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Carbon Nanotubes in Pharmaceutical Nanotechnology: An introduction to Future Drug Delivery System

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Abstract

Recent discoveries indicate that the materials are bought down in sizes in the range 1-100nm, these exhibits unique electrical, optical, chemical and pharmaceutical properties. Methods have now been established to obtain the monodispersed nanocrystals of various metallic and semi conducting materials, single walled and multiwalled nanotubes of carbon and other metallic and non metallic materials together with organic nanomaterials such as nanostructures composites with tailored functionalities. Carbon nanotubes (CNTs) have great impact on the development of newer methodologies and devices useful for the analysis and the detection of various types of chemicals. The detection sensitivity can be increased many folds. The extraordinary properties of carbon nanotubes have led to demonstration of several applications of CNTs. But commercial realization of these CNTs and CNTs based devices require consistent quality of CNTs and these should be free of any impurity. Such demanding requirements need development of elaborate purification and sorting of CNTs. In last few years, Carbon Nanotubes (CNTs) have shown unexpected advantages in the field of cancer treatment and drug delivery systems. Present review article discuss in brief about the methods of synthesis, with purification as well as sorting techniques for giving different grades to different types of CNTs. These show very good adsorption properties which helps in the detection of various chemicals, toxic agents etc. Research done using CNTs for cancer treatment is also discussed in brief.

Keywords: Carbon Nanotubes, Arc Discharge, Drug Delivery, Cancer Treatment, Detection of Toxins

Introduction

Drug particles in nanometer size range have unique characteristics that can lead to enhance performance in a variety of dosage forms .Scientists use nanotechnology to approach classical and novel drug delivery applications. Controlled and targeted delivery are the most enviable requirements expected from a carrier, which involves multi-disciplinary site specific or targeted approach .Nanoparticulate drug delivery system may offer platform of advantages over conventional dosage forms ,which includes improve efficacy, reduced toxicity, enhance biodistribution with improved patient compliance. Pharmaceutical nanoparticles are subnanosize based structure, contain drug or bioactive substances with in them and constituted of several tens or hundreds of atoms or molecules with a variety of sizes (from 5nm-300nm) and morphologies (amorphous, crystalline, spherical, needles, tubes etc.).

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 tumor is much needed. With the focus on these requirements the recent researches shows that Carbon Nanotubes holds good for desired drug delivery systems for the treatment of cancer disease, gene transfer and DNA applications. Functionalized carbon Nanotubes (f-CNTs) are emerging as new tools in the field of nanobiotechnology and nanomedicine.

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 nanometers, and serve as an instructive example of the Janus-like properties of nanomaterials

These shows unique chemical, physical and electrical properties [3,4].CNTs with 3Å diameter have been recently reported[5]The current review paper basically focused on the characterization of CNTs by all possible views to enhance their excellency towards pharmaceuticals nanotechnology .In present paper the different types of CNTs ,there methods of preparation & purification are discussed .The paper opens the recent trends towards CNTs in drug delivery .

Carbon nanotubes: some physiochemical aspects

Depending on their sheet direction and diameter,CNTs may classified in metallic and semiconducting categories. On depending on there atomic layer arrangement s there are of two types:

Single-Walled Carbon Nanotubes (SWCNTs).
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[6,7].The wave by which a Nanotubes is built from grapheme sheets does not only have an influence on the diameter chirality of CNTs but also for the electronic application [8,9].

Multi-Walled Carbon Nanotubes (MWCNTs).
The MWCNTs consists of multi walled grapheme sheets rolled up in concentric CNTs ,filling each other's inner cavities to end up with Nanotubes filled Nanotubes [10,11].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 [12,13]. SWCNTs are grapheme sheet rolled up into a tube form with nanodimensions .These are strikingly inert materials in the form of bundles due to Vander Waals attractive interactions. SWCNTs with additional grapheme tubes around the core of SWCNTs are called MWCNTs

Preparation of CNTS
Techniques have been developed to produce CNTs & well known techniques include arc discharge, laser ablation & chemical vapour deposition methods.

3.1 Arc Discharge Method for CNTs Synthesis.
CNTs were observed under microscope in carbon soot of graphite electrodes during arc discharge, by using current of 100 amps. It has been the most widely used method for CNTs were first developed by this method analysis of product shows that the yield by this method of CNTs, is approximately 30% by weight[14,15] .This method produces both SWCNTs and MWCNTs. However, these are quite short (50µ).

