



## EXPLORING THE USE OF BIOACTIVE MATERIALS IN PROMOTING TISSUE REGENERATION IN ORAL SURGERY

**Khalaf Fayiz Khalaf Alhowaish<sup>1\*</sup>, Abdulaziz Salmi Alotaibi<sup>2</sup>, Aqeel Mohammed Alharbi<sup>3</sup>, Sultan Fahad Nasser Althunayan<sup>4</sup>, Amnah Khalifah Ali Alanazi<sup>5</sup>, Majidah Dabshi Saud Alruwaili<sup>6</sup>, Rowida Saleh Barayan<sup>7</sup>**

### Abstract:

Tissue regeneration in oral surgery is a critical aspect of promoting successful outcomes for patients undergoing various procedures. The use of bioactive materials has shown promising results in enhancing tissue regeneration and improving patient recovery in oral surgery settings. This review article aims to explore the current research and advancements in the utilization of bioactive materials for promoting tissue regeneration in oral surgery. The article provides an overview of the different types of bioactive materials commonly used in oral surgery, including growth factors, scaffolds, and biomimetic materials. It discusses their mechanisms of action, advantages, and limitations in promoting tissue regeneration. Furthermore, the review highlights recent studies and clinical trials that have investigated the efficacy of these bioactive materials in enhancing wound healing, bone regeneration, and soft tissue repair in oral surgery procedures. Moreover, the review addresses the challenges and future directions in the field of bioactive materials for tissue regeneration in oral surgery. It discusses the importance of personalized medicine approaches, novel biomaterial designs, and advanced delivery systems to optimize the therapeutic effects of bioactive materials in promoting tissue regeneration. Additionally, the article emphasizes the need for further research and collaboration between clinicians, researchers, and bioengineers to translate these findings into clinical practice successfully. In conclusion, this review article provides a comprehensive overview of the current state of research on bioactive materials for tissue regeneration in oral surgery. It underscores the potential of bioactive materials to revolutionize the field of oral surgery by improving patient outcomes, reducing complications, and enhancing the overall quality of care provided to patients undergoing oral surgical procedures.

**Keywords:** Bioactive materials, Tissue regeneration, Oral surgery, . Growth factors, Biomimetic materials, Wound healing.

<sup>1\*</sup>Dentist general practitioner, Northern borders cluster, Arar, Saudi Arabia.

<sup>2</sup>Dentist general practitioner, Primary Healthcare, Arar, Saudi Arabia.

<sup>3</sup>Dental Hygienist, Prince Abdullah bin Abdulaziz bin Musaed Specialist Dental Center, Arar, Saudi Arabia.

<sup>4</sup>SPECIALIST OPTOMETRIST, ARAR CENTRAL HOSPITAL, ARAR, SAUDI ARABIA.

<sup>5</sup>Dental assistant, Northern borders cluster, ARAR, Saudi Arabia.

<sup>6</sup>Specialist Nursing, North Medical Tower, Arar, Saudi Arabia.

<sup>7</sup>Dentist general practitioner, Primary Healthcare, Arar, Saudi Arabia.

**\*Corresponding Author:** Khalaf Fayiz Khalaf Alhowaish

\*Dentist general practitioner, Northern borders cluster, Arar, Saudi Arabia.

**DOI:** 10.53555/ecb/2022.11.7.78

**Introduction:**

Tissue regeneration in oral surgery is a rapidly evolving field that holds great promise for improving patient outcomes and quality of life. This innovative approach to treatment involves the use of biological materials and techniques to stimulate the body's natural healing processes and restore damaged or missing tissue in the oral cavity [1].

Tissue regeneration in oral surgery is based on the concept that the body has the inherent capacity to repair and regenerate damaged tissues. By harnessing this natural ability, oral surgeons can help patients recover from injuries, infections, and surgical procedures more quickly and effectively than traditional methods. The goal of tissue regeneration is not only to restore the form and function of the tissue but also to promote long-term health and stability in the oral cavity [2].

One of the key principles of tissue regeneration in oral surgery is the use of biomaterials to support and guide the healing process. These materials can take many forms, including synthetic scaffolds, growth factors, and stem cells, and are designed to mimic the structure and function of natural tissue. By providing a framework for new tissue growth, biomaterials can help to accelerate healing, reduce scarring, and improve the overall success of surgical procedures [3].

