Bulletin of Electrical Engineering and Informatics
Vol. 12, No. 2, April 2023, pp. 891~901
ISSN: 2302-9285, DOI: 10.11591/eei.v12i2.4310

Carbon nanomaterials advancements for biomedical applications

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Article Info

Article history:

Received Jun 26, 2022
Revised Aug 18, 2022
Accepted Oct 7, 2022

Keywords:

Carbon nanomaterials
Carbon nanotubes
Fullerenes–based nanomaterials
Graphene–based nanomaterials
Tissue engineering

ABSTRACT

The development of new technologies has helped tremendously in delivering timely, appropriate, acceptable, and reasonably priced medical treatment. Because of developments in nanoscience, a new class of nanostructures has emerged. Nanomaterials, because of their small size, display exceptional physio-chemical capabilities such as enhanced absorption and reactivity, increased surface area, molar extinction coefficients, tunable characteristics, quantum effects, and magnetic and optical properties. Researchers are interested in carbon-based nanomaterials due to their unique chemical and physical properties, which vary in thermodynamic, biomechanical, electrical, optical, and structural aspects. Due to their inherent properties, carbon nanomaterials, including fullerenes, graphene, carbon nanotubes (CNTs), and carbon nanofibers (CNFs), have been intensively studied for biomedical applications. This article is a review of the most recent findings about the development of carbon-based nanomaterials for use in biosensing, drug delivery, and cancer therapy, among other things.

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1. INTRODUCTION

Nanomaterials do have a significant influence on the way health care is delivered and identified in the healthcare context [1]. Biomedical researchers have struggled to figure out the convenient materials for diagnosis and therapeutic applications [2]. Recently, significant progress has been attempted forward into the employ of carbon nanomaterials in medical field [3]. Since carbon nanomaterials are varied in structure, have large surface-to-volume ratios, easy fabrication, and unique optical characteristics on top of that, they have a lot going for them in biomedicine research [4].

There are a variety of nanoscale materials, including carbon nanotubes (CNTs), graphene, fullerenes, carbon fibers, and nanodiamonds. The number of nanoscale dimensions is commonly used to categorize carbon nanomaterials [5]. Consequently, fullerenes are nanomaterials that have no dimensions whatsoever. CNTs, and carbon fibers are one-dimensional nanomaterials, whereas two-dimensional graphene structures are nanomaterials with layered graphene structures [6].

This article will provide an overview of recent advancement in biomedical applications of carbon nanostructures, including fullerenes, graphene, CNTs and carbon nanofibers (CNFs). Applications of carbon–based nanomaterials in medical research. Medical research relies heavily on biomaterials. Nanoparticles have made their way into biomaterials as a result of their unique properties related to the nanoscale [1], [5]. To put it

another way, when there are many surfaces to one bulk, the chemical reactivity and physico-chemical properties are greatly altered as a result and they intended them for release, and their small size makes it easier for the body to absorb and distribute them quickly throughout the body [1], [7].

Carbon-based nanomaterials are becoming more and more popular in the science and technology fields [5]. Everyone in the carbon family has unique properties and has already been extensively used in different medical applications, including biosensing, medication delivery, and other biological applications [2]. Along with the emergence of numerous carbon allotropes, ranging from well-known allotropic phases such as amorphous to less well-known amorphous phases such as fullerenes, graphene, CNTs, and CNFs [8].

2. APPLICATIONS OF FULLERENES–BASED NANOMATERIALS IN BIOMEDICINE

Fullerenes had first been revealed in 1985, and the researchers who identified this new carbon allotrope were awarded the Nobel Prize in Chemistry in 1996 [9]. Among the various carbon nanostructures, fullerenes have the highest degree of symmetry and, as a result, exhibit exceptional structural and chemical stability [5], [10]. Diverse operational groups can be imprinted on fullerene surfaces to allow for the distribution of drugs and diagnostics with greater accuracy [11], [12]. Fullerenes, particularly C60, have photo-electrochemical characteristics that mark them appropriate for photothermally treatment [13]. Fullerenes are hydrophobic, making it difficult to use them in biomedicine due to its relatively low solubility in polar solvents like water (11). To address this drawback, various approaches have been proposed, which include synthesizing fullerene derivatives [14].

