Carbon Nanotubes in Pharmaceutical Nanotechnology: An introduction to Future Drug Delivery System
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ABSTRACT
Carbon nanotubes (CNTs) up to now are the most researched materials of the 21st century with an international intention of growing industrial quantities due to their superior properties for use in many applications either in medical or other potential applications. These compounds have become increasingly popular in various fields simply because of their small size and amazing optical, electric and magnetic properties when used alone or with additions of metals. These are often described as a graphene sheet rolled up into the shape of a cylinder. To be precise, they are graphene cylinders about 12 nm in diameter and capped with end containing pentagonal rings. Carbon nanotubes have potential therapeutic applications in the field of drug delivery, diagnostics, and biosensing. Functionalised carbon nanotubes can also act as vaccine delivery systems. The basic concept is to link the antigen to carbon nanotubes while retaining its conformation, thereby, inducing antibody response with the right specificity. In present paper the different types of CNTs, their methods of preparation & purification are discussed. The paper opens the recent trends towards CNTs in drug delivery. With the increasing interest shown by the nanotechnology research community in this field, it is expected that plenty of applications of CNTs will be explored in future. Current work is focused on the recent developments, particularly of Nanoparticles and Nanotubes. The materials developed from such as the hollow nanospheres, core shell structures, nanocomposites, nonporous materials, and nanomembranes will play a growing role in materials development for the Medical and Nonmedical industry.


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INTRODUCTION
Although fields to develop nanotechnology-based efficient drug delivery systems extend into all therapeutics classes of pharmaceuticals, many therapeutic agents have not been successful because of their limited ability to reach the target tissue. In addition, the faster growth opportunities are expected in developing delivery systems for anti-cancer agents, and vaccines because of safety and efficacy shortcomings in their conventional administration. For example, in cancer chemotherapy, cytostatic drugs damages both malignant and normal cells alike. Thus, a drug delivery strategy that selectively targets the malignant tumour is much needed. With the focus on these requirements the recent researches shows that Carbon gene transfer and DNA applications. As a group, Carbon Nanotubes typically have diameters ranging from <1 nm up to 50 nm. Their lengths are typically several microns, but recent advancements have made the Nanotubes much longer, and measured in centimetres. A Carbon Nanotubes is a tube-shaped material, made of carbon, having a diameter measuring on the nanometre scale. Carbon are a newly created material combining two previously discovered allotropes of carbon: carbon nanotubes and fullerenes. In this new material, fullerene-like "buds" are covalently bonded to the outer sidewalls of the underlying carbon Nanotubes. This hybrid material has useful properties of both fullerenes and carbon nanotubes. In particular, they have been found to be exceptionally good field emitters. In composite materials, the attached fullerene molecules may function as molecular anchors preventing slipping of the nanotubes, thus improving the composite’s mechanical properties.

Carbon Nanotubes (CNTs) have become strongest candidates mainly in the field of biomedical engineering, biotechnology; defense research and pharmaceutical nanotechnology after their discovery in 1991. These are an important new class of technological materials that have numerous novel and useful properties. They have received very much attention as new classes of nanomaterials. These are the long hollow seamless cylinders (single walled as well as multiwalled carbon Nanotubes) of graphene. The diameter of these tubes in the range of 1-100 nm. These tubes are normally capped with the half a full fullerence molecules at both the ends [1-2]. Carbon Nanotubes are cylinders of one or several coaxial graphite layer(s) with a diameter in the order of nanometres, and serve as an instructive example of the Janus-like properties of nanomaterials. Carbon nanotubes have generated huge activity in most areas of science and engineering due to their remarkable physical and chemical properties. No previous materials have displayed the combination of superlative mechanical, thermal and electronic properties attributed to them. These properties make nanotubes ideal, not only for a wide range of applications but as a test bed for fundamental science CNTs have received much attention from scientific communities up to this date mainly because of their superior properties such as having a wide band gap, high melting point, high tensile strength and high thermal conductivity [9]. The purpose of using nanotubes in the human body Provide efficient drug delivery and biosensing methods for disease treatment and health monitoring. CNTs as drug delivery vehicles have shown potential in targeting specific cancer cells with a dosage lower than conventional drugs used [34] that is just as effective in killing the cells, however does into harm healthy cells and significantly reduces side effect [35]. Current blood glucose monitoring methods by patients suffering from diabetics are normally invasive and often painful. [36].

CLASSIFICATION OF CARBON NANOTUBES:

Nanotubes are categorized as single-walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs). Individual nanotubes naturally align themselves into "ropes" held together by van der Waals forces, more specifically, pi-stacking.

1) Single walled carbon nanotubes (SWNTs) [1,13-14].
These can be imagined perfect graphene sheets in which grapheme being the same poly –aromatic mono-atomic layer made of hexagonal display of sp2 hybridized carbon atoms, rolled up into a cylinder, with the hexagonal rings put in contact to join seamlessly [1,13-14].

2) Multiple walled carbon nanotubes (MWNTs):
The MWCNTs consists of multi walled graphene sheets rolled up in concentric CNTs, filling each other’s inner cavities to end up with Nanotubes [15-16]. The intertube distance is in a MWCNTs is approximately that of inter-graphene distance in turbostratics poly aromatic solids & hence these MWCNTs are more stronger in their strength in comparisons to SWCNTs. SWCNTs are graphene sheet rolled up into a tube form with nanodimensions [17-18].

**Table 1: Differences between SWNT and MNWT:**

<table>
<thead>
<tr>
<th></th>
<th>SWNT</th>
<th>MWNT</th>
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<tbody>
<tr>
<td><strong>Differences</strong></td>
<td>Single layer graphene</td>
<td>Multiple graphene layer</td>
</tr>
<tr>
<td>Catalyst is required for synthesis</td>
<td>Can be produced without catalyst</td>
<td></td>
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<tr>
<td>Bulk synthesis is difficult as it requires proper control over growth and atmospheric conditions.</td>
<td>Bulk synthesis is easy</td>
<td></td>
</tr>
<tr>
<td>Purity is poor</td>
<td>Purity is high</td>
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<tr>
<td>A chance of defect is more during Functionalization</td>
<td>A chance of defect is less but once occurred it is difficult to improve</td>
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<tr>
<td>Less accumulation in body</td>
<td>More accumulation in the body</td>
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</tr>
<tr>
<td>Characterization and evaluation is easy</td>
<td>It has very complex structure</td>
<td></td>
</tr>
<tr>
<td>It can be easily twisted &amp; are more liable</td>
<td>It cannot be easily twisted</td>
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STRUCTURE AND MORPHOLOGY

Each atom joined to three neighbours, as in graphite so that bonding in carbon nanotubes is sp². The tubes can therefore be considered as rolled-up graphene sheets. This bonding structure, which is stronger than the sp³ bonds found in diamond, provides the molecules with their unique strength. Under high pressure, nanotubes can merge together, trading some sp² bonds for sp³ bonds, giving the possibility of producing strong, unlimited length wires through highpressure nanotube linking. Structure of nanotubes is as shown in fig.1.

