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An overview: Nanomaterials & Nanotubes with its Structure and using Applications

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ABSTRACT

The nanotubes may consist of one up to tens and hundreds of concentric shells of carbons with adjacent shells separation of 0.34 nm. The carbon network of the shells is closely related to the honeycomb arrangement of the carbon atoms in the graphite sheets. Cancer is a generic term that encompasses a group of diseases characterized by an uncontrolled proliferation of cells. There are over 200 different types of cancer, each of which gains its nomenclature according to the type of tissue the cell originates in. Many patients who succumb to cancer do not die as a result of the primary tumor, but because of the systemic effects of metastases on other regions away from the original site. One of the aims of cancer therapy is to prevent the metastatic process as early as possible. There are currently many therapies in clinical use, and recent advances in biotechnology lend credence to the potential of nanotechnology in the fight against cancer. Nanomaterials such as carbon nanotubes (CNTs), quantum dots, and dendrimers have unique properties that can be exploited for diagnostic purposes, thermal ablation, and drug delivery in cancer. CNTs are tubular materials with nanometer-sized diameters and axial symmetry, giving them unique properties that can be exploited in the diagnosis and treatment of cancer. In addition, CNTs have the potential to deliver drugs directly to targeted cells and tissues. Alongside the rapid advances in the development of nanotechnology-based materials, elucidating the toxicity of nanoparticles is also imperative. Hence, in this review, we seek to explore the biomedical applications of CNTs, with particular emphasis on their use as therapeutic platforms in oncology.

Keywords: Nanotubes, CNT, Quantum, Therapies, Dendrimers, Chemotherapy.

1. Introduction

In the UK there are more than 293,000 newly diagnosed cases of cancer each year. More than one in three people will develop some form of cancer in their lifetime [1]. The most commonly diagnosed cancers among people in the UK are cancer of the breast and lung and colorectal cancer. Lung and colorectal cancer are the most common causes of death from cancer. The current arsenal against cancer includes surgical resection, chemotherapy, radiotherapy, or a combination of these three modalities [2]. In spite of improvements in the efficiency of treatments over the last few decades, the majority of conventional chemotherapeutic formulations (tablet, capsule, injection) pose multiple problems, such as systemic toxicity and a destructive “bystander” effect to neighboring cells. In addition, there are risks of nephrotoxicity, neurotoxicity, vascular toxicity, infertility, and thromboembolic complications, as well as the more commonly anticipated side effects, such as hair loss, nausea, and myocardial infarction.

Other problems incurred with conventional chemotherapy include the inability of drugs to access tumor sites specifically, and difficulty in clinical administration of drugs [3]. For these reasons, the two main areas that have been addressed by different research groups are destruction of cancer cells with minimum harm to normal body tissue [4] and delivery of high doses of drug molecules to tumor sites for maximum treatment efficacy [5].

Carbon nanotubes (CNTs), discovered by Japanese scientist Iijima in 1991 [6]. They are now considered to be a top class subject in academic researches as well as in various industrial areas. These nanomaterials are allotropes of carbon, made of graphite, ad have been constructed in cylindrical tubes with nanometer scale in diameter and several millimeters in length [7,8]. Carbon nanotubes have been first used as additives to various structural materials for electronics, optics, plastics, and other materials of nanotechnology fields. Since the beginning of the 21st century, they have been introduced in pharmacy and medicine for drug delivery system in therapeutics. Thanks to their high surface area, excellent chemical stability, and rich electronic polyaromatic structure, CNTs are able to absorb or conjugate with a wide variety of therapeutic molecules (drugs, proteins, antibodies, DNA, enzymes, etc.). They have been proven to be an excellent vehicle for drug delivery by penetrating into the cells directly and keeping the drug intact without metabolism during transport in the body [9] Carbon nanotubes (CNTs), in particular, have been introduced in pharmacy and medicine for drug delivery

system in therapeutics since the beginning of the 21st century. They have an ultra-small size, large surface area to mass ratio, and high reactivity, which are different from bulk .
materials (in microscale) of the same composition; in addition, they are able to adsorb or conjugate with a wide variety of therapeutic molecules (drugs, proteins, antibodies, DNA, enzymes, etc.) and they have been proven to be an excellent vehicle for drug delivery by penetrating into the cells directly and keeping the drug intact without metabolism during transport in the body [10-11]. Although these characteristics are associated with highly desirable properties (e.g. mechanical, electrical, and chemical) for medical uses, they are also the main factors that make them potentially dangerous to human health. Importantly, this risk is not only for patients, but also for workers including researchers, manufacturers and people involved in the preparation of the therapeutic infusions.

