ABSTRACT
Aim: The aim is to review and discuss the strategies available for use of platelet rich fibrin (PRF) as healing aid in implant dentistry. This review article is also to sum up different types of platelet concentrates, classification, architecture, protocol and there salient features. Background: Platelet rich fibrin (PRF) is a fibrin matrix during which platelet cytokines, growth factors, and cells are trapped and may be released after a certain time which can serve as a resorbable membrane. Faster wound healing has always been a challenge for clinicians since ages. Choukroun et al (2001) were amongst the pioneers for using PRF protocol in oral and maxillofacial surgery to improve bone healing in implant dentistry. Autologous PRF is taken into account to be a healing biomaterial and presently, studies have shown its application in numerous disciplines of dentistry. Wound healing is a complex biological process where many cellular events taking place simultaneously leading to the repair or regeneration of damaged tissues. Blood platelets are the first cells to respond to wound healing. The ability of blood platelets to secret growth factors makes them the foremost requirement in wound healing. The aim of this review article is to sum up different types of platelet concentrates, classification, architecture, protocol and there salient features. Materials and Methods: By using specific keywords, electronic search of scientific papers was carried out on the whole PubMed database with a custom range of five years. The electronic search yielded 203 papers; based on inclusion and exclusion criteria which were specifically predetermined, 63 papers were identified as suitable to the inclusion criteria and the remaining 140 papers were excluded. After adding one selected papers through hand search, full text of all the articles retrieved and review was done. By pooling the extracted data from chosen papers, the reviewed data was synthesized. Conclusion: Recently by showing good promising results with use of the plasma rich fibrin (PRF), it has proved to have a good prospect for its use as healing aid in various aspects of the implant dentistry.

KEYWORDS: Plasma rich fibrin (PRF), platelet rich plasma (PRP), wound healing.

INTRODUCTION
Development of the bioactive surgical additives is one of the great challenges of clinical research which has been used to regulate inflammation and increase the speed of healing process.[1] A wide range of intra- and extra articular events and various signaling proteins mediate and regulate the healing process of both hard and soft tissues, respectively. But understanding this entire process is still incomplete; however, it is known that platelets play a crucial role not only in hemostasis, but also in the wound healing process.[2] In 1974, platelets regenerative potentiality introduced, Ross et al.[3] were first to describe a growth factor from platelets. After activation of platelets which are trapped within fibrin matrix, growth factors released and stimulate the mitogenic response in the bone periostium during normal wound healing for repair of the bone.[4] Better understanding of physiologic properties of platelets in wound healing since last two decades led to increase its therapeutic applications in the various forms showing varying results.

MATERIALS AND METHODS
Structured electronic search of scientific papers published up to December, 2018 was carried out on the (http://www.ncbi.nlm.nih.gov/pubmed) entire PubMed database with a custom range of 5 years and hand search for term PRF (platelet rich fibrin); which was further filtered using Boolean operators (AND, OR, NOT) and combination of specific keywords as following: “PRF Choukroun”, “PRF in dentistry”, “PRF dental”, “PRF in maxillofacial surgery”, “PRF dental implant”, “PRF periodontal”, “PRF extraction”, and “platelet rich fibrin oral”; abstracts of all relevant papers were thoroughly scrutinized and in the end and articles pertaining to the topic (Plasma rich fibrin) were included. The relevant literature for “Plasma Rich Fibrin” in common dental textbooks and for additional information bibliographies of the papers and review articles together with

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**PLATELET RICH FIBRIN (PRF) AND ITS ROLE AS HEALING AID IN IMPLANT DENTISTRY**

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appropriate and authentic peer reviewed journals were also scrutinized. The inclusion criteria set for this review were: All original research papers, review papers, case reports, case series in vitro/in vivo studies, animal studies, and controlled clinical trials on Plasma rich fibrin used in dentistry related studies. Exclusion criteria consisted of studies that did not meet above inclusion criteria. The electronic search yielded 203 papers, out of which 65 were identified as suitable papers to the inclusion criteria and the remaining 140 were excluded [Figure 1]. Only 65 papers selected, 63 from electronic search and one from other searches and full text of all articles retrieved and reviewed, out of which 19 in vivo studies, 11 in vitro studies, 13 case reports, 9 animal studies, 5 controlled clinical trials, 2 combined in vivo and in vitro studies, and 6 reviews [Figure 2].

