Nat. Volatiles & Essent. Oils, 2021; 8(4): 15602-15608

NVEO
Natural Volatiles &
Essential Oils

Beta Glucans As Potential Scaffold For Periodontal Regeneration – A Review

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ABSTRACT:

The periodontium is an integrated, functional unit of multiple tissues surrounding and supporting the tooth. Periodontal tissues can be destructed by chronic periodontal disease, which can lead to tooth loss. In support of the treatment for periodontally diseased tooth, various biomaterials have been applied starting as a contact inhibition membrane in the guided tissue regeneration that is the current gold standard in dental clinic. Recently, various biomaterials have been used in tissue engineering as a scaffold to facilitate the regeneration of damaged periodontal tissues. This review article elicits about the beta glucans as potential scaffold for periodontal regeneration.

INTRODUCTION:

The ultimate purpose of periodontal treatment is to regenerate periodontal tissues in harmony, whereby cementum, periodontal ligament, and alveolar bone are formed simultaneously in their right positions.[1]. Periodontitis is initiated by bacterial infection and involves increased infiltration of neutrophil and macrophages, activation of osteoclasts via RANKL signaling, followed by bone resorption [2]. The current clinical practices include a non-surgical, conservative treatment for removing the etiology of periodontitis (e.g. dental plaque and calculus) and surgical procedures performed to reduce periodontal pocket depth. However, the form of healing by these techniques is

frequently by the long junctional epithelium. To obtain a desirable outcome, regeneration of periodontal tissue should be characterized by the formation of cementum, periodontal ligament (PDL), alveolar bone and gingiva. Studies have proven that regeneration is a better outcome compared to repair of the periodontal structures [3].Guided tissue regeneration (GTR) is the best documented regenerative technique that utilizes a barrier membrane to promote the selective repopulation of the periodontal defect by cells derived from the remaining periodontal ligament [6]. Although histologically regeneration can be achieved in selected cases [7], the clinical outcomes are generally unpredictable [8].Challenges are faced by clinicians in achieving regeneration of the lost periodontal structures because there is loss of all three tissues like cementum, periodontal ligament and alveolar bone which are unique in their function and origin. The reconstruction of just a single tissue will not satisfy the healing process of the disease but requires the involvement of all the three tissues for regeneration [16].In recent years, tissue engineering, a new advancement in periodontal regeneration has been introduced for the complete regeneration of lost tissues [17]. Tissue engineering is the replacement of reconstructed living tissues in the place of lost or damaged tissues and is developed on the principles of cell biology, developmental biology and biomaterial sciences [18]. The tissue engineering involves a triad which includes cells, signalling molecules and scaffold matrices. The scaffold acts as a compartment for holding cells and enables attachment, migration, proliferation and three- dimensional structural organisation of the cells . In addition, it also guides the three dimensional (3D) arrangement of the cell population. Scaffolds act as a vehicle three dimensionally to assist the above processes for tissue regeneration. Polymeric scaffolds are a porous and biodegradable material that has been customised to form sheets, films, fibers and gels [19]. Recently, more advanced scaffold systems have been developed to guide integrated regeneration of periodontium. These scaffolds are designed to deliver bioactive cues for periodontal regeneration and to undergo degradation which is to be replaced by new tissues [01]. To date, many materials have predominantly been used to create biodegradable scaffolds, comprising polymers with the synthetic origin such as poly(α-hydroxy esters) including poly caprolactone (PCL), polyglycolic acid (PGA), polylactic acid (PLA), and their copolymer poly(glycolic acid) (PLGA); poly(ethers) containing poly(ethylene oxide) (PEO) and poly(ethylene glycol) (PEG), polyvinyl alcohol (PVA), polyurethane (PU), etc. In addition, naturally occurring biomaterials like polypeptides and polysaccharides are also studied [24].Polysaccharides are widely used with this purpose because they are non-toxic, biocompatible, biodegradable and are obtained from renewable sources in nature. In this context, β-glucans are a good option, since they are able to create a hydrogel easily by thermal changes. β-glucans are groups of dietary fibers or polysaccharides composed of D-glucose monomers, linked by 1,3; 1,4 or 1,6 β-glycosidic bonds, and are naturally found in the cell wall of bacteria, fungi, algae, and higher crops, such as cereals [22]. They offer some interesting biological properties, such as the ability to improve wound healing or modulate the immune system, and their anti-inflammatory and anti-bacterial properties, that increase their potential in medical and pharmaceutical applications [24]. However, in spite of the biocompatibility and various physiological activities of beta-glucan, there are limited research in which a support for tissue engineering has been developed or studied using beta-glucan. This review focusses on the role of β-glucans as potential scaffold material for periodontal regeneration.

