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MINIREVIEWS

Orthopedic revolution: The emerging role of nanotechnology

Wen-Jie Ruan, Si-Si Xu, Dong-Hui Xu, Zhi-Peng Li

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Abstract

This review summarizes the latest progress in orthopedic nanotechnology, explores innovative applications of nanofibers in tendon repair, and evaluates the potential of selenium and cerium oxide nanoparticles in osteoarthritis and osteoblast differentiation. This review also describes the emerging applications of injectable hydrogels in cartilage engineering, emphasizing the critical role of interdisciplinary research and highlighting the challenges and future prospects of integrating nanotechnology into orthopedic clinical practice. This comprehensive approach provides a holistic perspective on the transformative impact of nanotechnology in orthopedics, offering valuable insights for future research and clinical applications.

Key Words: Cerium oxide nanoparticles; Injectable hydrogels; Interdisciplinary research; Orthopedic nanotechnology; Selenium nanoparticles

Core Tip: Nanotechnology has become a new and popular technology in recent years. Combining nanotechnology with orthopedic medicine may open up new treatment methods for orthopedic diseases. Nanotechnology, such as metal nanoparticles, injectable hydrogels and nanofiber scaffolds, can improve the treatment of osteoarthritis, cartilage injury and sports injury. However, in the process of exerting its function, nanotechnology needs to be combined with many disciplines, and it also faces many ethical challenges, which need further research.

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INTRODUCTION

The field of orthopedic medicine faces many complex challenges, including cartilage damage, bone infection, tendon injury, bone defects, and osteoarthritis. These diseases not only affect patients’ quality of life but also increase medical burden. For example, due to their natural extracellular matrix, good biocompatibility, and strong plasticity, cartilage damage makes injectable hydrogels a promising tool for cartilage tissue engineering[1,2]. Osteoarthritis is a common chronic joint disease whose treatment mainly relies on nonsteroidal anti-inflammatory drugs (NSAIDs)[3-5], but these drugs have side effects. In recent years, the application of nanotechnology in orthopedic medicine has been increasing, especially in bone regeneration engineering[6-9]. Nanofiber-based scaffolds have attracted attention due to their similarity to natural tendon structures and their ability to promote tissue regeneration. For example, multiscale nanofiber-based scaffolds for Achilles tendon regeneration have demonstrated their potential in promoting tissue regeneration[10]. In addition, metal/metal oxide nanoparticles (such as manganese dioxide and cerium oxide) have shown potential in the treatment of osteoarthritis[11,12]. They can not only simulate the activity of antioxidant enzymes but also catalyze the degradation of superoxide anions and hydrogen peroxide. Moreover, cerium oxide nanoparticles promote the differentiation of bone precursor cells by activating the Wnt pathway[13], demonstrating their important role in fracture repair and bone tissue homeostasis. In addition, selenium nanoparticles have been shown to have anti-inflammatory effects on osteoarthritis both *in vitro* and *in vivo*[3], potentially making them potential anti-inflammatory agents for the treatment of osteoarthritis[14].

NANOTECHNOLOGY FOR BONE REGENERATION

Bone healing is a complex biological process that faces multiple challenges, including slow regeneration, risk of infection, and incomplete repair[15-17]. For example, osteoarthritis and postfracture infections (such as PTRLO) increase the complexity and difficulty of treatment. These challenges encourage researchers to seek more effective methods for bone regeneration. The application of nanotechnology in orthopedic medicine has shown great potential[6]. For example, hydroxyapatite (HA) nanoparticles have been widely studied because their composition and structure are similar to those of bone minerals. HA nanoparticles can promote the proliferation and differentiation of bone cells, thereby accelerating the bone healing process[18]. Research by Zhu *et al*[1] injectable hydrogels, due to their good biocompatibility and plasticity, have emerged as promising tools for cartilage tissue engineering. Zhu *et al*[10] also discussed the application of nanofiber-based scaffolds in Achilles tendon regeneration, emphasizing their potential in promoting tissue regeneration. A study by Luo *et al*[13] showed that cerium oxide nanoparticles can activate the Wnt pathway and promote the differentiation of bone precursor cells. Recent research has shown that the application of nanotechnology in bone regeneration is not limited to laboratory research but also has potential in clinical trials[19,20]. For example, the selenium nanoparticles mentioned earlier[3], along with metal/metal oxide nanoparticles[11], have shown great potential in the treatment of osteoarthritis. The application of nanotechnology in the field of bone regeneration provides new perspectives and solutions for the treatment of various orthopedic diseases. The versatility and efficiency of nanotechnology, ranging from cartilage tissue engineering to osteoarthritis treatment, make it an important area for future orthopedic medical research and clinical applications.

