



A Recent Study on Biomedical Applications of Carbon – Based Nanomaterial: An Overview

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ABSTRACT

Now a days, Biomaterials in the form of nanomaterial is being used in various fields, commonly in clinical and biomedical research. Carbon based nanomaterials (CBNs) have unique structural dimensions and excellent mechanical, electrical, thermal, optical, and chemical properties, that's why these materials have attracted significant interest in diverse areas, including biomedical applications. Due to these intrinsic properties, CBNs mainly include carbon nanotubes (CNT), Graphene oxide (GO), and Graphene quantum dots (GQDs), fullerenes, carbon-based quantum dots (CBQDs) have been extensively checked in biomedical field. This review summarizes the most recent studies in developing carbon-based nanomaterials for various biomedical applications including bio-sensing, drug delivery, cancer therapy, tissue engineering, antimicrobial etc.

Keywords:

carbon-based nanomaterials; Graphene (G); Graphene Oxides (GO); Carbon Nanotube (CNT); biomedical applications

INTRODUCTION

In the past 40 years, various nanomaterials with diverse shapes, sizes, and compositions have been used in daily life and are increasingly being used in the healthcare industry [1-2]. Nanoparticles are defined by their dimensions, such as size and shape, which enhance their chemical and physical properties and make them useful for a wide range of applications [3]. Nanotechnology aims to introduce new advancements and improve existing technologies for more effective and precise medical procedures [4]. Carbon-based nanomaterials (CBN) have received attention due to their mechanical properties, chemical resistance, and high distribution rate in the body [5]. Functionalized CBNs have been explored for use in nanomedicines and biocompatible scaffolds through chemical modification of their moieties [6]. Fullerenes are isotopic isomers of carbon nanomaterials known for their cage structures, with C60 being the most prominent representative [7-8]. Graphene and graphene oxide have attracted researchers due to their potential optical, structural, electrical, and mechanical properties, while carbon nanotubes have numerous biomedical applications but also drawbacks, such as potential cytotoxicity and excessive RES uptake [9-10]. Nano-toxicology is a division of toxicology that studies the toxicity of nanomaterials, which is associated with their physical and chemical features [10-11]. Carbon-based nanomaterials can cause various toxicities, such as hepatotoxicity, nephrotoxicity, cardiotoxicity, neurotoxicity, immunotoxicity, genotoxicity, epigenetic toxicity, carcinogenicity, and dermatotoxicity. However, some approaches, such as chemical structural modification, have

been established and effectively applied in bio-applications, such as drug delivery and detection of biomolecules, as well as therapy and tissue engineering for cancer [13]. Carbon-based nanomaterials hold potential for future biomedical applications.

BIOMEDICAL APPLICATIONS OF CARBON – BASED NANOMATERIAL-

CBNs can be used in diverse medical fields for optimum utilization of their specific characteristics to the best of their ability. Some of the applications are as follows:

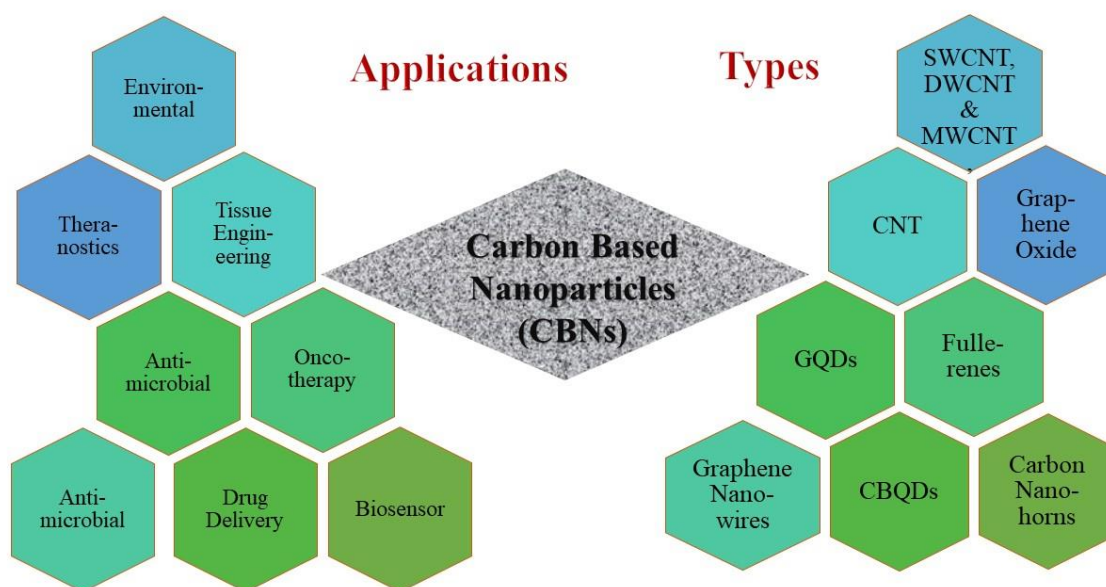


Fig.1 depicts the types and various applications of CBNs.

Anti-Cancer Therapy:

Cancer is a fatal illness and there are numerous variations of tumors which is responsible for an intense increase in death rates [5]. The fullerenes have the capability to mimic photoproduction sensitizers for singlet oxygen (1O_2) ROS, and as a result, it is used for photodynamic cancer therapy (PDT) and blood sterilization [9]. For the treatment of cancer, fullerenes can act as an active drug and gene delivery carrier with proper effectiveness. Additionally, we can treat cancer by photodynamic therapy (PDT) as fullerenes tend to create cytotoxic free radicals under photo-irradiation, so they function as free-radical scavengers. It is recognized that C_{60} can go into singlet state $^1C_{60}$ from the ground state due to photoexcitation, which consequently comes to the triplet state $^3C_{60}$, and singlet oxygen formation takes place because of energy transfer to peripheral oxygen. Furthermore, C_{60} can be easily reduced from $^1C_{60}$ and $^3C_{60}$ can be easily reduced through electron transfer. Free radicals have more attraction towards many biomolecules such as proteins, DNA, RNA, etc. Similarly, fullerenes are also considered to be effective in terminating tissue or cells by a feedback mechanism alike to that of photodynamic therapy (1).

