



Major clinical outcomes of the use of biostimulators (L-PRF and coenzyme Q10) in the optimization of buccomaxillofacial surgery: a systematic review

Patricia Consuelo Nacimba Medina^{1,3,4*}, Brian Steven López^{2,3,4}, Igor Mariotto Beneti^{3,4}

¹ Dental Sty Clinic. Av. Ignacio de Veintimillay 9 de Octubre-Quito, Ecuador.

² Autonomous Regional University of Los Andes. Ambato, Tungurahua, Ecuador.

³ Unorte - University Center of Northern São Paulo, Dentistry department, São José do Rio Preto, São Paulo, Brazil.

⁴ Unipos - Post graduate and continuing education, Dentistry department, São José do Rio Preto, São Paulo, Brazil.

*Corresponding author: Dr. Patricia Consuelo Nacimba Medina.

Dental Sty Clinic. Av. Ignacio de Veintimillay 9 de Octubre-Quito, Ecuador.

E-mail: pattynacimba@hotmail.com

DOI: <https://doi.org/10.54448/mdnt24110>

Received: 10-15-2023; Revised: 01-24-2024; Accepted: 01-27-2024; Published: 02-07-2024; MedNEXT-id: e24110

Abstract

Introduction: Tissue engineering combines three key elements matrix (three-dimensional structures that support growth, collagen cell, bone mineral), signaling molecules (growth factors (GF) and leukocyte cytokines), and cells (osteoblasts, fibroblasts or other adequate populations for tissue regeneration. Many studies suggest that antioxidants act as inhibitors of osteoclastogenesis and the inhibitory effect of CoQ10 on osteoclast differentiation. These findings highlight the potential therapeutic applications of CoQ10 for the treatment of bone diseases. **Objective:** The present study highlighted the main approaches to the use of fibrin-rich plasma (L-PRF) and coenzyme Q10 in buccomaxillofacial surgery through a systematic review.

Methods: The systematic review rules of the PRISMA Platform were followed. The search was carried out from October 2023 to January 2024 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases, using articles from 2006 to 2022. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed accordingly, according to the Cochrane instrument. **Results and Conclusion:** A total of 104 articles were found, 38 articles were evaluated and 23 were included and developed in this systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 36 studies with a high risk of bias and 20 studies that did not meet GRADE. The use of platelet and leukocyte-rich fibrin can reduce bone absorption, infection, pain, local edema, and wound healing. L-PRF presents itself as an autogenous biomaterial with great versatility, low cost,

easy acquisition and wide use, and infinite possibilities. It can be combined with other materials in the most diverse areas of dentistry. Also, CoQ10 concentrations can suppress ROS, which is needed as a signaling intermediate. CoQ10 acts as an enhancer of all stages of osteoblastic differentiation. Thus, CoQ10 suppresses osteoclast differentiation by eliminating generated intracellular ROS. Furthermore, CoQ10 enhances bone regeneration in all differentiation processes through transcription factor activity.

Keywords: Tissue engineering. Bone bioengineering. Fibrin-rich plasma. Coenzyme Q10. Buccomaxillofacial.

Introduction

Tissue engineering is a multidisciplinary field based on recent advances in medicine and surgery, molecular and cellular biology, polymer chemistry, and physiology. Its primary purpose is the development and manipulation of molecules, cells, tissues, or organs grown in the laboratory, artificial implants, and tissue generated without the laboratory capable of replacing, stimulating, or supporting the function of defective or injured parts of our body [1,2].

In this sense, tissue engineering combines three key elements: matrix (three-dimensional structures that support growth, collagen cell, bone mineral), signaling molecules (growth factors (GF) and leukocyte cytokines), and cells (osteoblasts, fibroblasts or other adequate populations for tissue regeneration) [2]. Tissue engineering principles have found wide applicability in various branches of dentistry, such as

periodontics, oral and maxillofacial surgery, and oral implantology, in the early 2000s when there was a significant development of tissue engineering within platelet concentrates where new generations emerged [2,3].