THE APPLICATION OF NANOMATERIALS IN THE MANAGEMENT OF JOINT DISEASES

Joint diseases, such as osteoarthritis and rheumatoid arthritis, are prevalent health issues globally[21-23]. These diseases often manifest as joint pain, swelling, and limited range of motion, significantly impacting patients' quality of life[24-26]. Current treatment methods, such as NSAIDs, can alleviate symptoms, but long-term use may lead to side effects and cannot fundamentally solve the problem of cartilage degeneration[27]. Due to their unique physical and chemical properties, nanomaterials have demonstrated tremendous potential in the treatment of joint diseases. For example, selenium nanoparticles have been shown in studies to have anti-inflammatory effects in the treatment of osteoarthritis[3]. These nanoparticles can effectively reduce the expression of inflammatory cytokines, such as inducible nitric oxide synthase and cyclooxygenase-2, thereby alleviating joint inflammation[3]. In addition, metal/metal oxide nanomaterials, such as cerium oxide and manganese dioxide, have also been studied for their ability to mimic the activity of antioxidant enzymes, which can help reduce oxidative stress and promote cartilage repair[11]. In clinical and laboratory studies, the application of nanomaterials has already shown positive results. For example, a study by Li *et al*[3] demonstrated the significant anti-inflammatory effect of selenium nanoparticles on osteoarthritis *in vitro* and *in vivo*. These studies not only demonstrate the effectiveness of nanomaterials in reducing joint inflammation and promoting cartilage repair but also provide promising directions for future clinical applications.

The application of nanomaterials in the management of joint diseases provides a new treatment strategy, particularly for reducing inflammation and promoting cartilage repair. With more research and clinical trials being conducted, nanomaterials are expected to become an effective means of treating joint diseases (Table 1).

NANOTECHNOLOGY IN TENDON AND LIGAMENT REPAIR

Tendon and ligament injuries are common sports injuries, especially among athletes[28]. The self-repair capacity of these tissues is limited, and the healing process is slow. It is even difficult to restore the original structure and corresponding functions[29], often leading to limited function and long-term discomfort[30]. Traditional treatment methods, such as physical therapy and surgical intervention, often fail to fully restore the original strength and function of damaged tissues [30]. For example, studies have shown that nanomaterials can interact with stem cells, thus exerting therapeutic effects. This provides a new idea for the treatment of Achilles tendon and ligament diseases[31]. In addition, Zhu *et al*'s study[10] showed that nanofiber-based scaffolds, due to their structural similarity to natural tendons and ligaments, can provide a good environment for cell attachment and proliferation, thereby promoting the repair of damaged tissues. Therefore, nanofiber-based scaffolds have demonstrated significant potential in Achilles tendon regeneration. Currently, the application of nanomaterials in tendon and ligament repair is mainly in the experimental research stage. These studies have shown that nanomaterials can mimic the biomechanical and biochemical environment of natural tendons and ligaments, thereby promoting cell proliferation and differentiation and accelerating the healing process. Additionally, nanomaterials can also serve as carriers for drugs and growth factors, directly targeting damaged tissue to further promote repair.

Although most current research is still in the laboratory phase, some preliminary clinical trials are already underway. These trials aimed to evaluate the safety and effectiveness of nanomaterials in actual clinical applications. Nanotechnology has demonstrated tremendous potential in tendon and ligament repair, especially in promoting the repair and regeneration of damaged tissues[32]. With more research and clinical trials being conducted, nanotechnology is expected to become an effective treatment for tendon and ligament injuries.

CHALLENGES AND OPPORTUNITIES IN ORTHOPEDIC NANOTECHNOLOGY

The challenges of orthopedic nanotechnology mainly arise from the biological compatibility, cost, scalability, long-term stability, and safety of nanomaterials (Table 2). A major challenge in the application of nanomaterials in orthopedics is ensuring their good compatibility with human tissues. Improper materials may be detected by the immune system and cause immune reactions or inflammation, which can affect the therapeutic effect[33]. The development and production costs of nanotechnology are relatively high, which can limit its widespread application in clinical practice. Additionally, scaling up production from the laboratory to the commercial scale remains a technical and economic challenge. The long-term biological stability and potential toxicity of nanomaterials are also important considerations[34]. Long-term studies are needed to ensure that these materials do not cause adverse reactions in the body.

