Article type:
Review Article
Volume 1, Issue 1, pp 70-75
Article history:
Received 20 June 2024
Revised 08 August 2024
Accepted 18 September 2024
Published online 01 October 2024

Biomimetic Nanomaterials in Regenerative Oral Medicine, a Minireview

1. Alireza. Asadi: Shiraz University of Medical Sciences, Shiraz, Iran
2. Melika. Rezaee: Faculty of Materials Engineering, Islamic Azad University, Najafabad, Isfahan, Iran
3. Yasamin. Ghahramani: Oral and Dental Disease Research Center, Department of Endodontics, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran*

Corresponding author email address: ghahramany@sums.ac.ir

ABSTRACT

Regenerative dentistry uses advanced biomaterials such as nano scaffolds to address oral defects. These scaffolds mimic the extracellular matrix (ECM), promoting cell attachment, proliferation, differentiation and eventually, tissue regeneration, Common fabrication methods include electrospinning, self-assembly and thermal-induced phase separation (TIPS), allowing precise control over scaffold properties. This article reviews the use of nano scaffolds in repairing dental pulp, enamel, periodontal ligaments and bone tissue.

Keywords: Regenerative dentistry, Nano scaffold, Nanomaterials, Nano mimicking structures.

How to cite this article:
Asadi, A., Rezaee, M., & Ghahramani, Y. (2024). Nano Scaffolds in Regenerative Dentistry. *Journal of Oral and Dental Health Nexus*, 1(1), 70-75. https://doi.org/10.61838/jodhn.1.1.7

Introduction

Nanomaterials are materials exhibiting nanoscale dimensionality, with at least one dimension or constituent component measuring within the 1-100 nm range (1). Nano-materials are of interest because of their unusual mechanical, thermo-mechanical, electrical, optical and magnetic properties (2, 3). Surface atoms possess extra energy, known as surface free energy(4). This energy is usually insignificant for bulk materials because it only affects a few atomic layers at the surface, and the proportion of surface atoms is tiny compared to the total volume. However, in nanomaterials like nanoparticles, nanowires, and thin films, the surface area becomes proportionally large. This increased surface-to-volume ratio makes surface free energy a significant factor in their behavior (3, 5, 6).

The diverse applications of nanomaterials range from nanoprobe sensing and point-of-care diagnostics to cancer biosensors and bone scaffolding. Further applications include protein separation, water purification, microbial fuel cells, lithium batteries, and electrochemical sensors and more (3, 7). Various methods are employed to synthesize nanomaterials, such as vacuum deposition, vacuum vaporization, and solution synthesis. Additional techniques include chemical vapor deposition, chemical vapor condensation, gas condensation, combustion synthesis, physical vapor deposition, mechanical attrition, self-propagating high-temperature synthesis, chemical precipitation, sol-gel methods, and electrodeposition, among others (7, 8).

Nano-scaffolds

Nano scaffolds are advanced three-dimensional structures engineered at the nanoscale. These structures are meticulously designed to replicate the extracellular matrix (ECM), which is the natural environment surrounding cells in living tissues (9). The ECM is a complex network of proteins and other molecules that provide structural and biochemical support to cells (10, 11). By mimicking the ECM, nano scaffolds create a similar supportive environment for cells in laboratory or clinical settings (12).

The primary function of nano scaffolds is to serve as a framework or scaffold for cells to attach, grow, and organize themselves. When cells are introduced to these scaffolds, they adhere to the surface, begin to multiply (proliferate), and eventually differentiate into specialized cell types (13). This process is crucial for tissue regeneration, as it allows damaged or lost tissues to be repaired or replaced with new, functional tissue (14, 15). For example, in dentistry, nano scaffolds can be used to regenerate dental pulp (16), periodontal ligaments (17), or even bone tissue (15, 18, 19).

Fabrication techniques

Electrospinning is a popular method for producing nanofiber scaffolds that mimic the natural ECM (20). It uses a strong electric field to create a charged jet from a polymer solution. The solvent evaporates as the jet travels, leaving behind nanofibers that collect on a surface. These scaffolds offer control over fiber properties like diameter and porosity. This makes them well-suited for periodontal ligament regeneration (21), dental pulp engineering (22), and other applications due to their high surface area that supports cell growth and nutrient exchange (23, 24).

Self-assembly is an innovative bottom-up technique for creating nano scaffolds in regenerative dentistry. In this method molecules spontaneously organize into nanostructures via non-covalent interactions, mimicking the natural ECM (25, 26). This allows for tailored mechanical properties, porosity, and bioactivity, making them ideal for endodontic tissue engineering (27, 28).

Thermal-induced phase separation (TIPS) is another technique used to create nano scaffolds for regenerative dentistry by cooling a polymer solution, causing it to separate into polymer-rich and polymer-poor phases. The polymer-rich phase forms the scaffold matrix, while the polymer-poor phase creates pores. After solvent removal, a highly porous, nanofibrous scaffold remains, mimicking the extracellular matrix (ECM). TIPS allows control over pore size, porosity, and fiber diameter, making it ideal for dental pulp regeneration, periodontal repair, and bone grafting. It is cost-effective, scalable, and can be enhanced with bioactive molecules to improve regenerative outcomes (29, 30).