![Fig. 1. Structure of nanotubes](image1)

Carbon occurs in many forms, and the properties depend of each form on its special structure makes carbon a truly unique building block for nanomaterials. Carbon nanotubes discovered in 1991 by Iijima and coworkers. Each of which is pair of fullerene caps connected by a tube that is a rolled up seamless graphene sheet. [Fig. 2.]

![Fig. 2. Single sheet of Graphene](image2)

METHODS OF PRODUCTIONS OF CNTs

1) Arc Discharge [19]

Arc discharge initially used to producing C60 fullerenes, is the most common and easiest way to produce CNTs. This method creates CNTs through arc-vaporization of two carbon rods placed end to end, separated by approximately 1mm, in an enclosure that is usually filled with inert gas at low pressure. A direct current of 50 to 100 A0, driven by a potential difference of approximately 20 V creates a high temperature discharge between the two electrodes. The discharge vaporizes the surface of one of the carbon electrodes and forms a small rod-
shaped deposit on other electrode. By changing metal catalyst, nanotubes with a diameter of 0.6 to 1.2 nm are produced. Catalysts used are Cobalt and Molybdeum. Fig.3.

2) Laser ablation [20]
In Laser ablation laser vaporization pulses were followed by a second pulse, to vaporize the target more uniformly. The use of two successive laser pulses minimizes the amount of carbon deposited as soot. The second laser pulse breaks up the larger particles ablated by the first one, and feeds them into the growing nanotubes structure. The material produced by this method appears as a mat of ropes, 10-20 nm in diameter and up to 100μm or more in length.

3) Chemical Vapor Deposition [21]
Chemical Vapor Deposition of hydrocarbons over a metal catalyst is that has been used to produce various carbon materials like carbon fibers and filaments. Large amount of CNTs can be formed by catalytic CVD of acetylene over cobalt and iron catalysts supported on silica or zeolite. High yields of single walled nanotubes have been obtained by catalytic decomposition of H2-CH4 mixture all over well dispersed metal particles such as cobalt, nickel and iron on magnesium oxide 10000C. The decomposition of CH4 over the freshly formed nanoparticles prevents their further growth and thus results in a very high proportion of SWNTs and few MWNTs.

4) Flame Synthesis Method [22]
SWNTs are formed in controlled flame environment from hydrocarbon fuels and small aerosol metal catalyst. Single-walled nanotubes have been observed in the post-flame region of a premixed acetylene/oxygen/argon flame operated at 50 Torr with iron pentacarbonyl vapor used as a source of metallic catalyst. Between 40 and 70 mm heights above burner nanotubes are observed to form and coalesce into clusters.

5) Silane Solution Method [23]
Carbon nanotubes were produced using a silane solution method, in which a substrate such as carbon paper or stainless steel mesh was immersed in a silane solution of a metal catalyst, referably Co: Ni in a 1:1 ratio and a feedstock gas containing a carbon source such as ethylene inserted through the substrate and the catalyst deposited thereon while the substrate was heated by applying an electrical current.

PURIFICATION OF CNTs [24]
Nanotubes usually contain a large amount of impurities such as metal particles, amorphous carbon, and multishell. There are different steps in purification of nanotubes.

1) Air Oxidation
The carbon nanotubes are having less purity, the average purity is about 5- 10%. So purification is needed before attachment of drugs onto CNTs. Air oxidation is useful in reducing the amount of amorphous carbon and metal catalyst particles (Ni, Y). Optimal oxidation condition is found to be at 673 k for 40 min.

2) Acid Refluxing
Refluxing the sample in strong acid is effective in reducing the amount of metal particles and amorphous carbon. Different acids used were hydrochloric acid (HCl), nitric acid (HNO3) and sulphuric acid (H2SO4), but HCl was identified to be the ideal refluxing acid.

3) Surfactant aided sonication, filtration and annealing
After acid refluxing, the CNTs were purer but, tubes were entangled together, trapping most of the impurities, such as carbon particles and catalyst particles, which were difficult to remove with filtration. So surfactant-
Aided sonication was carried out. Sodium dodecyl benzenesulphonate (SDBS) aided sonication with ethanol (or methanol) as organic solvent were preferred because it took the longest time for CNTs to settle down. The sample was then filtered with an ultra filtration unit and annealed at 1273 K in N2 for 4 h. Annealing is effective in optimizing the CNT structures. It was proved the surfactant-aided sonication is effective to untangle CNTs, thus to free the particulate impurities embedded in the entanglement.

**Purification process of CNTs:**

![Diagram of purification process of CNTs]

**Produced CNTs**  
(With impurities i.e. catalyst, graphite, carbon)

- **Purification**
- **Sorting**
  - Length based
  - Band based
  - Diameter based

**Purified Carbon Nanotubes (CNTs)**

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**Table 2. Purification of CNTs**

**Functionalized carbon Nanotubes in drug design and discovery**

In general drug delivery system is designed to improve the physiological and therapeutic profile of a drug molecule. The large inner volume of CNTs allows encapsulation of both low as well as high molecules of drugs. It also permits encapsulation of both hydrophilic and lipophilic drugs. More than one drug can also be loaded in CNTs in the case of multi-drug therapy. Ligands and diagnostic materials can also be conjugated to surface of CNTs by functionalization to target the drugs to specific site of action. The CNTs can act as controlled release system for drug by releasing the loaded drugs for along period of time. Carbon nanotubes (CNTs) have been proposed and actively explored as multipurpose innovative carriers for drug delivery and diagnostic applications. Their versatile physicochemical features enable the covalent and noncovalent introduction of several pharmaceutically relevant entities and allow for rational design of novel candidate nanoscale constructs for drug development. CNTs can be functionalized with different functional groups to carry simultaneously...
several moieties for targeting, imaging, and therapy. Among the most interesting examples of such multimodal CNT constructs described in this Account is one carrying a fluorescein probe together with the antifungal drug amphotericin B or fluorescein and the antitumor agent methotrexate.