Since the biological structures' dimensions are similar to carbon nanostructures, they create effective drug delivery system applicants [8]. Given that carbon nanostructures can be easily synthesized, they can be linked to therapeutics such as chemotherapeutics, antitumor drugs, and antibodies [2], [3], [15]. For advanced drug delivery systems, a number of fullerene derivative products with enhanced water solubility have been invented [16]. A combination of fullerenes' size and amphiphilicity allows them to pass through virtually all biological barriers. With conjugated fullerenes, drugs can be delivered to a specific area while putting as little stress as possible on the organs and tissues nearby [16], [17].

The pain-relieving drug ibuprofen is widely prescribed, but when taken orally, it can cause bleeding, ulceration, gastrointestinal issues, and diarrhea. Alipour *et al.* [18] demonstrated that use of C60 fullerenes with a porphyrin-like transition metal N4 as an ibuprofen deliver agent recently been observed using density functional theory. Recently, there has been interest in fullerenes as nucleic acid delivery systems (Figure 1). Minami *et al.* [19] confirmed that in vivo studies of tetra piperazino fullerene epoxide (TPFE) have already revealed that TPFE is no2ntoxic and has a higher knockdown efficiency for short interfering RNA (siRNA) delivery than the commonly used lipofectamine 2,000. Abstracting services depend on the accuracy of the title, extracting from it keywords useful in cross-referencing and computer searching. An improperly titled paper may never reach the audience for which it was intended, so be specific.

In another study Minami *et al.* [20] confirmed that TPFE used to stabilize and deliver unstable siRNA molecules in a latest in vitro study. In terms of delivering siRNA to the lung cells, we used TPFE-siRNA particles with a submicrometer size, and we saw an immediate agglutination of plasma proteins. Proteins made from the TPFE-siRNA plasma technology were steady initially, but after blocking the blood supply to the lungs, they became unstable and siRNA was released into the cells.

Huang *et al.* [21] discovered the existence among less alkane covalent bonds is bonded to the fullerene hutch, the lack of chlorine in the structure, and the existence of 2-phenoxyacetate by products correlate to a greater cytotoxic capacity of fullerene extracts against lung cancer cells. The C60-serinolamide compound can penetrate liver cancer cells; the C60-serinolamide conjugation with paclitaxel lowers tumor grade without causing weight gain as an adverse reactions. An investigation on C60-serinol's in vivo performance has revealed which includes its transport and removal from the renal system of mice [22]. Shi *et al.* [23] have developed a new method of delivering drugs to patients with advanced cancers utilizing C60. Doxorubicin is bonded to the fullerene utilizing reactive oxygen species, and a hydrophilic shell with a tumor-targeting characteristic is affixed to its surface. The reactive oxygen species are created by fullerenes in the 'on' mode, and doxorubicin is discharged as a by-product. Laser with 532 nm controls the shifting between "on" and "off" phases.

Antiviral applications for hydrophilic fullerenes are of major relevance. A fullerene cage's functional groups are tightly correlated to the fullerene's biological characteristics. The C60 is the most water-soluble form of fullerene and the synthesis of this substance has been greatly simplified lately [24], [25]. The water-soluble fullerene compound C60 has been shown in an in vitro investigation by Kraevaya *et al.* [26] to be active against influenza A and feline coronavirus. In light of these findings, FPA may also be a viable option for testing against emerging pandemic coronaviruses, such as middle east respiratory syndrome-coronavirus (MERS-CoV), acute respiratory syndrome (SARS-CoV), and SARS-CoV-2, which are all now under investigation.

