei M, Ostgaard K, Skjakbraek G, Smidsrod O, Soonshiong P, Espevik T. Induction of cytokine production from human monocytes stimulated with alginate. *J Immunother*, 1991; 10: 286-291. doi:10.1016/j.progpolymsci.2011.06.003.
- [20] Zimmermann U, Klock G, Federlin K, Haning K, Kowalski M, Bretzel RG, Horcher A, Entenmann H, Siebers U, Zekorn T. Production of mitogen contamination free alginates with variable ratios of mannuronic to guluronic acid by free flow electrophoresis. *Electrophoresis*. 1992;13:269-74. doi.org/10.1002/elps.1150130156.
- [21] Lee J, Lee KY. Local and sustained vascular endothelial growth factor delivery for angiogenesis using an injectable system. *Pharm Res* 2009; 26:1739-1744. doi: 10.1007/s11095-009-9884-4
- [22] Pelletier S, Hubert P, Payan E, Marchal P, Choplin L, Dellacherie E. Amphiphilic derivatives of sodium alginate and hyaluronate for cartilage repair: Rheological properties. *J Biomed Mater Res*. 2001; 54:102-108. DOI: 10.1002/1097-4636(200101)54:1<102::aid-jbm12>3.0.co;2-1.
- [23] Yao BL, Ni CH, Xiong C, Zhu CP, Huang B. Hydrophobic modification of sodium alginate and its application in drug controlled release. *Bioprocess Biosyst Eng*. 2010; 33:457-463. doi: 10.1007/s00449-009-0349-2.
- [24] Lehenkari PP, Horton MA. Single integrin molecule adhesion forces in intact cells measured by atomic force microscopy. *Biochem Biophys Res Commun*. 1999; 259:645-650. https://doi.org/10.1006/bbrc.1999.0827.
- [25] Koo LY, Irvine DJ, Mayes AM, Lauffenburger DA, Griffith LG. Co-regulation of cell adhesion by nanoscale RGD organization and mechanical stimulus. *J Cell Sci*. 2002; 115:1423-1433. doi.org/10.1242/jcs.115.7.1423
- [26] Miyazaki S, Kubo W, Attwood D. Oral sustained delivery of theophylline using in-situ gelation of sodium alginate. *J. Control Release* 2000, 67 (2-3), 275-280. doi.org/10.3109/03639045.2011.634809.
- [27] Katchalsky A, Cooper RE, Upadhyay J, Wassermann A. Counter-ion fixation in alginates. *J. Chem. Soc.* 1961; 5198. doi.org/10.1039/JR9610005198
- [28] Grant GT, Morris ER, Rees DA, Smith PJC, Thom D. Biological interactions between polysaccharides and divalent cations: The egg-box model. *FEBS Letters*. 1973; 32 (1):195-198. doi.org/10.1016/0014-5793(73)80770-7.
- [29] Smeds KA, Grinstaff M.W. Photocrosslinkable polysaccharides for in situ hydrogel formation. *J. Biomed. Mat. Res*. 2001, 54 (1),115-121. doi.org/10.1002/1097-4636(200105)55:2<254::AID-JBM1012>3.0.CO;2-5.
- [30] Kuo CK, Ma PX. Ionically crosslinked alginate hydrogels as scaffolds for tissue engineering: Part structure, gelation rate and mechanical properties. *Biomaterials*. 2001; 22: 511-521. doi.org/10.1016/S0142-9612(00)00201-5.
- [31] S. Al-Musa, D. A. Fara, and A. A. Badwan. Evaluation of parameters involved in preparation and release of drug loaded in crosslinked matrices of alginate *J. Controlled Release*, 57, 223 (1999). doi: 10.1016/s0168-3659(98)00096-0.
- [32] S. Giridhar Reddy, Akanksha Saxena Pandit, and Amrita Thakur. Study on

the Effects of crosslink agents on Sodium Alginate and Lignosulphonic Acid Blends Polymer(Korea), Vol. 40, No. 1, pp. 63-69 (2016). DOI:10.7317/pk.2016.40.1.63.

[33] Zhao XH, Huebsch N, Mooney DJ, Suo ZG. Stress-relaxation behavior in gels with ionic and covalent crosslinks. *J Appl Phys.* 2010; 107 063509/1-063509/5. doi: 10.1063/1.3343265.

[34] Suzuki Y, Nishimura Y, Tanihara M, Suzuki K, Nakamura T, Shimizu Y, Yamawaki Y, Kakimaru Y. Evaluation of a novel alginate gel dressing: Cytotoxicity to fibroblasts in vitro and foreign-body reaction in pig skin in vivo *J Biomed Mater Res.* 1998; 39:317-22. doi.org/10.1002/(SICI)1097-4636(199802)39:2<317::AID-JBM20>3.0.CO;2-8

[35] Eiselt P, Lee KY, Mooney DJ. Rigidity of two-component hydrogels prepared from alginate and poly(ethylene glycol)-diamines. *Macromolecules* 1999;32:5561-6. doi.org/10.1021/ma990514m.

