Utilization of Platelet Rich Fibrin (PRF) for Tissue Healing in Replantation of Avulsed Permanent Teeth: A Systematic Review

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Abstract

Avulsion is a serious dental injury with a high prevalence in young patients. These injuries account for 0.5%-3% of all trauma to replanted permanent teeth. Avulsed teeth stored in non-physiological conditions may increase the risk of periodontal cell necrosis, ankylosis, and root resorption of replacement teeth. Recent research has focused on the use of PRF in oral surgery and periodontics. Applications include bone augmentation, sinus tightening, and repair of gum recession. It has also been used for regenerative procedures such as apex regeneration and periapical surgery. Writing systematic review (SR) for study further regarding the use of PRF for tissue healing in replantation of avulsed permanent teeth SR writing is done with search and analyze journal from PMC, Pubmed and Science Direct portals with criteria inclusion and exclusion that have been determined. To determine framework right time For review, Google Scholar search regarding the use of PRF for tissue healing in replantation of avulsed permanent teeth 2014-2024. The Results of study showed that A total of 390 articles journal obtained through search through 3 databases (Pubmed, Science Direct and PMC) and identified 10 journals that met criteria. 10 articles journals identified three case articles report, five clinical studies, one retrospective study and one systematic reviews. Review results systematic This shows that the use of PRF is effective in recovery cell periodontal ligament (PDL). PRF increases the amount of growth factors in the wound and helps wound healing in avulsed tooth replantation.

Keywords: Avulsion, PRF, Tooth Replantation.

1. Introduction

Avulsion is a serious dental injury with a high prevalence in young patients. These injuries account for 0.5%-3% of all trauma to replanted permanent teeth. Challenges in dental implant placement occur due to bone atrophy and periodontal ligament trauma. The prognosis of tooth replantation is determined by the degree of mechanical trauma and the survival of periodontal ligament cells. Several important factors in the success of tooth replantation include the time

interval before replantation, storage media, and methods of treating avulsed teeth (Behnaz et al., 2021).

Avulsed teeth stored in non-physiological conditions may increase the risk of periodontal cell necrosis, ankylosis, and root resorption of the replacement tooth. Periodontal healing is difficult to achieve if there is rapid root resorption or tooth ankylosis with bone replacement. Loss of upper anterior teeth can cause aesthetic and functional problems. More effective management of this condition is needed (Zhao et al., 2013).

Recent research has focused on the use of PRF in oral surgery and periodontics. Applications include bone augmentation, sinus tightening, and repair of gum recession. It has also been used for regenerative procedures such as apex regeneration and periapical surgery (Hartshorne & Gluckman, 2016). The literature confirms the positive effects of PRF on bone healing, socket preservation and accelerated soft tissue healing. Furthermore, a systematic review also confirmed the potential benefits of PRF in periodontal regeneration after tooth replantation. However, in vivo there is still very little evidence for the use of this concentrate to treat tooth avulsion (Behnaz et al., 2021).

Use of PRF in intentional replantation of molar teeth, Deshpande et al. found success over two years without signs of inflammation or replacement resorption. In another case report by Rayana et al. Replantation of severely damaged teeth with PRF also showed no complications after 12 months of follow-up (Mall et al., 2021). This study aims to examine the use of PRF for tissue healing in replantation of avulsed permanent teeth.

2. Methods

Strategy and terms search developed consult with Oral and Maxillofacial Surgery specialist Faculty UNHAS Dentistry. Search strategy only covers studies human in English. Original research study from journal peer- review includes trials randomized controlled, trial comparative And studies prospective/retrospective Utilization of PRF for tissue healing in replantation of avulsed permanent teeth.

Search literature done by three authors (YAT, AF and EP) who are experts in their fields, because our goal to know Utilization of PRF for tissue healing in replantation of avulsed permanent teeth. We try For produce question Which wide, and terms key become focus main. MeSH used For get correct term for keywords. As for terms search key identified using truncated words (in matter this *) with the word form PRF * AND Replantation * AND/OR avulsed permanent * AND/OR Teeth *.

Search beginning Google Scholar done For determine relevance term key, but google scholar No used as machine search in this research Because machine search This No can doubled. For determine framework time Which appropriate For review, Google Scholar search regarding the use of PRF for tissue healing in replantation of avulsed permanent teeth year 201 4 - 202 4 so date This chosen Which in accordance For study This. Databases what you are looking for including PubMed, Science direct and PMC. Criteria inclusion and exclusion, consistent with objective review we, developed and outlined in Table 1.