3.2) Laser Ablation Method for CNTs Synthesis
The method developed by smalley[16] et al.In laser ablation method, pulsed laser vaporizes a graphite target in a high temperature reactor while a noble gas is blad into the chamber. The CNTs develop on the cooler surfaces of the reactor, as the vaporized carbon condenses. The collection of tubes is done at water cooled surface in the reactor. The analysis of the products shows that the yield is 70 percent and produce primary SWCNTs .However, this method is more expensive then the arc-discharge method.

3.3) Chemical Vapour Deposition Method for CNTs Synthesis
In Chemical Vapour Deposition method, substrate is first prepared with the help of metal catalyst particles[6]. The nanoparticles of metals as catalyst can be produced by reduction of oxide or solid solution of these oxides. The Diameters of the CNTs to be grown are related to the size of metal catalyst[16]. This is controlled by the patterned Deposition of metal or annealing or by plasma etching of a metal layer. This substrate is heated to approximately 700˚C. To initiation of CNTs growth, gases are blad into the reactor process gas (NH_3, N_2 etc) and carbon containing gas (acetylene, ethylene etc) [17-20].Ghosal[21] et al. synthesize CNTs in the reactor by CVD and PECVD (Plasma Enhanced Carbon Vapour Deposition) method. In CVD method the thermally – heated CVD reactor having 14mm dia quartz reactor tube was used .The substrate composed of

four layers [n-type Si (100) substrate of resistivity 4-6 Ωcm, precleaned to remove greasy material from the surface .on this layer consecutive layer of SiO2, chromium & SiO2] respectively were deposited .catalyst (iron) was deposited on to the substrate using slandered RF sputtering technique .Argon gas was passed to prevent the catalyst oxidation. The mixture of NH3 and C2H2 (process and carbon gas) passed. Growth temperatures were maintained at 1123K& 1023K for different cases, and the characterization of developed tube was taken out in PECVD method. Catalyst pattern with 20μ iron dots, were made over n-Si (100) by photolithography and than sputtering and lift- of were performed. After the Fe loading, the chamber was evacuated initially to 10-5 Torr by DP & after putting on rotatory pump the pressure maintained at 5 Torr using H_2 purging at 50 sccm. After 30 minutes H_2 was stopped and there is striking of plasma between the electrodes with NH_3 flow starting of 100 sccm after reaching 873 K, additional NH_3 plasma treated for few minutes which cause the break of Fe particle into small islands .the C_2H_2 and NH_3 were used with flow for 10 minutes and the substrate was cooled in N_2 ambience.

The CVD method shows the most promising for industrial scaled deposition in terms of its economy. There are some additional advantages to the CVD method synthesis of CNTs .CVD method is applicable on growing Nanotubes directly on a desired substrate where the CNTs must be collected by other growth techniques [22].

Properties and purifications of CNTS

Purification includes the removal of carbonaceous and the catalyst particles .Purification processes includes one or more of the process including the dispersion, dry-oxidation, wet oxidation, chemical treatment, filtration (including chromatographic methods) and annealing [23-30].

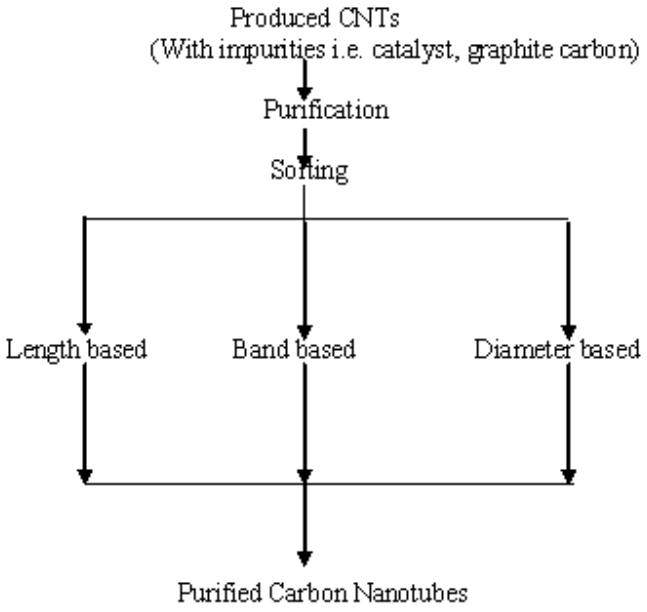

Figure1: Representing basic steps in CNTs purification

Technique like Ultrasonication is mainly used for the dispersion .Even after dispersion ,direct acid treatment is less effective for removal of catalyst particles due to carbon coating over them

