



# Vital Role of Carbon Nanotubes and its Application in Technology

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## Abstract

We know the Carbon nanotubes (CNTs) are nanostructures derived from rolled graphene planes and possess various interesting chemical and physical properties. Carbon nanotubes (CNTs) are allotropes of carbon with a nanostructure that can have a length-to-diameter ratio greater than 1,000,000. These cylindrical carbon molecules have novel properties that make them potentially useful in many applications in nanotechnology. Their unique surface area, stiffness, strength and resilience have led to much excitement in the field of pharmacy. CNTs can be conjugated with various biological molecules including drugs, proteins and nucleic acid to afford bio-functionalities. CNTs exist as single (SWNTs), and multi-walled (MWNTs) structures. They present several interesting properties, such as high aspect-ratio, ultra-light weight, strength, high thermal conductivity and electronic properties ranging from metallic to semiconducting. The CNTs are valuable in the field of drug delivery, blood cancer, breast cancer, brain cancer, liver cancer, cervical cancer, gene therapy, immune therapy, biomedical imaging, biosensors and tissue engineering.

**Keywords :** Carbon nanotubes, Single and multiple walled nanotubes, Nano medicines.

## Introduction

Carbon nanotubes (CNTs) are nanostructures derived from rolled graphene planes and possess various interesting chemical and physical properties, have been extensively used in biomedicine. The discovery of carbon nanotubes by Iijima in 1991 using High Resolution Electron Microscopy (HREM) has stimulated intense experimental and theoretical studies on carbon nanotubes [1]. Carbon nanotubes are allotropes of carbon that have a nanostructure, which can have a length-to diameter ratio more than 1,000,000. Theoretical studies have predicted exciting electronic properties for the nanotubes. The potential application of carbon nanotubes to the synthesis of nanowires has been demonstrated [2]. HREM is a robust approach for the characterization of microstructure and it is most suited to the study of nanotubes, it should be pointed out that the image obtained is a two-dimensional projection of a three-dimensional object [3]. CNTs can be conjugated with various biological molecules including drugs,

proteins and nucleic acid to afford bio functionalities [4, 5]. Moreover, the aromatic network existing on the CNT surface allows efficient loading of aromatic molecules such as chemotherapeutic drugs via stacking. The versatile chemistry of carbon nanotubes enables a wide range of their applications in biomedicine [6]. CNTs exist as single (SWNTs), and multi-walled (MWNTs) structures. They present several interesting properties, such as high aspect-ratio, ultra-light weight, tremendous strength [7], high thermal conductivity and remarkable electronic properties ranging from metallic to semiconducting [8]. It is not clear yet which of the two systems are more advantageous: SWCNTs offer the additional photoluminescence property that could be proficiently applied in diagnostics, while MWCNTs present a wider surface that allows a more efficient internal encapsulation and external functionalization with active molecules. They have both been used for diversified roles including biosensors, field-effect transistors (FET), and scanning probe elements longer blood circulation time than the anticancer drug on its own. This leads to more prolonged and sustained uptake of the drug by tumour cells via the enhanced permeability and retention effect. Once the functionalized of SWCNT releases the drug into a specific area, it is gradually excreted from the body via the biliary pathway and finally in the faeces. This suggested that SWCNTs are suitable candidates for drug delivery and a promising nano platform for cancer therapeutics.

### Advantages of carbon nanotubes

- Biocompatible, Non-biodegradable and non-immunogenic nature.
- Highly elastic nature and have the possibility of intracellular delivery.
- May exhibit minimum cytotoxicity.
- Excreted by urine 96% and remaining 4% by faeces.
  - Ultra-light weight and do not break down during processing.
- It has an open end on both sides, which makes the inner surface accessible and subsequent incorporation of species within nanotubes is particularly easy.
- Nanotubes have longer inner volume relative to the diameter of nanotubes for entrapment.
- CNTs are able to enter cells by spontaneous mechanism due to its tubular and nano needle shape.
- It has distinct inner and outer surface, which can be differentially modified for chemical biochemical functionalization.

