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Carbon nanotubes: Types, methods of preparation and applications

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Abstract
Carbon nanotubes (CNTs) are nanostructures derived from rolled graphene planes and possess various interesting chemical and physical properties. CNTs can be conjugated with various biological molecules including drugs, proteins and nucleic acid to afford bio-functionalities. CNTs exist as single (SWNTs), and multi-walled (MWNTs) structures. They present several interesting properties, such as high aspect-ratio, ultra-light weight, strength, high thermal conductivity and electronic properties ranging from metallic to semiconducting. The production of carbon nanotubes can be done by plasma based synthesis method or arc discharge evaporation method, laser ablation method, thermal synthesis process, chemical vapor deposition and by plasma-enhanced chemical vapor deposition. The CNTs are valuable in the field of drug delivery, blood cancer, breast cancer, brain cancer, liver cancer, cervical cancer, gene therapy, immune therapy, biomedical imaging, biosensors and tissue engineering. This review leads to a useful knowledge related to general overview, types, preparation methods and applications of CNTs.

Keywords: Arc discharge, Cancer, Laser ablation, Multiple walled, Nanotube, single walled

1. Introduction

Carbon nanotubes (CNTs) are nanostructures derived from rolled graphene planes and possess various interesting chemical and physical properties, have been extensively used in biomedicine. The discovery of carbon nanotubes by Iijima in 1991 using High Resolution Electron Microscopy (HREM) has stimulated intense experimental and theoretical studies on carbon nanotubes [1]. Carbon nanotubes are allotropes of carbon that have a nanostructure, which can have a length-to-diameter ratio more than 1,000,000. Theoretical studies have predicted exciting electronic properties for the nanotubes. The potential application of carbon nanotubes to the synthesis of nanowires has been demonstrated [2]. HREM is a robust approach for the characterization of microstructure and it is most suited to the study of nanotubes, it should be pointed out that the image obtained is a two-dimensional projection of a three-dimensional object [3].

CNTs can be conjugated with various biological molecules including drugs, proteins and nucleic acid to afford bio-functionalities [4, 5]. Moreover, the aromatic network existing on the CNT surface allows efficient loading of aromatic molecules such as chemotherapeutic drugs via stacking. The versatile chemistry of carbon nanotubes enables a wide range of their applications in biomedicine [6]. CNTs exist as single (SWNTs), and multi-walled (MWNTs) structures. They present several interesting properties, such as high aspect-ratio, ultra-light weight, tremendous strength [7], high thermal conductivity and remarkable electronic properties ranging from metallic to semiconducting [8]. It is not clear yet which of the two systems are more advantageous: SWCNTs offer the additional photoluminescence property that could be proficiently applied in diagnostics, while MWCNTs present a wider surface that allows a more efficient internal encapsulation and external functionalization with active molecules. They have both been used for diversified roles including biosensors, field-effect transistors (FET), and scanning probe elements [9].

2. Advantages of carbon nanotubes [10, 11]

- Biocompatible, Non-biodegradable and non-immunogenic nature.
- Highly elastic nature and have the possibility of intracellular delivery.
- May exhibit minimum cytotoxicity.
- Excreted by urine 96% and remaining 4% by faeces.
- Ultra-light weight and do not break down during processing.
- It has an open end on both sides, which makes the inner surface accessible and subsequent incorporation of species within nanotubes is particularly easy.
- Nanotubes have longer inner volume relative to the diameter of nanotubes for entrapment.
- CNTs are able to enter cells by spontaneous mechanism due to its tubular and nano needle shape.
- It has distinct inner and outer surface, which can he differentially modified for chemical biochemical functionalization.

3. Types of carbon nanotubes (CNTs):

The carbon nanotubes are of two types namely:

- Single walled carbon nanotubes (SWCNTs)
- Multiple walled carbon nanotubes (MWCNTs)

3.1. Single-wall carbon nanotubes (SWCNTs):

SWCNTs consist of a single cylindrical carbon layer with a diameter in the range of 0.4-2 nm, depending on the temperature at which they have been synthesized. It was found that the higher the growth temperature larger is the diameter of CNTs [12]. The structure of SWCNTs may be arm chair, zigzag, chiral, or helical arrangements [13]. The SWCNTs have an ultra-high surface area as large as 1300 m^2/g, which renders sufficient space for drug loading and bio conjugation [14]. In drug delivery, SWCNTs are known to be more efficient than MWCNTs. This is due to the reason that SWCNTs have ultra-high surface area and efficient drug-loading capacity. It has been found that a SWCNT anticancer drug complex has a much

longer blood circulation time than the anticancer drug on its own. This leads to more prolonged and sustained uptake of the drug by tumor cells via the enhanced permeability and retention effect. Once the functionalized of SWCNT releases the drug into a specific area, it is gradually excreted from the body via the biliary pathway and finally in the feces. This suggested that SWCNTs are suitable candidates for drug delivery and a promising nanoplatform for cancer therapeutics [15].

