

The role of chitosan in Regenerative Endodontics: A Review of Current Advances and Future Directions

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Abstract: Chitosan, a biopolymer derived from chitin, has gained attention in regenerative endodontics due to its biocompatibility, antibacterial properties, and capacity to promote tissue regeneration. This review explores the applications of chitosan in endodontics, particularly its role in scaffold development for pulp regeneration and as a drug delivery system for antibiotics and growth factors. Chitosan-based scaffolds exhibit excellent cellular compatibility, encouraging the proliferation and differentiation of dental pulp stem cells. The incorporation of chitosan into antibiotic formulations, enhances antimicrobial efficacy while mitigating cytotoxic effects of the drug. Innovations in chitosan, including nanoparticles and hydrogels, are showing promising clinical outcomes. This review aims to consolidate current findings and discuss the challenges and future prospects of chitosan in regenerative endodontics, emphasizing its potential to revolutionize treatment protocols and enhance treatment outcomes.

Keywords: Chitosan, Endodontics, Biomaterials, Antimicrobial Activity, Regenerative Dentistry, Drug Delivery , Outcome

INTRODUCTION

Traditional endodontic treatments focus on removing infected pulp tissue and filling the canal, regenerative endodontics aims to restore the vitality of the pulp and regenerate the tooth structure, offering a more biologically favourable solution . This field not only aims to enhance the clinical outcomes of root canal treatments but also restore the natural functions of the pulp-dentin complex .

The increasing prevalence of traumatic dental injuries, especially among children and adolescents, has further underscored the need for effective

regenerative techniques in endodontics. Traditional methods may result in compromised tooth structure and functionality, leading to complications such as root fracture and impaired tooth development . Regenerative endodontics offers an innovative strategy by employing biomaterials that facilitate the healing process and support the regeneration of dental pulp tissue [1,2].

Chitosan, a biopolymer derived from chitin, has emerged as a promising material in the field of regenerative endodontics due to its favourable biological properties. It is non-toxic, biodegradable, and exhibits excellent biocompatibility, making it suitable for dental applications [3]. Furthermore, chitosan possesses inherent antibacterial properties, which can help in reducing bacterial load within the root canal system, thereby enhancing the success of regenerative procedures . Its ability to promote cellular attachment and proliferation has been demonstrated in various studies, indicating its potential as a scaffold material in pulp regeneration [4].

In regenerative endodontics, chitosan can be utilized in various forms, including scaffolds, hydrogels, and drug delivery systems [2]. Chitosan-based scaffolds can provide a three-dimensional matrix that supports the growth and differentiation of dental pulp stem cells, facilitating the regeneration of functional pulp tissue [5]. Additionally, the incorporation of growth factors and bioactive molecules into chitosan matrices can further enhance the regenerative potential by promoting angiogenesis and neurogenesis, which are crucial for pulp healing [6]. Despite the promising applications of chitosan in regenerative endodontics, challenges remain

regarding its mechanical properties and the optimization of its formulations for clinical use. Research is ongoing to improve the physical characteristics of chitosan-based materials and to better understand their interactions with dental pulp cells [7].

This review aims to provide a comprehensive overview of the current applications of chitosan in regenerative endodontics, highlighting its benefits, limitations, and future directions for research and clinical practice.

METHODS

In the present review, the literature search was done by the online search regarding chitosan nanoparticles. The comprehensive literature search was conducted using different electronic databases like PubMed, Medline, Web of Science, Google etc. and the articles published in the different journals were obtained. The keywords used for the computer-based search were like 'Nanoparticle'; 'Nanotechnology'; 'Dentistry'; 'Review'; 'Endodontics'; etc. Further articles were sought by manually searching reference lists of the relevant article publications. The articles which were published only in the English language were selected. The review data consisted of different original articles, reviews, textbooks, etc. were documented. There was no patient involvement in the review.

Chitosan as a scaffold material

Chitosan facilitates the adhesion, proliferation, and differentiation of dental pulp stem cells (DPSCs), which are critical for effective pulp tissue regeneration [8]. The biodegradability of chitosan scaffolds allows for gradual degradation over time, which minimizes the risk of chronic inflammation and provides a dynamic environment for newly formed tissues to replace the scaffold naturally [9]. The mechanical properties of chitosan scaffolds can be optimized to closely mimic the natural extracellular matrix of dental pulp. Modifying the porosity and thickness of chitosan scaffolds enhances nutrient diffusion and facilitates cellular migration, both of which are essential for successful tissue regeneration [8,9]. Chitosan's intrinsic antibacterial properties are another critical factor in its application in regenerative endodontics. The positive charge of chitosan can disrupt bacterial cell membranes, providing a protective mechanism against infection during the regeneration process [10]. This is particularly beneficial in endodontic treatments,

where bacterial contamination can significantly compromise healing outcomes. Incorporating chitosan-based scaffolds can thus reduce bacterial colonization while promoting tissue regeneration [11].

Chitosan in Drug Delivery

Its application in drug delivery has been particularly promising in two specific areas: as an antibacterial drug carrier and in combination with growth factors for tissue regeneration.

