Chitosan as a Bone Graft Biomaterial Enhances Osteogenesis after Tooth Extraction: A Systematic Literature Review

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ABSTRACT

Tooth extraction often results in changes to the dimensions of the alveolar ridge due to resorption, which can affect the stability and comfort of dental prostheses. Socket preservation efforts are crucial for preventing bone resorption and supporting the regeneration of both soft and hard tissues. Chitosan, a biomaterial derived from crustacean exoskeletons, has shown potential as a scaffold and graft material for bone regeneration. With its biocompatible, biodegradable, and antibacterial properties, chitosan supports osteogenesis through its osteoconductive, osteoinductive, and osteogenic capabilities. Additionally, the cationic nature of chitosan allows interaction with bacterial cell membranes, preventing infection and facilitating the transformation of macrophages from pro-inflammatory to anti-inflammatory types. This systematic literature review evaluates the benefits of chitosan in bone regeneration after tooth extraction. The study employed a PRISMA flow diagram to select relevant literature, resulting in 15 studies meeting the inclusion criteria. The findings indicate that chitosan significantly enhances osteoblast activity, accelerates new bone formation, and supports bone healing during the inflammatory, reparative, and remodeling phases without toxicity or risk of disease transmission. Thus, chitosan presents an innovative solution for bone regeneration in clinical dental practice. This study demonstrates that chitosan is an effective natural material for supporting bone healing after tooth extraction. It helps increase bone cell activity, speeds up new bone growth, and prevents infection. These findings support the use of chitosan as a safe and promising option for improving dental bone regeneration.

Keywords: bone_regeneration, chitosan, osteogenesis, scaffold, tooth_extraction

INTRODUCTION

Tooth extraction is a dental treatment procedure that can cause significant changes in the dimensions of the alveolar ridge. The tooth socket is made of cortical bone, leaving a post-extraction wound where the periodontal ligament is severed. Tooth extraction aims to remove the tooth from the socket without or with opening the soft and hard tissues. Ideally, tooth extraction causes minimal trauma to the supporting tissues of the tooth, but is not accompanied by pain. Post-extraction wounds generally heal well without causing prosthetic problems.[1]

Tooth extraction can cause loss of the alveolar ridge due to resorption. Several studies have shown that, within three months after tooth extraction, two-thirds of the hard and soft tissues will undergo resorption. Most of this bone loss occurs in the first six months after tooth extraction. After that, the average resorption rate increases by 0.5-1% per year. It is estimated that there will be a loss of alveolar bone width of up to 50% within 12 months after tooth extraction. This loss of alveolar bone will affect the stability, retention, and support of dental prostheses, thereby reducing patient comfort. The best time to prepare the alveolar ridge is at the time of tooth extraction, namely by performing a socket preservation procedure. The use of graft material in the tooth extraction socket is expected to slow down the resorption process of the socket walls and regenerate soft and hard tissues.[2,3]

Chitosan is a biomaterial scaffold and bone graft for bone regeneration. Chitosan, produced from exoskeletons, has biocompatible, biodegradable, and antibacterial properties. As a natural material, chitosan is often used to reduce the side effects of synthetic materials. Chitosan has antibacterial properties that support the inflammatory phase of the bone healing process by preventing infection, accelerating the transformation of macrophages from pro-inflammatory to anti-inflammatory types, which supports osteoblastogenesis.[4]

Chitosan exhibits osteoconductive, osteoinductive, and osteogenic properties, allowing the deposition and mineralization of extracellular matrix to form osteocytes in the ossification process. In addition, the antibacterial ability of chitosan is based on its cationic nature, which allows interaction with bacterial cell membranes, disrupting material transfer processes, bacterial lysis, and inhibition of protein synthesis. Chitosan is also used in nanocomposite scaffolds with hydroxyapatite to support bone regeneration in the inflammatory, reparative, and remodeling phases. This article emphasizes the benefits of chitosan as a bone scaffold material that supports regeneration and healing without causing toxicity or risk of disease transmission.[4]

METHODS

Search strategy

A literature search is based on the scientific findings derived from the literature review conducted in 2015 to 2025 using electronic databases (PubMed, Scopus, ScienceDirect, Google Scholar) to obtain some information related to the use of chitosan in the relationship with bone regeneration. This study searched each of the databases using the combination of several keywords, including Chitosan AND bone regeneration AND bone graft AND scaffold.

