Growth Factor Enhanced Matrices in Periodontal Regeneration: A Literature Review

Abstract

Periodontitis is a chronic inflammatory disease that destroys the supporting structures of teeth, including the periodontal ligament, cementum, and alveolar bone. Conventional periodontal therapies primarily aim to control disease progression but often result in repair rather than true regeneration of lost periodontal tissues. The emergence of growth factor-enhanced matrices (GFEMs) has significantly advanced regenerative periodontology by combining biologically active signaling molecules with scaffold systems capable of controlled release and structural support.

This literature review evaluates the role of growth factor-enhanced matrices in periodontal regeneration from 2018 to 2026, with emphasis on their biological mechanisms, clinical applications, limitations, and future directions. Major growth factors used in regenerative therapy include platelet-derived growth factor (PDGF), bone morphogenetic proteins (BMPs), fibroblast growth factor-2 (FGF-2), enamel matrix derivatives (EMD), and platelet concentrates. Among currently available regenerative products, GEM 21S, which combines recombinant human platelet-derived growth factor-BB (rhPDGF-BB) with beta-tricalcium phosphate (β-TCP), remains one of the most extensively studied and clinically validated systems.

Growth factor-enhanced matrices have demonstrated significant clinical success in intrabony defects, furcation defects, gingival recession management, ridge preservation, sinus augmentation, peri-implant defect regeneration, and emerging applications in peri-implantitis reversal. Despite promising outcomes, challenges remain regarding high treatment costs, rapid degradation of growth factors, variability in scaffold performance, technique sensitivity, and limited long-term evidence.

Emerging regenerative strategies involving stem cells, exosome therapy, nanotechnology, gene-activated matrices, three-dimensional bioprinting, and artificial intelligence-based treatment planning may further improve the predictability of periodontal regeneration. Growth factor-enhanced matrices continue to represent a major advancement in regenerative dentistry and are expected to play an increasingly important role in preserving natural dentition and improving implant outcomes.

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Keywords

Periodontal regeneration; Growth factor enhanced matrices; GEM 21S; Recombinant human platelet-derived growth factor-BB; Periodontitis; Tissue engineering; Enamel matrix derivative; Bone morphogenetic proteins; Fibroblast growth factor; Peri-implantitis; Regenerative dentistry.

Introduction

Periodontitis is a chronic inflammatory disease characterized by progressive destruction of the supporting structures of teeth, including gingiva, periodontal ligament (PDL), cementum, and alveolar bone, ultimately resulting in tooth mobility and tooth loss if left untreated. Conventional periodontal therapy primarily focuses on eliminating etiologic factors and arresting disease progression through scaling and root planing, flap surgery, and osseous recontouring. Although these approaches successfully reduce inflammation, they often lead to healing by repair rather than true regeneration of the lost periodontal apparatus. True periodontal regeneration requires formation of new cementum, functionally oriented periodontal ligament fibers, and new alveolar bone on previously diseased root surfaces.[1]

Earlier regenerative approaches mainly relied on guided tissue regeneration (GTR), in which barrier membranes were used to exclude epithelial migration and allow selective repopulation of periodontal ligament cells. While GTR demonstrated success, complications such as membrane exposure, bacterial contamination, technique sensitivity, and inconsistent clinical outcomes limited its predictability.[2]

Advances in molecular biology and tissue engineering led to the development of biologically active regenerative materials. Growth factors regulate cellular migration, proliferation, differentiation, angiogenesis, and extracellular matrix synthesis during periodontal wound healing. However, direct application of isolated growth factors showed limited success due to rapid degradation and poor localization at defect sites. This led to the development of growth factor enhanced matrices (GFEMs), which combine bioactive molecules with scaffold systems capable of controlled release and structural support.[3]

These matrices represent a significant advancement in regenerative periodontology by integrating signaling molecules, scaffold biomaterials, and host cellular response. Current systems include platelet-derived growth factor matrices, enamel matrix derivatives, fibroblast growth factor systems, platelet concentrates, hydrogels, nanofiber scaffolds, and gene-activated biomaterials.[4]

