How can the use of platelet-rich fibrin benefit the extraction of mandibular third molars?

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Abstract: Surgery for the removal of third molars is a surgical procedure commonly performed in Dentistry. It is associated with inflammatory events and possible complications, being more evident after the removal of lower molars, since in most cases there is a need for more invasive approaches. It is essential for the dentist to minimize such effects, providing a more peaceful postoperative period with less morbidity for the patient. In this context, platelet-rich fibrin (PRF) was developed, which is considered a platelet aggregate obtained by centrifugation of the patient's own blood and proposes to minimize inflammatory effects, accelerate healing and repair processes, and reduce postoperative complications. A literature review on the effect of L-PRF in sockets after the removal of mandibular third molars was conducted, evaluating its efficacy on pain, swelling, trismus, and healing. A bibliographic survey was performed on the PubMed, Web of Science, and Elsevier databases, using the following descriptors: 'platelet rich fibrin', 'third molar', and 'surgery', limiting to articles written in English published from 2013 to 2023. Thus, we have a current scientific overview of the real effect of using this platelet aggregate in the extraction of lower third molars. The studies reviewed, for the most part, showed positive results in improving pain, swelling, trismus, and healing.

Keywords: Platelet-rich fibrin; Third molar; Surgery.

1. Introduction

Third molars, popularly known as wisdom teeth, represent the last teeth to develop in the human dental arch, typically erupting between the ages of 16 and 27 [1]. Despite their original function in chewing, their presence often associates with complications, generating a flow of patients in dental offices reporting painful complaints in the posterior region of the jaws. The indication for the extraction of wisdom teeth is based on the dentist's assessment, considering the difficulty of cleaning due to their location and consequently leading to the accumulation of bacteria that can cause severe inflammations and infections, being a determining factor for the removal of the third molars [2].

To perform a complete diagnosis, an imaging examination, preferably a panoramic radiography, is necessary to assess the position of the tooth to be extracted, any relationship with noble structures, the incidence of cavities or bone resorptions that may be occurring; as the decision and planning of the removal surgery (exodontia) will directly depend on such factors [3]. Various inflammatory events are related to the exodontia of mandibular third molars, mainly because most cases require ostectomy, which involves bone removal, odontosection, referring to the division of the tooth into smaller parts, or a possible access, making the surgery more complicated and with a higher incidence of undesirable post-operative signs and symptoms such

as pain, swelling, and trismus, which significantly interfere with the patient's quality of life [4].

Faced with this problem, researchers in the field seek innovations in techniques and materials to bring comfort and a postoperative period with less morbidity for patients. One technique that is gaining ground is the preparation of platelet-rich concentrates introduced in Dentistry in the field of surgery. By centrifuging a sample of the patient's blood until the red blood cells are removed, a suspension rich in white blood cells (platelets), which are body cells responsible for tissue healing [5], is obtained. This suspension acts as a surgical additive, inserted locally, increasing cell mitosis, collagen production, the growth of blood vessels, among other important factors in regeneration [6].

The first generation of autologous platelet aggregates (made from the patient's own blood) was called Platelet-Rich Plasma (PRP), such biomaterial after a long preparation time, is centrifuged and subsequently receives anticoagulant substances such as sodium citrate, which act by blocking the natural coagulation process, in addition to elements to initiate platelet movement and activation of the clot more quickly, such as thrombin, more specifically of the bovine type. PRP gained prominence in regenerative dentistry, especially in endodontics, periodontics, and oral and maxillofacial surgery [7]. However, the use of PRP presents some limitations, despite some positive results, criticisms arose due to the possible immune response to the presence of bovine thrombin factor V, which can lead to changes in coagulation [8]. Other characteristics that lead to a reduction in its applicability are the use of double centrifugation as a method of preparation, making the process more complex, the need to add anticoagulant, such as the previously mentioned thrombin, the short lifespan of the platelets, and a decrease in the concentration of cytokines and growth factors due to a rapid release, which will reduce their bioavailability [9].

Eager to find promising alternatives that would replace PRP with a material with better cost-benefit, presenting fewer risks, good availability, and meeting the needs for good tissue regeneration and efficient healing, Chockroun and his collaborators developed the Platelet-Rich Fibrin (PRF) method, the second generation of autologous platelet aggregates, now without the need for the use of anticoagulants in its preparation, being a simpler, cheaper, and safer option for the patient [10]. PRF uses the same collection technique as PRP, however, instead of blood plasma, fibrin is used. Fibrin is a protein present in the blood that is responsible for clot formation and can be used as a support agent for platelets. Thus, PRF presents advantages over PRP, such as the possibility of using a smaller amount of the patient's blood and greater stability of the platelet concentration [11].

