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Carbon Nanotubes in Oncology: From Diagnostic Biosensors to Cancer Therapy

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ABSTRACT

Carbon nanotubes (CNTs) represent one of the most significant advances in nanotechnology and have attracted considerable interest due to their extraordinary physicochemical properties. Their unique cylindrical nanostructure, high surface area, exceptional mechanical strength, and remarkable electrical and thermal conductivity make them promising materials for a wide range of scientific and biomedical applications. This review provides a comprehensive overview of carbon nanotubes, including their structural characteristics, classification into single-walled and multi-walled nanotubes, and the most commonly used synthesis methods such as arc discharge, laser ablation, and chemical vapor deposition. In addition, various purification and characterization techniques are discussed to highlight their importance in obtaining high-quality nanotube materials. Special attention is given to the functionalization of carbon nanotubes through covalent and non-covalent approaches, which significantly improve their solubility, stability, and biocompatibility. Furthermore, the review explores the growing role of CNTs in pharmaceutical and biomedical fields, particularly in drug delivery systems, targeted therapy, and nanomedicine, where they offer advantages such as high drug loading capacity and improved therapeutic efficiency. Despite their promising potential, several challenges including toxicity, safety concerns, and large-scale production remain critical issues that must be addressed before their widespread clinical application. Overall, carbon nanotubes continue to represent a powerful platform for the development of next generation nanotherapeutics and advanced biomedical technologies.

Keywords: Carbon Nanotubes, Oncology, Diagnostic Biosensors, Cancer Therapy

INTRODUCTION

The strategy of medicine intake can substantially influence its effectiveness. Few pharmaceuticals possess an ideal concentration range that yields maximal efficacy, while levels exceeding or falling short of this range may result in toxicity or lack therapeutic value entirely. Drug delivery system (DDS) is an interface between the drug and the patient **[1]**.

Nanoscience and nanotechnology have emerged as rapidly expanding fields of research over the past decades, attracting substantial attention from the scientific community due to their ability to manipulate and control matter at the nanometer scale (10^{-9} m).

At this scale, materials often exhibit unique physicochemical properties that differ significantly from those of their bulk counterparts, enabling a wide range of innovative technological and biomedical applications **[2]**.

Consequently, nanotechnology has become an interdisciplinary domain that integrates several scientific areas, including chemistry, biology, medicine, pharmacy, and engineering, with the primary objective of improving quality of life and advancing healthcare technologies **[3]**. The term nanotechnology was first introduced by Norio Taniguchi in 1974, referring to the processing, separation, consolidation, and deformation of materials at the atomic or molecular level **[4]**.

Since then, nanotechnology has evolved into a broad scientific field that investigates the structure, properties, and functionality of materials at the nanoscale, bringing transformative changes to modern science and everyday life **[5]**.

Among the wide variety of nanomaterials investigated to date, carbon nanotubes (CNTs) have attracted particular attention due to their extraordinary structural characteristics and exceptional physicochemical properties **[6]**.

Carbon nanotubes are considered a one-dimensional (1-D) allotrope of carbon, consisting of a cylindrical lattice of sp²-hybridized carbon atoms arranged in a hexagonal graphene network **[7]**. Structurally, CNTs can be described as graphene sheets rolled into seamless cylindrical nanostructures, resulting in an extremely high length-to-diameter ratio that distinguishes them from most conventional materials **[8]**.

Typically, the diameter of carbon nanotubes lies within the nanometer range, whereas their length may extend from several micrometers to even millimeters, creating highly anisotropic nanoscale structures **[9]**. Due to this unique architecture, carbon nanotubes exhibit remarkable mechanical strength, high elasticity, superior tensile properties, and outstanding electrical and thermal conductivity **[10]**.

These distinctive characteristics arise from the graphite-like arrangement of carbon atoms, similar to other carbon allotropes such as graphene and fullerenes, which provide CNTs with exceptional structural stability and functional versatility **[3]**. The discovery of carbon nanotubes by Iijima in 1991 marked a major milestone in nanomaterial research and stimulated extensive investigations into their synthesis, structural characteristics, and potential applications **[11]**.

Depending on the number of graphene layers forming the cylindrical structure, CNTs are commonly classified into single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs) as presented in figure 1 **[12]**.

Single-walled carbon nanotubes consist of a single graphene layer rolled into a cylindrical structure with diameters typically ranging from 0.4 to 2 nm, whereas multi-walled carbon nanotubes are composed of several concentric graphene cylinders with diameters that may reach tens of nanometers **[13]**.

In addition to their unique structural characteristics, CNTs possess a very high surface-to-volume ratio, which enables efficient interaction with a variety of biological molecules including proteins, nucleic acids, and pharmaceutical compounds **[14]**. Furthermore, chemical functionalization of CNT surfaces significantly improves their solubility, biocompatibility, and ability to interact with biological systems, enhancing their potential for biomedical and pharmaceutical applications. As a result, carbon nanotubes have been extensively explored in areas such as drug delivery systems, gene therapy, tissue engineering, biosensing, and cancer diagnostics **[15]**.

Finally, CNTs display unusual electronic, thermal, and optical properties, making future uses in biomedical sensors, reporters, or even simple circuits possible.