In this context, Fibrin Rich in Platelets and Leukocytes (L-PRF), is an autologous biomaterial, a second-generation blood product consisting of leukocytes, platelets, and a dense three-dimensional network of fibrins that are simple to process and without the biochemical manipulation of blood tissue used for healing. , which accumulates inflammatory cytokines (IL-1 β , IL-6, TNF- α , IL-4), several key CFs are the main ones: Transforming Growth Factor β (TGF β -1), Platelet-Derived Growth Factor (PDGF) and Insulin-Like Growth Factor (IGF), Vascular Endothelial Growth Factor (VEGF) [1,4].

The three-dimensional membrane composition of L-PRF creates an environment of slow degradation and gradual release of CF such as TGF β -1, PDGF, IGF, VEGF, and TSP-1 for at least seven days until the fibrin network disintegrates. Thus, L-PRF can anticipate the healing event and contribute to cell proliferation and movement [2,5].

The slow and progressive dispensation of L-PRF polymerization increases the incorporation of these chemical mediators into fibrin meshes increasing the life span of these fibrin meshes which are released and used only at the time of initial scar matrix restructuring, causing a long-term effect. The gelatinous consistency of the L-PRF film favors the stability of the clot and the grafting material [2]. The L-PRF film has its applicability widely indicated in the area of implant dentistry, periodontics, lesions, regenerative endodontics, and alveoli, among others due to its high potential for tissue restructuring [6].

Also, the main advantages of using L-PRF are rapid gingival tissue healing, angiogenesis, immunological control, high ability to transform adult stem cells into cells specific for gingival tissue growth and epithelial lining of the lesion; high capacity for tissue restructuring and regeneration capacity of tissue vascular network [4].

According to Choukron et al. (2006) [5], these factors are essential in achieving rapid tissue healing due to the successful development of neovascularization, intense rapid closure of lesions, scar tissue restructuring, and scarcity of infectious events. Therefore being configured as an ideal material for use in post-extraction alveoli because it can ensure rapid healing, prevent infection, and improve the capacity of local vascularization.

In this context, coenzyme Q10 (CoQ10) acts as a

powerful antioxidant and an important component in the transfer of mitochondrial bioenergy (ATP). Many studies suggest that antioxidants act as inhibitors of osteoclastogenesis and the inhibitory effect of CoQ10 on osteoclast differentiation. CoQ10 markedly attenuated the formation of nuclear factor κ B ligand-receptor activator (RANKL) induced by tartrate-resistant acid phosphatase (TRAP) positive multinucleated cells in bone marrow-derived monocytes (BMMs) and RAW 264.7 cells. Furthermore, CoQ10 strongly suppressed H₂O₂ -induced I κ B α , p38 signaling pathways for osteoclastogenesis. These findings highlight the potential therapeutic applications of CoQ10 for the treatment of bone diseases [7].

Therefore, the present study highlighted the main approaches to the use of fibrin-rich plasma and coenzyme Q10 in bucco-maxillo-facial surgery through a systematic review.

Methods

Study Design and Data Sources

This was followed by a systematic literature review model, according to the PRISMA rules. The literary search process was carried out from October 2023 to January 2024 and was developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, using scientific articles from 2006 to 2022, using the descriptors (MeSH Terms): *Tissue engineering*, *Bone bioengineering*, *Fibrin-rich plasma*, *Coenzyme Q10*, *Buccomaxillofacial*, and using the Booleans "and" between the descriptors (MeSH Terms) and "or" between the historical findings.

Study Quality and Risk of Bias

Quality was classified as high, moderate, low, or very low in terms of risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using the Cohen test (d).

Results and discussion

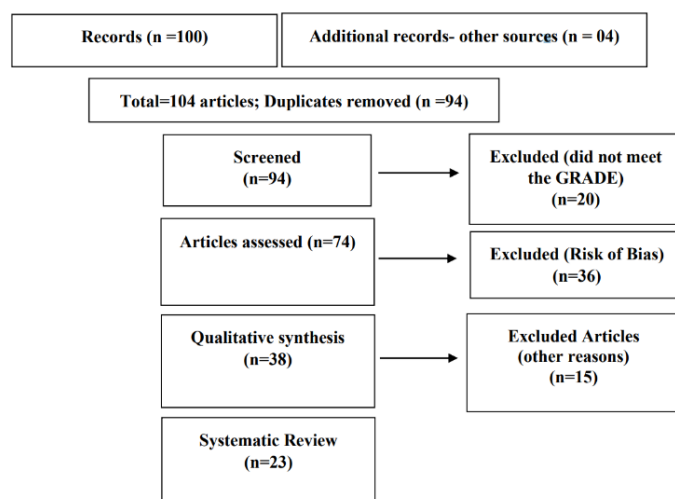
Summary

A total of 104 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 74 articles. A total of