In cancer therapy, the usage of carbon nanotubes is extensively accepted. Due to the intake of specific malignant cells without eroding healthy cells, they are incompetent of targeting the tumor. For chemotherapy, CNTs considered as a perfect vehicle for the transportation of proteins, anticancer drugs, and genes. To improve programmed cell death in cancer cells, a group utilized a PEG-coated CNT-ABT737 nano-drug to aim mitochondria. Programmed death of lung cancer cells via breaking-off of the mitochondrial membrane because

of the release of Cytosol of the nano-drug. Also, the restricted heating effect under the influence of NIR irradiation enhanced the performance therapeutically [14]. To produce and improve the scaffolds for pancreatic cancer cells MWCNTs were used. An anticancer drug named Methotrexate was restrained on the surface of the graphene to estimate the drug transporting ability of graphene-based nanomaterials. Breast cancer is treated with fabricated SWCNTs, this fabrication is done with infrared fluorescent cyanines. Polyvinylpyrrolidone (PVP) polymer is used for producing the homogeneous dispersion of single-walled carbon nanotubes in water stably. In the further step, the high iron oxide content was loaded into SWCNTs [15]. Thus, in a 4T1-induced breast cancer murine model, for active targeting of cancerous sites, the magnetic iron-tagged SWCNT complexes were labeled with a mouse Endoglin/ CD105 monoclonal antibody. The acquired results of bio-compatibility assays defined that the magnetic-based SWCNTs are harmless for administration in animals and may be used for tumor monitoring [16]. In tumor therapy, hydrogels of GO-based nano-fillers are used to deliver drugs and bind in a controlled release manner. Camptothecin and doxorubicin were loaded into G/GO-based hydrogels, which were able of delivering antitumor drugs dead slower than the Pluronic F-127 solution designating strong binding-interaction of lipophilic drugs due to the gel containing G/GO [17]. Based on pH-stimuli drug delivery, GO filled with 5-fluorouracil was produced and the drug is released in a controlled release manner at a pH of 5.8 while, in the normal physiological pH of 7.4. the release was decreased ominously Folic acid with functionalized GO work as a tumor-targeting molecule and cancer drugs named as doxorubicin and camptothecin, are loaded into the bulky surface area of GO through π - π stacking. The cancer-targeting ability and antitumor activity is improved by drug-loaded FA-GO in comparison with unaccompanied delivered drugs or unmodified GO carried drugs carried [11].

Biosensor

A biosensor is an analytical instrument that combines a biological component with a physicochemical detector to detect and measure the presence and amount of an analyte [14]. They are the most significant sensor for biological analyte determination. Biosensors based on nanomaterials have been utilized to detect antibiotics, poisons, proteins, and microorganisms in a quick, sensitive, and specific manner. These bio-macromolecules' specificity, or interaction strength, is often high for their biological substrates or targets [10]. Wide light absorption in the UV–Vis region, structural angle tension, a combination of nucleophilic and electrophilic dual properties, SOP (singlet oxygen production), photo-thermal effect, long life triple state, and the ability to act as an electron acceptor are all unique properties of fullerene [1]. Fullerene has the advantage of great sensitivity to numerous biological and biomedical analyses, high selectivity, real-time responsiveness, and quick signal transmission due to these unique features. Fullerenes are not harmful to biological systems, and their materials are small enough to detect near distances in biomolecules' active zones. Electron exchange between species can also be simple in the vicinity of biomolecules. Furthermore, they are an excellent substrate for receiving and releasing electrons from a transducer. In the identification of a biosensor, biological ingredients such as antibodies, cells, bacteria, organelles, enzymes, and tissues are used. Fullerenes operate as a mediator between the biosensor's identification component and the electrode to speed up the electron transfer caused by the biochemical reaction of the analyte in contact with the biological element at the identification field [15]. By leveraging graphene's unique physiochemical, optical, and electrical capabilities, many graphene-based biosensors with high sensitivities have been developed [9]. Because graphene has a wide lipophilic region on its surface, it has a strong π - π contact with single-stranded DNA (ssDNA), however this interaction would be diminished if double-stranded DNA (dsDNA) was produced by adding a comparable ssDNA. Based on this phenomenon, a variety of off/on fluorescence biosensors have been

conceived and built, demonstrating high sensitivity and selectivity for the detection of various targets in solutions or even living cells. CNTs are also being investigated for the manufacture of a wide range of biosensors due to their unique structure, NIR-II fluorescence, and resonance Raman scattering [18]. The immobilization of biomolecules on the surface of CNT-based biosensors is a key feature that improves identification and signal transduction. These biosensors are classified as electronic CNT-based biosensors, electrochemical biosensors, and optical biosensors based on their target transduction methods and recognition. CNTs are well-known for their ability to improve electron transfer, making them ideal for merging electrochemical and electronic biosensors [13]. In the development of biosensors, double-wall carbon nanotubes (DWCNTs) are also employed. An immuno-sensor for adiponectin, an obesity biomarker, was produced by grafting antibodies onto the surface of DWCNTs. Anti-salmonella was impregnated on the surface of DWCNT bundles employed as an electrode in this construction [19]. Graphene oxide can engage dynamically with the probe and/or to transmit a specific response to the target molecules. Electrochemical reaction, fluorescence, and Raman scattering are used to achieve this transmission process. GO are commonly utilized as biosensors because of this. The Rahigi group created reduced graphene nanowire (RGNW) biosensors that allow for the electrochemical detection of four DNA bases (adenine, tyrosine, guanine, and cytosine) by examining the oxidation signals of discrete nucleotide bases. With an increase in differential pulse voltammetry (DPV) up to 100 scans, the RGNW showed outstanding stability, with just 15% variance in the oxidation signals. A graphene surface modified vertically aligned silicon nanowire for detecting oligonucleotides with sensitivity and selectivity was produced using a single-layer graphene (SLG)-based FET biosensor that was able to detect a very low quantity of DNA (10 fM) [13]. GQD adapted form pyrolytic graphite (PG) electrode combined with single-stranded DNA probe can be used to develop various electrochemical biosensors for the sensitive and vigilant detection of diverse target molecules. GQDs are a one-of-a-kind platform for effective biomolecule sensing via fluorescence resonance energy transfer (FRET) from quantum dots (QDs) to graphene oxide (GO). Because these GQDs hybrids can detect target DNA and proteins, they have a wider range of applications [20].