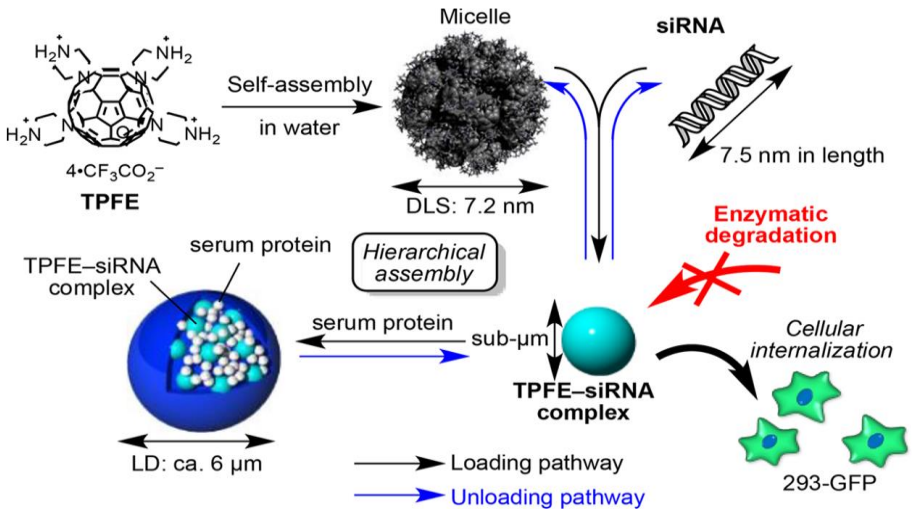

Figure 1. Diagram showing ternary complex synthesis from self-assembled TPFE pattern

Klimova *et al.* [27] discovered that ndC60, a water-soluble form of C60, exhibits antiviral efficacy against HSV-1 and CMV. Viral entry into host cells is prevented by ndC60's ability to interfere with virus's receptor connections, according to investigations in both vitro and vivo. By reacting C60Cl6 with dimethyl 2,2'-(1,4-phenylenebis-(oxy) diacetate. Voronov *et al.* [28] developed five novel water soluble fullerene constituents as HIV inhibitors. Using the five compounds, they discovered that they were effective against HIV-1 R5 and X4.

The hydrophobic phospholipid in the coronavirus's external surface is crucial for the virus's interactions with the host. In the presence of UVA irradiation, the aqueous colloidal fullerene produces singlet oxygen, which destroys the lipid layer of coronavirus. Thus, C60 coatings could be used as antiviral coatings. In addition, the virus's surface adherence can be reduced.

Reduced contact areas on fullerene-coated surfaces use both fullerenes' hydrophobic characteristics and lipid structure of viruses [25]. Research by Novir *et al.* [29], found that stabilizing chloroquine delivery with C60 fullerenes enhanced the efficacy of the chloroquine medication for COVID-19. Hence, Fullerene performs as an electron acceptor, and chloroquine serves as an electron donor due to the species' convenient electrochemistry.

3. APPLICATIONS OF GRAPHENE–BASED NANOMATERIALS IN BIOMEDICINE

Graphene is atoms. Graphene is a carbon allotrope composed of a single layer of atoms organized in a two-dimensional hexagonal arrangement nanostructure [5], [30]. It was in 2004 that Geim and Novoselov first disclosed the production and characterization of this carbon nanostructure; they were awarded the Nobel Prize in Physics for their work [7]. Scientifically, the nanostructure has a huge relative surface area as compared to bulk structures [2]. Graphene may be chemically functionalized and distributed in a variety of solvents, including water [7]. All of the atoms in graphene reside on the surface, providing sites for many different types of biomaterials to adhere (30). Graphene with all of these characteristics is an excellent contender for therapeutic, diagnostic imaging, biosensors, tissue regeneration, and regenerative medicine [31]. Whereas graphene has the possibility to be used as a drug delivery, it is harmful to organism body due to its ability to cluster in tissues and cause peroxidation [32]. Surface treatment of graphene is critical for overcoming this challenge. To get over these problems, the deep eutectic solvent technique can be used to bind specific functional groups to the graphene surface [33]. Graphene's functionalization opens the door to new uses in medication delivery technology. Graphene's high surface-to-volume ratio also makes it an attractive drug delivery candidate [32].

Recent work discussed the use of doxorubicin to load graphene that had been functionalized by Zainal-Abidin and co-researchers using the deep eutectic solvent method. There was a healthy amount of dispersion and loading capability with this material. Anti-cancer properties are enhanced because the synthesized graphene captures doxorubicin more effectively than plain graphene [34].

