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Role of injectable Platelet Rich Fibrin (iPRF) in Periodontal Therapy - A report on current evidence

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ABSTRACT

The advent and emergence of the use of platelet concentrate in wound healing and regeneration has opened up an arena of possibilities to explore the potential of these biomimetic agents in periodontal regeneration. This review narrates the role of platelet concentrates in wound healing, regeneration and the literature evidence of use of iPRF in periodontal therapy.

Keywords: *Periodontal, platelet rich fibrin, biofilm, evidence, plaque*

INTRODUCTION

Periodontal disease is the inflammatory condition of the supporting structures of the tooth initiated by polymicrobial biofilm and mediated by host immune response.[1] It is considered as the major cause of tooth loss resulting in compromised mastication, loss of self-confidence, and quality of life. According to the global burden of disease reported in 2017 periodontal disease is the 11th most prevalent condition in the world with a range of 20 - 50 %.[2] The initial stages of plaque induced periodontal disease presents as gingival inflammation which is a reversible condition on elimination of the plaque biofilm.[1] However if left untreated it progresses to deeper periodontal tissues resulting in its damage which is known as periodontitis.[3] An array of periodontal therapy are practised to remove the etiologic agents that are targeted to slow down the progression of active periodontal destruction. It includes scaling and root planing of the diseased root surface to remove the plaque and calculus and also the diseased cementum.[4] Although this results in considerable periodontal pocket depth reduction, the residual pocket depth remains inaccessible to routine home care thus harbouring pathogenic periodontal microflora that may facilitate further progression of active periodontal disease. To reduce or eliminate these residual pockets surgical periodontal therapy is advocated, either by resective or regenerative or combination approach. [5]

The possibility of regenerating lost periodontal structure has long been the ultimate goal in periodontal therapy. Initial attempts of periodontal regeneration are carried out using various types of bone and non - bone grafts.[6] These include autografts obtained from intraoral and extraoral origin that are considered to have osteogenic potential. Allografts are synthesised from different individuals of the same species

Which showed an osteoinductive property by allowing adjacent cells to become bone forming cells and result in regeneration of bone. Alloplasts are synthetic materials that have osteoconductive properties allowing adjacent bone cells to migrate into the grafted area and form bone tissue. [7]Even though all these modes have shown a good defect filling effect they failed to achieve a new attachment on to the treated tooth surfaces. This has resulted in the concept of tissue engineering triad where the combination of a scaffold, tissue forming cells and the signalling molecules for regeneration is a minimum prerequisite for periodontal regeneration.[8] Following this many regenerative approaches representing each component of the tissue engineering triad have been tested for achieving periodontal regeneration. Some of the materials used were as follows: guided tissue regeneration (GTR), root biomodification, use of enamel matrix derivatives, recombinant human bone morphogenetic proteins, recombinant human growth factors etc. However many of these materials have reported conflicting data with lack of predictability, allogenic or xenogenic in origin giving possibility of immunogenic reactions, and high cost of the materials. All these limitations point out the need for a more reliable, predictable, autologous biomaterial that can facilitate periodontal regeneration.

The advent and emergence of the use of platelet concentrate in wound healing and regeneration has opened up an arena of possibilities to explore the potential of these biomimetic agents in periodontal regeneration. This review narrates the role of platelet concentrates in wound healing, regeneration and the literature evidence of use of iPRF in periodontal therapy.

Platelets

The role of platelets in regeneration was reported first in 1970. [9] These reports state that the alpha granules in platelets are capable of stimulating cell division, differentiation, migration, neovascularization and collagen synthesis which all contribute to tissue regeneration. These platelet concentrates are categorised as fist generations and second generation which majorly includes platelet rich plasma (PRP) and platelet rich fibrin (PRF) respectively.[10] Although PRP showed considerable clinical effects, the need for sophisticated centrifuges, and the need for biochemical handling like addition of bovine thrombin had led to the development of PRF. [11]

Platelet Rich Fibrin (PRF)

PRF was developed in the year 2001 by Choukroun J from then its application in dentistry and other specialities have exponentially increased. The widespread acceptance of PRF was mainly due to the easy handling like absence of need for biochemical alteration like addition of bovine thrombin, need for highly sophisticated centrifuges etc.[12]

