ABSTRACT
Carbonnanotube a major investigation in nanotechnology seves a gift also to medical field. Carbon nanotubes (CNT) are considered ideal materials for several applications ranging from ultrastrong fibers to field emission displays. Recently, CNT have generated great interest in biology, where suitably modified CNT can serve as vaccine delivery systems or protein transporters. Due to their unique physical and chemical property combination Carbonnanotubes serves as a biomedical tool for delivering drugs and in treatment of cancer, gene delivery, peptide drug delivery DNA and gene therapy and neural applications.

KEYWORDS: Carbonnanotube, Nanotechnology, Cancer.

INTRODUCTION
During the past many years, tremendous progress has been made in the field of nanomaterials and these nano material has given a boon in biomedical applications.

The Carbonnanotubes and Carbonnanofibres have been investigated in many applications related to modern medical technology due their specialty in composite structural material, semiconductor devices and sensors. The Carbon nanotube and Carbon nanofibres have attracted increases attention due to their mechanical, structural, optical and thermal properties. But their major role has been explored as most promising and desirable tool for cancer diagnosis and therapy. \(^{[1,2]}\)

Earlier radical resection of tumor at early stage is the only way to cure Cancer. But the early symptom of cancer cannot be identified easily. For those unresectable patients and those who received palliative operation, chemotherapy and radiotherapy are needed. Since chemotherapy drugs target all rapid dividing cells, including healthy cells, they can cause
great damage to the patient's body. Therefore, it would be desirable to develop new methods to detect cancers at their early stage and directly target cancerous cells without affecting normal ones.

Bionanotechnology investigates the interactions between nanoscale materials and biological systems and creates the technologies for interfacing the two.

Carbon nanotubes (CNTs) are considered potential biomedical materials because of their flexible structure and propensity for chemical functionalization.

Recently, nanomaterial’s have gained wide application in biomedical field. They have been effectively utilized to deliver biologically active cargo into the sites of interest for the purposes of cancer diagnosis and therapy. Among diverse classes of nanomaterial’s, CNTs have attracted particular attention due to their unique physicochemical properties and the ability to cross the cell membrane.

Over the course of the past 18 years, numerous carbon nanotube preparations have been reported being used in cellular therapy, drug delivery, and more recently as sensors for detecting specific proteins and other bimolecular in serum. Recent research has focused on the targeted delivery of functionalized carbon nanotubes (f-CNTs) to the sites of interest.\cite{3,4}

**INTRODUCTION TO CARBONANOTUBE**

Carbon nanotubes, first discovered by Iijima in 1991 who is Japanese physicist, often cited as the inventor of carbon nanotubes. Although carbon nanotubes had been observed prior to his "invention", Iijima’s 1991 paper generated unprecedented interest in the carbon nanostructures and has since fueled intense research in the area of nanotechnology. For this and other work Sumio Iijima was awarded, together with Louis Brus, the inaugural Kavli Prize for nanoscience in 2008.

Carbonnanotube which are made up of thin sheets of benzene ring carbons rolled up into the shape of a seamless tubular structure. This novel structure belongs to the family of fullerenes, the third allotropic form of carbon along with graphite and diamond.\cite{5}

CNTs are generally produced by three major techniques: electric arc discharge, laser ablation, and thermal or plasma enhanced chemical vapor deposition (CVD). Based on their structure, CNTs can be classified into two general categories: Single walled (SWNTs), which consist
of one layer of cylinder graphene and multi-walled (MWNTs), which contain several concentric graphene sheets.

**CNTs have unique physical and chemical properties such as**

1. High aspect ratio,
2. Ultralight weight,
3. High mechanical strength,
4. High electrical conductivity, and
5. High thermal conductivity etc.

The combination of these characteristics makes CNT a unique nanomaterial with the potential for diverse applications, especially in biomedical Carbon nanotube-based diagnostic tools.