Theranostics

Theranostics is an emerging inter-discipline that is paving the way toward personalized medicine by combining medical diagnostics and therapies to achieve optimal efficacy and safety of a comprehensive regimen. Many nano-materials are being actively investigated for theranostic applications due to their large aspect ratio and/or surface area, which can allow for the attachment of multiple copies of various theranostic moieties such as imaging labels (e.g., radioisotopes, etc.), targeting ligands (e.g., peptides and antibodies), therapeutic agents (e.g., drugs, genes, etc.), as well as various polymers to improve their water so Activatable theranostic compounds can improve disease destruction selectivity and specificity with high localized cytotoxicity and minimal collateral harm [21]. For biomedical applications, fullerenes have a wide range of possibilities. Fullerenes could be useful building blocks for the development of a multifunctional theranostics platform due to their great biocompatibility and intriguing inherent features [1]. Most fullerenes (such as C60) have a spheroid shape, while oblong variants resembling a rugby ball do exist (e.g., C70). As a result, fullerenes that have been produced have the potential to be used as antibacterial, antiviral, and antioxidant agents. Fullerenes can self-assemble into vesicles known as fullerosomes, which can be used as multivalent drug delivery vehicles with various targeting features. Fullerenes' antioxidant properties, which include scavenging free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), have fueled its biological uses. Fullerenes have also been suggested as possible

photosensitizers. They may absorb photons in the ultraviolet and visible electromagnetic spectrum, resulting in photo-excited fullerene species in the triplet state and, depending on the polarity of the medium, singlet oxygen or reactive oxygen species (ROS) [22]. The interior space of fullerene and carbon nanotubes with hollow structures can be used to load various functional species for theranostic purposes. CNTs and graphene derivatives with high optical absorbance in the near-infrared region can also be used for cancer photothermal ablation [17]. Sp²-carbon nanomaterials, particularly single-walled carbon nanotubes (SWNTs) and graphene with all carbon atoms exposed on their surfaces, have a large surface area that can be used for drug loading and bio-conjugation. Graphene and its derivatives have been thoroughly investigated and found to be promising nanomaterials for drug and gene delivery, as well as cancer therapy [1]. Graphene-based materials are emerging as drug vehicles, cellular imaging agents, and sensors to overcome these barriers in cancer treatment [18]. Graphene and carbon nanotubes (CNTs) have similar electrical, optical, and thermal properties, but graphene's two-dimensional atomic sheet structure allows for a wider range of electronic properties; (Graphene oxide (GO), which is made by oxidizing graphite under acidic conditions, is more commonly used because it has several advantages over pure graphene. For starters, GO can be dispersed in aqueous conditions, which is crucial for biological applications. Second, GO contains hydrophilic functional groups that can be used to perform chemical functions. Third, because to its structural heterogeneity, GO has a wider variety of physical properties than pure graphene. Graphene materials have been investigated for a variety of biomedical applications, including injectable cellular labelling agents, drug delivery systems, and scaffold reinforcements, in the same way that CNTs have been [23]. Graphene materials interfere with macrophage metabolic activity, damaging the mitochondrial membrane and increasing reactive oxygen species (ROS) levels. When CBNs are taken up by cancer cells, they cause DNA and lipid damage, as well as cell death due to ROS activation [6]. A study conducted by Farahnaz Barahuie et al., the production of GO as a drug carrier for chlorogenic acid (CA) can be used as a pH-sensitive platform for the controlled discharge of CA from GO. CA loaded GO had a low and negligible harmful effect on normal cells, while it had a substantial toxic effect on cancer cell lines. Folic acid combined with polyethyleneimine (PEI), functionalized GO, and carboxymethylcellulose was shown to be non-toxic to normal cells and resulting in a regulated release of doxorubicin (Dox) [5]. Single wall carbon nanotubes (SWCNTs) and multiwall carbon nanotubes (MWCNTs) are separated by the number of graphene layers in the cylindrical tubes (MWCNTs). Arc discharge or chemical vapor deposition of graphite are routinely used to create carbon nanotubes. They have a cylindrical carbon structure and a wide range of electrical and optical properties due to their extended sp² carbon and tunable physical properties (e.g., diameter, length, single-walled vs multiwalled, surface functionalization, and chirality) [6]. CNTs have been studied for usage in a wide range of industrial applications due to their diverse set of characteristics [13]. CNTs, for example, are well-known for their exceptional mechanical strength: their measured stiffness and flexibility exceed those of certain commercially available high-strength materials (e.g., high tensile steel, carbon fibers, and Kevlar). As a result, they've been used as reinforcing elements in composite materials including plastics and metal alloys, resulting in several commercialized goods [24]. Carbon nanotubes are being studied in high-efficiency electron emission devices including electron microscopes, flat display screens, and gas-discharge tubes. Carbon nanotubes also have a bright luminosity due to field emission, which could be employed in lighting [11]. Because of their hydrophobic surface, carbon nanotubes, including SWCNTs and multi-walled carbon nanotubes (MWCNTs), are water insoluble. CNTs have been shown to be effective intracellular carriers for small pharmacological molecules and various biomacromolecules loaded by noncovalent attachment or covalent

conjugation, thanks to their efficient intracellular shuttling capabilities. SWCNTs have been discovered to be photoluminescent and exhibit a high optical absorbance in the near-infrared range, indicating that they are useful for bioimaging and tumor therapy. SWCNTs have been found to be useful Raman probes for selective detection and multiplexed imaging due to their strong resonance Raman scattering characteristic [1]. CNTs are divided into two categories based on the arrangement of graphite cylinders: single-walled carbon nanotubes (SWNTs) and multi-walled carbon nanotubes (MWNTs) (MWNTs). SWCNTs are highly absorbent materials with strong optical absorption in the near-infrared range, making them ideal for photothermal and photoacoustic imaging. Nanohorns are a modified type of SWCNTs. They have a single carbon hexagonal ring. They are employed in medication delivery and targeting therapeutic molecules to malignant cancer because of their unique trait of increasing diameter with length [6]. The CNT has long been seen as a sensing element for finding, detecting, and assessing a variety of disorders, particularly diabetes and viral diseases [5].