2. Carbon Nanotubes: Structures and Types

Carbon nanotubes (CNTs) consist exclusively of carbon atoms arranged in a series of condensed benzene rings rolled up into a tubular structure. This novel artificial nanomaterial belongs to the family of fullerenes, the third allotropic form of carbon along with graphite and diamond which are both natural sp2 (planar) and sp3 (cubic) forms, respectively [11,12,13]. Based on the number of layers, structures of CNTs are classified into two types: single-walled carbon nanotubes (SWCNTs) and multiwalled carbon nanotubes (MWCNTs) .

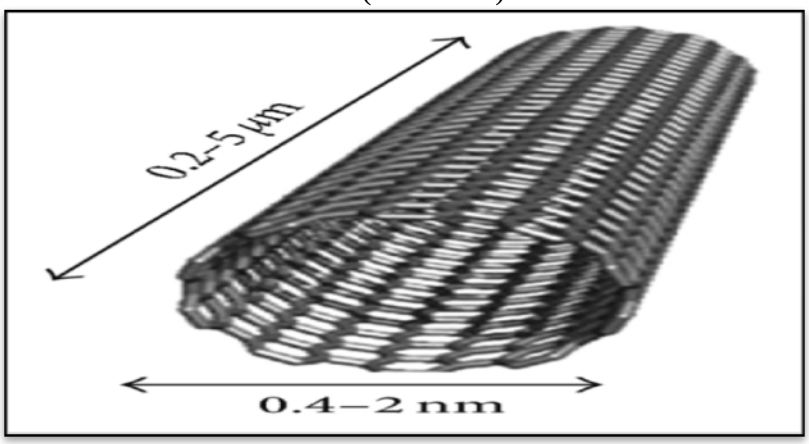

Figure 1: Conceptual diagrams of single-walled carbon nanotubes (SWCNT) (a) and multi-walled carbon nanotube.

SWCNTs consist of a single graphene cylinder with diameter varying between 0.4 and 2 nm, and usually occur as hexagonal close-packed bundles (Figure 2). MWCNTs consist of two to several coaxial cylinders, each made of a single graphene sheet surrounding a hollow core. The outer diameter of MWCNTs ranges from 2 to 100 nm, while the inner diameter is in the range of 1–3 nm, and their length is 0.2 to several μm [14].

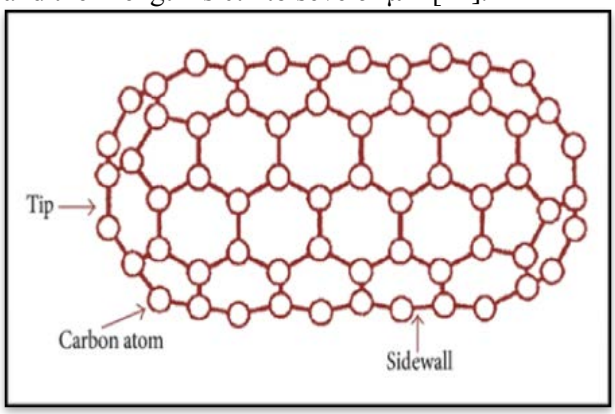

Figure 2: A carbon nanotube with closed ends

3. Properties Of Carbon Nanotubes

The most important properties of CNTs and their molecular background are stated below.

Chemical Reactivity

The chemical reactivity of a CNT is, compared with a graphene sheet, enhanced as a direct result of the curvature of the CNT surface. Carbon nanotube reactivity is directly related to the pi-orbital mismatch caused by an increased curvature. Therefore, a distinction must be made between the sidewall and the end caps of a nanotube.