### Types of carbon nanotubes (CNTs):

The carbon nanotubes are of two types namely:

- Single walled carbon nanotubes (SWCNTs)
- Multiple walled carbon nanotubes (MWCNTs)

#### Single-wall carbon nanotubes (SWCNTs):

SWCNTs consist of a single cylindrical carbon layer with a diameter in the range of 0.4-2 nm, depending on the temperature at which they have been synthesized. It was found that the higher the growth temperature larger is the diameter of CNTs [12]. The structure of SWCNTs may be arm chair, zigzag, chiral, or helical arrangements [13]. The SWCNTs have an ultrahigh surface area as large as 1300 m<sup>2</sup>/g, which renders sufficient space for drug loading and bio conjugation [14]. In drug delivery, SWCNTs are known to be more efficient than MWCNTs. This is due to the reason that SWCNTs have ultrahigh surface area and efficient drug-loading capacity. It has been found that a SWCNT anticancer drug complex has a much longer blood circulation time than the anticancer drug on its own. This leads to more prolonged and sustained uptake of the drug by tumour cells via the enhanced permeability and retention effect. Once the functionalized of SWCNT releases the drug into a specific area, it is gradually excreted from the body via the biliary pathway and finally in the faeces. This suggested that SWCNTs are suitable candidates for drug delivery and a promising nano platform for cancer therapeutics.

## Multiple walled carbon nanotubes (MWCNTs):

MWCNTs consist of several coaxial cylinders, each made of a single grapheme sheet surrounding a hollow core. The outer diameter of MWCNTs ranges from 2-100 nm, while the inner diameter is in the range of 1-3 nm, and their length is one to several micrometers [16]. The sp<sup>2</sup> hybridization in MWCNTs, a delocalized electron cloud along the wall is generated which is responsible for the interactions between adjacent cylindrical layers in MWCNTs resulting in a less flexible and more structural defects [17]. MWCNTs structures can be split into two categories based on their arrangements of graphite layers: one has a parchment-like structure which consists of a graphene sheet rolled up around it and the other is known as the Russian doll model where layers of graphene sheets are arranged within a concentric structure [18]. Decoration of multiwall carbon nanotubes (MWCNTs) consists of depositing nanoparticles on the MWCNT walls or ends, bonded by physical interaction with potential applications in catalysis, biosensors, biomedical, magnetic data storage, and electronic devices. The various methods used for this purpose include precipitation, hydrolysis at high temperature, or chemical decomposition of a metal precursor.

### Application of carbon nanotubes:

The functionalization of CNTs makes them useful in a range of different applications. Their structure means that the tubes have an inner and an outer core which can both be modified by different functional groups. Thus the CNTs can be designed for very specific purposes. In the area of biomedicine, the applications of CNTs are investigated in especially four main fields: drug delivery, biomedical imaging, biosensors and scaffolds in tissue engineering

### Drug delivery:

Specific drug delivery is an essential method used in medicine to deliver pharmaceuticals to the specific place in the body where it is needed. The method shows great promise in cancer therapy since one of the biggest challenges in treating cancer is the severe side effects caused by the chemotherapy. The harsh medication used to treat cancer attacks not only the cancer cells, but also the healthy cells of the body, and this is what causes the side effects of the treatment.

### Blood Cancer:

Leukemia is a cancer that begins in the bone marrow (the soft inner part of some bones), but in most cases, moves into the blood. It can then spread to other parts of the body, such as organs and tissues. Acute lymphoblastic leukemia (ALL), one of the four main types of leukemia, is a slow-growing blood cancer that starts in bone marrow cells called lymphocytes or white blood cells. Once these white blood cells are affected by leukemia, they do not go through their normal process of maturing. An intensified targeted delivery of daunorubicin (Dau) to acute lymphoblastic leukemia was achieved by Taghdisi et al., they developed a tertiary complex of Sgc8c aptamer (this aptamer targets leukemia biomarker protein tyrosine kinase-7

daunorubicin, and SWCNT named as Dau-aptamer SWCNTs. Flow cytometric analysis viewed that the tertiary complex was internalized effectively into human T cell leukemia cell (MOLT-4 cells) but not to U266 myeloma cells. Release of Dau-loaded nanotubes were pH-dependent. In a slightly acidic solution of pH 5.5, Dau was released from complex in 72 h at 37 °C, whilst Dau-aptamer-SWNTs tertiary complex was pretty stable after the same incubation at pH 7.4