3.2. Multiple walled carbon nanotubes (MWCNTs):

MWCNTs consist of several coaxial cylinders, each made of a single grapheme sheet surrounding a hollow core. The outer diameter of MWCNTs ranges from 2-100 nm, while the inner diameter is in the range of 1-3 nm, and their length is one to several micrometers [16]. The sp^2 hybridization in MWCNTs, a delocalized electron cloud along the wall is generated which is responsible for the interactions between adjacent cylindrical layers in MWCNTs resulting in a less flexible and more structural defects [17]. MWCNTs structures can be split into two categories based on their arrangements of graphite layers: one has a parchment-like structure which consists of a graphene sheet rolled up around it and the other is known as the Russian doll model where layers of graphene sheets are arranged within a concentric structure [18].

Decoration of multiwall carbon nanotubes (MWCNTs) consists of depositing nanoparticles on the MWCNT walls or ends, bonded by physical interaction with potential applications in catalysis, biosensors, biomedical, magnetic data storage, and electronic devices. The various methods used for this purpose include precipitation, hydrolysis at high temperature, or chemical decomposition of a metal precursor [19].

4. Methods of carbon nanotube synthesis

High temperature preparation techniques such as arc discharge or laser ablation were first used to produce CNTs however nowadays these methods have been replaced by low temperature chemical vapour deposition (CVD) techniques (<800 ^{0}C), since the orientation, alignment, nanotube length, diameter, purity and density of CNTs can be precisely controlled in which technique [20]. Most of these methods require supporting gases and vacuum. However, gas-phase methods are volumetric and hence they are suitable for applications such as composite materials that require large quantities of nanotubes and industrial-scale synthesis methods to make them economically feasible. On the other hand, the disadvantages of gas-phase synthesis methods are low catalyst yields, where only a small percentage of catalysts form nanotubes, short catalyst lifetimes, and low catalyst number density [21].

During the CNT preparation there are always produced a number of impurities whose type and amount depend on the technique being used. The above mentioned techniques produce powders which contain only a small fraction of CNTs and also other carbonaceous particles such as nanocrystalline graphite, amorphous carbon, fullerenes and different metals (typically Fe, Co, Mo or Ni) that were introduced as catalysts during the synthesis. All these impurities interfere with most of the desired properties of CNTs and cause a serious impediment in characterisation and applications. Therefore, one of the most fundamental challenges in CNT science is the development of efficient and simple purification methods. Most common purification methods are based on acid treatment of synthesized CNTs.

4.1. Plasma based synthesis method or Arc discharge evaporation method

In Arc discharge methods, use of higher temperatures (above 1700 ^{0}C) for CNT synthesis, which usually causes the growth of CNTs with fewer structural defects in comparison with other techniques. The electric arc method, initially used for producing C_{60} fullerenes, is the most common and perhaps the easiest way to produce CNTs. MWCNTs were discovered in 1991 by Iijima by the arc-discharge evaporation technique. SWCNTs were produced subsequently in 1993 by the same [22]. In this method, electric arc created between two graphite electrodes leads to an extremely high temperature which is sufficient to sublimate carbon. Either MWCNTs or SWCNTs can he formed when the carbon vapours cools and condenses Generally, MWCNT are formed when there is no catalyst particles between two graphite electrodes; and the SWCNT can be generated by adding Fe, Ni, or Co as catalysts. The catalysts can be introduced by packing metal powder into a hole in the anode. The metal was consumed along with the graphite and created catalyst particles favouring small-diameter SWCNTs [23].

In case of MWCNTs, the purity and yield depended sensitively on the gas pressure in the reaction vessel. Different atmospheres markedly influence the final morphology of CNTs. They used DC arc discharge of graphite electrodes in helium and methane. By evaporation under high pressured methane gas and high arc current, thick nanotubes embellished with many carbon nanoparticles were obtained. However, thin and long MWNTs were obtained under a methane gas pressure of 50 Torr and an arc current of 20 A for the anode with a diameter of 6 mm [24]. Moreover, It was found that the variation of carbon nanotube morphology was more marked in the case of evaporation in methane gas than that in helium gas [25].

