

Overview of Alginate: Its Antimicrobial Properties, Biocompatibility, Biodegradability and Range of Uses

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Abstract

Alginate is a polysaccharide that has been used extensively in the fields of biomedical and engineering, dentistry, pharmaceutical science, paper and textile industries, film formation, gelling, biocompatibility, biodegradability, readily available, medicine and antimicrobial properties. Its properties also include mucoadhesive properties, scaffolding, and welding roads.

Alginates' hydrogels are essential for tissue engineering, wound healing, and controlled or sustained release medication delivery. We shall give a thorough introduction to Alginate and its uses in this review paper. As far as we are aware, no such useful information about alginate and its connection to drug susceptibility is available. Here, we paid additional attention to alginate's antimicrobial potential and how it relates to bacterial resistance.

1. Introduction

Alginate is a polymer that is found in large quantities in the cell walls of species of brown algae, such as *Ascophyllum* and *Laminaria*. The general structure and characteristics of a cell are determined by the multiple repeating units of monosaccharides that make up polysaccharides. In order to create different gum pastes, alginate is frequently chemically reacted with water [1]. These pastes are perfect for moulding hands, feet, and other small objects. Alginate is a naturally gelling material because of its special ability to hold up to 200–300 times its own weight in water. Alginate is a versatile product for use in pharmaceutical, thickening, and medicinal applications. It can adjust to a useful thickness to fulfil specific tasks. Although a variety of polysaccharides are employed in the field of treatment, biodegradable polysaccharides are more beneficial [1,2]. The main component of brown algae is alginates, a carbohydrate polymer that is found in the water-insoluble composition of alginic acid salts of magnesium, sodium, potassium, and calcium. These salts are structural components of the cell walls of brown seaweed. They are all structural participants consisting of 1,4 bonds between α-1-Glucuronic (G) and β-D-Mannuronic (M) acids that react as unbranched binary polymers [2]. The source determines the composition of alginates, which varies with the G:M ratio. The molecular weight, G:M ratio, particle morphology, volume fraction, and cation availability can all be changed in a variety of ways. Alginates were initially used by researcher Edward Stanford in 1883, and commercial development of the substance started in 1927 [2,3]. The amount of algae produced annually in the world has increased to approximately 41 tonnes. Alginates are widely employed in the dental, food, cosmetic, and pharmaceutical industries. Currently, the pharmaceutical, dental, and medical sectors have a huge impact on biomolecules, particularly alginates [4]. Due to its unique properties, such as its natural disintegration, gel formation, biocompatibility, and nontoxicity, alginate is well-known in the pharmaceutical industry and has uses in drug delivery, wound healing, dermatology, and scaffolds [4]. Alginate functions as a natural gum and has several advantages over biosynthetic polymers, including the ability to form hydrogels, affordability, and ease of usage. Many medicinal uses are made possible by the less intrusive oral administration of alginate into the body. Alginate gels can be used in tissue engineering and cell transplantation to restore missing or failing organs or tissue in patients [5].

2. Alginate Properties

The well-known brown algae strains *Laminaria hyperborea*, *Laminaria Digitata*, *Laminaria japonica*, *Ascophyllum nodosum*, and *Macrocystis pyrifera* are derived from seaweeds and are used to produce alginates that are sold in stores [5,6]. Alginates are generally insoluble in water; however, they can be made soluble in water by washing, crushing, drying,

powdering, and treating them with basic chemicals, particularly NaOH or KOH. To put it another way, brown algae naturally contains edible carbohydrates that are known as algin, or alginic acid. When hydrated, it becomes a viscous gum due to its hydrophilic nature [7]. **Figure.1** displays the alginate properties in diagrammatic representations.

