International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 11; Issue 02 (A); February 2022; Page No.219-224
DOI: http://dx.doi.org/10.24327/ijcar.2022.224.0049

Review article

CONTEMPORARY REGENERATIVE MATERIALS FROM PEPTIDES AND PLATELET-DERIVED GROWTH FACTOR

Suchetha Aghanashini., Reshmi V Nair*., Darshan Basavaraj Mundinamane., Sapna Nadiger., Apoorva Sokke Mallikarjunappa., Divya Bhat and Poojitha Kommana

Department of Periodontics, D A P M R V Dental College Bangalore

A R T I C L E I N F O

Article History:
Received 4th November, 2021
Received in revised form 25th December, 2021
Accepted 23rd January, 2022
Published online 28th February, 2022

Key words:
Bone grafts; Periodontal regeneration; Peptides; Osteoconduction

A B S T R A C T

Periodontal regeneration is the reproduction or reconstitution of a lost or injured part to restore the architecture and function of the periodontium. Various regenerative materials have been used in the treatment of periodontitis. Mostly used regenerative materials are bone grafts, PRF, PRP, etc. which have been demonstrated to have significant regenerative potential. Recently, regenerative materials are developed from peptides (PepGen P-15) and platelet-derived growth factor (GEM 21S). PepGen P-15 is an anorganic bovine-derived hydroxyapatite bone matrix that is combined with cell-binding peptide P-15. GEM 21S is a combination of highly purified recombinant human platelet-derived growth factor (rhPDGF-BB) and beta-tricalcium phosphate (β-TCP). This article aims to provide an insight into these regenerative materials so as to provide the clinician with some practical rationale in the treatment of periodontal intrabony defects.

INTRODUCTION

Periodontitis causes pathological alterations of the periodontium, which is perceived as a loss of connective tissue attachment to the tooth, loss of supporting alveolar bone, and apical migration of the junctional epithelium along the root surface. The goal of periodontal therapy is to arrest the progression of these events, by stabilizing the long-term prognosis of the periodontium. They do not restore the anatomy of the normal periodontium though these treatments have been proven to be effective. Instead, they result in the repair of periodontal wounds, wherein the healed tissue does not replicate the original architecture and function.[1]Treatment modalities like surgical and nonsurgical periodontal therapy, have been attempted to repair/regenerate periodontal tissues damaged or lost due to disease.[2]

Periodontal repair can be defined as healing that does not completely restore the architecture or function of the part. Periodontal repair elicits the formation of a long junctional epithelium along the root surface.[3]

Regeneration has been defined as the reproduction or reconstitution of a lost or injured part to restore the architecture and function of the periodontium (Periodontology, 1992). To be considered as a regenerative modality, the material or the technique must demonstrate histologically that bone, cementum and a functional periodontal ligament (a new attachment apparatus) can be formed on a previously diseased root surface.[4] According to the definitions of these terms as suggested by Kalkwarf (1974) "new attachment" should be used when a fibrous attachment is re-established on a root surface that has been exposed to a periodontal pocket or to the oral environment, while "reattachment" should be used to describe the reunion of soft tissue and root separated by incision or injury.[5]Periodontal regenerations are now considered a successful and predictable procedure to treat deep pockets associated with intrabony defects.

And these regenerative procedures have been accomplished using grafts, PRF, PRP, etc. In order toachieve periodontal regeneration, soft and hard tissue replacement grafts, guided tissue/bone regeneration (GTR/GBR), root surface biomodifications, and delivery of growth factors have been developed.[2] Bone grafting is one of the most commonly used surgical methods in the medical field to enhance bone regeneration in orthopedic procedures.[6]

A bone graft is an embedded material that promotes bone healing when used alone or used in combination with other material(s).[7] Bone replacement grafts promote new bone formation and periodontal regeneration in periodontal therapy, especially in intrabony defects.[8] The goal of osseous replacement is to enhance the hard and soft tissue healing by maintaining the contour, eliminating the dead space, and reducing postoperative infection.[9]Human and animal histologic findings support the potential of barrier membranes, demineralized freeze-dried bone allografts (DFDBA), a combination of barrier membranes and grafts, and amelogenins to induce periodontal regeneration.[10]

Corresponding author:* **Reshmi V Nair
Department of Periodontics, D A P M R V Dental College Bangalore

Historical Review:[11]

Hegedus (1923): reconstructed intraosseous defects using bone grafts produced by periodontal disease.