The process involves collecting a small amount of blood (10-20 ml) in a special collection tube and then centrifuging the blood at a medium speed of 3,000 rotations per minute [9]. This separates the blood into three layers: platelet-rich plasma, platelet-rich fibrin, and a layer of red blood cells. The intermediate layer of PRF is then collected and can be used for therapeutic purposes. It has been used in dentistry as a safe and effective alternative to promote healing and tissue regeneration in various clinical situations, including the exodontia of third molars.

Platelet-Rich Fibrin (PRF) is a derivative of blood plasma that contains a high concentration of platelets and growth factors. There are various types of PRF, with L-PRF (Leukocyte-Platelet-Rich Fibrin) being a specific notable variant, especially used in procedures such as exodontia. L-PRF is employed in sockets after the extraction of mandibular third molars due to its regenerative and tissue healing properties [9]. Its application in this specific context has demonstrated effectiveness in reducing post-operative discomfort and promoting a faster recovery [12]. PRF is currently used in various areas, both dental and medical, in facial harmonizations, implants, treatments of gingival recessions, being a positive factor especially in the context of surgeries of mandibular third molars, which based on discussions in the literature, its use proved to be quite effective, where it is inserted into the patient's alveolus,

the cavity of the maxilla and mandible bones where the teeth are housed, to obtain a more comfortable postoperative period [13].

The use of L-PRF is very promising in third molar surgeries, yet it is not yet a practical reality for most dentists. Therefore, this work aims to highlight the importance and clinical benefits of this relatively new technique that has been widely used in dental procedures. A literature review can provide an overview of the clinical results of these procedures. This is extremely relevant for dental professionals seeking to offer increasingly effective and safe treatments to their patients. The use of platelet-rich fibrin is an example of how technology can be applied to improve dental procedures and offer a faster and more efficient recovery for patients. This review can contribute significantly to the understanding of the use of PRF in dental procedures of third molar exodontia, offering important information for professionals, researchers, and students interested in deepening their knowledge on this topic.

2. Methodology

To conduct this research, an adaptation of the method presented by Petter et al. [14] was used. The process was divided into four stages: characterization of the study where search, selection, and inclusion criteria are defined; data collection where the search is actually conducted, and the works are compiled; analysis of the data according to established criteria; and summarization and presentation of results.

2.1 Study Characterization

The first step is the study characterization, which was divided into seven activities:

1. Definition of the topic, "Use of platelet-rich fibrin in mandibular third molar extractions." This topic was chosen due to interest in delving into methods that assist in the recovery from extractions, specifically of the mandibular third molar, due to a higher incidence of inflammatory events and post-surgical complications.

2. Definition of descriptors. Based on the selected topic, three English-language descriptors were chosen due to the selection criterion that will be reported below. The descriptors are "Platelet rich fibrin," "Surgery," "Third Molar."

3. Boolean operators are used in bibliometric works to combine search terms and refine queries, allowing the construction of complex and precise queries to retrieve relevant information from bibliographic studies. In this work, the operator "And" was used, making the search functional only when all three descriptors are present in the resulting files.

4. Search platforms are the databases that were used to conduct the queries based on the previously mentioned descriptors. The databases PubMed, Web of Science, and Elsevier were chosen due to their popularity and credibility in the academic community.

5. Selection criteria were chosen to refine the search in the databases. The searches were limited to English-language works from the last 10 years (2013 - 2023).

6. For the selection of articles to be included or excluded, the Rayyan website was used, due to its capability to organize and highlight keywords in the title and body of the text.

7. The inclusion criteria were: complete articles, in English, being clinical trials, and dated from the last ten years, and excluded were works dealing with systematic reviews, meta-analyses, clinical trials that noted alveolar osteitis, and duplicated articles among the three platforms.