Criteria Inclusion and Exclusion

Criteria ink l usi analyzed based on component PICOS as following; (1) Published journals 2014 -2024; (2) English language articles and human species articles; (3) Mandibular Fracture; (4) Cross-sectional studies, cohort study, cases reports, cases controls and systematic review. Criteria ex cl usi with reason; (1) Studies in outside period time Which determined; (2) Articles are not in English.

Table 1. Description Table Criteria Inclusion based on PICOS criteria

P	Population	The patient has permanent avulsion
I	Intervention	Tooth replantation
C	Comparison	Platelet Rich Fibrin (PRF)
O	Outcomes	Tissue healing
S	Study Design	Case report,Clinical Study, cohort study, and systematic review

Risk of Bias Assessment

Risk of bias assessment using JBI critical appraisal checklist for analytical randomized type trials adjusted based on the type of research study. The assessment results are then categorized according to Saletta et al. (2019) where is the question calculated based on the percentage of positive answers ('yes') only. Then, the risk of bias (RoB) of each study was categorized according to the final score as 'high' (score equal to or lower than 49%, leading to exclusion of articles), 'medium' (score ranging from 50% to 69%) or ' low' (score higher than 70%).

Data extraction

Data retrieved from fulfilling article criteria inclusions and conditions that is author, year, country, research references, aim and number of research subjects, type studies and research results related to the use of PRF for tissue healing in replantation of avulsed permanent teeth.

Study selection

A total of 390 journal articles were obtained through searches in 3 databases (Pubmed, Science direct and PMC) and identified 10 journals that met the inclusion criteria (Fig 1). After through process filtering, from deletion duplicates (84), did not meet the requirements using automatic tools (272) and were removed for other reasons (15), excluded because they did not meet the criteria (15), obtained 19 full articles papers, some were excluded (9), found 10 that met the requirements, then re-evaluated those that did not have sufficient information (0), the final result was that 10 journal articles were reviewed (Figure 1).

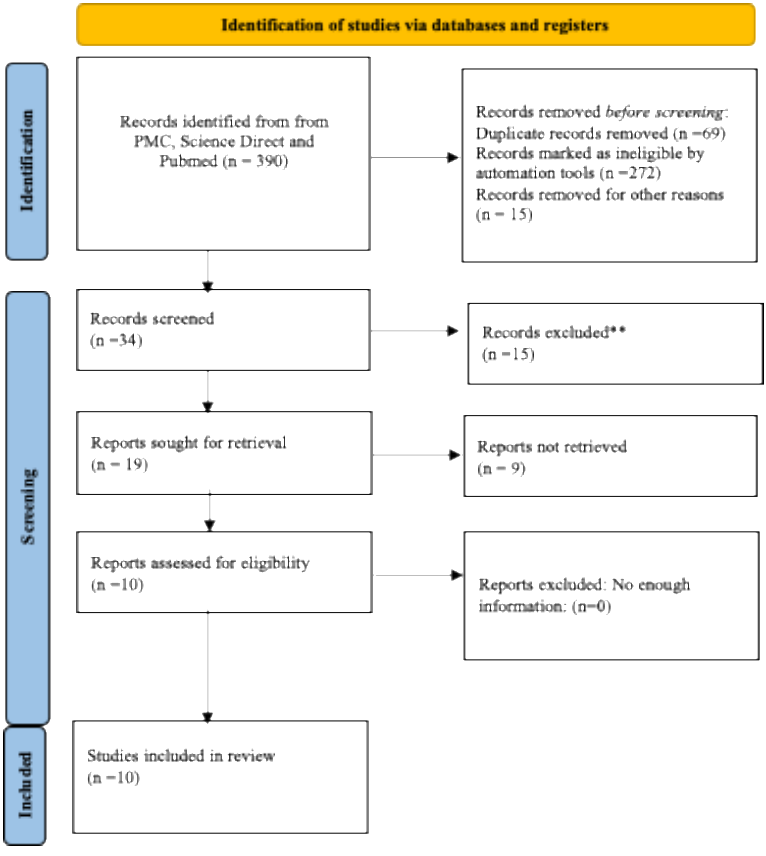

Figure 1. Study Flowchart Based on the 2020 PRISMA Guidelines

Characteristics Study

Characteristics studies in study of 10 article journal Which identified three case article report, five clinical studies, one retrospective study and one systematic reviews. As for summary results identification can be seen in Table 2 below:

Table 2. Summary of Selected Studies

No	Title	Author, Year, Country Reference	Objectives	Type Study	Results
1	Comparative Evaluation of Efficacy of Platelet-Rich Fibrin and Hank's Balanced Salt Solution as a Storage Medium for Avulsed Teeth	Shetty et al. (2019), India	To compare the efficacy of platelet-rich fibrin (PRF) and Hank 's balanced salt solution (HBSS) on the preservation of the periodontal ligament cells (PDL). Survival from tooth avulsion. Method:	Clinical Studies	Although the majority of the studies showed that autologous platelet concentrates (APCs) may improve the results of tooth replantation, the majority of the studies contained various sources of bias.
2	Surgical Re-entry of an Intentionally Replanted Periodontally	Ryana et al, (2016), India	To see effectiveness reentry using PRF periodontally	Case Report	Autologous PRF demonstrated effectiveness in preserving and restoring PDL cells from

	Compromised Tooth Treated with Platelet Rich Fibrin (PRF): Hopeless to Hopeful				extracted teeth and stored dry for up to 2 hours.
3	The Impact of Autologous Platelet Concentrates on the Periapical Tissues and Root Development of Replanted Teeth	8.Zhang et al, (2020), Saudi Arabia	To summarize and assess critically available literature moment This about prior use of APC replantation tooth.	Systematic Reviews	Utilization mixed autologous dentin particles with proven PRF effective as alternative material Conventional bone grafting on GBR and jaw on.
4	Assessment of platelet-rich fibrin in the maintenance and recovery of cell viability of the periodontal ligament	Navarro et al, Brazil, (2019)	To analyze the efficacy of autologous platelet -rich fibrin (PRF) in maintaining and restoring cell viability of the periodontal ligament (PDL)	Clinical Study	Implanted teeth repeat shows no symptoms resorption root inflammation or ankylosis on examination follow-up 3, 6, and 12 months after reimplantation with autologous PRF. Apart from teeth avulsion, tooth injury others are also being treated use appropriate conventional treatment methods.
5	Auto-dentin platelet-rich fibrin matrix is an alternative biomaterial for different augmentation procedures: A retrospective case series report	Alrmali et Al, (2023), USA	To evaluate material autologous dentin graft origin from fibrin extracted teeth.	Retrospective Study	Results from scanning electron microscopy showed that BMMSCs could tightly adhere to a fibrin scaffold only immediately after seeding. These data suggest that the BMMSCs /PRF construct has the potential to improve the clinical prognosis of reimplanted tooth avulsions in the future. Additional studies are required to be conducted prior to clinical use.
6	ibrin following delayed reimplantation: Two case reports	11.Hatwar et al, 2022, USA	For management tooth avulsion after replantation	Case Report	The study results suggest that clinical use of bone marrow suction concentrate, with PRF as a carrier, may have some potential to improve mineralization in fresh extraction sockets.
7	Design and Fabrication of a Novel Transplant Combined with Human Bone Marrow Mesenchymal Stem Cells and Platelet-rich Fibrin: New Horizons for Periodontal Tissue Regeneration after Dental Trauma	Moradiana et al, (2017), Iran	To design PRF scaffolding and determine feasibility and function of BMMSCs on the fabricated scaffolds. To test draft this is in-vitro, human BMMSC isolated and characterized based on markers surface cells, and their potential in differentiation osteogenic / adipogenic.	Clinical Study	study results confirm the feasibility of applying I-PRF as a promising addition to dental procedures.
8	Bone marrow aspirate concentrate and platelet-rich fibrin in fresh extraction sockets: A histomorphometric and immunohistochemical study in humans	Sousa et al, (2020), Brazil	To evaluate method transplant cell new this, we were at first aim designing PRF scaffolding and determine feasibility and function of BMMSCs on scaffolds artificial.	Clinical Study	Scan results microscope electrons show that BMMSC can attached tightly onto the fibrin scaffold immediately after seeding. These data indicate that the BMMSCs/PRF construct has potency For improve clinical prognosis tooth future replanted avulsion. Additional studies required For done before use clinical.