![Fig.4. CNTs as drug design](image)

The biological action of the drug in these cases is retained or, as in the case of amphotericin B constructs, enhanced, while CNTs are able to reduce the unwanted toxicity of the drug administered alone. Ammonium-functionalized CNTs can also be considered very promising vectors for gene-encoding nucleic acids. Indeed, we have formed stable complexes between cationic CNTs and plasmid DNA and demonstrated the enhancement of the gene therapeutic capacity in comparison to DNA alone. On the other hand, CNTs conjugated with antigenic peptides can be developed as a new and effective system for synthetic vaccine applications. What makes CNTs quite unique is their ability, first shown by our groups in 2004, to passively cross membranes of many different types of cells following a translocation mechanism that has been termed the nanoneedle mechanism. In that way, CNTs open innumerable possibilities for future drug discovery based on intracellular targets that have been hard to reach until today. Moreover, adequately functionalized CNTs as those shown in this Account can be rapidly eliminated from the body following systemic administration offering further encouragement for their development. CNT excretion rates and accumulation in organs and any reactivity with the immune system will determine the CNT safety profile and, consequently, any further pharmaceutical development. Caution is advised about the need for systematic data on the long-term fate of these very interesting and versatile nano-objects in correlation with the type of CNT material used. CNTs are gradually playing a bigger and more important role in the emerging field of nanomedicine; however, we need to guarantee that the great opportunities they offer will be translated into feasible and safe constructs to be included in drug discovery and development pipelines.

**The purpose of using nanotubes in the human body**

Carbon nanotubes are very prevalent in today’s world of medical research and are being highly researched in the fields of efficient drug delivery and biosensing methods for disease treatment and health monitoring. CNT technology has shown to have the potential to alter drug delivery and biosensing methods for the better, and thus carbon nanotubes have recently garnered interest in the field of medicine. The use of CNT’s in drug delivery and biosensing technology has the potential to revolutionize medicine. Fictionalization of SWNT’s
has proven to enhance solubility and allow for efficient tumour targeting/drug delivery. It prevents SWNT’s from being cytotoxic and altering the function of immune cells. Cancer, a group of diseases in which cells grow and divide abnormally, is one of the primary diseases being looked at with regards to how it responds to CNT drug delivery. Current cancer therapy primarily involves surgery, radiation therapy, and chemotherapy. These methods of treatment are usually painful and kill normal cells in addition to producing adverse side effects.

CNTs as drug delivery vehicles have shown potential in targeting specific cancer cells with a dosage lower than conventional drugs used [34] that is just as effective in killing the cells, however does not harm healthy cells and significantly reduces side effect [35]. Current blood glucose monitoring methods by patients suffering from diabetics are normally invasive and often painful. For example, one method involves a continuous glucose sensor integrated into small needle which must be inserted under the skin to monitor glucose levels every few days [36]. Another method involves glucose monitoring strips to which blood must be applied. These methods are not only invasive but they can also yield inaccurate results. It was shown that 70 percent of glucose readings obtained by continuous glucose sensors differed by 10 percent more and 7 percent differed by over 50 percent [36]. The high electrochemically accessible surface area, high electrical conductivity and useful structural properties have demonstrated the potential use of single-walled nanotubes and multi-walled nanotubes in highly.

Mode of break down of CNTs in the body.
Carbon nanotubes were once considered biopersistent in that they did not break down in body tissue or in nature. In recent years, research has shown that laboratory animals exposed to carbon nanotubes via inhalation or through injection into the abdominal cavity develop severe inflammation. This and the tissue changes (fibrosis) that exposure causes lead to impaired lung function and perhaps even to cancer. For example, a year or two ago, alarming reports by other scientists suggested that carbon nanotubes are very similar to asbestos fibres, which are themselves biopersistent and which can cause lung cancer (mesothelioma) in humans a considerable time after exposure [42]. A team of Swedish and American scientists has shown for the first time that carbon nanotubes can be broken down by an enzyme - Myeloperoxidase (MPO) -- found in white blood cells. Their discoveries are presented in Nature Nanotechnology and contradict what was previously believed, that carbon nanotubes are not broken down in the body or in nature. The scientists hope that this new understanding of how MPO converts carbon nanotubes into water and carbon dioxide can be of significance to medicine [42]. This current study thus represents a breakthrough in nanotechnology and nanotoxicology, since it clearly shows that endogenous MPO can break down carbon nanotubes. This enzyme is expressed in certain types of white blood cell (neutrophils), which use it to neutralise harmful bacteria. Now, however, the researchers have found that the enzyme also works on carbon nanotubes, breaking them down into water and carbon dioxide. The researchers also showed that carbon nanotubes that have been broken down by MPO no longer give rise to inflammation in mice [42].

APPLICATIONS OF CNTs
1) GENETIC ENGINEERING
CNTs are used to manipulate genes and atoms in the development of bioimaging genomes, proteomics and tissue engineering. The unwound DNA winds around SWNT by connecting its specific nucleotides and causes change in its electrostatic property. Wrapping of carbon nanotubes by singlestranded 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 to treat cancer and genetic disorders34. Their tubular nature has proved them as a vector in gene therapy. Nanotubes complexes 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 syncytical virus (RSV), a virus with severe bronchitis and asthma. The treatment is generally done by combining Nanoparicles and gene slicing technologies. RNA fragments capable of inhibiting a protein is encapsulated within nanotubes and administered in the form of nasal sprays or drops. Nanotubes are reported for helical crystallisation of proteins and growth of embryonic rat brain neurons [35-36].

2) BIOMEDICAL APPLICATIONS [36-37]
Bianca et al. have prepared soluble CNTs and have covalently linked biologically active peptides. This was demonstrated for viral protein VP1 of foot mouth disease virus (FMDV) showing immunogenicity and eliciting antibody response. 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.

