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Carbon Nanotubes as a Drug Delivery Systems

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.ABSTRACT

Carbon nanotubes (CNTs) are the most investigated materials of the twenty-first century, with a global goal of increasing industrial quantities due to their superior qualities for usage in a wide range of applications, including medicinal and other prospective applications. Because of their small size and outstanding optical, electric, and magnetic capabilities when used alone or with metal additions, these compounds have become increasingly attractive in a variety of sectors. These are commonly described as a graphene sheet wrapped into a cylindrical form. They're graphene cylinders with a diameter of roughly 12 nm and end caps comprising pentagonal rings. Drug transport, diagnostics, and biosensing are all possible therapeutic applications for carbon nanotubes. Carbon nanotubes that have been functionalized can also be used as vaccine delivery methods. The core idea is to attach the antigen to carbon nanotubes while maintaining its shape, resulting in a particular antibody response. With the growing interest in nanotechnology research in this subject, it is envisaged that a wide range of CNT applications will be investigated in the future.

Keywords:Carbon nanotube,SynthesisPurification,Functionalization,PharmacokineticApplication are some of the terms used in this paper.

1 INTRODUCTION

The main goal of creating nanocarrier drug delivery systems is to improve the therapeutic efficacy of therapeutically active compounds or reduce their toxicity. Liposomes, which are spherically shaped vesicle nanocarriers, are commonly used to do this. Carbon nanotubes (CNTs), on the other hand, are essentially cylindrical carbon atom molecules. CNTs are graphene sheets rolled into a seamless cylinder with a high aspect ratio with diameters as small as 1 nm and a length of several micrometres, which can be open ended or capped. Single-walled carbon nanotubes (SWNTs) are generated from a single graphene sheet, whereas multiwalled carbon nanotubes (MWNTs) are made from many graphene sheets [1, 2]. (Figure 1). Due to their unique physical and chemical properties and potential applications in a wide range of fields, from electronic devices and sensors to nanocomposite materials of high strength and low weight, these allotropes of carbon have sparked intense interest since their discovery in 1991 by Kijima [1]. CNTs that aren't pristine aren't soluble. CNT bioapplications were only possible following the invention of techniques to functionalize these molecules with organic groups and make them soluble. They can adsorb or conjugate with a wide range of medicinal compounds due to their large surface area. CNTs can thus be surface engineered (i.e., functionalized) to improve their aqueous phase dispersibility or to offer the proper functional groups to bind to the required therapeutic material or target tissue to elicit a therapeutic effect. CNTs may aid in the penetration of the attached therapeutic molecule through the target cell to treat diseases [3–6], and Figure 2 shows a recent example of CNTs with a range of functional groups important to cancer therapy [7]. Here, we give an overview of the therapeutic applications of carbon nanotubes, with a particular focus on cancer treatment.

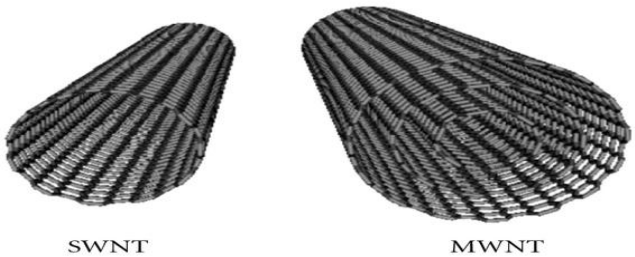

Figure.2-Carbon nanotubes (CNTs) are graphene sheets rolled into a cylindrical shape.

MWNTs are made up of several sheets, whereas SWNTs are made up of just one sheet.