Nabers and O'leary (1965): Cortical bone was removed with hand chisels during osteoplasty and ostectomy and its shavings were used to treat one, two-wall defect.

Schallhorn *et al*. (1970): Iliac bone and marrow wasused asallografts Mellonig *et al*. (1981): In his study, on treating with freeze-dried bone allografts (FDBAs), on re-entry it was found that 60–68% of the defects had 50% or more bone fill.

Meffert *et al*.(1985): Dense hydroxyapatite (HA) when compared with debridement showed a reduction in the probing depth and an increase in the clinical attachment level.

Yukna(1990):conducted a 6-month clinical study on hard tissue replacement (HTR) polymer (HTR synthetic bone) wherein his study showed a significant defect fill and improved attachment level relative to open flap debridement (OFD).

Richardson *et al*. (1999): introduced Bio-Oss, which is a bovine bone from which all inorganic components are removed and used for regeneration.

Bone grafts or Regenerative Materials

Bone grafts can be classified based on material groups as:[12]

1. Allograft‐based bone graft: consists of allograft bone that is used alone or in combination with other materials e.g., Grafton, OrthoBlast.
2. Factor‐based bone grafts: they are natural and recombinant growth factors e.g., transforming growth factor‐beta (TGF‐beta), platelet‐derived growth factor (PDGF), fibroblast growth factors (FGF), and bone morphogenetic protein (BMP).
3. Cell‐based bone grafts: They use cells to generate new tissue either when used alone or are added onto a support matrix, for example, mesenchymal stem cells.
4. Ceramic‐based bone graft substitutes include calcium phosphate, calcium sulphate, and bioglass; for example, OsteoGraf, ProOsteon, OsteoSet.
5. Polymer‐based bone graft uses degradable and nondegradable polymers alone or in combination with other materials, for example, open porosity polylactic acid polymer.
6. Different types of bone grafts are available. But, each bone graft varies in its composition and characteristics. Thus, the clinician has to select an appropriate bone graft material based on their characteristics.

Ideal characteristics of a bone graft are:[8] (Rosenberg and Rose, 1998; Nasr *et al*., 1999)

- It should be nontoxic.
- It should be nonantigenic.
- It should be resistant to infection.
- Should not cause any root resorption or ankylosis.
- Strong and resilient.
- Easily adaptable and available.
- Should require minimal surgical intervention.
- Should stimulate new attachment and be able to trigger osteogenesis, cementogenesis, and formation of a functional periodontal ligament.

Selection of graft material is guided by:[4]

1. Biologic acceptability (Schallhorn, 1977; Nasr *et al*., 1999)
2. Predictability (Schallhorn, 1977)
3. Resorbability (Nasr *et al*., 1999)
4. Clinical feasibility (Schallhorn, 1977; Nasr *et al*., 1999)
5. Minimal operative hazards (Schallhorn, 1977)
6. Minimal postoperative sequelae (Schallhorn, 1977)
7. Patient acceptance (Schallhorn, 1977; Nasr *et al*., 1999)

For it to be considered as a successful regenerative graft material, they should show clear histological, clinical, and radiographic evidence of the following criteria:[4]

- Biologic acceptability: the graft should not have any side effects or cause any unwanted tissue reaction.
- Resorbability: the graft should resorb slowly and be replaced by the patient's own bone.
- Regeneration: the graft should have evidence of regenerative ability with the formation of new bone, cementum, and periodontal ligament fibers.
- Defect fill: the graft should have evidence of bone fill.
- Stability: the outcome of the treatment should be stable at re-evaluation visits.