3) CARBON NANOTUBES IN DETECTION [38]
For detection of chemical and biological agents CNTs are used by forming its casting on suitable sensitized electrodes and can be exposed to enzymes solution for immobilization procedure.
A) Detection of Toxic Organophosphoric Compounds [39]
These Organophosphoric compounds are generally used in insecticides, pesticides. These chemicals are CNS affecting by inhibiting acetylcholine esterase which functions on acetylcholine neurotransmitters. Carbon Nanotubes are the electrode materials has the possibility of promoting electron transfer reaction at enzymes immobilization. Acetylcholine esterase is immobilized on Nanotubes surface and catalyses hydrolysis if thiocholine ester, forms thiocholine and oxidation of thiocholine can be detected by electrochemical techniques. On Organophosphoric compounds action acetylcholine esterase catalytic property become reduced and simultaneously the oxidation of thiocholine inhibited and this can be detected by amperometric analysis using CNTs electrodes.
B) Detection of Alkylating Agents Containing Sulphur and Nitrogen [40-41].
Alkylating agents such as Nitrogenmustards, Ethylamine, Alkylsulphonates, Triazenes, Piprazenes, and Nitrosureas can be detected by DNA sensing as the biological recognition element which could have numerous applications. To improve the sensitivity aligned CNTs should be used as nanoelectrodes array for DNA recognition.
C) Detection of Toxic Proteins and Micro Organisms
By change in electrical signals, the CNTs can be used as a measuring platform for various toxic proteins which will immobilized on the CNTs by both covalent and noncovalent means. This immobilization properties of antibodies by means of sensing improves their activity in antigen antibodies biosensors [42-44]. Scanning electron microscope (SEM) and electrochemical chemiluminescence (ECL) can be used to test the bonds of proteins with antibodies on CNTs platform. Finally the detection can be done by integrating these sensor tips to a single conditioning and processing circuits and measurements analysis of conductance and electrical signals obtained in presence of toxic proteins [45-48].
D) Detection of Chemical Substances
Colinet al. found that CNTs exhibit very good adsorption properties because of there high specific surface area and nanoscale structures which provide large number of sites where the chemical in gaseous form can react.
Young et al. achieved ultrahigh sensitivity detection of NO2 gas using composite film of SWCNTs mash doped with alkanethiol monolayer protected gold cluster (MPC). Penza, et al. Fabricated micro acoustic sensor, for organic vapour detection at room temperature, in which SWCNTs were imbedded in Cadmium arachidate(CdA) amphiphillic matrix [25-49]

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4) 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 [25-50].

5) 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 prevents oxidation of important skin components [51].

6) CARBON NANOTUBES IN DRUG DELIVERY
A) Carbon Nanotube Membranes for Transdermal Drug Delivery
The CNT patch represents a major step forward in developing a programmable, transdermal drug delivery system that can usefully treat a variety of syndromes and be tailored to an individual patient’s needs in a manner that will both improve therapeutic administration and efficacy. Dr. Hinds and his colleagues have developed a novel skin patch device for delivering nicotine based on an active layer of aligned carbon nanotubes (CNT) approximately 1.5-7 nm in diameter crossing through a solid polymer film [52].

B) CNT’S for cancer treatment
Though the current treatments of cancer by surgery, radiation and chemotherapy are successful in several cases, these curative methods also kill healthy cells and cause toxicity to the patient. The spread of cancer cells between organs, a process known as metastasis, is the cause of most cancer death. CNT’s can be considered as antitumor agents and when in combination with conventional drugs, can significantly enhance their chemotherapeutic effect with the help of the advanced drug delivery system. It has been reported that Paclitaxel loaded PEG--CNT’s are promising for cancer therapeutics. Aqueous solution of functionalized SWCNTs on exposure to radiofrequency (RF) field experiences efficient heating and this property has been exploited by Gannon et al for a noninvasive and selective thermal destruction of human cancer cells with minimal or no toxic effects to normal cells. This demonstrates that carbon nanotubes are capable of leading to new exciting directions and approaches in therapeutic oncology. A photo-thermal effect can be employed to induce thermal cell death in a noninvasive manner, provides important information on potential therapeutic targets for pancreatic cancer treatment. There are three key features of this nanoscale drug delivery system (DDS):

i) Use of functionalized SWCNTs as a biocompatible platform for the delivery of therapeutic drugs or diagnostics,
ii) Conjugation of prodrug modules of an anticancer agent that is activated to its cytotoxic form inside the tumor cells upon internalization and in situ drug release,
iii) Attachment of tumor-recognition modules to the nanotube surface [53-54].

C) CNTs for Cardiac Autonomic Regulation
Single walled carbon nanotubes share physicochemical properties with ultrafine Component
which may impair cardiovascular autonomic control proved after the study conducted in rats, suggest that SWCNTs may alter the baroreflex function, thus affecting the autonomic cardiovascular control regulation [55].

D) CNTs for platelet activation

SWCNTs using along with platelet P-selection when injected into anaesthetized mice, light induced thrombus formation was found and the platelet found to be activated. MWCNTs activate blood platelets by inducing extracellular Ca2+ influx that could be inhibited by calcium channel blockers SKF 96365 and 2-APB. CNT-induced platelet activation is associated with a marked release of platelet membrane microparticles positive for the granular secretion markers CD62P and CD6356.

E) CNT for tissue regeneration

CNTs are combined with polymers such as poly-l-lactase, Polylactide and poly-D, Llactide- glycolide copolymer which have been used as scaffolds in tissue regeneration. MacDonald et al., prepared composite materials comprised of a collagen matrix with embedded CNTs by mixing solubilised collagen with solution having carboxylated SWCNTs [20].

F) Carbon Nanotubes in Drug Delivery: Recent Trends [55-60]

Carbon Nanotubes (CNTs) have emerged as a recent and promising option especially in drug delivery, cancer therapy. This is mainly due to their unique properties, which render them extremely versatile through the incorporation of several functional groups and targeting molecules at the same time, while their natural shape allows them to selectively penetrate across biological barriers in a non-invasive way. Carbon Nanotubes (CNTs) are considered potential biomedical materials because of their flexible structure and propensity for chemical functionalization. Pharmaceutical excipients have been regarded as inert or nonactive components of dosage forms, but they are essential and necessary components of pharmaceutical preparations. Application of CNTs in biological systems depends on their compatibility with hydrophilic environments; therefore, the solubilisation of CNTs in pharmaceutical solvents is essential. Carbon Nanotubes have potential novel application in nanomedicine as biocompatible and supportive substrates, and as pharmaceutical excipients for creating versatile drug delivery systems. Single-Walled Carbon Nanotubes are currently under evaluation in biomedical applications, including in vivo delivery of drugs, proteins, peptides and nucleic acids as for gene transfer or gene silencing, in vivo tumor imaging and tumor targeting of Single-Walled Carbon Nanotubes as an anti-neoclassic treatment. Versatile physicochemical features of CNTs enable the covalent and noncovalent introduction of several pharmacologically relevant entities and allow for rational design of novel nanoscale candidate constructs for drug development. CNTs can be functionalized with different functional groups to carry simultaneously several moieties for targeting, imaging, and therapy. Among the most interesting examples of such multimodal CNT constructs described is one carrying a fluorescein probe together with the antifungal drug amphotericin B or fluorescein and the antitumor agent methotrexate. The biological action of the drug is retained or enhanced, while CNTs are able to reduce the unwanted toxicity of the drug administered alone. Ammoniumfunctionalized CNTs can also be considered very promising vectors for gene-encoding nucleic acids. Stable complexes between cationic CNTs and plasmid DNA and demonstrated the Drug delivery with Buckyballs. Scientists are also testing fullerenes for drug delivery. Many drug molecules can be attached to a fullerene. The medicine loaded fullerene can then be attached to an antibody. Antibodies are Y-shaped proteins that can recognize and attach to things in the body called antigens. Viruses, bacteria and diseases in the body each have unique antigens. The antibody finds the disease in the body then the attached fullerene delivers the appropriate medicine. Just like with magnetic nanoparticles, medicine can be sent only to place where it is needed, leaving healthy cells alone.
An antibody will only attach to a specific antigen that is the right shape. Fullerenes can be loaded with medicine (green) and attached to an antibody (pink) which will seek out the disease antigen.

