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Applications of seaweed biopolymers and its composites in dental applications

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ABSTRACT

Biopolymers are natural polymers derived from renewable sources such as plants, algae, and microbes. As a supportive material for regeneration in dental research, biopolymers are of prime importance. Biopolymers have been widely developed for periodontal, prosthodontics, orthodontic, and endodontic applications in dentistry, including scaffolds, biomembranes such as guided tissue regeneration (GTR), guided bone regeneration (GBR), nanocomposites, hydrogels, barrier membranes, nanofibers, and bioink for 3D printing. Different biopolymers have been traditionally used since time immemorial, such as chitosan, collagen, and hyaluronic acid which are non-versatile, difficult for availability, and not cost-effective in the present scenario. Agar, carrageenan, alginate, fucoidan, and ulvan are biopolymers effectively utilized for dental applications. Seaweed biopolymers are easily available and meet other biopolymers' characteristics for material fabrication. Blending of nanoparticles and antibiotics for slow release with seaweed polymers is possible, like that of other biopolymers. Seaweed biopolymers also support osteogenic processes and cytocompatibility and biocompatibility in nature. Its good resorbable nature and solubility in water with good gel strength favor physical and mechanical properties support for dental applications. Biopolymers derived from seaweeds also exhibit good biocompatibility, biodegradable nature, good structural strength, and induce cell proliferation and differentiation. Seaweed biopolymers exhibit antimicrobial, antioxidant, and anti-inflammatory activities.

1. INTRODUCTION

Since time immemorial, polymers have been used in medicinal applications [1,2]. Polymers are generally classified as natural and synthetically derived. Natural polymers are ones obtained from natural resources through extraction methods using plants, animals, seaweeds, etc. Whereas synthetic polymers are obtained from petrochemical sources as a value-added product while refining the chemicals during the process [3,4]. Alternate sources for synthetic polymers are gaining more attention from researchers and environmentalists to reduce plastic usage in dental applications [1].

Most of the dental materials are made of synthetic polymers and are widely used in various applications. Polymers such as poly (methyl methacrylate) (PMMA), ethylene glycol dimethacrylate (EGDMA), hydroxyethyl methacrylate (HEMA), triethylene glycol dimethacrylate (TEGDMA), polyacrylic acid (PAA), polycarbonate, polyethylene glycol, polyurethane, polypyrrole, hexamethyldisilazane, N-isopropylacrylamide, N-tert-butylacrylamide, hydrogel, and polydimethylsiloxane were frequently used in dental material preparation [1,5]. Most dental polymers are not recyclable and not biodegradable in nature [1,6]. To overcome this issue, an alternate and immediate solution providing material to replace synthetic polymers has been in search for a long time and alternate polymer coatings for biocompatibility will favor dentistry applications [7].

Seaweeds are a source of natural biomaterials that are gaining importance in the medicinal field, especially for dental applications [8]. Biopolymers such as agar, carrageenan, alginate, and ulvan are widely used in different fields [9]. Biopolymers are reversible (agar, carrageenan) and irreversible (alginate) in nature, especially used in dental applications [10-12]. Applications such as impression making, scaffold preparation are some common applications in the dental domain. Apart from dental applications, these polymers are used in food and drug delivery applications [13-15].

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2. SEAWEED DERIVED BIOPOLYMERS IN DENTAL APPLICATIONS

Seaweeds are macroalgae and differentiated into red (Rhodophyta), brown (Phaeophyceae), and green (Chlorophyta) in color based on external appearance [16]. Seaweeds are rich in pigments, biopolymers, and other bioactive compounds (e.g., polyphenols) [17-19]. Apart from biopolymers, seaweeds also have important bioactive pigments such as carotenoids, phycobiliproteins, and some polyphenols, which are biologically active compounds with good medicinal properties and applications in a wide area [20-22]. Biopolymers are gaining importance in the medicinal field for different applications [23], especially in dental impressions and other cancer-related scaffold applications [5,8,19]. The major components of seaweeds are biopolymers/hydrocolloids/polysaccharides (50–70%) [24], followed by proteins (5–47 %) [25,26], pigments, lipids, and polyphenols.