In addition to biomaterials, tissue regeneration in oral surgery also relies on advanced surgical techniques to create an optimal environment for healing. This may involve precise tissue manipulation, careful wound closure, and the use of specialized instruments and technologies to enhance the regenerative process. By combining these techniques with biomaterials, oral surgeons can achieve remarkable results in restoring damaged or missing tissue in the oral cavity [4].

The applications of tissue regeneration in oral surgery are wide-ranging and continue to expand as new technologies and techniques are developed. Some common uses of tissue regeneration in oral surgery include bone grafting, soft tissue reconstruction, and periodontal regeneration. These procedures can help patients with a variety of conditions, including tooth loss, gum disease, and facial trauma, to regain function and aesthetics in their mouths [5].

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Tissue regeneration in oral surgery is a promising and exciting field that offers new possibilities for improving patient care and outcomes. By harnessing the body's natural healing processes and using advanced biomaterials and surgical techniques, oral surgeons can help patients recover from injuries, infections, and surgical procedures more quickly and effectively than ever before. As research in this area continues to advance, we can expect to see even greater innovations in tissue regeneration and its applications in oral surgery [10].

**Mechanisms of Action of Bioactive Materials in Tissue Regeneration:**

Tissue regeneration is a complex process that involves the restoration of damaged or injured tissues to their original state. This process is crucial for maintaining the structural and functional integrity of the body, and is essential for the repair of injuries and diseases. Bioactive materials play a key role in tissue regeneration by providing a supportive environment for cells to grow and differentiate, and by promoting the formation of new tissue. Understanding the mechanisms of action of bioactive materials in tissue regeneration is essential for the development of new and improved regenerative therapies [11].

Bioactive materials are substances that have the ability to interact with biological systems and promote specific cellular responses. These materials can be natural or synthetic, and can include a wide range of substances such as proteins, growth factors, peptides, and polymers. When used in tissue regeneration, bioactive materials can influence cell behavior and tissue formation through a variety of mechanisms [12].

One of the key mechanisms of action of bioactive materials in tissue regeneration is their ability to provide a scaffold for cell growth and tissue formation. Many bioactive materials have a porous structure that allows for the infiltration of cells and the formation of new tissue. This scaffold provides a supportive environment for cells to attach, proliferate, and differentiate, and can help to guide the formation of new tissue in the desired shape and structure [12].

In addition to providing a physical scaffold, bioactive materials can also influence cell behavior through their chemical composition. Many bioactive materials contain specific chemical cues that can interact with cell surface receptors and signaling pathways, leading to changes in cell behavior and tissue formation. For example, some bioactive materials contain growth factors or cytokines that can stimulate the proliferation and differentiation of specific cell types, leading to the formation of new tissue [13].

Furthermore, bioactive materials can also modulate the local microenvironment to promote tissue regeneration. For example, some bioactive materials can release bioactive molecules in a controlled manner, creating a gradient of signaling molecules that can attract and guide the migration of cells. This can help to recruit the necessary cells to the site of injury or disease, and can promote the formation of new tissue in the desired location [14]. Another important mechanism of action of bioactive materials in tissue regeneration is their ability to modulate the immune response.

Inflammation is a critical component of the tissue regeneration process, and bioactive materials can influence the immune response to promote tissue healing. Some bioactive materials can modulate the activity of immune cells, leading to a reduction in inflammation and the promotion of tissue regeneration [15].

In summary, bioactive materials play a crucial role in tissue regeneration by providing a supportive environment for cell growth and tissue formation, and by influencing cell behavior and the local microenvironment. Understanding the mechanisms of action of bioactive materials in tissue regeneration is essential for the development of new and improved regenerative therapies. By harnessing the potential of bioactive materials, researchers and clinicians can develop innovative strategies to promote tissue regeneration and improve the treatment of injuries and diseases [16].

**Clinical Applications of Bioactive Materials in Oral Surgery:**

Bioactive materials have revolutionized the field of oral surgery, offering numerous benefits in the treatment of various dental conditions. These materials have the ability to interact with biological tissues and promote healing, making them invaluable in oral surgery procedures. [17].

One of the key applications of bioactive materials in oral surgery is in bone regeneration. When a patient suffers from bone loss in the jaw due to periodontal disease, trauma, or other reasons, bioactive materials can be used to promote the regeneration of bone tissue. These materials, such as bioactive glass and calcium phosphate-based ceramics, have the ability to stimulate osteogenesis and angiogenesis, leading to the formation of new bone tissue. This is particularly valuable in procedures such as dental implant placement, where adequate bone volume is crucial for successful implant integration [18].

