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Nano-Hydroxyapatite: A Driving Force for Bone Tissue Regeneration in Orthopedic Surgery: Challenges and Future

(Review Article)

Abstract
Nanotechnology is currently recognized as a technology with vast application potential across multiple fields, particularly in medicine. Nanomaterials and nanostructures, owing to their ultra-microscopic dimensions, high surface area, and unique physicochemical properties, are increasingly employed in orthopedic surgeries. These materials, due to their distinctive features in interacting with living tissues, are considered key components in prostheses and medical devices, and they have led to significant advancements in bone tissue engineering, the design of implantable materials, and diagnostic as well as therapeutic processes. In this study, various databases including ISI Web of Science, PubMed, SID, Scholar, Scopus, and ScienceDirect were utilized. The keywords applied consisted of nanohydroxyapatite, bone defect repair, prosthesis, clinical evaluation, and fracture healing. The use of biocompatible nanomaterials in orthopedic prostheses—particularly due to their ability to stimulate cellular growth, regenerate damaged tissues, and improve cellular microenvironmental properties—has had a profound impact on enhancing orthopedic therapies. These technologies have successfully facilitated bone repair processes. This article has been prepared to provide a deeper understanding of the application of hydroxyapatite at the nanoscale and its potential therapeutic objectives in orthopedic surgeries.

Keywords: Limb prosthesis, Biotechnology, Nano hydroxyapatite collagen, Bone regeneration.

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Introduction

In recent years, the application of biomaterials in the medical field has increased substantially. These materials generally possess properties that ensure both biocompatibility and favorable mechanical–physical characteristics. Among the most significant and promising applications of biomaterials is the physical replacement of organs in humans and other animals. Since the external surfaces of prostheses remain in constant contact with living tissues, they are fabricated from alloys that demonstrate high resistance within the body. A critical application of prostheses in orthopedic surgery is the support of bones and the repair of skeletal defects(1).

The objective of this study was to review the effects of hydroxyapatite nanoparticles in accelerating bone fracture healing and their application as coatings for orthopedic prostheses/implants.

Keywords included nanohydroxyapatite, bone defect repair, prosthesis, clinical evaluation, and fracture healing. For this purpose, relevant publications were retrieved from databases such as ISI Web of Science, SID, Google Scholar, PubMed, Scopus, and ScienceDirect, and articles meeting the inclusion criteria were analyzed.

Micro- and Nanostructure of Bone Tissue

Bone tissue is a specialized and dynamic connective tissue that fulfills both structural and metabolic roles, including mechanical support, organ protection, and the storage of minerals such as calcium and phosphorus. The bone matrix consists of type I collagen fibers and hydroxyapatite crystals, which provide mechanical strength and hardness. Bone remodeling is regulated through the coordinated activity of osteoblasts and osteoclasts. During fracture repair, angiogenesis plays a crucial role by supplying nutrients and growth factors such as vascular endothelial growth factor (VEGF). Impaired vascularization or inadequate mechanical stability may result in delayed union or nonunion, particularly in bones with limited blood supply(2,3).

Bone tissue is classified into two major types: compact bone and spongy bone.

- **Compact bone:** This type appears dense and structureless to the naked eye and forms the outer cortical layer. Owing to its compact architecture, it exhibits high resistance to compressive forces.
- **Spongy bone:** This type is composed of trabeculae with visible intertrabecular spaces. Its porous and lightweight structure reduces overall bone mass while enhancing resistance to mechanical impacts(2,3).

Chemical Composition of Bone

Bones are composed of approximately 70% mineral content and 30% organic content. This chemical composition is responsible for their hardness and mechanical strength(2,3).

Bone Cells

Several distinct cell types contribute to bone structure and function. Osteoblasts are responsible for synthesizing the bone matrix. Mature osteocytes, embedded within lacunae, maintain bone tissue. Osteoclasts perform bone resorption and are essential for remodeling processes(2–4).