Screening process using the PRISMA flowchart diagram

Figure 1 shows the process of writing an article review through the Prisma flow chart. The article screening process was carried out based on journal selection criteria, including publications (original articles or review articles) published within the last 5 years, including free journals, journals that have discussions on increasing osteoblasts in bone graft material, Indonesian language journals, and or in English. The article screening strategy is carried out through three stages: looking at the article title, abstract, and full-text article.

PRISMA Flowchart

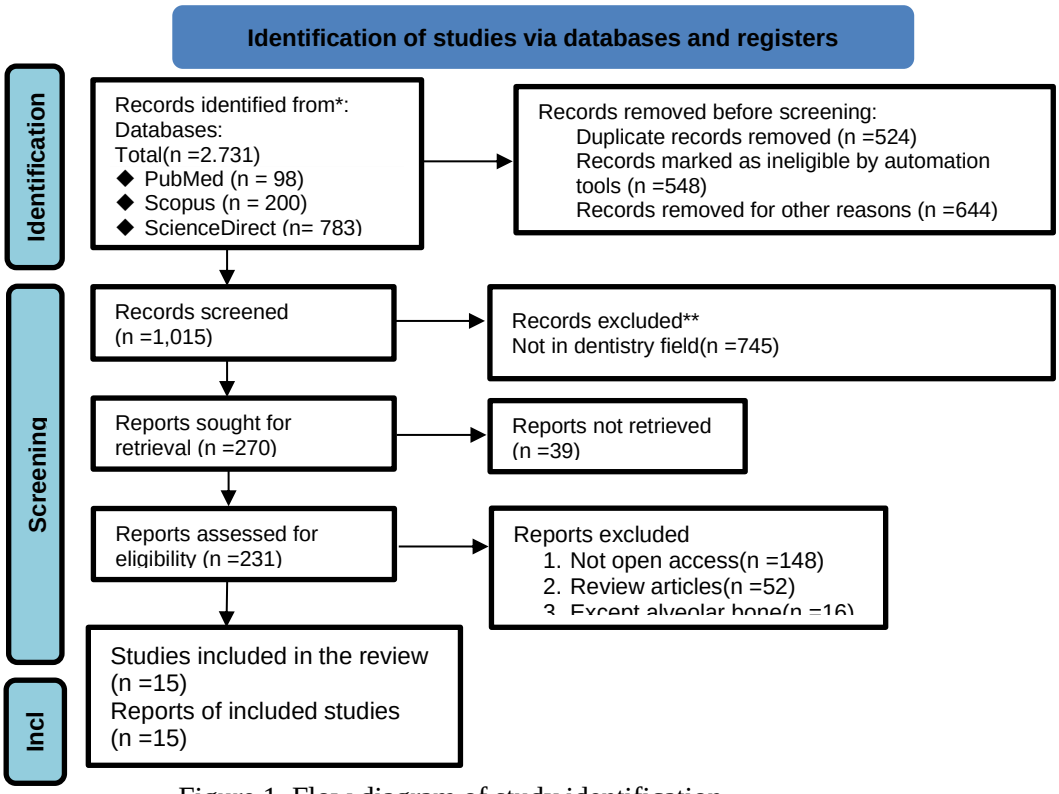

Figure 1. Flow diagram of study identification

RESULTS AND DISCUSSION

Experimental Studies Discussing the Efficacy of Chitosan in Dental Socket Preservation