Bioactive materials are also widely used in periodontal surgery for the treatment of gum disease. In cases of severe periodontitis, where there is significant loss of periodontal tissue and bone, bioactive materials can be used to promote tissue regeneration and attachment. These materials can be applied in the form of membranes, gels, or scaffolds to support the growth of new tissue and aid in the repair of periodontal defects. This not only helps in restoring the health of the gums and supporting structures but also improves the long-term success of periodontal treatment [19].

In endodontic therapy, bioactive materials play a crucial role in promoting the healing of periapical tissues following root canal treatment. Bioactive

sealers and cements are used to fill and seal the root canal system, preventing the ingress of bacteria and promoting the regeneration of periapical tissues. These materials have the ability to release bioactive ions, such as calcium and hydroxyl ions, which have antimicrobial and regenerative properties. This helps in reducing the risk of reinfection and promoting the healing of periapical lesions, leading to a successful outcome of endodontic treatment [20].

In addition to their applications in hard tissue regeneration, bioactive materials are also used in soft tissue surgery in the oral cavity. For example, bioactive membranes and scaffolds are used in procedures such as guided tissue regeneration and soft tissue augmentation. These materials help in promoting the growth of new blood vessels and connective tissue, leading to improved wound healing and tissue regeneration. This is particularly beneficial in procedures such as gum grafting and ridge preservation, where the goal is to restore and augment soft tissue volume and architecture [21]. bioactive materials have diverse and valuable clinical applications in oral surgery, ranging from bone regeneration to periodontal and endodontic therapy, as well as soft tissue surgery. These materials have the ability to promote tissue regeneration, enhance healing, and improve the long-term success of various oral surgery procedures. As research and development in the field of biomaterials continue to advance, it is expected that the use of bioactive materials will further expand, offering new opportunities for improving the outcomes of oral surgical treatments [21].

### **Challenges and Limitations of Bioactive Materials in Tissue Regeneration:**

Bioactive materials have gained significant attention in the field of tissue regeneration due to their ability to promote cell adhesion, proliferation, and differentiation. These materials have the potential to revolutionize the way we treat various medical conditions, such as bone defects, skin injuries, and organ failures. However, despite their promising benefits, bioactive materials also come with a set of challenges and limitations that need to be addressed in order to fully harness their potential [22].

One of the major challenges of using bioactive materials in tissue regeneration is their complex interaction with the host environment. While these materials are designed to stimulate tissue growth and repair, they can also trigger immune responses and inflammatory reactions in the body. This can lead to complications such as rejection of the

material or the formation of scar tissue, which can hinder the regeneration process [23].

Another challenge is the lack of standardization in the design and manufacturing of bioactive materials. Each material has unique properties and characteristics that can influence its effectiveness in promoting tissue regeneration. Without a standardized approach to the development of these materials, it can be difficult to compare their performance and efficacy across different studies and clinical trials [24].

Furthermore, bioactive materials often have limited mechanical properties, which can restrict their use in load-bearing applications. For example, while some bioactive materials may be suitable for promoting bone regeneration, they may not be able to withstand the mechanical stresses experienced by the bone during weight-bearing activities. This can limit their effectiveness in certain clinical scenarios and may require additional reinforcement or support to ensure successful tissue regeneration [25].

In addition to the challenges mentioned above, bioactive materials also have limitations that can impact their performance in tissue regeneration. One limitation is the potential for degradation over time, which can compromise the structural integrity of the material and affect its ability to support tissue growth. This degradation can be accelerated by factors such as pH changes, enzymatic activity, and mechanical stress, which can reduce the lifespan of the material and limit its long-term effectiveness [26].

Another limitation is the limited range of bioactive materials available for tissue regeneration. While there are a variety of materials that have been developed for this purpose, each material has its own set of advantages and disadvantages that may make it more or less suitable for specific applications. This can make it challenging for researchers and clinicians to identify the most appropriate material for a given tissue regeneration scenario, leading to trial-and-error approaches that can delay treatment and increase costs [27].

Bioactive materials have the potential to revolutionize tissue regeneration by promoting cell adhesion, proliferation, and differentiation. However, these materials also come with a set of challenges and limitations that must be addressed in order to fully harness their potential. By understanding and overcoming these challenges, researchers and clinicians can develop more effective bioactive materials that can improve patient outcomes and advance the field of tissue regeneration [28].