PRF is prepared from immediate centrifugation of blood after collection in a glass tube in 3000 rotations per minute (RPM) for 10 minutes. This results in a segregation of blood into 3 compartments namely: top - platelet poor plasma, middle platelet rich fibrin with buffy coat, bottom red blood cell compartment.[12,13] The middle PRF contains a fibrin matrix in which the majority of platelets and leukocytes are entrapped along with circulating stem cells. This also enmeshes the cytokines released from activated platelets and leukocytes like transforming growth factor, vascular endothelial growth factor, platelet derived growth factor, beta defensins etc. These cytokines, especially the growth factor, are thought to be responsible for the enhanced healing and regenerative potential of PRF with the fibrin matrix additionally playing a crucial role in facilitating the healing process.[14] Literature evidence shows beneficial effects of PRF in a variety of periodontal applications flap surgery, intrabony defects, furcation defects

Injectable platelet rich fibrin (IPRF)

iPRF was developed as an advanced product of PRF by altering the centrifugation protocol by lowering the centrifugation speed and force to 700 rotations per minute (RPM) and 40 grams of force in the year 2014[15]. This results in segregation of the blood into 2 compartments: the top layer being the liquid platelet rich fibrin (Liquid PRF) and the bottom red blood cells. The

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top layer of liquid PRF can be aspirated in a syringe and stays in the injectable form for an average of 5 - 10 minutes.[15] During this the liquid fibrinogen is slowly polymerising into a fibrin matrix after which it becomes a fibrin clot. Thus the transient liquid form of iPRF allows for the clinician to utilise it in injectable forms for various clinical applications like for both soft and hard tissue management in periodontal and oral surgical procedures. Similar to PRF, iPRF brings about clinical benefits because of the fibrin matrix, their degradation and release of various cytokines including growth factors into the surgical wound area for regeneration and healing. [15]

The I-PRF preparation method differs according to the centrifugation time and speed, centrifuge device, and the site from which sample is collected.[16] Most of the published reports used an optimum centrifugation speed of 700 rate per minute (rpm) for obtaining I-PRF, based on the notion that the number of platelets, inflammatory factors, and cytokine significantly increases with a reduction in relative centrifugal force (RCF).[17] In most of the studies the protocol used was 700 RPM for 3 minutes, however some reports have used 2300 rpm for three minutes [18], and Jasmine et al[19] implemented a method of 1000 rpm for five minutes. Further exceptions were the study by Val- ladão et al. in which I-PRF was acquired after centrifuging two non-ridged tubes holding 8 ml blood at 2700 rpm for three minutes in a centrifugal machine, the research by Kyyak et al.[20] which centrifuged the tubes at 1200 rpm for eight minutes. For periodontal regeneration purposes, all the studies centrifuged blood at 700 rpm for three minutes. Only, Ay- dinyurt et al. [21]applied a protocol of 3300 rpm for two minutes.

There are two types of centrifugation devices that can be used to procure iPRF. blood for I-PRF preparation: either fixed-angle or horizontal centrifuge devices. While the most common centrifugation system used for PRF preparation is the fixed-angle centrifugation system, the horizontal centrifugation system is more favourable. Most of the I-PRF studies usied the fixed- angle method with either Duo, IntraSpin, MF-20R, PC-02, Eppendorf Centrifuge, VE-4000, Ample Scientific Champion F-33D, EBA20, Dy- namica Velocity 14R, or TC-SPINPLUS-6 Digital Desktop, except for the study by Fujioka-Kobayashi on I-PRF [22]which used horizontal centrifugation with the Eppendorf Centrifuge. Despite fixed angle centrifuges being more commonly used and available for PRF preparation, horizontal centrifuges are more effective than fixed angle devices. It separates the blood cells very effectively facilitating a more optimised segregation of blood components. Further horizontal centrifuges results in more inclusion of platelets & leukocytes into iPRF to an average of 3.5 time than fixed angle devices with reduced trauma to the cells thus preserving active platelets and leukocytes.

