Research article

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A NOVEL APPROACH OF CARBON NANOTUBES IN DRUG DELIVERY SYSTEM

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ABSTRACT
Nowadays carbon nanotubes (CNT's) have achieved the concern in the field of novel drug delivery system. CNT's can be surface modification (example, functionalized) with certain groups in order to change their physicochemical and biological characteristics to improve the solubility of many drugs for efficiency tumour targeting as drug delivery. Due to the larger surface are, this unique characteristic of CNT's able to penetrate into target cells and free the drug molecules at the targeted site without leaking to non-targeted cells or broken up. CNT's also serve as a protein carrier, as vectors in gene delivery, delivery of vaccine and involved in treatment of broken bone. The method involved in production of nanosized CNT's including arc discharge, laser vaporization, chemical vaporization and electric arc technique. Furthermore, study structures of the CNT's are important to gain the properties and characteristics of CNT's, which including strength, kinetic, electric, thermal and etc. Those properties of CNT's will affect the efficient of delivery of drug to the target site. Therefore, the present review described about application, properties, production and classification of carbon nanotubes in drug delivery system.

Keywords: Single-walled carbon nanotubes, Double-wall nanotubes, MWNTs

INTRODUCTION

In 1991, first carbon tube is produced by Iijima**,** carbon tubes are cylindrical molecules created by rolling single (SWCNTs) or multiple (MWCNTs) layer of graphene sheets into a cylinder [1]. Since the start of the 21st century, carbon nanotubes (CNTs) have been bring in the pharmacy and medicine for drug delivery system in therapeutics. Thanks to their high surface area, outstanding chemical stability, and affluent electronic polyaromatic structure, CNTs are capable to adsorb or associate with a broad range of therapeutic molecules (drugs, proteins, DNA, enzymes, etc.). They have been proven to be an excellent medium for drug delivery by penetrating into the cells directly and preserving the drug unbroken without metabolism during transport in the body [2–5]. Many studies have verified that when bonded to CNTs, these molecules are delivered more efficiently and undamaged into cells than by traditional methods [3–5]. This fantastic discovery has opened a new technique for drug preparations that is totally different with traditional techniques used in pharmaceutical industry before and completely changed the anterior idea of pharmacology [3,4]. It has been first implemented to bind antineoplastic drug and antibiotic drugs to CNTs for cancer and infection treatments, respectively. Then, other linkages of biomolecules (included: genes, proteins, DNA, antibodies, vaccines, biosensors and cells) to CNTs have been also evaluated for cancer therapy, immunotherapy, tissue regeneration treatment and examination of different nutrition [6–10]. Therefore, in a very short time, CNTs have become the focal point of attention by scientists in a wide variety of preparation. In this paper, an overview of major synthesis method, characterization, classification and application of CNTs in the field of drug delivery system.

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CLASSIFICATION OF CARBON NANOTUBES

CNTs are seamlessly tubes of graphite sheets with nanosized diameter. They are included, "Single walled carbon nanotubes (SWNTs) and Multi walled carbon nanotubes (MWNTs)". Some nanotubes are opened at their terminal part; the others are closed with full fullerene caps. Carbon nanotubes can be either metallic or semi-conducting in nature by depend on graphite sheet direction and diameters. CNTs have highest theoretical strength when compared with all types of natural materials. It is 100 times tougher than steel, although their specific gravity are only one sixth that of the latter. Carbon nanotubes special benefit in the field of absorbing electro-magnetic radiation (EMR), field emission, thermal conducting, hydrogen storing, adsorbing and catalyzing process. Depending on number of layer of graphite sheets, CNTs can be separated as SWNTs, Double Walled Carbon Nanotubes (DWNTs) and MWNTs.

Single-Walled Carbon Nanotubes (SWNTs):

SWNTs have a diameter of about 1 to 10 nanometers, with a tube length that can be several thousands of times larger. Wrapping a one atom thick layer of graphite called graphene into a seamless cylinder can be conceptualize the structure of a SWNT (Fig A).

