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Mini Review

The Application of NOLFs and Variegated Fullerene Materials in Orthopedic Diseases and Disorders

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Abstract

Since the 1980s, carbon fullerene materials have been investigated for medical applications in humans. Nanocarbon onion-like fullerenes (NOLFs) and variegated fullerene materials are composed of carbon atoms and compatible with the human body. They reduce free radicals in cells, provide anti-inflammatory effects, and inhibit tumor growth. The primary antioxidant benefit of fullerene materials might be through the activation of Nrf2. Fullerene materials are utilized in molecular scaffolds, aiding bone reformation and repair and supporting the growth, proliferation, osteogenetic differentiation, and differentiation of bone-derived stem cells. Fullerene materials improve the outcomes and shorten the recovery time in joint replacement and orthopedic bone cement procedures. Although fullerene materials have demonstrated beneficial applications in a variety of bone, muscle, and cartilage conditions, their manufacture, dosage, timing, and duration should be further evaluated and established for therapeutic use in specific conditions by evidence-based research.

Keywords: *Biocompatibility; Bone Tissue Engineering; Graphitization; Nanocarbon; Osteoporosis; Scaffold*

Abbreviations

C_{60}: Carbon 60; CaMKIIα: Calcium/Calmodulin-Dependent Protein Kinase IIα; CD: Carbon Dot; CNO: Carbon Nano-Onion; CNT: Carbon Nanotube; NOLF: Nanocarbon Onion-Like Fullerene; Nrf2: Nuclear Factor (Erythroid-Derived 2) Factor 2; OI: Osteogenesis Imperfecta; ROS: Reactive Oxygen Species

Introduction

Nanocarbon fullerene materials have various physical structures and features; however, their chemical properties are similar. These qualities have led to diverse applications in many fields, such as medicine, veterinary medicine, and agriculture [1–3]. Carbon allotropes and nanotechnology materials, such as nanoparticles, nanotubes, graphene, and fullerene, have been widely applied in research [4–7] and specific orthopedic diseases and disorders. Due to their biocompatibility and minimum interference with metabolic processes in humans, fullerene materials can be used to diagnose and treat a variety of specific medical conditions [8–12].

Nanocarbon fullerene materials are stable and biocompatible in human organs, tissues, and cells. Nanocarbon onion-like fullerenes (NOLFs) and other fullerene materials have been vigorously researched for their beneficial application in humans, animals, and plants [1–3,13–15]. Due to their varied physical structures and analogous and complementary chemical properties [16], they are integrated into diverse medical diagnosis and treatment procedures. Specific fullerene materials, introduced into the human body, support various biological processes. Also, these molecules do not interfere with primary metabolism.

Specific fullerene materials have been utilized in tissue engineering and the repair and replacement of defective or damaged muscles or bones [17]. Numerous skeletal defects can occur in the human body, thus fullerene materials will likely play a more significant role in the repair of such defects. Nanocarbon fullerenes are utilized in scaffolds, supporting bone reformation and repair. Fullerene materials help treat orthopedic diseases and disorders, promoting the growth, proliferation, osteogenetic differentiation, and differentiation of bone-derived stem cells [18].

Typically, the various fullerene materials applied in orthopedics include carbon dots (CDs), graphene nanoparticles, and carbon nanotubes (CNTs). Specific fullerene materials directly impact or influence new bone growth in the human body [19]. Bone degenerative diseases result in weakened cartilaginous structures and osseous destruction over time. Osteoporosis and osteogenesis imperfecta (OI) compromise bone tissue in humans [20]. However, the introduction of fullerene materials in skeletal sections augments the formation of scaffolds—the initial framework in the bone reformation system. Due to the biocompatibility of these fullerene materials in humans, the growth of bone-derived stem cells for the scaffolds is encouraged. As older bones deteriorate or "die away", the intake of specific fullerene materials allows for the mechanical extension of bone tissue from the scaffolds. Ultimately, fullerene materials regulate skeletal growth at various sites to repair or replace damaged or weakened bone structures.

