

## Platelet-Rich Fibrin in Periodontal Regeneration

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### Abstract

**Background:** Periodontal disease is multifactorial regarding potential etiological factors and modifiers of achieved therapeutic effects. The treatment of this disease has been a challenge for periodontists for years. In recent years, new methods have begun to be implemented to regenerate periodontal tissue. One of these methods is platelet-rich plasma therapy in regenerating periodontal tissue. This study aimed to assess the potential benefits of platelet-rich fibrin (PRF) in periodontal regeneration.

**Material and Methods:** An electronic literature search was conducted using the National Library of Medicine, PubMed/MEDLINE, and the Scopus database, covering articles published from 2000 to 2023. Keywords used included "platelet-rich fibrin (PRF)," "PRF in periodontology," "PRF on gingival recession," and "PRF in infrabony pocket." The articles were selected based on title and abstract, focusing on clinical applications of PRF in periodontology. Inclusion criteria encompassed case reports, case series, original research, review papers, and both in vitro and in vivo studies, including animal studies and controlled clinical trials.

**Conclusion:** The use of PRF in the treatment of periodontal diseases, especially advanced platelet-rich fibrin, offers additional benefits in periodontal regeneration. Simplicity in the preparation, minor interventions, cost efficiency, and favorable clinical results have made this treatment method attractive for the regeneration of gingival recessions and the treatment of bone defects. The relatively small volume of PRF obtained from a single blood sample and the dependence on accurate handling and preparation are limitations that must be considered. (International Journal of Biomedicine. 2025;15(1):31-36.)

**Keywords:** platelet-rich fibrin • periodontal disease • gingival recession

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### Abbreviations

**A-PRF**, advanced platelet-rich fibrin; **CTG**, connective tissue graft; **DFDBA**, demineralized freeze-dried bone allograft; **L-PRF**, leukocyte- and platelet-rich fibrin; **OFD**, open flap debridement; **PRF**, platelet-rich fibrin; **PRP**, platelet-rich plasma; **SCTG**, subepithelial connective tissue graft.

### Introduction

Periodontal disease is a complex, multifactorial disease characterized by the loss of connective tissue attachment with the destruction of periodontal tissues. The aim of periodontal therapy is to eliminate the inflammatory process, prevent the progression of periodontal disease, and regenerate the lost periodontal tissues. Periodontal regeneration is a complex

multifactorial process involving biological events like cell adhesion, migration, proliferation, and differentiation in an orchestrated sequence.<sup>1</sup>

Periodontal regenerative procedures include soft tissue grafts, bone grafts, root biomodifications, guided tissue regeneration, and combinations of these procedures. The current perspective is that regenerative periodontal therapies can only restore a fraction of the original tissue volume<sup>2</sup> and

have a limited potential for complete periodontal restoration.<sup>3</sup> Often, tissues in the oral cavity are complex with bordering mineralized and soft tissue components, both of which harbor unique progenitor populations residing within specialized extracellular matrix frameworks.<sup>4,5</sup>

Mimicking such complex environments using chemically homogenous scaffolds and uniform stem cell populations is often challenging. Instead, recent approaches favor complex natural scaffolds that allow for repopulation with the patient's own cells, thereby producing an autologous tissue-engineered organ.<sup>6</sup>

One such complex natural scaffold ideally suited for autologous tissue regeneration is platelet-rich fibrin (PRF), a second-generation platelet concentrate developed as an improvement over the earlier introduced platelet-rich plasma (PRP) to aid tissue repair and regeneration.<sup>7</sup>

Platelets play a key role in wound healing, and hence, wound healing after periodontal treatment can be accelerated by the use of platelet concentrates. The wound healing process initiated by the formation of blood clots and after tissue injury in periodontal surgery causes adherence and aggregation of platelets, favoring the formation of thrombin and fibrin.<sup>8</sup>

The main aim of this review was to briefly describe the novel platelet concentrate PRF and its potential role in periodontal regeneration.

## Material and Methods

An electronic literature search was conducted using the National Library of Medicine, PubMed/MEDLINE, and the Scopus database, covering articles published from 2000 to 2023. Keywords used included "PRF," "PRF in periodontology," "PRF on gingival recession," and "PRF in infrabony pocket." The articles were selected based on title and abstract, focusing on clinical applications of PRF in periodontology. Inclusion criteria encompassed case reports, case series, original research, review papers, and both in vitro and in vivo studies, including animal studies and controlled clinical trials.

## Topics

### *Biological Aspects*

Platelet-rich fibrin (PRF), classified as a leukocyte- and platelet-rich fibrin (L-PRF), often named Choukroun's PRF after its inventor, to avoid any confusion with other techniques using similar names such as Vivostat PRF (Vivolution, Allerød, Denmark), a pure platelet-rich plasma (PRP) or Fibrine PRF (Cascade Medical, Wayne, NJ) matrix (without leukocyte).<sup>9,10</sup> Platelet-rich fibrin (PRF) belongs to the second-generation platelet concentrate, collecting on a single fibrin membrane containing constituents of blood samples favorable for healing and immunity.<sup>11,12</sup>

### *Platelet Concentrate Evolution*

Kingsley in 1954 first used the term PRP to earmark thrombocyte concentrate during experiments related to blood coagulation.<sup>13</sup> In 1970, fibrin glue was introduced by Matras, which improved the healing of skin wounds in rat models.