.wet oxidation is coupled with dry oxidation to break these coatings and expose the catalyst particles with acid . This step is performed with strict control on oxidation temperature ,because the metal particle catalyze in discriminate oxidation of carbon and destroys the CNTs .To circumvent this problem ,Chiang[31-32],et al. proposed a scheme that starts with long, low-temperature oxidative cracking of shells (carbonaceous) which encapsulates the metal particles . It is performed by wet-oxygen by bubbling 20percent O2 in argon through water. This process removes coating over metals and the acid treatment become possible. Microwave heating[29-30]has also been employed to achieve the metal acid treatment which leads to other purification processes i.e. dry-oxidation, wet oxidation, filtration, annealing etc. Sorting of CNTs[33] give the idea to sort them into different grades with narrow distribution of band gap, length and diameter. CNTs first separated from the bundles and then the sorting procedures are performed. Fei[34], et al. used phosphotungstic acid (HPW) for separation of CNTs from bundles and the purification proceeded. HPW provides the static repulsion, the CNTs aggregates are divided into individual small bundles and turned into a stable solution by sonication in presence of HPW. Sorting based on length is important in light of potential applications. Techniques like chromatography (size-exclusion chromatography over DNA -wrapped CNTs), capillary electrophoresis, AC dielectrophoresis, DNA assisted separation ion exchange lipid chromatography, using structure discriminating surfactants (elimination of DNA),density-gradient ultracentrifugation, employing complete mixtures of surfactants ,dispersions – centrifugation etc. are some methods developed for sorting. Purity of CNTs can be evaluated in sense of qualitative and quantitative analysis .generally the scanning electron microscopy (SEM),transmission electron microscope(TEM), and scanning tunneling microscopy(STM) are used for purity evaluation .Other techniques such as thermal gravimetric analysis(TGA), near-infrared(NIR)spectroscopy[35], Raman spectroscopy[36]etc were introduced for quantitative analysis

5. CARBON NANOTUBES IN DETECTION

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[37].

5.1 Detection of Toxic Organophosphoric Compounds.

These Organophosphoric compounds are generally used in insecticides, pesticides .These chemicals are CNS affecting by inhibiting acetylcholine esterase which functions on acetylcholine neurotransmitters. To monitor these toxic compounds, the electrochemical detection is necessary[37].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 [38]. 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

5.2 Detection of Alkylating Agents Containing Sulphur And Nitrogen

Alkylating agents (nitrogen mustards; ethylenimes ;alkylsulphonates ;triazenes; piprazenes ;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[39].

5.3 Detection of Toxic Proteins and Micro Organisms

Schematic explores [14] gives the mechanism of CNTs using as biosensors devices.

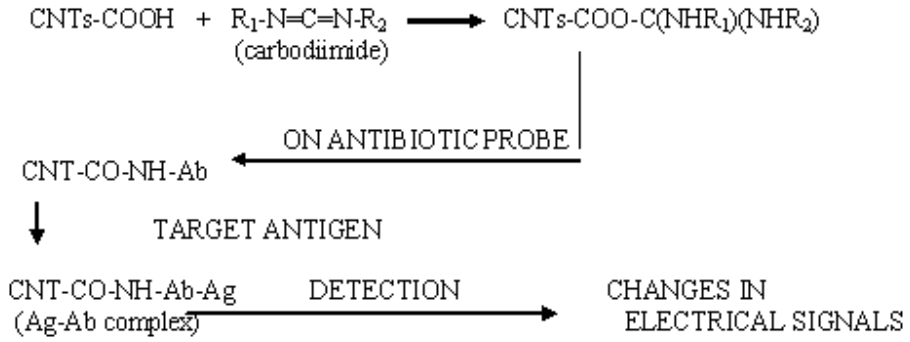

Figure 2: Targeting on antibody binding on COOH generated Carbon Nanotubes (showing binding of desired protein on CNTs)

By change in electrical signals, the CNTs can be used as a measuring platform for various toxic proteins [40] 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[40-45].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[46-47].

5.4 Detection of Chemical Substances

Colin[48]et 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 .This adsorption of chemicals on CNTs surface after the CNTs electrical properties, enable the CNTs to act as a gas sensor . Kong[49], et al. developed a gas sensor based on SWCNTs whose electrical conductance, on exposure to gaseous molecules, changes quickly (e.g. NO_2, NH_3).Young[50] et al. achieved ultrahigh sensitivity detection of NO2 gas using composite film of SWCNTs mash doped with alkanethiol monolayer protected gold cluster (MPC).

Penza[51],et al. fabricated micro acoustic sensor, for organic vapour detection at room temperature, in which SWCNTs were imbedded in Cadmium arachidate(CdA) ampiphillic matrix .