Mechanism of action

The biologic mechanisms that provide a principle for bone grafting are osteoconduction, osteoinduction, osteogenesis, and osteopromotion.[13,14]

- Osteogenesis is the formation of new bone by the cells contained within the graft materials such as cancellous bone/bone marrow that contain living cells that are capable of differentiation and formation of bone.[8]
- Osteoinduction is a chemical process in which molecules contained within the grafts such as DBM (bone morphogenetic proteins [BMPs]), that provide a biologic stimulus that induces the progression of mesenchymal stem cells and other osteoprogenitor cells toward the osteoblast lineage to convert.[8]
- Osteoconduction is a physical effect by which the matrix of the graft forms a scaffold on which cells in the recipient site can form new bone (osteogenesis) in a closed environment.[4]
- Osteopromotionoccurs when the grafted material does not possess osteoinductive properties but enhances osteoinduction by promoting bone formation. E.g., EMD does not stimulate Denovo bone growth alone, but when used with DFDBA, it enhances the osteoinductive effect of DFDBA.

Emerging Regeneration Materials

There are various regenerative materials used in dentistry that has shown variable efficacy in the development of new bone in the intraosseous defects and augmentation of bone. The clinicians use a particular type of graft material taking into consideration the depth of the defect, dimension of the defect, the duration it takes for the bone to form, and the condition of the patient. Both the clinicians as well as the patient prefer the material that has faster regeneration potential, iscost-effective, biocompatible, and effective for a longer duration of time. There are few newer regeneration materials that are introduced

in the field of dentistry that has shown to incorporate a few of these preferences. A few of these new materials are:

- PepGen P-15
- GEM

Pepgen P-15

PepGen P-15 (Dentsply Friadent, Mannheim, Germany) is an anorganic bovine-derived hydroxyapatite bone matrix or ABM that is combined with a synthetic cell-binding peptide, P-15.It is derived from the cortical bone.[15,16]

ABM is a pure anorganic bovine-derived polycrystalline form of hydroxyapatite, that provides the structure and calcium phosphate required for bone formation and is manufactured as naturally porous, radiopaque, irregularly shaped particles, sized from 250 to 420 micrometers, while the P-15 provides the collagen analog receptor site for cell-receptor initiation of morphogenesis. It is a synthetic peptide, that modulates cell binding, migration, proliferation, and differentiation. ABM is processed at 1,100 C to remove organic matter.[16,17] It is a type I collagen, a 15 amino acid, identicalto the sequence (766) GTPGPQGIAGQRGVV (780), that provides a similar anatomic scaffold, composition, and structure as that of autogenous bone for cellular invasion. It serves as a bone-like substitute for autogenous bone grafts and also provides a tissue-engineered hospitable biomimetic habitat for cells like osteoblasts and fibroblasts.[18,19]

The P-15 peptide is a 15 amino acid sequence of the α1 chain of Type I human collagen, a synthetic clone, and is a biologically active segment of collagen that facilitates cell migration and binding. The P-15 peptide is adsorbed to ABM to enhance bone growth in the defect site.[19]

Pep-Gen P-15 is available in particulate and gel form when 200 nanograms of P-15 is combined with 1 gram of ABM which when combined with other regenerative materials hasbeen shown to result in better regeneration potential for the management of intrabony defects.[20]

A study was conductedto compare and evaluate the efficacy of peptide-enhanced bone graft (PepGen P-15) and resorbable GTR (Artisorb) barrier with PepGen P-15 alone in the treatment of human mandibular class II furcation both clinically and radiographically and observed that the use of ABM along with a bioresorbable membrane and without a membrane is both beneficial for the treatment of grade 2 furcation but did not provide a benefit for the clinical outcome of the mandibular grade II furcation defect treatment.[18]

Mechanism of Action

A short sequence of collagen forms the major component of the organic components of bone that forms about 85% and has been identified as a cell-binding domain for mesenchymal progenitor cells wherein the osteoblast progenitor cells bind thus initiating proliferation and differentiation. The integrin initiates a connection of the extracellular matrix (ECM) on the cellular membrane and they represent a transmembrane hierarchy of molecular responses viz. receptor clustering and recruiting of signal and cytoskeleton proteins to focal adhesion through the transfer of information via an "outside-in-signaling" process.

The amino acid P-15 can be produced via the synthetic process in any desired quantity, and as it is irreversibly bound to a carrier (Osteograf/N), they can form a substitute for the physiological collagen thus triggering the differentiation cascade of the target cells by binding to this synthetically manufactured analogue, PepGen P15.