Biological Basis of Periodontal Regeneration

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Periodontal wound healing involves highly coordinated interactions between inflammatory cells, fibroblasts, osteoblasts, cementoblasts, endothelial cells, and mesenchymal stem cells. Growth factors function as biological mediators that regulate these processes.[5]

Following periodontal surgery, platelets release several growth factors including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), insulin-like growth factor (IGF), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF). These factors stimulate chemotaxis of progenitor cells and initiate early wound healing.[6]

During the proliferative phase, fibroblasts synthesize collagen and extracellular matrix proteins while angiogenesis provides nutrition for newly forming tissues. Osteoblastic differentiation promotes alveolar bone regeneration, while cementogenesis and periodontal ligament formation are necessary for complete regeneration.[7]

A major challenge in regenerative therapy is maintaining therapeutic concentrations of growth factors at the defect site for sufficient periods. Matrix delivery systems help overcome this limitation by improving localization and controlled release.[8]

Platelet-Derived Growth Factor Enhanced Matrices

Platelet-derived growth factor remains one of the most extensively studied growth factors in periodontal regeneration because of its ability to stimulate fibroblast proliferation, angiogenesis, collagen synthesis, and osteoblastic activity.[9]

The most significant advancement in this category is GEM 21S, an FDA-approved regenerative product composed of recombinant human platelet-derived growth factor-BB (rhPDGF-BB) combined with beta-tricalcium phosphate (β-TCP).[10]

The β-TCP component acts as an osteoconductive scaffold that maintains space and gradually resorbs during bone regeneration, while rhPDGF-BB promotes migration and proliferation of periodontal ligament fibroblasts and osteogenic cells.[11]

Clinical studies have shown significant improvements in probing depth reduction, clinical attachment gain, and radiographic bone fill compared with conventional grafting techniques. Long-term studies have demonstrated stability of regenerated tissues.[12]

GEM 21S has also demonstrated promising results in ridge preservation, peri-implant defect regeneration, and treatment of peri-implantitis-associated bone loss.[13]

Enamel Matrix Derivative Systems

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102 Enamel matrix derivatives are composed primarily of amelogenin proteins that mimic natural
103 root development and stimulate cementogenesis and periodontal ligament regeneration.[14]

104 Emdogain remains one of the most widely used enamel matrix derivative products in
105 regenerative periodontology. It has demonstrated effectiveness in intrabony defects, furcation
106 defects, and root coverage procedures.[15]

107 Systematic reviews have consistently reported improvements in clinical attachment levels,
108 probing depth reduction, and radiographic defect fill.[16]

109

110 Bone Morphogenetic Protein Matrices

111 Bone morphogenetic proteins (BMPs) belong to the transforming growth factor-beta superfamily
112 and possess strong osteoinductive properties. BMP-2 and BMP-7 stimulate differentiation of
113 mesenchymal stem cells into osteoblasts and promote mineralized tissue formation.[17]

114 Despite successful applications in oral surgery, periodontal use remains limited because of risks
115 such as ankylosis, root resorption, and uncontrolled mineralization.[18]

116

117 Fibroblast Growth Factor Matrices

118 Fibroblast growth factor-2 (FGF-2) promotes angiogenesis, fibroblast proliferation, and
119 periodontal ligament regeneration. Clinical studies have shown improved bone fill and
120 attachment gain in intrabony defects.[19]

121 FGF-based regenerative therapies are becoming increasingly important in contemporary
122 periodontal treatment protocols.[20]

123

124 Platelet Concentrate Matrices

125 Autologous platelet concentrates such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF),
126 leukocyte-PRF, and concentrated growth factor matrices serve as natural reservoirs of growth
127 factors.[21]

128 These matrices release PDGF, VEGF, TGF-β, and IGF, thereby enhancing wound healing and
129 regeneration. Their autologous nature reduces immunological risks and lowers treatment
130 costs.[22]

131 However, lack of standardization in preparation protocols remains a major limitation.[23]

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Hydrogel and Nanotechnology-Based Matrices

Recent regenerative strategies focus on advanced biomaterials such as injectable hydrogels, nanofibers, and electrospun scaffolds.[24]

Hydrogels provide adaptability to irregular periodontal defects and permit controlled release of growth factors. Nanofibrous scaffolds mimic extracellular matrix architecture and improve cellular adhesion and proliferation.[25]

