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# Scaffolds in Periodontal Regeneration

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

The periodontium is a well-designed central core made up of numerous tissues that surround and support the tooth. Sustained periodontitis has the ability to create havoc on periodontal tissues, leading to tooth loss. Diverse biomaterials are used as obstacle layers in the coordinated-tissue-recuperation (GTR), which at present is the highest quality level under the dentistry community, to treat periodontally weak teeth. Unique biomaterials have recently been structured in a tissue planning stage to aid in the recovery of injured periodontal tissues. In recent decades, innovations in stage manufacture have ranged from a genuine substrate to aid in the recovery of a specific kind of periodontal tissue to a multiphase/bioactive stage structure to coordinate a coordinated periodontal tissue recovery. This article discusses the new sorts of phrases that are being developed for periodontal tissue recovery.

*Keywords: Cementum; gingival; periodontal ligament; periodontal; periodontium; periodontitis; regeneration; scaffolds, syndrome torrent.*

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## 1. INTRODUCTION

Oral diseases are the most common cause of periodontal disease. If the periodontal ligament, cementum, alveolar bone, and gingiva are not treated, microscopic organisms that cause aggravation could spread and ruin them. Periodontitis is diagnosed when x-rays reveal Alveolar bone destruction is a condition under which the alveolar bone is eliminated, and it is usually believed to be an irreversible condition. Gingivitis is non-medication-required chronic gum disease. As a result, gingival recession is frequently connected with functional and cosmetic issues such as root caries and black triangles. In addition to cosmetic and functional concerns, periodontitis is associated with systemic illnesses including congestive heart failure, diabetes, respiratory disease, etc [1]. As a result, gingivitis is becoming a serious general public health problem in which finding effective periodontal therapies should be a key focus for health researchers. The frequency of mild to moderate periodontitis was highest in the urban population (21.7%). (CI: 16.3-27.5). Females exhibited a lower frequency of periodontitis (33.4%) than males (43.2%).

As per by the National Health & Nutrition Examination Survey (NHANES), nearby 7.9% of grown people (ages 18 to 62) and 18.6% of seniors (ages 60-70) in the United States have Periodontitis, while tooth caries affects 39% of children (ages 3 to 9) in their baby tooth and 60% of growing people (ages 11 to 21) in there fix the tooth. Two disorders continue to be a major public health issue that requires more effective preventive and management techniques [2].

## 2. OBJECTIVE OF PERIODONTAL REGENERATION VIA BIOMATERIAL SCAFFOLDS

### 2.1 Ancient Legacy of Periodontal Regeneration

The focusing aim for therapy in periodontitis is to recreate periodontal tissues that work together, in which cementum, PDL, and AB fibers aligned longitudinally between CM and AB and CM, PDL, and AB are created synchronously in their proper places. The bacterial infection causes periodontitis, which seems characterized by increased neutrophil and macrophage infiltration, osteoclast activation via RANKL signaling, and bone resorption [3]. Plaque and calculus on the teeth increase the risk of bacterial infection and periodontitis by creating a space between the teeth and the periodontium [4]. Non-surgical, conservative therapy that addresses the causes of gingivitis (e.g, calculus and dental plaque).

Tissue engineering technologies for periodontal regeneration have lately been studied as a novel way to overcome such limitations [5]. GTR can be used with a variety of biomaterial scaffolds that include cells and/or bioactive. More improved scaffold technologies for guiding integrated periodontal regeneration have recently been developed [6]. Until they degrade and are replaced by new tissues, these scaffolds are meant to offer bioactive indicators for periodontal regeneration.

### 2.2 Scaffolds to Aid in Periodontal Wound Repair

In tissue engineering, scaffolds are utilised to create a platform for cell adhesion, tissue ingrowth, and early structural support [7]. Non-degradable or degradable membranes impede epithelium formation in GTR, enabling periodontal connective tissue and PDL to heal slowly (4–6 weeks) [8]. A long period of periodontitis, on the other hand, may aggravate the result of GTR by decreasing PDL cell repairability, hindering the host immunity, or significantly denaturalizing the cememtum [9]. Periodontal tissue regeneration scaffolds may provide contact guidance, allowing cells to move more quickly into periodontal abnormalities and speed up periodontal tissue regeneration scaffolds [10].

