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Review: Carbon Nanotubes in Cancer Therapy

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ABSTRACT

Cancer is an uncontrolled proliferation of cells. There are currently many therapies in clinical use and recent advances in biotechnology against cancer. Carbon nanotubes (CNTs) have been introduced recently as a novel carrier system for both small and large therapeutic molecules. CNTs are tubular materials with nanometer-sized diameters and axial symmetry, giving them unique properties that can be exploited in the diagnosis and treatment of cancer. CNTs have the potential to deliver drugs directly to targeted cells and tissues. CNTs can be functionalized (i.e., surface engineered) with certain functional groups to manipulate their physical or biological properties. In addition to the ability of CNTs to act as carriers for a wide range of therapeutic molecules, their large surface area and the possibility to manipulate their surfaces and physical dimensions have been exploited for use in the photothermal destruction of cancer cells. This paper will discuss the therapeutic applications of CNTs with a major focus on their applications for the treatment of cancer.

INTRODUCTION

Carbon nanotubes are one of the most commonly mentioned building blocks of nanotechnology. With one hundred times the tensile strength of steel, thermal conductivity better than all but the purest diamond, and electrical conductivity similar to copper, but with the ability to carry much higher currents, they seem to be a wonder material.

Nanotubes come in a variety of types: long, short, single-walled, multi-walled, open, closed, with different types of spiral structure, etc. (Figure no 1). Each type has specific production costs and applications. Some have been produced in large quantities for years while others are only now being produced commercially with decent purity and in quantities greater than a few grams. In this brief white paper, we hope to resolve some of the confusion surrounding what may be one of the most significant new materials since plastics. Carbon nanotubes were 'discovered' in 1991 by SumioIijima of NEC and are effectively long, thin cylinders of graphite, which you will be familiar with as the material in a pencil or as the basis of some lubricants. Graphite is made up of layers of carbon atoms arranged in a hexagonal lattice, like chicken wire. Though the chicken wire structure itself is very strong, the layers themselves are not chemically bonded to each other but held together by weak forces called Van der Waals. It is the sliding across each other of these layers that gives graphite its lubricating qualities and makes the mark on a piece of paper as you draw your pencil over it[1].

Due to their high surface area, they are capable of adsorbing or conjugating with a wide variety of therapeutic molecules. Thus, CNTs can be surface engineered (i.e., functionalized) to enhance their dispersibility in the aqueous phase or to provide the appropriate functional groups that can bind to the desired therapeutic material or the target tissue to elicit a therapeutic effect[2]. CNTs might help the attached therapeutic molecule to penetrate through the target cell to treat diseases and a recent example of CNTs with a variety of functional groups relevant to cancer therapy[3]. Here, we provide an overview of the therapeutic applications of CNTs with a major focus on their use in the treatment of cancer.