Electrical Conductivity

The differences in conductivity can easily be derived from the graphene in conductivity can easily be derived from the grapheme. The resistance to conduction is determined by quantam mechanical aspects and was proved to be independent of the nanotube leanth.

Optical Activity

Theoretical studies have revealed that the optical activity of chiral nanotube disappears if the nanotubes become larger.

Mechanical Strength

Carbon nanotubes have a very large Young modulus in their axial direction. The nanotubes as a whole is very flexible because of the great length. Therefore, these compounds are potentially suitable for applications in composite materials [15]. In the past several years, there have been numerous papers that studied the behavior of carbon nanotubes in animals. The *in vivo* pharmacokinetics, biodistribution, long-term fate, and toxicology of CNTs, which are closely associated with their surface chemistries, sizes, doses, and administration routes, are rather complicated issues, and thus not the focus of this current review article [16]. Although there are certain debates on the clearance mechanism of nanotubes, the majority of studies have suggested that functionalized CNTs, when intravenously injected into animals (e.g., mice, rats), tended to accumulate in the reticular endothelial system including the liver and spleen, and were gradually excreted, likely via both fecal and renal excretion · Recent work by our group investigated the behavior of SWNTs *in vivo* at early time points after intravenous injection. The SWNTs were tracked using their intrinsic near-infrared photoluminescence (NIR PL) for several minutes after injection. Utilizing principle component analysis (PCA), our group was able to identify the time course of SWNTs through individual organs, including the liver, lungs, spleen, and kidneys .

3. Carbon Nanotubes Used for Cancer Therapy

By Drug Delivery

CNTs can be used as drug carriers to treat tumors [17, 18–19]. The efficacy of anticancer drugs used alone is restrained not only by their systemic toxicity and narrow therapeutic window but also by drug resistance and limited cellular penetration. Because CNTs can easily across the cytoplasmic membrane and nuclear membrane, anticancer drug transported by this vehicle will be liberated in situ with intact concentration and consequently, its action in the tumor cell will be higher than that administered alone by traditional therapy.

Thus, the development of efficient delivery systems with the ability to enhance cellular uptake of existing potent drugs is needed. The high aspect ratio of CNTs offers great advantages over the existing delivery vectors, because the high surface area provides multiple attachment sites for drugs [20].

By Local Antitumor Hyperthermia Therapy

The hyperthermia therapy using CNTs has been recently suggested as an efficient strategy for the cancer treatments. SWCNTs exhibit strong absorbance in the near-infrared region (NIR;700–1100 nm). These nano-materials are considered as potent candidates for hyperthermia therapy since they generate significant amounts of heat upon excitation with NIR light [21–22]. The photothermal effect can induce the local thermal ablation of tumor cells by excessive heating of SWCNTs shackled in tumor cells such as pancreatic cancer. Some progress in the technique has been achieved in recent years, and it has shown feasibility in clinical application.

By Antitumor Immunotherapy

Some studies have demonstrated that CNTs used as carriers can be effectively applied in antitumor immunotherapy [23]. This therapeutic consists of stimulating the patient's immune system to attack the malignant tumor cell In vitro, the conjugate of CNTs and tumor immunogens can act as natural antigen presenting cells (such as mature dendritic cells) by bringing tumor antigens to immune effector T cells; this action is due to the high avidity of antigen on the surface and the negative charges B Cells.

4. Applications of CNTS

Carrier for drug delivery

1. They can be used as lubricants or glidants in tablet manufacturing due to nanosize and sliding nature of graphite layers bound with venders Waals forces.
2. Functionalized carbon nanotubes are reported for targeting of amphoterecin.
3. Anticancer drug Polyphosphazene platinum given with nanotubes had enhanced permeability, distribution and retention in the brain due to controlled lipophilicity of Nanotubes.
4. The gelatin CNT mixture (hydro-gel) has been used as potential carrier system for biomedicals.

Genetic Engineering

In genetic engineering, CNTs and CNHs are used to manipulate genomes and atoms in the development of bioimaging genomes, proteomics and tissue engineering. The unwound DNA winds around SWNT by connecting its specific

nucleosides and causes ch ange in its electrostatic properties. Their tubular nature has proved them as a vector in gene therapy.