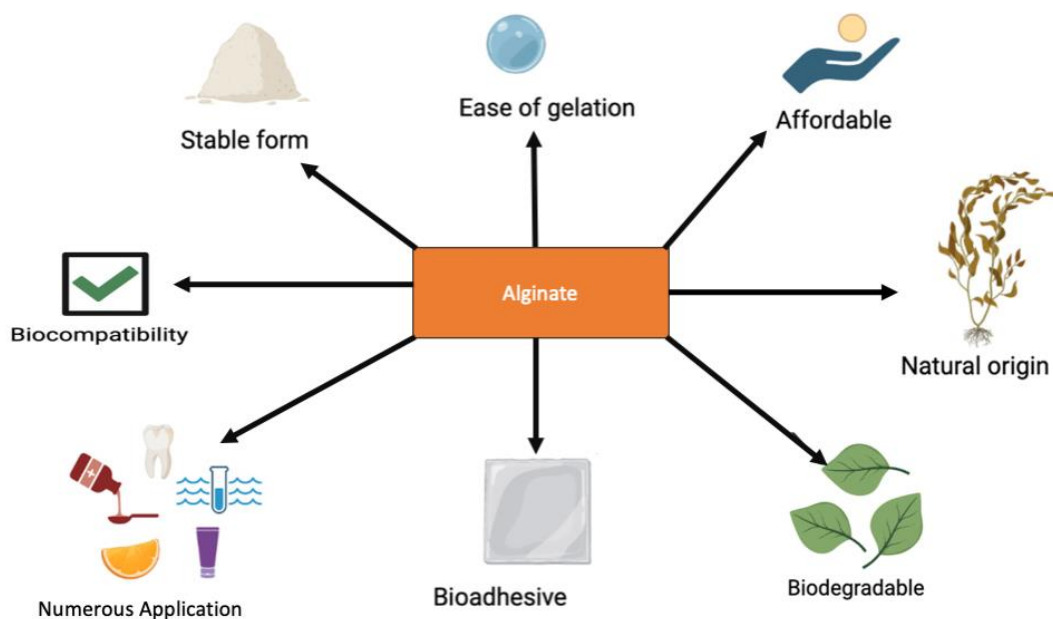


Figure.1 Schematic presentation of alginate properties (graphic was prepared with ppt accessed on 29 May 2024).

Its salts are referred to as alginates when they contain metals like calcium and sodium. It might be white or have a golden brown hue. These two names are the most well-known for alginates on the market: sodium alginate and alginic acid of sodium salt. A vital component of the biofilms that *Pseudomonas aeruginosa* produces is alginic acid [8,9]. Because of their acidic properties, alginate is a suitable biodegradable biopolymeric product for use in pharmaceutical and biomedical settings. Owing to their acidic behaviour, alginates gel more quickly when Guluronic acid (G) monomer is present, particularly when Ca^{2+} ions are present [10]. Alginate's ability to gel allowed for a variety of uses, such as the encapsulation of different fragments or even cells inside the alginate matrix, with very little drawbacks. For a variety of uses, alginates have a carboxylic group that can be changed according to the use [11]. *Pseudomonas* and *Azotobacter* bacteria have exopolysaccharide forms of alginates [11,12]. These two bacterial classes have the ability to synthesise alginates with specific monomer formulations, are very potent alginate producers, and may be able to create 'tailor-made' bacterial alginates through the use of protein engineering and recombinant DNA technologies.

2.1 Alginate structure and characterization

Alginates belong to the family of unbranched biopolymers. Partial acid hydrolysis [13] demonstrates that the alginates have a homogeneous (Poly-G, Poly) or heterogenous (MG) block combination consisting of 1,4- β -D-mannuronic acid (M) and 1,4 α -L-guluronic acid (G) monomers. **Figure.2** displays the structural details of Alginate in diagrammatic representations.

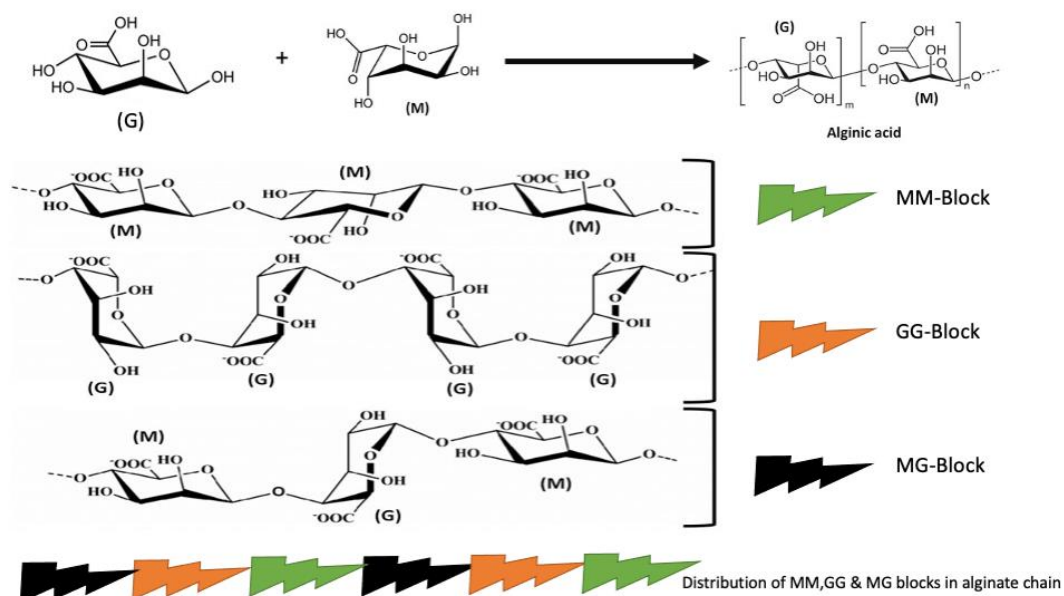


Figure.2 The structural details of alginate. (M) refers to D-mannuronic acid and (G) refers to L-guluronic acid. (graphic was prepared with ppt accessed on 29 May 2024).

Alginates range in molecular weight from fifty thousand to five lakhs and are found in various parts of the sea bed. Alginate is found in varying forms and concentrations in the cell walls of different seaweed components [14]. Alginates provide seaweeds a mechanical, flexible structure and protect them from potential inflammation when the seaweeds are exposed to vigorous water motion. Because the carboxylic groups in guluronic acid are the part of the alginate structure that become protonated and form hydrogen bonds, alginate viscosity is always pH sensitive. An increase in viscosity is the primary indicator of a pH decrease and reaches a pH of approximately 3.5 [15,16]. Alginates can handle varying molecular weights based on whether a separate analysis of the solution's pre-gel viscosity or post-gelling dispersion strength is needed. A combination of alginate polymers with high and low molecular weights keeps the solution viscous [16].