Various experimental studies using animal models have investigated the effectiveness of chitosan in preserving dental sockets after tooth extraction (Tabel 1). In these studies, chitosan was applied to extraction sockets in animals such as Wistar rats or guinea pigs (Cavia cobaya) to observe its ability to reduce alveolar bone volume loss and accelerate new bone regeneration. The results showed that chitosan has significant pro-osteogenic properties, stimulating osteoblast proliferation and enhancing faster bone matrix formation compared to untreated controls. Chitosan also plays a role in reducing local inflammation and accelerating wound closure in the dental socket. Studies using chitosan scaffolds combined with biphasic calcium phosphate and additives like trichostatin A in rat models demonstrated improved bone fill and better preservation of alveolar shape. Additionally, chitosan gels derived from various sources, including crab shells and fish scales, proved effective in promoting biological responses in bone tissue of animal dental sockets. Overall, these animal model experimental studies provide strong evidence that chitosan is a promising biomaterial for dental socket preservation and could be further developed for clinical applications in humans.[16-30]

Table 1. Experimental Study Summary

	Research Name and Year	Research Title	Research Design	Data Sources and Data Collection Methods	Number of Samples or Informants	Key Findings
1	Sularsih and Endah Wahjuningsih (2015); [16]	*Expression of BMP-2 after Using Chitosan Gel with Different Molecular Weight on Wound Healing Process of Dental Extraction*	Experimental	Experimental laboratory study using Wistar rats with 3 treatment groups. 1. Use of immunohistochemistry to assess BMP-2 expression. 2. Time-based research (7, 14, 21 days).	21 Wistar rat	High molecular weight chitosan gel is more effective in increasing BMP-2 expression and accelerating bone healing.
2	Gani A., et al (2022); [17]	*Effectiveness of Chitosan Gel and Hydroxyapatite as Bone Graft on Periodontal Regeneration*	Experimental	Laboratory experiment with 3 groups (negative control, positive control, chitosan and HA combination). Immunohistochemical analysis for IL-1 and BMP-2.	27 Wistar rats	The combination of chitosan and HA increased BMP-2 expression and reduced IL-1 compared to the control, supporting regeneration.
3	Lopes MS., et al (2020); [18]	*Bone Regeneration Driven by Nano-Hydroxyapatite/Chitosan Composite Bioaerogel for Periodontal Regeneration*	Experimental	In vitro evaluation on human dental follicle mesenchymal cells (DFMSCs) and in vivo rat bone defect model. n-depth biological mechanism evaluation via genetic and histological analysis.	12 Wistar rats	Nano-hydroxyapatite/chitosan bioaerogel increased DFMSC proliferation, osteogenic differentiation, and new bone formation significantly.
4	Dewi RK., et al (2024); [19]	*Potential of Chitosan Black Soldier Flies Pupae on Post-Extraction Wound Healing Process*	Experimental	Histological measurements of macrophages and fibroblasts.	18 Male Cavia cobaya	The application of chitosan BSF pupae accelerates the post-extraction wound healing process in Cavia cobaya by increasing the number of macrophages and also increasing the number of fibroblasts which may be good for accelerate wound healing process.
5	Maula N., et al (2025); [20]	*The impact of chitosan derived from black soldier fly (Hermetia illucens) pupae on bone remodeling post-tooth extraction: an in vivo study*	Experimental	This study employed a true experimental design. The left mandibular incisor of guinea pigs was extracted. In the control group (n=9), the socket was filled with polyethylene glycol (PEG) gel as a placebo, while in the treatment group (n=9), the	18 guinea pigs	The application of chitosan BSF pupae gel can increase osteoblast numbers and decrease osteoclast numbers after tooth extraction, potentially accelerating bone formation and offering benefits for future bone regeneration.