Background of Tissue engineering approach for periodontal regeneration

The term 'Tissue Engineering' was framed by Langer and Vacanti in 1993 [26]. Tissue engineering is surfacing as a potential solution to replace the damaged or lost tissues by implanting natural,

synthetic or semi-synthetic tissues which gains function from the start orgrows into functionality [12]. The periodontal healing is a complex process which involves cells of five or more tissue types which includes the epithelium, gingival connective tissue, periodontal connective tissue, cementum and the alveolar bone to have a new connection with the nonvascular hard tissues [27]. Healing of these tissues must happen under a significant bacterial load and rendered to this complexity is the action of occlusal forces in the transverse and axial planes which affects the pattern of wound healing by disrupting the periodontal tissue resorbing horizontally. Hence without the introduction of the triad theory (Figure 1) [12] it may be difficult to overcome these limitations.

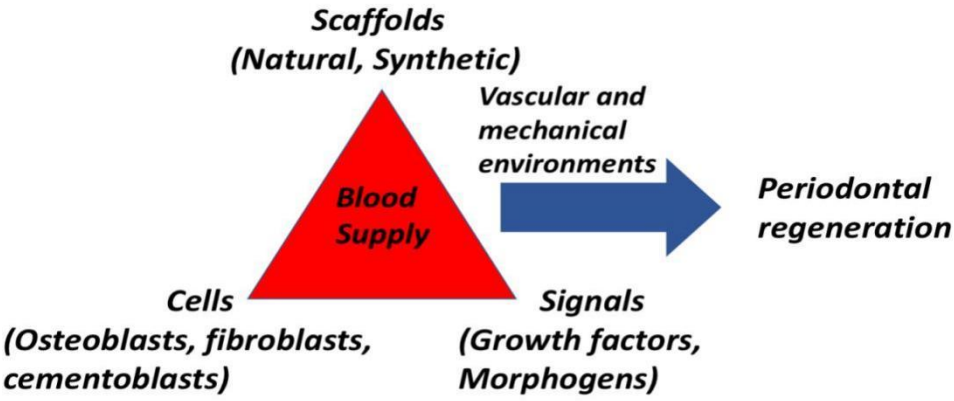

Figure 1: Tissue engineering triad

Role of scaffolds in Tissue engineering

The term "scaffold" refers to an artificial temporary platform applied to support, repair, or to enhance the performance of a structure. This can be done on different size and length scales, with various methods of support depending on the form and use. Biocompatibility, biodegradability, mechanical characteristics, pore size, porosity, osteoinductivity, osteoconductivity, osteogenesis, and osteointegration are the key design considerations for the scaffold [29]. Some of the essentials of scaffolds used in tissue engineering are illustrated in Figure 2 [20].

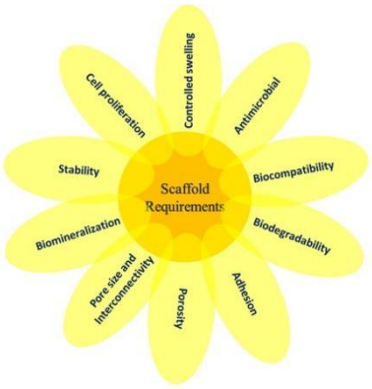

Figure 2: The essential variables involved in scaffold desiign for TE. [20]

Scaffolds used for the regeneration of periodontal tissues can provide a contact guidance that enables timely migration of cells into periodontal defects, followed by promoted regeneration [28]. Given the complexity of the periodontal tissue architecture and the need for a precisely coordinated

wound healing response, the use of advanced scaffold designs that are able to guide the spatiotemporal requirements for periodontal regeneration has the potential to significantly improve therapeutic outcomes. The use of such scaffolds could be complementary to current clinical procedures such as GTR and the use of bioactive molecules, and have the ability to be combined with cell- based approaches [3]. To further facilitate cell migration and tissue ingrowth, various bioactive cues including growth factors (GFs) and cytokines have also been delivered with the scaffolds.

Natural Biopolymer-Based Scaffolds

Natural biopolymers have resurged over the past few decades as primary bioactive substances used in the applications of medical materials. Based on their monomeric units and structure, biopolymers are categorized roughly into three classes: [30]

- Polypeptide- and protein-based: collagen, fibrin, fibrinogen, gelatin, silk, elastin, myosin, keratin, and actin.
- Polysaccharide-based: chitin, chitosan, alginate, hyaluronic acid, cellulose, agarose, dextran, and glycosaminoglycans.
- Polynucleotide-based: DNA, linear plasmid DNA, and RNA.