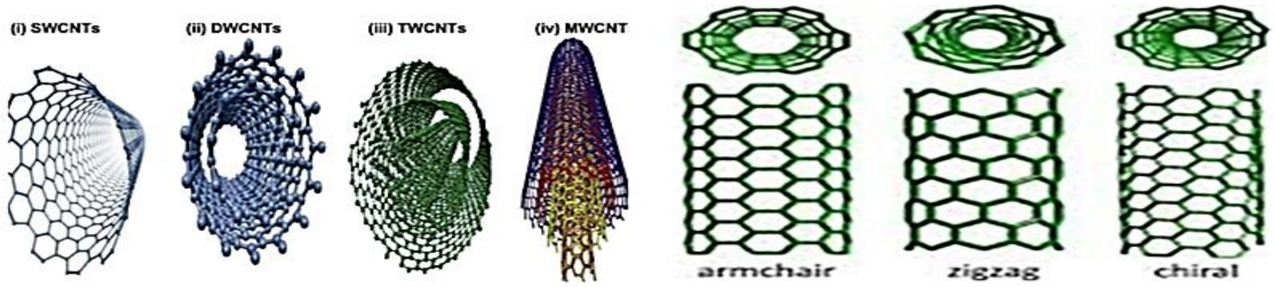

Figure 1: Diagram illustrating the different type of CNTs **[16].**

Physicochemical properties of CNTs

- Carbon nanotubes are cylindrical tubes of nanoscopic dimensions. Typical diameters range from a few nanometers (~ 5-30 nm); typical lengths are in the range of a few millimeters **[17]**.

- The substructure of CNTs (“armchair”, “zigzag”) is derived from the type of process used during synthesis, and affects features such as the existence of semiconductor properties **[18]**.

- The electric and thermal properties of the raw materials are greatly superior to those of conventional materials. In particular, correct insertion of the CNTs into a material matrix will cause a significant shift of the percolation curve towards reduced material concentrations. These promising properties are based on the emergence of a network that takes advantage of the high aspect ratio between the length and the diameter. The formation of networks also supports the improvement of mechanical properties within the matrices, particularly as the basic material has a tensile strength 20 times that of steel **[19]**.

- One important property of carbon nanotubes is that their electrical resistance changes when molecules attach to their surface.**[20]**

- CNTs can penetrate cell membranes depending on their size and surface functionalization. In fact, nanotubes long, narrow shape make them look like miniature needles, so it makes sense that they can function like a needle at the cellular level. Medical researchers are using this property by attaching molecules that are attracted to cancer cells to nanotubes to deliver drugs directly to diseased cells **[19]**.

Advantages of carbon nanotubes as drug delivery system [20]

- Highly uniform ordered structure with high aspect ratio.
- Ultra-light weight.
- Biocompatibility and non-immunogenicity.
- Highly elastic nature.
- Ferromagnetism and non-linear property.
- Cellular internalization *via* endocytosis and passive diffusion mechanisms.
- Exhibit relatively low cytotoxicity after proper functionalization.
- Excretion through biliary pathway.
- Cell membrane penetration due to its tiny nanoneedle tubular structure.
- Open ends on both sides of CNTs make the inner surface accessible and further incorporation of bioactive within the tubes.
- Longer inner volume for endohedral filling relative to diameter.
- High mechanical strength, thermal conductivity, superconductivity metallic or semi-metallic behavior.
- Rare retention of well functionalized CNTs in reticuloendothelial system (RES) due to small size (<1 µm).

Disadvantages of carbon nanotubes as drug delivery system [20].

- Low solubility in aqueous, organic and in organic solvents.
- Bundling/aggregation phenomena.
- Accumulation in liver.

Types of carbon nanotubes

CNTs can be divided into single walls or multiple walls. Nanotubes with single well are described as single-wall carbon nanotubes (SWCNTs) and were first reported in 1993, while the ones with more than one well is multiwall carbon nanotubes (MWCNTs) and were first discovered in 1991 by Iijima **[21]**.

Single walled carbon nanotubes are graphene sheets rolled in the form of seamless cylinder of radius on nanometer scale having a hexagonal lattice of carbon. SWCNT diameter differs 0.4 to 2 to 3 nm, and their length is typically of the micrometer range. SWCNTs usually can come together and form bundles (ropes).

Dependent on wrapping to a cylinder way, there are three different forms of SWCNTs such as armchair, chiral, and zigzag. A SWCNT's structure is characterized by a pair of indices (n, m) that describe the chiral vector and directly have an effect on electrical properties of nanotubes. The number of unit vectors in the honeycomb crystal lattice of graphene along two directions is determined by the integer's n and m. As a common opinion, when m = 0, the nanotubes are named zigzag nanotubes; when n = m, the nanotubes are named armchair nanotubes, and other states are called chiral **[22]**.

Multiwalled carbon nanotubes can be formed in two structural models: Russian Doll model and Parchment model. When a carbon nanotube contains another nanotube inside it and the outer nanotube has a greater diameter than thinner nanotube, it is called the Russian Doll model. On other hand, when a single graphene sheet is wrapped around itself manifold times, the same as a rolled-up scroll of paper, it is called the Parchment model as presented in figure 1 **[21]**.

Preparation of carbon nanotubes

There are several techniques that have been developed for fabricating CNTs structures which mainly involve gas phase processes **[23]**.

