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Mini Review

Biomedical Application of Halloysite Nanotubes: Advances and Prospects

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Abstract

Recently, several difficulties have been faced in the biomedical field, which prompted scientists to explore a wide variety of nanomaterials that can be used to solve issues using tissue regeneration strategies. For decades, Titanium, steel, and metals have been explored for the fabrication of medical implants due to their excellent properties such as hardness, strength, and biocompatibility, but these materials have limitations. Several reports have documented the increase in the human body rejecting Titanium, resulting in revision surgery [1]. Therefore, there is a need to develop materials that can be highly biocompatible, nontoxic, and biodegradable, leading to the development and use of nanomaterials. Additional Halloysite Clay Nanotubes (HNTs) have shown several properties that meet and exceed those needed to replace Titanium, steel, and Metals. This paper reviews the advances and prospects of the biomedical application of HNTs.

Introduction

Joint replacement surgery has significantly advanced orthopedics, providing a solution for patients suffering from chronic joint pain and dysfunction. 3D printing and regenerative medicine are two areas of orthopedics with potential benefits since new treatments and methods are constantly being introduced to improve patient care, such as nanomaterials used as bone substituents have been developed. 3D printing is used to customize and revolutionize patient's specific bone implants, surgical tools, and body screws. One of the most exciting aspects is the capability to 3D print different nanomaterials or polymers of complex geometry in a short period and low manufacturing costs [2], which makes scientists start exploring different materials to upgrade the durability and properties of implants to fulfill the needs.

Halloysite Nanotubes (HNT)

HNTs are a type of clay nanotubes that are abundantly and naturally available as clay particles at a cheap price [3]. It comprises an aluminosilicate multilayer [4]. HNTs have a negatively charged external layer of about 50-80nm diameter and a positively charged inner layer of about 10-15nm diameter with 1µm length, making them cation and anion absorbents. They are majorly hollow tubular shapes with a pore size of 0.353 cm^3/g, attracting interest for their drug delivery applications as drug carriers increasing their use as antibacterial agents [5]. They are considered nontoxic and biocompatible, and their high mechanical properties and easy functionalization enable their use in scientific research [6]. Due to their weak intermolecular forces, the external layer can undergo modification by improving with polymers, biopolymers, or other materials capable of reinforcing their properties, resulting in improved dispersibility and thermal stability [3] used in biomedical and industrial applications [7].

Drug Delivery Application

HNTs can be loaded with growth factors and drugs, and can be released in a controlled and sustained manner. Cancer therapy is one of the applications that helps to reduce any side effects by increasing life efficacy. A recent study shows clay nanotubes loaded with Potassium Iodide and sustained released over a period for the treatment of Anaplastic Thyroid Cancer (ATC); potassium iodide helps in the homoaggregation of the nanotubes while the nanotubes act as the nanocarrier for transporting [8]. Similarly, the HNTs lumen was loaded with deferiprone while growing ceria nanozyme on the external layer to relieve iron stress and for radiation colitis therapy [9].

Some researchers prepared a hydrogel scaffold utilizing HNT, chitosan, and graphitic-carbon nitride to lower the side effects of anticancer agents by loading Quercetin (QC) into the lumen of the HNT and controlled release against MCF-7 cells (breast cancer cells) and the resulting outcome shows an improved cytotoxicity pH-sensitive drug delivery system [10]. Also, Curcumin was loaded into HNT to develop wound dressing with hyaluronic acid and polyamide 6, which produces increased antibacterial properties against pathogens. When tested *in vivo*, the outcome shows a reduced wound size, signifying the delivery capability properties [11].

Antimicrobial Agent Application

A pH-sensitive scaffold made up of clay nanotubes such as HNT can effectively inhibit the growth of microorganisms; they contain inherent antimicrobial properties in addition to the capability of loading additional antimicrobial agents into the lumen, which will enhance the antimicrobial properties; they also possess high surface area, excellent surface chemistry, biocompatibility and mechanical properties, which can be used in reinforcing different polymers [12]; Ciprofloxacin was also shown to be loaded into the HNT and sustain release over a period at different pHs [13].

Tissue Regeneration Application

Due to the weak mechanical hardness and osteoinductive capability of Hydroxyapatite (HAP) in designing nanocomposite scaffolds for tissue regeneration, HNT has been reported to improve these limitations by reinforcing HAP by improving the scaffold microstructure and porosity [14]. Engineered scaffolds provide better results than biological grafts for tissue reconstruction due to their excellent properties, but they are poor in tissue healing properties; therefore, researchers loaded exendin-4 (growth factor – EX-4) in the lumen of the HNT) to attain the desired bioactivity and to protect and avoid burst release resulting in improving tendon healing [15].

Similarly, Nanoclay enhanced the properties of a self-healing nanocomposite hydrogel, such as the mechanical properties, biocompatibility, and porosity intended for cartilage tissue defect treatment [16]. Nano clay was incorporated in a scaffold composed of chitosan-polyethylene oxide to improve the regeneration of bone tissue mainly because of their morphological and mechanical properties [17].

Medical Coatings Application

Several scientists have reported that HNT can be used as nanofillers for different nanocomposite scaffolds to enhance their protective coatings, mechanical and antimicrobial properties. One example documented was the coating of the HNT lumen with dopamine derivatives covalently modified and characterized to prevent microbial biofilm formation, resulting in a material that can coat medical implants [18]. HNT has been documented to be used in enhancing the fire safety of polyester-cotton fabrics by initially loading HNT with silver nanoparticle (AgNP) before coating with nitrogen, phosphorus, and silicon, which results in a self-extinguish composite coating, providing excellent fire safety [19].

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