Tissue Engineering

In many areas of biomedical research, Carbon-based biomaterials have been applied to tissue scaffold reinforcements, drug delivery systems, and cellular sensors. (11) Scaffolds are called “the beating heart” of the tissue engineering field (19) CS has various desirable properties for tissue engineering like biodegradability, biocompatibility, and non-toxicity. CS was used in numerous tissue-engineering applications such as bone, separation membranes, liver, tendons, ligaments, wound healing, nerves, fat-sequestering agent, blood anticoagulants, contact lenses, controlled release of drugs p, hydrogel preparations, and food packaging material. (25) To recently, the use of carbon nanotubes as composite reinforcements in tissue engineering scaffolds has primarily been focused on increasing mechanical properties. To mimic the rigidity of natural tissues, commonly utilized scaffold materials such as fibre scaffolds and hydrogels are intrinsically soft, and so often lack structural support and strength. CNTs have been found to improve the mechanical properties of these nanomaterials when they are included. Shin et al., for example, found that including CNTs into photo-cross-linkable gelatin hydrogels resulted in a negligible increase in tensile strength. CNTs' multifunctional nature has recently piqued the interest of academics who want to use them to create tissue scaffolds. CNTs have been used to make electrically conductive scaffolds. (26)

DWCNTs, rather than SiO₂, provide a suitable surface texture for growing neuron cells in tissue engineering. After neuron growth on DWCNT, improved cell differentiation was reported (1) Materials are classified in vivo uses of GO-based on passive targeting, enhanced permeability, and retention effects. These effects are frequent in a variety of tumor types and are attributable to excessive vascularization. As a result of the active targeting of GO, nanomaterials can now be accumulated in the target cancer tissue, boosting efficacy, and decreasing side effects. (5) Fullerene C₆₀ enhances the MAPK expression level as well as proliferation, stem cell survival, and cardio myogenesis. Furthermore, at a concentration of 100 g/mL, fullerene C₆₀ had no cytotoxic effects on brown adipose-derived stem cells (BADSCs). Additionally, fullerene C encourages cell6s0 to develop gap junctions. These findings have significant implications for the use of fullerenes in the treatment of myocardial infarction in the clinic. Peripheral nerve injury is a common clinical injury, and its repair and reconstruction have always been a worldwide problem (Qian et al., 2019a, 2020a, 2021). At present, the main methods of treating peripheral nerve injury are autologous nerve transplantation and the construction of tissue engineered nerve scaffolds, autologous nerve.

In the development of bioimaging genomes, proteomics, and tissue engineering, carbon nanotubes (CNTs) and carbon nanohorns (CNH) are utilized to control genes and atoms. Nanotubes and nanohorns can bind to numerous antigens on their surfaces, making them potential antigen sources for vaccinations. Treatment of orofacial fractures, bone augmentation, temporomandibular joint cartilage regeneration, pulp repair, periodontal ligament regeneration, and implant osseointegration are all possible applications of tissue engineering and stem cell research in dentistry. Tissue engineering allows for the implantation of implants that have a shorter recovery time, are more biologically and physiologically stable than earlier implants, and can safely support early loading. Because it encourages the cell proliferation required for periodontal tissue remodeling, nanocrystalline hydroxyapatite can help generate bone grafts (27) Graphene has been shown to successfully adsorb nucleobases via the π - π interaction, as well as shield nucleotides from enzyme breakage. In the field of regenerative medicine, gene therapy has recently become a popular treatment option. Protecting DNA from degradation and guaranteeing high transfection efficiency are two of the most basic requirements for a gene delivery vector. In addition, both non-viral and viral vectors have been extensively studied in the field of gene delivery. As a result, graphene nanosheets may be useful as a vector that cells may easily absorb. Chen et al., for example, used a poly(ethylenimine)-GO (PEI-GO) carrier to transfect plasmid DNA into HeLa cells, demonstrating that PEI-GO might improve transfection efficiency through a proton-sponge effect. To create 2D or 3D graphene-based constructions, many researchers have used coating, hydrogel blending, wet/dry spinning processes, and 3D printing. Other biomaterials can be attached to graphene and its derivatives to improve their mechanical, physical, and electrical properties for tissue engineering applications. We previously demonstrated that the modulus of GO-hybrid gels could be adjustable within a range of 8-24 kPa by utilizing varying amounts of GO (16). Nanomaterials were then used to create 3D tissue-engineered scaffolds for skin, bone, blood vessels, and other tissues. In addition, nanostructures have been discovered to affect the adhesion, proliferation, and differentiation of primordial stem cells. MNPs have recently gotten a lot of attention because of their extraordinary magnetic characteristics and unusual size. MNPs are smaller (20–300 nm) and have magnetization directions that allow for thermal fluctuations at room or biological temperatures. (28)

Drug delivery

Several sub-group of CBNs possess as a carrier for effective delivery of a wide range of drugs. In recent years, these materials have been extensively used for cancer therapy. Concurrently, the scope of CBNs towards other diseases is also exploring gradually. As the size of nanodiamonds are less in size basically less than 1nm their physical and chemical properties make them suitable for their use in technological as well as high scientific works. As per the size, nanodiamonds are of three types :type 1- nanocrystalline particle of size 1-150nm, type2- ultra nanocrystalline particle of size 2-10nm and type3- Diamondoids of size 1-2nm ,due to extremely small size they have significantly increase large surface is to volume ratio due to this the surface property of nanodiamond dominate and improve their pharmaceutical properties , in the drug delivery system the chemical bonding and physical adsorption mechanism are involved.as in liver cancer the ionic bonding properties of nanodiamonds conjugates with doxorubicin and form complex(ND-PEG-DOX) and due to formation of this complex the half-life of doxorubicin increase its twice and by using clathrin dependent pathway(inside nucleus) this complex prevents cell proliferation . [29]