Biocompatibility

In general, a biocompatible material is defined as a synthetic or natural non-living substance that is employed as part of a living system, or for a specific function, in direct contact with living tissue for a defined period of time. For proper performance, the material must meet specific standards for interaction with biological systems. These standards include mechanical properties appropriate for the intended site, biological stability, and the minimization of adverse biological or immunological responses(5).

One of the common approaches to improving the biocompatibility of polymer surfaces is the grafting of monomers onto the polymer surface. Since biocompatibility is primarily related to the surface rather than to the bulk properties of polymers, surface modification is largely dependent on altering physicochemical characteristics such as wettability. For this reason, hydrophilic monomers can be employed for surface modification(5). Nanobiotechnology, as an advanced and innovative branch of nanotechnology, represents the convergence of nanoscience and biology. By integrating molecular biology, physics, and materials engineering, this field has contributed to significant advancements in biotechnology, which in turn have led to transformative developments across various scientific disciplines. In other words, nanobiotechnology constitutes the interface between life sciences and materials science(6).

Nanocomposites

Nanocomposites are composites in which one or more components exist at the nanometer scale. Specifically, at least one constituent exhibits dimensions below 100 nm. At present, nanocomposites are recognized as a class of nanomaterials with broad and promising application potential. They are composed of two phases: a matrix (base material) and nanoparticles that serve as reinforcements. These nanoparticles, generally introduced in very small amounts (up to 10%), are dispersed within the matrix to enhance strength and other mechanical properties.

Bone itself is inherently a nanocomposite composed of organic and inorganic nanostructures. These nanoscale features play a fundamental role in bone formation and remodeling, where they act as key elements in initiating the repair process(7,8).

Fabrication of Hydroxyapatite-Based Prostheses/Implants

Hydroxyapatite is the naturally occurring mineral form of calcium apatite with the formula $Ca_5(PO_4)_3(OH)$, although it is commonly written as $Ca_{10}(PO_4)_6(OH)_2$ (Figure 1). This material is considered the most important bioceramic used in medicine and dentistry due to its unique biological properties and its close structural similarity to the mineral component of bone tissue. Among its notable properties are the ability to stimulate bone growth, to form direct bonding with bone, and to provide excellent osteointegration.

Hydroxyapatite has been applied extensively in the medical field, including in the filling of bone defects, the fabrication of bone scaffolds, the coating of metallic prostheses, and the preparation of injectable bone cements. It exhibits favorable biocompatibility with various cell types such as osteoblasts, osteoclasts, and bone-forming cells. Due to the structural resemblance between hydroxyapatite and natural bone, cells do not distinguish between the two(9,10).

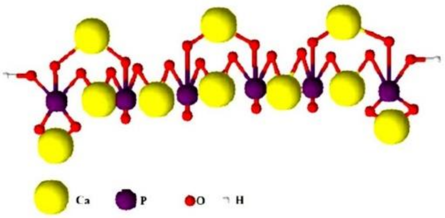

Figure 1: Hydroxyapatite Structure (https://www.researchgate.net)