Seaweed-derived polysaccharides are biopolymers usually called hydrocolloids, which are soluble in different solvents and biodegradable in nature. These biopolymers are interlinked with monomers to form a long chain with chemical bonding through electrostatic interactions. Monomers of agar polysaccharide consist of agarose (d-galactose and 3,6-anhydro-L-galactopyranose) and agaropectin units. Carrageenan consists of 1,3 linked β-galactose and 1,4 linked α-d-galactose units [27] and alginates molecules are chains of d-mannuronic acid and l-guluronic acid. Fucoidan consists of galactose, mannose, glucose, and laminaran consists of β-(1-3)-linked glucan backbone with β-(1-6)-linked side chains of various lengths [28-31]. Ulvans consist of rhamnose, xylose, and uronic acid as monomers.

Biopolymers are gaining huge applications in the dental field due to their versatile nature and flexibility with binding to additional monomers/polymers [Table 1]. Alginates are a widely used polymer material for dental impression making and it is an irreversible polymer with better compatibility with other chemicals and miscible with water without difficulty. In general, impression materials are mucocompressive, thermoplastic, and rigid in nature [32]. Impression materials are used to make replicas of oral structures. Alginates were used for making impressions [33] for partial dentures, complete dentures [34,35], and orthodontic and study models [1,5,36,37]. Alginate monomers are linked through (1–4) glycosidic bonds. By dispersing different ceramics and fillers in the alginate, polymers using nanoparticles will enhance the property suitable for dental applications [38].

2.1. Thin Films Derived from Biopolymers

The use of biopolymeric materials and films is gaining importance in medicinal and dental research [5,39]. Biopolymeric films have been used in different aspects of dentistry, such as preventive, restorative, and regenerative therapies [40]. Some biologically synthesized polymers such as polylactic acid are used in dental pulp and dentin regeneration applications. Polymeric films are widely used in dentistry [Figure 1a], such as for preventing biofilm and dental caries development [41], preventing tooth erosion, drug delivery, restorative dentistry, prosthetic dentistry, implantology, periodontics, reducing corrosion in dentistry, and reducing friction in dentistry [42]. In addition, of nanoparticles through surface, modification techniques will also favor nanocapsule development with bioadhesive properties [5]. As of now, most of the polymeric films are synthetic and semi-synthetic in nature, but the applications of seaweed polymers in dentistry are minimal and need a lot of research to replace the synthetic polymers [5].

2.2. Fabrication of Membranes/Graft Materials

Hydrogel membranes are usually used in tissue engineering, NiTi implants, and orthodontics. However, some of them do not have proper mechanical strength and compatibility. Hence, biomembranes [43] which are made up of naturally derived polymers are much of use in biocompatibility and have natural tissue regeneration capacity like natural tissue [44] [Figure 1b]. Since the membranes are used for periodontal applications, biopolymer should possess lubrication and antiwear formation, anti-biofouling, cellular adhesion promotion, drug delivery, and biosensing [45,46].

2.3. Drug Delivery Applications

Biopolymers from seaweed such as carrageenan and alginates are widely used as gels for drug delivery [47]. Some bioactive polymers are used as advanced drug delivery systems [5]. Hydrogels are made of polymers either derived naturally or in a synthetic form used as a drug delivery system [48-51]. The development of stimuli-responsive blends of biopolymers is a dynamic field of research, due to the effect of the nature of the medium, heat, presence of ions, and electropositivity or electronegativity of ions [13,52]. Thermoresponsive (agarose and cellulose), pH-responsive (alginate and carrageenan), and physicochemical-responsive biopolymers (fucoidan and ulvan) derived from seaweeds can be used as smart materials in dental and other biomedical applications as it is possible to be tuned to make them economically affordable [53-56].

2.4. Dental Impression

Alginates are a widely used material for dental impressions [57]. Alginates are sulfated polysaccharides derived from brown seaweeds such as kelp [58]. There are many commercial companies producing ready-to-use impression material using alginate as one of the setting ingredients, such as Neocolloid (Zhermack), Palgat Plus (3M ESPE), and Blueprint Cremix (Dentsply). First and foremost, the important thing in making an impression is the set time, which determines