38 articles were evaluated and 23 were included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 36 studies with a high risk of bias and 20 studies that did not meet GRADE.

The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with $X^2=59.7\%>50\%$. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 21 studies with a high risk of bias and 21 studies that did not meet GRADE and AMSTAR-2.

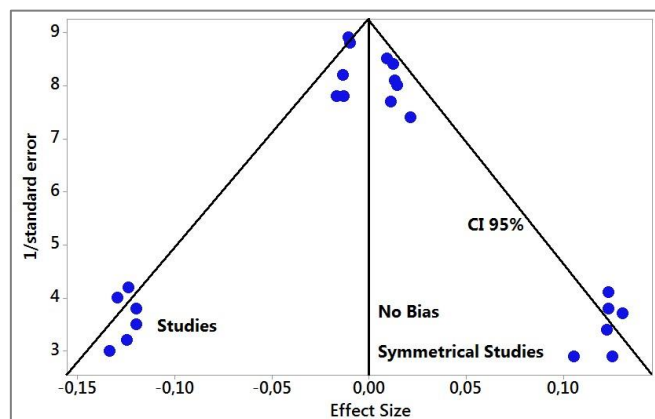
Figure 1. Selection of studies.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the bottom of the graph and in studies with a large sample size that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=23 studies).



Source: Own authorship

Main Clinical Outcomes

Initially, the study in tissue engineering developed fibrin glue in 1970 and the fibrinogen polymerization with thrombin and calcium using donor plasma. However, due to the low concentration of fibrinogen in plasma, the low stability and quality of fibrin glue, and the threat of hepatitis transmission, much allogeneic fibrin glues commercialized so far have been banned in the US since 1978 [1].

Some commercial fibrin patches, such as Tisseel® (Baxter Healthcare Corp.) are commercially available and are heat-treated products with minimal risk of disease transmission, but not eliminating their use is still controversial. This is due to the complexity of the protocols for their production, in the case of autologous adhesives, and the risk of cross-infection in commercially available allogeneic adhesives [2].

Authors innovated the medical sciences by pioneering the discovery of the regenerative capacity of platelets. Describe and demonstrate that when isolated in peripheral blood samples, they presented themselves as an autologous source of growth factors (GF). The GF contained in platelet alpha granules can stimulate cell proliferation, matrix remodeling, and angiogenesis [1-3].

Since 1990, medical science has recognized the importance and power of various blood components that are part of the natural restoration of homeostasis; when added to injured tissues or surgical sites, able to anticipate healing. In possession of this knowledge, there have been numerous attempts to develop autologous fibrin adhesives. The use of autologous blood materials then focused on the use of platelet concentrates associated with GF. These chemical mediators obtained from platelets, in addition to their action on tissues, interact with other GF, resulting in the activation of gene expression and the production of proteins that favor cellular activity [8,9]. The use of platelet concentrates aimed at improving healing in oral and maxillofacial surgery in place of fibrin glues, such

results were first described by Whitman and colleagues in 1987 [10].

Other protocols were developed. The described protocols generally used double centrifugation to increase the concentration of collected platelets: the first spin, the soft spin, separated the blood sample into three distinct layers, and the hard spin, where there was longer and faster, obtaining, again, three distinct layers [10]. The potential risks associated with the use of PRP through these protocols was the thrombin used (usually of bovine origin) that could be associated with the emergence of antibodies to both anti-thrombin and anti-factors V and XI, resulting in a risk of coagulation changes. There was also the possibility of a foreign body immune reaction due to the presence of factor V in the thrombin used [8-10]. The original goal of PRP autologous preparations was to concentrate platelets and GF in a plasma solution, and to make them a fibrin gel for surgical site use to favor the healing process [10].