The SWNTs can be produced when the transition metal catalyst is used. The process of SWNTs growth in arc discharge utilizes a composite anode, usually in hydrogen or argon atmosphere. The anode is made as a composition of graphite and a metal, such as Ni, Fe, Co, Pd, Ag, Pt. etc. or mixtures of Co, Fe, Ni with other elements like Co-Ni, Fe-Ni, Fe-No, Co-Cu, Ni-Cu, Ni-Ti etc. The metal catalyst plays a significant role in the process yield. To ensure high efficiency, the process also needs to be held at a constant gap distance between the electrodes which ensures stable current density and anode consumption rate. In this process, unwanted products such as MWNTs or fullerenes are usually produced too [26].

4.2. Laser Ablation Method

The laser ablation method uses a pulsed and continuous laser to vaporize a graphite target in an oven, which is filled with helium or argon gas to keep pressure. The laser ablation is similar to the arc discharge, both taking advantage of the very high temperature generated, with the similar optimum background gas and catalyst mix observed. The very similar reaction conditions needed to indicate that the reactions probably occur with the same mechanism for both the laser ablation and electric arc methods [27]. SWNTs were prepared by continuous wave carbon dioxide laser ablation without

applying additional heat to the target. They found that the average diameter of SWNTs produced by carbon dioxide laser increased with increasing laser power [28].

Stramel *et al.*, have successfully applied commercial MWNTs and MWNTs-polystyrene targets (PSNTs) for deposition of composite thin films onto silicon substrates using PLD with a pulsed, diode pumped, Tm: Ho: LuLF laser (a laser host material LuLF (LuLiF4) is doped with holmium and thulium in order to reach a laser light production in the vicinity of 2 mm. They found that usage of pure MWNTs targets gives rise to a thin film containing much higher quality MWNTs compared to PSNTs targets [29]. Similarly, prepared MWNTs thin films were deposited by PLD techniques (with Nd: YAG laser) ablating commercially polystyrene-nanotubes pellets on alumina substrates [30].

4.3. Thermal Synthesis Process

Arc discharge and laser ablation methods are fundamentally plasma based synthesis. However, in thermal synthesis, only thermal energy is relied and the hot zone of reaction never goes beyond 1200 ^{0}C, including the case of plasma enhanced CVD. In almost all cases, in the presence of active catalytic species such as Fe, Ni, and Co, carbon feedstock produce CNTs depending on the carbon feedstock; Mo and Ru are sometimes added as promoters to render the feedstock more active for the formation of CNTs. In fact, thermal synthesis is a more generic term to represent various chemical vapor deposition methods. It includes Chemical Vapor Deposition processes, Carbon monoxide synthesis processes and flame synthesis [31].

4.4. Chemical vapor deposition (CVD)

Catalytic CVD synthesis is achieved by putting a carbon source in the gas phase and using plasma or a resistively heated coil to heat the gaseous carbon containing molecules. The heat is used to "crack" the molecule into reactive atomic carbon. The most frequently used catalysts are transition metals, primarily Fe, Co, or Ni. Sometimes, the traditionally used catalysts are further doped with other metals, e.g. with Au. Concerning the carbon source, the most preferred in CVD are hydrocarbons such as methane, ethane, ethylene, acetylene, xylene, eventually their mixture, isobutane or ethanol. In the case of gaseous carbon source, the CNTs growth efficiency strongly depends on the reactivity and concentration of gas phase intermediates produced together with reactive species and free radicals as a result of hydrocarbon decomposition.

These studies showed that growth efficiency strongly depends on the reactivity and concentration of gas phase intermediates produced as a result of complex gas phase reactions. On this basis, it can be expected that the most efficient intermediates, that have the potential of chemisorption or physisorption on the catalyst surface to initiate CNT growth should be produced in the gas phase. The overall kinetics of the growth process depend on the interaction, competition of gas phase and surface reaction [32].

Hydrocarbon molecules are often used as carbon sources, and ferrocene (FeCp2) as a catalyst. Yang *et al.*, obtained SWCNTs with a mean diameter of 3.23 nm through the catalytic decomposition of a hydrocarbon with hydrogen, helium as the carrier gases [33]. Zhang *et al.*, 2010 prepared MAVNTs with diameters of 40-60 nm by the catalytic decomposition of methane at 680 ^{0}C for 120 min using nickel oxide-silica binary aerogels as the catalyst [34].