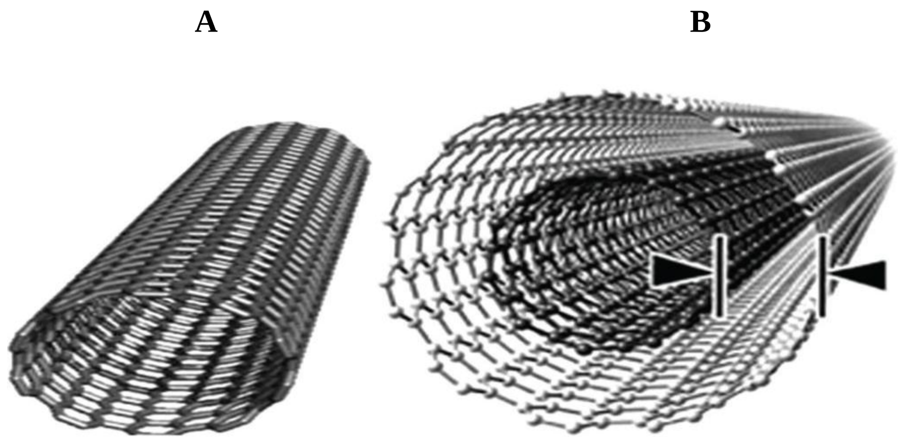

Figure No. 1: A) Single-walled CNTs B) Multi-walled CNTs

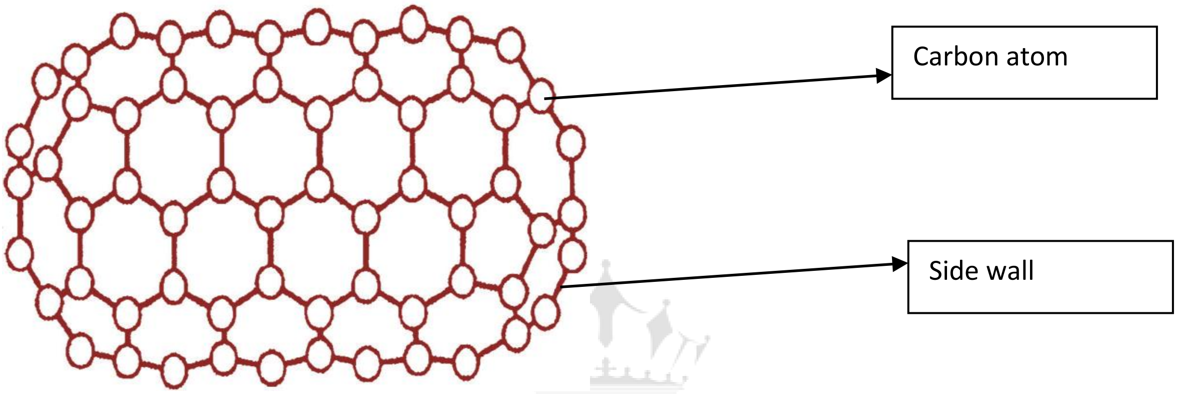

Figure No. 2: A carbon nanotube with closed ends.

Applications of Carbon Nanotubes in pharmacy and Medicine[5]

The main applications of CNTs in pharmacy and medicine include drug, biomolecule, gene delivery to cells or organs, tissue regeneration, and biosensor diagnostics and analysis. They are summarized in Figure 1. For drug delivery, the general process using CNTs can be briefly resumed as follows. The drug is fixed on the surface or the inside of functionalized CNTs. The conjugate obtained is then introduced into the animal body by classic ways (oral, injection) or directly to the target site through the use of a magnetic conjugate, for example, guided by an external magnet to the target organ, such as lymphatic nodes. The cell ingests the drug CNT capsule and finally, the nanotube spills its contents into the cell and thus the drug is delivered.

Functionalized CNTs possess the ability to carry molecules of interest across the cytoplasmic membrane and nuclear membrane without producing a toxic effect; therefore, the drug CNT conjugate proves to be safer and more effective than a drug used alone by traditional preparation after reaching the targeted cells, there are two possibilities to deliver the drugs. The drug enters the cell without internalization of the CNT carrier of both the drug and the CNT carrier enters the cells. The latter internalization method is more effective than the first one because after entering the cells, the intracellular environment degrades the drug carrier conjugate releasing drug molecules in situ, that is, inside the cells. While, in the non-internalization method, the extracellular environment helps to degrade drug carrier conjugates and the drug then crosses itself the lipid membrane to enter the cells, thereby, there is a possibility of drug degradation during this penetration by itself. There are two possible mechanisms of CNT internalization: either via the endocytosis pathway or via the insertion and diffusion with the ability to enhance cellular uptake of existing potent drugs are needed. The high aspect ratio of CNT's offers great advantages over the existing delivery vectors because the high surface area provides multiple attachment sites for drugs. Many anticancer drugs have been conjugated with functionalized CNTs and successfully tested in vitro and vivosuchas epirubicin, doxorubicin, cisplatin, methotrexatequercetin, and paclitaxel. chemotherapeutic, agents can be bound to a complex formed by CNT and antibody against antigen overexpressed on the cancerous cell surface.

Carbon Nanotubes Used for CancerTherapy[5]

A. By Drug Delivery.

CNTs can be used as drug carriers to treat tumors. The efficacy of anticancer drugs used alone is restrained not only by their systemic toxicity and narrow therapeutic window but also by drug resistance and limited cellular penetration. Because CNTs can easily cross the cytoplasmic membrane and nuclear membrane, anticancer drugs transported by this vehicle will be liberated *in situ* with intact concentration and consequently, its action in the tumor cell will be higher than that administered alone by traditional therapy. Thus, the development of efficient delivery systems. By the attraction of antigen-antibody, the CNTs can be taken up by the tumor cell only before the anticancer drug is cleaved off CNTs; thus, targeting delivery is realized.