A natural blood clot is made up of 95% red blood cells, 5% platelets, less than 1% white blood cells, and numerous amounts of fibrin filaments. A PRP blood clot contains 4% red blood cells, 95% platelets, and 1% white blood cells. Therefore, the properties of PRP are based on the production and release of multiple GF and differentiation in platelet activation. These factors are essential in regulating and stimulating wound healing and play a key role in regulating cellular processes such as mitogenesis, chemotaxis, differentiation, and metabolism [10].

The major watershed after the emergence of PRP was the technique developed by Choukroun and collaborators who were pioneers in trying to alleviate the limitations of PRP and eventually developed a new generation of platelet concentrates. Choukroun and colleagues developed in 2000 in France a specific technique for the acquisition of PRF, a second-generation platelet concentrate, an autologous scar matrix for use in oral and maxillary surgery, revolutionized dentistry with a new concept: fibrin gel, a platelet concentrate on a fibrin film with a very high lesion repair potential [5,6]. Thus Choukroun and collaborators eventually created a new material that could not be considered either fibrin glue or a classic platelet concentrate, PRF, which eliminated the possible risks associated with the use of bovine thrombin [6].

Moreover, the technique does not require anticoagulant, thrombin, or any other gelling agent. Blood is centrifuged without any addition and forming a film from an autologous blood sample without the addition of external factors, PRF, an autologous platelet-rich fibrin concentrate acquired in a small volume of plasma from sample collection. venous blood in collection tubes [2]. Fibrin gel is based on the concept

of continuous release therapy of HR and protein by the gel and induces fibroblast collagen synthesis, which can speed up wound healing and tissue healing process [3].

Besides, with continuous advances and research in the area, Choukroun and collaborators developed L-PRF, a second-generation blood product or immune processing and platelet concentrate that is simple and without biochemical manipulation of blood. which is a determinant for the conformation of the fibrin network consisting of leukocytes, platelets in a dense three-dimensional fibrin network, a high-density fibrin 3D tissue capable of generating a system that accumulates inflammatory cytokines (IL-1 β , IL-6, TNF - α , IL-4), VEGF, PDGF, epidermal growth factors (EGF family), fibroblast-derived growth factors and IGF-I [5,6].

According to Guedes (2017) [11], the L-PRF was developed to obtain bone regeneration but its superior qualities indicate a much higher potential. Concentrates can also be divided into two major referenced groups: PRP and PRF. PRP is the first group of the precursor group and consists of a modification of fibrin glue (produced in the 1970s by Matras) resulting from the donor's two-stage centrifugation of the blood that contains the HRs that influence healing, tissue adjustment, and cell regulation mechanisms that include chemotaxis, differentiation, and metabolism. Generally, PRP is used as a gel achieved by mixing PRP (resulting from double autologous whole blood centrifugation) with thrombin and calcium chloride. Obtaining PRP is divided into two more protocols: P-PRP and PRP-L.

The Applicability of Fibrin-Rich Plasma and Leukocyte (L-PRF) Post Extraction Alveoli

After an extraction, a set of inflammatory events for local repair arises where the alveolus is filled with blood due to ruptured blood vessels of the periodontal ligament, and a fibrin network is immediately formed. At this stage, platelets lead to clot creation, then there is the presence of erythrocytes and neutrophils. If the primary clot is retained, alveolar healing will follow a natural course. Between the third and fourth day, the emergence of epithelialization and the creation of immature connective tissue is observed. Some small clot fragments are already replaced by granulation tissue. One week after the immature bone trabeculae event is already visualized, an initial angiogenesis stage is noted [12].

Alveolar bone healing during post-extraction repair is associated with tissue remodeling resulting in bone volume loss, approximately 50% both vertically and horizontally. Such resorption occurs mainly within the first three months and triggers the deformation of the lip that causes aesthetic and functional difficulties. Post-extraction bone resorption in both the maxilla and

mandible is a major challenge for oral rehabilitation. This resorption and loss of the physiological alveolar process after tooth removal is a natural, undesirable phenomenon that can impair the installation of prostheses and implants [11].