Since radical resection of the tumor at its early stage is the only way to cure the disease, early screening and detection are of vital importance. However, most cancers are asymptomatic during their early stage. Also conventional clinical cancer imaging techniques, such as X-ray, CT and MRI, do not possess sufficient spatial resolution for early detection of the disease. Since distinct morphologic changes are absent in most early neoplastic disorders, they can easily avoid being detected by these imaging techniques.[2,6,4]

**Positron emission tomography (PET)**

PET is a highly sensitive and accurate imaging technology that relies on changes in tissue biochemistry and metabolism. It is the most valuable means we have so far to identify early-stage alterations in molecular biology, often before there is any morphologic change.

**Positron emission tomography (PET) has inherent advantages**

- Attenuation correction is easily accomplished; positron-emitting isotopes of carbon, nitrogen, oxygen, and fluorine occur naturally in many compounds of biological interest, and can therefore be readily incorporated into a wide variety of useful radio-pharmaceuticals; and collimation is done electronically, so no collimator is required, leading to relatively high sensitivity.

- The major problem with PET is its cost. The short half-life of most positron emitting isotopes requires an on-site cyclotron, and the scanners themselves are significantly more expensive than single-photon cameras.
Nevertheless, PET is widely used in research studies and is finding growing clinical acceptance, primarily for the diagnosis and staging of cancer.

Nevertheless, fluoro-desoxy-glucose (FDG), the most commonly used PET tracer in clinical oncology (more than 95% of the molecular imaging procedures make use of FDG at present), is not a specific tracer for malignant diseases but for increased metabolism.\textsuperscript{[8,9,10]}

Therefore, it is imperative to develop new tools for early cancer diagnosis.

Over the past few years, imaging studies with SWCNTs have flourished. Hong et al. reviewed molecular imaging with singlewalled carbon nanotubes. In this review, the state-of-the-art applications of SWNTs as contrast agents in a number of imaging modalities, such as magnetic resonance, near-infrared fluorescence, Raman spectroscopy, photoacoustic tomography, and radionuclide-based imaging, are summarized. When Gd\textsuperscript{3+}-functionalized SWCNTs was applied to MRI, high resolution and good tissue penetration were achieved. But the level of sensitivity still remained low. Similarly, medium resolution, high sensitivity and good tissue penetration were obtained from radioisotopes labeled SWCNTs with radionuclide based imaging techniques (PET and SPECT).

Besides, cancer cells often overexpress characteristic protein biomarkers, which provide an opportunity for early diagnosis of the disease. Clinically, some important tumor markers, such as carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), carbohydrate antigen 19-9 (CA19-9), carcinoma antigen 125 (CA125), prostate specific antigen (PSA), and human chorionic gonadotropin (hCG), have been widely applied to the diagnosis of colorectal cancer, hepatocellular carcinoma, pancreatic cancer, epithelial ovarian tumor, prostate cancers, and so on are used as of most existing tumor markers for the early detection of malignancies. Hence, markers are mostly used in determining prognosis, predicting therapeutic response, maintaining surveillance following curative surgery, and monitoring therapy in advanced disease.\textsuperscript{[11,12,13]}

Since CNTs exhibit unique electronic, mechanical and thermal properties, they have been proposed as a promising tool for detecting the expression of indicative biological molecules at early stage of cancer. With this novel approach, high sensitivity, ultralow detection limits and wide linear ranges have been achieved Among the various biomarkers, PSA has been widely used in cancer detection. A detection limit as low as 4 pg/mL was achieved through
CNT-based detection systems, which surpassed detection limits of PSA by commercial immunoassay methods, as well as most recently reported experimental biosensor approaches.

CNTs-based detecting measurement may serve as an alternative method for cancer biomarkers diagnosis in clinical analysis in the future.\textsuperscript{[2,12,14]}

**Role of CNTs in cancer therapy**

**Cancer** known medically as a malignant neoplasm, is a broad group of diseases involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and spread by invading nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream.