2.2 Data Collection

In the data collection, the second stage, there were four activities. The first was the search of works, which consisted of conducting the search of articles using the Boolean operator and the determined descriptors in the previous stage and applying the available filters on each platform regarding the type of work, publication year, and language. In the second activity, the articles were selected, and the following quantities of works were obtained: 73 on PubMed, 44 on Web of Science, and 42 on Elsevier, totaling 159 works. These works were downloaded and allocated on the online platform Rayyan, which is a site to assist researchers in the method section of systematic review articles, being these the third and fourth step.

2.3 Data Analysis

In the data analysis stage, with the use of the Rayyan software, the inclusion and exclusion criteria defined in item 7 of topic 2.1 were applied, considering the title and summary of the articles. 29 works were deleted for being duplicated among the platforms. Of the remaining 130, 108 articles were excluded due to the chosen criteria, leaving 22 works to be analyzed more deeply. Of these, 12 came from PubMed, 7 from Web of Science, and 3 from Elsevier. The remaining 22 works were read, summarized, and critically analyzed taking into consideration the objective of the work to identify the outcome of the use of PRF in the postoperative period of third molar extractions.

2.4 Results

To conclude the work, we have the last stage with two activities: identification of the studies and summarization. First, a thorough reading of the articles and identification of the results of the authors concerning the use of PRF in the proposed works were conducted. The results, whether positive or negative, were summarized to be presented to the reader. In this stage, an attempt was made to ascertain similar results among various authors, confirming the beneficial or harmful use of this material in surgeries of mandibular third molars.

3. Results and discussion

The literature review conducted in this study aimed primarily to identify the influence of platelet-rich fibrin in the context of mandibular third molar extractions, with a particular focus on the reduction of postoperative pain, swelling, and trismus. In some studies, it was also analyzed whether healing benefited from the use of this platelet aggregate. All 22 articles were read to gather information such as the inclusion criteria used by each author, the number of patients studied in each work, the year of publication, and, as the most important criterion, the results obtained in each study. All the works and this obtained information were then summarized and condensed and can be verified in Table 1.

Table 1: Summary of the information obtained from the analyzed studies.

| Reference	Inclusion Criteria	Number of Patients	Pain	Swelling	Trismus	Soft Tissue Healing
[15]	Patients with an average age of 26 years	31	Positive	Positive	Positive	Not Evaluated
[16]	Patients aged 18 to 28 years	20	Not Evaluated	Not Evaluated	Not Evaluated	Positive
[17]	Patients aged 19 to 31 years, both genders,	20	Positive	Not Evaluated	Positive	Not Evaluated

	no systemic diseases, impacted lower third molars					
[18]	Patients aged 18 to 31 years, normosystemic	59	Positive	Negative	Negative	Not Evaluated
[19]	Patients aged 16 to 27 years, no blood coagulation issues	30	Not Evaluated	Not Evaluated	Not Evaluated	Positive
[20]	Patients over 18 years old, asymptomatic, normosystemic	30	Negative	Negative	Negative	Not Evaluated
[21]	Patients aged 17 to 27 years, both genders, no systemic diseases, bilaterally impacted lower third molars	30	Positive	Positive	Not Evaluated	Not Evaluated
[22]	Patients aged 18 to 30 years, both genders, no systemic alterations, partially erupted unilateral M3	60	Positive	Positive	Positive	Not Evaluated
[23]	Patients aged 18 to 50 years, both genders, surgery site free of infection, no systemic diseases	60	Not Evaluated	Positive	Not Evaluated	Positive
[24]	Patients over 18 years, presenting clinical signs like abscess, pericoronitis, chronic pain from the third molar	60	Positive	Positive	Positive	Not Evaluated
[25]	Patients aged 18 to 35 years, no systemic diseases	25	Not Evaluated	Not Evaluated	Not Evaluated	Positive
[26]	Patients aged 18 to 60 years, both genders, no systemic diseases and no NSAIDs use in	34	Positive	Positive	Not Evaluated	Not Evaluated