Commonly, three procedures are being used for producing CNTs: the chemical vapor deposition (CVD) technique, the laser-ablation technique, and the carbon arc-discharge technique. High temperature preparation techniques for example laser ablation or arc discharge were first used to synthesize CNTs, but currently, these techniques have been substituted by low temperature chemical vapor deposition (CVD) methods (<800°C),since the nanotube length, diameter, alignment, purity, density, and orientation of CNTs can be accurately controlled in the low temperature chemical vapor deposition(CVD) methods **[24]**.

1. Arc Discharge Method

In the arc-discharge method used in the initial experiments in the early 1990s, a high DC current is passed between carbon electrodes, leading to carbon evaporation and the formation of MWCNTs. The first demonstration of controlled SWCNT synthesis also used arc discharge, with the inclusion of a transition metal catalyst. Electric arc discharge uses higher temperatures (above 1,700°C) for CNT synthesis, which typically causes the expansion of CNTs with fewer structural defects compared to other methods. The most utilized methods use high-purity graphite electrodes, usually water-cooled, with diameters between 6–12 mm and separated by 1–2 mm in a chamber filled with helium at sub atmospheric pressure . The chamber contains a graphite cathode and anode, evaporated carbon molecules, and some metal catalyst particles (such as Co, Ni, and/or Fe) . Direct current is passed through the chamber, which is pressurized and heated to approximately 4,000 K . During this process, about half of the evaporated carbon solidifies on the cathode tip, forming a “cylindrical hard deposit or cigar-like structure,” while the rest condenses into chamber soot . The inner core, cathode soot, and chamber soot yield either single-walled or multi-walled carbon nanotubes and nested polyhedral graphene particles **[25]**. In MWNT synthesis, catalysts are generally not required, but SWNT synthesis requires metal catalysts or complex anodes made of graphite combined with metals like Gd, Co, Ni, Fe, Ag, Pt, Pd, or mixtures such as Co-Pt, Co-Ru, Ni-Y, Fe, Ni, Co-Ni, Co-Cu, Ni-Cu, Ni-Ti, Ni-Y, Ni-Y-graphite mixtures can produce high yields (<90%) of SWNTs with average diameters of 1.4 nm and are widely used worldwide. The main advantage of the arc-discharge method is its ability to produce large quantities of nanotubes, while the main disadvantage is relatively little control over the alignment (chirality) as presented in Figure 2 **[26]**.

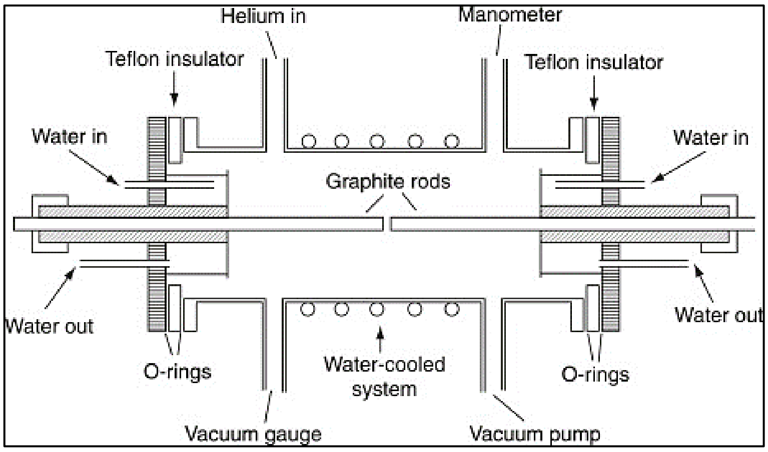

Figure 2: Diagram illustrating Arc Discharge Method of CNTs preparation **[25]**

2. Laser Ablation Method

Laser ablation uses high-power lasers (YAG type) to vaporize a pure graphite block containing metal catalysts in an are atmosphere, inside a furnace heated to approximately 1,200°C 0. The principles and mechanisms are similar to the arc-discharge method, but the energy is provided by a laser hitting a pure graphite pellet holding catalyst materials (frequently cobalt or nickel) **[27]**. The diameter of SWCNTs can be controlled by increasing the laser pulse power, and ultrafast (subpicosecond) laser pulses can produce large amounts of SWCNTs. The main advantage of this technique is high yield and relatively low metallic impurities since metallic atoms tend to evaporate from the tube ends once closed. Other advantages include the ability to produce high-purity SWCNTs with controlled diameters. Disadvantages include non-uniformity, branching of tubes, high cost due to high-purity graphite rods, high laser power requirements, and lower daily production compared to arc discharge .Many parameters affect the properties of CNTs synthesized by laser ablation, including structural and chemical composition of the target, laser properties (peak power, pulse vs CW, energy fluence, oscillation wavelength, repetition rate), buffer gas flow and pressure, chamber pressure and chemical composition, distance between target and substrates, and ambient temperature. Studies indicate that laser ablation can produce up to 1.5 g/h of nanotube material under optimized conditions as presented in Figure 3 **[28]**.