B. By Antitumor Immunotherapy.

Some studies have demonstrated that CNTs used as carriers can be effectively applied in antitumor immunotherapy. This therapeutic consists of stimulating the patient’s immune system to attack the malignant tumor cells. This stimulation can be achieved by the administration of a cancer vaccine or therapeutic antibody as a drug. In vitro, the conjugate of CNTs and tumor immunogens can achieve by the administration of a cancer vaccine or therapeutic antibody as a drug. *In vitro*, the conjugate of CNTs and tumor immunogens can act as natural antigen-presenting cells (such as mature dendritic cells) by bringing tumor antigens to immune effector T-cells; this action is due to the high avidity of antigen on the surface and the negative charge.

C. By Local Antitumor Hyperthermia Therapy

Hyperthermia therapy using CNTs has been recent suggested as an efficient strategy for cancer treatments. SWCNTs exhibit strong absorbance in the near-infrared region (NIR;700–1100 nm). This unique property of CNTs has been exploited as a method to kill cancer cells via thermal effects. These nanomaterials are considered potent candidates for hyperthermia therapy since they generate significant amounts of heat upon excitation with NIR light. The photothermal effect can induce the local thermal ablation of tumor cells by excessive heating of SWCNTs shackled in tumor cells such as pancreatic cancer. Some progress in the technique has been achieved in recent years, and it has shown feasibility in clinical application.

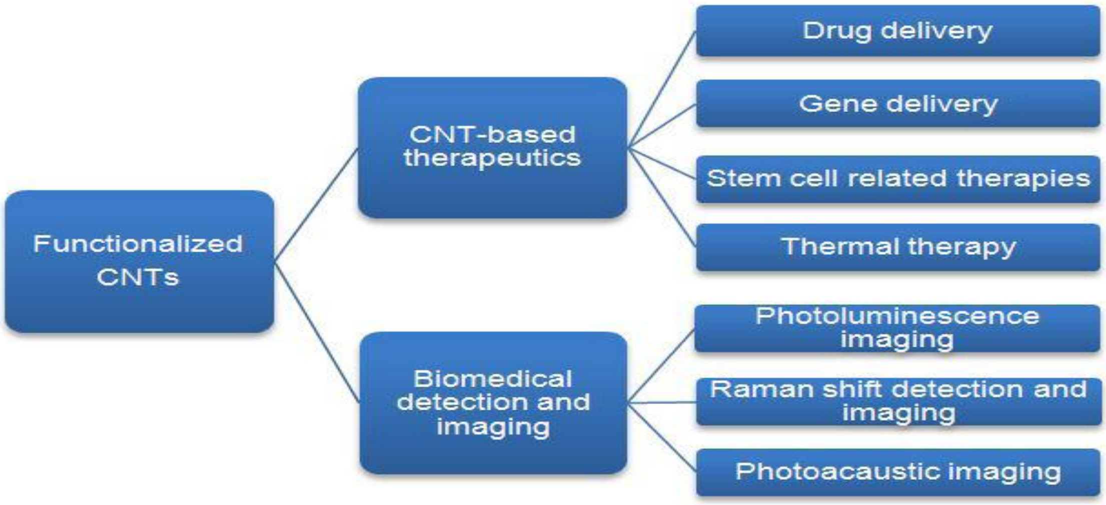

Figure No. 3: Schematic of carbon nanotube applications in therapeutics and biomedical diagnosis and analysis.

SUMMARY

The unique physical properties of carbon nanotubes and structure as a nanoscale tool for many different applications in cancer treatment and diagnostics. Unlike conventional inorganic nanoparticles, CNTs are easily functionalizable in many different ways and possess intrinsic physical properties, including resonance photoluminescence strong NIR optical absorption, and Raman scattering, which can be exploited for multiple purposes, like static and functional imaging, passive and active tracking, drug and gene vectoring and targeting. Most of these "abilities" can be joined together on a single CNT, making them a unique platform for potential multimodality cancer therapy and imaging. They can also be used in synergy with standard tumor treatment, like chemo- and radiotherapy. Despite numerous encouraging results using CNTs in the tumor fight having been published in the past few years, much more work is still needed before they can enter the clinic. The combination of diagnostic and therapeutic capabilities in a single nanometric agent, and may bring unknown opportunities for the future of cancer diagnosis and therapy.

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