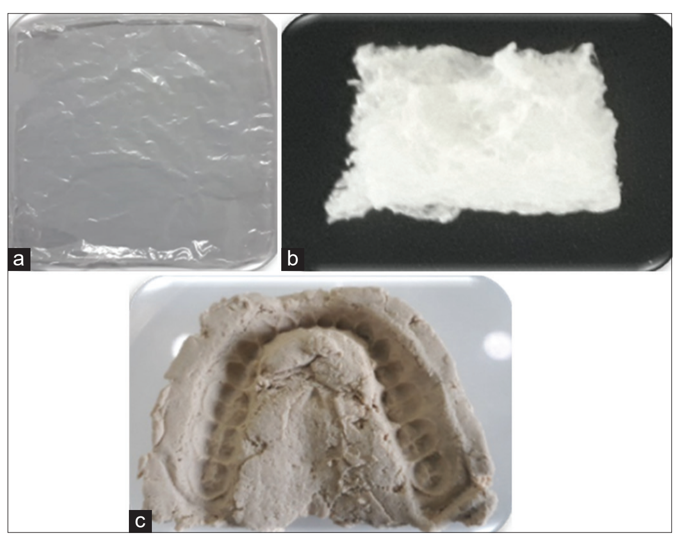

Figure 1: Biomembrane/Scaffold made using carrageenan biopolymer (a). Graft material fabricated using carrageenan biopolymer (b). Dental impression composition developed using alginate and carrageenan, and (c). The above materials are developed in Saveetha Dental College.

the proper teeth impressions of patients within a short period of time [59]. Impression materials composition consists of polymers, cross-linker agents, pH modifiers, sequestrants, fillers, and other color changers [60]. There are other natural polymers from seaweed that may help in making impression materials, such as carrageenan, ulvan, fucoidan, and agarose. Impression material [Figure 1c] must pass the following tests such as hardness, tear test, setting time, thickness, dimensional changes, solubility, and weight changes before it is useful in dental applications [10].

2.5. Bioink Development for 3D Printing

3D printing is an emerging field in the medical sector, especially in dental and oral surgery [61]. There are many synthetic polymers widely used for 3D printing [62,63]. Due to their cytotoxicity and biocompatibility issues with humans, those polymers are now used at a minimal level. Now, bioink development using natural biopolymers shows promising advantages in this field [64-66]. Bioink is naturally derived, and it is compatible in nature without causing toxicity to human cells [Figure 2]. Seaweed biopolymers, especially alginate and carrageenan, are already existing bioinks [67,68]. Due to versatile chemical properties and easy blending with other materials, seaweed biopolymers can be used as a better source for bioink development. Seaweed-based biopolymers also possess good rheological properties [28] and are emerging as a new avenue in 3D printing technology in the dental domain [69]. In the dental field, dentin-derived bioink development shows promising results in 3D printing technology. It is also helpful in craniofacial tissue engineering applications [70-72]. Currently, polymers/biopolymers are used in creating anatomical 3D models, guides, and, scaffolds/membrane for bone defects in oral and maxillofacial surgery, 3D printed dentures and prosthesis in prosthodontics, 3D printed dental models and clear aligners in orthodontics, computed tomography-based endodontic guides for root canal treatments, 3D printed scaffolds in periodontics [73].

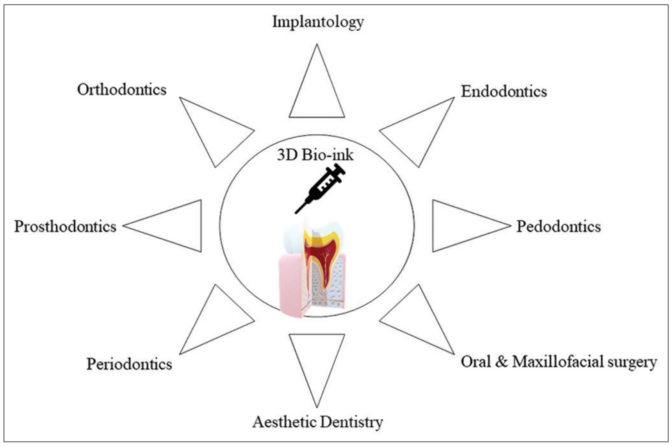

Figure 2: Bioink development using seaweed-derived biopolymer and its applications in the dental field.

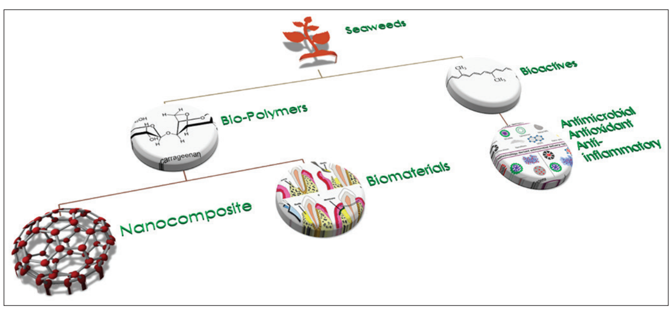

Figure 3: Schematic representation of the overview of seaweed use in the medical field.