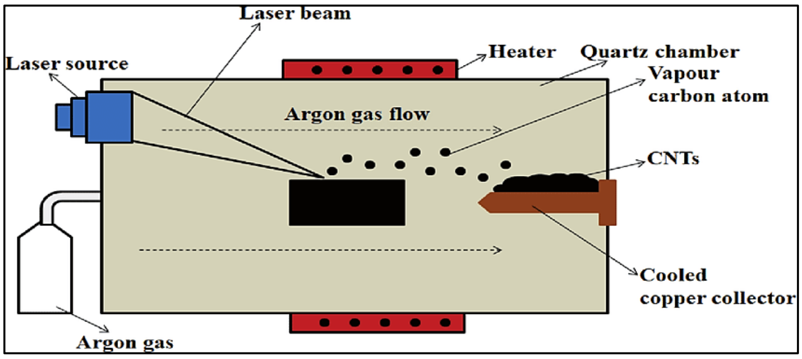

Figure 3: Diagram illustrating Laser ablation Method of CNTs preparation **[29]**

3. Chemical Vapor Deposition (CVD) of Carbon Nanotubes (CNTs)

One of the standard methods for production of carbon nanotubes is chemical vapor deposition (CVD).

There are many different types of CVD, such as:

- Catalytic chemical vapor deposition (CCVD)—either thermal or plasma-enhanced (PE) oxygen-assisted CVD
- Water-assisted CVD
- Microwave plasma (MPECVD)
- Radio-frequency CVD (RF-CVD)
- Hot-filament CVD (HFCVD)

But CCVD is currently the standard technique for the synthesis of CNTs. CVD is based on the passage of a carbon-containing precursor gas over a substrate in a reactor, allowing reaction between the precursor and the surface, which leads to the gradual buildup of CNTs.

The substrate can incorporate a catalyst, commonly nanoparticles made of Fe, Ni, Co, or combinations of these metals, which can nucleate CNT growth and allow it to proceed at lower temperature. A catalyst is generally not needed for MWCNT synthesis, but is required for SWCNTs, since the size and composition of the catalyst determine the initial stages of CNT growth, which in turn determines the diameter and chirality of the final nanotube **[30]**.

The advantages of CCVD are:

- Economically practical method for large-scale CNT production

- High purity of the obtained CNTs
- Reaction can be easily controlled.
- Excellent alignment, as well as positional control on nanometer scale, can be achieved **[31]**.

The overwhelming prevalence of CVD can be attributed to advantages such as scalability, industrial maturity, and adaptability and flexibility of the reactor. An example of this adaptability is floating catalyst CVD, where catalyst particles are suspended in a stream of gas containing a hydrocarbon precursor, which decomposes and forms CNTs on the catalyst surface. The floating catalyst process can generate a range of CNT macrostructures, including films, fibers, arrays, and sponges **[32]**.

In plasma-enhanced CVD (PE-CVD) , plasma above the substrate is used to partially dissociate precursor molecules before surface reactions take place. This allows CVD to be achieved at lower temperatures, providing better control of CNT properties in some cases as presented in Figure 4 **[33]**.

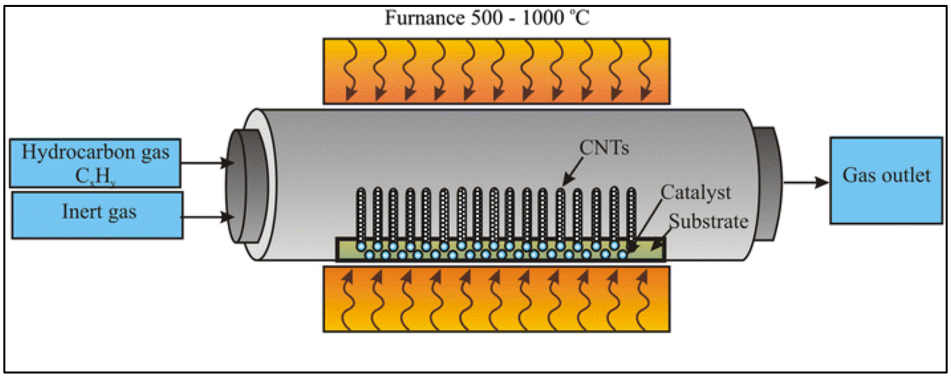

Figure 4: Diagram illustrating Chemical Vapor Deposition (CVD) of CNTs preparation **[8]**

4. Silane Synthesis method

In this method, carbon paper or stainless-steel mesh was immersed in a Silane solution of a metal catalyst, preferably Co: Ni in a 1:1 ratio and a feedstock gas containing a carbon source such as ethylene were fed through the substrate and catalyst deposited. When the substrate was heated by applying an electric current. Thus, a reaction occurs between the catalyst and gas to yield CNTs **[34]**.

5. Flame Synthesis method

SWNTs are formed in control environment from hydrocarbon fuel and small metal catalyst. SWNTs observed in the post-flame region of premixed acetylene / argon / oxygen flame operated at 50 Torr with iron pentacarbonyl vapors used as a source of metallic catalyst **[34]**.

Chemistry of carbon nanotubes for biologic applications

Single-walled carbon nanotubes and MWCNTs can be produced through several methods such as high-pressure carbon monoxide conversion, chemical vapor deposition, plasma arc methods, or the use of cobalt/molybdenum catalysts, among several others. In most preparations, the resulting product is a polydisperse mixture of both metallic and semiconducting species of several diameters and lengths. Technological advances have enabled improved purification of nanotubes by length, diameter, and chirality separation **[35]**. Regardless of the method of production or purification, pristine CNTs are insoluble in most organic or aqueous solvents. For applications in biologic environments, CNTs require further chemical modifications to render the nanotubes dispersible in aqueous media, and an array of strategies has been developed **[36].** Adequate dispersion of nanotubes is necessary to ensure that nanotube solutions are free from large aggregates or bundles of nanotubes, which have been associated with induction of inflammatory pathways and ultimately toxicity **[37].** Indeed, adequate dispersion and individualization is one of the key predictors of biocompatibility of nanotubes and can significantly impact their pharmacologic behavior, including pharmacokinetics, biodistribution, and cellular uptake **[38].** Data suggest that adequately functionalized CNTs can be nontoxic, biocompatible agents for drug delivery applications **[39]**.