For this physiological condition, it was suggested to use the L-PRF technique, which acts on bone formation and maintenance in post-extracted teeth alveoli, thus minimizing the loss of height and thickness of the alveolar process. The 4 fundamental events that structure L-PRF is angiogenesis, immunity, stem cell chemotaxis, and epithelization [9].

Also, the three-dimensional structure of the fibrin gel maintains key cytokines and HR such as FGFb, VEGF, and PDGF, immersed in the mesh that, added to the rigidity of the PRF matrix, directly influences angiogenesis, supporting stem and mesenchymal cells to populate this primary matrix. vigor and speed. Fibrin affinity with the various GF is the key to rapid angiogenesis. This difference in PRF matrix configuration is what clinically differentiates the higher efficiency of L-PRF from fibrin glue and PRP. The expression of integrin (AVP3) by endothelial cells allows fibrin to bind to fibronectin and vitronectin, and this expression is regulated by fibrin itself which does not happen in collagen [9].

Also, the cytokines controlling immune reactions are present in PRF, due to the artificially induced leukocyte induction in the tube, these cytokines give L-PRF infinitely great protection against infections by increasing the expression of proinflammatory cytokines (IL-1b, IL6, TNF-a), anti-inflammatory (IL4), angiogenic factor (VEGF) that mobilize immune cells to protect the wound against infectious agents [1,2,9].

The mesh formed by Fibrina in L-PRF is a great asset of this biomaterial as it robustly traps Platelets that in time will release the GF and cytokines that will modulate and promote regeneration. The addition of L-PRF to dental extraction sites has the function of sustaining the required bone volume. The L-PRF film stimulates clot production, favoring the physiological healing process. According to Choukroun et al. (2006a) [5] and Ehrenfest et al. (2006) [13] after tooth extraction the local bone structure changes rapidly and rapid bone resorption occurs. PRF-L can boost accelerated bone regeneration, faster vigorous angiogenesis and accelerate epithelialization.

In addition, according to Rao et al. (2013) [14] state that the costs of L-PRF film are much cheaper when compared to the costs of other recombinant CFs. Another advantage that the use of L-PRF enables is the prevention of mandibular osteitis in 90% of cases of wisdom teeth extraction. Suttapreyasri and Leepong

(2013) [15], agree that L-PRF is a compatible biomaterial in filling post-extraction alveoli concerning better healing and preservation.

In another study, changes in bone crest associated with the healing of 21 extraction sites using L-PRF alone as a graft were quantified. Measurements of crest width and height at extraction were recorded after graft placement and after 4 months of healing. What was observed was that the grafted sites only using L-PRF exhibited rapid clinical healing, minimal flap reopening, and excellent bone density. The advantages of platelet-rich fibrin alone include shorter surgical time, elimination of techniques, better membrane-associated healing, and less resorption during healing when compared to guided bone regeneration procedures [16].

The study by Suttapreyasri, Leepong (2013) [15] investigated the influence of L-PRF on early wound healing and preservation of alveolar crest shape after tooth extraction. Platelet-rich fibrin has clinically shown early healing of soft tissue orifice holes within the first 4 weeks. L-PRF entered the stable stage after the fourth week after tooth extraction, while in the control group, the progression of oral contour contraction was still detected until the eighth week. In this study, the preliminary result showed no better preservation of the alveolar ridge nor the increased bone formation of PRF in the extraction socket, but the use of L-PRF revealed limited efficacy by accelerated soft tissue healing in the first 4 weeks.

Furthermore, L-PRF can accelerate physiological healing, and when associated with bone grafts accelerates the bone regeneration process, regulates inflammation, and stimulates the chemotaxis immune process [4]. L-PRF can support the development of three phenomena simultaneously: Angiogenesis, immune response, and epithelial coverage, which are the main factors involved in the healing and tissue maturation process [5].

The study by Hauser et al. (2013) [17] investigated whether the use of L-PRF membranes for cavity filling could improve the microarchitecture and quality of alveolar bone intrinsic bone tissue after premolar extraction. Twenty-three patients requiring premolar extraction were divided into groups in the first, simple extraction and loop filling with L-PRF were performed, in group II mucosal flap extraction and loop filling with L-PRF. and in group III control with simple extraction without filling. Post-computed tomography analysis showed better bone healing with improved microarchitecture in group I. The results support the use of a minimally traumatic procedure for tooth extraction and cavity filling with L-PRF to preserve hard tissue and minimize potential impact reabsorption.