[36] Lee KY, Bouhadir KH, Mooney DJ. Controlled degradation of hydrogels using multifunctional cross-linking molecules. *Biomaterials*, 2004;25: 2461-6. doi.org/10.1016/j.biomaterials.2003.09.030.

[37] Lu MZ, Lan HL, Wang FF, Chang SJ, Wang YJ. Cell encapsulation with alginate and phenoxycinnamylidene-acetylated poly(allylamine). *Biotechnol Bioeng* 2000;70:479-83.doi.org/10.1002/1097-0290(20001205)70:5<479::AID-BIT1>3.0.CO;2-E.

[38] Das M K, Senapati PC. Furosemide-loaded Alginate microspheres prepared by ionic cross-linking technique: Morphology and release characteristics. *Indian J. Pharm. Sci.* 2008, 70, 77-84. doi: 10.4103/0250-474X.40336.

[39] da Silva TL, Vidart JM, da Silva MG, Gimenes ML, Vieira MG. Alginate and Sericin: Environmental and Pharmaceutical Applications. In *Biological Activities and Application of Marine Polysaccharides*; InTech: Rijeka, 2017; pp 57-86. DOI: 10.5772/65257.

[40] Liu, X. D.; Yu, W. Y.; Zhang, Y.; Xue, W. M.; Yu, W. T.; Xiong, Y.; Ma, X. J.; Chen, Y.; Yuan, Q. Characterization of structure and diffusion behaviour of Ca-Alginate beads prepared with external or internal calcium sources. *J. Microencapsul.* 2002, 19, 775-782. doi.org/10.1080/0265204021000022743.

[41] Mahmoodi, NM. Magnetic ferrite nanoparticle-Alginate composite: Synthesis, characterization an binary system dye removal. *J. Taiwan Inst. Chem. Eng* 2013, 44,322-330. doi.org/10.1016/j.jtice.2012.11.014.

[42] Martinsen, A.; Skjåk-Braek, G.; Smidsrød, O. Alginate as immobilization material: I. correlation between chemical and physical properties of Alginate gel beads. *Biotechnol. Bioeng.* 1989, 33, 79-89. DOI: 10.1002/bit.260330111.

[43] Vandebossche,G.M. R.; Remon,J.P. Influence of the sterilization process on alginate dispersions. *J. Pharm. Pharmacol.* 1993, 45 (16),484-486. <https://doi.org/10.1111/j.2042-7158.1993.tb05582.x>.

[44] Gombotz,W.R. ; Wee,S.F. Protein release from alginate matrices. *Adv Drug Deliv. Rev.* 1998, 31 (1-2), 267-285. DOI: 10.1016/s0169-409x(97)00124-5.

[45] Becker TA, Kipke DR, Brandon T. Calcium alginate gel: A biocompatible and mechanically stable polymer for endovascular embolization. *J. Biomed. J Biomed Mater Res.* 2001;54(1):76-86. DOI: 10.1002/1097-4636(200101)54:1<76::aid-jbm9>3.0.co;2-v.