### Breast cancer:

Over expression of human epidermal growth factor receptor 2 (HER2), also known as c-erbB-2 or HER2/neu, is approximately 20-25% responsible for invasive breast cancer. Liu et al., studied SWNT delivery of paclitaxel (PTX) into xenograft tumors in mice with higher tumor suppression efficacy than the clinical drug formulation Taxol. The PTX conjugated to PEGylated SWNTs showed high water solubility and maintains alike toxicity to cancer cells as Taxol in vitro. SWNT-PTX affords much longer blood circulation time of PTX than that of Taxol and PEG ylated PTX, leading to high tumor uptake of the drug through EPR effect. The strong therapeutic efficacy of SWNT-PTX is shown by its ability to slow down tumor growth even at a lower drug dose [37]. Pan et al., investigated the efficiency of MWCNTs to deliver the gene to the tumor cell for cancer therapy. In this work, they fabricated MWCNTs modified with polyamidoamine dendrimer which were further conjugated with FITC-labelled antisense c-myc oligonucleotides (asODN). Human breast cancer cell line MCF-7 cells and MDA-MB-435 cells were incubated with modified MWCNTs (asODN-dMNTs). Fluorescence developed by the FITC revealed the cellular uptake of asODN-dMNTs within 15 min. These composites inhibit the cell growth in time and dose dependent means and down regulated the expression of c-myc gene (over expression of this gene amplify the expression of HER2) and C-Myc protein [38].

**Liver Cancer:**

Polyamidoamine dendrimer modified CNTs (dMWCNTs) were fabricated for the efficient delivery of antisense c-myc oligonucleotide (asODN) into liver cancer cell line HepG2 cells. As ODN-dMWCNTs composites were incubated with HepG2 cells and confirmed to enter into tumor cells within 15 min by laser confocal microscopy. These composites inhibited the cell growth in time and dose dependent means and down regulated the expression of the c-myc gene and C-Myc protein. These composites exhibit maximal transfection efficiencies and inhibition effects on tumor cells when compared to CNTNH - asODN and dendrimer (asODN) alone [38].

**Brain cancer:**

Xing et al., synthesized phospholipid-bearing polyethylene glycol (PL-PEG) functionalized SWCNTs conjugated with protein A, which was further coupled with the fluoresceinlabeled integrin monoclonal antibody to form SWCNTintegrin monoclonal antibody (SWCNT-PEGmAb). Confocal microscopy revealed that SWCNT-PEG-mAb showed a much higher fluorescence signal on integrin positive U87MG cells and presented a high targeting efficiency with low cellular toxicity, whilst, for integrin -negative MCF-7 cells, no obvious fluorescence was observed, which clearly reveals low targeting efficiency of the functionalized SWCNTs, demonstrating that the specific targeting of integrin positive U87MG cells was caused by the specific recognition of integrin on the cellular membrane by the monoclonal antibody [39].

**Lymph Node Metastasis:**

Yang et al., compared the in vitro and in vivo potential therapeutic effect of gemcitabine (GEM) loaded magnetic MWCNTs (mMWCNTs) with that of gemcitabine loaded magnetic-carbon particles (mACs). The result reflects that mACs and mMWCNTs effectively enhanced GEM cytotoxicity in vivo and inhibited lymph node metastasis, especially when using high dose agents and/or applying implanted in vivo magnets. Systems offer the possibility to enhance therapeutic effects and decrease side-effects associated with chemotherapeutic agents by utilising the synergistic effects of magnetic targeting and lymphatic chemotherapy. Due to the super paramagnetic behaviour of mMWCNTs-GEM, their magnetic moments tend to align along the applied field leading to net magnetization which greatly affects the interaction of mMWCNTs-GEM with the cellular membrane and thus they were found to be superior than mACs-GEM in successful inhibition of lymph node metastasis after following subcutaneous administration under the impact of magnetic field [40].

**Cervical Cancer:**

Wu et al., developed a novel approach of utilizing natural biocompatible polymer chitosan for imaging the tumor cells. In this assay, SWCNTs were modified by chitosan (CHIT) fluorescein isothiocyanate (FITC). This was further conjugated with folic acid (FA), as mostly cancer cells overexpress folic acid receptors, to construct the functional FITC-CHIT-SWCNT-FA conjugate. These novel functionalized SWCNTs were found to be soluble and stable in phosphate buffer saline and can be readily transported inside the human cervical carcinoma HeLa cells [41]. Combining the intrinsic properties of CNTs, versatility of chitosan, and folic acid, FITC-CHIT-SWCNT-FA can be used as potential devices for targeting the drug into the tumor cells and also for imaging [42].