Artificial Implants

Normally body shows rejection reaction for implants with the post administration pain. But, miniature sized nanotubes and nanohormone get attached with other proteins and amino acids avoiding rejection. Also, they can be used as implants in the form of artificial joints without host rejection reaction. Moreover, due to their high tensile strength, carbon nano tubes filled with calcium and arranged/grouped in the structure of bone can act as bone substitute.

Preservative

Carbon nanotubes and nanohormones 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 zincoxide.

Diagnostic Tool

Protein-encapsulated or protein/enzyme filled nanotubes, due to their fluorescence ability in presence of specific biomolecules have been tried as implantable biosensors. Even, nanocapsules filled with magnetic materials, radioisotope enzymes can be used as biosensors. Nanosize robots and motors with nanotubes can be used in studying cells and biological systems.

Other applications

The linkages of other biomolecules such as genes, proteins, DNA, and biosensors to CNTs have been also assessed for gene therapy and tissue regeneration. CNTs can effectively transport the genes inside mammalian cells, maintaining their integrity. In fact, when bound to SWCNTs, DNA probes are protected from enzymatic cleavage and interference from nucleic acid binding proteins; consequently, DNA-SWCNT complex exhibits superior biostability and increased self-delivery capability of DNA in comparison to DNA used as free moieties. CNTs can interact directly with DNA through Van der Waals and hydrophobic forces [24].

SWCNTs have strong optical absorption from ultraviolet (UV) to near-infrared (NIR) regions, which can be used for photothermal therapy and photoacoustic imaging from the heat they generate from NIR light absorption. SWCNTs appear to be an excellent platform for biomedical molecular imaging [25].

Polymethyl methacrylate denture base material modified with multiwalled carbon nanotubes showed better results in terms of fatigue resistance, flexural strength, and resilience compared to conventional materials used in dentistry. Besides these main applications of CNTs, they have been shown as a powerful tool for enantiomer separation of chiral drugs and chemicals in the pharmaceutical industry.

6. Toxicity of CNT

The results of CNT toxicological assays found in the literature seem to be contradictory. Some preliminary in vitro tests have showed that CNTs are toxicologically benign to certain cells, while other further studies have indicated that CNTs, especially raw materials are potentially dangerous to many living systems [26, 27].

***In Vitro* Toxicological Studies of Carbon Nanotube**

Some in vitro cytotoxicity assessments of water dispersible single-walled carbonnanotubes(SWCNT) on A549 cells, a human lung cell line, confirmed that there was no intracellular localization of SWCNT in A549 cells and demonstrated that SWCNT could induce an indirect cytotoxicity by alteration of cell culture medium which caused a false-positive toxic effect [28-27]. Dumortier et al. observed that water soluble SWCNTs marked with fluorescein were nontoxic to cultures of mouse B- and T-lymphocytes and macrophages and preserved the function of these immune cells.

In Vivo Toxicological Studies of Carbon Nanotubes

According to the interesting review article about CNT toxicity recently published by Yang et al., [29] many in vivo toxicological assessments have been performed by IV or SC injections and gastrointestinal exposure with functionalized or dispersed SWCNTs or/and MWCNTs in different animals (rats, mice). The available safety data collectively indicate that CNTs are of low toxicity via various exposure pathways for biomedical applications. CNTs induced meaningful toxicity only when a very high dosage (60 mg/kg) under Polyethylene-Glycol-MWCNTs (PEG-MWCNTs) form was administrated in mice. The toxicity of SWCNTs is closely related to the oxidative stress in despite of the administration routes.

Human Toxicity of Carbon Nanotubes

As applications of functionalized CNTs linked with therapeutic molecules are still not assayed in man for clinical studies, most publications found in the literature suggested that pristine CNTs could be the source of occupational lung diseases in workers of CNT industries like asbestos pathology previously observed in man.

Based on several rodent studies in which test dusts were administered intratracheally or intrapharyngeally to assess the pulmonary toxicity of manufactured CNTs, these authors concluded that CNTs were capable of producing inflammation, epithelioid granulomas, fibrosis, and biochemical changes in the lungs.

