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Review Article

Carbon nanomaterials for biomedical applications: A comprehensive review

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ABSTRACT: Carbon-based nanomaterials have emerged as promising candidates for a wide range of biomedical applications due to their unique physicochemical properties and biocompatibility. This comprehensive review aims to provide an overview of the recent advancements and potential applications of carbon-based nanomaterials in the field of biomedicine. The review begins by discussing the different types of carbon-based nanomaterials, including carbon nanotubes, graphene, and fullerenes, highlighting their distinct structures and properties. It then explores the synthesis and functionalization strategies employed to tailor their physicochemical properties, facilitating their integration into various biomedical platforms. Furthermore, the review delves into the applications of carbon-based nanomaterials in biomedicine, focusing on three major areas: diagnostics, therapeutics, and tissue engineering. In diagnostics, carbon-based nanomaterials have demonstrated their utility as biosensors, imaging agents, and platforms for disease detection and monitoring. In therapeutics, they have been utilized for drug delivery, gene therapy, and photothermal therapy, among others. Additionally, carbon-based nanomaterials have shown great potential in tissue engineering, where they have been employed as scaffolds, biosensors, and substrates for cell growth and differentiation. The review also highlights the challenges and considerations associated with the use of carbon-based nanomaterials in biomedical applications, including toxicity concerns, biocompatibility, and regulatory considerations. Moreover, it discusses the current trends and future prospects in this rapidly evolving field, such as the development of multifunctional nanomaterials, combination therapies, and personalized medicine.

KEYWORDS: carbon-based nanomaterials; biosensors; diagnostics; therapeutics; tissue engineering

1. Introduction

Carbon-based nanomaterials have gained considerable attention in the field of biomedicine due to their remarkable physicochemical properties and high biocompatibility. These nanomaterials, primarily derived from carbon allotropes such as carbon nanotubes, graphene, and fullerenes, exhibit unique structural and functional characteristics that make them appealing for various biomedical applications[1–4]. A variety of carbon-based nanomaterial forms are shown in **Figure 1**. Carbon-based nanomaterials possess a large surface area-to-volume ratio, enabling high loading capacities for therapeutic agents, imaging probes, and biomolecules. This property is particularly advantageous for drug delivery systems, where the nanomaterials can efficiently encapsulate and transport therapeutic compounds to target sites, improving drug efficacy and minimizing side effects[5–9].