Two types of I-PRF can be attained following centrifugation: red and yellow I-PRF. In the case that the I-PRF is collected merely from the liquid yellow site over the buffy coat, it is referred to as the yellow I-PRF. On the other hand, the sample collected from the red and yellow zone with the buffy coat is considered as the red I-PRF. . According to a previous research [22], even minor alterations in the fractionation method can influence the biological and physical properties of the collected sample. Previous studies have reported a higher number of cells (erythrocytes, platelets, and leukocytes) and platelet-derived growth factor (PDGF) for the red I-PRF, and superior fibrin clot formation for yellow I-PRF. [22] Additionally, the viscoe- lastic properties (clot-forming time, α-angle, and maximal clot firmness) of the yellow I-PRF are substantially greater than that of the red I-PRF due to the above-described variations in cellular components and fibrin network of red and yellow I-PRF[23]. In this regard, Miron et al. [23]have recently introduced a novel metho- dological approach in order to measure cells and platelets within platelet concentrates in which 100-µL sequential layers were pipetted from approximately 1.2- to 1.5-ml layers above the buffy coat to the red blood cell layer. The results from sequential 100-µL layers in the I-PRF protocol have demonstrated that there was a 3-fold in- crease in leukocytes and 5- to 6-fold increase in monocytes directly at the buffy coat layer in comparison with the baseline. Furthermore, there was a 2.5-fold increase in

platelets in all of the aforementioned obtained layers compared to the baseline. Most of the reported studies have utilised yellow iPRF that is obtained from the top layer of the test tube not involving the buffy coat.

Assessment of periodontal ligament cellular activities,[16] using the 2 types of iPRF showed that red iPRF had a better influence on cellular activity like proliferation, migration etc. However, evaluation on calcification and bone formation showed a significantly better effect by yellow iPRF than the red type.[16,24]

Wound healing and anti-inflammatory efficacy of IPRF

In an in vitro study by Dohle et al[25] the evaluation of the effect of PRF on antiinflammatory effect and wound healing showed a positive effect. There was a renounced antiinflammatory effect seen as decreased proinflammatory cytokine production from the cell culture studies. Also the wound healing efficacy was shown to be higher with evidence of increased secretion of cytokine and proangiogenic growth factors involved in wound healing mechanisms like vascular endothelial growth factor, platelet derived growth factor, alkaline phosphatase, bone morphogenetic protein, intercellular adhesion molecules, E selectin etc.

In other animal studies the researcher evaluated the wound healing effect of iPRF compared to melatonin. The results showed both iPRF and melatoningroup increased the SMGs but when compared between groups it was in favour of melatonin with iPRF showing inferior effect compared to melatonin with regard to SMGs and histomorphometric analysis.

In another animal study in 2020, Mu et al. evaluating the angiogenic potential in a rabbit sinus model, comparing 2 modes of regeneration: grafted using deproteinized bovine bone mineral (DBBM) particles mixed with I-PRF and plain DBBM without iPRF. The results showed that the iPRF mixed with the DBBM group had better wound healing angiogenic effect than the DBBM without iPRF. There was a significant sustained release of growth factors in the iPRF with DBBM group which was not interrupted due to the bone graft.[26]

A recent case report by Gasparro et al. [26,27]showed that repeated intra-leisional delivery of iPRFin plasma cell mucositis resulted in reduction of perilesional inflammation with reduction of pain after 4th infiltration with 0 visual analogue scale (VAS). The authors concluded that the use of iPRF resulted in reduction of inflammation and pain while iPRF was used. Another case report concluded that the use of iPRF showed a good improvement in reimplantation of avulsed teeth in spite of longer extraoral dry time. The follow up showed a successful reimplanted teeth with no postoperative complications like pain mobility ankylosis.[26]

There are about 4 clinical trials that evaluated the effect of iPRF therapy in wound healing and antiinflammatory effect. In one study reported on 2020 iPRF application on palatal wound healing was studied. The wound healing was assessed based on the epithelialization using hydrogen peroxide bubbling test, landry Turnbell Howley (LTH) index for soft tissue healing, Manchester scar scale (MSS), bleeding on palpation, palatal tissue thickness were evaluated. The result showed that the use of iPRF showed a significant beneficial effect on palatal wound healing by having higher epithelialization and lower bleeding than the autologous fibrin group. However the autologous fibrin group showed better effect in higher LTH index, lower MSS score, lower VAS score compared to iPRF after 1 month evaluation.Kiziltoprak et al. Another study on the comparison of iPRF versus triamcinolone acetonide in lichen planus treatment reported on 2021 Bennardo et al.[28] showed a higher reduction of VAS score and extension of lesion in iPRF group after 4 weeks evaluation however not showing statistical significance. One more study in treatment of lichen planus Saglam et al [29]evaluated the efficacy of iPRF compared to corticosteroids (methylprednisolone) and assessed the parameters like lesion extension, VAS score, pain score. Results showed that both groups had significantly reduced the pain, VAS score, lesion size, however there was no statistically significant difference between the groups at 6

month evaluation. In a final study by Negah at al which evaluated the efficacy of iPRF in treatment of internal root resorption showed a marked reduction in internal inflammatory process root resorption, and periapical lesion in the IPRF use[30]d patients after 12 months evaluation.