4.5. Plasma Enhanced CVD (PECVD)

Plasma-enhanced chemical vapour deposition (PECVD) systems have been used to produce both SWNTs and MWNTs. PECVD is a general term, encompassing several differing synthesis methods. In general PECVD can be direct or remote. Direct PECVD systems can be used for the production of MWNT field emitter towers and some SWNTs. A remote PECVD can also be used to produce both MWNTs and SWNTs. For SWNT synthesis in the direct PECVD system, the researchers heated the substrate up to 550-850 ^{0}C utilized a CH_4-H_2 gas mixture at 500 mT, and applied 900 W of plasma power as well as externally applied magnetic field. The plasma enhanced CVD method generates a glow discharge in a chamber or a reaction furnace by a high frequency voltage applied to both electrodes. A substrate is placed on the grounded electrode. In order to form a uniform film, the reaction gas is supplied from the opposite plate. Catalytic metal, such as Fe, Ni and Co are used on a Si, SiO_2 or glass substrate using thermal CVD or sputtering. As such, PECVD and HWCVD as essentially a crossover between plasma-based growth and CVD synthesis. In contrast, to arc discharge, laser ablation, and solar furnace, the carbon for PECVD synthesis comes from feedstock gases such as CH_4 and CO, so there is no need for a solid graphite source. The argon-assisted plasma is used to break down the feedstock gases into C_2, CH, and other reactive carbon species (CxHy) to facilitate growth at low temperature and pressure [31].

5. Application of carbon nanotubes

The functionalization of CNTs makes them useful in a range of different applications. Their structure means that the tubes have an inner and an outer core which can both be modified by different functional groups. Thus the CNTs can be designed for very specific purposes. In the area of biomedicine, the applications of CNTs are investigated in especially four main fields: drug delivery, biomedical imaging, biosensors and scaffolds in tissue engineering [35].

5.1. Drug delivery

Specific drug delivery is an essential method used in medicine to deliver pharmaceutics to the specific place in the body where it is needed. The method shows great promise in cancer therapy since one of the biggest challenges in treating cancer is the severe side effects caused by the chemotherapy. The harsh medication used to treat cancer attacks not only the cancer cells, but also the healthy cells of the body, and this is what causes the side effects of the treatment.

5.2. Blood cancer

Leukemia is a cancer that begins in the bone marrow (the soft inner part of some bones), but in most cases, moves into the blood. It can then spread to other parts of the body, such as organs and tissues. Acute lymphoblastic leukemia (ALL), one of the four main types of leukemia, is a slow-growing blood cancer that starts in bone marrow cells called lymphocytes or white blood cells. Once these white blood cells are affected by leukemia, they do not go through their normal process of maturing.

An intensified targeted delivery of daunorubicin (Dau) to acute lymphoblastic leukemia was achieved by Taghdisi *et al.*, they developed a tertiary complex of Sgc8c aptamer (this aptamer targets leukemia biomarker protein tyrosine kinase-7),

daunorubicin, and SWCNT named as Dau-aptamer SWCNTs. Flow cytometric analysis viewed that the tertiary complex was internalized effectively into human T cell leukemia cell (MOLT-4 cells) but not to U266 myeloma cells. Release of Dau-loaded nanotubes were pH-dependent. In a slightly acidic solution of pH 5.5, Dau was released from complex in 72 h at 37 ^{0}C, whilst Dau-aptamer-SWNTs tertiary complex was pretty stable after the same incubation at pH 7.4 [36].

5.3. Breast cancer

Over expression of human epidermal growth factor receptor 2 (HER2), also known as c-erbB-2 or HER2/neu, is approximately 20-25% responsible for invasive breast cancer. Liu *et al.,* studied SWNT delivery of paclitaxel (PTX) into xenograft tumors in mice with higher tumor suppression efficacy than the clinical drug formulation Taxol. The PTX conjugated to PEGylated SWNTs showed high water solubility and maintains alike toxicity to cancer cells as Taxol *in vitro*. SWNT-PTX affords much longer blood circulation time of PTX than that of Taxol and PEG ylated PTX, leading to high tumor uptake of the drug through EPR effect. The strong therapeutic efficacy of SWNT-PTX is shown by its ability to slow down tumor growth even at a lower drug dose [37].