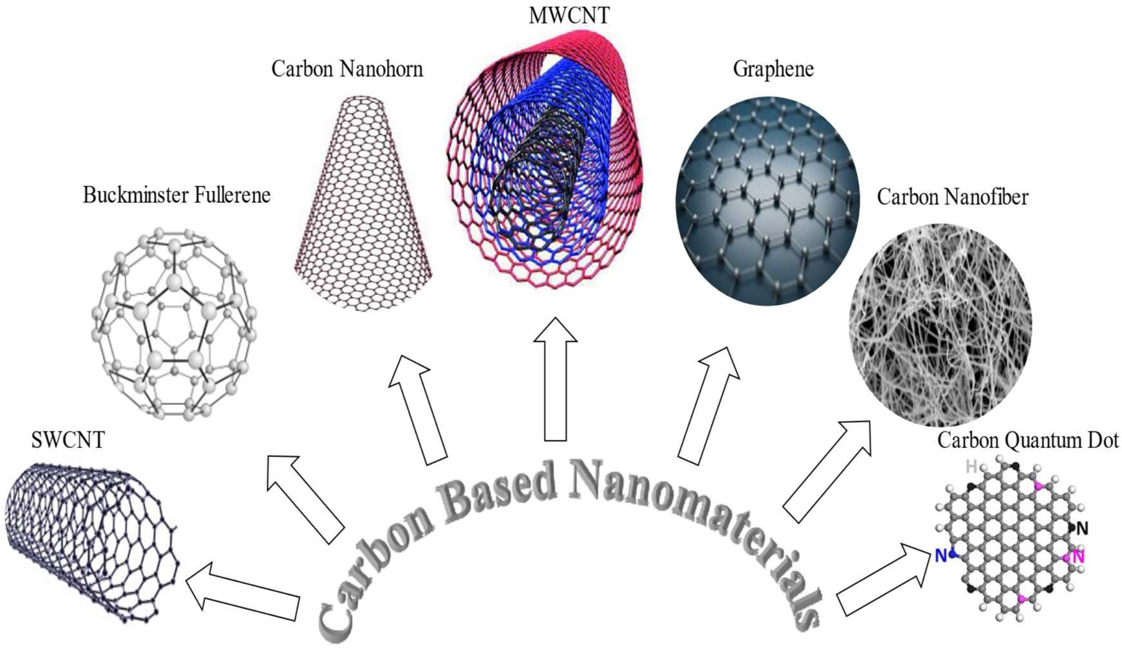

Figure 1. Various forms of carbon-based nanomaterials.

Carbon-based nanomaterials exhibit excellent mechanical strength and stability, allowing them to withstand physiological conditions and retain their structural integrity. This robustness is essential for their applications as scaffolds in tissue engineering, where they provide support for cell growth, proliferation, and tissue regeneration[10–13].

Moreover, carbon-based nanomaterials possess unique electrical and optical properties. For instance, graphene exhibits exceptional electrical conductivity, making it suitable for biosensing platforms and electrical stimulation of cells. Carbon nanotubes, on the other hand, display excellent optical properties, enabling their utilization as imaging agents for various imaging modalities, including fluorescence imaging, magnetic resonance imaging (MRI), and photoacoustic imaging[14–17]. Biocompatibility is another crucial attribute of carbon-based nanomaterials. They have been extensively investigated for their interactions with biological systems, and studies have shown minimal cytotoxicity and immunogenicity when appropriately functionalized and used at appropriate concentrations. This biocompatibility is vital for their safe integration into biological systems and their potential use in clinical applications[18–20]. Furthermore, carbon-based nanomaterials offer versatility in terms of their surface functionalization and modification. By introducing various functional groups, biomolecules, or targeting ligands onto their surface, their properties can be tailored to achieve specific functionalities, such as targeted drug delivery, cellular imaging, or selective interactions with biomolecules[21–24].

Overall, the unique physicochemical properties and biocompatibility of carbon-based nanomaterials make them highly promising candidates for a wide range of biomedical applications. Their potential applications span areas such as drug delivery, biosensing, tissue engineering, imaging, and regenerative medicine. However, further research is still needed to address challenges related to their large-scale synthesis, long-term biocompatibility evaluation, and regulatory considerations to ensure their safe and effective translation into clinical practice.

2. Carbon-based nanomaterials

There are various types of carbon-based nanomaterials, each with its own unique physicochemical properties. Carbon Nano-tubes (CNTs) are cylindrical structures composed of rolled-up graphene sheets. They can be single-walled (SWCNTs) or multi-walled (MWCNTs), with different layers of graphene concentrically arranged[25–27] Several types of carbon-based nanomaterials are depicted in **Figure 2**. CNTs possess exceptional mechanical strength, high electrical conductivity, and high thermal stability. They exhibit unique one-dimensional electronic properties, depending on their structure (metallic or semiconducting)[28–30]. Graphene is another carbon-based material and it has a single layer of carbon atoms arranged in a hexagonal lattice[31–33]. It exhibits remarkable properties such as high electrical conductivity, excellent thermal conductivity, and exceptional mechanical strength. It is also nearly transparent, flexible, and has a large surface area[34,35]. Fullerenes are hollow carbon molecules with cage-like structures. The most well-known fullerene is Buckminsterfullerene (C60), which has a spherical shape composed of 60 carbon atoms arranged in a soccer ball-like structure[36,37]. It possesses unique electronic properties and high stability. It can act as electron acceptors and exhibit photophysical properties, making them useful in various applications, such as organic solar cells and biomedical research.