7. Conclusion

This review on carbon nanotubes reveals the overview on structure, morphology, synthesis and purification methods of carbon nanotubes along with their properties, benefits and applications. The distinct structural properties of carbon nano particles, in particular their high aspect ratio and propensity to functional modification and subsequent use as carrier vectors, make them useful for pharmaceutical nano delivery. Carbon nanotubes have the added advantage of being potential nanodevices for controlled drug delivery. As the carbon nanotubes allow the easy functionalization on their sidewall and also in the core, many drugs can easily be sited on them, thus giving them the property as targets in drug delivery systems. The remarkable physical properties of nanotubes create a host of application possibilities, some derived as an extension of traditional carbon fiber applications, but many are new possibilities, based on the novel electronic and mechanical behaviour of nanotubes. It needs to be said that the excitement in this field arises due to the versatility of this material and the possibility to predict properties based on its well-defined perfect crystal lattice. Nanotubes truly bridge the gap between the molecular realm and the macro-world, and are destined to be a star in future technology. With the prospect of gene therapy, cancer treatments, and innovative new answers for life-threatening diseases on the horizon, the science of nanomedicine has become an ever-growing field that has an incredible ability to bypass barriers. The properties and characteristics of CNTs are still being researched heavily and scientists have barely begun to tap the potential of these structures. They can pass through membranes, carrying therapeutic drugs, vaccines, and nucleic acids deep into the cell to targets previously unreachable. They also serve as ideal non-toxic vehicles which, in some cases, increase the solubility of the drug attached, resulting in greater efficacy and safety. Overall, recent studies regarding CNTs have shown a very promising glimpse of what lies ahead in the future of medicine.

8. References

[1]. Westlake S, Cooper N. Cancer incidence and mortality: Trends in the United Kingdom and constituent countries, 1993 to 2004. Health Stat Q. 2008;38:33–46.

[2]. Utreja P, Jain S, Tiwary AK. Novel drug delivery systems for sustained and targeted delivery of anti-cancer drugs: Current status and future prospects. Drug Delivery, 2010;7:152–161.

[3]. Batra R, Davies JN, Wheatley D. Extensive arterial and venous thrombo-embolism with chemotherapy for testicular cancer: A case report. Cases J. 2009; 2:9082.

[4].Dhar S, Liu Z, Thomale J, Dai H, Lippard SJ. Targeted single-wall carbon nanotube-mediated Pt(IV) prodrug delivery using folate as a homing device. J Am Chem Soc. 2008;130: 11467–11476.

[5]. Liu Z, Chen K, Davis C, et al. Drug delivery with carbon nanotubes for in vivo cancer treatment. Cancer Res. 2008;68:6652–6660.

[6]. S. Iijima, “Helical microtubules of graphitic carbon,” Nature, vol. 354, no. 6348, pp. 56–58, 1991.

[7]. R. Hirlekar, M. Yamagar, H. Garse, M. Vij, and V. Kadam, “Carbon nanotubes and its applications: a review,” Asian Journal of Pharmaceutical and Clinical Research, vol. 2, no. 4, pp. 17–27, 2009.

[8]. B. G. P. Singh, C. Baburao, V. Pispati et al., “Carbon nanotubes. A novel drug delivery system,”International Journal of Research in Pharmacy and Chemistry, vol. 2, no. 2, pp. 523–532, 2012.

[9].Y. Zhang, Y. Bai, and B. Yan, “Functionalized carbon nanotubes for potential medicinal applications,”Drug Discovery Today, vol. 15, no. 11-12, pp. 428–435, 2010.

[10]. Liu Z, Chen K, Davis C, et al. Drug delivery with carbon nanotubes for in vivo cancer treatment. Cancer Res. 2008;68:6652–6660.

[11]. R. Hirlekar, M. Yamagar, H. Garse, M. Vij, and V. Kadam, “Carbon nanotubes and its applications: a review,” Asian Journal of Pharmaceutical and Clinical Research, vol. 2, no. 4, pp. 17–27, 2009

[12]. B. G. P. Singh, C. Baburao, V. Pispati et al., “Carbon nanotubes. A novel drug delivery system,”International Journal of Research in Pharmacy and Chemistry, vol. 2, no. 2, pp. 523–532, 2012.