Not all tumors are cancerous; benign tumors do not invade neighboring tissues and do not spread throughout the body. There are over 200 different known cancers that affect humans.\textsuperscript{[5]} Among all cancer treatment options, such as surgery, chemotherapy, radiotherapy, thermotherapy, and immunotherapy etc., surgery continues to play a major role in early-stage cancer survival by removing detectable tumor. For those patients with advanced cancer and those received palliative operation procedures, chemotherapy and radiotherapy are required. Even for those patients who underwent radical resection of the tumor, radiochemotherapy and other treatments are sometimes recommended to prevent relapse caused by residual micrometastases. Although these modalities are successful in some cases, systemic toxicity may develop at the same time due to lack of selectivity for these treatments.\textsuperscript{[12,14]}

![Figure 1](image-url): (A) spherical C60 fullerene (Buckyball structure), (B) conical structure of a carbon nanohorn (CNH), (C) cylindrical structure of a single-walled carbon nanotube (SWNT), and (D) cylindrical structure of a multiwalled carbon nanotube (MWNT), composed of concentric SWNTs.
Drug delivery by CNTs IN CANCER TREATMENT

As mentioned above, conventional administration of chemotherapeutic agents is often compromised by their systemic toxicity due to lack of selectivity. In addition, limited solubility, poor distribution among cells, inability of drugs to cross cellular barriers, and especially a lack of clinical procedures for overcoming multidrug resistant (MDR) cancer, all limit the clinical administration of chemotherapeutic agents.

Notably, due to the unique properties of CNTs, especially their ultrahigh surface area, many other beneficial molecules such as drugs, peptides and nucleic acids can be integrated to their walls and tips.

Researchers have found that functionalized CNTs can cross the mammalian cell membrane by endocytosis or other mechanism. With the help of specific peptides or ligands on their surface to recognize cancer-specific receptors on the cell surface, CNTs can carry therapeutic drugs more safely and effectively into the cells that are previously unreachable, which makes them ideal candidates for drug delivery. Recently, novel SWNT-based tumor-targeted drug delivery systems (DDS) have already been developed by several investigators. These delivery systems generally consist of three parts: functionalized SWNTs, tumor-targeting ligands, and anticancer drugs. When SWNT-based tumor-targeted drug delivery systems interact with cancer cells, they could recognize cancer-specific receptors on the cell surface and then induce receptor-mediated endocytosis. It has been demonstrated by an research that the complex was taken up efficiently and specifically by cancer cells with subsequent intracellular release of chemotherapeutic agents, which suppressed proliferation of cancer cells more effectively than untargeted controls containing the same drug. Meanwhile, with this novel approach, the cytotoxicity was decreased to some extent and hence serious and harmful side effects might be avoided.

A lymphatic targeted drug delivery system using magnetic multi-walled carbon nanotubes (mMWCNTs), which successfully delivered gemcitabine to lymph nodes with high efficiency under the guidance of a magnetic field. No obvious systemic toxicity was observed. The result suggests that this novel drug delivery system could confer an advantage over the way chemotherapeutic agents are currently delivered to lymph nodes.[5,10]

Besides, with very high surface area per unit weight SWNTs provide higher capacity of drug loading, compared to that reported for conventional liposomes and dendrimer drug carriers.
In addition, the intrinsic stability and structural flexibility of CNTs may prolong the circulation time as well as improve the bioavailability of drug molecules conjugated to them. Overall, these results clearly indicate the potential applications of CNTs in tumor-targeted drug delivery in the near future.\textsuperscript{[5,6]}

**OTHER PROSPECTIVES OF CARBONANOTUBE**

1. **DNA and Gene therapy**

The identification of disease-related genes and their complete nucleotide sequence through the human genome project provides a marked significance in treating gene related disorders.

However, gene therapy relies on the efficient and nontoxic transport of therapeutic genetic medicine through the cell membranes, and this process is very inefficient.

Carbon nanotubes, due to their large surface areas, unique surface properties, and needle-like shape, can deliver a large amount of therapeutic agents, including DNA and siRNAs, to the target disease sites. In addition, due to their unparalleled optical and electrical properties, carbon nanotubes can deliver DNA/siRNA not only into cells, which include difficult transfecting primary-immune cells and bacteria, they can also lead to controlled release of DNA/siRNA for targeted gene therapy.

Furthermore, due to their wire shaped structure with a diameter matching with that of DNA/siRNA and their remarkable flexibility, carbon nanotubes can impact on the conformational structure and the transient conformational change of DNA/RNA, which can further enhance the therapeutic effects of DNA/siRNA. Synergistic combination of the multiple capabilities of carbon nanotubes to deliver DNA/siRNAs will lead to the development of powerful multifunctional nanomedicine to treat cancer or other difficult diseases.