Now a days, Carbon Dots (CQDs) are an exceptional research nanomaterial and it contains small carbon nanoparticles with sizes typically less than 10 nanometers[38,39]. Carbon dots exhibit excellent photoluminescence, making them useful for applications in bioimaging, optoelectronics, and sensing. Their properties can be tuned by controlling their size, surface functionalization, and composition[40,41].

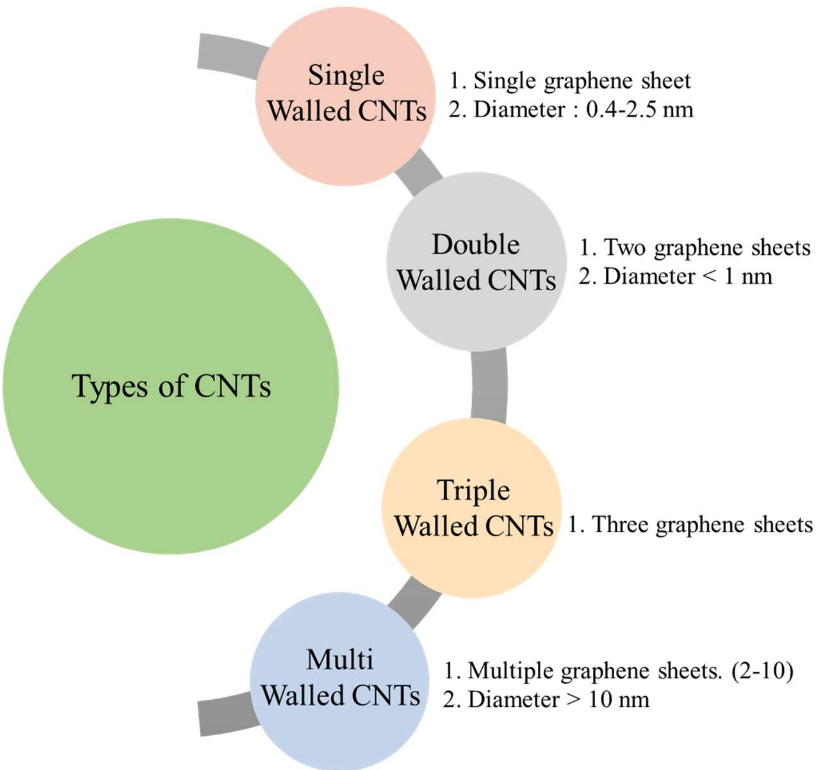

Figure 2. Types of carbon nanotubes.

Carbon Nanofibers (CNFs) are fibers made of carbon with diameters in the nanometer range. CNFs possess high mechanical strength, high electrical conductivity, and excellent thermal stability. It evolves into platforms for artificial intelligence that can be utilized for a variety of purposes, including biomedical applications. In addition, the exceedingly large surface areas of CNFs enable them to be customized and functionalized as needed[42]. They have a high aspect ratio and can be used as reinforcements in composite materials[43,44]. Besides this, Carbon nanohorns are horn-shaped nanostructures composed of graphene sheets. Single walled carbon nanohorns (SWNHs) are conical carbon nanostructures constructed from a sp^2 carbon sheet of about 2–5 nm of diameter and 30 to 50 nm long (see **Figure 3**). It has a unique spiky morphology, high surface area, and excellent adsorption properties. SWCNHs have been shown to be efficient carriers for cisplatin, dexamethasone, prednisolone, and other anti-cancer and anti-inflammatory drugs. They are also used in energy storage, catalysis, drug delivery, and biosensing[45–47].

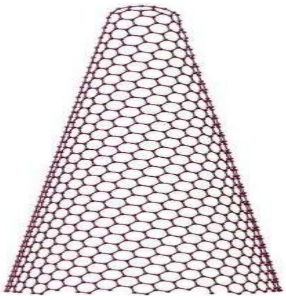

Figure 3. The structure of carbon nanohorn[47].

3. Carbon-based nanomaterials for clinical diagnostic applications

Carbon-based nanomaterials have shown great promise in diagnostic applications due to their unique properties, including high surface area, excellent biocompatibility, and versatile surface chemistry.