In addition Consales [52]et al. fabricated multilayer SWCNTs with different thickness and detected the toluene and xylene and the results showed higher sensitivity. Besides CNTs the

nanoparticles (NPs) of metal oxides are in under research and development, for example MCO_2O_4 (M=Ni,Cu,Zn), SnO_2.nanoholes array[53-54].

CARBON NANOTUBES IN DRUG DELIVERY

6.1 Carbon Nanotubes in Drug Delivery: Recent Trends

Functionalized carbon Nanotubes (f-CNTs) are emerging as new tools in the field of nanobiotechnology and nanomedicine. F-CNTs have been demonstrated to deliver proteins, nucleic acids, drugs, antibodies and other therapeutics. Emerging developments in this area are pointing towards the successful utilization of carbon nanotubes for drug delivery. This is because they can be easily manipulated and modified by encapsulation with biopolymers or by covalent linking of solubilising groups to the external walls and tips. The possibility of incorporating f-CNTs into biological systems has opened the way to the exploration of their potential applications in biology and medicinal chemistry. Within the different fields of applications (i.e., biosensors, composite materials, molecular electronics), one use of CNTs is as new carrier systems for the delivery of therapeutic molecules[55].Amidst the myriad of Drug Delivery Systems able to enhance delivery, absorption and intracellular uptake of a bioactive molecule while protecting it from deactivation, 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[56].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[57].Carbon Nanotubes have potential novel application in nanomedicine as biocompatible and supportive substrates, and as pharmaceutical excipients for creating versatile drug delivery systems[58]. 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-neoplastic treatment

Versatile physicochemical features of CNTs enable the covalent and noncovalent introduction of several pharmaceutically relevant entities and allow for rational design of nove 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. Ammonium-functionalized CNTs can also be considered very promising vectors for gene-encoding nucleic acids. 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 antigenic peptides can be developed as a new and effective system for

synthetic vaccine applications. What makes 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[59].

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. They have been modified with several molecules of therapeutic interest. Excellent progress has been made in harnessing the potential of Carbon Nanotubes for several drug deliveries and other applications[60].

Towards the drug delivery and treatment for cancer treatment, CNTs are very good candidates in the field of cancer therapy. For example, dispersion of single walled carbon nanotubes (SWCNTs) by ultrasonication with phospholipid-polyethylene glycol (PL-PEG) fragments it, thus interfering with its ability to block nonspecific uptake by cells. However, unfragmented PL-PEG promoted specific cellular uptake of targeted SWCNTs to two distinct classes of receptors expressed by cancer cells[61].

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 leukemia cell line) by means of confocal 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 (PEG-DXR) 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 axillary 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 sensoring and drug delivery on the cellular level. Filling carbon nanotubes with tailored materials realises nanoscaled 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(NH 3) 2Cl 2(O 2CCH 2CH 2CO 2H)(O 2CCH 2CH 2CONH-PEG-FA)] (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-NH 2) 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 folate-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 d(GpG) 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((NH 3) 2} 1,2-intrastrand d(GpG) cross-link in nuclear DNA[68] .

Nanocomposite films based on single wall carbon nanotubes (SWCNTs) and poly (DL-lactide-co-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].

By controlling size, nanoparticles can be effectively taken up into lymphatics. On this basis, various nanoparticles have been investigated for transporters of chemotherapeutic pharmaceuticals, but only a few were retained in the draining lymph node. Here, a technology using a magnetic carbon nanotubes (MNTs) delivery system is more effective in facilitating the targeted delivery of drugs in the lymphatic tissue more effectively. Chemotherapeutic agents were incorporated into the pores of functionalized MWCNTs synthesized with a layer of magnetite nanoparticles on the inner surface of the nanotubes. To improve drug delivery to cancer cells in the lymph nodes, individualized MNTs were noncovalently functionalized by folic acid (FA). By using an externally placed magnet to guide the drug matrix to the regional targeted lymph nodes, the MNTs can be retained in the draining targeted lymph nodes for several days and continuously release chemotherapeutic drugs. Selective killing of tumor cells over expressing the folate receptors (FRs) in the lymph nodes can be achieved, as FR is over expressed across a broad spectrum of human tumors[70]. The lack of solubility, nonbiodegradability, circulation half-life of 3-3.5 hours, biocompatibility, and immunogenicity are some limitations of CNTs which produce the challenges associated with the.These limitations indicate the need for modifications in order to explore the feasibility of CNTs as delivery vehicles[71].

6.2 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[72].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].

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