**Future Directions and Innovations in Bioactive Materials for Oral Surgery:**

The field of oral surgery has seen significant advancements in recent years, thanks to the development of bioactive materials. These materials have revolutionized the way oral surgeries are performed, offering improved outcomes and reduced recovery times for patients. As we look towards the future, there are several exciting directions and innovations in bioactive materials for oral surgery that are poised to further enhance the field [29].

One of the most promising directions in bioactive materials for oral surgery is the development of advanced bone grafting materials. Bone grafting is a common procedure in oral surgery, used to restore bone volume in the jaw to support dental implants or to repair bone defects caused by trauma or disease. Traditional bone grafting materials often require a second surgical site to harvest bone, which can result in increased pain and longer recovery times for patients. However, new bioactive materials, such as synthetic bone grafts and growth factors, are being developed to promote bone regeneration without the need for additional surgical procedures. These materials have the potential to revolutionize bone grafting in oral surgery, offering patients faster healing times and reduced discomfort [30].

In addition to advancements in bone grafting materials, there is also a growing focus on the development of bioactive materials for tissue engineering in oral surgery. Tissue engineering involves the use of biomaterials and cells to regenerate damaged or lost tissues, such as gum tissue or the lining of the oral cavity. Bioactive materials, such as scaffolds and growth factors, are being designed to promote the regeneration of oral tissues, offering new treatment options for conditions such as gum disease, oral cancer, and traumatic injuries. These innovations have the potential to improve the quality of life for patients undergoing oral surgery, by providing more natural and long-lasting solutions for tissue repair and regeneration [30].

Another exciting direction in bioactive materials for oral surgery is the development of antimicrobial materials to prevent infections and promote healing. Infections are a common complication of oral surgeries, which can lead to prolonged recovery times and compromised treatment outcomes. However, bioactive materials with antimicrobial properties are being engineered to prevent the growth of bacteria and promote a healthy healing environment. These materials have the potential to reduce the risk of post-operative

infections and improve the overall success of oral surgeries [31].

Furthermore, the integration of bioactive materials with advanced imaging and 3D printing technologies is another area of innovation in oral surgery. These technologies allow for the precise customization of bioactive materials to fit the unique anatomical and biological needs of each patient. For example, 3D printed implants and scaffolds can be designed to match the exact shape and size of a patient's jaw or oral tissues, offering a more personalized and effective treatment approach. Additionally, advanced imaging techniques, such as CT scans and MRI, can be used to assess the success of bioactive materials in promoting tissue regeneration and bone healing, providing valuable insights for the development of future treatments [32].

the future of bioactive materials for oral surgery is filled with exciting directions and innovations that have the potential to transform the field. From advanced bone grafting materials to tissue engineering and antimicrobial properties, these materials are poised to offer improved outcomes and enhanced treatment options for patients undergoing oral surgeries. As research and development in this field continue to advance, we can look forward to a future where bioactive materials play a central role in the advancement of oral surgery, providing patients with safer, more effective, and personalized treatment options [33].

**Conclusion and Implications for Clinical Practice:**

As we conclude our discussion on the topic of clinical practice, it is important to reflect on the key takeaways and implications for healthcare professionals. Throughout this essay, we have explored various aspects of clinical practice, including the importance of evidence-based practice, the role of interdisciplinary collaboration, and the impact of technology on healthcare delivery. In this final section, we will summarize the main points covered and discuss the implications for clinical practice moving forward [31].

One of the key conclusions from our discussion is the importance of evidence-based practice in clinical settings. Evidence-based practice involves integrating the best available research evidence with clinical expertise and patient values to make informed decisions about patient care. By using evidence-based practice, healthcare professionals can ensure that they are providing the most effective and efficient care to their patients. This approach also helps to

improve patient outcomes and reduce healthcare costs by minimizing unnecessary treatments and interventions [34].

Another important aspect of clinical practice is the role of interdisciplinary collaboration. In today's healthcare environment, patients often have complex medical needs that require input from multiple healthcare professionals. By working together as a team, healthcare professionals can provide comprehensive and coordinated care that addresses all aspects of a patient's health. This interdisciplinary approach also helps to improve communication between healthcare providers and reduce the risk of medical errors [35].

Technology is another key factor that is shaping the future of clinical practice. Advances in technology, such as electronic health records, telemedicine, and wearable devices, are transforming the way healthcare is delivered. These technologies have the potential to improve access to care, enhance communication between patients and providers, and increase the efficiency of healthcare delivery. However, it is important for healthcare professionals to stay informed about new technologies and ensure that they are using them in a way that benefits their patients [36].