From the above studies it can be observed that iPRF has a potent antiinflammatory action equal to some of the gold standard treatment options available now proving it could be a viable autologous alternative to these antiinflammatory drugs and aids in wound healing.

Antimicrobial Efficacy of IPRF

Few studies have evaluated the antimicrobial efficacy of iPRF by assessing the inhibition of biofilm formation and antimicrobial efficacy. Study by Jasmine et al[19] evaluating the biofilm formation by staphylococcus aureus pathogen reported that iPRF showed a potent inhibition of biofilm formation by staphylococcus pathogen which was concentration dependent showing week to moderate effect at MIC concentrations and strong antibiofilm effect at MBC of iPRF. Another study by Rafiee et al.[31] evaluated the antimicrobial efficacy comparing iPRF loaded with triple antibiotic paste against iPRF alone against actinomyces species. The results showed there was more antimicrobial activity by iPRF containing triple antibiotics compared to iPRF alone. A study evaluating the antimicrobial efficacy of iPRF against periodontal pathogens (Porphyromonas gingivalis, Aggregatibactor actinomycetumcomitans) showed iPRF having significantly wider zone of inhibition by iPRF compared to PRF and PRP against P gingivalis while PRP showed better efficacy with respect to A actinomycetumcomitans Kour et al. Similar results were seen in another study evaluating antimicrobial efficacy against pathogens obtained from periodontitis patients showing iPRF having significantly higher efficacy than other platelet concentrates.[32]

IPRF in Periodontal regeneration

The initial studies evaluating potential of iPRF in periodontal; regeneration were of in vitro design in which the influence of iPRF on periodontal ligament, gingival fibroblast and mesenchymal stem cells activity with respect to proliferation, migration, differentiation ability to secrete collagen, fibronectin, transforming growth factor, platelet derived growth factor etc. the results were mostly supporting the beneficial effects of iPRF like increased survival of gingival fibroblast on implant surfaces coated with iPRF.[33] Further in one more study iPRF showed a dose dependent increase in cellular activity like osteogenic potential on periodontal ligament fibroblast. [34] However a study by Fujioka-Kobayashi et al.[35] reported that Concentrated-PRF had significantly better influence on cellular activity against periodontal ligament fibroblast than iPRF. In one animal study evaluating iPRF in controlling bone loss reported decreased bone loss when iPRF was used however dint show any statistical significance.

IPRF in Periodontal Pocket Therapy

Clinical studies evaluating iPRF effect in periodontal regeneration were basically assessed its use in periodontal pocket therapy and gingival recession coverage. iPRF in periodontal pocket therapy showed significantly more probing depth reduction when iPRF was used compared to control groups. In one study by Vučković et al.[36] showed better clinical effects when iPRF combined with scaling root planing compared to scaling root planing alone. However Albonni et al. evaluated scaling and root planing alone and in addition iPRF infiltration in treatment of periodontal pockets in a split mouth study design evaluated for 3 months. The results reported that there were no significant better results from additional use of iPRF when compared to scaling and root planing alone in periodontal pocket depth reduction.

IPRF in Gingival recession coverage

The additional use of iPRF in gingival recession coverage therapy mostly assessed the outcomes like gingival recession coverage, gingival thickness, keratinised tissue increase etc. In a study İzol and Üner evaluating free gingival graft (FGG) use of iPRF as root biomodifying agent showed enhanced root coverage with new gingival tissue formation. Another study

evaluated connective tissue graft with iPRF showing significant reduction in probing depth and increase in keratinised tissue dimension compared to connective tissue graft alone[37] which was not seen at 6 month evaluation. Other studies also used iPRF with micro needling for gingival augmentation showing iPRF increased gingival tissue thickness and keratinised tissue dimension Ozsagir et al.[38] Its use in coronally advanced flap for recession coverage showed use of iPRF along with bone graft formed labial bone plate and increased gingival thickness.