2.2 Alginate molecular weight and solubility

Commercial sodium alginate has a molecular weight that falls between 32,000 and 400,000 g/mol. Because of its varied molecular weights, alginate handles a wide variety of solubilities [17]. Alginates containing divalent or trivalent cations are likewise water-insoluble [18]. This is because the alginates have a terminal carboxylic ion (COO^-), to which these cations form bonds and produce a non-water-soluble product. Both hot and cold water will dissolve alginic acid salts containing monovalent cations, such as propylene glycol alginate, Na, K, and NH_4 salts. The cell walls of maritime brown algae contain sodium alginate, which has an approximate concentration of 30 to 60% alginic acid [19]. Alginic acid is converted to sodium alginate, which makes it soluble in water and facilitates extraction. Alginate forms a hydrophilic gel when it absorbs bodily fluids and H_2O up to 20 times its weight.

2.3 Biocompatibility of Alginate

Alginate's biocompatibility has been thoroughly tested both in-vitro and in-vivo, with variations depending on the material's purity. Due to its biocompatibility and mild gelation when divalent cations like Ca^{2+} are added, alginate a naturally occurring anionic polysaccharide has been thoroughly studied and utilised for a variety of applications [20]. The degree of purity and biocompatibility of alginate is determined by its composition. In terms of biocompatibility, alginate with a high concentration of M monomers has been shown to be more immunogenic and to promote cytokine biosynthesis ten times more strongly than alginate containing G monomers; aside from this, however, reports of very little or no immune response have been made across alginate implants [21]. Alginates can contain impurities such as heavy metals, endotoxins, proteins, and polyphenolic compounds, which can cause a variable reaction at the injection or implantation sites. However, there haven't been many reports of significant tissue injury or inflammatory cases with alginates that came from reputable or branded companies, were commercially available, or were certified [22].

2.4 Derivatives of Alginate

There are numerous beneficial uses for alginate derivatives in pharmaceutical and biomedical fields, as described to date. By adding non-water-resistant moieties (such as alkyl chains or non-water-resistant polymers) to the backbone of alginate, derivatives of alginate with amphiphilic character have been created [23]. These compounds have the ability to form gels and particles in aqueous conditions, as well as self-organized structures. They are also helpful in drug delivery applications. Long alkyl chains have been conjugated to the alginate backbone via ester bond formation to create sodium alginate amphiphilic derivatives [24]. One example of a long-chain alkyl group that forms bonds with the alginates matrix by esterification is dodecyl or octadecyl. For cartilage healing and bone regeneration, rheology, gelling, and crosslinking qualities are crucial [25]. Alginate, which is generated from poly butyl methacrylate, is used to create sustained or regulated drug delivery vehicles. Peptides with cell sticky peptides are also present in alginate and are created by joining peptides as side chains and junctions with carboxylic groups of sugar residues [25,26]. Scientific interest in the use of Alginate derivatives containing cell sticky peptides in human health has grown. Peptides are chemically introduced as side chains to create these derivatives. The sodium salt of alginic acid is used to make sodium alginate ($\text{NaC}_6\text{H}_7\text{O}_6$), and the potassium salt is used to make potassium alginate ($\text{KC}_6\text{H}_7\text{O}_6$) [27]. Sodium alginate is the precursor of calcium alginate ($\text{CaC}_{12}\text{H}_{14}\text{O}_{12}$), and in the process of making calcium alginate, sodium ions are exchanged for calcium ions.