**Platelet Concentrate Evolution**
Platelets are the end product of megakaryocytes having no nuclei and cannot replicate by themselves. They contain many granules among which alpha granules form an intracellular storage pool of substances necessary for wound healing. These granules fuse with the platelet cell membrane after activation producing bioactive molecules which bind to transmembrane receptors of the target cell, leading to activation of intracellular signal protein within the target cell. This results in expression of gene sequence that leads to various events of wound healing. The substances necessary for wound healing stored in the granules of platelets are the growth factors, also called cytokines. They are small proteins each of 25,000 daltons molecular weight and perform some vital roles in wound healing. A natural blood clot on an average contains just 5% platelets and as high as 95% RBC. Now “platelet concentrates” are actually the concentrated
Platelets in a natural clot. As high as 95% platelets can be obtained from a platelet concentrate which means more availability of growth factor at the wound site thus faster healing.

**Platelets Rich Plasma (Prp)**
Platelets rich plasma (PRP) was introduced by Marx et al in 1998.\(^5\) It has been defined as a high concentration of autologous platelets in a small volume of autologous plasma.\(^6,7\) Platelets rich plasma (PRP) was used as a method of introducing concentrated growth factors platelet derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and insulin-like growth factor 1 (IGF-1) to the surgical site, thereby enriching the natural blood clot in order to hasten wound healing and stimulate bone regeneration.\(^8\) A platelets rich plasma (PRP) blood clot, contains 4% RBCs, 95% platelets, and 1% WBCs.\(^9\) The platelets rich plasma (PRP) preparation protocol requires collection of blood with anticoagulant, centrifugation in 2 steps, and induced polymerization of the platelet concentrate using calcium chloride and bovine thrombin.\(^10\) Platelets rich plasma (PRP) has been used in conjunction with different grafting materials in bone augmentation procedures since the day of its introduction; the results from these studies are controversial and no conclusions can be drawn regarding the bone regenerative effect of platelets rich plasma (PRP) till now.

**Platelet Rich Fibrin (Prf)**
Platelet rich fibrin (PRF) represents a revolutionary step in the platelet gel therapeutic concept.\(^11\) Platelet rich fibrin (PRF), developed in France by Choukroun et al.\(^12\) in 2001, is a 2nd generation platelet concentrate widely used to accelerate soft and hard tissue healing. PRFs are strictly autologous fibrin matrix containing a large quantity of platelet and leukocyte cytokines. With its strong fibrin architecture and slow release of growth factors and glycoprotein over several days this natural bioactive membrane can enhance soft and hard tissue healing while protecting both surgical and grafted sites.

**Advantages of Prf Over Prp**
- No biochemical handling of blood.\(^13\)
- Simplified and cost-effective process.\(^13\)
- Use of bovine thrombin and anticoagulants not required.\(^13\)
- Favorable healing due to slow polymerization.\(^13\)
- More efficient cell migration and proliferation.\(^13\)
- PRF has supportive effect on immune system.\(^13\)
- PRF helps in hemostasis.\(^13\)

**Classification of Platelet Concentrate**
According to the classification proposed by Ehrenfest et al. (2009), four main families of preparations can be defined, depending on their cell content and fibrin architecture.\(^14\)

1. **P-PRP** (Pure Platelet Rich Plasma) products are preparations without leucocytes and with a low density fibrin network after activation.
2. **L-PRP** (Leucocyte and PRP) products are preparations with leucocytes and with a low-density fibrin network after activation.
3. **P-PRF** (Pure platelet-rich fibrin) preparations are without leucocytes and with a high density fibrin network. These products only exist in strongly activated gel form, and cannot be injected or used like traditional fibrin glues.
4. **L-PRF** (Leucocyte and platelet-rich fibrin) or second generation PRP products are preparations with leucocytes and with a high-density fibrin network.

**Second Generation Platelet Concentrate**
Includes -

**Properties Of Prf**
1. The biochemical analysis of the platelets rich fibrin (PRF) composition indicates that this biomaterial consists of an assembly of glycanic chains, cytokines, structural glycoproteins enmeshed within a slowly polymerized fibrin network. These biochemical components have well known synergetic effects on healing processes.\(^14\)
2. PRF is not only a platelet concentrate but also stimulate defense mechanisms. It is likely that the significant inflammatory regulation noted on surgical sites treated with PRF is the outcome of effects from cytokines trapped in the fibrin network and released during the remodeling of this initial matrix.\(^19\)

**Role of Fibrin Matrix of Prf**
- Fibrin is the natural guide of angiogenesis.
- Fibrin constitutes a natural support to immunity.
- Fibrin and wound coverage: Fibrin matrix guides the coverage of injured tissues, affecting the metabolism of epithelial cells and fibroblasts.\(^18\)

**Mode of Action of Prf**
At due to the lack of anticoagulant blood begins to clot as soon as it comes in contact with the glass surface of the test tube. Fibrinogen is converted to fibrin and the platelets get tapped into the fibrin network. This fibrin network could work as a resorb able membrane for guided bone regeneration.