Future research directions for nanomaterials may focus on the development of advanced materials, personalized medicine, and combination therapies. The development of nanotechnology will support more personalized orthopedic treatment options, such as nanocarrier systems customized to the specific needs of individual patients. The combination of nanotechnology with other treatment methods, such as cell therapy and gene therapy, may open up new treatment avenues and improve therapeutic outcomes[35-37].

THE IMPORTANCE OF CONTINUOUS RESEARCH AND FUNDING

Nanotechnology is an emerging technology covering many disciplines and fields[38]. The development of orthopedic nanotechnology requires close collaboration between biologists, materials scientists, engineers, and clinicians. Continuous research funding is essential for overcoming technical challenges, conducting long-term studies, and translating laboratory findings into clinical applications. As nanotechnology evolves, there is a need to establish corresponding policies and ethical guidelines to guide its safe and effective application in orthopedics[39].

Nanotechnology in the field of orthopedics offers significant opportunities but also faces various challenges. Through interdisciplinary collaboration, continuous research, and appropriate funding support, these challenges can be overcome, leading to comprehensive applications and innovative breakthroughs in the use of nanotechnology in orthopedic treatment.

ETHICAL, LEGAL, AND REGULATORY ASPECTS

When using nanotechnology for treatment, it is crucial to ensure that patients fully understand the potential risks and benefits of the treatment. This includes transparent discussions about the long-term effects and possible side effects of nanotechnology. The long-term impact of nanotechnology in medicine is not completely clear. Therefore, researchers and

Table 1 Related nanomaterials and their functions

Nanomaterials	Functions
HA	Promote the proliferation and differentiation of bone cells and accelerate the process of bone healing
Injectable hydrogel	Promote the repair of cartilage
Nanofiber-based scaffold	Interact with related stem cells to promote the repair of tendons and ligaments
Cerium dioxide	Activate Wnt pathway, promote the differentiation of bone precursor cells and treat osteoarthritis
Selenium nanoparticles	Reduce the expression of inflammatory factors and treat osteoarthritis
Manganese dioxide	Reduce oxidative stress and treat osteoarthritis

HA: Hydroxyapatite.

Table 2 Challenges and opportunities for nanomaterials

Challenges	Opportunities
Biocompatibility: Improper materials may be attacked by the body's immune cells, leading to rejection and inflammation	Research and development of advanced nanomaterials: Nanomaterials provide new treatment ideas for orthopedic medicine and even the entire healthcare industry, and can improve medical standards through research and development of nanomaterials
Cost: Due to the research on nanomaterials being in its initial stages, a significant amount of human, material, and financial resources are required for its investigation	Personalized orthopedic treatment: Orthopedic diseases are becoming increasingly common, and the number of patients is generally on the rise. There is an urgent need to provide personalized treatment based on the condition of each patient in order to achieve the best therapeutic effect
Long-term stability: Currently, most research on nanomaterials is still in the laboratory stage, with few clinical studies and even fewer long-term studies. Therefore, the stability of these materials remains to be further investigated	Combination therapy: As a new treatment method, nano therapy can be combined with other treatment methods to achieve better results
Potential toxicity: Since nanomaterials are not the body's own tissues, it remains to be further studied whether they have adverse toxic or side effects on the human body	Promote multidisciplinary development: The research and application of nanomaterials require the support of multiple disciplines, such as chemistry, biology, and materials science. Therefore, increasing efforts in the research and development of nanomaterials can promote multidisciplinary development

doctors need to consider long-term health effects and incorporate patient well-being into treatment decision-making. The use of nanotechnology may involve the collection and processing of large amounts of patient data. Protecting these data from unauthorized access is an important ethical consideration. The legal and regulatory frameworks for medical nanotechnology vary across different countries and regions. Typically, these laws aim to ensure the safety and effectiveness of new technologies while protecting patient rights. Medical professionals should receive training on the ethical and legal issues of nanotechnology to ensure that they can provide optimal treatment to patients while adhering to relevant regulations.

When using nanotechnology in medicine, careful consideration must be given to ethical, legal, and regulatory issues. By strengthening education, promoting interdisciplinary collaboration, increasing public participation, and ensuring policy flexibility, these challenges can be effectively addressed.

MULTIDISCIPLINARY METHOD OF ORTHOPEDIC NANOTECHNOLOGY

The collaboration between biologists and materials scientists is crucial in the development of orthopedic nanotechnology. For instance, biologists provide in-depth knowledge about bone tissue biology, while materials scientists utilize this information to design nanomaterials that mimic bone tissue. This cooperation has facilitated the development of nanofiber-based scaffolds that can promote the regeneration of tendons and ligaments.