3. BIOPOLYMERS COMPOSITES

A biopolymer composite refers to a combination or mixture of supporting materials to form a final material for various or specific applications [74]. A composite may be a nanoparticle, different polymers, synthetic polymers, compatible polymers, cross-linking agents, plasticizers, and antimicrobial or antioxidant agents. Most of the polymers used for dental applications are polylactic acid (PLA), poly lactic-*co*-glycolic acid (PLGA), polycaprolactone (PCL), glycidyl methacrylate, methyl methacrylate, and others [75-82]. However, these materials are somehow toxic to the patient and the environment once disposed of. Different composite materials have been developed over the past decade with the help of nanoparticles, but seaweed nanocomposites are emerging in different biomedical and dental applications [Figures 3 and 4]. Different bionanocomposites are made using carrageenan biopolymer blended with ZnO, SiO_2, hydroxyapatite, TiO_2, CuO nanoparticles [83], alginate-carrageenan combination blended with green synthesized nanoparticles, fucoidan-based nanoparticles fused with another natural biopolymer, etc. [84-88]. These bionanocomposites are biocompatible, and also showing activities such as antimicrobial, antioxidant and anti-inflammatory properties. Some nanocomposites are even non-toxic to blood cells possessing anti-coagulant properties with hemocompatibility. Some bionanocomposites are less cytotoxicity in cell lines proved using *in vitro* MTT assay [38,89-92].

Table 1: Seaweed biopolymers in dental applications.

Seaweeds	Biopolymers	Dental applications	References
Red seaweeds			
Kappaphycus sp., *Gracilaria* sp., *Gelidium* sp.	Agar, Carrageenan (Kappa, Lambda, Iota)	Hydrogels, Oral drug delivery, Scaffolds, Biomembrane, Anti-microbial activity medium, Nanoparticles coatings, Bionanocomposites, Bone tissue engineering, Nanofibers, 3D printing (bioink)	[23,27,67,68,93-105]
Brown seaweeds			
Laminaria sp., *Ascophyllum* sp., *Sargassum* sp., *Fucus* sp., *Turbinaria* sp.	Alginic acid and alginate, Sodium alginate, Fucoidan	Impression plaster, Wound healing/dressing for oral cavity/drug delivery, Hydrogels, Scaffolds, Biomembrane, GTR, GBR, Adhesives/resins, 3D printing bioink, Nanoparticles coatings, Bone tissue engineering, Nanocomposites, Nanofibers	[106-114]
Green seaweeds			
Ulva sp.	Ulvan, Cellulose	Hydrogels, Scaffolds, Biomembrane, Nanocomposites, Nanofibers	[31,115-116]

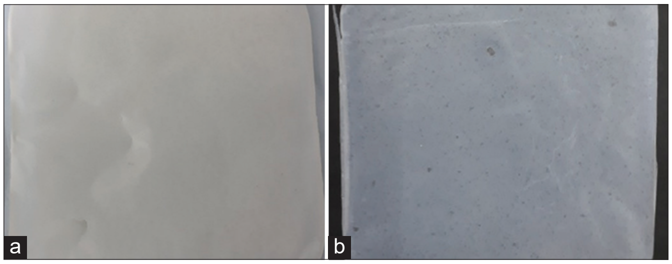

Figure 4: Bionanocomposite membrane films developed using seaweed biopolymers such as (a) alginate and (b) carrageenan.

4. CONCLUSION

Seaweed-derived biopolymers are widely used in a variety of industries. However, their use in dentistry is significantly less. Alginates have been utilized for creating dental impressions for a very long time. Other biopolymers found in seaweeds are still in the research stage in the dental industry. A developing field and biopolymer-based 3D printing technology-based biomaterials with desired qualities through the development of bioink formulation helps in dental domain material research. There is still a scope for improvement in the production of nanofibers, particularly from seaweed biopolymers. The use of seaweed biopolymers is not without its problems. This might be due to the polymer extraction procedure, its associated costs, and the durability of the current biopolymer materials being developed. However, soon, these challenges will be overcome with the aid of nanoparticles and composite designs, leading to the development of new biopolymeric materials with superior biocompatibility for dental use.

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6. AUTHORS' CONTRIBUTIONS

M.P. Sudhakar: Conceptualization, Writing – Original Draft, Formal analysis, and Investigation;

V. Deepak Nallasamy: Visualization, Supervision, and Project administration; G. Dharani: Supervision, Drafting, and Language correction; and Alejandro H. Buschmann: Language correction, Drafting, and Analysis

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8. CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

9. ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

10. DATA AVAILABILITY

All the data is available with the authors and shall be provided upon request.

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