The chemistry used to render nanotubes dispersible in aqueous media usually falls into two broad categories covalent and noncovalent approaches. Covalent approaches functionalize the nanotubes either on their side walls or at defect sites containing sp^3 hybridized carbons (such as open nanotube ends) **[40]**. Covalent approaches serve to provide highly stable linkages, but can also significantly alter the spectroscopic and electronic properties of the nanotube material **[41].** Noncovalent approaches typically use an amphiphilic molecule such as surfactants, DNA, or proteins in order to strongly adsorb a hydrophilic structure that allows for interactions with water molecules to disperse the material.

Another class of nanotube chemistry, which is not directed toward solubilization or dispersion, involves filling of the interior cavities of the nanotubes, known as ''endohedral filling.'' In biologic applications, this type of chemistry has been used to load paramagnetic gadolinium atoms into nanotube defect sites, which leads to greatly enhanced relaxivity. Ultimately, chemical approaches will depend on the biologic application of the nanotubes as a therapeutic or diagnostic device. After functionalization of CNTs, the materials can be characterized through an array of techniques **[42]**. Microscopic approaches such as TEM or atomic force microscopy provide high-resolution images of the material, allowing qualitative description of nanotube length and purity. However, microscopic techniques are limited by their ability to sample only tiny fractions of the material and are also prone to artifacts of sample preparation, making it difficult to describe how the nanotubes exist in aqueous solutions. Spectroscopic techniques include near-IR spectroscopy and Raman spectroscopy. Near-IR spectroscopy can provide important information about nanotube purity and chirality due to the unique van Hove transition peaks characteristic of CNTs. Such spectroscopic features are highly disrupted by covalent modification of nanotube side walls, so their utility may be limited in such materials **[43].**

Properties of CNTS

1. Mechanical properties

CNTs are among the strongest and stiffest material, because they possess very high resistance and flexibility Characteristics.

Their high strength results from the strong sp^2 covalent bonds between the carbon atoms strength ranges from 2.5 to 3.5 GPa, which is higher than steel. Because of these special properties, CNTs are used in many areas of modern technology **[13]**.

2. Electrical properties

CNTs are very tough materials and they also show unique behavior when electricity passes through them. A thin layer of graphite is considered a semimetal, acts like something between a metal and a semiconductor.
When this layer rolled to form a nanotube, the carbon atoms arrange themselve around -the tube. At the same time, the movement pattern of electrons must fit together according to the rules of quantum physics. Because of these special structure, carbon nanotubes can transfer extremely large amounts of electric charge, reaching about 4×109 A/cm² **[15]**.

3. Thermal properties

The incorporation of pristine and functionalized nanotubes can double the thermal conductivity, showing that nanotube composite materials may be useful for managing heat in industries **[15]**.

Characterization of CNTs [44]

- **Scanning Electron Microscopy**, SEM image used to show the morphological characterization and distribution of CNTs.
- **Transmission Electron Microscopy**, TEM image used to show the diameter of CNTs.
- **Thermal Properties Measurements**, thermogravimetric analysis (TGA) provide information about the amount of catalyst particles in CNTs.
- **Mechanical properties Measurements**, used to measure the strength of CNTs.

Functionalization of CNTS

Pristine CNTs have highly hydrophobic surfaces and are not soluble in aqueous solutions whereas pristine CNTs are not soluble in any solution. A solution to this problem is functionalization **[45].** Functionalization of CNTs is a process of chemical synthesis where desired functional groups can be introduced onto the walls of CNTs for various applications producing functionalized CNTs. The aim of this process in cancer treatment is the enhancement of biocompatibility within the body, enhancement of encapsulation tendency and solubility, multimodal drug delivery, and imaging with the specific properties imparted related to the desired function. Modifications to CNTs can be divided into two categories; covalent and noncovalently bonded **[46].**

Covalent functionalization of carbon nanotubes

Covalent modification can be classified as either side wall or defect site covalent modifications. Side wall covalent modification can be accomplished through halogenation, addition of radicals, and cycloadditions, among many other techniques. For biologic applications the most common approach has been the cycloaddition of azomethine ylides, sometimes referred to as the Prato reaction **[41].** This reaction offers a versatile set of functional groups that can be bound to the nanotubes. By adding hydrophilic poly ethylene glycol (PEG) chains terminated with a primary amine, this approach has produced highly aqueous compatible nanotubes with minimal toxicity and a high propensity for cellular uptake **[47].** In this approach, the incorporated primary amine serves as a versatile chemical handle for attachment of a wide array of molecules, including radioisotopes, whole proteins, short peptides, and oligonucleotides **[48].** One drawback of covalent side wall modification is the loss or reduction of characteristic electronic properties due to disruption of the π-electron network that can alter the nanotubes' spectroscopic properties.