2.5 Gelling Properties of Alginate

Alginates react with divalent cations, such as Ca^{2+} , to create gels; the key to alginate gelation and crosslinking is the interchange of sodium ions from glucuronic acids with divalent cations in solution [28]. One of alginate's key characteristics is gelation, which is brought on by Ca^{2+} . The gelation phenomenon has been extensively investigated over the past fifty years, and it is well-known. It has been described as an egg-box model. Numerous variables, such as reactant concentration, heating temperature, pH, and salts, influence the formation of alginate gel [29]. These variables include the gel's viscosity, storage, and loss moduli as well as its rheological characteristics, which determine its strength. When calcium ions are present, sodium alginate's G monomer undergoes a chemical reaction to form a crosslink with another molecule, which is how sodium alginate thickens and gels in the presence of calcium [30,31]. Calcium alginate gel can be easily disrupted by EDTA sodium citrate or monovalent ions complex ions (phosphate and citrate), which are strong complex-forming agents with a strong chemical affinity for Ca^{2+} . Instability is also influenced by the large quantities of non-gelling ions, such as Na^+ and Mg^{2+} [32]. Alginate can only chemically combine with trivalent (Fe^{3+}) or divalent (Ca^{2+} , Sr^{2+} , and Ba^{2+}) ions to produce gels. The production of carriers for the well-controlled and sustained release distribution of pharmaceuticals has been investigated using divalent and trivalent ions [33]. This is the result of intramolecular bond formation and ionic interactions between carboxylic acid groups on the polymer matrix. Alginate is a blend of two uronic acids; each uronic acid unit has a negatively charged carboxyl group with a high capacity for ionic exchange. These groups combine to form chains, which give Alginate its polymer structure [34,35,36]. By means of electrostatic repulsion, the molecules of alginate in an aqueous solution push against one another, creating a smooth, viscous liquid. Positively charged calcium ions are drawn to negatively charged alginate molecules when calcium ions are added, creating a salt [36]. Calcium ions with negatively charged alginate come into touch with other alginate molecules and join through a calcium ion when more positive charge is added. Because of its resemblance to an egg in an egg carton, this occurrence is often referred to as "egg box junction." Alginate gels come into touch with calcium ions as a result of this instantaneous reaction that takes place throughout the solution [37,38]. A sodium alginate aqueous solution forms beads as it gels due to surface tension, controlling the ionisation of calcium to create a jelly, when added dropwise to an aqueous solution of calcium salt and gels instantly wherever it comes into contact with calcium ions [39]. The entire solution can be gelled into any desired shape; this technique is known as the "ion control method." The ion control approach states that calcium ions must first be sequestered so that alginate cannot chemically react with them. Once sequestered, calcium does not chemically react with the aqueous alginate solution and mixes evenly throughout the solution [40]. As a solution's pH drops gradually, sequestered calcium is freed and reacts uniformly with the gels of alginate solution. By adjusting the kind and quantity of these two types of agents, calcium responds as a sequestering agent and a pH reduction agent. This allows for the free adjustment of the gelation period, which can range from a few minutes to an overnight operation [41]. Alginate is utilised as a gelling agent in a variety of pharmaceutical and medical applications by taking advantage of this characteristic.

2.6 Effect of pH on Alginate

A few criteria that affect the alginate's water solubility are pH and ionic strength. Because of the deprotonation of carboxylic groups ($-\text{COO}^-$), alginates have a lower pH and are less water soluble [42]. Above $\text{pH} > 5$, the alginates' viscosity remains constant. While the COO^- group present in alginates will get protonated to COOH in solutions with pH less than 5, electrostatic repulsion between chains would then decrease [42,43]. Together, they can go closer to forming hydrogen bonds, which results in a drop in viscosity. Alginates' viscosity has been found to

diminish owing to de-polymerization at pH values greater than 11. The concentration of an ionic solution affects crosslinking and can raise the molecular weight and viscosity of alginates [44]. Moreover, the crosslinking is dependent on the presence of M groups in the alginate matrix and the confirmation of G monomers. The molecules synthesised from sodium alginate were described by Pawar and Edgar in 2012, and it was found to be stable between pH 5 and 10 [1,44].

2.7 Sterilization

Alginate's viscosity reduces during autoclave sterilisation because the random breaking of alginate chains occurs during autoclave heating. This indicates that alginate is not well suited for autoclave sterilisation [45,46]. The emergence of different types of components in the solution serves as a gauge for the extent to which this loss happens. For the safe sterilisation of alginate solutions, ethylene oxide and gamma radiation are essential [46]. Prior to use, alginate sterilisation is crucial for eliminating and conquering contamination from alginate solution.

2.8 Immunogenicity of Alginate

Alginates play a critical role due to their immunogenicity and biocompatibility; drug administration in a controlled or sustained release way is the newest trend in pharmaceutical dosage forms requirements for appropriate application in drug vehicles [47]. Alginate immunogenicity is caused by two factors: chemical composition and mitogenic contaminants. Alginate is thought to have modest cytotoxic effects and reduced hemolysis when it comes into contact with blood. Although alginate is a poor immunogen, it elicits powerful or highly effective immune responses that effectively eradicate the *Pseudomonas* bacteria [47,48]. Alginate immunogenicity is increased by SLN, which is also helpful for drug distribution and can extend its effectiveness. The findings of ELISA and opsonophagocytosis assays demonstrate that the SLN-Alginate conjugate stimulates the immune system to produce a higher number of immunoglobulins with effective outcomes than Alginate antigen alone. According to the challenge experiment, mice treated with Alg-SLN exhibited a greater degree of immunity against *Pseudomonas aeruginosa* infections compared to mice treated with pure Alginate [48]. Overall findings demonstrate the newly synthesised vaccine's ability to produce immunogenicity, and as a result, it will be taken into consideration as a potential potent vaccination against *Pseudomonas aeruginosa*.

2.9 Alginate Bioadhesion

The phenomena by which synthetic and natural macromolecules adhere firmly to mucosal surfaces in the body is known as bioadhesion or mucoadhesion. When these components are added to formulations, there may be an increase in the amount of medicine absorbed by mucosal cells or a longer duration of drug release at the location [49]. Alginates' carboxyl group exemplifies mucoadhesive qualities with its mucoadhesive anionic polymeric layer. When comparing polycation with non-ionic polymers, it is shown that polyanion polymers have superior bioadhesive qualities. When compared to polymers such as polystyrene, chitosan, carboxymethyl cellulose, and poly (lactic acid), alginate exhibits superior mucoadhesive strength [50]. Alginate's mucoadhesive qualities are essential for its function as a mucosal drug delivery vehicle to the GI tract and nasopharynx because they increase the duration of the medication's residence time at the site. Because of its biodegradability, biocompatibility, and ability to interact electrostatically with positively charged substances, alginate is frequently utilised as a bioadhesive [51,52]. Intimate contact between a dosage form and the absorbing tissue is made possible by alginate bioadhesive systems, which may lead to high concentration in a specific area and consequently high drug flux through the absorbing tissue.