9	A Comparative Evaluation of Revascularization Done in Traumatized Immature, Necrotic Anterior Teeth with and without Platelet-rich Fibrin: A Case Report	Nagaveni et al, (2020), India	For presents two methods revascularization performed on immature nonvital anterior teeth that have experienced trauma with using platelet-rich fibrin (PRF) and clots blood experience as material scaffolding.	Case Report	After 12 months, on clinical examination, both teeth showed a negative response to percussion and palpation tests but a positive response to cold and electrical pulp tests. On radiographic examination, teeth treated with PRF showed faster root elongation, complete root apex coverage, greater root dentin wall thickening, and narrowing of the root canal space compared with conventionally revascularized teeth.
10	Management of internal inflammatory root resorption using injectable platelet -rich fibrin revascularization technique: a clinical study with cone beam computed tomography evaluation	Nageh et al, Egypt, (2021)	To assess clinically and radiographically management resorption root internal inflammation (IIRR) in permanent anterior teeth with or without lesion periapical use approach regenerative platelet -rich fibrin (i -PRF) which can injected.	Clinical Studies	The use of i-PRF can stop and allow healing in permanent adult teeth and allows periapical healing with successful clinical results.

Risk Biased in Studies

The risk of bias from the eleven studies is summarized in Table 3 using case report, clinical study, retrospective study and systematic reviews. As for summary For results evaluation from four case articles reports of them, two got a result of 100, which means it was in the low category (>70%)(Ryana et al., 2016; Hatwar et al., 2022), and one study (Nagaveni et al., 2020) (score 75.0%) did not include anticipatory steps and case reports providing learning, but met other criteria such as explaining the patient's demographic characteristics completely, However, the history, current clinical conditions, diagnostic tests, treatment procedures, conditions after intervention, anticipatory steps and case reports are explained.

For assessing the risk of bias in systematic studies review show result 90.9 which means it is in the low category (>70%), the study only had no data extraction error, the remaining 8met the criteria including inclusion criteria, keyword search strategy, and bias assessment, valid instrument, consisting of a review team of more than 2 reviewers for the feasibility of the study, there are efforts in data extraction to minimize errors, appropriate methods of combining studies where descriptive information and explanations are adequate to support the final synthesized findings, tests to assess potential publication bias, have suggestions that are appropriate to the study or reported data as well as recommendations for future researchers.

For assessment risk of bias from three clinical studies is 100% which means is at in category low (>70%) and fulfilling nine indicator form because clear consequences, same characteristics from second groups, the same treatment and care, exist group control, measurement several times, follow complete further, method the same measurements, reliable measurements and appropriate statistical tests (Navarro et al., 2019; Moradiana et al., 2017; Sousa et al., 2020; Nageh et al., 2021). However One studies other No fulfil One indicator that is No There is repeated (Shetty et al., 2019).

For studies type retrospective study own value 81.8 which means in category low (>70%) of them studies mention limitations and fulfillment indicator like patients within and across group own the same characteristics, steps exposure defined with clear and explained in detail in procedure clinical, measurement valid exposure, quite long research time in action research reporting Complete advanced and statistical analysis right, however No there is criteria inclusion For minimize exists factor confounder with give criteria inclusion and its strategies (Choy et al., 2021).

Cases Reports

Studies	Demographics characteristics clearly	History clearly	Current clinical condition	Diagnostics tests or assessment	Treatment procedure (s) clearly multiple measurements	Post-intervention clinical condition	Unanticipated events identified	Cases reports provide takeaway lessons	Ratings results (%)
Ryana *et al,* [7]	+	+	+	+	+	+	+	+	100
Yang *et al,* [11]	+	+	+	+	+	+	+	+	100
Nagaveni *et al,* [14]	+	+	+	+	+	+	-	-	75

Systematic Reviews

Study i	Reviews Questions Clearly	Inclusion criteria	Search Strategy	Sources and Resources Used	Criteria For Appraising Studies	Reviewers > 2	Minimize Errors in Data Extraction	Methods Used to Combine Studies	Bias Assessed	Recommendations For Policy	Specific Directives For New Research	Ratings Results (%)
8.Zhang *et al,* **(2020)**	+	+	+	+	+	+	-	+	+	-	+	81.8