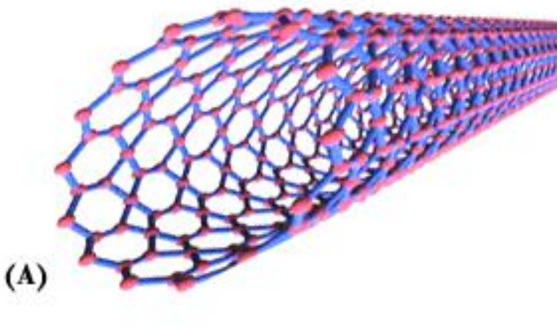

Figure-1: Shows structure of single-walled carbon nanotubes

Double-wall Nanotubes (DWNTs):

Double-wall Nanotubes (DWNTs) combine similar morphology and other properties of SWNT, as significantly improving their resistance to chemicals. DWNTs are concept systems for studying the interwall interactions affecting the properties of nanotubes with two or more walls (Fig B). This property, especially essential when functionality is required to add new properties to the nanotube. Since DWNTs are synthetic blend of both SWNT and MWNT, they display the electrical and thermal stability of the latter and the flexibility of the former [11].

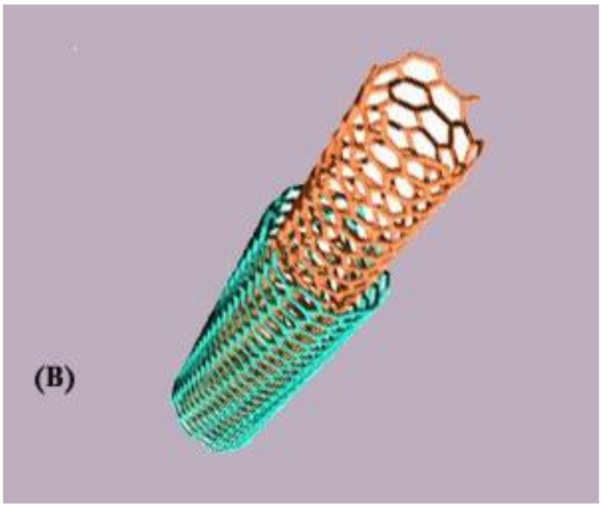

Figure-2: Shows structure of double-wall nanotubes

Multi-walled carbon nanotube (MWNTs):

MWNTs consists of multiple layers of graphite sheets coiled on themselves to form a tube shape (Fig C). There are two models which can be used to illustrate the structures of multiwalled nanotubes. The sheets of graphite are presented in concentric cylinders, known as the Russian Doll model. Such as, a SWNT in a larger single-walled nanotube. A single sheet of graphite is covered in around itself, like a rolled up newspaper, it known as Parchment model. The MWNT's are much stiffer than the SWNT's, particularly in compression.

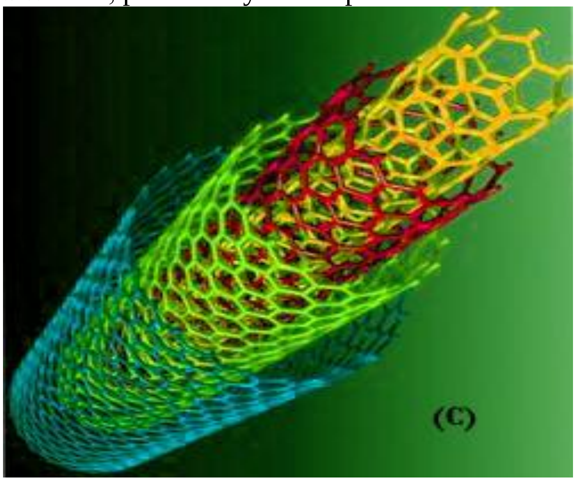

Figure-3: Shows structure of multi-walled carbon nanotube

SYNTHESIS OF CARBON NANOTUBES

The theory of CNT production is uncomplicated. All known manufacture techniques connected to a carbon feedstock, a metal catalyst, and heat. All techniques for producing of MWNTs, carbon arc discharge is the one exception that without require of any metal catalyst.