Sequencing of the human genome and functional genomics offer unprecedented opportunities to combat a large number of diseases with designed genes either in the form of therapeutic oligonucleotides (ONs) or plasmids DNA carrying gene sequences.\textsuperscript{[14,15]}

**CNFs/CNTs for neural applications**

As an emerging interdisciplinary field, neural tissue engineering has evoked increasing interest from scientists wishing to develop novel and improved biological scaffolds that restore, maintain, or improve neural tissue functions. Since natural neural tissues have
numerous nanostructured features (such as nanostructured extracellular matrices that neural cells interact with), CNFs/CNTs which also have such nanofeatures and exceptional electrical, mechanical and biocompatible properties, are excellent candidates for neural tissue repair. Specifically, with the rapid development of CNT production technologies, a variety of CNTs with nanometer to millimeter lengths and widths have been synthesized and widely investigated for various neural applications. Similarly, CNFs have excellent properties comparable to CNTs but at a lower cost and are fabricated through an easier scale-up process, thus, CNFs have generated much interest in regenerative neural tissue engineering applications.[14]

Delivery of genes
Gene therapy is a method to use a gene to promote cells to produce their own therapeutic proteins. Methods to deliver genes to cells can be divided into two main categories: viral gene delivery (also called viral vector) and non-viral gene delivery (or non-viral vector).

In viral gene delivery, the genes are carried by a virus into the cells due to the ability of viruses to enter the cells. The advantages of this method include high delivery efficacy and high levels of gene expression.

However, several disadvantages such as immunogenic and inflammation responses of host tissue have halted the applications of viral vectors in human use.[10,15]

On the other hand, non-viral delivery of genes to cells uses means other than viruses to transport genes inside the cells. The methods used in non-viral vectors can be either physical or chemical. Physical forces can be used to “push” genes into cells. Chemical means use other materials (such as lipids, polymers or proteins) to conjugate with genes and then direct them to the cells. One of the challenges for non-viral gene delivery is to achieve high gene transfer efficiency. There are several barriers for
(i) Delivering DNA to the targeted cell population,
(ii) Internalizing DNA by the cells and
(iii) Transporting the DNA to desired cellular compartments.

Those barriers include physical barriers (including biological membranes, such as the endothelium, the plasma membranes, and the nuclear membranes) and chemical barriers (including extracellular, endosomal/lysosomal, and cytosolic degradation pathways).
Microinjection (that is, using micro-needle-injected DNA) is a common method that can bypass both physical and chemical barriers to deliver DNA cells.

**However, the microinjection method has disadvantages of**

(i) Having to manipulate cells one at a time under a microscope and
(ii) Micron-sized tip radii which cause damage to cell membranes.

Recently, vertically aligned CNFs grown on flat substrates have been employed for delivering DNA to cells. These VACNFs were coated with DNA and then pressed onto cellular matrices to deliver coated DNA to the cells (Chinese hamster ovary cells) **Chinese hamster ovary (CHO) cells** are a cell line derived from the ovary of the Chinese hamster, often used in biological and medical research and commercially in the production of therapeutic proteins. They were introduced in the 1960s, are grown as a cultured monolayer and require the amino acid proline in their culture medium.

CHO cells are used in studies of genetics, toxicity screening, nutrition and gene expression, particularly to express recombinant proteins. Today, CHO cells are the most commonly used mammalian hosts for industrial production of recombinant protein therapeutics.

The advantages of this method include its minimal cell membrane disruption its ability to simultaneously deliver DNA to a large number of cells.\(^5,15\)

**Future perspective**

As we can see, due to their amazing properties, imaging agents, targeting ligands, chemotherapeutic drugs, SiRNA and many other therapeutic agents can all be integrated into carbon nanotubes, which have great potential in molecular diagnosis and targeted therapy of tumors. Overall, a detailed understanding of the pharmacological and toxicological properties of carbon nanotubes and a balanced evaluation of risk/benefit ratio are required before they can be recommended for routine clinical use.

**REFERENCES**

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