When compared to the conventional graft materials, the materials coated with P-15, showed higher cell proliferation, as they allow for immediate activation of all osteoblast progenitor cells while physiologically a collagen network is formed first. Thus they form the prerequisite for a multifocal formation of new bone, resulting in the accelerated formation of new, highly vascularized bone.[21]

A study was conducted to evaluate the long-term benefit of PepGen P-15 (Dentsply Friadent CeraMed, Lakewood, CO), used for ridge augmentation and Onlay bone grafting. The radiographic and clinical evaluations were continued for the site treated with PepGen P-15 over a period of 8 years to confirm the stability of the onlay/ridge augmentation site. They observed enhanced bone formation within a shorter time period when compared with the composite graft of HA and autogenous bone in human maxillary sinus augmentation. Thus the study concluded that PepGen P-15 has the potential to provide long-term clinical and radiographic stability for endosseous implants.[22]

Types

P-15 bone graft substitute (P15-BGS) is a combination of the mineral component of bone and a peptide that represents the cell-binding domain of type I collagenand has been observed as an alternative to the conventional autografts in the repair of the ununited fracture.[19]

PepGen P-15 Flow contains the particles, suspended in a biocompatible hydrogel, that is composed of carboxymethylcellulose and glycerol. The hydrogel properly spaces the particles, thus permitting the faster transfer of cells to the P-15 binding sites. A study compared the efficacy of PepGen P-15 Particulate and PepGen P-15 Flow to the natural bone in the extraction socket of the same individual. The radiographic, histologic, and histomorphometric evaluations showed enhanced bone formation and faster particle resorption with PepGen P-15 Flow compared to the PepGen P-15 particulate and concluded that accelerated bone formation with faster implant placement was observed in PepGen P-15 Flow.[17]

Safety

PepGen P-15 showed potential for mutagenicity and toxicity when a nonclinical safety testing was conducted by the FDA.[16]
Indications and Contraindication

PepGen P-15 is indicated in the treatment of intrabony periodontal osseous defects in moderate or severe periodontitis.

There are no known contraindications.[16]

Growth Factor Enhanced Matrix (GEM):

Platelet-derived growth factor (PDGF) is a naturally occurring protein growth factor that is found in blood platelets. They stimulate the recruitment of chemotactic cells of mesenchymal lineage, as well as monocytes and macrophages that are required for normal wound healing and thus act early in the wound healing cascade. The mesenchymal lineage cells such as osteoprogenitor cells divide and their numbers are increased

at the site of injury as a result of receptor-ligand binding. In addition, cell signaling by PDGF supports angiogenesis and assist in wound healing by upregulating the expression of VEGF. PDGF-BB binds to both PDGF α and β cell-surface receptors with high affinity.[23]

Recombinant human PDGF-BB (rhPDGF-BB) expressed in yeast, is purified and formulated in a 20 mM sodium acetate solution at pH 6.0 for clinical applications. Numerous studies have been conducted demonstrating the preclinical and clinical efficacy of rhPDGF-BB for the repair and regeneration of bone. The rhPDGF-BB treatment improved bone healing, increased bone density, and accelerated fracture repair in preclinical animal models of orthopedic bone repair and regeneration.[24]

GEM 21S® (Growth-factor Enhanced Matrix) was developed using innovative tissue engineering principles that combine a bioactive protein (highly purified recombinant human platelet-derived growth factor, rhPDGF-BB) with an osteoconductive matrix (beta-tricalcium phosphate, β-TCP).[25]β-TCP particles ranging in size from250 to 1000 μm, ("small β-TCP"), are approved by the United States Foodand Drug Administration (FDA).[24]

It is engineered to stimulate wound healing and bone regeneration when they are implanted in the body thus triggering a cascade of molecular events that continues, even after the implanted PDGF is gone.[25] An in vivo study was conducted on calvarial defect in rat models by Young *et al*. to evaluate the rate of release of GEM 21S (small β-TCP) with that of Augment™ (big β-TCP) wherein they found that radioactive rhPDGF-BB was released rapidly from the implantation site over the first 60 min and a secondmore gradual phase of release of a small proportion (10–20%) of the implanted radioactivity remained localized at the implantation site for up to 72 h.[24]Following release at the wound site, PDGF stimulates:

- Chemotaxis - directed cell migration
- Mitogenesis - bone and periodontal ligament cell proliferation
- Matrix formation - e.g. collagen for new tissue formation
- Angiogenesis - revascularization of the surgical site

It promotes regeneration of bone, cementum, and periodontal ligament. Also, it is the only material that contains PDGF, one of the vital growth factors found in the human body, well known for its role in wound healing. PDGF exerts its effects by recruiting and stimulating the cells within the surrounding tissues.