Fullerens is made up of carbon60 molecule forming a cage like structure the core is having hydrophobic structure and shows complexity because of functional group attached at its core so attaching compatible hydrophilic group helps in generation of water soluble C60 and further makes it capable for carrying drug and delivery. The hydrophilic functional group (hydroxy group) present on surface of fullerenes helps in functionalization stabilization and super positioning of fullerene with drug this leads to overcome the safety and drug load concerns (30). The lipid-based vector in cos1 cells show less efficacy to enhance it the DNA functionalized fullerene is used which makes it better efficacy and increasing the life of DNA in endosomes through chromosomal incorporation. The peptide fullerenes conjugates show mechanical flexion in skin organization that increases its penetration power and permeability. Taking example first esters are used to create hollow spaces in cells membrane which helps to generate the delayed release carriers for anti-cancerous and anti-tumor like delayed release dosage form of docataxel in tumor cells and 5-fluoro uracil and cyclophosphamide in cancer cells. [31]

Nanotube is a rolled-up Graphene sheet having size of 100nm due to their broad absorption spectra a in UV-vis-NIR region and large surface area as well as RAMAN bands they are used in nanomedicine. They work on adsorption mechanisms (covalent adsorption and non-covalent adsorption). Size and shape of nanotubes is a major key factor for its site selectivity and targeted drug delivery. [32]

Carbon quantum dots commonly known by the name Carbon Dots with size less than 10nm are produced by several techniques such as chemical vapor deposition, laser ablation, pyrolysis etc. They are highly chemically stable ,they have strong fluorescence property .In CDQ are widely used because of their chemical property they also are low cytotoxic ,shows high cell permeability and water solubility(hydrophilicity) use of CDQ with Quercetin {7-(3-bromopropoxy)-2-quinomethy chlorambucil} through covalent bonding showed a controlled release of drug to target cell by irradiation CDQ are also used in gene therapy/gene delivery because of their electrostatic interaction between positively charged functionalized Carbon Dots and nucleic acid (negatively charged)they also have good properties to condense plasmid-DNA .They are used as gene vector too for chondrogenesis from fibroblast the plasmid SOX9 in combination with CDs are used to form nanoparticle with size range from 10 to 30nm .Also because of their hollow nanostructure they have increase efficacy in drug loading the CDQ used in drug delivery becomes magnetic so it is also used in MRI(magnetic resonance imaging). [33]

Carbon nanohorns shows structural similarity with nanotubes having opening and apex made of 5 pentagonal rings they show sponge like structure with diameter of about 100nm due to its specific shape it has high porosity and high surface area which leads high adsorption property functionalization of carbon nanohorns make them biocompatible taking example of in lung cancer PEG-Doxorubicin complexed with carbon nanohorns have shown lower apoptosis of cell than normal controlled drug of doxorubicin this is due to retention of PEG-DOX on the surface this leads to therapeutic effect. [6]

Graphene nanoribbons (GRNs) have a definite Nature, virtually one-dimensional and flat graphene structures. Minuscule (<10nm) with higher aspect ratio fragments of Graphene sheets create GNRs. The Observed stable Bandgap is not more than 10nm and when this width is increased the conductive nature of these materials increases as they turn into a semi-metallic compound from the original semiconductor nature. The thermal conductivity, as well as the electrical conductivity, is very high in Graphene Nanoribbons due to this exponential conductivity shift and thermal stability it resembles property that is suitable for a material to be used in an integrated circuit and thus it may replace copper in an integrated circuit.

The bandgap of GNRs is unstable and variable thus they are modified to suit the structure's dimension. The Armchair GNRs can be either metallic or semiconductor, in contrast to the metallic zigzag form of GNRs. [7]

Its irreversible aggregation performance, which is mostly the result of strong van der Waals interactions, has some limits, although some cleverly engineered modulations are done to alter the surface chemistry for its multidimensional practical applications. Such Graphene oxide based engineered devices is being used nowadays largely because of their excellent qualities such as their large surface area, honeycomb-like structure that provides hollow interstitial space for compounds, sp² hybridized carbon, good biocompatibility, and cell membrane penetration caused by electronic effect. [8]

With the larger surface area and advantageous physicochemical characteristics, the porous carbon compounds are gaining popularity. Activated carbons are another name for this kind of carbon. Based on the size of their pores, they can be categorized into three types based on their size: macroporous (greater than 50 nm), mesoporous (greater than 2 nm), and microporous (2 nm). They are typically produced through pyrolysis and through different carbon-based precursors which are chemically or physically activated at high temperatures. According to observations, the mixture of all microporous, mesoporous, and microporous gives the most surface area of any carbon type. They are widely utilized in adsorption, separation, and a variety of other processes and may be made in huge quantities). Microporous and Mesoporous structures may create mass transfer resistance in the 3D bulk form Mezzoporous carbon nanoparticles (MCNs) are widely used in the delivery of pharmaceuticals. [34]

Antimicrobial Application:

Antimicrobial action can be seen in carbon-based nanomaterials against a variety of microorganisms, such as viruses, bacteria, and fungi. The exact mechanism by which carbon-based nanomaterials exert their antimicrobial activity is not yet fully understood, but it is believed to be due to several factors including larger surface area, ability to penetrate cell membranes, and ability to generate reactive oxygen species. For example, carbon nanotubes can inhibit the growth of bacterial strains such as *Escherichia coli* and *Staphylococcus aureus*, while graphene oxide has been shown to be effective against a range of bacteria, including *Pseudomonas aeruginosa* and *Salmonella typhimurium*. Fullerene has also shown antimicrobial action against a variety of microorganisms such as bacteria and fungus. [35]

While the antimicrobial activity of carbon-based nanomaterials shows promise for their potential use in biomedical applications. It requires more research for Understanding their exact mechanism of action and assessing their potential toxicity and environmental impact. One proposed mechanism is that the sharp edges and large surface area of carbon-based nanomaterials can physically damage the cell membrane of microorganisms, causing leakage of cellular contents and eventually leading to cell death. Another proposed mechanism is that carbon-based nanomaterials can generate reactive oxygen species (ROS) upon exposure to light, which induces oxidative stress and damages microbial cells.