Figure 4 illustrates the many applications of carbon-based nanomaterials in several biomedical fields. Here are some specific ways carbon-based nanomaterials are utilized in diagnostics.

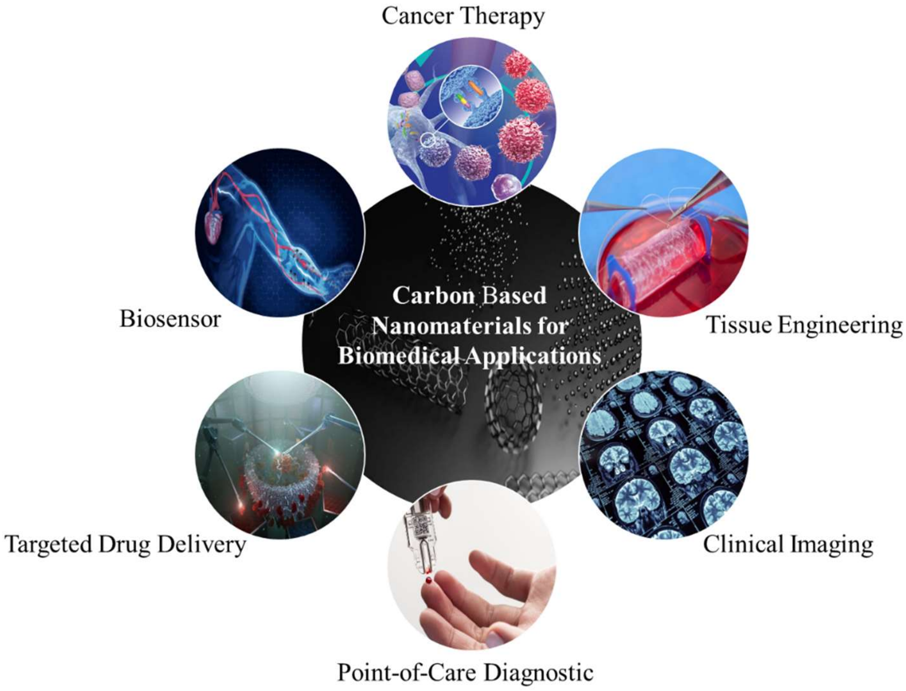

Figure 4. Biomedical applications of carbon-based nanomaterials.

3.1. Contrast agents in clinical imaging

3.1.1. Carbon nanotubes (CNTs)

CNTs have been explored as contrast agents for various imaging techniques, including magnetic resonance imaging (MRI) and computed tomography (CT). They possess high magnetism and strong X-ray attenuation, enabling enhanced imaging resolution and sensitivity[48,49].

3.1.2. Graphene-based materials

Graphene and graphene oxide (GO) have excellent optical properties, making them suitable for fluorescence imaging. They can be functionalized with targeting ligands and fluorescent dyes to specifically label and visualize targeted cells or tissues[50,51].

3.2. Biosensors

3.2.1. Field-effect transistors (FETs)

Carbon nanotubes and graphene can be integrated into FET-based biosensors. When biomolecules, such as proteins or DNA, bind to the nanomaterial surface, it induces changes in the electrical properties of the FET, enabling highly sensitive and label-free detection of biomarkers[52–54]. **Table 1** presents specific biomedical uses of several carbon-based nanomaterials.

Table 1. Several specific biomedical applications of different carbon-based nanomaterials.

Nanomaterials	Biomedical Applications	References
Carbon nanofiber	Cancer therapy, Biosensor, Neurotransmitter detection, Food preservatives detection.	[55]
Graphene	Gene delivery, Bio-FET, Fluorescence biosensor, Neural, cardiac and bone tissue engineering, Fluorescence imaging, Photoacoustic imaging, Photothermal and photodynamic therapy.	[56]
Carbon nanotubes	Transistor, Electrochemical sensor, Filtration membrane, Optical biosensor, Electrochemical actuator, Photo luminescence. Vaccine delivery, Regenerative medicine, Bone, muscle and neural regeneration, Biomolecular detection.	[57]
Carbon quantum dots	Multicolor photoluminescence, In vitro and in vivo imaging, Photoacoustic imaging, Drug delivery, Crossing blood-brain barrier.	[58]
Carbon nanohorn	Methane storage, Catalyst support, Fuel cells, Supercapacitors, Electrochemical detection, Gas sensor, Drug carriers, Biomedicine.	[59]

