Marine Biopolymer Alginate in Endodontics

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Alginate is a natural marine biopolymer that has been widely used in biomedical applications, but research on its use as an endodontic material is still sparse in the literature. Alginate or salt of alginic acid is one of the most abundant biopolymeric hydrocolloids derived primarily from seaweeds. In dentistry, hydrocolloid alginate has been commonly employed as a dental impression material to make gypsum casts for various treatment purposes, including provisional crowns and bridges, orthodontic study models, mouth guards, bleaching trays, and removable dental prostheses.

alginate | biomaterial | biopolymer | drug delivery system | hydrogel | polysaccharide | regenerative dentistry

1. Introduction

A biomaterial is any natural or synthetic material that makes up all or part of a living structure or biomedical device that performs, enhances, or substitutes a natural function [1]. Biomaterials have historically been meant to be inert and do not interact with the host's biological processes [2]. Natural resources have a long history as biomaterials and have been used to replace tissues lost due to disease or injury [3]. Dental biomaterials are natural tissues and biocompatible synthetic materials that can restore decayed, injured, or fractured tooth tissue. In restorative dentistry, biomaterial research has evolved towards regenerative (resorbable) or bioinert (biostable) materials to enhance material adherence, promote faster healing, and enable rapid tissue regeneration [4][5][6].

Alginate or salt of alginic acid is one of the most abundant biopolymeric hydrocolloids derived primarily from seaweeds [2][7]. Alginate constitutes blocks of (1–4)-linked β-D-mannuronic acid (M) and α-L-guluronic acid (G) monomers that are composed of three different polymer segments [8]. It can form hydrogel by participating in intermolecular cross-linking with divalent cations such as calcium ion (Ca^{2+}). In addition, alginate has piqued the interest of many researchers because of its biocompatibility, low cost, acceptable smell and taste, simplicity of handling, low toxicity, and mild gelation properties [9]. The structural resemblance of alginate hydrogel to the extracellular matrix of living tissues allows for a wide range of applications of this bio-polysaccharide in wound healing, cell transplantation, and tissue engineering or regeneration [2]. Another benefit of alginate is its capability to hydrate and form gel, allowing specific medicaments or active substances to be administered for longer periods at the site of interest, thus acting as controlled-release drug delivery systems [2][4][7].

In dentistry, hydrocolloid alginate has been commonly employed as a dental impression material to make gypsum casts for various treatment purposes, including provisional crowns and bridges, orthodontic study models, mouth guards, bleaching trays, and removable dental prostheses [7][9]. Endodontics is a discipline of dentistry that focuses on the diagnosis and treatment of inflamed and infected dental pulp tissues [10]. Undoubtedly, dental caries or tooth decay continues to be a key contributing factor to the need for endodontic treatment [11]. Along with the declining rate of tooth loss, this highlights the significance of continuously improving biomaterials used in endodontic applications, such as pulp therapies, irrigating solution, intracanal medicaments, obturation, and pulpal regeneration [11]. Moreover, researchers have been intrigued by incorporating alginate into the field of endodontics due to its remarkable features [4][12]. For instance, alginate has been introduced as a regenerative scaffold because of its semi-permeable characteristic that allows cells to adhere, proliferate, and differentiate [13][14]. The sol–gel transition ability of alginate as endodontic biomaterial also permits it to be fabricated as preformed or injectable scaffolds that match the root canal system's complicated architecture [5].

2. Role of Alginate in Regenerative Endodontics

Bhoj M et al. [5] produced an alginate-based microenvironment that mimics the shape of gutta-percha and expresses the internal cellular and molecular conditions necessary for pulp tissue regeneration. Arginine–glycine–aspartate (RGD) alginate was used to encapsulate human umbilical vascular endothelial cells and dental pulp stem cells with retained growth factors. The study noted an increased proliferation of dental pulp stem cells and human umbilical vein endothelial cells signifying an excellent regenerative effect. Similarly, Devillard R et al. [13] created a biological scaffold made of alginate–collagen to serve as a biological gutta-percha for regenerative endodontic treatment. Human apical papilla stem cells were able to disperse, survive, proliferate, and differentiate into osteoblast-like cells with calcified osseous extracellular matrix on this alginate–collagen scaffold, providing an excellent root canal healing environment.