**Gene therapy**

CNTs can deliver a large amount of therapeutic agents, including DNA and RNA, to the target disease sites, Gene therapy and RNA have presented a great potential for antitumor treatment. The wire shaped structure (with a diameter matching that of DNA/siRNA) and their remarkable flexibility, CNTs can influence the conformational structure and the transient conformational changes of DNA RNA, which can further enhance the therapeutic effects of DNA or RNA. The treatment of a human lung carcinoma model in vivo using siRNA sequences, which led to cytotoxicity and cell death using amino-functionalized multiwalled carbon nanotubes (MWNT-NH<sub>3</sub><sup>+</sup>). This is believed to activate biologically in vivo by triggering an apoptotic cascade that leads to extensive necrosis of the human tumor mass followed by a concomitant prolongation of survival of human lung tumor-bearing animals [43].

**Immune therapy**

Chemotherapy faces the issues of accumulative toxicity and drug resistance, anti-tumour immunotherapy usually has few

adverse effects, good patient tolerance, and the potential to improve the prognosis significantly. CNTs have also shown the potential to boost the antigenicity of the carried proteins or peptides. Xu et al., studied that MWNTs conjugated to tumor lysate protein will enhance the efficacy of an anti-tumor immunotherapy that employs tumor cell vaccine (TCV) in a mouse model bearing the H22 liver cancer [44]. The study showed that MWNTs conjugated to tumor lysate protein enhanced the specific anti-tumor immune response and the cancer cure rate of a TCV immunotherapy in mice [45].

### **Biomedical imaging**

Besides having unique electrical and mechanical properties CNTs also have optical properties that are very useful in applications such as biomedical imaging. SWNTs have strong optical absorption from ultraviolet (UV) to near infra-red (NIR) regions and are useful in a range of different imaging techniques. These include photo acoustic imaging, Raman imaging, fluorescence imaging, and with functionalization of the CNTs also positron emission tomography (PET) imaging and magnetic resonance (MR) imaging [46]. Dai et al., the CNTs were functionalized with a specific receptor for internalization into a specific cell type thus imaging these cells with very low auto fluorescence background. In an in vivo study the bio distribution of SWNTs in live drosophila larvae was monitored by fluorescence imaging [47]. In photo acoustic imaging deeper tissue penetration can be achieved compared to most other optical imaging techniques. The technique makes use of certain light absorbing molecules (for example CNTs) that converts laser pulses delivered into the biological tissue to heat. Thereby transient thermoelastic expansion is induced giving rise to wideband ultrasonic emission which can then be detected by an ultrasonic microphone. With their high optical absorption in the NIR range. SWNTs make a useful contrast agent in this kind of biomedical imaging [48].

### **Biosensors**

Biosensors are used for monitoring biological processes or for recognition of biomolecules and differ from other sensors by having a sensing element consisting of a biological material such as proteins, oligo- or polynucleotides or microorganisms. The most popular type of biosensors is the electrochemical biosensor and carbon materials have been used in these devices for a long time. Electrochemical biosensors are popular for detecting biomolecules in solutions because of their simplicity and the relative ease of calibration. These sensors are normally based on enzymatic catalysis of a reaction that either produces or consumes electrons and CNT-based biosensors incorporating enzymes have been produced for detection of glucose and other biomolecules [49].

### **Tissue Engineering**

Besides all these applications, CNTs are also useful in enhancing tissue matrices. The matrix, or scaffold, has played an important part in tissue engineering, since this is what provides the structural support for the new tissue. It is responsible for defining the space the new tissue occupies, and for aiding the process of tissue development. Arrangement of different criteria have to be fulfilled by such a scaffold. Among other things the scaffold should show: high mechanical strength, good biocompatibility (supporting cell adhesion viability, proliferation and differentiation), biodegradability. All three criteria seem to be possible to meet using CNTs in the production of the scaffold and with superior results compared to other materials used in tissue engineering. Studies have shown that scaffolds of CNTs seem to be biocompatible both in vitro and in vivo when mixed with other materials such as in a polymer matrix of chitosan which itself is highly biocompatible.