Table 1. Experimental Study Summary

	Research Name and Year	Research Title	Research Design	Data Sources and Data Collection Methods	Number of Samples or Informants	Key Findings
				socket was filled with BSF pupae chitosan gel.		
6	Rusdy H., et al (2024); [21]	*Effect of Black Crab (Scylla Serrata) Chitosan Gel on the Three-Dimensional Socket Response and Fibroblasts after Tooth Extraction in Rattus Norvegicus*	Experimental	This research is an experimental study with a post-test only with a controlled group design. Observations were made by measuring the mesial-distal, lingual-buccal, and socket depths using calipers and the UNC15 probe and observing the number of fibroblasts histologically on Days 1, 3, and 7.	30 Wistar rats	Black crab (*Scylla serrata*) chitosan gel is effective in accelerating socket wound closure and stimulating fibroblasts in socket wounds after tooth extraction.
7	Hendrijantini N., et al (2019); [22]	*The Effect of a combination of 12% spirulina and 20% chitosan on macrophage, PMN, and lymphocyte cell expressions in post extraction wound*	Experimental	Determine macrophage, PMN, and lymphocyte cells of animal models treated with a combination of 12% spirulina and 20% chitosan on the 1st, 2nd, and 3rd post-extraction day	42 Cavia cobaya	A combination of 12% spirulina and 20% chitosan decreases PMN cells, also increases macrophage and lymphocyte cells on days 1, 2, and 3 after tooth extraction.
8	Siti Rochmah, Y. (2018); [23]	*Analisa Gel Kombinasi Platelet Rich Plasma Dan Chitosan Terhadap Peningkatan Jumlah Osteoblas Sebagai Bone Regeneration Pada Luka Pasca Ekstraksi Gigi Tikus Wistar.*	Experimental	Analyze the combination of PRP and Chitosan gel to increase the number of osteoblasts in post extraction wound of Wistar rat teeth	28 wistar rats	The combination of PRP and chitosan gel had a more optimal and effective effect in increasing the number of osteoblasts in post-extraction socket bone regeneration compared to PRP gel and chitosan gel.
9	Ragab M., et al (2025); [24]	*Evaluation of the Healing Potential of Silicon Carbide/Bioactive Glass/Carboxymethyl Chitosan Nanocomposites on Extraction Socket in Albino Rats*	Experimental	Healing efficacy of the materials was evaluated histologically, histomorphometricaly and by using real-time polymerase chain reaction (qRT-PCR) for quantitative analysis of osteopontin (OPN) gene expression.	36 male Albino rats	The SiC/BG/CMC group can have superior results as more mature bone formation with a more regularly arranged osteocytes as compared to other groups
10	Gharib HS., et al (2023);	*Histological And Immunohistochemical Evaluation Of*	Experimental	The effect of CS/nHA was evaluated histologically and	40 New Zealand	CS/nHA scaffolds could be used to augment bone healing and improve the