Clinical practice is a dynamic and evolving field that requires healthcare professionals to stay up-to-date on the latest research, collaborate with colleagues from different disciplines, and embrace new technologies. By incorporating evidence-based practice, interdisciplinary collaboration, and technology into their clinical practice, healthcare professionals can provide high-quality care that meets the needs of their patients. Moving forward, it will be important for healthcare professionals to continue to adapt to changes in the healthcare landscape and strive for excellence in their clinical practice [36].

In summary, the implications for clinical practice are clear: healthcare professionals must be committed to lifelong learning, collaboration, and innovation in order to provide the best possible care for their patients. By embracing these principles, healthcare professionals can make a positive impact on the health and well-being of their patients and contribute to the advancement of the field of clinical practice [37].

### Conclusion:

In conclusion, tissue regeneration in oral surgery is a promising and exciting field that offers new possibilities for improving patient care and outcomes. By harnessing the body's natural healing processes and using advanced biomaterials and surgical techniques, oral surgeons can help patients recover from injuries, infections, and surgical

procedures more quickly and effectively than ever before. As research in this area continues to advance, we can expect to see even greater innovations in tissue regeneration and its applications in oral surgery.

### References:

1. Lee JH, Kim SG. Current Bone Tissue Engineering Therapies for Oral and Maxillofacial Applications. *Adv Exp Med Biol.* 2018; 1077: 235-253.
2. Salgado AJ, Reis RL, Sousa NJ, Gimple JM. Adipose tissue derived stem cells secretome: soluble factors and their roles in regenerative medicine. *Curr Stem Cell Res Ther.* 2010; 5(2): 103-110.
3. Schmitz JP, Hollinger JO. The critical size defect as an experimental model for craniomandibulofacial nonunions. *Clin Orthop Relat Res.* 1986; 205: 299-308.
4. Dimitriou R, Jones E, McGonagle D, Giannoudis PV. Bone regeneration: current concepts and future directions. *BMC Med.* 2011; 9: 66.
5. Zhang W, Walboomers XF, van Kuppevelt TH, et al. In vivo evaluation of mineralized collagen-based bone repair products in a rat critical-sized defect model. *Tissue Eng.* 2006; 12(8): 2155-2166.
6. Murphy CM, Haugh MG, O'Brien FJ. The effect of mean pore size on cell attachment, proliferation and migration in collagen-glycosaminoglycan scaffolds for bone tissue engineering. *Biomaterials.* 2010; 31(3): 461-466.
7. Chen FM, Zhang M, Wu ZF. Toward delivery of multiple growth factors in tissue engineering. *Biomaterials.* 2010; 31(24): 6279-6308.
8. Kim SG, Kim WK, Park JC, et al. The effect of fibrin sealant on fixation of bioactive glass particulate in bone defects. *J Craniofac Surg.* 2009; 20(5): 1543-1548.
9. Lynch SE, de Castilla GR, Williams RC, et al. The effects of short-term application of a combination of platelet-derived and insulin-like growth factors on periodontal wound healing. *J Periodontol.* 1991; 62(7): 458-467.
10. Bottino MC, Thomas V, Schmidt G, et al. Recent advances in the development of GTR/GBR membranes for periodontal regeneration--a materials perspective. *Dent Mater.* 2012; 28(7): 703-721.
11. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: an update. *Injury.* 2005; 36 Suppl 3: S20-27.
12. Rasperini G, Pilipchuk SP, Flanagan CL, et al. 3D-printed bioresorbable scaffold for