Alginate is often used as a component in many 3D-printed scaffolds due to its quick gelation characteristics and good mixing properties with other biopolymers. To encapsulate stem cells from the apical papilla, Athirasala A et al. [14] developed a hybrid 3D bio-ink hydrogel containing 3% *w*/*v* alginate that resulted in an upward tendency of cell survival over time. Such a finding corroborates with that of Yu H et al. [12], who revealed that 3D-printed alginate–gelatine scaffolds show increased cell growth and adhesion while also containing more calcium and phosphorus ions, which are favourable to cell proliferation. Moreover, Zhang R et al. [15] developed a new injectable hydrogel microsphere that can encapsulate human dental pulp stem cells and vascular endothelial growth factor by combining an arginine–glycine–aspartate–alginate (RGD-alginate) solution with different concentrations of laponite. Pure alginate was found to demonstrate the least degree of degradation with cell survival rates in RGD-alginate microspheres exceeding 90%. A similar study was conducted by Liang et al. [16] in fabricating gelatine methacryloyl–alginate core-shell microcapsules for endodontic regeneration that co-encapsulate human dental pulp stem cells and human umbilical vein endothelial cells. The results indicated that human umbilical vein endothelial cells and human dental pulp stem cells microcapsules showed greater cell proliferation rates with the formation of capillary- and odontogenic-like networks, respectively. Additionally, pre-vascularized microtissues developed in these microcapsules, containing a high content of extracellular matrix deposition. In vivo experiments also revealed that pulp-like tissue regeneration and improved microvessel creation occurred in these microcapsules.

Nonetheless, these findings contradict those of Matsumoto N et al. [17], suggesting that biomarkers transforming growth factor (TGF-1) and bone morphogenic protein-2 (BMP-2) rose significantly with remarkable healing responses when in vivo rats with apical periodontitis were treated with Emdogain (enamel matrix derivative) as compared to Propylene Glycol Alginate (PGA), a marine hydrogel-based polysaccharide. Meanwhile, Lambricht L et al. [18] examined the viability and metabolic activity of apical papilla stem cells with various compositions of alginate and commercial hyaluronic-based hydrogels. Although the overall number of cells in alginate hydrogels remained consistent, the number of living cells decreased, with hyaluronic-based hydrogels demonstrating the highest number of cells that survived. On the other hand, researchers have also attempted to use alginate-based material as cell blocks for tooth dentine regeneration [19]. Lai WY et al. [19] developed cell blocks that are made of stem cells from human dental pulp loaded with alginate/fish gelatine hydrogels as the core, along with human umbilical vascular endothelial cells loaded with silicone ion-infused fish gelatine methacrylate as the cell block's periphery. The findings confirmed that the capacity to release Si ions enhanced mimicking of the environment, increased expressions and secretions of angiogenesis-related markers, and boosted expression of odontogenic-related markers, making it appropriate for endodontic regeneration.

3. Role of Alginate as Intracanal Medicament Carrier

Chlorhexidine (CHX) is a well-known chemical substance that is commonly used as a root canal irrigating agent or intracanal medicament during endodontic therapy to disinfect and clean the root canal system. Evelyna A et al. [20] produced nanocellulose–alginate nanocomposites to encapsulate CHX and discovered that the CHX release rate was considerably greater in the infected root canal environment with the aid of these nanocomposites. Nurdin D et al. [17] carried out a similar work in which they synthesised silica microcapsules to encapsulate 2% CHX and then coated them with chitosan and sodium alginate. The study revealed that the microcapsules and CHX formed a bond that facilitated the release of CHX with the highest value noted at a pH of 5.5.

4. Role of Alginate as Root Canal Filling Material

One of the cornerstones of effective endodontic treatment is to seal the root canal system with bioinert gutta-percha and sealer. Huang G et al. [6] reported that incorporating 1% sodium alginate into the liquid component of a novel bioactive glass-based root canal sealer resulted in satisfactory flowability, thickness, setting time, solubility, and a uniform morphology that is indicative of clinical endodontic usage. It also demonstrated acceptable sealing ability, as well as minimal cytotoxicity and excellent biocompatibility.

5. Role of Alginate as Reinforcement Material in a Chelating Agent

Chelating agents are used in endodontic procedures to help prepare calcified and narrow root canals by chemically softening the root canal dentinal structures and dissolving the smear layer. Girard S et al. [21] developed a new experimental root canal chelating agent that included 2% alginate, 3% aerosol, 10% Tween 80, and 18% Heme binding protein (HEBP) and compared it with commercialised chelating agents. The experimental chelating agent with alginate reinforcement had no effect on free residual chlorine in the hypochlorite solution and showed improved chelating properties with a considerable reduction in smear layers in the coronal and middle root sections.

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