Hydroxyapatite, as a bioceramic, has significant applications in orthopedic surgery, particularly as a surface coating on prostheses and for localized drug delivery with controlled release capabilities. Due to these properties, it is considered an ideal material for bone tissue engineering and various orthopedic prostheses. Hydroxyapatite nanocomposites are being developed as scaffolds for bone tissue engineering not only because of their high chemical and structural similarity to natural bone but also due to unique features such as high porosity, increased surface area, and enhanced mechanical strength compared to pure hydroxyapatite. These characteristics contribute to improved mechanical performance and protein adsorption in vivo(7,9,10). Hydroxyapatite can be synthesized using various methods, each offering specific advantages and applications(11). The use of hydroxyapatite in the form of nanoparticles for bone tissue repair not only avoids significant side effects but can also considerably reduce the time required for grafting or regenerating bone tissue lost due to trauma, disease, or other conditions. Compared with natural bone grafts, which carry multiple risks, hydroxyapatite nanoparticles have demonstrated higher success rates(12). Orthopedic implants are medical devices designed to reinforce or replace joints and bones in damaged or deformed regions. For instance, a patient may require an implant due to congenital conditions(13,14). Orthopedic surgeons, depending on patient-specific conditions, replace the affected tissue with implants using specialized surgical instruments. Most of these implants are fabricated from titanium alloys or stainless steel, while some may incorporate polymer coatings. The metallic structure provides mechanical strength, and the polymer coating functions as an artificial cartilage layer(12–14). Because cells can sense chemical and physical surface properties and respond through behaviors such as preferential adhesion, migration, and proliferation, the use of nanoscale structures can control initial protein adsorption on implant/prosthesis surfaces. This, in turn, regulates cellular attachment and subsequent cellular responses. Consequently, prosthesis designers carefully select materials and engineer surface structures to minimize adverse biological reactions. Despite advances in this field, research and development continue to optimize implant materials and designs to reduce complications and improve in vivo performance(11–13).

Prostheses made from conventional materials may be subject to rejection by the body. Incorporating hydroxyapatite nanoparticles into prosthesis fabrication enhances bone adhesion and improves mechanical properties. Nanostructured coatings, in particular, minimize fracture and rejection rates. In addition, orthopedic implants with antibacterial coatings are currently being developed to further improve clinical outcomes(15,16).

The Necessity of Nanotechnology in Prosthesis Fabrication

The surface of artificial prostheses can activate the immune system, potentially leading to implant rejection, which is particularly critical in orthopedic surgery. Therefore, prosthesis design aims to engineer surfaces that are as irregular as possible, incorporating microstructures similar to the nanostructure of natural bone, in order to mimic native tissue and integrate harmoniously with the surrounding biological environment. Additionally, porous structures in prostheses facilitate the transport of essential nutrients for cellular growth. Such designs not only reduce the contact area between the prosthesis and host tissue but also significantly decrease the likelihood of rejection(17). Studies have shown that applying these modifications in orthopedic implants stimulates osteoblast activity, the cells responsible for bone growth and regeneration, thereby reducing the probability of implant rejection. These findings underscore the importance of nanotechnology in enhancing the interaction between prosthetic materials and body tissues(17).

Antifungal and Antibacterial Nanocoatings

A major challenge in orthopedic implants is the risk of infection, which can compromise surgical outcomes. Nanocoatings with antimicrobial properties can mitigate this risk. These coatings are applied to implant surfaces using silver nanoparticles, gold nanoparticles, or carbon nanotubes, preventing bacterial colonization and biofilm formation(18,19).

Structural Reinforcement and Prosthesis Strength

The application of nanotechnology to reinforce prosthetic structures can substantially increase durability and mechanical strength. Nanoparticles or thin nanolayers applied to the surface of prostheses enhance mechanical properties, reducing wear and the risk of cracking or fracture, thereby extending implant lifespan. Additionally, these modifications promote osteointegration and stimulate bone cell activity[20].

Future Perspectives

Hydroxyapatite nanoparticle coatings on prostheses play a key role in improving design and clinical performance. Biocompatible nanomaterials, compared with macrostructured alternatives, facilitate better cellular adhesion, enhance durability, and accelerate osteogenesis, collectively reducing fracture and rejection rates. Overall, the use of nanohydroxyapatite as a prosthetic coating represents a significant advancement in tissue engineering and clinical medicine.

Conclusion

Despite the numerous advantages, challenges remain, including precise control of mechanical properties, large-scale cost-effective production, and long-term clinical evaluation. Nevertheless, with ongoing advances in material fabrication and assessment technologies, hydroxyapatite-coated prostheses are expected to play a vital role in disease treatment and in improving human quality of life in the near future.

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