Scaffold systems have proved to offer a lot of promise for periodontal regeneration. The current technological advancement in micro precise regional under scaffold designing is marked as an essential step toward integrated multi tissue periodontium regeneration. There are numerous scaffolds and delivery systems used to regenerate integrated periodontium.

### 2.3 Scaffolds for Periodontal Regeneration have an Antimicrobial Impact

Bacteria are the significant cause of periodontitis, and the ailment is triggered by the host's defensive resistance to them [11]. Despite the fact that modern periodontal therapy involves eliminating dental biofilm and calculation, which

are the main sources as well as niches of microbes that produce clinical indicators, periodontitis reoccurrence is tightly tied to maintenance to avoid secondary infection [12]. Current periodontal treatments provide a risk of bacterial re-infection. As a result, antimicrobial activity has been included in various scaffolds meant to improve periodontal regeneration while also lowering the likelihood of re-infection following periodontal treatment. Antibacterial material components have been incorporated into scaffold materials in a simple and straightforward manner. Chitosan is a bio-adhesive, antifungal, antibacterial, and hemostatic polymer generated from natural seashells [13].

### 2.4 Scaffolds for Periodontal Regeneration with Anti-inflammatory Characteristics

Periodontitis is a multifaceted inflammatory condition, an illness that causes the periodontium to deteriorate over time [14]. Despite the fact that bacterial infection appears to be the primary cause of periodontitis, Periodontitis is triggered by an overactive immunological response from the host and/or an absence of inflammation resolution. As a result, pharmacological medications which include NSAIDS medicines which are used to try to reduce inflammation [15]. Treatments that target just proinflammatory pathways and /or signaling without addressing causative factors, on the other hand, have minimal benefits [16]. Only as a supplement are they used. The removal of the causative causes (such as dental biofilm as well as calculus), the initial stage in periodontal treatment is to remove inflammatory granulation tissue.

## 3. BIOMATERIALS FOR PERIODONTAL REGENERATION SCAFFOLD (TOTAL A1)

### 3.1 Natural Materials

Cell affinity and biocompatibility are often high in natural biomaterials. They are less toxic and elicit inflammatory and immunological reactions less frequently. As a result, natural biomaterials have become popular as periodontal tissue regeneration scaffolds [17]. By its immunogenicity, biodegradability, biocompatibility, biodegradability, and anti-bacterial capability as opposed to fungus and bacteria. chitosan has been frequently employed for periodontal regeneration [18]. Chitosan is typically combined with other scaffold materials which can provide antimicrobial action due to its drawbacks as standalone scaffold material, it includes particle aggregation as well as limited solubility [19].

### 3.2 Bioceramics

Bioceramic scaffolds are ideal for the regeneration of the periodontium because of their mechanical durability and biodegradability [20]. The key benefits of bio-ceramic-based scaffolds over all the other natural and synthetic materials are their excellent osteoconductive and osteoinductive properties [21]. Bioceramics can be used to treat periodontal disorders and come in a variety of forms, including granules, pastes, and injectables [22]. Bio-active glass, a popular bioceramic having high osteogenesis qualities that are often used for periodontal tissue regeneration, is another well-known bioceramic with high osteogenic capabilities [23].

### 3.3 Synthetic Polymers

To replace the non-resorbable PTFE membrane, synthetic polymers have been predominantly employed as 2$^{nd}$ Generation degradable membrane materials. Many polyester-based polymers have been employed as periodontal scaffold materials [24]. Synthetic polymers offer some advantages, including highly variable physio-chemical capabilities, variable biodegradation rates, and a low-cost, conventional manufacturing technology that enables mass production [25].

## 4. TISSUE ENGINEERING FOR PERIODONTAL REGENERATION RECENT PROGRESS

### 4.1 Scaffolds having Intelligence

Thanks to recent breakthroughs in polymer engineering, functional scaffolds have been constructed. Cell culture surface modification or polymer design can alter cell orientation and kind rhPDGF- BB [26]. was used to construct a 3D printed bioresorbable scaffold for periodontal regeneration. The treated area remained intact for 11 to 12 months after the therapy, according to the authors [27].

### 4.2 Scaffold-free Culture Technique

A spheroid culture strategy was devised for PDL-MSCs with improved osteogenic capacity, and

this technique may be effective for hard tissue regeneration [28]. Another study discovered that spheroid culture altered the expression of anti-inflammation and angiogenesis genes in PDLSCs. These alterations are thought to be linked to apoptosis signaling [29]. These data suggest that culture conditions affect the characteristics of PDL-MSCs.