Cancer cells, in contrast to normal cells, exist in an acidic medium. As a result, pH-sensitive materials could be beneficial in medication delivery platforms. pH-responsive materials could be beneficial in drug carriers approaches. Graphene-based pH-sensitive drug carriers have recently been implemented [35]. Ganguly *et al.* [36] fabricated rubber-like nanohybrid hydrogels that can be used for pH-sensitive drug delivery

applications. In addition, the hydrogel's conductivity allowed for adjustable and pulsatile drug delivery (Figure 2). This material displayed drug release with variations in pH. Graphene and acrylic acid in the structure of the nanohybrid hydrogel were shown to be pH-responsive and conductive, according to this study.

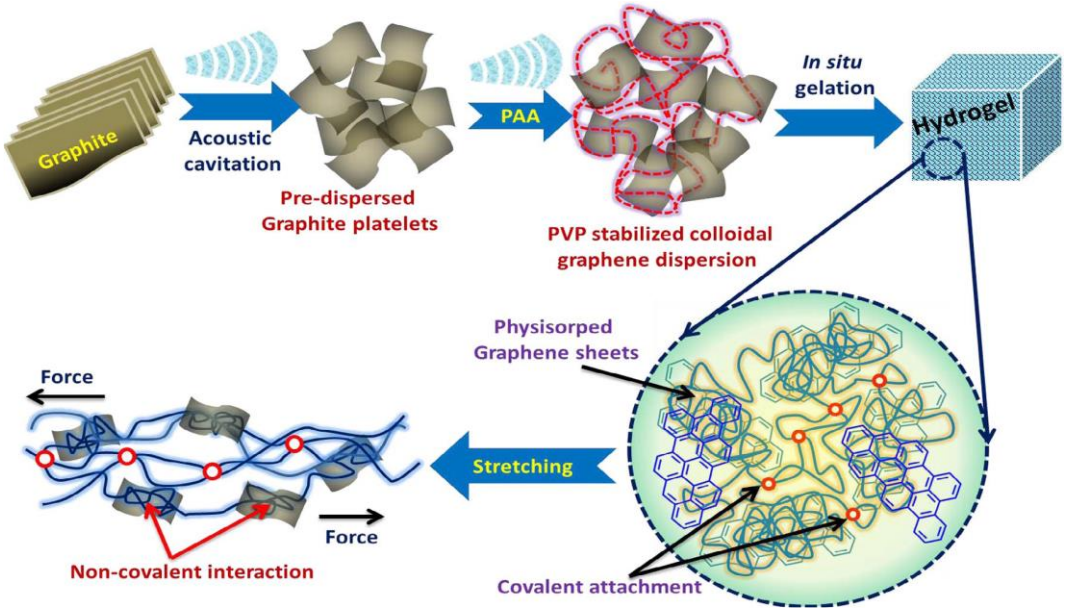

Figure 2. Schematic representation of the synthesis of G-AA nanocomposite hydrogel and the role of chemical and physical crosslinking in the hydrogel matrix

To aid in the treating of human immunodeficiency virus (HIV), graphene quantum dots (GQDs) were mixed with two anti-HIV drugs, CDF119 and CHI499. This investigation identified the reverse transcriptase inhibitors (RTI)-conjugated molecule GQD-CHI499 as a promising option for HIV treatment [37]. Lucherelli *et al*. [38] employed a polyethylene glycol chain to link folic acid to graphene for active targeting of DOX; they used indocyanine green to monitor the molecule inside cancer cells to evaluate its dispersity and anticancer effect. In vitro and in vivo research revealed that multi-role graphene has lower toxicity.

Jahanshahi proposed a new curcumin delivery system for cancer therapy by using fluorination of graphene dissolved in an ionic liquid. The nanostructures material demonstrated improved drug loading capacity and antitumor activity in vitro study since it has a folded edged sheet-like texture. An excellent anti-cancer impact was observed when cancerous cells were used for in vitro testing [39].

Multimodal drug distribution is critical in chemotherapeutic agents because single-drug treatments are often not effective. Graphene is a potential material for combination medication delivery because of its simple functionalization and huge relative surface area [40]. Paclitaxel and doxorubicin have been shown in computational experiments to be synthesized with graphene concurrently. Through strong intra-bonding interactions, folic acid functionalized graphene is potential of co-delivering doxorubicin and cyclophosphamide [41], [42].