**Advantages of Prf**
It is a single step centrifugation process which is comparatively simple as compared to PRP preparation
- It is obtained from autologous blood sample and does not require external thrombin; the risk of immunological reaction is negligible.
- The polymerization is a completely natural process.
- Economical, efficient, simple and quick procedure.
- The studies of PRF present it to be more efficient and with less controversies on its final clinical results when compared to PRP.\(^20\)
Table 1: A major content in various platelets concentrates.

<table>
<thead>
<tr>
<th>Platelet Concentrate</th>
<th>L-PRF</th>
<th>A-PRF</th>
<th>I-PRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucocytes +</td>
<td>Leucocytes +</td>
<td>Leucocytes + Platelets</td>
<td>Leucocytes + Platelets</td>
</tr>
<tr>
<td>Platelets + CD 34</td>
<td>Platelet</td>
<td>Higher levels of monocytes</td>
<td>+ Higher levels of monocyte.</td>
</tr>
<tr>
<td>T-lymphocytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD34+ B-lymphocyte (CD20+)</td>
<td></td>
<td>Higher quantity of lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Monocyte (CD68+)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Applications of PRF in various fields of dentistry:

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENDODONTICS</td>
<td>Revitalization of tooth with necrotic pulp and open apex</td>
</tr>
<tr>
<td>PEDODONTICS</td>
<td>Pulp capping, Pulpotomy, Apexogenesis.</td>
</tr>
<tr>
<td>ORTHODONTICS</td>
<td>Periodontally accelerated osteogenic orthodontics.</td>
</tr>
<tr>
<td>ORAL SURGERY</td>
<td>Wound healing</td>
</tr>
<tr>
<td>IMPLANTOLOGY</td>
<td>Enhance implant stability</td>
</tr>
<tr>
<td>PERIODONTOLOGY</td>
<td>Treatment of peri implant bone defect.</td>
</tr>
<tr>
<td></td>
<td>Early immediate loading</td>
</tr>
<tr>
<td></td>
<td>Treatment of mucogingival recession.</td>
</tr>
<tr>
<td></td>
<td>Periodontal regeneration in repair of intraboney and furcation defects.</td>
</tr>
<tr>
<td></td>
<td>Guided bone regeneration</td>
</tr>
</tbody>
</table>

DISCUSSION

PRF first described by Choukroun et al. is a new second generation of platelet concentrate. Simplified processing technique without any complex handling makes it superior to PRP. PRF can be used to promote wound healing, bone regeneration, graft stabilization, wound sealing, and hemostasis. Because the fibrin matrices are better organized, it is able to more efficiently direct stem cell migration and the healing program. Release of growth factors from PRF through in vitro studies and good results from in vivo studies led to optimize the clinical application of platelets rich fibrin. It was shown that there are better results of platelets rich fibrin over platelets rich protein. Dohan et al. proved a slower release of growth factors from PRF than PRP and observed better healing properties with platelets rich fibrin (PRF). It was observed and shown that cells are able to migrate from fibrin scaffold; while some authors demonstrated the PRF as a supportive matrix for bone morphogenetic protein as well.

CONCLUSION

Although PRF belongs to a new generation of platelet concentrates, the biologic activity of fibrin molecule is enough in itself to account for significant cicatricial capacity of the PRF. The slow polymerization mode confers to platelets rich fibrin (PRF) membrane as a particularly favorable physiologic architecture to support the healing process. However, it is necessary to look further into platelet and inflammatory features of this biomaterial. Only a perfect understanding of its components and their significance will enable us to comprehend the clinical results obtained and subsequently extend the fields of therapeutic application of this protocol.

Abbreviations

PRP = platelet-rich plasma
PRF = platelet-rich fibrin
L-PRF = leukocyte- and platelet-rich fibrin
T-PRF = Titanium-prepared platelet-rich fibrin
A-PRF = Advanced Platelet-Rich Fibrin
I-PRF= Injectable Platelet-Rich Fibrin
PDGF = platelet-derived growth factor
TGF-β = transforming growth factor-beta
PGRF = platelet rich in growth factor

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