CNTs quite unique is their ability, to passively cross membranes of many different types of cells following a translocation mechanism that has been termed the nanoneedle mechanism. In that way, CNTs have open innumerable possibilities for future drug discovery based on intracellular targets. Moreover, adequately functionalized CNTs can be rapidly eliminated from the body following systemic administration offering further encouragement for their development. CNTs excretion rates and accumulation in organs and any reactivity with the immune system, determine the CNTs safety profile and, consequently, any further pharmaceutical development. Caution is advised about the need for systematic data on the long-term nano-objects in correlation with the type of CNT material used. CNTs are gradually playing a bigger and more important role in the emerging field of nanomedicine. Outstanding progress has been made in drug delivery approaches of CNTs. However, challenges still exist in delivering clinically optimal levels of therapeutic molecules. Advances in nanotechnology and nanomedicine have heralded the advent of several innovative nanomaterials which are set to revolutionize the field of drug delivery. Carbon Nanotubes are one such novel class of nanomaterials that are gaining increasing attention. There are three key features of this nanoscale drug delivery system (DDS): (a) use of functionalized SWCNTs as a biocompatible platform for the delivery of therapeutic drugs or diagnostics, (b) conjugation of prodrug modules of an anticancer agent (taxoid with a cleavable linker) that is activated to its cytotoxic form inside the tumor cells upon internalization and in situ drug release, and (c) attachment of tumor-recognition modules (biotin and a spacer) to the nanotube surface. To prove the efficacy of this DDS, three fluorescent and fluorogenic molecular probes were designed, synthesized, characterized, and subjected to the analysis of the receptor mediated endocytosis and drug release inside the cancer cells (L1210FR leukaemia cell line) by means of co focal fluorescence microscopy. The specificity and cytotoxicity of the conjugate have also been assessed and compared with L1210 and human noncancerous cell lines. Then, it has been proven that this tumor-targeting DDS works with high potency toward specific cancer cell lines, thereby forming a solid foundation for further development [62].Chemically functionalized single-walled carbon nanotubes (SWNT) have shown promise in tumor-targeted accumulation in mice and exhibit biocompatibility, excretion, and little toxicity. Here, we show in vivo SWCNTS drug delivery for tumor suppression in mice. Conjugating paclitaxel (PTX), a widely used cancer chemotherapy drug, to branched polyethylene glycol chains on SWCNTs via a cleavable ester bond to obtain a water-soluble SWNT-PTX conjugate. SWCNTs-PTX affords higher efficacy in suppressing tumor growth than clinical Taxol in a murine 4T1 breast cancer model, owing to prolonged blood circulation and 10-fold higher tumor PTX uptake by SWNT delivery through enhanced permeability and retention. Drug molecules carried into the reticuloendothelial system are released from SWCNTs and excreted via biliary pathway without causing obvious toxic effects to normal organs. Thus, nanotube drug delivery is promising for high treatment efficacy and minimum side effects for future cancer therapy with low drug doses [63]. Functional analyses of water-dispersed carbon nanohorns with antitumor activity were performed to explore their potential as a drug carrier for local cancer chemotherapy. Water-dispersed carbon nanohorns were prepared by adsorption of polyethylene
glycol-doxorubicin conjugate (PEGDXR) onto oxidized single-wall carbon nanohorns (oxSWNHs). PEG-DXR-bound oxSWNHs were administered intratumorally to lung cancer-cell NCI-H460-bearing mice. When injected intratumorally, PEG-DXR-bound oxSWNHs caused significant retardation of tumor growth associated with prolonged DXR retention in the tumor. In accordance with this DXR retention, a large number of oxSWNH agglomerates was found in the periphery of the tumor. Histological analyses showed migration of oxSWNHs to the axillaries lymph node, which is a major site of breast cancer metastasis near the tumor, possibly by means of interstitial lymphatic-fluid transport. These results suggest that water-dispersed oxSWNHs may thus be useful as a drug carrier for local chemotherapy [64]. Hampel [65], et al. prescribed CNTs as feasible carriers for carboplatin, a therapeutic agent for cancer treatment. The drug was introduced into CNTs to demonstrate that they are suited as nanocontainers and nanocarriers and can release the drug to initialize its medical virtue. The filling was accomplished by a wet-chemical approach after the CNTs were opened.