When tested against several bacteria, including *E. coli*, *Salmonella*, and *Streptococcus* spp., fullerenes showed antibacterial action. Once the nanoparticles were internalized by the bacteria, energy metabolism was likely inhibited, resulting in antimicrobial action. Moreover, it has been proposed that fullerene derivatives can prevent the development of germs by affecting the respiratory chain. An initial drop in oxygen intake is followed by an increase in oxygen uptake, which increases the formation of hydrogen peroxide.

The stimulation of cell membrane rupture is another bactericidal mechanism that has been put forth (fullerenes surface is hydrophobic which helps to interpolate into microorganisms by interfering with membrane lipids). Fullerenes can bear positive or negative charges and can also exist as neutral compounds and all exhibited antibacterial action against *E. coli* and *Shewanellaoneidensis*, although cationic derivatives had the most antibacterial activity. [36]

Chemically modifying graphene by suspending different functional groups yields GO nanosheets that are easily dispersed in water. The primary antibacterial mechanism of GO is due to established membrane stress when they are in direct contact with sharp nanosheets. Graphene as well as GO was shown to limit the development of *E. coli*, the direct contact of the associated very sharp edges with bacteria results in a damaged cell membrane which leads to RNA Efflux in both gram-negative (*E. coli*) and gram-positive (*S. aureus*) bacteria. Ag-carbon nano complexes also inhibited the growth of many pathogens, including *Burkholderiacepacia*, *MRSA*, *MDR-A.baumannii*, and *Klebsiella pneumoniae*. These nanostructures may also hinder the growth of bio-defense bacteria like *Yersinia pestis*. [37] The interaction of the QDs with the phospholipid bilayer roughens and shrinks the cell membrane. Additionally, the cell is torn because of the QDs' direct connection, resulting in the ejection of cellular components. Membrane tension is caused by the electrostatic interaction of the positive charge of QDs with the negative charge of cellular components. The introduction of metals/ions into the cell enhances toxicity, resulting in cell death. QDs generate a significant number of free electrons and holes due to their strong electron transport. Photoactivated QDs generate an abundance of free radicals, such as hydroxide anions (OH), superoxide singlet oxygen (O₂), triplet oxygen, and per-hydroxyl anions. The concentration of ROS within the cell hampers respiration and reproduction, resulting in microbial cell death. Some QDs can enter the nucleus and accumulate. QDs and nuclear content combine to decrease cell respiration, division, replication, and adenosine triphosphate (ATP) generation. Cell apoptosis is the end effect of nucleus damage. [38]

The antimicrobial activity of nanotubes is not well defined however it is a potent antimicrobial it works through several mechanism firstly it adheres to the microbes cell surface, there it interrupts transmembrane electron transfer and cause breakage of membrane and cell walls thus leading to penetration to bacterial cell which results to damage and protein dysfunction and formation of reactive oxygen species. [16]

Environmental application

The capability of fullerenes to generate ROS has potential to be exploited to generate oxidative species that hasten the degradation of organic moieties in water. Our motive is to study the oxidation reaction in under investigation organic compounds by reactive oxygen species generated by solutions of hydroxy fullerene which rapidly create stable suspensions of fulleranol (C₆₀(OH)₂₂₋₂₄) masses by using ultrasonic technology. After exposure to UV light, the pollutants are damaged with an efficacy like known photosensitizers generating singlet oxygen. A slight specific degradation of the compound occurs. By exploiting the specificity of the reaction, a chemical can be destroyed while avoiding unwanted byproducts of oxidation. [39]

C₆₀ and C₇₀ fullerenes are also thought to have potential antimicrobial properties that can damage DNA and inactivate viruses, bacteria, and tumor cells, suggesting that these materials could be used to disinfect or render surface resistant to growth of microbes. We take the example of the deactivation of marine bacterial viruses and the formation of antifouling films, where biofouling is a disadvantage. [40]

The application of quantum dot nanomaterials and connection to optical or chemical sensor transducers, it is possible to assemble powerful detection equipment capable of detecting various metals under complex conditions. The zero-dimensional graphene dots have been utilized due to their attractive properties, which includes exceptional optical characteristics, tunable absorbing surface groups, decent stability, and easy fabrication as well as preparation procedures, by doping in heavy metal ion nano sensors in optical detector species. [41]

Silica-based mesoporous constituents belonging to the class of inorganic nanocarriers are commonly utilized as a suitable mode for delivery of drug. This method uses the extremely stable porous surface of mesoporous silicon constituents to plug in bioactive substances. Ideally, the charged pores are plugged, and the cargo is released inside the cell [21]. One of the most important benefits of using MPSNPs is the stability of MPSNP, making them capable of coping with physical stresses like change in pH and temperature of adjacent medium [22].

There is indication that the uptake of nanoparticles by plants is largely dependent on the cell wall pore size, which differs between diverse tissues and organs. The repulsive size limit of plant cell walls is up to 50 nm [23]. MSNs are designed such that the gold nanoparticles coat the pores to prevent cargo leakage and release the contents into the intended target to activate gene expression within the controlled release conditions [42].

Nanocarriers based on chitosan are found to be a capable system for delivering cargo into plant cells as they are having positive charges. An investigation verified targeted delivery to organelles and temporary expression of genetic material through chitosan-based nanotube carriers of single walled carbon. Effective chloroplast transformation has been attained in mature mustard, nasturtium, tobacco, and spinach plants, as well as in isolated mesophyll protoplasts of Arabidopsis. [25,38,44]

Starting from the chemical sensitivity of pure nanotubes, many articles have shown that single-walled carbon nanotubes (SWCNTs) as well as multi-walled carbon nanotubes (MWCNTs) can be applied for detection of Oxygen or for minute chemical sensors for detecting toxic gas molecules in low concentrations with high sensitivity.

Carbon nanotubes are found to be an excellent adsorbent for the elimination of several kinds of organic and inorganic pollutants in marine environments and air. The adsorption capability of CNTs is primarily attributed to the porous structure as well as the presence functional groups on the surface of the nanotubes, which are obtained by chemical or thermal alteration to give the CNTs the desired properties. [43,45]

CONCLUSION-

Over the last two decades, widespread research efforts have been conducted on CBNs as one of the most widely used classes of nanomaterials. Interestingly, CBNs are becoming promising materials due to the existence of both inorganic semiconducting properties and organic π - π stacking characteristics. Hence, it could effectively interact with biomolecules and response to the light simultaneously. By taking advantage of such aspects in a single entity, CBN-based nanomaterials could be used for developing biomedical applications in future. This review article provides some achievements in the use of CBNs for biomedical applications. Moreover, in this paper we also focus on some recently found key features of CBNs and their utilizations for superior bio-applications. However, as CBNs still contain toxicity, more systematic studies are needed to determine the toxicity and pharmacokinetics of CBNs.