Natural polymers make important contributions to tissue engineering, especially in the manufacture of scaffolds for therapeutic agent delivery. Novel and natural polymeric materials are aimed at enhancing different therapies due to their inherent bioactivity, biocompatibility, and bioresorbability [31]. Naturally derived polymers including collagen, chitin, chitosan, gelatin, silkfibroin, soybean, fibrinogen (Fbg), fibrin (Fbn), elastin, proteoglycan, hyaluronan, and laminin have displayed great potential in the biomedical sector [20].

β-Glucans As Scaffold

Natural polysaccharides are abundant in nature which are useful in many applications due to their unique properties. One of the most predominant class of polysaccharides is the β-glucans which are carbohydrate polymers that are found in the cell walls of many organisms such as bacteria, fungi, yeasts and some cereals like barley and oat[32]. All β-glucans comprises of glucose polymer linked by 1-3 linear glycosidic chain core of varying length and branching structures. These branches that are derived from the glycosidic chain core are highly different with two main group of branching such as 1-4 or 1-6 glycosidic chains[33]. Also, different types of β-glucans exhibit distinct molecular weight, solubility and viscosity causing diverse physiological functions. It is also most known for its powerful immune stimulant, antagonist effect on benign and malignant tumors, antimicrobial properties and lowering blood pressure or cholesterol levels [22]. Beta-glucan enhances the production of growth factors and promotes collagen biosynthesis [34]. β-glucan have a broad spectrum of effects on different cell types that can evident their proficiency on wound healing[07]. The ability of β-glucan to stimulate wound healing was first described by Leibovich and Danon in 1980[35], who observed faster re-epithelialisation and increased macrophage activity and fewer polymorphonuclear neutrophils in the wound bed during inflammatory stage of repair. Curdlan; 1,3-β-glucan, a linear polysaccharide first observed in bacteria and able to be sourced biologically is biocompatible and has been approved for human use by the American Food and Drug Administration (FDA). Its commercially accessible version is produced by Alcaligenes faecalis [36] .In the field of bone regeneration, curdlan is

a particularly interesting material as it enhances bone growth by helping mesenchymal stem cell adhesion onto the scaffold and by favouring their differentiation into osteoblasts [37] . It also has an inhibiting effect on osteoclastogenesis through its interaction with the dectin-1 receptor leading to a further increase in the speed of the regeneration of bone tissue [38]. Przekora et al. studied the properties of a scaffold composed of bacterial 1,3-β-glucan (curdlan) with chitosan drying the hydrogels. They found out that the addition of β-glucan to hydroxyapatite increased the elasticity and water uptake capacity of the scaffold, suggesting a better adaptation into the implant site, although mechanical strength was decreased [37]. Toullec et al., used curdlan-chitosan electrospun fibers as scaffold for bone regeneration and demonstrated that curdlan expressed immunomodulatory properties by enhancing cell migration and these electrospun curdlan-chitosan scaffolds show great potential for bone tissue engineering [4]. In another study by M. Salgado et al., β-glucans derived from barley and yeast were used as raw materials to create hydrogels due to their easy gelation and biological properties and assessed the ability of these materials to sustainably deliver dexamethasone. They concluded that the scaffolds had good morphology and provided a controlled release, thus being suitable to be used as scaffolds and drug delivery vehicles [25]. Song et al., developed a beta-glucan based scaffold for biological tissue engineering using radiation fusion technology. They concluded that the beta-glucan based scaffold (extracted from Schizophyllum commune (schizophylan)) can be successfully employed as a filler for tissue regeneration, cell culturing and plastic surgery, as a filler for voids in biological tisue,as a scaffold for reconstructive and corrective plastic surgery, and for cell transplantation and drug delivery [39].

CONCLUSION

The natural biopolymers possesses exclusive features in terms of biophysical and biochemical characteristics such as biocompatibility, biodegradability, more body fluid adsorption capacity, more gel forming ability, non-toxic, non-immunogenic properties, along with antifungal, antibacterial, and antitumor properties. This made the biopolymers as a promising candidate for application in tissue engineering and some other health care applications [21]. The antitumor, antigenotoxic, antimutagenic and/or antioxidative effects of β-glucans have been widely studied using in vitro and animal-based in vivo studies, but human-based clinical trials are rarely reported. The medical significance and effectiveness of β-glucans, as antimicrobial, anticancer, anti-diabetic and anti-hyperchloresterolemic polysaccharides, have been reviewed. Various in vivo and in vitro studies discussed are evident to confirm the wound healing activity of beta- glucans from various sources. Also the β-glucans induces the proliferation and migration of keratinocytes and fibroblasts through specific receptors such as Dectin-1, CR3 or TLRs. These data also confirmed that β-glucans directly or indirectly modulate the activity of diverse cells and growth factors that are central to the reparative process. However, systematic study of the clinical and physiological significance of β-glucans is scarce [22] . Thus research has to be done in this direction, focusing on the potential of β-glucans as scaffold material for periodontal regeneration.

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