Coenzyme Q10 and Osteoclast and Osteoblast Differentiation

In the setting of bone regeneration and formation in maxillofacial surgery, CoQ10 provides membrane-stabilizing properties and acts as an antioxidant with cellular protective effects [18-22]. CoQ10 at low concentrations (below 5 μ M) acts as an inhibitor of osteoclastogenesis by suppressing ROS generation. Therefore, we investigated the molecular mechanism of both the inhibitory effect of CoQ10 on osteoclastogenesis and the promoting effect of CoQ10 on osteoblastogenesis. CoQ10 at high concentrations (above 10 μ M) disrupts ROS production and attenuates H₂O₂-induced early signaling activities, including p38, I κ B α , and JNK signaling pathways. Furthermore, CoQ10 promoted the induction of osteoclastogenic gene markers and also promoted matrix mineralization increasing bone nodule formation. In RANKL-mediated osteoclast differentiation, RANKL stimulates the intracellular generation of ROS [23].

Conclusion

The use of platelet and leukocyte-rich fibrin can reduce bone absorption, infection, pain, local edema, and wound healing. L-PRF presents itself as an autogenous biomaterial with great versatility, low cost, easy acquisition and wide use, and infinite possibilities. It can be combined with other materials in the most diverse areas of dentistry. Also, CoQ10 concentrations can suppress ROS, which is needed as a signaling intermediate. CoQ10 acts as an enhancer of all stages of osteoblastic differentiation. Thus, CoQ10 suppresses osteoclast differentiation by eliminating generated intracellular ROS. Furthermore, CoQ10 enhances bone regeneration in all differentiation processes through transcription factor activity.

Acknowledgement

Not applicable.

Funding

Not applicable.

Ethical Approval

Not applicable.

Informed consent

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate®.

Peer Review Process

It was performed.

About the License

© The authors (s) 2024. The text of this article is open access and licensed under a Creative Commons Attribution 4.0 International License.

References

1. Farshidfar N, Amiri MA, Jafarpour D, Hamedani S, Niknezhad SV, Tayebi L. The feasibility of injectable PRF (I-PRF) for bone tissue engineering and its application in oral and maxillofacial reconstruction: From bench to chairside. *Biomater Adv.* 2022 Mar;134:112557. doi: 10.1016/j.msec.2021.112557.
2. Alrayyes Y, Al-Jasser R. Regenerative Potential of Platelet Rich Fibrin (PRF) in Socket Preservation in Comparison with Conventional Treatment Modalities: A Systematic Review and Meta-Analysis. *Tissue Eng Regen Med.* 2022 Jun;19(3):463-475. doi: 10.1007/s13770-021-00428-y.
3. Azevedo, MCMPS et al. Application of PRF in Dentistry. 36 pages 2014. Dissertation (Master in Dental Medicine) – Faculty of Dental Medicine, University of Porto, Porto 2014.
4. Correia VG, Castilio D. Use of platelet- and leukocyte-rich fibrin (L-PRF) in maxillary sinus lift surgery. 67 pages 2015. Monograph (Specialization in Implantology) - Bahiana School of Medicine and Public Health, Salvador, Bahia, 2015.
5. Choukroun J et al. Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part V: Histologic evaluations of PRF effects on bone all graft maturation in sinus lift. *Oral Surg Oral Med Oral Pathol Oral EndodRadiol*, 2006, v. 101, p.299-303.
6. Choukroun J et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 2006a, v. 101, no. 3, p. e56-e60.
7. Moon HJ, Ko WK, Jung MS, Kim JH, Lee WJ, Park KS, Heo JK, Bang JB, Kwon IK. Coenzyme q10