CONFLICTS OF INTEREST

There are no conflicts of interest among the authors.

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REFERENCE

1. Vikash, Dr. P.M. *Nanomaterials and Nanotechnology in medicine*. 2022.
2. K. SenthilKannan, G. Flora, S. Gunasekaran, H. Abdul Jaffar Ali, M. Vimalan & S. Balasubramanian. *Nanotechnology for advances in medical microbiology* 2021, Springer Science and Business Media LLC.
3. Jyotsna, L. Stanley Abraham, Rathore Hanumant Singh, Ramesh C. Panda., *Biomedical Applications. Nanomaterials and their biomedical application*. 2021, P. 157.
4. L. Stanley Abraham, Rathore Hanumant Singh, Ramesh C. Panda., *Biomedical Applications of carbon based nanomaterial. Nanomaterials and there biomedical application*. 2021, P. 161.
5. *Nanooncology* 2018, Springer Science and Business Media LLC
6. Ajima K, Yudasaka M, Murakami T, Maigné A, Shiba K, Iijima S. Carbon nanohorns as anticancer drug carriers. *Carbon nanohorns as anticancer drug carriers*. 2005, P. 475-480.
7. srivastava, sujit kumar debnath and rohit. *Drug Delivery With Carbon-Based Nanomaterials as Versatile Nanocarriers: Progress and Prospects*. 2021, Frontiers In Nanotechnology.
8. Neha Karki, a Himani Tiwari, Chetna Tewari, a Anita Rana, Neema Pandey, Souvik Basakb and Nanda Gopal Sahoo. *Functionalized graphene oxide as a vehicle for targeted drug delivery and bioimaging applications* 2020, Journal of Materials Chemistry B.
9. . Ma, Yufei, He Shen, Xiaolong Tu, and Zhijun zhang. *Assessing in vivo toxicity of graphene materials: current methods and future outlook* 2014, Future Medicine.
10. Zhanjun Gu, Shuang Zhu, Liang Yan, Feng Zhao, Yuliang Zhao. *Graphene based small platforms for combination cancer therapy* 2018, Advnaced Material .
11. Dr. Svetlana A. Chechetka, Dr. Benoit Pichon, Dr. Minfang Zhang, Dr. Masako Yudasaka, Dr. Sylvie Bégin-Colin, Dr. Alberto Bianco, Dr. Eijiro Miyako. *Multifunctional Carbon Nanohorn Complexes for Cancer Treatment*. 2014, Wiley Online Library.
12. Nishtha Panwar, Alana Mauluidy Soehartono, Kok Ken Chan, Shuwen Zeng, Gaixia Xu, Junle Qu, Philippe Coquet, Ken-Tye Yong, and Xiaoyuan Chen. *Nanocarbons for Biology and Medicine: Sensing, Imaging, and Drug Delivery* 2019, ACS Publication.
13. Mariia Faustova, Elena Nikolskaya, Nikita Yabbarov, Rem Petrov. *Metalloporphyrins in Medicine: From History to Recent Trends*. 2020, ACS Publication.
14. Tang, L., Xiao, Q., Mei, Y. et al. Insights on functionalized carbon nanotubes for cancer theranostics. *J Nanobiotechnol* 19, 423 (2021). <https://doi.org/10.1186/s12951-021-01174-y>
15. Singh Gural, Kaur Harinder, Sharma Akanksha, Singh Joga, Alajangi Hema Kumari, Kumar Santosh, Singla Neha, Kaur Indu Pal, Barnwal Ravi Pratap, *Carbon Based Nanodots in Early Diagnosis of Cancer*, *Frontiers in Chemistry*, 9, 2021. 10.3389/fchem.2021.669169
16. Hosnedlova, B.; Kepinska, M.; Fernandez, C.; Peng, Q.; Ruttkay-Nedecky, B.; Milnerowicz, H.; Kizek, R. Carbon Nanomaterials for Targeted Cancer Therapy Drugs: A Critical Review. *Chem. Rec.* 2019, 19, 502–522.
17. Zhuang Liu, Joshua T. Robinson, Scott M. Tabakman, Kai Yang, Hongjie Dai, *Carbon materials for drug delivery & cancer therapy*, *Materials Today*, 14(7-8), 2011. [https://doi.org/10.1016/S1369-7021\(11\)70161-4](https://doi.org/10.1016/S1369-7021(11)70161-4).
18. Hazal Gergeroglu, Serdar Yildirim & Mehmet Faruk Ebeoglugil. *Nano-carbons in biosensor applications: an overview of carbon nanotubes (CNTs) and fullerenes (C60)*. 2020, SN Applied Sciences.
19. Sadia Afreen, Kasturi Muthoosamy, Sivakumar Manickam, Uda Hashim, *Functionalized fullerene (C60) as a potential nanomediator in the fabrication of highly sensitive biosensors*. 2014, Elsevier.
20. Li Zhang a, Dong Peng a, Ru-Ping Liang a, Jian-Ding Qiu. *Graphene-based optical nanosensors for detection of heavy metal ions* ,2018, *TrAC Trends in Analytical Chemistry-Elsevier*, Vol. 102.
21. Patel, K. D., Singh, R. K., & Kim, H. W. *Carbon-based nanomaterials as an emerging platform for theranostics*. 2019, *Materials Horizons*, P. 434-469.