Applications of nano scaffolds in regenerative dentistry

Pulp

A significant application of nano scaffolds lies in dental pulp regeneration. Nano scaffolds can be utilized to regenerate pulp tissue within teeth that have been damaged or infected. This process involves seeding the scaffolds with dental stem cells, ultimately restoring the tooth's vitality (31, 32). The scaffolds function by providing a supportive environment that promotes odontoblast differentiation, leading to the formation of dentin (33), and thus presenting a potential alternative to conventional root canal treatments specially for complicated cases (31, 34, 35). Furthermore, nano scaffolds can be functionalized with growth factors, such as Bone Morphogenetic Proteins (BMPs) or Vascular Endothelial Growth Factor (VEGF). This functionalization enhances cell recruitment and tissue regeneration, consequently improving the overall outcomes associated with pulp therapy (36, 37).

Alveolar bone

Nano scaffolds have also become a cornerstone in alveolar bone regeneration, offering a highly effective solution for repairing bone loss caused by trauma, periodontal disease, or tooth extraction (38). Alveolar bone, which supports the teeth, is critical for maintaining oral function and aesthetics (39). Traditional bone grafts, while effective, have limitations such as donor site morbidity, limited availability, and risk of rejection (40-42). Nano scaffolds address these challenges by providing a synthetic, biocompatible, and biodegradable framework that mimics ECM (15).

These scaffolds are typically fabricated from materials like nano-hydroxyapatite (nHA) (43), bioactive glass (44), or composite polymers, which closely resemble the mineral composition of natural bone (13, 15). Techniques such as electrospinning and thermal-induced phase separation (TIPS) are used to create scaffolds with precise pore sizes, high porosity, and interconnected networks, ensuring optimal nutrient exchange and cell migration (31). Additionally, scaffolds infused with TGF-β3 + BMP-2 have shown stimulation bone regeneration in alveolar defects (45). By integrating with the host tissue and gradually degrading as new bone forms, nano scaffolds offer a promising, minimally invasive approach to alveolar bone regeneration, restoring both function and aesthetics in patients with bone loss (15).

Root canal disinfection

Nanofibrous scaffolds have also emerged as a promising tool in regenerative dentistry, particularly for root canal disinfection and tissue regeneration (31, 46). It is essential to use biomaterials that minimize bacterial presence in the root canal while being non-toxic to cells and promoting tissue regeneration (47). Advanced nano scaffolds have been developed to act as controlled drug delivery systems tailored to specific therapeutic needs(48). Unlike propylene glycol, the most commonly used carrier for antimicrobial pastes in root canal treatment, nanofibers offer the advantage of a larger surface area and the potential for sustained, controlled drug release over a longer period (28, 49, 50).

Enamel

Enamel, the hard outer layer of teeth (51), cannot regenerate naturally once damaged due to its acellular structure (52). Nano scaffolds offer a promising solution by mimicking the natural enamel matrix and promoting the growth of hydroxyapatite crystals (53), the primary component of enamel (54). These scaffolds are designed with a biomimetic structure that attracts calcium and phosphate ions, facilitating the formation of organized enamel-like material (19, 55). Functionalized with bioactive molecules, nano scaffolds encourage mineralization and integrate seamlessly with existing enamel, restoring its strength and function. This approach is particularly useful for repairing early-stage cavities, restoring worn enamel, and enhancing tooth aesthetics without the need for invasive procedures (56, 57).

Salivary glands

Nano scaffolds offer a promising solution for regenerating damaged salivary glands, which are essential for saliva production and oral health. By mimicking the natural extracellular matrix, nano scaffolds provide a supportive 3D structure for stem cell growth and differentiation into functional salivary gland cells, such as acinar and ductal cells. They also promote angiogenesis (new blood vessel formation) and stimulate secretory function(58), helping to restore saliva production in conditions like xerostomia (dry mouth) caused by radiation therapy, autoimmune diseases (e.g., Sjögren's syndrome), or aging (37, 59-64).

Periodontal Ligament (PDL)

Nanofibrous scaffolds and hydrogels replicate the PDL's complex structure, offering a framework for periodontal fibroblasts to attach and align. These materials also stimulate the production of extracellular matrix, essential for tissue repair. By mimicking natural tissue architecture, they promote functional regeneration of the PDL. This approach enhances cell behavior and tissue integration, improving overall periodontal healing. Such innovations hold promise for advanced periodontal therapies (37, 65).

Conclusion

Nano scaffolds in regenerative dentistry offer groundbreaking potential for tissue regeneration, particularly in dental pulp, enamel, periodontal ligaments and alveolar bone repair. Various fabrication techniques can be employed to create nano scaffolds, each with specific applications in dentistry. Further research needs to be done in order to provide solutions for possible future applications.

Authors' Contributions

All authors equally contributed to this study.

Acknowledgments

We would like to express our appreciation and gratitude to all those who cooperated in carrying out this study.

Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

Funding

This research was carried out independently with personal funding and without the financial support of any governmental or private institution or organization.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

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