2.10 Toxicity of Alginate

Numerous studies have concluded that alginates are not hazardous, and when they are crosslinked with sodium or calcium, they become harmless to cells and even safe for the skin and eyes. Alginate, on the other hand, has found a variety of uses in the biomedical, food, paper, pulp, and biomedical industries due to its benign nature and fully controlled and sustained release medication delivery [53]. When added to food goods, sodium alginate is completely safe and harmless. There is no cap on the amount taken because sodium alginate is generally recognised to be harmless.

2.11 Biodegradation of Alginate

Because mammals lack the enzyme alginase, which cleaves polymer chains, alginate is intrinsically non-degradable. Partial oxidation of alginate chains is necessary for alginate to become degradable in a physiological setting [54]. The oxidised form of alginate degrades in an aqueous media, and these materials have several applications as drug delivery vehicles and cells [55]. Alginate can be oxidised by sodium periodate. Periodate oxidation disrupts the cis-diol group's carbon-carbon link in the uronate residue, changing the chair's conformation to an open-chain adduct that can't break down the alginate backbone [56]. It is anticipated that oxidation will cause a small shift in the

molecular weight of alginate. The mechanical characteristics and rate of decomposition of alginate gels can be significantly influenced by modifying the molecular weight distribution of alginate. Through ionic or covalent cross linking, binary alginate gels with low and high molecular weights have been produced from partially oxidised alginates [57].

3. Alginate various applications

Alginate has a very broad variety of uses in biomedical engineering, such as rate-controlling studies in drug delivery systems, a matrix for biomolecules and excipients in the growth and development of biopharmaceuticals for local administration. Since alginates are harmless, as **Figure. 3** illustrates, they can only be used in food additives and medication compositions.

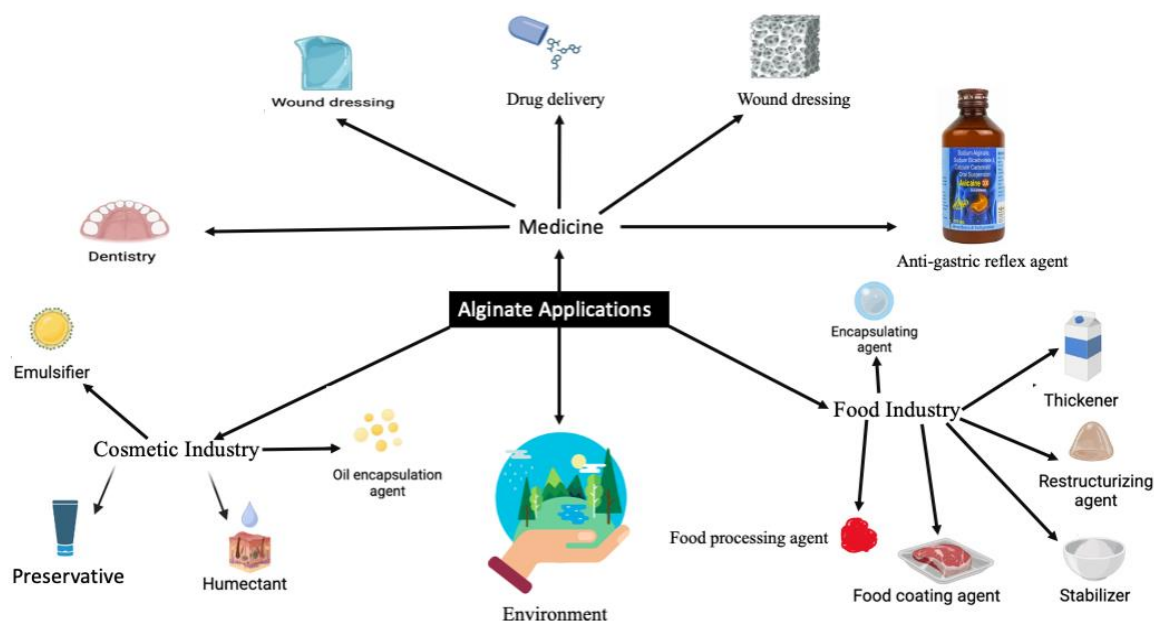


Figure.3 Alginate applications (graphic was prepared with program ppt, accessed on 29 May 2024).

3.1 Alginate in pharmaceuticals, food industry and its clinical relevance

Since alginate can be a key component of prolonged release medication solutions, alginates are commonly used in the pharmaceutical industry as gel-forming, thickening, and stabilising agents [58]. In the current medical field, a vast range of side effects are caused by different medications or prescriptions that are given to patients. The majority of alginates are used in pharmaceutical applications for oral medications; nevertheless, the use of alginate hydrogels as a storage medium for tissue-confined drug delivery is expanding [59]. Alginate gels are being researched for a variety of low molecular weight drug delivery, and they are highly useful at the time because kinetics of drug release can be started by either a primary or secondary bond between the drug and the alginate [60]. Alginate gel is usually nonporous; which controls how quickly tiny molecules diffuse through the gel.