### 4.3 Tissue-engineered Constructs that have been Decellularized

Decellularized materials have as of late been made for periodontal recovery. Chemical decellularization of HPDL cell sheet with DNase and NH4OH/Triton X-100 resulted in positive extracellular matrices are intact, and growth factors are accessible, which can lead to promoting allogeneic cell proliferate [30]. Before being implanted into rat periodontal insufficiency models [31]. The absence of essential cells in the decellularized construct aided attachment formation, implying that the construct itself aided periodontal regeneration. As a result, this product may be authorized to be acquired off the shelf [32].

## 5. FUTURE CYTOTHERAPY FOR PERIODONTAL REGENERATION:- A PERIODONTAL REGENERATION PERSPECTIVE

### 5.1 Cell Bank Establishment and Allogeneic Cell Sources

PDL-MSC sheets were found to be safe and feasible for therapeutic application in autologous transplantation research [33]. However, some of the strategy's flaws have become apparent. For starters, individuals without redundant teeth are unable to get this treatment due to a lack of a cell supply almost all older people seem to be missing wisdom teeth, that are most likely extracted when they were younger Cell growth and phenotypic differences between individuals are seen in certain patients with duplicated teeth. As a result, it's challenging to make things that are both reliable and stable [34]. This cellular design is produced from the tooth and takes four weeks to generate, making it an expensive technique. As a result, we made a decision to modify our opinions.

### 5.2 ES/ IPS Cells (Embryonic Stem/ Induced Pluripotent Stem)

Furthermore method to establish a cell bank is to IPS /ES cells, which are projected to reproduce indefinitely. Overexpression of 4 key factors of transcription is c-Myc, Sox2, Klf4, Oct4, and can be used to give rise to iPS cells from somatic cells that resemble ES cells. Despite the fact that the approach and methodology for producing PDL cells are unclear, a strategy for generating MSCs from ES/iPS cells utilizing neural crest cells has been created [35]. PDL cells are derived from dental follicle cells during development [36]. As a result, recognizing the economic growth from dental follicles to PDL tissues and cells is critical. MSC growth can be modified by the stiffness of cultureware, according to recent studies [37].

### 5.3 MSCs' Condition Medium

According to a recent study, MSCs generate and release proteins and extracellular vesicles into the culture medium, and conditioned media possesses regeneration potential. Nagataetal collected and condensed PDL-MSC conditioned media to mimic periodontal deficits in rats [38]. TNF mRNA levels were also lower in periodontal tissues treated with PDL-MSC conditioned medium. According to these findings, PDL-conditioned MSC's medium improved regeneration of the periodontitis by reducing inflammatory responses via TNF production. Although the specific mechanisms are unknown, current research suggests that in addition to proteins, conditioned media contains extracellular vesicles (EVs) that carry proteins, mRNAs, mi RNAs, and DNA. The EV fractions from the conditioned medium were the focus of our research [39].

## 6. CONCLUSION

The cell—scaffold interaction that might also occur when tissue-engineering technologies are adopted for regeneration of periodontitis was the center of this review. Biomaterial treatments can still be used in dental clinics thanks to recent innovations in periodontal regeneration technology**.** Whether stem cells are being used not, the biocompatible scaffold is another key technique in tissue engineering technology that has been embraced for the construction of new tissue [40]. Recent developments in the design and fabrication of excellent biomaterial scaffolds are a massive breakthrough in periodontal regeneration utilizing tissue engineering technologies. The periodontium is a complex multi-tissue structure, and its renewal is inextricably related to periodontitis' severe / chronic inflammation.

Several newer hydrogel-based delivery technologies also allowed for said timely and/or stimulation-sensitive release of numerous components that could be included under different scaffold architectures [41]. We spoke about the prospective periodontal cell- scaffold interactions, which might be a helpful technique for searching for the perfect scaffold. Many cellular and molecular processes involved in periodontal tissue healing systems have been discovered to date. These breakthroughs in knowledge might be the catalyst for a breakthrough in cell-based regeneration techniques in our profession. Rapid advances in material sciences and micro/nanofabrication technologies are also paving the door for novel tissue engineering approaches for "perfect" periodontal regeneration.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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