2. METHODS FOR OPENING, FILLING AND CAPPING CARBON NANOTUBES

Carbon nanotubes are endcapped, as previously stated, and hence there are essentially two options for drug loading: filling carbon nanotubes during synthesis or after synthesis. Adding the contents of the nanotubes in-situ is a less efficient way, yielding roughly 10%, whereas the post-synthesis process can be more regulated, resulting in yields of 50-100 percent (Mantoux, 2002). The method to use is determined by the material to be introduced into the CNT. Melting temperature, reactiveness, surface tension, and material sensitivity are among the criteria. The ends of CNTs must be opened after synthesis, which can be done by running electric currents through the tube, attacking the tube with acid that corrodes the angled regions of the tube the most (i.e., the ends), or oxidizing with carbon dioxide (Tsang et al., 1994; Ajayan et al., 1993). Foreign particles can be introduced into CNTs in two ways. The method of attaching a functional group to CNTs falls into one of these categories (Ebberson et al., 1996). Because carbon is relatively inert, oxidation is utilized to provide a more reactive attachment surface.

3.1 Drug loading

The medicine to be given by the CNT can be delivered either internally or externally. Internalization, also known as encapsulation, relies on Van der Waals forces for insertion into the CNT and is best suited to pharmaceuticals that are sensitive to external conditions and easily degraded.

3.2 Drug targeting

Drug delivery is inherently indiscriminate in traditional cancer treatments utilizing chemotherapeutic drugs. The toxic drug treatment is thus administered to both tumor and normal cells, with the result that, at best, the patient experiences several unpleasant side effects and, at worst, the patient dies as a result of the drugs' toxicity.

Figure.3- drug targeting genetic mutation.

3.3 Passive and active targeting

Previous attempts at antibody-mediated drug delivery have mainly failed due to the antibodies' loss of specificity when bound to drug molecules. It was discovered that employing nanotubes to support antibodies had no effect on their characteristics, and thus had no effect on their ability to target. Functionalisation is a direct effect of targeting approaches such as active or passive targeting. The macromolecule's inertness and physical size "hide" it from the immune system, resulting in passive targeting. To avoid cellular opsonisation (the susceptibility of a macromolecule to absorption by phagocytes, resulting in its destruction) by the innate immune system, CNTs must be nanosized, but also functionalized with molecules/polymer chains such as PEG that do not promote an adaptive immunological response. A trade-off is required because the CNT must be large enough to take advantage of the EPR effects.

3.4 Crossing the blood-brain barrier

The difficulty of many medications to reach tumors is also a problem. Drugs can't kill brain tumors because of the blood-brain barrier. Because CNTs may traverse the blood-brain barrier, this difficulty can be solved by attaching chemotherapeutic medicines to them.

3.5 Drug delivery targeted to lymphatic system

Many malignancies spread through the lymphatic system. Cancer metastasis can be effectively halted using drug delivery devices that target the

lymphatic system. Polyacrylic acid (PAA) can be attached to CNTs using radical polymerization, making them very hydrophilic. Fe3O4-based magnetic nanoparticles can be adsorbed on the PAA-CNT surface by coprecipitation.

3.6 Functionalisation

Carbon nanotubes with highly hydrophobic surfaces are insoluble in aqueous solutions, but pure CNTs are insoluble in all liquids. Functionalisation is a solution to this problem. Functionalisation of carbon nanotubes is a chemical synthesis method that involves introducing desired functional groups onto the walls of carbon nanotubes for a variety of purposes, resulting in functionalised carbon nanotubes (f-CNT). The goal of this method in cancer treatment is to improve biocompatibility within the body, encapsulation propensity and solubility, multimodal drug administration, and imaging, all while imparting specific qualities linked to the desired function. Covalent and noncovalently bonded modifications to CNTs fall into two groups.

3.7 Covalent bonding

Strong chemical connections between nanotubes and the connected molecule emerge from covalent chemical bonding of polymer chains to CNTs. Grafting to and grafting from processes, which entail the addition of premade polymer chains or the polymerisation of monomers from surface generated initiators on CNTs, respectively, have been devised to graft molecules based on their changing properties. Functionalisation reactions are used to react to the surface of CNT in both the to and from approaches.