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	Research Name and Year	Research Title	Research Design	Data Sources and Data Collection Methods	Number of Samples or Informants	Key Findings
	[25]	*Chitosan–Nanohydroxyapatite Scaffold On Regenerative Bone Healing In Osteoporotic Rabbits*		immunohistochemically using ALP, OP, and BMP-2 markers.	white rabbits	quality of newly formed bone after extraction in patients with osteoporosis required for future surgical procedures such as dental implantation.
11	Dewi RK., et al (2025); [26]	*Chitosan Black Soldier Fly (Hermetia Illucens) Pupae Improves Osteoblasts and Decreases Osteoclasts Post-Tooth Extraction: In Vivo Studies*	Experimental	Expression of the number of osteoblasts and osteoclasts.	18 Cavia cobaya	BSF chitosan pupae can potentially accelerate bone formation Through increasing the number of osteoblasts and decreasing the number of osteoclasts posttooth extraction which may be good for bone regeneration
12	Putranto, R., et al (2022); [27]	*Effects Of Clamshell (Amusium Pleuronectes) Chitosan Extract On The Increase Number Of Osteoblast Of The Alveolar Bone Under Periodontitis*	Experimental	The increase in the number of osteoblasts was compared and analyzed.	30 Wistar rats	An increasing effect of alveolar bone osteoblasts from chitosan in scallop shell extract (*Amusium Pleuronecte*) in Wistar rats with periodontitis
13	Sukpaita T., et al (2023); [28]	*Alveolar ridge preservation in rat tooth extraction model by chitosan-derived epigenetic modulation scaffold*	Experimental	Micro-Computed Tomography (micro-CT), polyfluorochrome labeling, and histological analysis were used to evaluate the ridge-preservation ability	16 male Wistar	Chitosan biphasic calcium phosphate loaded with trichostatin A showed a significantly higher potential to induce bone formation and complete healing in the extraction socket than the other groups
14	Hendrijantini N., et al (2018); [29]	*The Effect of Combination Spirulina–chitosan on Angiogenesis, Osteoclast, and Osteoblast Cells in Socket Models of Hyperglycemic Rattus norvegicus*	Experimental	The capillary lumen, osteoblasts, and osteoclast cells were counted in tooth socket models of type 1 diabetes.	36 Wistar rats	Significant increment in the number of capillary lumen, osteoblast cells, and a decrease in osteoclasts in all three treated groups
15	Salim S., et al (2015); [30]	*Effect Spirulina Chitosan Combination as A Socket Preservation to Osteoblast, Osteoclast, and Collagen Density*	Experimental	Histopathology examination on the amount of osteoblast, osteoclast and collagen density.	28 Cavia cobayas	Combination spirulina 12% chitosan 20% can increase the amount of osteoblas and collagen density also reduce the amount of osteoclast on day 14th.

Bone Wound Healing

The wound healing process in bones includes several phases: the inflammatory phase, the reparative phase, and the bone remodeling phase. In the reparative phase, bone callus formation occurs due to the differentiation of progenitor cells into chondrocytes and osteoblast cells, vascular growth, and deposition of fibrous bone. Pro-inflammatory cytokines and chemokines produced in the reparative phase are Transforming Growth Factor-β (TGFβ1, TGFβ2, TGFβ3), Bone Morphogenic Protein (BMP), Vascular Endothelial Growth Factor (VEGF), Platelet-Derived Growth Factor (PDGF), and Fibroblast Growth Factor-2 (FGF-2), which are the main mediators of the reparative and bone remodeling processes. Bone Morphogenic Protein (BMP) is a pro-inflammatory cytokine that has osteoinductive properties, so that it stimulates osteoprogenitor cells to proliferate and differentiate to form new bone.[4]

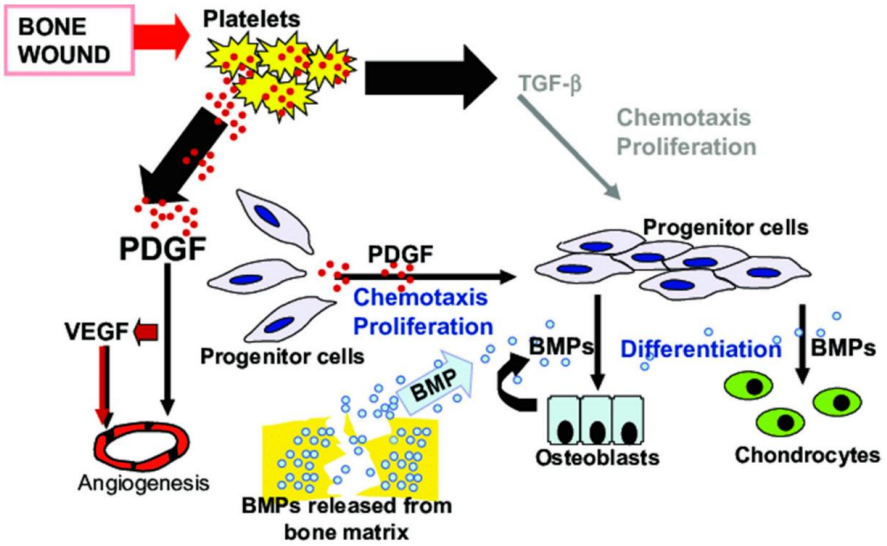

Figure 2. Growth factors expressed in bone wound healing. (PDGF, platelet-derived growth factor; VEGF, Vascular endothelial growth factor; BMPs, bone morphogenetic proteins; TGF-β, transforming growth factor beta) (Park et al., 2019).[7]