Pan *et al.,* investigated the efficiency of MWCNTs to deliver the gene to the tumor cell for cancer therapy. In this work, they fabricated MWCNTs modified with polyamidoamine dendrimer which were further conjugated with FITC-labelled antisense c-myc oligonucleotides (asODN). Human breast cancer cell line MCF-7 cells and MDA-MB-435 cells were incubated with modified MWCNTs (asODN-dMNTs). Fluorescence developed by the FITC revealed the cellular uptake of asODN-dMNTs within 15 min. These composites inhibit the cell growth in time and dose dependent means and down regulated the expression of c-myc gene (over expression of this gene amplify the expression of HER2) and C-Myc protein [38].

5.4. Liver Cancer

Polyamidoamine dendrimer modified CNTs (dMWCNTs) were fabricated for the efficient delivery of antisense c-myc oligonucleotide (asODN) into liver cancer cell line HepG2 cells. As ODN-dMWCNTs composites were incubated with HepG2 cells and confirmed to enter into tumor cells within 15 min by laser confocal microscopy. These composites inhibited the cell growth in time and dose dependent means and down regulated the expression of the c-myc gene and C-Myc protein. These composites exhibit maximal transfection efficiencies and inhibition effects on tumor cells when compared to CNT-NH -asODN and dendrimer (asODN) alone [38].

5.5. Brain cancer

Xing *et al.,* synthesized phospholipid-bearing polyethylene glycol (PL-PEG) functionalized SWCNTs conjugated with protein A, which was further coupled with the fluorescein-labeled integrin monoclonal antibody to form SWCNT-integrin monoclonal antibody (SWCNT-PEGmAb). Confocal microscopy revealed that SWNT-PEG-mAb showed a much higher fluorescence signal on integrin positive U87MG cells and presented a high targeting efficiency with low cellular toxicity, whilst, for integrin -negative MCF-7 cells, no obvious fluorescence was observed, which clearly reveals low targeting efficiency of the functionalized SWCNTs, demonstrating that the specific targeting of integrin positive U87MG cells was caused by the specific recognition of integrin on the cellular membrane by the monoclonal antibody [39].

5.6. Lymph Node Metastasis

Yang *et al.,* compared the *in vitro* and *in vivo* potential therapeutic effect of gemcitabine (GEM) loaded magnetic MWCNTs (mMWCNTs) with that of gemcitabine loaded magnetic-carbon particles (mACs). The result reflects that mACs and mMWNTs effectively enhanced GEM cytotoxicity *in vivo* and inhibited lymph node metastasis, especially when using high dose agents and/or applying implanted *in vivo* magnets. Systems offer the possibility to enhance therapeutic effects and decrease side-effects associated with chemotherapeutic agents by utilising the synergistic effects of magnetic targeting and lymphatic chemotherapy. Due to the super paramagnetic behaviour of mMWCNTs-GEM, their magnetic moments tend to align along the applied field leading to net magnetization which greatly affects the interaction of mMWCNTs-GEM with the cellular membrane and thus they were found to be superior than mACs-GEM in successful inhibition of lymph node metastasis after following subcutaneous administration under the impact of magnetic field [40].

5.7. Cervical Cancer

Wu *et al.,* developed a novel approach of utilizing natural biocompatible polymer chitosan for imaging the tumor cells. In this assay, SWCNTs were modified by chitosan (CHIT) fluorescein is othyocyanate (FITC). This was further conjugated with folic acid (FA), as mostly cancer cells overexpress folic acid receptors, to construct the functional FITC-CHIT-SWCNT-FA conjugate. These novels functionalized SWCNTs were found to be soluble and stable in phosphate buffer saline and can be readily transported inside the human cervical carcinoma HeLa cells [41]. Combining the intrinsic properties of CNTs, versatility of chitosan, and folic acid, FITC-CHIT-SWCNT-FA can be used as potential devices for targeting the drug into the tumor cells and also for imaging [42].

5.8. Gene therapy

CNTs can deliver a large amount of therapeutic agents, including DNA and RNA, to the target disease sites, Gene therapy and RNA have presented a great potential for antitumor treatment. The wire shaped structure (with a diameter matching that of DNA/siRNA) and their remarkable flexibility, CNTs can influence the conformational structure and the transient conformational changes of DNA RNA, which can further enhance the therapeutic effects of DNA is RNA. The treatment of a human lung carcinoma model *in vivo* using siRNA sequences, which led to cytotoxicity and cell death using amino-functionalized multiwalled carbon nanotubes (MWNT-NH^{3+}). This is believed to activate biologically *in vivo* by triggering an apoptotic cascade that leads to extensive necrosis of the human tumor mass followed by a concomitant prolongation of survival of human lung tumor-bearing animals [43].