3.8 non-covalent bonding

According to the literature, non-covalent bonding of molecules to CNTs is the most extensively employed technique of drug administration. The features of an ideal non-covalently functionalized CNT should be specified; the closer they are, the more beneficial they are in biological tasks. This can be accomplished by coating amphiphilic chemicals onto CNTs in micelle-like structures.

4. EVOLUTION STUDIES

4.1 Electronics for Carrying Out Evolution

The computationally expensive algorithms were executed on a PC via a serial interface provided by an Amed microcontroller. To give signals and record the output of the material system, the med was in charge of regulating a set of analogue-to-digital and digital-to-analogue converters. The inputs and outputs, which were in the form of voltage signals, were buffered to prevent measurement errors caused by high resistance material samples.

4.2 Electrode Fabrication

For the evolutionary training experiments, electrodes were made on glass, while for the SEM imaging, they were fabricated on silicon substrates. To create an electrically insulating support, the silicon has a 100 nm oxide layer. Electrodes in chromium/gold metal were constructed using traditional etch-back photo-lithography in both cases. The gold seed layer was 50 nm thick and the chromium seed layer was 5 nm thick. To hold the material while it was being tested on the glass substrates for evolutionary tests, an M3 nylon washer was affixed to the electrode array with epoxy.

5. Applications

The expense of carbon nanotubes has been a major impediment to their use. As of March 2010, retail pricing for single-walled nanotubes had dropped from approximately $1500 per gram in 2000 to around $50 per gram of as-produced 40–60 percent by weight SWNTs. The retail price of 75 percent by weight SWNTs as-produced in 2016 was $2 per gram.

The current use and application of nanotubes has mostly been limited to bulk nanotubes, which are a mass of disorganized nanotube fragments. Although bulk nanotube materials will never have the same tensile strength as individual tubes, such composites may have enough strength for many purposes. Carbon nanotubes in bulk have already been employed as composite fibres in polymers to improve the bulk product's mechanical, thermal, and electrical qualities.

Easton-Bell Sports, Inc. has collaborated with Savex Performance Materials to use carbon nanotube technology into a variety of bicycle components, including flat and riser handlebars.

Amory Europe Oy is a company that produces.

6. Factors found to affect CNT toxicity

The following is a list of factors that have been observed to influence the degree of toxicity of CNTs (Thurn Herr et al., 2011):

- Concentration / dose of CNTs.
- SWCNTs or MWCNTs. Length of the tubes
- Catalyst residues left over during synthesis or functionalization
- Degree of aggregation · Oxidisation · Functionalist

7. Kinetics of CNTs

The delivery, absorption, and transportation of CNTs as drug carriers must all be considered in order to achieve the desired treatment outcomes. Oral and injection routes of CNT delivery, such as subcutaneous injection, abdominal injection, and intravenous injection, have been explored. When CNTs are delivered by various routes, there are several mechanisms of absorption and transportation. The absorbed CNTs are transferred by blood or lymphatic circulation from the administration sites to the effect-relevant areas. Absorption is the first critical step for drug carriers to perform their drug-delivery mission after administration. CNTs have been shown to be capable of being absorbed in studies. Physically shorter CNTs that are orally delivered have also been shown to be absorbed via the columnar cells of the intestinal mucous membrane, as validated by transmission electron microscopy.

8. PROPERTIES OF CARBO NANOTUBES: -

The orderly production of carbon atoms in graphene cylinders results in a number of features. Carbon nanotubes are a big cylindrical molecule made up of a hexagonal arrangement of sp2 hybridized carbon atoms (the C-C distance is around 1.4). CNTs' walls are made up of single or multiple layers of graphene sheets, with single-walled carbon nanotubes (SWCNTs) being generated by rolling up a single sheet and multi-walled carbon nanotubes (MWCNTs) being formed by rolling up multiple sheets (MWCNTs). Both SWCNTs and MWCNTs have fullerenes, a hemispheric arrangement of carbon networks distorted up by the graphene sheet, capped at both ends of the tubes (Figure 1). MWCNTs' graphene layers have an average interlayer separation of 0.34 nm, generating individual tubes with a greater outer diameter (2.5 to 100 nm) than SWCNTs (0.6 to 2.4 nm). MWCNTs are more prone to contain structural faults, resulting in a less stable nanostructure, whereas SWCNTs have a better wall. Three key properties of CNTs have been used in the medical field:

- Their small size.
- Their high surface area to volume ratio.
- Their ability to contain chemicals.