	the 4 weeks prior to surgery					
[27]	Patients aged 18 to 40 years	30	Positive	Positive	Positive	Positive
[28]	Patients aged 16 to 29 years, both genders, no systemic alterations, bilateral extraction of lower third molars	20	Positive	Not Evaluated	Not Evaluated	Positive
[29]	Patients aged 18 years, reporting pain, swelling, or sensitivity in the third molar region	25	Positive	Positive	Not Evaluated	Not Evaluated
[30]	Patients aged 18 to 40 years, normosystemic, impacted third molar with indication for extraction	75	Negative	Negative	Negative	Not Evaluated
[31]	Patients aged 18 to 30 years, no systemic diseases, no local infection, third molars with level A class I	20	Positive	Not Evaluated	Not Evaluated	Positive
[32]	Patients aged 18 to 40 years, no systemic diseases	75	Positive	Positive	Not Evaluated	Not Evaluated
[33]	Patients aged 18 to 40 years	44	Positive	Positive	Positive	Not Evaluated
[34]	Patients aged 18 to 35 years	10	Positive	Positive	Positive	Not Evaluated
[35]	Patients over 18 years, healthy teeth, normosystemic	30	Not Evaluated	Positive	Not Evaluated	Not Evaluated
[36]	Patients aged 18 to 50 years, normosystemic, asymptomatic third molar	48	Positive	Positive	Positive	Not Evaluated

The studies were organized by year of publication, and it was identified that the largest number of studies was from the year 2018, as shown in Figure 1, with a total of 5 articles (23% of the selected articles). Eight works, representing 36%, are from 2020 to 2023, with at least one work found in each year, indicating that this remains a highly relevant and recurrent academic topic. The frequency of these studies and the updating of results with the advancement of technologies and methods make the findings more significant.

The summarization of the works can be found in Table 1, with columns separated into: author, year of publication, inclusion criteria used by the authors, number of people analyzed in each study, the database from which the work was found, and results obtained with improvements in pain, swelling, trismus, and healing. For the inflammatory criteria, the results were classified as "positive", where the study analyzed the issue and noted improvement with the use of L-FRP; "negative", when the author considered that the use was not significantly beneficial compared to the control group without the use of the platelet aggregate; and "not evaluated" when the author did not present results indicating positive or negative improvements regarding the reduction of one or more chosen inflammatory events.

Figure 1: Number of articles by year of publication.
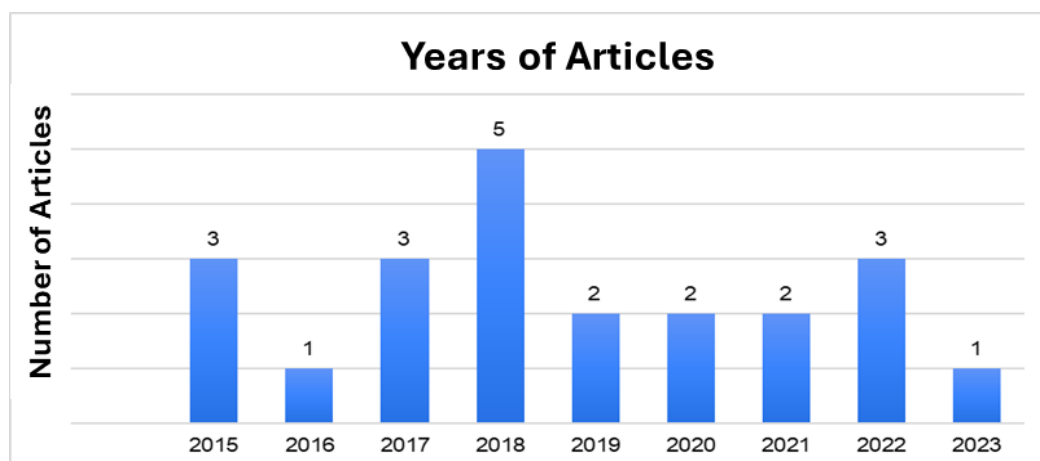
In total, adding the patients from all the studies, there are 836 patients (Figure 2). More than half of the studies used a minimum group of 30 people for their research, and two studies selected 75 people each, making the results of these studies more significant. Conversely, the study by Donmezer and Bilginaylar (2021) showed positive results, while the study by Torul, Omezli, and Kahveci (2020) showed negative results, cancelling each other out if analyzed only by the end result without considering the methodology. The two studies that presented negative results will be further analyzed at the end of the Discussion section.