The effect on cell proliferation and cytotoxicity of the carboplatin-filled CNTs was investigated by using viability assays. Using different analysis methods such as electron energy loss spectroscopy and x-ray photoelectron spectroscopy the structure of carboplatin incorporated into the CNTs was found to be retained. In vitro studies showed that carboplatin-filled CNTs inhibited growth of bladder cancer cells whereas unfilled, opened CNTs barely affected cancer cell growth [66]. Besides the cancer treatment advances of CNTs shows their extraordinary physical and chemical properties carbon nanotubes reveal promising potential as biomedical agents for heating, temperature censoring and drug delivery on the cellular level. Filling carbon nanotubes with tailored materials realises nanoscale containers in which the active content is encapsulated by a protecting carbon shell. In particular, the filling with magnetic materials offers the potential for hyperthermia applications while the insertion of NMR active substances allows the usage as markers and sensors. The potential of carbon nanotubes for biomedical applications is highlighted by hyperthermia studies which prove their applicability for local in situ heating. In addition, a non-invasive temperature control by virtue of a carbon-wrapped nanoscaled thermometer and filling with anti-cancer drugs is possible [67]. Most low-molecular-weight platinum anticancer drugs have short blood circulation times that are reflected in their reduced tumor uptake and intracellular DNA binding. A platinum (IV) complex of the formula c, c, t-[Pt(NH3)2Cl2(O2CCH2CH2CO2H)(O2CCH2CH2CONH2)] (1), containing a folate derivative (FA) at an axial position, was prepared and characterized. Folic acid offers a means of targeting human cells that highly over express the folate receptor (FR). Compound (1) was attached to the surface of an amine-functionalized single-walled carbon nanotube (SWCNTS-PL-PEG-NH2) through multiple amide linkages to use the SWCNTs as a "longboat delivery system" for the platinum warhead, carrying it to the tumor cell and releasing cisplatin upon intracellular reduction of Pt(IV) to Pt(II). The SWCNTs deliver the foliated-bearing Pt(IV) cargos into FR(+) cancer cells by endocytosis by the localization of fluorophore-labeled SWCNTs using fluorescence microscopy. Once inside the cell, cisplatin, formed upon reductive release from the longboat oars, enters the nucleus and reacts with its target nuclear DNA, by platinum atomic absorption spectroscopy of cell extracts. Formation of the major cisplatin 1,2- intrastrand (dGpG) cross-links on the nuclear DNA was demonstrated by use of a monoclonal antibody specific for this adduct. The SWNT-tethered compound 1 is the first construct in which both the targeting and delivery moieties have been incorporated into the same molecule; intracellular reduction of a Pt(IV) prodrug leads to the cis-{Pt((NH3)2} 2} 1,2-intrastrand (dGpG) cross-link in nuclear DNA [68]. Nanocomposite films based on single wall carbon nanotubes (SWCNTs) and poly (DL-lactideco- glycolide) copolymer (50:50 PLGA) were processed and analyzed. The effect of different functionalization systems on the physical stability and morphology of PLGA films were studied. Both covalent and non covalent functionalization of carbon nanotubes were considered in order to control the interactions between PLGA and SWCNTs and to understand the role of the filler in the
biodegradation properties. Using a solvent casting process, different PLGA/SWNT nanocomposites were prepared and incubated using organic solution under physiological conditions. In-vitro degradation studies were conducted by measurements of weight loss, infrared spectroscopy, glass transition temperature and SEM observations as a function of the incubation time, over a 9-week period. All PLGA films were degraded by hydrolitical degradation. However, a different degradation mechanism was observed in the case of functionalized SWCNTs with respect to pristine material. It has been observed that system composition and SWCNTS functionalization play a crucial role on the autocatalytic effect of the degradation process. These studies suggest that the degradation kinetics of the films can be engineered by varying carbon nanotube (CNTs) content and functionalization. The combination of biodegradable polymers and CNTs opens a new perspective in the self-assembly of nanomaterials and nanodevices [69].

FUNCTIONALIZATION OF CARBON NANOTUBES FOR BIOLOGICAL APPLICATIONS:

Raw carbon nanotubes have highly hydrophobic surfaces, and are not soluble in aqueous solutions. For biomedical applications, surface chemistry or functionalization is required to solubilise CNTs improve biocompatibility and low toxicity. covalent and noncovalent two type of Surface functionaization of carbon Nanotubes [25]. Chemical reactions forming bonds with nanotube sidewalls are carried out in the covalent functionaization.

1. Covalent functionalization of carbon nanotubes

Functionalize carbon nanotubes have been developed by Various covalent reactions and oxidation being one of the most common. CNT oxidation is carried out with oxidizing agents such as nitric acid [26-27]. During the process, carboxyl groups are formed at the ends of tubes as well as at the defects on the sidewalls. Zeng et al. observed sp3 carbon atoms on SWNTs after oxidation and further covalent conjugation with amino acids28. Modification can be achieved by attaching hydrophilic polymers such as poly ethylene glycol (PEG) to oxidized CNTs, yielding CNT-polymer conjugates stable in biological environments. Now used covalently PEGylated SWNTs synthesized by this strategy for both In vitro and in vivo applications. [2+1] Cycloadditions can be conducted by photochemical reaction of CNTs with azides or carbine generating compounds via the Bingel reaction. A 1, 3-dipolar cycloaddition reaction on CNTs developed by Prato et al. is now a commonly used reaction . An azomethine-ylide generated by condensation of an α-amino acid and an α-aldehyde is added to the graphitic surface, forming a pyrrolidine ring coupled to the CNT sidewall. Functional groups e.g., amino terminated PEG introduced via a modified α-amino acid can be used for further conjugation of biological molecules [29-30].

FIG.6. Covalent functionaization of CNTS with surface activity
2. Noncovalent functionalization of carbon nanotubes

In contrast to covalent functionalization, noncovalent functionalization of CNTs can be carried out by coating CNTs with amphiphilic surfactant molecules or polymers. Since the chemical structure of the π-network of carbon nanotubes is not disrupted, except for shortening of length due to the sonication employed in the fictionalization process, the physical properties of CNTs are essentially preserved by the noncovalent approach. The polyaromatic graphic surface of a carbon nanotube is accessible to the binding of aromatic molecules via π -π stacking. Taking advantage of the π- π interaction between pyrene and the nanotube surface, Chen et al. showed that proteins can be immobilized on SWNTs functionalized by an aminereactive pyrene derivative. A recent study conducted by Wu et al. Beside pyrene derivatives, single-stranded DNA molecules have been widely used to solubilise SWNTs by virtue of the π-π stacking between aromatic DNA base units and the nanotube surface. A recent report by Moon et al. showed that DNA molecules coated on SWNTs could be cleaved by nucleases in the serum, suggesting that DNA functionalization of SWNTs might not be stable in biological environments containing nucleases [30-32]. Cherukuri et al used Tween-20 and a Pluronic triblock copolymer to noncovalently functionalize nanotube surfaces to reduce the nonspecific binding of proteins in the case of SWNT-based biosensors Pluronic tri-block polymer. An ideal noncovalent functionalization coating on CNTs for biological applications should have the following characteristics. First, the coating molecules should be biocompatible and nontoxic. Second, the coating should be sufficiently stable to resist detachment from the nanotube surface in biological solutions, especially in serum having high salt and protein contents [31-33]. Noncovalent functionalization of SWNTs by PEGylated phospholipids (PL-PEG) was developed by our group to meet the above requirements, including high water solubility of nanotubes and versatile functionalities Phospholipids are the major component of cell membranes, and are safe to use in biological systems. The two hydrocarbon chains of the lipid strongly anchor onto the nanotube surface with the hydrophilic PEG chain extending into the aqueous phase, imparting water solubility and biocompatibility [33].