Gao *et al*. [43] demonstrated that ibuprofen is an efficient adsorbent for graphene with FeN4 coupled; the ibuprofen/FeN4-graphene combination has a strong chemical binding capability to engage biochemical mechanisms, according to recent density functional model. Graphene can interact directly with viruses in addition to being conjugated with antiviral compounds. Electrostatic and hydrophobic actions between graphene and the virus may alter the virus's sheath. Matharu *et al*. [44] presented on a unique direct contact system they discovered. Graphene nanostructured platelets were tested for antiviral activity against the double-stranded DNA virus Escherichia coli T4 by incubating a graphene suspension for 24 hours. In just three hours, graphene nanoplatelets drastically reduced the viral replication and entirely avoided infections. They blamed graphene's antiviral properties on its shape and reactive oxygen species (ROS) production. Another recent study found that a graphene-copper hybrid was effective in preventing influenza. Within 30 minutes of disintegrating the virus sheath, a virus adhesion and penetration into the host organism [45].

There are antiviral agents that can be attached to graphene such as negatively charged sulfates. Functionalization of graphene with the positively charged residues of viral replication [46] increases this interaction. Functionalization of graphene by Donskyi *et al.* [47] increased its antiviral activity. Synthesis of graphene derivatives with polyglycerol sulfate and alkyl chains was carried out (C3eC18). Vero cells were extremely sensitive to graphene with the C12 alkyl chain, which was the best HSV-1 inhibitor. Shorter chains than C12 were safe for Vero cells and effective HSV-1 inhibitors, whereas longer chains were hazardous.

As a COVID-19 inhibitor, graphene has been suggested by research on additional coronavirus RNA viruses' computer models and experiments [48]. COVID-19 virus may be stabilized by graphene's excellent light absorption characteristics [49]. Nguyen *et al.* [50] reported that an antibody-coupled graphene alters its dopant density and photonic energy when it comes into contact with the SARS-CoV-2 spike protein. If you're looking for SARS, CoV-2 spike protein in artificial saliva or phosphate-buffered saline, this graphene device can identify it. It was also selective towards salivary proteins and the spike protein of the MERS. This optical platform can be duplicated for various COVID variations and specific-binding-based bio-detection applications since the change in graphene photonics is monitored instead of the analyses' photonic fingerprint.

Zhang *et al.* [51] integrated the unprecedentedly sensitive graphene field-effect transistor (Gr-FET) with highly selective antibody-antigen interaction to produce a coronavirus immunosensor in an effort to make screening and diagnosis of the unique COVID-19 easier and faster. As a result, the Gr-FET immunosensors are able to identify and capture the COVID-19 spike protein S1 (which has a receptor binding domain (RBD)) in real-time and label-free in a matter of minutes (approximately two minutes). Using Gr-FET immunosensors to screen for high-affinity antibodies at concentrations down to 0.1 pM has shown to be a viable application of the technology. Consequently, our electrical Gr-FET immunosensors offer an attractive alternative to address the early screening/diagnosis and the analysis and rational design of neutralizing-antibody locking strategies in this ongoing public health dilemma.

Another study by Ali *et al.* [52] demonstrated that 3D nonprinting of three-dimensional electrodes, covering the electrodes with nanoflakes of reduced-graphene-oxide, and immobilizing specific viral antigens on the nanoflakes developed a biosensing platform. A microfluidic device is then utilized to connect the electrode to a normal electrochemical cell. Impedance spectroscopy can be used to identify the presence of antibodies on the electrode surface, which attach to antigens and alter the electrical circuit's impedance. Smartphone-based user interfaces read antibodies to SARS-CoV-2 spike protein and its receptor-binding-domain, respectively, at the limit of detection. Low pH chemistry can be used to regenerate the sensor in just one minute, making it possible to use the same sensor for multiple tests. No cross-reactivity between S1 antibodies and proteins such as interleukin-6 has been observed. An Ebola, HIV, and Zika biomarker detection platform is also possible with the suggested sensing platform.

A class of carbon nanomaterial known as GQDs has the ability to be used in the medical field as drug delivery and bioimaging. GQD-based biosensors have long been widely established for use in clinical diagnosis. GQDs have been extensively applied for identifying biomacromolecules such as DNA, RNA, proteins, and glucose molecules due to their outstanding photoluminescence, electro chemiluminescence, and electrochemical characteristics [53], [54]. GQD have various distinguishing characteristics, such as single atomic planes with a modest lateral size and an oxygen-rich surface, which makes it excellent for delivering medicinal molecules and considered capable in physiological fluids. Furthermore, the fluorescent feature of GQD makes it an excellent vehicle for tracked drug carrier into cancerous cells [55], [56].