Fibrin glue was made by polymerizing fibrinogen with thrombin and calcium. However, due to the low concentration of fibrinogen in donor plasma, the quality and stability of fibrin glue were suboptimal.<sup>14</sup> Simultaneously, Choukroun et al., in 2000, developed another form of platelet concentrate in France, which was labeled as PRF, based on the strong fibrin gel polymerization found in this preparation. It was stamped as a "second-generation" platelet concentrate because it was obviously different from other PRPs. This proved an important milestone in the evolution of terminology.<sup>7</sup>

In 2009, Dohan Ehrenfest et al.<sup>15</sup> proposed the first classification of platelet concentrate. The authors classified the different platelet concentrates into four categories, depending on their leucocyte and fibrin content: "pure platelet-rich plasma (P-PRP), such as cell separator PRP, Vivostat PRF or Anitua's PRGF; leucocyte- and platelet-rich plasma (L-PRP), such as Curasan, Regen, Plateltex, SmartPREP, PCCS, Magellan or GPS PRP; pure platelet-rich fibrin (P-PRF), such as Fibrinet; and leucocyte- and platelet-rich fibrin (L-PRF), such as Choukroun's PRF." A major advantage of PRF is that it has a simple preparation protocol.

Choukroun,<sup>16</sup> in 2014, introduced an advanced PRF called A-PRF (claimed to contain more monocytes).

### *Protocol of Preparation*

The initial protocol for PRF production, introduced by Choukroun et al. in 2001, requires 10 mL of blood sample to be collected without anticoagulant in glass-coated plastic tubes, which is immediately subject to centrifugation at 2,700 rpm (around 400g) for 12 min. The obtained PRF is usually termed Choukroun's PRF or leukocyte- and platelet-rich fibrin (L-PRF). However, the PRF protocol underwent several modifications in the last few years. These protocols led to the formation of various products with different biology and potential uses.<sup>17</sup>

Since it is well-known that high centrifugal forces shift cells to the bottom of the tube, it was proposed that decreased centrifugation speed may prevent cell loss and increase leukocyte number in the PRF matrix. Advanced PRF (A-PRF) was provided using a reduced centrifugal force of 1,500 rpm (230 g) for 14 min and glass-based vacuum tubes. The obtained A-PRF is richer in the total number of viable cells compared to the L-PRF. Among them, an increase in the number of neutrophils, lymphocytes, and platelets was observed.<sup>18</sup>

Production of A-PRF may also be obtained using the same centrifugation time (14 min) but with a centrifugation speed of 1,300 rpm (200g), as was suggested later.<sup>19</sup>

Recent research provided a new protocol for a liquid variation of PRF called injectable PRF (i-PRF). This injectable form of PRF is produced by using blood without anticoagulant and centrifuged at 700 rpm (60g) for 3 min in plastic tubes without any coatings.<sup>20</sup> Plastic tubes used in this protocol do not effectively activate the coagulation process since they possess hydrophobic surfaces.<sup>21</sup>

### *Advantages and Disadvantages in the Use of PRF*

Some advantages are reported in the literature related to the use of PRF, such as the following: its preparation is

a simplified and efficient technique, with centrifugation in a single step, free and openly accessible for all clinicians.<sup>22,23</sup> Platelet-rich fibrin is obtained by an autologous blood sample,<sup>24</sup> and blood manipulation is minimized.<sup>25</sup> It does not require the addition of external thrombin because polymerization is a natural process without any risk of suffering from an immunological reaction.<sup>25</sup>

Platelet-rich fibrin has a natural fibrin framework with growth factors that may keep their activity relatively long and stimulate tissue regeneration effectively. Used as a membrane, it avoids a donor-site surgical procedure and results in a reduction in patient discomfort during the early wound-healing period.<sup>26</sup> The studies of platelet-rich fibrin present it to be more efficient and with less controversies on its final clinical results when compared to platelet-rich plasma.<sup>27</sup>

Platelet-rich fibrin may present some disadvantages: The final amount available is low because it is autologous blood.<sup>28</sup> The success of the PRF protocol depends directly on the handling, mainly related to blood collection time and its transference for the centrifuge.<sup>29</sup> A glass-coated tube is needed to achieve clot polymerization.<sup>23</sup>

### ***Use of PRF in Gingival Recession***

Gingival recession or soft tissue recession is defined as the displacement of the gingival margin apical to the cement-enamel junction (CEJ) of a tooth or the platform of a dental implant.<sup>30,31</sup>

This condition is associated with the loss of periodontal tissues, including gingiva, periodontal ligament, root cementum, and bone at dental sites, as well as the loss of mucosa and bone around dental implants. It has been suggested that the term 'periodontal recession' rather than 'gingival recession' would represent a more accurate definition of this condition at teeth.<sup>32</sup>

In the context of gingival recession therapy, the regenerative capacity of advanced platelet-rich fibrin (A-PRF) is applied to stimulate the growth of gingival tissues, promoting more proper wound healing and the restoration of a healthful periodontium.<sup>32-35</sup>

Clinical efficacy of subepithelial connective tissue graft and A-PRF in treating gingival recession was performed by Anegundi et al.<sup>36</sup> in 17 patients. The authors compared and evaluated subepithelial connective tissue graft (SCTG) and advanced platelet-rich fibrin (A-PRF) membrane-based root coverage in the treatment of gingival recession type 1 (RT1). Their study results suggested that both SCTG and A-PRF can be used in treating gingival recessions. However, SCTG was better for achieving root coverage and increasing keratinized tissue width.