These technologies have shown promising preclinical and early clinical outcomes.[26]

Clinical Applications of Growth Factor Enhanced Matrices

Growth factor-enhanced matrices have broad applications in both periodontal and peri-implant regenerative therapy.[27]

Intrabony Defects

The most well-established use of GFEMs is in treatment of intrabony periodontal defects, where they improve clinical attachment gain, probing depth reduction, and radiographic bone fill.[28]

Furcation Defects

Class II furcation defects remain challenging due to complex anatomy. Growth factor matrices combined with grafts or membranes have shown improved regenerative outcomes.[16]

Gingival Recession Treatment

rhPDGF-BB has demonstrated improved root coverage, increased keratinized tissue width, and enhanced soft tissue healing in mucogingival procedures.[9]

Ridge Preservation

GEM 21S has been used in extraction socket preservation to reduce post-extraction bone loss and improve future implant placement outcomes.[12]

Sinus Augmentation

Growth factor-enhanced matrices have been used to improve bone maturation and implant stability in sinus lift procedures.[27]

Peri-Implant Bone Defects

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160 These matrices are increasingly used for regeneration of peri-implant osseous defects and
161 enhancement of osseointegration.[28]

162 **Peri-Implantitis Reversal**

163 One of the emerging applications of GEM 21S (Fig.1) is treatment of peri-implantitis-associated
164 bone loss. Following implant surface decontamination, rhPDGF-BB combined with β-TCP has
165 demonstrated improved bone fill, reduced probing depths, improved implant stability, and partial
166 reversal of peri-implant bone loss in selected contained defects. Although long-term evidence
167 remains limited, early clinical outcomes are promising.[28]

168

169
170 Fig.1 The commercial packaging of GEM 21S

171 ## Limitations

172 Despite promising outcomes, growth factor-enhanced matrices have several limitations. Rapid
173 degradation of growth factors may reduce therapeutic efficacy.[29]

174 Current scaffold systems may demonstrate poor degradation kinetics, inadequate mechanical
175 stability, or insufficient bioactivity.[30]

176 High treatment cost remains a major barrier, especially for recombinant products such as GEM
177 21S.[31]

178 Patient-related factors such as smoking, diabetes, poor plaque control, and unfavorable defect
179 morphology may compromise regenerative outcomes.[32]

180 Potential complications such as ankylosis, root resorption, and ectopic mineralization remain
181 concerns with BMPs.[33]

182 Long-term randomized controlled trials remain limited, and histologic confirmation of true
183 regeneration remains difficult.[34]

184

185 ## Future Directions

186 Future regenerative therapy is shifting toward personalized and biomimetic treatment
187 approaches. Stem cell-based therapies using periodontal ligament stem cells, dental pulp stem
188 cells, and bone marrow stem cells are being actively investigated.[35]

189 Exosome-based therapies may provide regenerative benefits without the limitations of stem cell
190 transplantation.[36]

191 Three-dimensional bioprinting may enable fabrication of customized scaffolds that precisely fit
192 periodontal defects.[37]

193 Nanotechnology may improve controlled release systems and tissue integration.[38]

194 Gene-activated matrices capable of prolonged local growth factor production represent another
195 promising innovation.[39]

196 Artificial intelligence may help predict regenerative outcomes and improve treatment planning.[40]

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Conclusion

Growth factor-enhanced matrices have revolutionized periodontal regeneration by combining biological signaling molecules with scaffold systems to improve regenerative outcomes.

Among currently available products, **GEM 21S** remains one of the most clinically validated systems and has expanded beyond traditional periodontal defects into peri-implant regenerative therapy and peri-implantitis management.

Enamel matrix derivatives, platelet concentrates, fibroblast growth factor systems, hydrogels, nanotechnology-based scaffolds, stem cells, and gene therapies continue to expand the future scope of regenerative periodontology.

Although limitations related to cost, biological instability, and technique sensitivity remain, ongoing advances may help achieve more predictable and complete regeneration of periodontal tissues.[41]

Ultimately, growth factor-enhanced matrices are expected to play a critical role in preserving natural dentition, enhancing implant success, and advancing personalized regenerative dentistry.

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