- [46] Stabler C, Wilks K, Sambanis A, Constantinidis. The effects of alginate composition on encapsulated bTC3 cells. *Biomaterials* 2001, 22 (11), 1301-1310. doi.org/10.1016/S0142-9612(00)00282-9.
- [47] Shamkhani A, Duncan R. Radioiodination of alginate via covalently-bound tyrosinamide allows monitoring of its fate in vivo. *J Bioact Compat Polym* 1995;10:4-13. doi.org/10.1177/088391159501000102.
- [48] Torres ML, Fernandez JM, Dellatorre FG, Cortizo AM, Oberti TG. Purification of alginate improves its biocompatibility and eliminates cytotoxicity in matrix for bone tissue engineering. *Algal Research*, 2019;40:101499, doi.org/10.1016/j.algal.2019.101499.
- [49] Peppas NA, Buri PA. Surface interfacial and molecular aspects of polymer bioadhesion on soft tissues. *J. Control Release*. 1985; 2: 257-275. Doi.org/10.1016/0168-3659(85)90050-1.
- [50] Serp D, Cantana E, Heinzen C, Stockar UV, Marison IW. Characterization of an encapsulation device for the production of monodisperse alginate beads for cell immobilization. *Biotech. Bioeng.* 2000; 70 (1):41-53. doi.org/10.1002/1097-0290(20001005)70:1<41::AID-BIT6>3.0.CO;2-U
- [51] Gaserod, O, Jolliffe I.G, Hampson FC, Dettmar PW, Skjak-Braek G. The enhancement of the bioadhesive properties of calcium alginate beads by coating with chitosan. *Int. J. Pharm.* 1998; 175 (2): 237-246. doi.org/10.1016/S0378-5173(98)00277-4.
- [52] Bernkop-Schnurch A, Kast CE, Richter MF. Improvement in the mucoadhesive properties of alginate by the covalent attachment of cysteine. *J. Control Release*. 2001;71(3):277-285. doi.org/10.1016/S0168-3659(01)00227-9.
- [53] Dusel R, McGinity J, Harris MR, Vadino W A, Cooper J. Sodium alginate. In *Handbook of Pharmaceutical Excipients*; Published by American Pharmaceutical Society: USA and The Pharmaceutical Society of Great Britain: London. 1986; 257-258.
- [54] Anu Shilpa, S. S. Agrawal; Alok R. Ray, *Polymer Reviews*. 2003;43(2):187 -221. DOI: 10.1081/MC-120020160.
- [55] Mallikarjuna B, Madhusudana Rao K, Siraj S, Chandra Babu A, Chowdoji Rao K, Subha, MCS. Sodium alginate/poly (ethylene oxide) blend hydrogel membranes for controlled release of Valganciclovir hydrochloride. *Designed Monomers and Polymers*. 2013;16(2);151. doi.org/10.1080/15685551.2012.705503.
- [56] Okunlola A, Patel R.P, Odeku OA. Evaluation of freeze-dried pregelatinized Chinese yam (*Dioscorea oppositifolia*) starch as a polymer in floating gastroretentive metformin microbeads. *Journal of Drug Delivery Science and Technology*. 2010; 20 (6): 457-465. doi.org/10.1016/S1773-2247(10)50079-0
- [57] Nayak PL, Debasish Sahoo. Chitosan-alginate composites blended with Cloisite 30B as a novel drug delivery system for anticancer drug paclitaxel. *International Journal of Plastics Technology*. 2011; 15(1): 68. DOI:10.1007/s12588-011-9000-6.
- [58] Zeng WM. Oral controlled release formulation for highly water-soluble drugs: Drug-sodium Alginate-xanthan gum-zinc acetate matrix. *Drug Development and Industrial*

Pharmacy.2004; 30 (5):491-495. doi.org/10.1081/DDC-120037479

[59] Cui-Yun Yu, Bo-Cheng Yin, Wei Zhang, Si-Xue Cheng, Xian-Zheng Zhang, Ren-Xi Zhuo. Composite microparticle drug delivery systems based on chitosan, alginate and pectin with improved pH-sensitive drug release property. *Colloids and Surfaces B: Biointerfaces*, 2009;68 (2):245.doi.org/10.1016/j.colsurfb.2008.10.013.

[60] Nayak AK, Pal. D. Development of pH-sensitive tamarind seed polysaccharide-alginate composite beads for controlled diclofenac sodium delivery using response surface methodology. *International Journal of Biological Macromolecules*. 2011; 49(4):784. doi: 10.1016/j.ijbiomac.2011.07.013.

[61] Ramesh Babu V, Malladi Sairam, Kallappa M, Hosamani, Tejraj Aminabhavi M. Preparation of sodium alginate–methylcellulose blend microspheres for controlled release of Nifedipine. *Carbohydrate Polymers*. 2007; 69(2): 241-250. doi.org/10.1016/j.carbpol.2006.09.027.

[62] Oya Şanlı, Nuran Ay , Nuran Işıklan. Release characteristics of diclofenac sodium from poly (vinyl alcohol)/sodium alginate and poly(vinyl alcohol)-grafted-poly(acrylamide)/sodium alginate blend beads. *European Journal of Pharmaceutics and Biopharmaceutics*. 2007; 65(2): 204. doi: 10.1016/j.ejpb.2006.08.004.

[63] Rajesh N, Siddaramaiah, Gowda DV, Somashekar CN. Formulation and evaluation of biopolymer based transdermal drug delivery, *International Journal of Pharmacy Pharmaceutical Sciences*, 2010, 2, Suppl 2:142-148. <https://innovareacademics.in/journal/ijpps/Vol2Suppl2/569.pdf>.

[64] Rohit chaudhary, MD. Shamim Qureshi, Jitendra Patel, Uttam prasad panigrahi, Giri, I.C. Formulation, Development and in-vitro evaluation of mucoadhesive buccal patches of methotrexate. *International Journal of Pharma Sciences and Research*.2010; 1(9):357.

[65] Lee DW, Hwang SJ, Park JB, Park HJ. Preparation and release characteristics of polymer-coated and blended alginate microspheres. *Journal of Microencapsulation*. 2003; 20(2): 179-192. doi.org/10.3109/02652040309178060.