The success of any grafting procedure is its adequate blood supply. Many ex-vivo and in vivo studies have observed that PDGF is a powerful stimulant of angiogenesis and also stabilizes newly formed blood vessels.

GEM 21S® contains at least 1,000 times more active growth factors than either PRP or PRGF preparations.[25]

Mechanism of action

PDGF is a broad-acting growth factor with mitogenic and chemotactic properties that affects the cells of osteoblasts, Cementoblasts, and periodontal ligament which is demonstrated through various in vitro and animal studies.

β-TCP releases PDGF into the surrounding environment which then binds to the specific cell receptors on the target cells thus initiating a cascade of intracellular signaling molecules. This leads to the migration and proliferation of osteoblasts, fibroblasts of the periodontal ligament, and cementoblasts, resulting in new alveolar bone, periodontal ligament, and cementum due to the increased matrix synthesis. Clinical data suggests that over time of approximately 6 months, there is the maturation of supporting alveolar bone, cementum, andthe periodontal ligament that occurs. Thus, the result showed an enhanced boneand periodontal regeneration and retention of the natural tooth.[25]

Few studies have been conducted that show their regenerative property in both hard and soft tissue.

S.No	AUTHOR	RESULTS
1	Michael K. McGuire, E. Todd Scheyer, and Peter Schupbach (2009)[26]	A randomized controlled clinical trial compared GEM 21S® Growth-factor Enhanced Matrix to Subepithelial Connective Tissue Grafts (CTG).The study concluded that both the CTG and GEM 21S® treatments resulted in clinically significant improvements over the six-month evaluation periods and were effectivetreatments for the correction of recession defects and also resulted in the increase in keratinized tissue.
2	McGuire MK, Scheyer ET, Nevins M, Schupbach P. (2009)[27]	A histologic and Microcomputed Tomographic Examination was conducted to evaluate the human recession defects treated with coronally advanced flap in combination with either purified rh-PDGF and β-TCF or connective tissue. The results showed that the sites treated with GEM 21S consistently led to the formation of cementum with inserting connective tissue fibers and alveolar bone, which was not determined in the sites treated with a connective tissue graft.
3	Preetinder Singh *et al.* (2011)[28]	The study revealed a favorable tissue response to GEM 21S® and collagen membrane. Froma clinical and aesthetic point of view recombinant human platelet-derived growth factor-bb, beta-tricalcium phosphate with collagen membrane showed excellent plastic surgery results for gingiva.
4	Preetinder Singh, D. K. Suresh (2012)[29]	The study showed better results in both the groups treated in a combination of GEM 21S® andcollagen (Healiguide) and treated only with collagen showing a statistically significant difference in clinical parameters at various intervals. In comparison, there was no statistically significant difference observed between the groups, suggestive that both GEM 21S® with collagen combined and collagen(Healiguide) alone can be used effectively in root coverage procedures.
5	Preetinder Singh *et al.* (2016)[30]	The study revealed an increase in the clinical attachment level, reduced pocket depth, increased width of attached gingiva, and 100% reduction in gingival recession at 6 months when compared to baseline when treated with coronally advanced flap in combination with recombinant human platelet-derived growth factor-BB (rhPDGF-BB) (GEM 21S) to treat multiplegingival recession defects.

There have been studies wherein they showed a minimal to mild granulation tissue formation in the implant site treated with GEM 21S compared to control sites, which may be caused by a local reaction to ß-TCP. But there were no neoplastic changes noted after 1 year of treatment. And also there are no studies that show animals treated with GEM 21S showing positive for anti-PDGF-BB antibodies.[23]

Indications:[25]

rhPDGF-BB plus beta-tricalcium phosphate (GEM 21S®) is indicated in the following periodontally related defects:

- Intrabony defects;
- Furcation defects; and
- Gingival recession associated with periodontal defects.