Carbon nanotubes can be manufactured in sizes tiny enough to pass through tumor pores or transfer DNA (Singh et al.,2005) The high surface-to-volume ratio provides an excellent platform for chemical transfer and reactions required for ultra-sensitive glucose detection.

9. ADVANTAGES OF CARBON NANOTUBES OVER CONVENTIONAL CANCER THERAPY: -

Access to tumorous cells and the risk of operating near or on crucial organs make traditional treatments like surgery difficult. In addition, targeted chemotherapy and radiation treatment is limited. Overall, current treatment options are ineffective at preventing cancer's spread or recurrence. Nanomedicine allows medications to be delivered to specific locations. Because malignant cells are on the nanoscale, highly efficient drug delivery is possible (Misran et al., 2010). This offers two significant advantages. First, the total amount of drug required is lower, which is primarily an issue with more expensive drugs. Furthermore, there is no need for a solvent to transport the medicine, which implies that any negative health consequences from the solvent can be avoided. Second, a reduced concentration of the toxin is given to other places of the body while the protective nanocarrier remains intact. As a result, the patient experiencing therapy will experience less health adverse effects. Another benefit of nanocarriers is that a variety of medications can be attached for therapeutic, diagnostic, targeted, and barrier avoidance purposes, thereby allowing a toolkit to enable treatment tailored to each patient's cancer.

10. Medical applications: -

1) Nanotubes coupled to a chicken antibody have been demonstrated to be effective in destroying breast cancer tumors in lab experiments.
2) Proteins released by one type of breast cancer cell bind antibody-carrying nanotubes. The nanotubes then absorb light from an infrared laser, which incinerates the nanotube as well as the tumor to which it is attached.
3) Delivering quantum dots and proteins into cancer cells using nanotubes as a cellular scale needle.
By providing a carbon nanotube framework for new bone material to form, the healing process for damaged bones can be improved.
4) Combining carbon nanotubes with biological systems has the potential to dramatically advance medical science, particularly in the areas of diagnostics and illness treatment. Nothing has been fully developed or finalized yet, but we are making progress.
5) Let's look at an anti-cancer medicine as an example. When a patient receives frequent chemotherapy, he loses his hair and experiences various side effects for a variety of reasons, one of which is that chemotherapy does not simply destroy "bad" cells.

6) It also kills healthy cells in addition to tumor cells. That is why scientists are working so hard to prevent this from happening. Carbon nanotubes may be able to help with this. When nanotubes are subjected to infrared light, they heat up to 160°F (70°C) in just 120 seconds, according to Stanford University researchers.
7) They just destroy cancer cells if they are introduced within them. Infrared has little effect on cells that do not contain nanotubes, according to tests. This could lead to the creation of a cancer-killing drug. Carbon nanotubes could also help improve gene therapy.
8. Assume a damaged or absent gene can be replaced with a gene from the outside. However, this is compounded by the fact that DNA cannot cross through the cell membrane. A transporter is required, and modified carbon nanotubes fill this duty.

11. Biocompatibility of CNTs and its Enhancement: -

The following are the characteristics of an ideal (non-covalent) functionalization coating:

- Nontoxic and biocompatible coatings should be used.
- Amphiphilic coating molecules should have a low critical micelle concentration so CNT remains stable once removed from solution
- Coating should have functional groups that can be bioconjugated with antibodies or other molecules to create various CNT conjugates for various applications.