Carbon Nanotubes: Some Toxicological Aspects:

Nanotechnology is the science involving manipulation of materials at the nanometer scale. Concerns over adverse and unanticipated effects on human health have also been raised. In fact, the same properties that make nanomaterials attractive from a technological and biomedical application could also make these novel materials harmful to human health and the environment. Numerous in vitro and in vivo studies have shown that Carbon Nanotubes and associated contaminants or catalytic materials that arise during the production process may cause oxidative stress and prominent pulmonary inflammation. Recent studies also suggest some similarities between the pathogenic properties of multi-walled Carbon Nanotubes and those of asbestos fibers. On the other hand, Carbon Nanotubes can be readily functionalized and several studies on the use of Carbon Nanotubes as versatile excipients for drug delivery and imaging of disease processes have been reported, suggesting that Carbon Nanotubes may have a place in the armamentarium for treatment and monitoring of cancer, infection, and other disease conditions. However, concerns about the potential toxicity, with a potential, of single-walled Carbon Nanotubes have been raised. Examinations on the acute and chronic toxicity of functionalized single-walled Carbon Nanotubes when injected into the bloodstream of mice were performed and clinical and laboratory parameters reveal no evidence of toxicity over 4 months. Histology and Raman microscopic mapping demonstrate that functionalized Single-Walled Carbon Nanotubes persisted within liver and spleen macrophages for 4 months without apparent toxicity [73]. CNTs are an important new class of technological materials that have numerous novel and useful properties. The forecast increase in manufacture makes it likely that increasing human exposure will occur, and as a result, CNTS are beginning to come under
toxicological scrutiny. Seeks to set out the toxicological paradigms applicable to the toxicity of inhaled CNTS, building on the toxicological database on nanoparticles (NP) and fibers. Relevant workplace regulation regarding exposure is also under consideration. CNTS could have features of both NP and conventional fibers, and so the current paradigm for fiber toxicology, which is based on mineral fibers and synthetic vitreous fibers, is discussed. The available literature suggests that CNTS may have unusual toxicity properties. The predicted increase in manufacture and use makes human exposure likely, and so CNTS are beginning to come under toxicological scrutiny in order to assess the hazard they present. The toxicological paradigms that can be used to investigate the toxicity of CNTS, building on the toxicological database on NP and fibers. Regulation regarding exposure to particles and fibers and make suggestions about potential problems associated with Nanotubes exposure. Toxicology of Carbon Nanotubes 17 measurement. The increasing use of CNT in industry means that the safety of those who are working with Nanotubes requires consideration of the workplace regulation in the light of the peculiar problems presented by monitoring such small materials and the uncertainty of the nature, mechanism, and exposure response for adverse effects. Until better information becomes available, CNTS should be considered in the same way as other biopersistent fibers in workplace risk assessments implying similar control and assessment approaches [74].

**DNA and carbon nanotubes as medicine:**

The identification of disease-related genes and their complete nucleotide sequence through the human genome project provides us with a remarkable opportunity to combat a large number of diseases with designed genes as medicine. 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.

**Carbon Nanotube Delivery of Anticancer Drugs**

In essence, carbon nanotubes are stable tubes of graphene. They have unique electronic properties and high surface areas. These properties, combined with their stability on the nanoscale, has made them a big focus in the development of novel nano materials, especially for use in solar cells. The field of carbon nanotubes is growing rapidly as many more research groups are attempting to exploit their novel properties. Recently, carbon nanotubes have been studied for their utility in the safe delivery of anticancer drugs. Delivery of carbon nanotubes poses several problems, due mostly to their extremely low aqueous solubility and high hydrophobicity. Carbon nanotubes can form aggregates in the blood, which are extremely susceptible to opsonization and phagocytosis. Additionally, chemical synthesis of carbon nanotubes requires the use of heavy metal catalysts, which can cause mammalian cell death if residual amounts are introduced into the body. Thus, functionalization of carbon nanotubes is necessary to ensure safety, efficacy, and biocompatibility. Acid treatments are commonly used to covalently attach functional groups to carbon nanotubes. Additionally, groups
can be added through non-covalent methods such as pi-stacking interactions. One common approach has been covalent attachment of varying molecular weight PEG groups. Drug molecules can then be conjugated to PEG, along with conjugation of folate, biotin, and arginine-glycine-aspartic acids for targeting purposes. Functionalization of carbon nanotubes with PEG and other moieties leads to a reduction in both in vivo and in vitro cytotoxicity. PEG functionalization allows for prevention of opsonization, extended circulating times due to avoidance of the RES, as well as renal excretion.

In addition to conjugation to PEG, drugs can be conjugated directly to the functionalized carbon nanotubes. This has proven effective with taxoid, paclitaxel, methotrexate, doxorubicin, and camptothecin derivatives. Conjugation to PEG chains has proven effective for doxorubicin and paclitaxel. Due to the large pi network of carbon nanotubes, drugs can also be physically attached via pi-stacking interactions. This is accomplished by simple dissolution of the drug and carbon nanotubes in appropriate media, followed by mixing. Finally, drugs can be introduced into the centre of carbon nanotubes via capillary action. This is accomplished by immersion of carbon nanotubes in a saturated drug solution. This method has proven problematic, however, if carboxyl or ester groups are present on the walls of the carbon nanotubes.

For the drugs mentioned above, conjugation with functionalized carbon nanotubes has shown reduced half maximal inhibitory concentrations (IC50) compared to free drugs. The exception to this is doxorubin, which has shown higher or lower IC50s depending on the cell target and the groups that are functionalized onto the nanotubes. Physical conjugation of drugs is preferred over covalent attachment, due to the preservation of the drug properties.

The mechanism of nanotube entry into the cell is not completely understood. Several methods of entry have been proposed, including endocytosis and passive transport via 'nanosyringe piercing' of the cell membrane by the nanotube. It is hypothesized that nanotube size and degree of hydrophilicity might be a determinant of the mechanism of entry. Larger, more hydrophilic functionalized tubes are believed to enter through endocytosis, while smaller, less hydrophilic tubes are believed to 'pierce' the membrane. To ensure proper delivery to the cell, nanotubes that are homogeneous in size and functionalization are desirable. This can pose some problems in the development of nanotube delivery devices, as commercially available carbon nanotubes are often polydisperse and contain fragments as well as aggregates. Commercially available carbon nanotubes must be purified through ultracentrifugation following their dissolution in aqueous media by surfactant mediated tip-sonication. This can be a very time consuming process that produces only small amounts (millilitres) of purified nanotubes in solution. This might be a hindrance to the utility of carbon nanotube drug delivery on the large scale, until better purification methods are developed.

Carbon nanotubes themselves provide many options in terms of length of drug exposure. Radiolabeling of single walled carbon nanotubes with indium 111 has shown they are renally excreted within 3 hours of IV injection. This would be desirable for drugs that only require short term exposure at the target site to elicit a therapeutic response. In contrast, drugs that require long term exposure for therapeutic effect can be conjugated to PEGylated nanotubes. These PEGylated nanotubes have been detected in spleen and liver macrophages 4 months following IV injection with no apparent toxicity observed. Additionally, single walled carbon nanotubes with carboxyl groups conjugated to them have shown a reduced pulmonary inflammatory response following inhalation. This property could be exploited to create new Carbon nanotubes (CNTs) constitute a class of nanomaterials that possess characteristics suitable for a variety of possible applications. Their compatibility with aqueous environments has been made possible by the chemical functionalization of their surface, allowing for exploration of their interactions with biological treatments for asthma and COPD.