Doxycycline -loaded aptamer/GQD capped fluorescent mesoporous silica nanoparticles could be used for cellular drug carrier and real-time drug release tracking. The adenosine triphosphate biosensor induced the release of GQDs from nanocarriers in the adenosine triphosphate -rich cytoplasm of cancer cells, leading to the release of DOX [57]. Sui *et al.* [58] created a cisplatin-GQD nanoconjugate to improve anticancer efficacy. GQD improved cellular uptake in this nanoconjugate, whereas cisplatin improved nuclear uptake by interacting with DNA. That GQD-capped magnetic mesoporous silica nanoparticle can generate heat in an external magnetic field and/or with NIR irradiation has been investigated by the authors of this study. An in vitro investigation showed that the material was capable of chemo-photothermally treatment and magnetic hyperthermia [59].

4. APPLICATIONS OF CARBON NANOTUBES IN BIOMEDICINE

CNTs are folded graphene layers that take the cylindrical form of fullerenes. Single-walled and multi-walled CNTs are the corresponding names for these nanomaterials (8). In 1991, Iijima produced fullerenes using the laser ablation method to produce the first CNTs [60]. CNTs are both stretchy and flexible, with high mechanical stress. They are electrically and thermally very conductive and chemically highly reactive. To employ CNTs in large quantities, there are a few limitations, such as the inability to synthesis CNTs with a predictable architecture [61], [62].

Hydrophobic CNTs have a non-uniform dispersion in biological settings; synthesis method of the CNT surface can overcome this constraint. Oxidative substances cause CNTs to generate carboxylated surfaces once treated to them. It is possible to load pharmaceuticals onto the carboxylated CNT materials since they are evenly disseminated and biocompatible. The amine and carboxylate groups of carboxylated CNTs can be utilized to deliver droxidopa, which could be used to cure hypotension and Parkinson's disease. This material's endurance is predicted to be good by molecular dynamic modelling [63].

The multi-walled CNTs have been designed and synthesized to targeting cancerous cells (65). Antitumor activity, enhanced permeable of the blood-brain barrier and anti-glioma activity were demonstrated by the results with the material given (Figure 3). The anticancer properties of the substance were linked to its penetration and selectivity for glioma cells [64].

Figure 3. Synthetic scheme for TBCNT@OXA

Diseases induced by the viral nerve necrosis, impair the central nervous system, making it difficult to provide medications to the damaged tissue. Fluorescein isothiocyanate and an anti- drug have been coupled with CNTs to enhance Isoprinosine distribution. It was found that a distribution strategy containing bovine serum albumin, Isoprinosine, and CNTs improved anti-viral nerve necrosis ability while reducing fatality in vivo study [65]. Pearl gentian grouper juveniles were successfully vaccinated against the iridovirus with the aid of CNTs. The CNTs were used as a vaccine carrier to enhance the effectiveness of the immune genes [66].

The aggregation of CNTs precludes a clear calculation of an anticancer delivering platform's toxicity, in addition to increasing toxicity for healthy tissues. Covalently linked with doxorubicin, Pennetta *et al*. synthesized CNTs and multi-walls CNTs with pyrrole polypropylene glycol in order to improve CNT dispersion and biocompatibility, respectively. Melanoma and lung cancer cell killing was observed at minor doses of doxorubicin in the innovative delivery systems. The homogeneous distribution of chemotherapy agents also made cytotoxicity testing easier [67]. In particular, CNTs have a remarkable capacity to target a specific receptor or molecular compound. To improve the efficacy of breast cancer treatment, a dual-target method has been proposed. CNTs loaded with doxorubicin -conjugated glycoblock copolymers and folic acid concurrently targeted cancer cells' folic acid receptor and glucose transporter proteins [68].