3.1.1 Alginate in Controlled drug delivery

Alginate gels typically have pore sizes of about 5 nm, which allow low molecular weight medicines to fill the pore size through two different types of bonding: chemical and physical. The release of a loaded medicine is regulated when it comes into contact with a hydrated environment [61]. Additionally, because the loaded drug porters are soluble in water and may degrade in a diluted media, crosslinking alginates with a bivalent or trivalent cation will strengthen the gels or films. These items support the kinetics of drug release studies. For the regulated release of valganciclovir HCL as an anti-HIV medication in vitro, blends of polyethylene oxide and sodium alginic acid are described [61,63]. The most powerful example of common oral medicine dosage forms are tablets and capsules, which can be made into immediate release systems to facilitate quick drug absorption. The coating of fast release devices has the potential to delay the amount of medication released. Alginates are widely utilised for this kind of coating. Sodium alginate can be employed as a tablet binding agent and alginic acid plays a significant function as a disintegrant in rapid release dosage forms [64,65]. A physical or chemical barrier is used to release the medication dosage forms from the formulation in a regulated manner. When it comes to oral dosage forms, there are various ways to create a barrier, such as coating the active ingredient or trapping it within a polymer matrix [62]. Alginate is frequently employed in the design of dosage forms such as prolonged release systems and quick release systems.

3.1.2 Alginate in Food Industry

In the food sector, restructured meals are produced in a variety of shapes and sizes by enhancing their texture, appearance, and structural qualities. This gives the product originality and satisfies consumer desires [66]. Because of its many uses in food, alginate has been recognised by FAO/WHO as the safest food additive. Many food goods, such as ice cream toppings, fruit jams, jelly, milk products, food packaging, instant noodles, beer, etc., include alginate [67]. The stability of food products at both high and low temperatures depends on alginates. The concentration of Ca^{2+} and H^{+} in the solution controls the gelation rate and gel strength of alginates [68]. As things stand, work has been done on the expansion and advancement of food packaging made of alginate. Biodegradable and renewable biopolymers are frequently employed in short-term packaging. Bioactive compounds are combined with alginate films for long-term storage, which allows them to be released and prevents lipid oxidation and microbial growth in food while also extending its shelf life [69]. The Alginate films that are created by combining biologically active protein hydrolysate and cottonseed by-product have strong antioxidant and antibacterial lipid qualities. They also have lipid barrier and visible light-absorbing qualities that are enhanced by pH adjustment [69,70]. A few synthetic and natural additives that improve the functional, mechanical, and nutritional qualities of food products are necessary for the preservation of food ingredients. Alginates are helpful in the ice cream industry; they are used as stabilising, thickening, and gelling agents. Alginate gives baking creams freeze/thaw stability by overcoming syneresis. Additionally, it provides favourable melting properties, inhibits shrinkage and crystal formation, and improves resistance to heat shock [70].

3.1.3 Alginate in protein delivery

Because they may prevent or overcome denaturation and shield from degradation until their release, alginates are essential for the trapping of protein drugs. The pace at which protein is released can also be regulated using alginate gels [71]. Because of its flexible nature, alginate hydrogels reversibly bind with heparin-binding growth factors, such as fibroblast growth factor or vascular endothelial growth factor, and result in prolonged release [71]. Alginate microspheres and highly polydispersed index proteins, such as chymotrypsin and lysosome, can be cross-linked with success. The continual release method and cross linking benefit from the usage of sodium alginate.

3.1.4 Alginate in cell delivery

The alginate gel that contains arginine glycine aspartic acid peptides (RGD) has been used in vitro cell culture because it is biocompatible, non-immunogenic, and simple to administer in the body [72]. The enhancement of the phenotypes of interacting myoblasts, chondrocytes, osteoblasts, ovarian follicles, and bone marrow stromal cells is brought about by RGD peptides in alginate gel. Compared to non-modified alginate, chemical fusion is the cause of the increased adherence and proliferation of RGD peptides to the alginate backbone [72,73]. The density of RGD in gels has a significant impact on cell adhesion and proliferation. Changes in the spacer arm length between the alginate chain and RGD peptide can influence cellular responses.

3.1.5 Alginate in Wound dressing

There are several benefits to using an alginate-based wound dressing instead of a gauze [74]. Maintaining a dry wound can prevent the entry of infections, whereas an alginate dressing provides a moist wound form that facilitates wound healing [74,75]. Increased antibacterial activity and antioxidant properties of Alginate combined with Silver in wound dressings can boost binding affinity for immune regulators ($\text{TNF-}\alpha$, IL-8) and proinflammatory cytokines (elastases, matrix metalloproteases-2) [75]. Alginate polyethylene glycol, methyl ether methacrylate, and *M. oleifera* are scaffolds on which aloe vera with wound-healing properties is established. Alginate-treated calcium ions (Ca^{2+}) are what cause the alginate blocks to interconnect, forming an egg-box structure [76]. It causes handling and stability issues due to its poor integrity for tissue scaffolding [77]. Thus, plasticization—which maintains the alginate plasticizer ratio while overcoming the intermolecular attraction forces between polymer chains—can be used to remedy this problem. Consequently, it led to advancements in the stability and management of alginate. Problems with handling and stability can be resolved by adding plasticizer, such as polyethylene glycol and methyl ether methacrylate in the right amounts [78].