Contraindications:[25]

rhPDGF-BB plus beta-tricalcium phosphate (GEM 21S®) is contraindicated inone or more of the following clinical situations:

- Surgical sites with untreated acute infections;
- Surgical site with untreated malignant neoplasm(s);
- Patients with a known hypersensitivity to any of the component (ß-TCP or rhPDGF-BB);
- Intraoperative soft tissue coverage is not possible; or
- Conditions in which general bone grafting is not advisable.

CONCLUSION

PepGen P15 and GEM 21S are introduced recently for regeneration of periodontal intrabony defects. The studies have shown their efficacy in the successful treatment of periodontal intrabony defects. Each regenerative material shows variable potency in the regeneration of the periodontal tissue which can be appreciated by conducting various in vitro, preclinical and clinical studies. But these materials also exhibit certain contraindications, wherein they cannot be used in patients allergic to β-TCP and rh-PDGF. To my knowledge, there are no studies conducted wherein these materials have proven their efficacy in treating peri-implantitis. Thus, further studies have to be conducted to assess their regenerative potential in treating peri-implantitis. This review is intended to provide guidance for the clinicians on the newer regenerative material that assists in bringing about satisfactory results.

Bibliography

1. Lowenguth RA, Blieden TM. Periodontal regeneration: root surface demineralization. Periodontology 2000. 1993 Feb;1(1):54-68.
2. Sheikh Z, Hamdan N, Ikeda Y, Grynpas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review. Biomaterials research. 2017 Dec;21(1):1-20.
3. Becker W, Becker BE. Periodontal regeneration: A contemporary re-evaluation. Periodontology 2000. 1999 Feb;19(1):104-14.
4. AlGhamdi AS, Shibly O, Ciancio SG. Osseous grafting part I: autografts and allografts for periodontal regeneration--a literature review. Journal of the International Academy of Periodontology. 2010 Apr 1;12(2):34-8.
5. Isidor F, Karring T, Nyman S, Lindhe J. New attachment–reattachment following reconstructive periodontal surgery. Journal of clinical periodontology. 1985 Oct;12(9):728-35.
6. Wang W, Yeung KW. Bone grafts and biomaterials substitutes for bone defect repair: A review. Bioactive materials. 2017 Dec 1;2(4):224-47.
7. Pellegrini GG, Mattiuzzi AS, Pellegrini MA, Corso LA, Morales CP, Osinaga EA, Zeni SN. Update on Bone Grafting Materials Used in Dentistry in the Bone Healing Process: Our Experience from Translational Studies to Their Clinical Use. InBone Grafting-Recent Advances with Special References to Cranio-Maxillofacial Surgery 2018 Dec 19. IntechOpen.
8. Jangid MR, Rakhewar PS, Nayyar AS, Cholepatil A, Chhabra P. Bone Grafts and bone graft substitutes in periodontal regeneration: A review. Int J Curr Res Med Sci. 2016;2(8):1-7.
9. Kumar P, Vinitha B, Fathima G. Bone grafts in dentistry. Journal of Pharmacy and Bio Allied Sciences. 2013 Jun 1;5(5):125-.
10. Cortellini P. Reconstructive periodontal surgery: a challenge for modern periodontology. International dental journal. 2006 Aug 1;56:250-5.
11. Kumar J, Jain V, Kishore S, Pal H. Journey of bone graft materials in periodontal therapy: A chronological review. Journal of Dental and Allied Sciences. 2016 Jan 1;5(1):30.
12. Laurencin C, Khan Y, El‐Amin SF. Bone graft substitutes. Expert Rev Med Devices 2006;3:49‐57.
13. Balaji VR, Manikandan D, Ramsundar A. Bone grafts in periodontics. Matrix Science Medica. 2020 Jul 1;4(3):57.
14. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: An update. Injury 2005;36(Suppl 3):S20‐7.
15. Figueiredo M, Henriques J, Martins G, Guerra F, Judas F, Figueiredo H. Physicochemical characterization of biomaterials commonly used in dentistry as bone substitutes—comparison with human bone. Journal of Biomedical Materials Research Part B: Applied Biomaterials: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials. 2010 Feb;92(2):409-19.
16. https://kundoc.com/download/bone-grafting-material_5bc5c242d64ab2ff9573b75a.html
17. Hahn J, Rohrer MD, Tofe AJ. Clinical, radiographic, histologic, and histomorphometric comparison of PepGen P-15 particulate and PepGen P-15 flow in extraction sockets: a same-mouth case study. Implant dentistry. 2003 Jun 1;12(2):170-4.
18. Khashu H, Vandana KL. Clinical and radiographic evaluation of human periodontal osseous defect (mandibular grade II furcation) treated with PepGen P-15 and a bioresorbable membrane (Atrisorb). Journal of Indian Society of Periodontology. 2012 Oct;16(4):569.
19. Gomar F, Orozco R, Villar JL, Arrizabalaga F. P-15 small peptide bone graft substitute in the treatment of non-unions and delayed union. A pilot clinical trial. International orthopaedics. 2007 Feb;31(1):93-9.
20. Goyal, J., Sachdeva, S., Salaria, S.K., Vakil, N. and Mittal, A., 2020. Comparative assessment of periodontal regeneration in periodontal intraosseous defects treated with PepGen P-15 unaided or in blend with platelet-rich fibrin: A clinical and high-resolution computed tomography scan-assisted volumetric analysis. *Journal of Indian Society of Periodontology*, *24*(2), p.156.
21. Valentin AH, Weber J. Receptor technology—cell binding to P-15: a new method of regenerating bone quickly and safely-preliminary histomorphometrical and mechanical results in sinus floor augmentations. The Keio journal of medicine. 2004;53(3):166-71.
22. Hahn J. 8-year onlay bone graft and ridge augmentation with PepGen P-15: A clinical and radiographic case study. Implant dentistry. 2004 Sep 1;13(3):228-31.
23. Solchaga LA, Hee CK, Roach S, Snel LB. Safety of recombinant human platelet-derived growth factor-BB