Clinical Studies

Studies	*Cause and effect clear*	*Comparisons similar*	*Receiving similar treatment*	*Controls groups*	*Multiple measurements*	*Follow up complete*	*Comparisons measured in the same*	*Measured reliably*	*Appropriate statistical analysis*	Rating result (%)
Shetty *et al,* (2019)	+	+	+	-	+	+	+	+	+	88.9
Navarro *et al,* (2019)	+	+	+	+	+	+	+	+	+	100
Moradiana *et al,* (2017)	+	+	+	+	+	+	+	+	+	100
Sousa *et al,* (2020)	+	+	+	+	+	+	+	+	+	100
Nageh *et al,* (2021)	+	+	+	+	+	+	+	+	+	100

Cohort Study (Retrospective Study)												
Studies	**The Two Groups are Similar**	**Measured Similarly**	**Valid Rating**	**Identification of Founders**	**Strategy**	**Groups free of the outcomes**	**Valid and Reliable measurements**	**Follow up time**	**Complete follow up**	**Treatment strategy**	**Statistics Analysis**	**Ratings results (%)**
Choy et al. (2021)	+	+	+	-	-	+	+	+	+	+	+	81.8

3. Study Results and Research Synthesis

Review results systematic This shows that the use of PRF is effective in recovery cell periodontal ligament (PDL). In research related to regeneration pulp and periodontal of tooth incisor mature permanent avulsion using PRF after replantation pending: studies case clinical over 12 months, the results showed that PRF use showed 87% radiographic improvement and clinical parameters are achieved.16 Re-entry surgery on periodontally compromised and PRF - treated teeth, autologous PRF effective in maintaining and restoring periodontal cells ligament (PDL) (Ryana et al., 2016).

Deep PRF assessment maintenance and recovery viability cell periodontal ligament, Implanted teeth repeat shows no symptoms resorption root inflammation or ankylosis on examination follow-up 3, 6, and 12 months after reimplantation with autologous PRF (Navarro et al., 2019). Utilization mixed autologous dentin particles with proven PRF effective as alternative material Conventional bone grafting on GBR and jaw on (Choy et al., 2021). In two cases management tooth avulsion after replantation suggests PRF as a carrier, may have some potential to increase mineralization in fresh extraction sockets (Hatwar et al., 2022). After 12 months, on clinical examination, both teeth showed a negative response to percussion and palpation tests but a positive response to cold and electrical pulp tests. On radiographic examination, teeth treated with PRF showed faster root elongation, complete root apex coverage, greater root dentin wall thickening, and narrowing of the root canal space compared with conventionally. The use of i-PRF (PRF derivative) can stop and allow healing of IIRR in permanent adult teeth and allows periapical healing with successful clinical results (Nageh et al., 2021).

At three studies compare with efficacy material other like Hank's Balanced Salt Solution, Bone marrow mesenchymal stem cells (BMMSCs), (Moradiana et al., 2017) and autologous dentin particles (Zhang et al., 2020). Third result studies the proves that PRF can utilized in replantation tooth. Evaluation result comparison efficacy of PRF and Hank's Balanced Salt Solution as Storage Media for Avulsed Teeth, shows that PRF can used as replacement for Hank's Balanced Salt Solution (HBSS) as a storage medium tooth avulsion, p this is based on the number of viable periodontal ligament cells. PRF concentrates and blends autologous dentin particles proven effective as alternative material Conventional bone grafting on GBR and jaw on (Zhang et al., 2020). Results from scanning electron microscopy showed that BMMSCs could tightly adhere to a fibrin scaffold only immediately after seeding. These data suggest that the BMMSCs /PRF construct has the potential to improve the clinical prognosis of reimplanted tooth avulsions in

the future. Additional studies are required to be carried out before clinical use (Moradiana et al., 2017).

4. Discussion

Avulsion, one of the most severe forms of dental trauma, is defined as complete displacement of a tooth out of its alveolar socket (Martin & Pileggi, 2004). Replantation is widely accepted as the standard treatment option for avulsions with the assumption that the avulsed tooth is immediately replanted within an hour and during the extra-alveolar time the tooth is maintained in an appropriate medium such as milk or physiological saline. However, this causes drying of the root surface and leads to loss of vitality of cells in the remaining periodontal ligament (PDL), resulting in rapid root resorption, ankylosis, and ultimately tooth loss (Flores et al., 2007).