3.2 Alginate in cosmetics

Alginates have long been the subject of research in the cosmetics industry to create superior products that offer special benefits to skin. Alginates have the ability to absorb UV radiation, counteract the damaging effects of the sun, moisturise the epidermis, smooth the skin, and ensure the renewal of tiny cells [79]. Alginates have been shown to produce gels, retain moisture, and thicken a variety of cosmetic products. Alginate helps to keep face creams, body lotions, and lipstick colour on lips because of its gel-forming properties [80]. Sunflower wax is combined with alginate, a natural thickening agent, to create popular all-over body lotions. One type of naturally occurring polysaccharide with a high viscosity and significant water absorption capability is alginates. To provide maximal

viscosity, alginates viscosity can be improved [81]. Alginates are being investigated for use in face masks and antiaging masks that lift the skin, reduce wrinkles, and slow down the ageing process. Alginates are also helpful in dentures, which are a removable pair of gum tissue and replacement teeth with a full support and a stylish appearance [82]. Alginates are used in dentures as a detachable set of gum tissue and restorative dentistry that can provide us a full foundation and a lovely appearance even as we age.

3.3 Alginate in Textile Industry

Colour paste substrates can be made with textile-grade alginates, which are used in a wide variety of textile items such as towels, shawls, and print fabrics. When compared to other substrates, alginates are employed as a cleaner and simpler substrate to break down for textile printing [83]. Wastewater can be handed away more easily when alginates are used to print on cotton, jute, and rayon. In the textile business, sodium alginates are used as thickeners to thicken colour paste for printing. Using screen roller printing equipment, the pastes can be applied to fabric. After reactive dyes were discovered, alginates were used as a general thickening agent. These compounds undergo a chemical reaction with the cellulose content of garments. Reactive dyes react chemically with a number of well-known thickeners, such as starch, resulting in reduced colour yields and occasionally challenging product washout [84]. Because alginates are non-reactive with dyes and quickly wash out of the finished textile, they can be one of the strongest thickeners for reactive dyes. Although even low viscosity alginates are producing incredibly appealing printing in modern high speed roller printers, traditional screen roller printing uses mediums with high viscosity alginate [84].

3.4 Alginate in Welding rods

Welding is a well-known and practical method for creating a wide range of metal structures. Coating is employed as a flux and to monitor conditions surrounding the weld, such as temperature, hydrogen, and oxygen, during the welding process [85]. To provide part of the plasticity needed for coating extrusion into rods and to attach dried coating to rods, sodium silicate can be used with dry coating materials in this situation. On the other hand, the silicate does not bond or provide enough lubrication to enable successful and smooth extrusion [86]. To keep the wet mass together before to extrusion and to maintain the coating on the rod during drying and baking, a lubricant and a binder are required. Alginates can use in order to meet these norms.

3.5 Alginate use in Animal feed

Sodium and potassium alginate salts are widely used in industry as binders, thickeners, stabilisers, emulsifiers, and gelling agents. No competent authority has recommended the use of sodium alginate in fish, dogs, or other non-food producing animals' diets [87]. On the other hand, dogs and cats can consume potassium alginate as food. Alginates are beneficial for fish feed and do not negatively impact the customer. Alginate may cause mild ocular irritation, but not skin irritation [88]. The aquatic ecosystem is not negatively impacted by the inclusion or application of these substances in fish feed. Alginate, water, feed minerals, and a calcium content that is insoluble in water are combined to create gel-type cattle feed combinations [89]. After the feed mixture is generated, the calcium component is soluble in water or the sequester that affects the reactivity between the alginate and calcium component is removed, resulting in a gel feed that contains the feed nutrient elements [90]. After that, the gel meal can be given to the animals.

3.6 Biotechnological applications of Alginate

Through the use of matrix shields that incorporate biological agents and immobilise them from chemical and physical agents, alginate offers a stable support for microbial cells exposed to a range of ambient variables, including pH, temperature, and shear stress [91]. Comparatively speaking, immobilised cells have many more uses in biotechnological processes than do free cells. A well-known method for immobilising microbial cells inside micrometric and monodisperse particles is microfluidics, which can be used to advance bioprocessing [91,92].

Alginate microparticles immobilise proteins, microbes, and mammalian cells. By immobilising cells using a microfluidic technology, techniques for cell separation, cellular response to various stimuli, and cell division have been examined. *Bacillus subtilis* synthesises lipase, an enzyme with good thermal stability and enzymatic activity, at high alkaline pH levels by a submerged fermentation process [91,92,93]. Nevertheless, when immersed in the bioreactor, *Bacillus subtilis* that has been immobilised in alginate microparticles using the microfluidic approach boosts lipase synthesis. One of the major issues with industrially processed fruit-based beverages is the end product's undesirable turbidity, which is caused by the presence of polysaccharide inner cell walls, such as pectin, cellulose, hemicellulose, starch, and lignin particle suspension [94]. Pectin is the substance that gives fruit juices their turbidity; the enzyme pectinase can be used to break down and eliminate this undesired solid suspension.