Biomaterials used in socket preservation after tooth extraction will enhance bone growth induced by their osteoconductive activity. New bone formation can differ significantly depending on the osteoconductive material used as graft material in the socket.[5] Bone tissue engineering innovations in socket preservation procedures include biomaterial selection and bone scaffold design. The requirements for making an ideal scaffold include osteoconductive, osteoinductive, osteogenic, biodegradable, good microstructure, and proper mechanical properties. Chitosan (poly-β-1,4-glucosamine) is a biomaterial that is still being developed to date, because it has been proven to be non-toxic, has excellent biocompatibility and biodegradability compared to other polymers, so chitosan is very useful in bone regeneration.[5,6] Chitosan has a remarkable effect on bone regeneration and healing. Several studies have shown that spongy chitosan increases osteoblast activity, enhances osteogenesis, and helps bone formation.[6]

Chitosan as Scaffold and Graft Material for Bone Regeneration

Chitosan, a natural polymer derived from the exoskeleton of crustaceans such as shrimp and crab, has attracted attention as a multifunctional biomaterial. With its biodegradability, biocompatibility, and antibacterial properties, chitosan has great potential in the field of regenerative medicine, especially in applications as scaffolds and graft materials for bone regeneration.[4]

Chitosan has several unique characteristics that make it ideal as a biomaterial. Its non-toxic, biodegradable nature and low inflammatory response make it safe for use in the human body. The chitosan production process involves partial deacetylation of chitin using chemical or biological methods, which determines its molecular weight and solubility in traditional solvents. In addition, the

metabolites resulting from the degradation of chitosan are easily absorbed by the body without any harmful side effects.[5]

The Role of Chitosan in the Bone Healing Process

In cases of bone damage, chitosan acts as a scaffold that supports the regeneration process through osteoconductive, osteoinductive, and osteogenic properties. As a natural material, chitosan can encourage the formation of new osteoblast cells and accelerate the deposition and mineralization of the extracellular matrix until mature osteocytes are formed through the ossification process.[4]

One of the important mechanisms of chitosan is its ability to control the inflammatory phase, the first phase in bone healing. The cationic nature of chitosan allows electrostatic interaction with the bacterial cell membrane, thereby disrupting membrane permeability and causing bacterial lysis. In addition, chitosan can inhibit bacterial protein synthesis by binding to bacterial DNA. This process helps reduce the risk of infection and supports the change of macrophages from the pro-inflammatory type to the anti-inflammatory type, which is important in supporting osteoblastogenesis and accelerating healing.[4.5]

Chitosan is often used in combination with other materials such as hydroxyapatite to form nanocomposite scaffolds. This combination produces a structure that supports adhesion, proliferation, differentiation, and mineralization of osteoblast cells. In its application, this nanocomposite scaffold can support all phases of bone regeneration, from inflammation to repair, to remodeling, by improving bone structure and function as a whole.[4]

Regenerative Benefits of Chitosan

As an antibacterial agent and biomaterial scaffold, chitosan not only prevents infection but also accelerates the bone regeneration process through a mechanism that supports the balance between bone resorption by osteoclasts and new bone formation by osteoblasts. Thus, chitosan is a superior alternative compared to traditional graft materials such as autograft or allograft, which have higher risks of complications and disease transmission.[4]

Conclusion

Chitosan offers an innovative solution for bone regeneration with its multiple regenerative benefits, including antibacterial properties and the ability to support osteoblastogenesis. The combination of its safety in the human body and efficiency in accelerating the bone healing process makes chitosan a superior choice for clinical applications in regenerative medicine.

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