22. Zhuang Liu¹ and Xing-Jie Liang². *Nano-carbons as theranostics* 2012, Theranostics, P. 235.
23. Kai Yang, Liangzhu Feng, Hao Hong, Weibo Cai & Zhuang Liu. *Preparation and functionalization of graphene nanocomposites for biomedical applications*. 2013, Nature Protocols.
24. Mirae Kim , Jinhyeong Jang , Chaenyung Cha . *Carbon nanomaterials as versatile platforms for theranostic applications*. 2017, Drug Discovery Today-Elsevier.
25. Reza Eivazzadeh-Keihan , Ali Maleki , Miguel de la Guardia , Milad Salimi Bani , Karim Khanmohammadi Chenab , Paria Pashazadeh-Panahi, Behzad Baradaran , Ahad Mokhtarzadeh , Michael R. Hamblin. *Carbon based nanomaterials for tissue engineering of bone: Building new bone on small black scaffolds: A review*. 2019, Journal of Advanced Research, Vol. 18.
26. Carlos David Grande Tovar, Jorge Iván Castro ,Carlos Humberto Valencia ,Diana Paola Navia Porras ,José Hermínsul Mína Hernández ,Mayra Eliana Valencia, José Daniel Velásquez and Manuel N. Chaur. *Preparation of Chitosan/Poly(Vinyl Alcohol) Nanocomposite Films Incorporated with Oxidized Carbon Nano-Onions (Multi-Layer Fullerenes) for Tissue-Engineering Applications*. 2019, Biomolecules.
27. Zhao, Y., Shen, X., Ma, R., Hou, Y., Qian, Y., & Fan, C . *Biological and biocompatible characteristics of fullerene nanomaterials for tissue engineering*. 2021, Histol. Histopathol.
28. Hasan, A., Morshed, M., Memic, A., Hassan, S., Webster, T. J., & Marei, H. E. S. *Nanoparticles in tissue engineering: applications, challenges and prospects* 2018, International Journal of Nanomedicine.
29. Chun Xu¹, Chang Lei and Chengzhong Yu². *Mesoporous Silica Nanoparticles for Protein Protection and Delivery* , 2019, Frontiers in Chemistry.
30. Roman A. Perez, Rajendra K. Singh, Tae-Hyun Kim and Hae-Won Kim , *Silica-based multifunctional nanodelivery systems toward regenerative medicine*. 2017, Materials Horizon.
31. Francis J. Cunningham , Natalie S. Goh , Gozde S. Demirer , Juliana L. Matos, Markita P. Landry, *Nanoparticle-Mediated Delivery towards Advancing Plant Genetic Engineering*, 2018, Trends in Biotechnology, Vol. 39.
32. P. Bhatt et al., Structural modifications and strategies for native starch for applications in advanced drug delivery, *Biomed Res. Int.*, vol. 2022, pp. 1–14, 2022.
33. François Torney, Brian G. Trewyn, Victor S.-Y. Lin & Kan Wang. *Mesoporous silica nanoparticles deliver DNA and chemicals into plants*. 2007, Nature Nanotechnology.
34. Seon-Yeong Kwak, Tedrick Thomas Salim Lew, Connor J. Sweeney, Volodymyr B. Koman, Min Hao Wong, Karen Bohmert-Tatarev, Kristi D. Snell, Jun Sung Seo, Nam-Hai Chua & Michael S. Strano. *Chloroplast-selective gene delivery and expression in planta using chitosan-complexed single-walled carbon nanotube carriers* 2019, Nature Nanotechnology.
35. Sławomir Boncel , Piotr Zajac , Krzysztof K.K. Koziol, *Liberation of drugs from multi-wall carbon nanotube carriers*. 2013, Journal of Controlled Release.
36. Solmaz Maleki Dizaj, Afsaneh Mennati, Samira Jafari, Khadejeh Khezri, and Khosro Adibkia , *Antimicrobial Activity of Carbon-Based Nanoparticles*. 2015, National Library Of Medicine.
37. . Keerthiga Rajendiran ORCID, Zizhen Zhao ,De-Sheng Pei ,ORCID and Ailing Fu, *Antimicrobial Activity and Mechanism of Functionalized Quantum Dots* 2019, Polymers-MDPI
38. Liu, Dan, Mao, Yiqin and Ding, Lijun. *Carbon nanotubes as antimicrobial agents for water disinfection and pathogen control*. 2018, Journal of water and health.
39. S. P. Chand, S. Debnath, M. Rahimi, M. S. Ashraf, P. Bhatt, and S. A. Rahin, Contextualization of trait nexus and gene action for quantitative and qualitative characteristics in Indian mustard, *J. Food Qual.*, vol. 2022, pp. 1–24, 2022.
40. So-Ryong Chae, Ernest M. Hotze and Mark R. Wiesner. possible application of fullerene nanomaterial in water treatment and reuse. *Nanotechnology application for clean water*. s.l. : William Andrew Applied Science Publisher, 2014.
41. Huang, P., Lin, J., Wang, X., Wang, Z., Zhang, C., He, M., & Chen, X. *Light-triggered theranostics based on photosensitizer-conjugated carbon dots for simultaneous enhanced-fluorescence imaging and photodynamic therapy*, 2012, Advanced Materials.
42. Chaenyung Cha, Su Ryon Shin, Nasim Annabi, Mehmet R. Dokmeci, and Ali Khademhosseini. *Carbon-Based Nanomaterials: Multifunctional Materials for Biomedical Engineering*. 2013, ACS Publication.
43. Govindasamy Rajakumar , Xiu-Hua Zhang ,Thandapani Gomathi ,Sheng-Fu Wang ,Mohammad Azam Ansari ,Govindarasu Mydhili ,Gnanasundaram Nirmala ,Mohammad A. Alzohairy and Ill-Min Chung ,

- Current Use of Carbon-Based Materials for Biomedical Applications—A Prospective and Review.* 2020, Processes.
44. Debabrata Maiti, Xiangmin Tong, Xiaozhou Mou and Kai Yang¹. *Carbon-Based Nanomaterials for Biomedical Applications: A Recent Study.* 11 March 2019, Front. Pharmacology Sec. Experimental Pharmacology and Drug Discovery.
45. . Rasoul Madannejad , Nahid Shoaie , Fatemeh Jahanpeyma , Mohammad Hasan Darvishi, Mostafa Azimzadeh , Hamidreza Javadi. *Toxicity of carbon-based nanomaterials: Reviewing recent reports in medical and biological systems.* 2019, Chemico-Biological Interactions-eEsevier.