There has recently been a lot of interest in developing new antiviral systems, including vaccines and medications, to combat emerging viruses. Antiviral properties of carbon nanomaterials, such as viral suppression and virus enzyme blockage, have demonstrated promising results in the fight against viruses [69]. The influenza nanoscale protein 1 (NS1) RNA-binding domain A helps the virus to survive and stops the host cell's mRNA from being exported. As predicted by molecular mechanics models, CNTs are capable of binding and stretching the RNA-binding domain rapidly, disrupting the virus protective system [70].

An investigation of the effects of nano-functionalized single wall CNT and hydroxylated CNTs (IAV) in lung tissue by Chen *et al*. [71] has been completed. While CNTs and IAV can alter antiviral responses without affecting viral titers or producing severe lung damage in animals, CNTs can cause increased viral titers and lung damage in animals exposed to CNTs. It has been shown that CNTs are phagocytosed by macrophages and that their excretion qualities are significantly faster than CNTs. Based on density functional theory investigations, CNTs could be used as an antiviral coating on surfaces. H_2O_2 molecules, which are harmful to viruses like coronaviruses, are substantially absorbable by Cu-functionalized CNTs, that according density functional theory studies [72].

5. APPLICATIONS OF CARBON NANOFIBERS IN BIOMEDICINE

CNFs are one dimension carbon nanomaterial with mechanical and electrical properties, CNF have the potential to be used in biomedicine due to their flexibility, biocompatibility, and electrical conductivity [73]. Carbon-based nanofibers have received increased interest in recent decades due to their exceptional tensile stress and cytocompatibility. They are employed in the biomedicine field for a variety of purposes [74].

A high-density CNF structures are dispersed in a nanostructure film with polytetrafluoroethylene was developed by Li *et al*. [75]. It has been claimed that this nanofibrous dressing material has a unique and distinct technique of clotting blood. Because of its superhydrophobic qualities, this causes the blood to clot quickly owing to the production of fibrin microfibrils and prevents any bleeding that occurs as a result.

Salesa *et al*. [76] revealed the integration of alginate films with nanofibrous of carbon and graphene oxide for diverse biomedicine applications; includes the healing of cutaneous wounds. The usage of CNFs resulted in improved the ability of cells to adhere and proliferate without further toxicity. In 2019, They optimized the qualities for wound dressings, calcium alginate sheets, and the included CNFs were proven for the first time for their antibacterial activities. Additionally, these CNFs were found to be safe for human keratinocytes when exposed to them for an extended period of time, independently of concentration variation.

El-Aziz *et al*. [77] sought to create a hydroxyapatite (HA) and bovine serum albumin (BSA) operationalized carbon nanofibrous films for bone regeneration. The primary goal of this study was to examine the biocompatibility of the animal models. BSA, a key growth factor, improves the material's biocompatibility, whereas HA, along with its biocompatibility, it is widely used as an alternative for artificial bone (Figure 4).

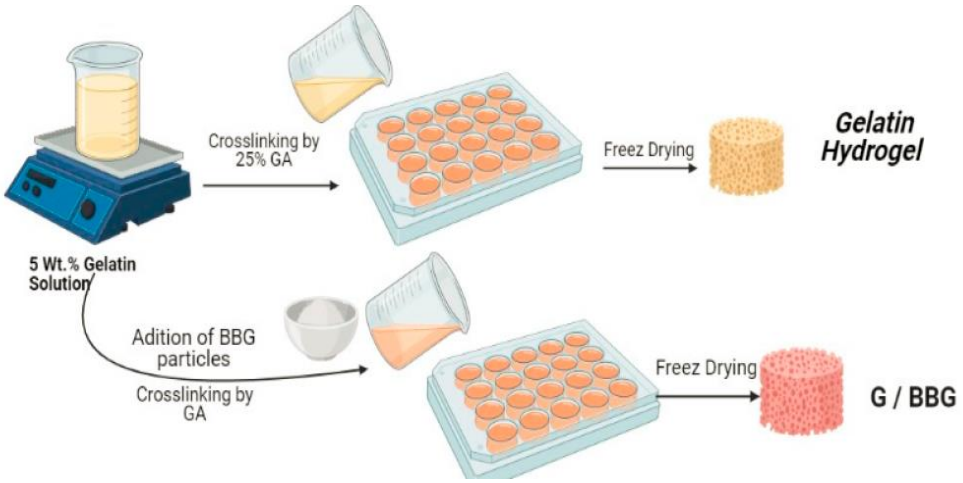

Figure 4. Schematic representation of the synthesis of gelatin/borosilicate bioactive glass nanomaterial

Samadian *et al*. [78] created a two-step process to create an electro-conductive carbon nanostructures fibers procedure in a 2020 study. With a DC electrical stimulation within particular parameters, these nanostructures fibers were able to respond, they increased MG-63 seeded cell proliferation and alkaline phosphatase levels, indicating that the cells were more osteogenic. The explanation has been explained as electrical stimulation penetrating the cell cytoplasm and entering the ion channels through the membranes.