Furthermore, fullerene materials have high electron-affinity properties, supporting the treatment of specific orthopedic conditions. The formation of new bone cells and the continuous growth of bone in the treatment of various orthopedic disorders are aided and accelerated by nanocarbon fullerenes [21]. The repair of damaged cartilage in humans can be enhanced by the application of fullerene materials.

Relevant fullerene materials boost bone-derived stem cells at the sites of degeneration or damage, displaying little to no toxicity. Over time, musculoskeletal disorders adversely affect the durability of bones. However, the conjoined treatment of medication and fullerene materials boosts treatment outcomes [22]. When coupled with other functional molecules, fullerene materials promote bone development at the molecular level, resulting in the strengthening of previously injured or deficient skeletal muscles. Fullerene materials aid in the production of several vital proteins. In particular, nanocarbon crystals activate calcium/calmodulin-dependent protein kinase IIα (CaMKIIα), facilitating stem cell progression and the repair of skeletal muscle [23].

The application of these nanocrystals are useful in tumor suppression [24]. Based on the fullerene free radical scavenging mechanisms at the cellular level, tumor growth and development are suppressed [25]. NOLFs and specific fullerene derivatives reduce free radicals in cells, provide anti-inflammatory effects, and inhibit tumor growth. The primary antioxidant benefit of fullerene materials might be through the activation of Nrf2 [25–30]. At the molecular level, fullerene materials accelerate recovery and provide antitumor effects (with low to no toxicity). Also, they help repair overused or decaying bone tissue through cellular processes and neutralize and reduce reactive oxygen species (ROS) [31–34].

Joint replacement surgeries and orthopedic bone cement procedures are reinforced by fullerene materials [35,36] and the reduction of ROS. Over time, the nanoparticles enhance bone-derived stem cell growth, reduce inflammation, and promote healing [29–31]. The use of fullerene materials in cemented joint replacements allows for a broader range of medical treatment options for individuals with associated orthopedic disorders.

The future seems promising for the application of fullerene materials in specific orthopedic diseases and disorders. However, the outcomes in the manufacturing process of experimental-grade and pharmaceutical-grade fullerene materials can be inconsistent (even within the same batch), making it challenging to perform reliable assessments and reproducible studies regarding their biological benefits, biocompatibility, and potential toxicity. Also, their dosage, timing, and duration should be further evaluated and established for therapeutic use in specific conditions by evidence-based research [1–3].

Conclusion

NOLFs and variegated fullerene materials are used to treat orthopedic diseases and disorders, given their high biocompatibility and low toxicity. Fullerene materials are utilized in scaffolds that aid in bone reformation and repair, supporting the growth, proliferation, osteogenetic differentiation and differentiation of bone-derived stem cells. They reduce free radicals in cells, provide anti-inflammatory effects, and inhibit tumor growth. They bolster joint replacement surgeries and orthopedic bone cement procedures. Overall, fullerene materials provide a more extensive range of medical treatment options for individuals with orthopedic diseases and disorders.

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

Supplementary Note

This paper, as a mini-review, is designed as a brief introduction to nanocarbon onion-like fullerenes (NOLFs), regarding their application in orthopedic medicine. Other articles have been or will be published on the application of NOLFs and variegated fullerenes in the respiratory system, cardiovascular system, gastrointestinal system, neurological system, veterinary medicine, agriculture, pharmacology and toxicology, and other topics. These distinct mini-review articles could have been combined into a much lengthier review or research article. However, to have done so, the subject matter would have resulted in only one publication in one journal, excluding other medical specialties. The purpose of these papers is to disseminate the purported biocompatibility and beneficial effects of fullerene materials to the broadest audience of students, researchers, and medical practitioners as possible. The authors hope that the introduction to fullerenes'applications in various and diverse disciplines spawns curiosity and further research regarding NOLFs and fullerene derivatives. Fullerene materials seem poised to become a vital part of the future of medicine, veterinary medicine, and agriculture. However, more research is needed to determine any adverse effects of their long-term use. Also, the NOLF manufacturing process requires standardization to provide consistent quality and batch samples. Dosage and duration of treatment with fullerene materials for specific conditions need to be established by evidence-based research.

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