To make biocompatible CNT, it must be low in toxicity and easy to process by the body. This is made possible by attaching polyethylene glycol (PEG) to phospholipids, as both elements are easily eliminated from the body over time. The toxicity of a substance is considerably lowered when it is functionalized. The circulation time in vivo, which in vitro testing cannot establish, is a troublesome aspect of many contemporary medications. Low circulation times diminish effectiveness because the medicine is eliminated from the body too rapidly, whereas high circulation times harm healthy tissue and increase side effects. For example, f-CNT can tune the blood circulation half-life to increase tumor absorbance while minimizing buildup in the skin dermis. Biodistribution is influenced by the degree of functionalization with polymers such as PEG and the length of these chains. In in vivo investigations on mice, increasing the extent (i.e., density) of PEGylation (PEGylation is the process of covalent bonding of polyethylene glycol polymer chains) and polymer chain lengths enhanced circulation time. PEGylation densities of 10% and chain lengths of 5k monomer units were found to have optimal half-life circulation durations of 12-13 hours, with high uptakes in tumors but low uptakes in other cells, such as the dermis of the skin. This is an excellent illustration of how functionalization may be fine-tuned to improve f-CNT in vivo behavior and applications in general. Cell absorption is influenced in part by the length of CNTs, which is another factor to consider when developing design requirements for CNT carrier systems. CNTs with submicron lengths were shown to efficiently aggregate in cells, implying that surface chemistry plays only a minimal role in absorption. The majority of studies made use of.

12. Toxicity of Carbon nanotubes: -

Carbon nanotubes are a high-profile, nano-scale technology that is being examined in several technological disciplines, as noted in this study. However, worries regarding potential toxicity issues with carbon nanotubes have grown in recent years, and there is currently a dearth of evidence and understanding about their influence on biological systems. Because CNTs are likely to be widely used in the future, it is critical to understand their effects on biological systems before they can be used in mainstream medication delivery. Nanomaterials' most appealing qualities for biomedical applications, such as their small size, vast surface area, high reactivity, and high aspect ratio, are also major contributors to potential cytotoxicity. Although there may be various mechanisms generating cell damage, it is assumed that DNA damage is the most common. According to the findings, SWCNTs can cause negative cellular responses by activating oxidative stress-related molecular signaling. When tested on mice, several researchers have discovered that CNTs can behave similarly to asbestos fibres. When the structures of these molecules are compared, this issue becomes understandable. Above are structures of chrysotile asbestos (left) and MWCNT (right). The fundamental issue with asbestos (and the concern with CNTs) is that they quickly become airborne and are taken into the lungs due to their nano-scale and light weight. Asbestos has been linked to pulmonary scarring (pulmonary fibrosis). While there is reason to be concerned about the potential resemblance to asbestos fibers, research suggests that high dosages of industrially manufactured MWCNTs do not cause cell death in lung epithelial (tissue) in the same manner as asbestos fibres do. Furthermore, long-term exposure to pristine MWCNTs at low concentrations had no significant negative consequences. CNT toxicity is influenced by a number of factors. A list of variables that have been discovered to have an impact.

13. CONCLUSION: -

Despite the fact that a number of medications have been given using carbon nanotubes, the issues surrounding CNT toxicity remain ambiguous in the field of CNT technology for cancer treatment. There are multiple conflicting studies revealing both toxic and non-toxic behavior. [1st Table] This appears to be attributable in part to the type of the research being carried out. That is, there is no genuine standard against which to compare results. Because of the wide range of characteristics that have been proven to affect CNT toxicity, toxicologists will need to pay close attention to this field in the future. For example, some evidence suggests that large concentrations of Fe (iron) impurities on CNTs increase the reported cytotoxic reaction, whereas other study indicates the contrary. Clearly, more research is needed in this area before CNT technology may be used to cure cancer. However, it is an incredibly promising application of nanotechnology that merits more investigation, as conventional cancer therapy methods are both indiscriminately destructive and only partially effective.

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