5.9. Immune therapy

Chemotherapy faces the issues of accumulative toxicity and drug resistance, anti-tumor immunotherapy usually has few

adverse effects, good patient tolerance, and the potential to improve the prognosis significantly. CNTs have also shown the potential to boost the antigenicity of the carried proteins or peptides. Xu *et al.*, studied that MWNTs conjugated to tumor lysate protein will enhance the efficacy of an anti-tumor immunotherapy that employs tumor cell vaccine (TCV) in a mouse model bearing the H22 liver cancer [44]. The study showed that MWNTs conjugated to tumor lysate protein enhanced the specific anti-tumor immune response and the cancer cure rate of a TCV immunotherapy in mice [45].

5.10. Biomedical imaging

Besides having unique electrical and mechanical properties CNTs also have optical properties that are very useful in applications such as biomedical imaging. SWNTs have strong optical absorption from ultraviolet (UV) to near infra-red (NIR) regions and are useful in a range of different imaging techniques. These include photoacoustic imaging, Raman imaging, fluorescence imaging, and with functionalization of the CNTs also positron emission tomography (PET) imaging and magnetic resonance (MR) imaging [46].

Dai *et al.*, the CNTs were functionalized with a specific receptor for internalization into a specific cell type thus imaging these cells with very low autofluorescence background. In an *in vivo* study the biodistribution of SWNTs in live drosophila larvae was monitored by fluorescence imaging [47]. In photoacoustic imaging deeper tissue penetration can be achieved compared to most other optical imaging techniques. The technique makes use of certain light absorbing molecules (for example CNTs) that converts laser pulses delivered into the biological tissue to heat. Thereby transient thermoelastic expansion is induced giving rise to wideband ultrasonic emission which can then be detected by an ultrasonic microphone. With their high optical absorption in the NIR range. SWNTs make a useful contrast agent in this kind of biomedical imaging [48].

5.11. Biosensors

Biosensors are used for mentioning biological processes or for recognition of biomolecules and differ from other sensors by having a sensing element consisting of a biological material such as proteins, oligo- or polynucleotides or microorganisms. The most popular type of biosensors is the electrochemical biosensor and carbon materials have been used in these devices for a long time. Electrochemical biosensors are popular for detecting biomolecules in solutions because of their simplicity and the relative ease of calibration. These sensors are normally based on enzymatic catalysis of a reaction that either produces or consumes electrons and CNT-based biosensors incorporating enzymes have been produced for detection of glucose and other biomolecules [49].

5.12. Tissue Engineering

Besides all these applications, CNTs are also useful in enhancing tissue matrices. The matrix, or scaffold, has played an important part in tissue engineering, since this is what provides the structural support for the new tissue. It is responsible for defining the space the new tissue occupies, and for aiding the process of tissue development. Arrange of different criteria have to be fulfilled by such a scaffold. Among other things the scaffold should show: high mechanical strength, good biocompatibility (supporting cell adhesion, viability, proliferation and differentiation), biodegradability. All three criteria seem to be possible to meet using CNTs in the production of the scaffold and with superior results compared to other materials used in tissue engineering. Studies have shown that scaffolds of CNTs seem to be biocompatible both *in vitro* and *in vivo* when mixed with other materials such as in a polymer matrix of chitosan which itself is highly biocompatible.

6. Conclusion

Nanoparticulate as drug delivery systems is designed to improve the pharmacological and therapeutic properties of conventional drugs. The incorporation of drug molecules into nanocarrier can protect a drug against degradation as well as offers possibilities of targeting and controlled release. In comparison with the traditional form of drugs, nanocarrier-drug conjugates are more effective and selective; they can reduce the toxicity and other adverse side effects in normal tissues by accumulating drugs in target sites. In consequence, the required doses of drugs are lower. However, so far, the scientific paradigm for the possible (adverse) reactivity of nanoparticles is lacking and we have little understanding of the basics of the interaction of nanoparticles with living cells, organs and organisms. A conceptual understanding of biological responses to nanomaterials is needed to develop and apply safe nanomaterials in drug delivery in the future. Furthermore a close collaboration between those working in drug delivery and particle production is necessary for the exchange of concepts, methods and know-how to move this issue ahead.

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