Abu-Ta'a<sup>37</sup> compared the clinical outcomes of advanced platelet-rich fibrin (A-PRF) and connective tissue graft (CTG) in treating marginal tissue recessions. His study demonstrates that A-PRF and CTG effectively manage gingival recession defects. However, connective tissue graft resulted in better clinical outcomes in terms of reduction in recession height and width.

Tadepalli et al. compared the clinical efficacy of leukocyte platelet-rich fibrin (L-PRF) and advanced platelet-

rich fibrin (A-PRF) in combination with coronally advanced flap (CAF) in the treatment of gingival recession defects. Based on the findings of this study, both L-PRF and A-PRF may be suggested as viable treatment options for managing gingival recession in the maxilla.<sup>38</sup>

### ***Use of PRF for the Treatment of Periodontal Infrabony Defects***

True and complete periodontal regeneration is complex since it involves a complex interaction of epithelium, gingival connective tissue, periodontal ligament, and alveolar bone. True periodontal regeneration should also include Sharpey's fibers spanning from the cementum through the periodontal ligament (PDL) and into the alveolar bundle bone. Many attempts utilizing various strategies, including bone grafts, barrier membranes, and biologic agents, have been proposed, yet to date, complete periodontal regeneration remains very challenging and unpredictable.<sup>39</sup> One strategy proposed several years ago to regenerate infrabony defects was platelet concentrates.<sup>40</sup>

In a study by Agarwal et al.,<sup>41</sup> 60 interproximal infrabony defects in 30 healthy, non-smoker patients diagnosed with chronic periodontitis were randomly assigned to PRF/demineralized freeze-dried bone allograft (DFDBA) group or the DFDBA/saline group. Compared with baseline, 12-month results indicated that both treatment modalities significantly changed all clinical and radiographic parameters. However, a combination of PRF and DFDBA was more effective than DFDBA with saline for treating infrabony periodontal defects.

Platelet-rich fibrin can be used with open flap debridement (OFD) to treat infrabony defects. In a study by Ajwani et al.,<sup>42</sup> the clinical efficacy of open flap debridement with or without platelet-rich fibrin in the treatment of infrabony defects was evaluated. It was found that adjunctive use of platelet-rich fibrin with open flap debridement significantly improves defect fill compared to v alone. Platelet-rich fibrin has consistently been showing regenerative potential; it is a simple, easy, and inexpensive biomaterial compared with bone grafts.

The same results were shown by Sharma & Pradeep.<sup>43</sup> Fifty-six infrabony defects were treated with either autologous platelet-rich fibrin with open flap debridement or open flap debridement alone. The researchers found more significant probing depth reduction, periodontal attachment level gain, and bone fill at sites treated with platelet-rich fibrin with conventional open flap debridement compared to conventional open flap debridement alone.

In a study by Martande et al.,<sup>44</sup> the combined efficacy of platelet-rich fibrin and 1.2% atorvastatin gel with open flap debridement in the treatment of infrabony defects in individuals with chronic periodontitis showed similar improvements in clinical parameters with a greater percentage of radiographic defect depth reduction compared with platelet-rich fibrin alone.

Autologous platelet-rich fibrin combined with bioactive glass was found to be more effective in gaining clinical attachment levels, reducing probing pocket depth, and achieving greater bone fill compared to treatment with bioactive glass alone in periodontal infrabony defects.<sup>45</sup>

## Conclusion

The use of platelet-rich fibrin in the treatment of periodontal diseases, especially advanced platelet-rich fibrin, offers additional benefits in periodontal regeneration. Simplicity in the preparation, minor interventions, cost efficiency, and favorable clinical results have made this treatment method attractive for the regeneration of gingival recessions and the treatment of bone defects. Current studies, *in vitro* and *in vivo*, have confirmed safe and encouraging results related to using platelet-rich fibrin alone or in a mixture with other biomaterials. PRF treatment has several indications and advantages for periodontal tissue regeneration. It has been shown to improve and promote natural support for tissue healing. Although platelet-rich fibrin has shown favorable clinical results, challenges still exist in the efficiency of its application and in ensuring consistent and predictable results in different clinical situations. The relatively small volume of platelet-rich fibrin obtained from a single blood sample and the dependence on accurate handling and preparation are limitations that must be considered.

## Competing Interests

The authors declare that they have no competing interests.

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