[66] Mukesh Shinde B, Ganesh Dama. Studies on development of in situ gelling system of ciprofloxacin. *Journal of Advanced Drug Delivery*.2014;1(1),2. <http://www.jadd.in/Content/Paper/201919575310000112019195753100001.pdf>.

[67] Lee KY, Peters MC, Mooney DJ. Comparison of vascular endothelial growth factor and basic fibroblast growth factor on angiogenesis in SCID mice. *J Control Release* 2003; 87:49-56. DOI: 10.1016/s0168-3659(02)00349-8.

[68] Silva EA, Mooney DJ. Effects of VEGF temporal and spatial presentation on angiogenesis. *Biomaterials* 2010; 31: 1235-1241. doi: 10.1016/j.biomaterials.2009.10.052

[69] Wells LA, Sheardown H. Extended release of high pI proteins from alginate microspheres via a novel encapsulation technique. *Eur J Pharm Biopharm* 2007;65: 329-335. DOI:10.1016/j.ejpb.2006.10.018.

[70] Gao CM, Liu MZ, Chen SL, Jin SP, Chen J. Preparation of oxidized sodium alginate-graftpoly((2-dimethylamino) ethyl methacrylate) gel beads and in vitro controlled release behavior

of BSA. *Int J Pharm.* 2009; 371:16-24. doi: 10.1016/j.ijpharm.2008.12.013.

[71] Yu CY, Yin BC, Zhang W, Cheng SX, Zhang XZ, Zhuo RX. Composite microparticle drug delivery systems based on chitosan, alginate and pectin with improved pH-sensitive drug release property," *Colloids and Surfaces B: Biointerfaces*, 2009; 68(2):245-249. DOI: 10.1016/j.colsurfb.2008.10.013

[72] Chen AZ, Chen MY, Wang SB, Huang XN, Liu YG, Chen ZX. Poly(L-histidine)-chitosan/alginate complex microcapsule as a novel drug delivery agent. *Jol of App Polymer Science*. 2012; 124(5): 3728-3736. Doi.org/10.1002/app.35371.

[73] Alejandro Sosnik, Alginate Particles as Platform for Drug Delivery by the Oral Route: State-of-the-Art International Scholarly Research Notices. 2014, Article ID 926157. <http://dx.doi.org/10.1155/2014/926157>.

[74] AlgiSite M™. <http://www.smith-nephew.com/professional/products/advanced-woundmanagement/algisite-m>.

[75] SMTL Dressings Databcard.: <http://www.dressings.org/Dressings/comfeel-plus.html>.

[76] KALTOSTAT Calcium Sodium Alginate Dressing. <https://fsastore.com/KALTOSTATCalcium-Sodium-Alginate-Dressing-3-x-4-34-Box-of-10-P23356.aspx>.

[77] Sorbsan Flat. http://www.aspenmedicaleurope.com/specialist_wound_car/sorbsan-flat/

[78] HYALOGRAN, Biodegradable Wound Dressing. Available online: <http://www.anikatherapeutics.com/products/dermal/hyalogran/>

[79] Algivon. Available online: <http://www.advancis.co.uk/products/activon-manuka-honey/algivon>.

[80] FIBRACOL™ Plus. Collagen Wound Dressing with Alginate. <http://www.woundsource.com/product/fibracol-plus-collagen-wound-dressing-alginate>.

[81] Szekalska M, Puciłowska A, Szymańska E, Ciosek P, Winnicka K. Alginate: Current Use and Future Perspectives in Pharmaceutical and Biomedical Applications. *Int. J. Polym. Sci.* 2016; 8:1-17. Doi.org/10.1155/2016/7697031.

[82] <https://www.directmedicalinc.com/catalog/product/1514/derma-sciences-medihoney-calcium-alginate-dressing-31045/>

[83] <https://www.lodaites.com/blogs/news/algues-cosmetique?lang=en>

[84] https://www.makingcosmetics.com/ICE-Alginate_p_129.html?locale=en

[85] <https://kimica-algin.com/alginate/application/>

[86] <https://glidewell dental.com/solutions/removable-prosthesis/partial/flexible-partial>

[87] <https://www.pinterest.com/LVSmileCenter/dentures/>

[88] <https://www.iroalginate.com/app-welding.htm>.

[89] Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Gerhard Flachowsky, Boris Kolar, Maryline Kouba, Marta Lopez-Alonso, Secundino Lopez Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace, Pieter Wester, Anne-Katrine

Lundebye, Carlo Nebbia, Derek Renshaw, Safety and efficacy of sodium and potassium alginate for pets, other nonfood producing animals and fish. EFSA Journal 2017; 15(7):4945.

[90] Kent Lanter, Brenda de Rodas, Bill L. Miller, Gary E. Fitzner, US Patent US 8092853 B2., Jan 2012. doi: 10.2903/j.efs.2017.4945.

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