4. Discussion

Among the three inflammatory events (pain, swelling, and trismus), pain showed the best results, with improvement noted in 15 studies (68%). Swelling also showed significant improvement, reported in 13 studies (two fewer than pain). Trismus and healing were the least evaluated, with trismus assessed in only 11 studies (50%) and healing in just 6, as shown in Table 2 and Figure 3. Based on the data, it is evident that improvement in pain and swelling is an expected outcome with the use of L-FRP and is positive in most cases. However, trismus, which is also a symptom that could be improved, was not evaluated by all authors. Some focused mainly on the analgesic and anti-inflammatory effects of platelet-rich fibrin, considering these aspects crucial for postoperative success [21, 26, 29, 32]. There may be a lack of con-

sensus in the scientific community about the clinical importance of trismus as a relevant parameter in postoperative studies of third molar extraction. This might have influenced the decision of some authors not to evaluate trismus. Considering the three inflammatory events: pain, swelling, and trismus; seven studies presented in Table 1 showed positive results in all three variables simultaneously.
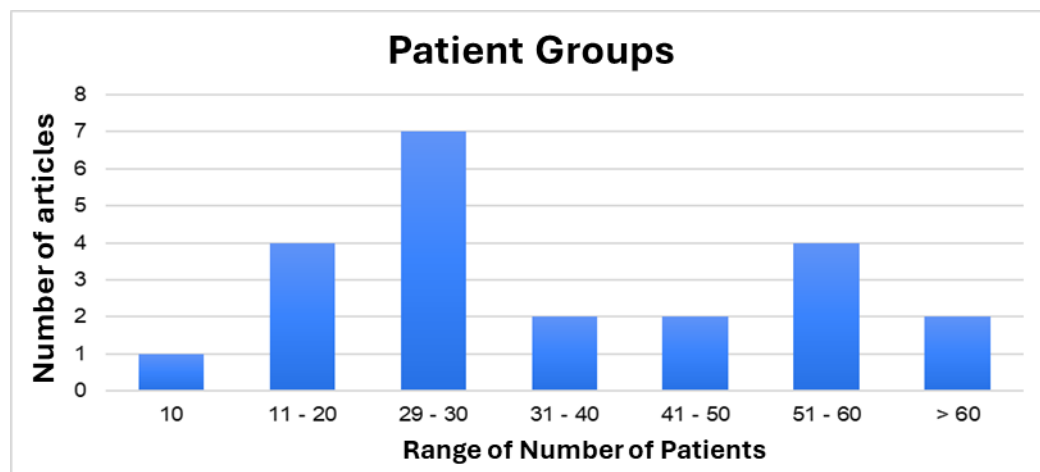
Figure 2: Patient Groups.

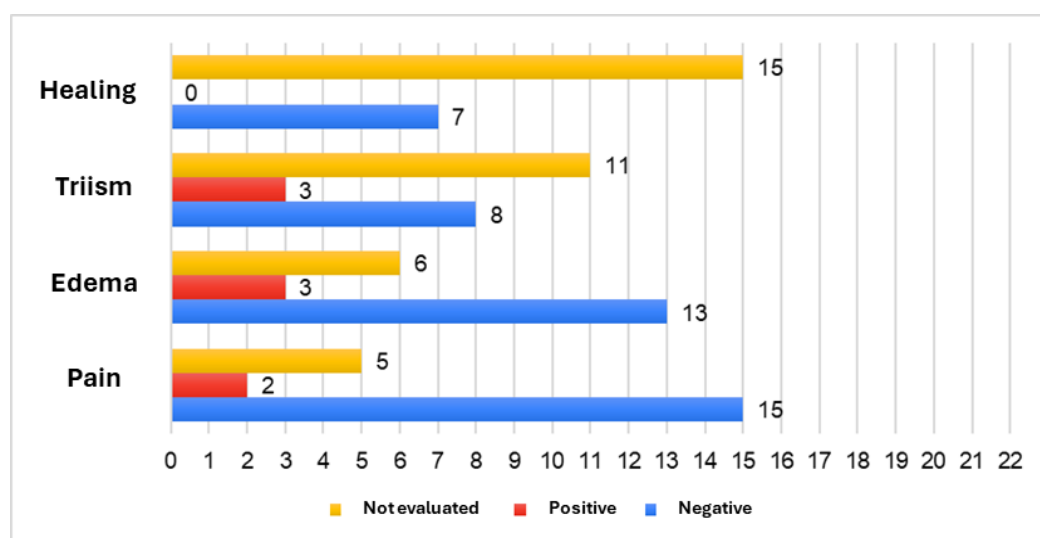**Figure 3:** Graph of Results in the Improvement of Observed Symptoms.

Table 2: Positive, Negative, and Not Evaluated Results.