In their 2020 research, Yadav *et al*. [79] described the use of electrospun CNFs in bone tissue regeneration. These nanostructures fibers were created 3-D structure by using polyacrylonitrile nanofibers and then thermally treating them at 1000 °C with argon gas. The results demonstrated that accelerated bone development occurred throughout the trials utilizing an anabolic signalling molecule (rhBMP-2) that is also employed in the treatment of several bone diseases.

Anodic and cathodic current amplitudes are significantly increased in the presence of glucose when TiO_2 coated CNFs are fixed with cobalt–nickel nanoparticles [80]. So, it's an ideal composite material for measuring blood glucose levels. Quantitative measurements of uric acid, ascorbic acid, and particularly dopamine levels in the body, which can be utilized to detect Parkinson's disease in its early stages, have also been made utilizing CNFs. Measurements made by Yue *et al*. [81] of dopamine, uric acid, and ascorbic acid revealed an irreversible, while a Quasi reversible, reaction to the latter.

Carbon-ceramic electrodes modified with single-wall CNTs were reported to be reversible in the presence of acetaminophen and dopamine by Habibi *et al*. [82] but not the pure carbon-ceramic electrodes. As a result of recent developments in this field, we now have the ability to detect disease at its earliest stages. An electrospun CNFs framework was coated with a new molybdenum disulphide ball-like nanosheet by Yue *et al*. [83]. A combination of two nanomaterials gives the final product outstanding electrochemical characteristics. Dopamine detection in urine samples has also been tested with this method. Carbon-based nanomaterials have been studied extensively for their potential medical applications; a summary of these uses is provided in Table 1.

Table 1. Summary of reviewed biomedicine applications of carbon-based nanomaterials

Carbon nanomaterials	Application	Advantages	Reference
Fullerenes	Drug delivery, anticancer and antithrombotic	High structural and chemical stability and surface functional groups	[18]-[29]
Graphene	Tissue engineering, anticancer and antithrombotic	Great electrical and thermal conductivity and electrostatic biomolecular interactions	[35]-[59]
CNTs	Tissue engineering, anticancer and drug delivery	high electrical and thermal conductivity, significant chemical reactivity and surface functional groups	[63]-[72]
CNFs	Wound dressings, tissue engineering and drug delivery	Flexible, electrical conductivity, high aspect ratio, and biocompatible	[75]-[83]

6. CONCLUSION AND FUTURE PERSPECTIVES

Carbon-based nanomaterial as one of the most employed kinds of nanomaterials, have been the subject of extensive research over the last two decades. Carbon-based nanomaterials have been widely used in a variety of applications due to their inherent mechanical, optical, electrochemical, and electrical capabilities. Furthermore, throughout the last decade, CBNs have received a lot of attention in biomedical engineering because of their variable surface characteristics, size, and form.

Interestingly, carbon-based nanomaterials are emerging as interesting materials due to the presence of both inorganic semiconducting and organic stacking capabilities. As a result, it could successfully interface with biomolecules while also responding to light. By combining such properties in a single organism, carbon-based nanomaterials could be exploited to produce biomedical applications in the future. Regarding their toxic effect on biological systems, numerous chemical modifying procedures have been devised and effectively implemented in biomedical applications such as drug delivery, tissue engineering, biomolecule identification, and cancer treatment. This review article discusses some of the advancements made in the use of carbon-based nanomaterials for biomedical applications. Furthermore, in this study, we emphasize upon those widely investigated essential properties of CBNs and their applications for enhanced bio-applications. However, because carbon-based nanomaterials still have toxicity, more systematic investigations are required to assess carbon-based nanomaterials' toxicity and bioavailability.

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