Arc discharge method:

Production of SWCNTs by arc discharge technique [12] in which applying a current of 40-100A in He(Helium) with the pressure of 100-700 torr at the electrode, the arc is generated. Due to the constant distance of electrode, electric discharge is produced which is collected in the inner wall of the chamber. Product is extracted by cesium oxide and washed with 1:1 concentration hydrochloric acid and dried at 100 degree Celsius to remove the impurities, fullerenes and catalyst.

Laser-Vaporization or Laser-Ablation Technique:

The laser-vaporization technique operates at similar conditions to arc discharge. Both techniques use the condensation of carbon atoms generated from the vaporization of graphite targets containing catalyst, such as Nickel, Cobalt and platinum [13-16], are vaporized by a laser. A Furnace (at~1200°C) is surrounding the quartz tube where the graphite target is placed. A constant gas flow (Argon or Helium) is passed through the tube in order to transfer the soot generated to a water-cooled Copper collector. The SWNTs generally condense as ropes or bundles containing of a number of individual SWNTs. By products such as amorphous carbon or encapsulated metal catalyst particles are also present. The laser-ablation technique favour the development of SWNTs; MWNTs are regularly not created with this method. Those SWNTs growth by arc discharge are believed to be comparable with the quality, length, diameter, and chirality distribution of material.

Catalyst Chemical Vaporization Method:

CNTs produced by catalytic chemical vaporization method could be very low cost in large scale. Flahaut et al. reported the synthesis of mixture of SWCNT and MWCNT by decomposition of H_2 /methane on nano composite powder of Fe aluminia [17].By addition of MgO (magnesium oxide) with ethanol solution of metal salts with corresponding concentration mixture is sonicated for one hour, the SWCNT is synthesized which reported in Colomer et al. By using of the rotary evaporator, the ethanol is eliminated and at 130°C the material is dried (for 12-15 hours). The obtained coarse material is grind into fine powder. Final portion of each catalyst is hydrogenated in H_2/N_2. SWCNT synthesis is carried out in fixed bed reactor at 1000oC with a typical reaction time for 10 mins for every synthesis; 1gm of catalyst is placed in center of reactor. Hydrogen and methane are used as catalyst. Carrier gas allows the methane and hydrogen to flow through fixed bet reactor. Once reaction completes catalyst are removed by using conc. HCl. 1gm of sample and 50ml of HCl is placed in to Sonicator for 15 mins and then filtered, washed and dried at 130°C [18].

Electric arc technique:

The laser production of SWCNT is reported by Journet, W. K. Masser and their co workers by electric arc technique [19]. Arc is produced between two electrodes under helium atmosphere. A voltage of 100A is applying to both cathode and anode which are drilled and filled with metallic catalyst and graphite powder. A voltage drop of 30V is produced between two electrode during this condition, rubbery products condensed on chamber wall and it forms web like structure between cathode and the reactor walls, at cathode end deposits black, very light porous material is formed around the cathode.

PROPERTIES OF CARBON NANOTUBES

There are four different physical properties associated with carbon nano tubes. Unique properties of CNTs are attributed to these properties. The section below attempts to discuss these properties reasonably.

Strength of nanotubes:

Carbon nanotubes are one of the strongest materials (in terms of tensile strength and elastic modulus) known to man. This strength results from the covalent Sp2 bonds formed between the individual carbon atoms. Since year of 2000, MWNTs was examined to find out the tensile strength in comparison to high-carbon steel. Tensile strength value of MWNT was found to be 63 GPa which is significantly higher than steel of 1.2 GPa. CNTs have very high elastic modulus of 1TPa (Tera Pascal). Under the applied strain, the tubes undergo changing in shape of plastic and tube undergoes fracture at a point of maximum strain by liberating energy.

Kinetic property:

MWNTs, multiple concentric nanotubes accurately fixed within one another, display a striking telescoping property by which an inner nanotube core may slide, approximately without friction, in the range of its outer nanotube shell thus forming an naturally ideal linear or rational bearing. This characterization has already been applied to build the smallest motor in the world and a nanorheostat.

Electrical property:

Because of symmetry and distinct electronic structure of graphene, the structures of nanotube greatly influence its electrical properties. Theoretically metallic nanotubes may have an electrical current density 1,000 times higher than metals like Ag(silver) and Cu(copper).