[13]. Z. Liu, X. Sun, N. Nakayama-Ratchford, and H. Dai, “Supramolecular chemistry on water-soluble carbon nanotubes for drug loading and delivery,” ACS Nano, vol. 1, no. 1, pp. 50–56, 2007.

[14]. E. Bekyarova, Y. Ni, E. B. Malarkey, et al., “Applications of carbon nanotubes in biotechnology and biomedicine,” Journal of Biomedical Nanotechnology, vol. 1, no. 1, pp. 3–17, 2005.

[15]. Dhar S, Liu Z, Thomale J, Dai H, Lippard SJ. Targeted single-wall carbon nanotube-mediated Pt(IV) prodrug delivery using folate as a homing device. J Am Chem Soc. 2008;130:11467–11476

[16]. G. Prenciple, et al J Am Chem Soc, 131 (2009), p. 4783

[17]. W. Zhang, Z. Zhang, and Y. Zhang, “The application of carbon nanotubes in target drug delivery systems for cancer therapies,” Nanoscale Research Letters, vol. 6, pp. 555–577, 2011

[18]. H. Liao, B. Paratala, B. Sitharaman, and Y. Wang, “Applications of carbon nanotubes in biomedical studies,” Methods in Molecular Biology, vol. 726, pp. 223–241, 2011.

[19]. A. M. A. Elhissi, W. Ahmed, I. U. Hassan, V. R. Dhanak, and A. D'Emanuele, "Carbon nanotubes in cancer therapy and drug delivery," Journal of Drug Delivery, vol. 2012, Article ID 837327, 10 pages, 2012.
[20]. W. Zhang, Z. Zhang, and Y. Zhang, "The application of carbon nanotubes in target drug delivery systems for cancer therapies," Nanoscale Research Letters, vol. 6, pp. 555–577, 2011.
[21]. S. Y. Madani, N. Naderi, O. Dissanayake, A. Tan, and A. M. Seifalian, "A new era of cancer treatment: carbon nanotubes as drug delivery tools," International Journal of Nanomedicine, vol. 6, pp. 2963–2979, 2011.
[22]. A. M. A. Elhissi, W. Ahmed, I. U. Hassan, V. R. Dhanak, and A. D'Emanuele, "Carbon nanotubes in cancer therapy and drug delivery," Journal of Drug Delivery, vol. 2012, Article ID 837327, 10 pages, 2012.
[23]. M. S. Digge, R. S. Moon, and S. G. Gattani, "Applications of carbon nanotubes in drug delivery: a review," International Journal of PharmTech Research, vol. 4, no. 2, pp. 839–847, 2012
[24]. Graphene and carbon nanotube nanocomposite for gene transfection. Materials Science and Engineering: C 39: 288–298.
[25]. M. S. Digge, R. S. Moon, and S. G. Gattani, "Applications of carbon nanotubes in drug delivery: a review," International Journal of PharmTech Research, vol. 4, no. 2, pp. 839–847, 2012
[26].W. Yang, P. Thordarson, J. J. Gooding, S. P. Ringer, and F. Braet, "Carbon nanotubes for biological and biomedical applications," Nanotechnology, vol. 18, Article ID 412001, 12 pages, 2007
[27].Y. Chang, S. Yang, J. Liu et al., "In vitro toxicity evaluation of graphene oxide on A549 cells," Toxicology Letters, vol. 200, no. 3, pp. 201–210, 2011
[28]. C. P. Firme III and P. R. Bandaru, "Toxicity issues in the application of carbon nanotubes to biological systems," Nanomedicine, vol. 6, no. 2, pp. 245–256, 2010.
[29]. S. Yang, J. Luo, Q. Zhou, and H. Wang, "Pharmacokinetics, metabolism and toxicity of carbon nanotubes for bio-medical purposes," Theranostics, vol. 2, no. 3, pp. 271–282, 2012.