in Augment® Bone Graft. Journal of tissue engineering. 2012 Dec;3(1):2041731412442668.

24. Young, C.S., Ladd, P.A., Browning, C.F., Thompson, A., Bonomo, J., Shockley, K. and Hart, C.E., 2009. Release, biological potency, and biochemical integrity of recombinant human platelet-derived growth factor-BB (rhPDGF-BB) combined with AugmentTM Bone Graft or GEM 21S beta-tricalcium phosphate (β-TCP). *Journal of controlled release*, *140*(3), pp.250-255.
25. https://www.indyperio.com/Brochures/GEM-21S-Brochure.pdf
26. Michael K. McGuire, E. Todd Scheyer, and Peter Schupbach. Growth Factor-Mediated Treatment of Recession defects: A Randomized Controlled Trial and Histologic and Microcomputed Tomography Examination. Journal of Periodontology 2009; 80(4): 550-56.
27. McGuire MK, Scheyer ET, Nevins M, Schupbach P. Evaluation of a Human Recession Defects Treated with Coronally Advanced Flaps and Either Purified Recombinant Human Platelet-Derived Growth Factor-BB with Beta Tricalcium Phosphate or Connective Tissue: A Histologic and Microcomputed Tomographic Examination. *Int J Periodontics Restorative Dent* 2009; 29
28. Singh P, Kaushal S, Dabra S, Kaushik A. Evaluation of recombinant human platelet derived growth factor-bb, beta-tricalcium phosphate with collagen membrane in the treatment of gingival recession. *International Journal of Dental Clinics*. 2011 Jul;3(3).
29. Singh P, Suresh DK. Clinical evaluation of GEM 21S® and a collagen membrane with a coronally advanced flap as a root coverage procedure in the treatment of gingival recession defects: A comparative study. *Journal of Indian Society of Periodontology*. 2012 Oct; 16(4):577.
30. Singh P, Dev YP, Nitin K, Singh A, Kaur P, Singh YR. rhPDGF Mediated Root Coverage Procedure Using Coronally Advanced Flap in Treatment of Multiple Recession Defects: A Case Report. *Dental Journal of Advance Studies*. 2016 Apr;4(01):059-64.

How to cite this article:

Suchetha Aghanashini *et al* (2022) 'Contemporary Regenerative Materials from Peptides and Platelet-Derived Growth Factor', *International Journal of Current Advanced Research,* 11(02), pp.219-224.
DOI: http://dx.doi.org/10.24327/ijcar.2022.224.0049

****