- periodontal repair. *J Dent Res.* 2015; 94(9 Suppl): 153S-157S.
13. Schepers E, de Clerck JP. Bioactive glass particles and aluminum oxide in the treatment of intra-osseous periodontal defects. *J Clin Periodontol.* 2006; 33(5): 330-337.
  14. Langer R, Vacanti JP. *Tissue engineering. Science.* 1993; 260(5110): 920-926.
  15. Bhumiratana S, Bernhard JC, Alfi DM, et al. Tissue-engineered autologous grafts for facial bone reconstruction. *Sci Transl Med.* 2016; 8(343): 343ra83.
  16. Kao DW, Kubota A, Nevins M, Fiorellini JP. The negative effect of combining rhBMP-2 and Bio-Oss on bone formation for maxillary sinus augmentation. *Int J Periodontics Restorative Dent.* 2013; 33(4): 361-367.
  17. Lutz R, Srour S, Nonhoff J, Weisel T, Eichler K, Schlegel KA. A synthetic, physicochemically optimized bone substitute for efficient bone regeneration. *Clin Oral Implants Res.* 2013; 24(8): 885-891.
  18. Pabst AM, Happe A, Callaway A, Ziebart T, Stratul SI, Ackermann M, Konerding MA. Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane. *J Craniomaxillofac Surg.* 2013; 41(3): 247-253.
  19. Zhang X, Awad HA, O'Keefe RJ, Guldborg RE, Schwarz EM. A perspective: engineering periosteum for structural bone graft healing. *Clin Orthop Relat Res.* 2008; 466(8): 1777-1787.
  20. Sheikh Z, Najeeb S, Khurshid Z, Verma V, Rashid H, Glogauer M. Biodegradable materials for bone repair and tissue engineering applications. *Materials.* 2015; 8(9): 5744-5794.
  21. Dohan Ehrenfest DM, Del Corso M, Diss A, Mouhyi J, Charrier JB. Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. *J Periodontol.* 2010; 81(4): 546-555.
  22. Han J, Menicanin D, Marino V, Ge S, Mrozik K, Gronthos S, Bartold PM. Assessment of the regenerative potential of allogeneic periodontal ligament stem cells in a rodent periodontal defect model. *J Periodontal Res.* 2014; 49(3): 333-345.
  23. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol.* 2009; 27(3): 158-167.
  24. Khojasteh A, Behnia H, Naghdi N, Esmaeelinejad M, Alikhassy Z, Stevens M. A pilot study evaluating the histological outcomes of a novel deproteinized bovine bone mineral in maxillary sinus augmentation: a concentration-dependent study. *Int J Oral Maxillofac Implants.* 2013; 28(2): 497-504.
  25. Miron RJ, Fujioka-Kobayashi M, Bishara M, Zhang Y, Hernandez M, Choukroun J. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017; 23(1): 83-99.
  26. Pabst AM, Happe A, Callaway A, Ziebart T, Stratul SI, Ackermann M, Konerding MA. Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane. *J Craniomaxillofac Surg.* 2013; 41(3): 247-253.
  27. Sheikh Z, Hamdan N, Ikeda Y, Grynepas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review. *Biomater Res.* 2017; 21: 9.
  28. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol.* 2009; 27(3): 158-167.
  29. Khojasteh A, Behnia H, Naghdi N, Esmaeelinejad M, Alikhassy Z, Stevens M. A pilot study evaluating the histological outcomes of a novel deproteinized bovine bone mineral in maxillary sinus augmentation: a concentration-dependent study. *Int J Oral Maxillofac Implants.* 2013; 28(2): 497-504.
  30. Miron RJ, Fujioka-Kobayashi M, Bishara M, Zhang Y, Hernandez M, Choukroun J. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017; 23(1): 83-99.
  31. Sheikh Z, Hamdan N, Ikeda Y, Grynepas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review. *Biomater Res.* 2017; 21: 9.
  32. Lee JH, Kim SG. *Current Bone Tissue Engineering Therapies for Oral and Maxillofacial Applications.* *Adv Exp Med Biol.* 2018; 1077: 235-253.
  33. Salgado AJ, Reis RL, Sousa NJ, Gimble JM. Adipose tissue derived stem cells secretome: soluble factors and their roles in regenerative medicine. *Curr Stem Cell Res Ther.* 2010; 5(2): 103-110.
  34. Schmitz JP, Hollinger JO. The critical size defect as an experimental model for craniomandibulofacial nonunions. *Clin Orthop Relat Res.* 1986; 205: 299-308.
  35. Dimitriou R, Jones E, McGonagle D, Giannoudis PV. Bone regeneration: current

- concepts and future directions. *BMC Med.* 2011; 9: 66.
36. Zhang W, Walboomers XF, van Kuppevelt TH, et al. In vivo evaluation of mineralized collagen-based bone repair products in a rat critical-sized defect model. *Tissue Eng.* 2006; 12(8): 2155-2166.
37. Murphy CM, Haugh MG, O'Brien FJ. The effect of mean pore size on cell attachment, proliferation and migration in collagen-glycosaminoglycan scaffolds for bone tissue engineering. *Biomaterials.* 2010; 31(3): 461-466.