Thermal property:

Nanotubes are predicted to behave as excellent thermal conductors along the tube axis, a feature known as ‘ballistic conducting’, but at the same time a good insulator, lateral to the tube axis.

APPLICATION OF CARBON NANOTUBES

Cancer targeting:

It is well understand that cancer cell over express folic acid receptors, from various researches it was accomplished that nano carrier’s which was surface functionalized to which folic acid can be connected for cancer targeting. Furthermore CNTs have been noted that it has high retaining capacity to collect in the lymph nodes for longer period of time when compared with other nano carriers. Hence, CNTs may be used for targeting cancer cells as shown by various investigators. Such as cisplatin anticancer drug which was prepared into magnetic nano particles incorporated into MWCNTS and functionalized with folic acid. With external magnet, CNTs were direct to lymph nodes and free the drug for longer duration in order to suppress the tumor development. In a recent study by Yang et al. revealed anticancer drug gemcitabine was loaded into magnetic MWCNT, which was studied with mice module shows high activity against lymph node metastasis when formulation was injected subcutaneously [20]. Further, N. Gsahoo, et al. reported that camphothecin low water soluble drug filled into PVA(Polyvinyl Alcohol) functionalized MWCNT was very efficient for therapy of skin and breast cancer [21]. Addition, platinum anticancer drug carboplatin after integrating into CNTs presented to obstruct the proliferation of urinary bladder cancer cells in an *In vitro* examination. Conjugation of iron nano particles and folate molecules leading to develop the dual targeting drug nano carrier which reported by LIi and co worker (2011) ,which was loaded with doxorubicin and it showed that there was superior deliver of drugs to HeLa cells when compared to free doxorubicin [22]. Bio adhesive polymers such as chitosan and sodium alginate were used to enhance the aqueous dispersability of the nano tubes and folic acid was use to improve targeting properties.

Vaccine delivery via CNTs:

Peptide functionalized CNTs are capable of penetrating mammalian cell membrane and translocating to the nucleus. The basic concept for vaccine delivery by CNTs is to link an antigen to CNTs while retaining its conformation and inducing an antibody response with right specificity. CNTs can also bind to enzyme-linked immunosorbent assay plates, overcoming potential problems that may be encountered with the direct coating of peptide onto a solid support [23,24].

CNTs as protein carriers:

CNTs can transport various types of proteins into the cells. The proteins must have a molecular weight less than 80 KDa, and may be covalently or non-covalently bound to nanotube sidewalls. Proteins bound to SWNTs transported inside the cell by endocytosis. Streptavidin, Fibrinogen, Protein-A, Bovine Serum Albumin, Erythroprotien and Apolipoprotien transported inside the cell by CNTs following the said mechanism [25,26].

CNTs as vectors in gene delivery:

CNTs have considerably been used as a vector in gene delivery. A nanotube for its small size, cells don’t recognize them as harmful intruders. The most common gene therapy today involves modified viruses as the vector for gene delivery. The virus vector is associated with limitations like immune response which however not the case with CNTs [7].

Carbon nanotubes in the treatment of broken bones:

The success of bone grafting depends on the ability of the scaffold which assists the natural healing process. The scaffolds are made from a wide variety of materials, such as polymers or peptide fibers which however, associated with few drawbacks like low strength and many times may experience body rejection. Bone tissue is a natural complex of collagen fibers and hydroxyapatite crystals. Study unveils that the nanotubes can copy the similar role of collagen as the scaffold formation material for growth of hydroxyapatite into bone [28].

CONCLUSION

In this review, we have made an effort to provide the most contemporary overview possible of the major method of synthesis, application, classification and properties of CNTs in the field of drug delivery system. The SWCNTs and MWCNTs are proven to serve as safer and more efficiency compared to previous drug delivery technique. Functionalized CNTs can incorporated with therapeutic drugs molecules and carry them deep into targeted cell which previous drug unreachable. Exceptional of drug delivery system, CNTs also can be used in area of biomedical detection and imaging. Overview, the CNTs are proven useful in cancer treatment, due to quickly absorption and deep penetration to target site in the human body.

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