Effect	Positive Count	Positive (%)	Negative Count	Negative (%)	Not Evaluated Count	Not Evaluated (%)
Pain	15	68%	2	9%	5	23%
Swelling	13	59%	3	14%	6	27%
Trismus	8	36%	3	14%	11	50%
Healing	7	32%	0	0%	15	68%
Total Articles			22			

Soft tissue healing was not heavily debated among authors and considered in the evaluations we analyzed, with 73% of the studies not assessing this factor. However, three authors focused their results specifically on this improvement, as was the case with Yelamali et al. [16], Guzmán Castillo et al. [19], and Revathy et al. [25]. Measuring parameters like pain is subjective, while edema and trismus are assessed through measurements and consequently more concrete results are found. However, quantifying them objectively compared to the visual or instrumental assessment of healing can still be a challenging task. This may lead some studies to opt for a more tangible and measurable approach, which does not necessarily mean that there were no improvements in other symptoms, just that they were not assessed. The positive results we identified in the healing studies may be directly related to the fact that platelet-rich fibrin fills the alveolus to prevent the entry of food and debris and presents a pattern similar to healing by first intention, thereby favoring the postoperative healing process [9].

The age range of patients in the studies varies, spanning from teenagers to older adults. Most studies seem to focus on young adults, generally between 18 and 40 years old. This can be attributed to the prevalence of third molar extraction in this age group, indicating a specific clinical application for this group. The clinical relevance of using platelet-rich fibrin may vary with age. For example, in younger patients, rapid recovery may be crucial, while in older adults, special attention may be necessary due to possible comorbidities. Dar et al. [23] in their work, noted that the bone around the teeth in younger patients is more malleable and elastic than in older patients, where the bone is more rigid. This implies that extracting teeth in older patients may require the removal of more bone, making the procedure more challenging and potentially causing more pain, swelling, and trismus postoperatively. However, no significant differences were observed in demographic variables, including sample size, sex, and age in the work of Daugela et al. [26], which included people from 18 to 60 years old.

It is important to consider that the diversity in age range highlights the importance of conducting specific studies for different age groups. This may include considerations about physiological response, tolerance to procedures, and specific challenges associated with recovery at different ages. In summary, the conclusion about the age of patients suggests the need to consider age range when interpreting and applying the results of these studies. A personalized approach for different age groups may be crucial to optimizing the postoperative benefits of platelet-rich fibrin in third molar extraction surgeries.

Overall, the results consistently indicate favorable outcomes for the use of platelet-rich fibrin in the postoperative period of third molar extraction surgeries, encompassing pain reduction, edema, trismus, and improved healing. This convergence of results may strengthen the evidence of the efficacy of this intervention in this specific context. However, two specific studies showed results that question this consistency, as they presented negative results in all three inflammatory events. In an attempt to identify the reason behind these negative results, relationships were investigated in common between the methodology of the two studies. The authors Asutay et al. [20] and Torul et al. [30] reported in each of their studies that no antibiotic prophylaxis measures were taken, which may have allowed the development of infections, contributing to adverse outcomes in the analyzed parameters. Negative results may highlight the importance of antibiotic prophylaxis in oral surgery, especially in procedures involving the extraction of third molars. However, despite these studies presenting negative results, Gülşen et al. [21] also did not use anti-inflammatories or antimicrobials but obtained positive results regarding the use of L-FRP.

4. Conclusion

Most of the analyzed studies show positive results regarding the use of L-FRP. This suggests consistency in the potential benefits of using platelet-rich fibrin in the postoperative period of third molar extraction. The assessment of inflammatory

events: pain, edema, and trismus, revealed that pain obtained the most consistently positive results, closely followed by the improvement of edema. However, trismus and healing were underestimated in many studies, demonstrating a gap in comprehensive understanding of these parameters. Despite the general consistency of favorable results for L-FRP, two studies highlighted negative results, hypothesizing that these outcomes were associated with the absence of antibiotic prophylaxis measures. This would emphasize the importance of antibiotic prophylaxis in oral surgery, especially in procedures that involve the extraction of third molars.

The systematic use of L-FRP appears to be a very promising option to foster and accelerate tissue healing and reduce inflammatory events resulting from the extraction of third molars. However, research with larger samples on this topic is necessary, with the aim of making the use of L-PRF an increasingly predictable alternative.

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