### **Genetic Engineering**

In genetic engineering, CNTs and CNHs are used to manipulate genes and atoms in the development of bioimaging genomes, proteomics and tissue engineering[33]. The unwound DNA (single stranded) winds around SWNT by connecting its specific nucleotides and causes change in its electrostatic property. This creates its potential application in diagnostics (polymerase chain reaction) and in therapeutics. Wrapping of carbon nanotubes by single-stranded DNA was found to be sequence-dependent, and hence can be used in DNA analysis. Nanotubes due to their unique cylindrical structure and properties are used as carrier for genes (gene therapy) to treat cancer and genetic disorders. Their tubular nature has proved them as a vector in gene therapy. Nanotubes complexed with DNA were found to release DNA before it was destroyed by cells defense system, boosting transfection significantly. Nanostructures have showed antiviral effect in respiratory syncytial virus (RSV), a virus with severe bronchitis and asthma<sup>34</sup>. The treatment is generally done by combining nanoparticles and gene slicing technologies. Here RNA fragments capable of inhibiting a protein (which is needed for virus multiplication) is encapsulated within nanotubes and administered in the form of nasal sprays or drops. The promising results have been noted inhibiting further growth of virus<sup>34</sup>. Nanotubes are reported for helical crystallisation of proteins and growth of embryonic rat brain neurons. Streptavidin protein is successfully immobilized on CNT via 1-pyrene butanoic acid and succinimidyl ester[32]. Nanotubes and nanohorns can adhere various antigens on their surface, hence act as source of antigen in vaccines. Hence, by use of nanotubes, use of dead bacteria as source for antigen which is sometimes dangerous can be avoided.

### **Biomedical applications**

Bianco et al. [35] have prepared soluble CNTs and have covalently linked biologically active peptides with them. This was demonstrated for viral protein VP1 of foot mouth disease virus (FMDV) showing immunogenicity and eliciting antibody response. In chemotherapy, drug embedded nanotubes attack directly on viral ulcers and kills viruses. No antibodies were produced against the CNT backbone alone, suggesting that the nanotubes do not possess intrinsic immunogenicity. Combination of all the described features of the vaccine system with the fact that the capacities of the anti-peptide antibodies to neutralize FMDV have been enhanced has indicated that CNT can have a valuable role in the construction of novel and effective vaccines<sup>34</sup>. In vitro studies by Kam et al.<sup>36</sup> showed selective cancer cell killing obtained by hyperthermia due to the thermal conductivity of CNT internalised into those cells. The work developed regarding the use of CNT as gene therapy vectors have shown that these engineered structures can effectively transport the genes and drugs inside mammalian cells. The CNT-transported genetic material has conserved the ability to express proteins<sup>[33]</sup>. **Artificial implants**

Normally body shows rejection reaction for implants with the postadministration pain<sup>35</sup>. But, miniature sized nanotubes and nanohorns get attached with other proteins and amino acids avoiding rejection. Also, they can be used as implants in the form of artificial joints without host rejection reaction. Moreover, due to their high tensile strength, carbon nanotubes filled with calcium and arranged/grouped in the structure of bone can act as bone substitute<sup>[37]</sup>.

### **Preservative**

Carbon nanotubes and nanohorns are antioxidant in nature. Hence, they are used to preserve drugs formulations prone to oxidation. Their antioxidant property is used in antiaging cosmetics and with zinc oxide as sunscreen dermatological to prevent oxidation of important skin components<sup>[33]</sup>.

### **Diagnostic tool**

Protein-encapsulated or protein/enzyme filled nanotubes, due to their fluorescence ability in presence of specific biomolecules have been tried as implantable biosensors<sup>37</sup>. Even, nanocapsules filled with magnetic materials, radioisotope enzymes can be used as biosensors<sup>38</sup>. Nanosize robots and motors with nanotubes can be used in studying cells and biological systems<sup>[38]</sup>.

### **As catalyst**

Nanohorns offer large surface area and hence, the catalyst at molecular level can be incorporated into nanotubes in large amount and simultaneously can be released in required rate at particular time. Hence, reduction in the frequency and amount of catalyst addition can be achieved by using CNTs and CNHs<sup>[38]</sup>.

### **Conclusion**

With the prospect of gene therapy, cancer treatments, and innovative new answers for life-threatening diseases on the horizon, the science of nano medicine has become an ever-growing field that has an incredible ability to bypass barriers. The properties and characteristics of CNTs are still being researched heavily and scientists have barely begun to tap the potential of these structures. Single and multiple walled carbon nanotubes have already proven to serve as safer and more effective alternatives to previous drug delivery methods. They can pass through membranes, carrying therapeutic drugs, vaccines, and nucleic acids deep into the cell to targets previously unreachable. They also serve as ideal non-toxic vehicles which, in some cases, increase the solubility of the drug attached, resulting in greater efficacy and safety. Overall, recent studies regarding CNTs have shown a very promising glimpse of what lies ahead in the future of medicine.

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