3.2.2. Electrochemical biosensors

Carbon-based nanomaterials, such as graphene and carbon nanofibers, can be used to design electrochemical biosensors. These nanomaterials provide a large surface area for immobilizing biomolecules, facilitating efficient electron transfer, and enabling the detection of target analytes through electrochemical signals[60–62].

3.3. Targeted drug delivery

Functionalized carbon nanotubes

Carbon nanotubes can be functionalized with targeting ligands, such as antibodies or peptides, to specifically deliver therapeutic agents to diseased cells or tissues. The large surface area of carbon nanotubes allows for high drug loading capacity, and their ability to penetrate cell membranes facilitates intracellular drug delivery[63–66].

Graphene-based Nanocarriers: Graphene and graphene oxide can be utilized as carriers for targeted drug delivery. By functionalizing their surfaces with specific targeting moieties, they can selectively bind to target cells or tissues, improving drug delivery efficiency and reducing off-target effects.

3.4. Point-of-care diagnostics

Paper-based biosensors

Carbon nanomaterials, such as graphene or carbon nanotubes, can be incorporated into paper-based biosensors for rapid and low-cost diagnostics. These biosensors can detect various analytes, including pathogens, biomarkers, or toxins, through colorimetric or electrochemical signals, enabling point-of-care testing in resource-limited settings[67–69].

3.5. Carbon based nanomaterials for tissue engineering application

Carbon-based nanomaterials have shown great potential for tissue engineering applications in humans. Their unique properties, including high surface area, electrical conductivity, mechanical strength, optical properties and biocompatibility, make them attractive for designing scaffolds and promoting tissue regeneration. Graphene, a single layer of carbon atoms arranged in a hexagonal lattice, has garnered significant interest in tissue engineering. Nanomaterials from graphene-family such as graphene, graphene oxide, or reduced graphene oxide, support the adhesion and proliferation of mammalian cells including human mesenchymal stem cells (hMSCs), human osteoblasts, fibroblasts, and adenocarcinoma cells[70]. Graphene-based scaffolds can provide structural support for cell growth and facilitate electrical signaling in engineered tissues. They can be functionalized with bioactive molecules to promote cell attachment, proliferation, and differentiation[71–73]. Besides this, CNTs, cylindrical structures made of rolled-up graphene sheets, have been explored for tissue engineering applications. They possess high mechanical strength, excellent electrical conductivity, and a large surface area. CNTs can be incorporated into scaffolds to improve their mechanical properties and electrical conductivity, which can be beneficial for tissues such as nerves, muscles, and cardiac tissues. CNTs can also serve as nanocarriers for controlled drug delivery to support tissue regeneration[74–76].

CNFs are fibrous structures composed of carbon atoms. They have a high aspect ratio, resembling the structure of natural extracellular matrix (ECM). The extracellular matrix (ECM) is the noncellular substance found in all tissues and organs. It serves as both a physical support structure for cells and a source of important chemical and mechanical signals needed for tissue development, specialization, and maintenance[77]. CNFs can provide physical cues and a favorable microenvironment for cell adhesion, proliferation, and differentiation. They can be fabricated into three-dimensional scaffolds that mimic the native tissue architecture, promoting tissue regeneration[78,79]. Moreover, CQDs are small carbon nanoparticles with unique optical properties. They have been investigated for tissue engineering and regenerative medicine applications, particularly in bioimaging and cell tracking. CQDs can be used as fluorescent markers to label and track cells in tissue engineering constructs, enabling real-time monitoring of cell behavior and tissue growth[80,81].