IPRF in Bone Regeneration

Initial in vitro studies evaluating the role of iPRF in bone regeneration using human osteoblast cells assessed the cellular activity like proliferation, migration, differentiation, mineralisation capacity, adhesion etc. Wang et al study[39] showed that iPRF resulted in a 3 fold increase in migration and proliferation of human osteoblast cells with more alkaline phosphatase secretion after 14 days. While another study reported the formation of lumina and microvessel like configurations in cell cultures with iPRF. Contrary to this iPRF concentration more than 60 % were showing detrimental effects on cell proliferation, migration and viability etc. Additionally the combination of iPRF with different bone grafts showed consistent results on osteoblast cell viability, proliferation, metabolic activity, mineralisation & differentiation markers etc. iPRF combination with bone grafts showed significant increase in all the parameters compared to bone grafts alone. In specific the combination of allograft with iPRF resulted in superior results compared to iPRF with xenografts.[40] This is further supported by recent studies where iPRF coating on titanium discs improve the ostoblast cell proliferation and migration, alkaline phosphatase secretion. [41]

Up to now, three animal studies have evaluated the regenerative effects of I-PRF on inducing bone formation. In two studies on I-PRF- induced maxillary bone regeneration, Mu et al. [42]assessed the effect of I-PRF modified with gelatin nanoparticles (GNPs) and DBBM for rabbit sinus augmentation. The authors found significantly greater bone creation surrounding the raised Schneiderian mem- brane for the sinus cavities treated with GNPs-I-PRF hydrogels compared with GNPs gels and the control.[42] Similarly, Mu et al. reported that I-PRF combined with DBBM led to new bone creation in the Schneiderian membrane zone and the basal bone wall. At four weeks, the group treated with GNPs-I-PRF was reported to have significantly higher values for the number of trabecular bones and new bone formation volume. However, lower tra- becular separation was reported for GNPs-I-PRF compared with control groups and GNPs. It was concluded that bone resorption was significantly decreased by treating the sinus cavities with GNPs-I- PRF hydrogels. Moreover, Mu et al. concluded that despite the augmented vascular formation and bone remodelling at the early stages of healing using I-PRF incorporated DBBM, the bone volume did not significantly change in a long-term period. Recently, Yuan et al. evaluated the angiogenesis, osteogenesis, and bone mass reduction using deproteinized bovine bone mineral (DBBM), gelatin nanoparticles (GNPs), and I-PRF in male beagle dogs. The researchers showed that the GNPs combined with I-PRF significantly enhanced angiogenesis and woven bone, and reduced osteoclast activity in extraction sockets 2 weeks following the operation. Significant corticalization on the alveolar ridge crest was also reported at 8 weeks post-operation.

There are several attempts of bone regeneration using various grafts materials like bone grafts, titanium mesh, combined with iPRF to augment defective ridges. Most of the cases reported have shown a good clinical outcome in terms of ridge widge and height evaluated both clinically and radiographically suggesting a possible influence of iPRF in enhancing both horizontal and vertical bone augmentation. However the concrete evidence of iPRF role in bone augmentation should be assessed using clinical trails evaluating its combination with bone grafts in ridge augmentation, sinus lifting etc. In this context there were some retrospective and prospective studies reported on iPRF in bone augmentation. 2 retrospective studies evaluating bone formation using combination of collagen plugs and bone grafts with iPRF in sinus lift and horizontal ridge defect respectively were reported. CBCT

analysis showed that iPRF enhanced the augmentation of the defects compared to the grafts or collagen plugs alone. Another study evaluating the combination of iPRF with iliac bone grafts compared to iliac bone grafts alone in periodontal regeneration reported significantly better outcome with iPRF iliac bone combination group compared to plain iliac bone graft group. Generally, all three clinical studies verified the positive effects of injectable PRF application in bone gain as an adjunct to bone graft materials in both maxilla and mandible. In a clinical study by Irdem et al. in 2021, [43]the effectiveness of the DBBM combined with liquid PRF was assessed on new bone formation in patients with bilateral maxillary sinus atrophy in need of maxillary sinus aug- mentation. It was found that the combination of DBBM with li- quid-PRF did not significantly affect new bone formation. Işık et al.[44] compared the effectiveness of particulate allograft combined with I-PRF and autogenous block bone graft on vertical bone aug- mentation. It was reported that while the particulate allograft material combined with i-PRF is rich in osteoblast cells compared to autogenous block bone graft, it resulted in similar vertical bone gain. In another study by Işık and colleagues [44]on guided bone re- generation simultaneous with implant placement, greater augmen- tation thickness as well as less marginal bone loss was detected for the bovine-derived xenograft mixed with liquid PRF compared to the xenograft only group. Thanasut et al. inspected the efficacy of autologous ABSM with and without liquid and solid PRF in bone regeneration in al- veolar clefts and found no significant differences in regenerated bone volume and density between autologous ABSM alone and combined with liquid PRF. In a digital workflow for guided bone regeneration using XBSM and I-PRF inspected by Wang et al,[45] a positive effect on the labial thickness of hard tissue was observed with XBSM and i-PRF. Moreover, the authors also investigated the effect of different guided bone regeneration procedures on graft contour in lateral ridge augmentation and found that labial graft thickness was greater when XBSM was combined with I-PRF.