The other major class of covalent nanotube functionalization is addition to defect sites, which are present predominantly at open nanotube ends. These defect sites are often oxidized to yield carboxylic acid moieties that can be readily modified through amidation or, less frequently, esterification **[44].** Amidation is often performed through activation of the carboxylic acid groups with carbodiimides, which can then be directly reacted with primary amines or indirectly through a succinimidyl ester intermediate. The groups attached in this way are often hydrophilic polymers such as long PEG that provide the hydrophilicity necessary for dispersion **[49].** The PEG derivatized nanotubes produced in this approach have also demonstrated good biocompatibility and aqueous solubility, and groups have also attached a range of biologically active species **[46].**

Noncovalent functionalization of carbon nanotubes

Noncovalent approaches are characterized by strong adsorption of amphiphilic molecules onto nanotube surfaces. The hydrophobic anchor that adsorbs molecules onto the nanotube side wall can be an aromatic species, such as pyrenes, or aliphatic carbon chains. Most commonly, phospholipid surfactants terminated with PEG chains have been used for adequate functionalization of CNTs **[50, 51].** These approaches preserve the inherent electronic and spectroscopic properties of nanotubes, and are useful for applications that take advantage of these unique properties, such as Raman imaging **[52].** The phospholipid surfactant can be derivatized with a range of species including biological macromolecules and small molecule drugs **[53]**. While there is a strong hydrophobic interaction of hydrocarbons or aromatic species with the nanotube, in some cases there is some evidence that in the protein rich environment of biologic organisms, these molecules can be rapidly displaced by hydrophobic protein sequences **[54]**. It is also important to distinguish between noncovalent approaches that use strongly bound specific functionalization agents versus suspension of pristine nanotubes in surfactants or detergents, which are likely to be less stable **[55].**

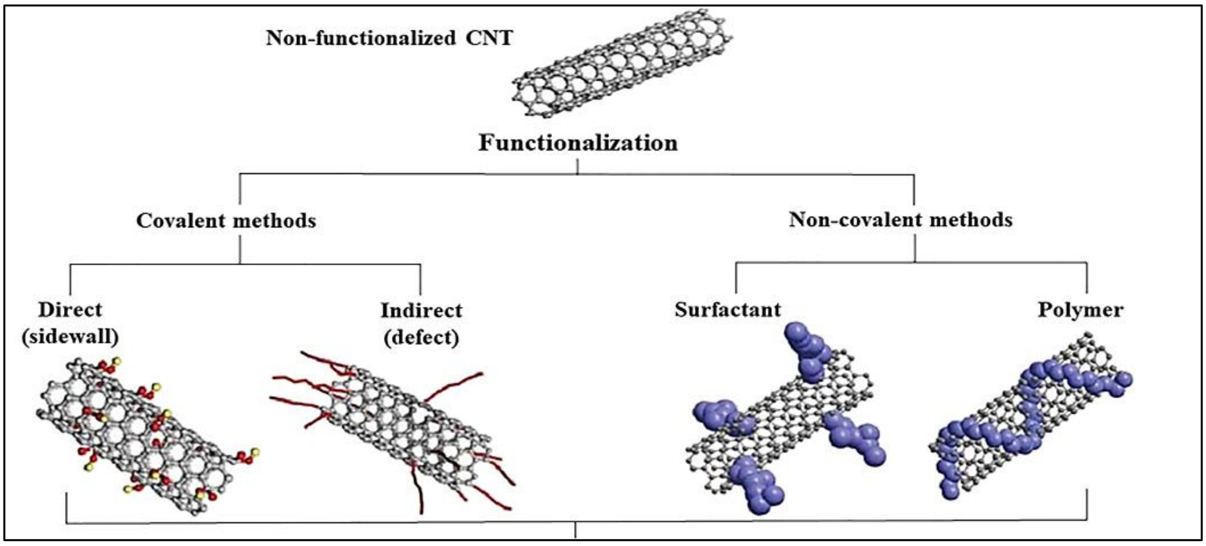

Figure 5: Diagram illustrating the Covalent and Noncovalent functionalization functionalization methods of CNTs.

Pharmacology of CNTs

According to various articles, CNTs pharmacology includes several number of key aspects as presented in Figure 6:

1. Pharmacokinetics (absorption, distribution, metabolism, and excretion)
2. Intracellular fate and cellular uptake
3. Targeted delivery and drug-carrier characteristics
4. Safety and toxicology
5. Therapeutic applications

1. Pharmacokinetics of CNTs (ADME) [56]

a. Absorption

There are various ways that CNTs might enter the body: Intravenous injection, inhalation, oral delivery and dermal route.

Following administration , CNTs may pass through biological barriers like membranes of cells, The blood-brain barrier and asculature of tumors.

Research shows that cellular uptake occurs through passive diffusion, phagocytosi, and endocytosis.

b. Distribution

Once in circulation, CNTs mostly disperse to: liver, spleen, lung, kidney and tumors (after functionalization).

Because the reticuloendothelial system (RES) frequently absorbs CNTs, this dispersion takes place.

Because of the enhanced permeability and retention (EPR) effect, functionalized.

CNTs exhibit better tumor targeting.

c. Metabolism

The metabolism of CNTs happens slowly. Among the potential mechanisms are macrophages' oxidative degradation and degradation by enzymes (peroxidases as myeloperoxidase).

d. Excretion

CNT size affects excretion. Renal clearance (urine) of small, functionalized carbon nanotubes. Hepatic clearance of large CNTs by bile and feces. Research indicates that CNTs functionalized with PEG have quicker renal clearance.