The collaboration between engineers and orthopedic surgeons is crucial in translating laboratory research into practical clinical applications. For instance, engineers require input from doctors to ensure that nanocarriers designed for bone repair meet clinical needs. This cooperation is essential for the development of effective and safe nanotherapies that can be used in orthopedic procedures.

Collaboration between chemists and pharmacologists is crucial for the development of novel nanopharmaceutical delivery systems that can more effectively deliver therapeutic agents directly to damaged bone tissue. This cooperation allows for the design of targeted and controlled drug delivery systems that can improve the efficacy and safety of orthopedic treatments.

With the continuous development of orthopedic nanotechnology, interdisciplinary collaboration will become key to addressing future challenges such as safety, efficiency, and sustainability. The multidisciplinary approach plays a crucial role in advancing orthopedic nanotechnology. Through close cooperation between different disciplines, more innovative

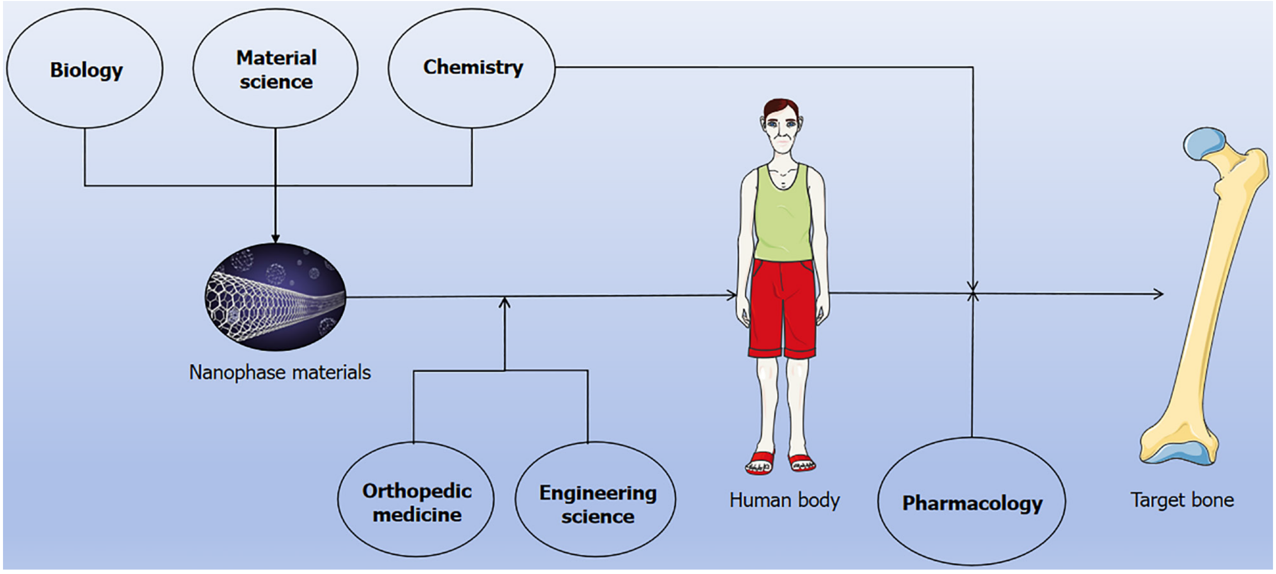

Figure 1 Interdisciplinary cooperation network. The combination of biology, materials science and chemistry can promote the research, development and upgrading of nanomaterials, while orthopedic medicine and engineering can allow nanomaterials to enter the human body and then target defective bone through chemical and pharmacological research.

breakthroughs can be achieved, clinical translation of research findings can be accelerated, and future challenges can be effectively addressed (Figure 1).

CONCLUSION

Nanotechnology in the field of orthopedics has demonstrated significant transformational potential, mainly in promoting bone and soft tissue repair, targeted drug delivery, the development of innovative treatment methods, and as a model for interdisciplinary collaboration. These technologies not only improve treatment outcomes but also reduce systemic side effects, providing more effective treatment options for patients with chronic diseases. Future research will focus on the safety and long-term effects of nanomaterials while also addressing legal and ethical challenges. The advancement of personalized medicine and the necessity for global collaboration will further drive the development of this field. Overall, the application of nanotechnology in orthopedics represents a promising future, representing the cutting edge of medical technology and foreshadowing important directions for future medical innovation. Through continued research, interdisciplinary collaboration, and appropriate regulation, nanotechnology is expected to revolutionize the treatment of orthopedic diseases.

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