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RESEARCH ARTICLE

GROWTH FACTOR ENHANCED MATRICES IN PERIODONTAL REGENERATION: A LITERATURE REVIEW

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Abstract

Periodontitis is a chronic inflammatory disease that destroys the suppor ting 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 facto r-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, limitati ons, and future directions. Major growth factors used in regenerative therapy include platelet derived growth factor (PDGF), bone morphoge netic proteins (BMPs), fibroblast growth factor-2 (FGF-2), enamel matrix derivatives (EMD), and platelet concentrates. Among currently available regenerative products, GEM 21S, which combines recombina nt 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

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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.

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:-

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:-

Enamel matrix derivatives are composed primarily of amelogenin proteins that mimic natural root development and stimulate cementogenesis and periodontal ligament regeneration.[14] Emdogain remains one of the most widely used enamel matrix derivative products in regenerative periodontology. It has demonstrated effectiveness in intrabony defects, furcation defects, and root coverage procedures.[15] Systematic reviews have consistently reported improvements in clinical attachment levels, probing depth reduction, and radiographic defect fill.[16]

Bone Morphogenetic Protein Matrices:-
Bone morphogenetic proteins (BMPs) belong to the transforming growth factor-beta superfamily and possess strong osteoinductive properties. BMP-2 and BMP-7 stimulate differentiation of mesenchymal stem cells into osteoblasts and promote mineralized tissue formation.[17] Despite successful applications in oral surgery, periodontal use remains limited because of risks such as ankylosis, root resorption, and uncontrolled mineralization.[18]

Fibroblast Growth Factor Matrices:-
Fibroblast growth factor-2 (FGF-2) promotes angiogenesis, fibroblast proliferation, and periodontal ligament regeneration. Clinical studies have shown improved bone fill and attachment gain in intrabony defects.[19] FGF-based regenerative therapies are becoming increasingly important in contemporary periodontal treatment protocols.[20]

Platelet Concentrate Matrices:-
Autologous platelet concentrates such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), leukocyte-PRF, and concentrated growth factor matrices serve as natural reservoirs of growth factors.[21] These matrices release PDGF, VEGF, TGF-β, and IGF, thereby enhancing wound healing and regeneration. Their autologous nature reduces immunological risks and lowers treatment costs.[22] However, lack of standardization in preparation protocols remains a major limitation.[23]

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

Peri-Implantitis Reversal:-

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

Fig.1 The commercial packaging of GEM 21S

Limitations:-

Despite promising outcomes, growth factor-enhanced matrices have several limitations. Rapid degradation of growth factors may reduce therapeutic efficacy.[29] Current scaffold systems may demonstrate poor degradation kinetics, inadequate mechanical stability, or insufficient bioactivity.[30] High treatment cost remains a major barrier, especially for recombinant products such as GEM 21S.[31] Patient-related factors such as smoking, diabetes, poor plaque control, and unfavorable defect morphology may compromise regenerative outcomes.[32] Potential complications such as ankylosis, root resorption, and ectopic mineralization remain concerns with BMPs.[33]Long-term randomized controlled trials remain limited, and histologic confirmation of true regeneration remains difficult.[34]

Future Directions:-

Future regenerative therapy is shifting toward personalized and biomimetic treatment approaches. Stem cell-based therapies using periodontal ligament stem cells, dental pulp stem cells, and bone marrow stem cells are being actively investigated.[35] Exosome-based therapies may provide regenerative benefits without the limitations of stem cell transplantation.[36] Three-dimensional bioprinting may enable fabrication of customized scaffolds that precisely fit periodontal defects.[37] Nanotechnology may improve controlled release systems and tissue integration.[38] Gene-activated matrices capable of prolonged local growth factor production represent another promising innovation.[39] Artificial intelligence may help predict regenerative outcomes and improve treatment planning.[40]

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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