- regulates osteoclast and osteoblast differentiation. *J Food Sci.* 2013 May;78(5):H785-891. doi: 10.1111/1750-3841.12116.
8. Del Corso M, Toffler M, Ehrenfest DM. Use of an autologous leukocyte and platelet-rich fibrin (L-PRF) membrane in post-avulsion sites: an overview of Choukroun's PRF. *J Implant Adv Clin Dent*, 2010, v. 1, no. 9, p. 27-35.
 9. Diniz PC. Use of PRF-L as an additive in dentistry. 52 pages 2017. Monograph (Specialization in Implant Dentistry) - Faculty of Dentistry Federal University of Minas Gerais, Belo Horizonte, MG, 2017.
 10. De Almeida RCC et al. The applicability of the platelet-leukocyte-rich fibrin membrane (L-PRF) IN DENTISTRY: A literature review. Extension, Teaching and Scientific Initiation Meeting (EEDIC), 2017, v. 3, no. 1.
 11. Guedes, Camila Sessim. Evaluation of the preservation of sockets, post-extraction, using concentrate of platelets and leukocytes produced with the L-PRF technique. 49pages 2017. Dissertation (Master in Dentistry) - University of Grande Rio "Prof. José de Souza Herdy"-UNIGRANRIO, Duque d'Caxias, RJ, 2017.
 12. Figueira, Leticia de Miranda; Goncalves, Luiz Felipe Salles. "Biomaterials applied in volumetric maintenance in post-extraction alveoli – Literature review". 27 pages 2015. Monograph (Bachelor of Dentistry) - Fluminense Federal University, Nova Friburgo, RJ, 2015.
 13. Ehrenfest D.M.Dohan et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biological features. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 2006, v. 101, no. 3, p. e45-e50.
 14. Rao S. Girish et al. Bone regeneration in extraction sockets with autologous platelet rich fibrin gel. *Journal of maxillofacial and oral surgery*, 2013, v. 12, no. 1, p. 11-16.
 15. Suttapreyasri, Srisurang; Leepong, Narit. Influence of platelet-rich fibrin on alveolar ridge preservation. *Journal of Craniofacial Surgery*, 2013, v. 24, no. 4, p. 1088-1094.
 16. Simon BI, Gupta P, Tajbakhsh S. Quantitative evaluation of extraction socket healing following the use of autologous platelet-rich fibrin matrix in humans. *International Journal of Periodontics & Restorative Dentistry*, 2011, v. 31, no. 3.
 17. Hauser F et al. Clinical and histological evaluation of postextraction platelet-rich fibrin socket filling: a prospective randomized controlled study. *Implant dentistry*, 2013, v. 22, no. 3, p. 295-303.
 18. Sood B, Keenaghan M. Coenzyme Q10. 2022 Jan 19. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2023 Jan–.
 19. PDQ Integrative, Alternative, and Complementary Therapies Editorial Board. Coenzyme Q10 (PDQ®): Health Professional Version. 2022 Jun 7. In: *PDQ Cancer Information Summaries [Internet]*. Bethesda (MD): National Cancer Institute (US); 2002–.
 20. Na HS, Woo JS, Kim JH, Lee JS, Um IG, Cho KH, Kim GH, Cho ML, Chung SJ, Park SH. Coenzyme Q10 encapsulated in micelles ameliorates osteoarthritis by inhibiting inflammatory cell death. *PLoS One*. 2022 Jun 24;17(6):e0270351. doi: 10.1371/journal.pone.0270351.
 21. Arenas-Jal M, Suñé-Negre JM, García-Montoya E. Coenzyme Q10 supplementation: Efficacy, safety, and formulation challenges. *Compr Rev Food Sci Food Saf*. 2020 Mar;19(2):574-594. doi: 10.1111/1541-4337.12539.
 22. Hargreaves I, Heaton RA, Mantle D. Disorders of Human Coenzyme Q10 Metabolism: An Overview. *Int J Mol Sci*. 2020 Sep 13;21(18):6695. doi: 10.3390/ijms21186695.
 23. Moon HJ, Ko WK, Jung MS, Kim JH, Lee WJ, Park KS, Heo JK, Bang JB, Kwon IK. Coenzyme q10 regulates osteoclast and osteoblast differentiation. *J Food Sci.* 2013 May;78(5):H785-891. doi: 10.1111/1750-3841.12116.