2. Intracellular fate and cellular uptake [57]

CNTs are internalized by cells in several ways. Endocytosis (Primary mechanism): Most studies show that CNTs enter cells via energy-dependent endocytosis **[58]**. Typical for short CNTs (<200 nm) also CNTs bind to membrane receptors → vesicle formation, caveolae-mediated endocytosis, micropinocytosis that engulfs larger CNTs bundles or aggregates.

Factors Affecting Cellular Uptake of CNTs:

Many physicochemical factors influence CNT uptake.

a. Length

- Short CNTs (<1 µm) → efficient uptake
- Long CNTs (>5 µm) → difficult to internalize

b. Diameter

- Smaller diameters enhance cellular internalization.

c. Surface functionalization

- Functionalization improves dispersibility and targeting.

3. Targeted delivery and drug-carrier characteristics [57]

Drug loading techniques like covalent bonding, adsorption that is not covalent and encapsulation. CNTs are able to provide, Anticancer medications, Peptides, Proteins, RNA and DNA Agents for imaging **[58]**.

Examples of medications that CNTs can deliver: Doxorubicin, Paclitaxel and Cisplatin.

CNTs enhance pharmacological results through: Improving the stability of drugs, Improving focused delivery and lowering the toxicity of the system. CNTs can regulate medication release [58].

4. Aspects of Safety and Toxicology [59]

Toxicity is dependent upon the length,diameter, functionalization of the surface, aggregation, and contamination of metal catalysts. Significantly harmful effects also include reactive oxygen species (ROS) that may be produced by CNTs **[58]**.

Inflammation can occur by CNTs that can trigger inflammatory cytokines and immunological reactions.

CNTs' benefits in pharmacology

- High capacity for drug loading
- Capacity to overcome biological obstacles
- Targeted medication administration
- Controlled release
- Multipurpose (imaging + treatment)

5. Therapeutic applications [58]:

- Targeted drug delivery for anticancer medications like doxorubicin
- Gene transfer like delivery of RNA, siRNA, and DNA treatments.
- Cancer therapy CNTs targeted tumor destruction with reduced systemic toxicity.

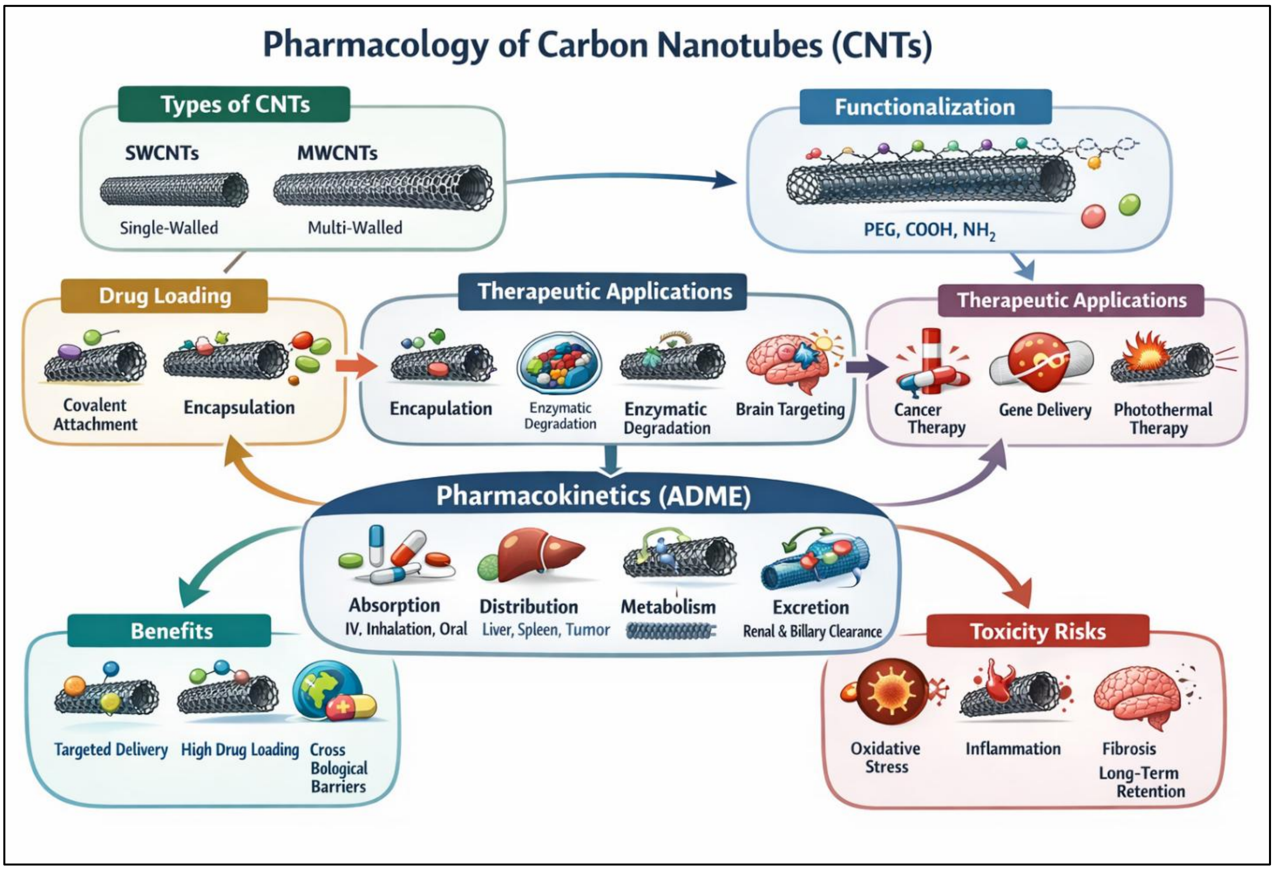

Figure 6: Diagram illustrating the Pharmacology of CNTs [18]