3.7 Environmental Applications of Alginate

A more dependable method for treating environmental contaminants is adsorption. Alginate-based composites, which are thought to be the most effective adsorbent, can help remove pollutants from water and waste water, such as heavy metals, industrial dyes, pesticides, and antibiotics [95]. Because alginates are rich in carboxyl and hydroxyl groups, they can target contaminants such as heavy metals and dyes by cation cross-linking to stop the exchange of metallic or cationic ions. Alginate gels' poor mechanical qualities, elasticity, high stiffness, and fragility are their drawbacks [96]. Composites made of both organic and inorganic alginates have been properly synthesised to get over these restrictions.

3.8 Alginate in Liposomes

As demonstrated by recently approved commercial goods, liposomes are biodegradable, biocompatible carriers with biological cell membrane characteristics and strong delivery capabilities [97]. According to reports, liposomes are a revolutionary drug delivery technology that can be used to deliver pharmaceutical and biological goods. Because of their high flex, they can incorporate both lipophilic and hydrophilic medicines. Liposomes boost the biodistribution of medicines and raise the therapeutic index [98]. Apart from free drug administration, liposomes have many other uses, such as medication delivery, diagnosis, and therapy monitoring. Because of their enhanced permeability and retention function, drug-loaded liposomes concentrate at the tumour site in cases of chemotherapeutic drugs' antitumor efficacy [99]. The FDA has approved a variety of liposome types for use in cancer therapy, and the toxicity of these drugs has been reduced to non-tumor tissues.

3.9 Alginate in Microspheres

Small spherical structures known as microspheres are free-flowing microparticles with a typical particle size of 1 μm to 1000 μm . They are typically made up of synthetic polymer and protein. Drugs, vaccines, antibiotics, and hormones can all be released under regulated conditions with the help of microparticles. Microspheres have a wide surface area and make it simpler to assess the mass transfer and diffusion characteristics [100]. Microspheres encapsulate small molecules that regulate the release of medications into bodily fluids. When compared to conventional dose forms, the use of sustained release drug systems has shown to be beneficial since they can reduce toxicity and increase the medicine's effectiveness. According to stability experiments, when the formulation is broken down under accelerated conditions and at room temperature, Eudragit S-100 coated sodium alginate microspheres of naproxen sodium show a steady rate of degradation of microspheres with a two-year shelf life [34].

3.10 Alginate in Microcapsule

Microcapsules are a type of delivery method used in the food and agriculture industries because of them engulf able external shell and inside core made of a combination of liquid and solid polymers. Though they are unstable in the gastrointestinal tract environment, probiotics are used to treat gastrointestinal irregularities [101]. The application of double alginate coating microencapsulation, which includes *Lactobacillus plantarum* and *Lactobacillus casei* probiotics, reduces this issue. Probiotics that are microencapsulated have higher temperature resistance and are more alive in simulated intestinal and gastric fluids. *Dietzia natronolimnea* has a functional pigment called canthaxanthin, which has strong antioxidant qualities [102]. They are heat, light, oxygen, and pH sensitive. Alginates with high methoxy pectin content and canthaxanthin microencapsulation facilitate retention in both neutral and acidic pH ranges. These strengthen canthaxanthin's antioxidant qualities. As of right now, Type-1 diabetes mellitus is being treated with the sophisticated insulin release system [103,104]. In contrast to chitosan or starch films, this approach reduces the thermal degradation of alginate films by synthesising hyaluronic films that are easily obtained commercially.

4. Conclusions

Alginate has been discovered to possess favourable qualities such as swelling characteristics, mucoadhesiveness, gelling, sol-gel transition, and metrics. Because of these benefits, alginate can be employed in the controlled drug delivery or sustained release drug delivery systems as well as in novel drug delivery systems like liposomes, microcapsules, microspheres, nanoparticles, hydrogels, metrics, membranes, tablets, cochleates, and supersaturation drug delivery. Alginate finds extensive use in the fields of biotechnology (biotechnology), biomedical (wound dressings, bone regeneration, neovascularization, cellular and protein), and pharmaceuticals (raft formulation, oral drug delivery, modulated systems, and controlled release structures). Tissue engineering, compound cell physiology research, and drug development can all benefit from the use of three-dimensional cell cultures or tissue based on alginate. The most recent method involving the usage of alginates is the encapsulation of pig pancreatic islet cells employing monolayer cellular apparatus technology to create cell-built nanoparticles for type-1 diabetes diagnosis and treatment. Researchers have always faced the difficulty of determining whether

alginate may be modified by grafting with other low- or high-molecular-weight polymers to increase its strength depending on the application.

Ethics approval and consent to participate

The ethical approval is not required for this study. The authors declare that their participation in writing this review as well as its publication is completely voluntary without affecting their actual research work.

Authors contribution

A.K & B.J.O, Conceptualization, conceived the structure of the review, writing, draft, editing and made figures, project administration. G.K.V, and P.S, writing reviewing and data curation. A.B, P.N, J.G and A.K edited, critically revised and approved the final manuscript. All authors have read and agreed to the published version of the manuscript.

Consent for publication

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