1. Antibacterial Drug Carrier :

The positive charge of chitosan enables it to interact with bacterial cell membranes, enhancing the uptake of antimicrobial agents and improving their efficacy. Various studies have demonstrated that chitosan-based formulations can significantly enhance the antibacterial activity of loaded drugs, such as amoxicillin and tetracycline, against common pathogens like *Escherichia coli* and *Staphylococcus aureus* [12,13]. The release kinetics of these drugs can be tailored by modifying the chitosan polymer's molecular weight and degree of deacetylation, resulting in controlled release profiles that sustain drug availability at the infection site [14]. Moreover, the ability of chitosan to form nanoparticles enhances drug solubility and stability, further contributing to its effectiveness as an antibacterial drug carrier.

2. Combination with Growth Factors :

In regenerative medicine, chitosan has shown great potential as a delivery system for growth factors, which are crucial for tissue repair and regeneration. When combined with growth factors like platelet-derived growth factor (PDGF) or vascular endothelial growth factor (VEGF), chitosan can create a synergistic effect that enhances cellular proliferation and differentiation. The biodegradable nature of chitosan allows for the sustained release of these growth factors, promoting long-term therapeutic effects in tissue engineering applications. Chitosan-based scaffolds can effectively deliver growth factors to targeted tissues, improving healing outcomes in bone and soft tissue repair [15]. The ability to engineer chitosan-based systems to provide controlled release and targeted delivery of growth factors makes it a promising candidate for advancing regenerative therapies.

Chitosan for Pulp Regeneration

Two significant aspects of chitosan in pulp regeneration include its cellular response and its role as a carrier for antibiotic delivery.

1. Cellular Response to Chitosan :

The interaction between chitosan and dental pulp cells is crucial for pulp regeneration. Studies have shown that chitosan promotes the proliferation and differentiation of pulp stem cells, leading to enhanced tissue regeneration. The biocompatibility of chitosan facilitates cell adhesion and growth, while its bioactive properties stimulate the expression of growth factors essential for tissue healing [11]. Chitosan has been found to enhance the synthesis of extracellular matrix components, which are vital for the structural integrity and function of regenerated pulp tissue. Moreover, the immunomodulatory effects of chitosan can help regulate inflammation during the healing process, further supporting pulp regeneration [16]. This cellular response makes chitosan a promising material for developing scaffolds in pulp regeneration therapies.

2. Chitosan-Loaded Antibiotic Paste :

Chitosan's ability to serve as a drug delivery system is particularly relevant in the context of pulp regeneration, especially in cases where infection is a concern. Chitosan-loaded antibiotic paste can effectively deliver antimicrobial agents directly to the pulp tissue, aiding in infection control while promoting healing. Studies have demonstrated that chitosan-based formulations can enhance the antibacterial efficacy of loaded antibiotics, such as chlorhexidine and minocycline, against root canal pathogens [17]. The controlled release properties of chitosan allow for sustained drug delivery, which helps maintain therapeutic levels of antibiotics in the pulp chamber over time. This approach not only minimizes the risk of bacterial reinfection but also creates a conducive environment for pulp tissue regeneration. The combination of chitosan's regenerative capabilities with its role as a carrier for antibiotics represents a significant advancement in regenerative endodontics.

LIMITATIONS

1. Mechanical Properties: Chitosan lacks the mechanical strength required for certain dental applications. Its mechanical properties may not be sufficient to withstand the forces encountered in the oral environment.

2. Solubility Issues: Chitosan's solubility in neutral or alkaline conditions can limit its effectiveness as a scaffold for pulp regeneration. Strategies to enhance its stability in such conditions are necessary .

3. Variability in Sources: The properties of chitosan can vary depending on its source, degree of deacetylation, and molecular weight, potentially affecting its consistency and performance in clinical applications .

FUTURE DIRECTIONS

The future of chitosan in pulp regeneration holds exciting possibilities:

1. Nanotechnology Integration: Combining chitosan with nanomaterials can enhance its mechanical properties and drug delivery capabilities, making it more effective in clinical applications .

2. Composite Scaffolds: Developing composite scaffolds that incorporate chitosan with other biopolymers or bioactive materials can improve mechanical strength and functional performance in pulp regeneration.

4. Clinical Trials: Further clinical studies are needed to evaluate the long-term efficacy and safety of chitosan-based materials in human subjects, ensuring their applicability in routine dental practice .

CONCLUSION

Chitosan has emerged as a promising biomaterial for pulp regeneration, demonstrating significant potential due to its biocompatibility, biodegradability, and antimicrobial properties. Its ability to enhance cellular responses and serve as a drug delivery system for antibiotics is particularly valuable in managing pulpitis and promoting tissue regeneration. While there are limitations regarding its mechanical properties and variability, ongoing research and advancements in nanotechnology and composite materials offer exciting opportunities for improving chitosan's application in regenerative dentistry. Future studies and clinical trials will be essential in establishing its efficacy and safety in clinical settings, ultimately contributing to the advancement of pulp regeneration strategies in endodontics.

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