Thus, these carbon-based nanomaterials can be incorporated into scaffolds or used as surface coatings to enhance the properties of the biomaterials used in tissue engineering. They can promote cell adhesion, proliferation, and differentiation, and provide a conductive and supportive environment for tissue regeneration. Moreover, their biocompatibility and tunable properties make them versatile tools for tailoring scaffold characteristics to match specific tissue engineering requirements. However, it’s important to note that the translation of carbon-based nanomaterials into clinical tissue engineering applications requires extensive research and validation to ensure their safety, long-term biocompatibility, and efficacy in human systems. Regulatory approval and thorough testing are necessary before their widespread use in tissue engineering.

4. The challenges associated with the use of carbon-based nanomaterials in biomedical sector

The use of carbon-based nanomaterials in biomedical applications holds great promise for various fields, including drug delivery, tissue engineering, biosensing, and medical imaging. However, there are several challenges and considerations that need to be addressed to ensure their safe and effective use. Some of these challenges include toxicity concerns, biocompatibility, regulatory considerations and long-term effects.

4.1. Toxicity concerns

Carbon-based nanomaterials, such as carbon nanotubes (CNTs) and graphene, possess unique physical and chemical properties that make them attractive for biomedical applications. However, their potential toxicity becomes a substantial issue when not employed under ideal conditions. The small size and high surface area of these nanomaterials can lead to unintended interactions with biological systems. It is crucial to understand their potential adverse effects on cells, tissues, and organs. Studies have shown that certain carbon nanomaterials can induce oxidative stress, inflammation and different types of cytotoxicity such as DNA damage, lysosomal damage, mitochondrial dysfunction and cell death. In addition to cytotoxicity, immunological effects such as pulmonary macrophage activation also induced by carbon nanomaterials. Assessing and mitigating the toxicity of carbon-based nanomaterials is essential for their safe use in biomedical applications[82–84].

4.2. Biocompatibility

Biocompatibility refers to the ability of a material to perform its desired function without causing any adverse reactions in living organisms. Carbon-based nanomaterials need to be biocompatible to ensure their successful integration into biological systems. Factors such as surface chemistry, purity, size, shape, and functionalization of these nanomaterials can influence their biocompatibility. Surface modifications or coatings can be applied to enhance biocompatibility and reduce potential toxicity. Thorough testing and evaluation of carbon-based nanomaterials in relevant biological models are necessary to assess their biocompatibility before their application in clinical settings[85,86].

4.3. Regulatory considerations

The use of carbon-based nanomaterials in biomedical applications is subject to regulatory oversight to ensure patient safety. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), have specific guidelines and requirements for the approval and commercialization of nanomaterial-based products. These guidelines address aspects such as preclinical testing, toxicity evaluation, manufacturing standards, labeling, and post-market surveillance. Compliance with these regulations is crucial to ensure the safe and effective use of carbon-based nanomaterials in biomedical applications.

4.4. Long-term effects

While carbon-based nanomaterials have shown promise in biomedical applications, the long-term effects of their exposure and accumulation in the body are not yet fully understood. It is important to conduct comprehensive studies to evaluate the potential risks associated with their long-term use. This includes investigating their potential for bioaccumulation, persistence, and chronic toxicity. Long-term safety studies are necessary to assess the potential risks and benefits of using carbon-based nanomaterials in biomedical applications.

To address these challenges and considerations, interdisciplinary collaborations between scientists, engineers, clinicians, and regulatory authorities are essential. Robust testing protocols, standardized characterization methods, and thorough risk assessments should be employed to ensure the safe and effective translation of carbon-based nanomaterials into clinical practice.

5. Conclusion

The use of carbon-based nanomaterials in biomedical applications offers tremendous potential for advancements in medicine and healthcare. These nanomaterials, such as carbon nanotubes, graphene, and fullerenes, possess unique properties that make them attractive for a wide range of applications, including drug delivery, tissue engineering, biosensing, and medical imaging. However, the challenges and considerations associated with their use cannot be overlooked. Toxicity concerns, biocompatibility, regulatory considerations and long-term effects are critical factors that need to be carefully addressed to ensure their safe and effective utilization.

Conflict of interest

The authors declare no conflict of interest.

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