Drug delivery with CNTs [60] [61]

1. A drug delivery system is designed to improve the pharmacological and therapeutic effect of a drug molecule. The ability of f-CNTs to penetrate into cells offers the potential of using f-cnt as vehicles for the delivery of small drug molecules. The development of delivery systems able to carry one or more therapeutic agents with recognition capacity, optical signals for imaging and specific targeting is of fundamental advantage, for example in the treatment of cancer and different types of infectious diseases.

2. CNTs can act as efficient carriers for drug delivery systems.

3. CNTs have the unique properties such as Surface area which make them as promising potential Delivery of drugs, peptides, and nucleic acids. Specific drug or gene can be integrated to walls and tips of CNTs and recognize cancer-specific receptors on the Surface, by these means CNTs can cross the Cell membrane by endocytosis or other mechanisms.

4. CNTs have been extensively explored due to their ability to encapsulate drugs and form stable conjugate forming complexes or conjugates on their surfaces through covalent bonds that promote drug release as presented in Figure 7.

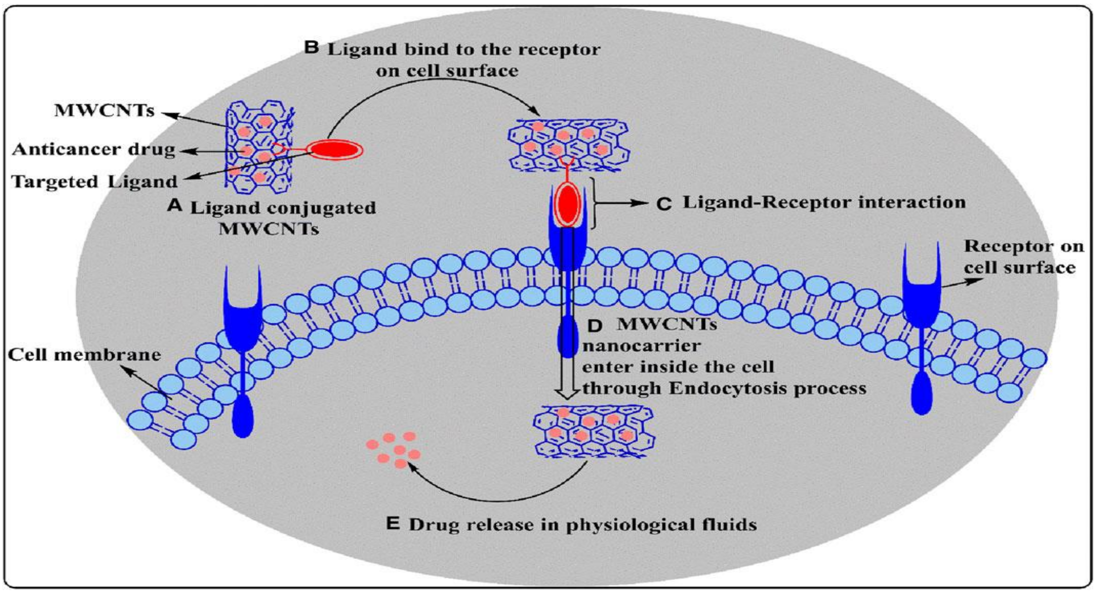

Figure 7: Diagram illustrating the Drug delivery with CNTs [61]

Conclusion

The conclusion for a review article on Carbon Nanotubes (CNTs) as drug delivery systems for cancer therapy should synthesize their revolutionary potential, the critical role of surface engineering, and the persistent safety hurdles that remain before clinical translation. CNTs represent a promising platform in nanomedicine because their nanoneedle shape allows them to penetrate cell membranes directly, delivering a high payload of therapeutic agents including small molecules (Doxorubicin, Paclitaxel) and macromolecules (DNA, siRNA). Their large surface area enables a multi-modal approach, where a single nanotube can carry targeting ligands (e.g., folic acid), imaging agents, and the drug itself, effectively creating a "theranostic" platform. A primary conclusion of most reviews is that pristine (raw) CNTs are unsuitable for clinical use due to their hydrophobicity and insolubility. Surface functionalization—either covalent (chemical bonding) or non-covalent (physical adsorption)—is mandatory to:

a. Improve Biocompatibility: Modification with polymers like PEG (PEGylation) drastically reduces immune recognition and systemic toxicity.

b. Enhance Solubility: Covalent oxidation (adding -COOH groups) or coating with surfactants makes them dispersible in physiological fluids.

c. Enable Selective Targeting: Tethering antibodies or ligands allows CNTs to distinguish cancer cells from healthy ones through active targeting, reducing "bystander" side effects.

Conflict of interest:

The authors declare that there is no conflict of interests.

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