The use of carbon nanotubes for drug delivery has not yet been perfected. Work still needs to be done in the areas of size homogenization, development of PEG alternatives to better introduce targeting ligands, studies on
biocompatibility and safety, increase in drug load capability, and studies on efficacy. Overall, the use of carbon nanotubes for drug delivery has shown promise and utility, but more development of the method is necessary before they can be considered viable treatment options.

Nanotube-Based Gene Delivery Vectors:
components including mammalian cells. Functionalized CNTs (f-CNTs) are being intensively explored in advanced biotechnological applications ranging from molecular biosensors to cellular growth substrates. We have been exploring the potential of f-CNTs as delivery vehicles of biologically active molecules in view of possible biomedical applications, including vaccination and gene delivery. Recently we reported the capability of ammonium-functionalized single-walled CNTs to penetrate human and murine cells and facilitate the delivery of plasmid DNA leading to expression of marker genes. To optimize f-CNTs as gene delivery vehicles, it is essential to characterize their interactions with DNA. In the present report, we study the interactions of three types of f-CNTs, ammonium-functionalized single-walled and multiwalled carbon nanotubes (SWNT-NH$_3^+$; MWNT-NH$_3^+$), and lysine-functionalized single-walled carbon nanotubes (SWNT-Lys-NH$_3^+$), with plasmid DNA. Nanotube–DNA complexes were analyzed by scanning electron microscopy, surface Plasmon resonance, Pico Green dye exclusion, and agarose gel shift assay. The results indicate that all three types of cationic carbon nanotubes are able to condense DNA to varying degrees, indicating that both nanotube surface area and charge density are critical parameters that determine the interaction and electrostatic complex formation between f-CNTs with DNA. All three different f-CNT types in this study exhibited upregulation of marker gene expression over naked DNA using a mammalian (human) cell line. Differences in the levels of gene expression were correlated with the structural and biophysical data obtained for the f-CNT:DNA complexes to suggest that large surface area leading to very efficient DNA condensation is not necessary for effective gene transfer. However, it will require further investigation to determine whether the degree of binding and tight association between DNA and nanotubes is a desirable trait to increase gene expression efficiency in vitro or in vivo. This study constitutes the first thorough investigation into the physicochemical interactions between cationic functionalized carbon nanotubes and DNA toward construction of carbon nanotube-based gene transfer vector systems.

The Potential Applications for Carbon Nanotubes:
Carbon Nanotube Technology can be used for a wide range of new and existing applications:

- Conductive plastics
- Structural composite materials
- Flat-panel displays
- Gas storage
- Antifouling paint
- Micro- and nano-electronics
- Radar-absorbing coating
- Technical textiles
- Ultra-capacitors
- Atomic Force Microscope (AFM) tips
- Batteries with improved lifetime
- Biosensors for harmful gases
- Extra strong fibers

Non Medical Applications:  Contents
1. Structural
2. Electromagnetic
3. Electoracoustic

4. Chemical

5. Mechanical

1. Structural

They are used for various purposes:

- Textiles – with the help of CNT we can make waterproof and tear resistant fabrics
- Body armor – using CNT fibres MIT was able to stop bullets and monitor the condition of the wearer [47].
- Concrete – CNTs in concrete increase the tensile strength and stops the crack propagation [48].
- Sports equipment – Stronger and lighter tennis rackets, bicycle parts, golf balls, golf clubs and baseball bats can be made.
- Bridges – CNT may be able to replace steel in suspension.
- Fire protection – Thin layers of buckypaper can significantly improve fire resistance due to the efficient reflection of heat by the dense, compact layer of CNT or carbon fibers [49].
- Aircraft using carbon nanotubes to increase strength and flexibility in highly stressed components [32].

2. Electromagnetic

- Optical ignition – A layer of 29% iron enriched single-walled nanotubes (SWNT) is placed on top of a layer of explosive material such as PETN, and can be ignited with a regular camera flash [50].
- Superconductor – Nanotubes have been shown to be superconducting at low temperatures [51].
- Ultra capacitors - MIT is researching the use of nanotubes bound to the charge plates of capacitors in order to dramatically increases the surface area and energy storage ability [52].
- Electromagnetic antenna – CNTs can act as antennas for radios and other electromagnetic devices [53].

3. Electro acoustic

- Loudspeaker – In November 2008 Tsinghua-Foxconn Nanotechnology Research Centre in Beijing announced that it had created loudspeakers from sheets of parallel CNT, generating sound similar to how lightening produces thunder. Near term commercial uses include replacing piezoelectric speakers in greeting cards [54].

4. Chemical

- Desalination – water molecules can be separated from salt by forcing them through networks of carbon nanotubes, which require far lower pressures than conventional reverse osmosis methods [55].
- Air pollution filter – CNT membranes can filter carbon dioxide from power plant emissions.
- Hydrogen storage – CNTs have the potential to store between 4.2 and 65% hydrogen by weight. If they can be mass produced economically, 13.2 litters (2.9 imp gal; 3.5 US gal) of CNT could contain the same amount of energy as a 50 litters (11 imp gal; 13 US gal) gasoline tank.

5. Mechanical

- Oscillator- Oscillators based on CNT have achieved higher speeds than other technologies (> 50 GHz).
- Infrared detector – The reflectivity of the buckypaper produced with “super growth” chemical vapour deposition method is 0.03 or less, potentially enabling performance gains for pyroelectric infrared detector [56-57].
- Thermal radiation – For thermal emission in space such as space satellites.
CONCLUSION

Current work is focused on the recent developments, particularly of Nanoparicles and Nanotubes. The materials developed from such as the hollow nanospheres, core shell structures, nanocomposites, nonporous materials, and nanomembranes will play a growing role in materials development for the Medical and Nonmedical industry.

As Carbon Nanotubes used in cancer treatment can guarantee 85% of the cure which other treatments cannot afford and having 100% site target with its body friendly nature adds to its advantage. CNTs and their composite materials are likely to become important biomaterials in the near future due to their superior and unique characteristics over conventional biomaterials. CNTs will find numerous applications as biomaterials and have important roles in the development of emerging technologies. CNTs are also promising new materials for molecular delivery in biological systems. Functionalized carbon Nanotubes (f-CNTs) are emerging as new tools in the field of Nanobiotechnology and Nanomedicine. A number of significant challenges remain to be overcome with superior CNTs for application as biomaterials, which will be of great benefit to large numbers of patients in the near future.

Nanomedical physicians of the 21st century will still make good use of the body's natural healing powers and homeostatic mechanisms, because all else equal, those interventions are best that intervene least.

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