PRF has been developed to overcome the limitations associated with the use of PRP. In addition, it is a highly resistant and elastic membrane that does not dissolve rapidly after application (Dohan et al., 2006); allowing a slow and continuous release of growth factors (Naik et al., 2013) that efficiently direct stem cell migration, proliferation, coagulation, and angiogenesis (Naik et al., 2013). PRF can enhance soft and hard tissue healing. A clear advantage over platelet-rich plasma (PRP) is its ease of application and cost, without the need for biochemical modifications. In addition, PRF forms an elastic fibrin mesh, which supports various cytokine traps and preserves growth factors from proteolysis (Ehrenfest et al., 2009). PRF scaffolds are considered effective. PRF growth factors can improve the overall prognosis of avulsions.

Use of PRF Choukroun (factor growth platelets generation second) with replantation has reported previously for the treatment of sprains extrusive that shows the results clinical and radiographic success (Patel et al., 2013). PRF, concentrate platelets generation secondly, consisting from Suite chain glycans, cytokines, and glycoproteins trapped structure in polymerized fibrin tissue slowly with potency promotes regeneration (Chang et al., 2010). A case handled with use combination PRF, Xenograft and Collagen membranes Type -I and is one report rare indications of deep use of PRF replantation affected teeth periodontal disorders. Sharma & Predeep (2011) and Thorat et al. (2011) investigated potency regenerative PRF in intrabony defects in chronic periodontitis patients and report significant increase in bone filling. PRF increase regulated Protein Kinase (p-ERK) expression signal extracellular stimulating phosphorylation production Osteoprotegerin (OPG) which in turn cause proliferation and differentiation of osteoblasts.

Tsai et al. (2009) revealed that the PRF encouraged effective periodontal healing, represented by PDL- like tissue regeneration and reduction inflammation and ankylosis. A report case about replantation tooth series jaw above the avulsion using PRF showed good results after 6 months of follow -up carry on. According to author, nature osteoconductive and osteoinductive PRF are responsible answer on that success (Johnset al., 2013). PRF plays role important in speed up site healing with provide derivative blood in concentrated amounts that increase activity macrophages and factors growth, as supported by existing research. PRF supporters underscore its height concentration factor the growth it contains, with focus specifically on platelet derivatives.

Dohan et al. (2006) explains platelet-rich fibrin (PRF) easily obtained through centrifugation new blood collected and without treatment biochemistry, where present domination platelets and fibrin within concentration different, with or without leukocytes (Choukroun et al., 2001). Draft Tissue engineering is based on three important pillars: cells, matrix biocompatible and molecular responsible bioactive answer on signal morphogenic. PRF delivers superiority compared to aggregate platelets other like making it in One step production product blood experience Because No presence of anticoagulants (He et al., 2009), in addition produce structure three dimensions (3-D) that support delivery and support sheet cells in areas of tissue that have been damaged. This fibrin matrix capable copy matrix extracellular in matter structural, and creating optimizing environment function cell and because contain glycosaminoglycans (heparin and acid hyaluronic acid) has strong affinity with peptide circulating small like platelet cytokines (Khiste & Naik, 2013; Miron & Du, 2017).

PRF processing with centrifugation push degranulation platelets directly which means release significant cytokines, in particular: factors growth derivative platelets (PDGF) that stimulate cell lines mesenchyme and constitute regulator important For migration and survival life cells this, factor growth beta transformation (TGF-β1) induces formation collagen I synthesis fibronectin, fibroblasts, osteoblasts, and factors growth insulin -like (IGF) is agent protection powerful cells, because increase potency continuity life part big cell type (Dohan Ehrenfest et al., 2010).

In medicine teeth, research with PRF is more concentrated on the field medical tooth implants and periodontal and partial large, shows good results in restoration and repair of soft and hard tissue (Simonpieri et al., 2012; Miron et al., 2021). These biomaterials have also been tested as matrix in the regeneration process periodontium implanted teeth return, and describe the PRF as matrix biocompatible and specific For delivery sheet therapeutic that will be increase efficacy clinical and will sustain cells in the spaces between teeth. alveolar bone and cementum (Chang & Zhao, 2011; Wang et al., 2016). During fibrin polymerization, which takes place slow Because No exists activator, there is merger intrinsic cytokines platelets and chains glycans in fibrin dough and action local from factors This produce continuity life, migration, proliferation and differentiation of cells (Wang et al., 2016; Su et al., 2009).

5. Conclusion

One of the main goals of platelet concentrate therapy is to provide a source of growth factors to promote tissue regeneration. Recent literature confirms the ability of PRF to increase the amount of growth factors in the wound and aid wound healing in replantation of avulsed teeth.

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