IPRF in Orthodontic Tooth movement

Most of the studies [45,46] evaluated the influence of tooth retraction time during orthodontic tooth movement when iPRF was used. In one study evaluating the retraction time of incisors, the iPRF infiltration group showed a significantly faster retraction of teeth compared to the control group. This was further supported by another study evaluating canine retraction where iPRF again showed a faster tooth retraction compared to the control group. Added to this the iPRF group also showed enhanced bone remodelling markers in the iPRF group that facilitated the faster tooth movement. The markers evaluated were interleukin 1 beta (IL-1β), matrix metalloproteinase-8 (MMP-8), re- ceptor activator of nuclear factor kappa-B ligand (RANKL), and os- teoprotegerin (OPG). In a study evaluating piezocision with iPRF in orthodontic tooth movement showed better results compared to piezocision alone in terms of amount, speed, duration of tooth movement and periodontal parameter. Furthermore, in another recent study by Zeitounlouian et al. [47]on the efficacy of I-PRF in preserving bone and preventing root resorption in orthodontic patients, it was found that I-PRF is not effective in preventing canine root resorption during canine retraction. In addition, the investigators showed that the prevalence of dehiscence and fenestration was not reduced by I-PRF.

IPRF in Dental pulp revascularization / regeneration

Similar to the influence of iPRF on periodontal ligament cells, its role on dental pulp cells was evaluated [48]in which iPRF showed to influence the dental pulp cells proliferation, migration, differentiation, mineralisation potential, collagen production etc. All these prove that iPRF has the potential to form reparative dentin and odontoblastic differentiation in human dental pulp cells. Another study evaluating the combination of iPRF with triple antibiotic paste (metronidazole (MET), ciprofloxacin (CIP), minocycline (MINO)) was carried out in which iPRF was used as a drug carrier vehicle. The pattern of drug release was evaluated using UV spectroscopic methods showing a burst release in the initial 24 h after which there was a period of

sustained release of the drugs from the iPRF vehicle for up to 14 days. In another similar study by Rafiee et al. iPRF loaded with triple antibiotic paste was evaluated for antimicrobial efficacy against E faecalis and A naeslundii in root canals. Its reported the iPRF group showed significantly better results.

Future prospects

The recent development in platelet concentrate family is the concentrated liquid PRF (C-PRF), which constitutes the yellow buffy coat layer adjacent to the red blood cell layer produced through standard L-PRF protocols of 2700 rpm for 12 minutes.[23] Research showed the concentrated -PRF resulted in a multi fold increase in the levels of platelets and leukocytes in the final centrifuged product without anticoagulant. Approximately there was 2-3 fold increase in platelet concentrate and 1 to 2 fold increase in leukocyte concentrate compared to baseline whole blood composition.[23] Despite all the modifications in centrifugation techniques and protocols to increase the platelet and leukocyte levels in the different platelet concentrates, all these products gradually resorb releasing the the entrapped cytokine into the surrounding environment allowing theirs presence for a period of maximum 14 days which limits their long term application.[49] various studies have reported that this degradation of PRF can be delayed so that the growth factor release can be slowed down resulting in prolonged availability of the growth factors to the regeneration site. In this context a novel product called albumin - PRF (Alb-PRF)[50] was developed by combining the liquid PRF layer with heated albumin to form a final product which could be stable for months. Nevertheless further research is needed to identify the additional benefits of the newer products compared to iPRF.

CONCLUSION

From the above evidences it can be concluded that iPRF seems to be a potential agent in enhancing wound healing, regeneration, bone augmentation, repair of endodontic lesions, periodontal regeneration, accelerating orthodontic tooth movements, antimicrobial effect, antiinflammatory effect etc. further it has the advantage of being autologous and biomimetic in nature thus eliminating the possibility of immune reaction and other adverse effects related to biocompatibility.

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