CARBON NANOTUBES: A PROMISING NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT:

Background: CNT's are nanomaterials that are one-dimensional structure, which are considered to be the 2nd generation allotrope of carbon. They usually constitute pure carbon and carbon atoms are present in a repetitive manner in a hexagonal pattern and thus make up cylindrical tubes. CNT's can be functionalized such that bio molecules can be attached on their surfaces by covalent or noncovalent linkages and the needle like shape of the CNT's enable them to perforate cellular membranes and delivers the carried drug molecules to targeted sites. They have the ability to carry drugs to the specific site as they are hollow and much smaller than blood vessels.

Methods: Previously published articles relating carbon nanotubes as an effective drug delivery system have been collected and reviewed.

Observations: Some of the important properties of CNT that makes them eligible as a novel nanomaterial for potential drug delivery are their characteristic configuration, excellent functionalisation ability and dynamic surface modification properties. They have high elasticity which enhances the chances of intracellular drug delivery. CNT's have emerged as an efficient drug delivery system in the field of medicine for targeted delivery of drug molecules to the specific site of action. The large inner volume of CNTs allows enclosing of both low and high molecular weight drugs. It also permits encapsulation of both hydrophilic as well as lipophillic drugs. They have exclusive characteristics like ability to absorb pathogenic molecules and heat conduction that would enhance their use in the medical field.

Keywords: Nanotubes, allotrope, carbon, nanomaterial, drug delivery system, encapsulation

INTRODUCTION:

Since its accidental discovery in1991 by sumo Ijima, CNT 's have received much attention from scientific communities in most areas of science as well as engineering and continues to be one of the most researched material in this century. They have unique chemical, optical, electrical and structural properties that make them potential drug delivery systems that can be functionalized with variety of bio molecules like antibodies, proteins or DNA. This contributes to targeted drug delivery to particular tissue, organs or cells.

CNT's are nano tubes that are one-dimensional structure, which are considered to be of the 2nd generation allotrope of carbon. They usually constitute pure carbon and carbon atoms are present in a repetitive manner in a hexagonal pattern and thus make up cylindrical tubes. They are also considered to be coming under the fullerene family [(1).]

Some of the important properties of CNT that makes them eligible as a novel nanomaterial for potential drug delivery are their characteristic configuration, excellent functionalisation ability and dynamic surface modification properties[(2).] CNT's can be functionalized such that bio molecules can be attached on their surfaces by covalent or noncovalent linkages and the needle like shape of the CNT's enable them to perforate cellular membranes and delivers the carried drug molecules to targeted sites [(3)].Drug delivery systems improves the pharmacological and therapeutic profile as well as the efficacy of the drug and lower the chances of off target drug delivery [(4)].

CNT's have the ability to carry drugs to the specific site as they are hollow and much smaller than bloodvessels.DNA and protein molecules are attached to the inside and outside of the nanotubes by various methods, thus provides it the potential to target and destroys the infected or cancerous cells. CNT's with enzyme attached can act as a long term enzymatic biosensor that could simultaneously detect and measure various biological molecules [(5)].

This study is aimed at reviewing various literatures on carbon nanotubes and determining their role as an efficient drug delivery system

CLASSIFICATION OF CARBON NANOTUBES

Based on their shape and structural confirmations, they are of 4 types

1. Single walled CNT's
2. Double walled CNT's
3. Multi walled CNT's
4. Functionalised CNT's

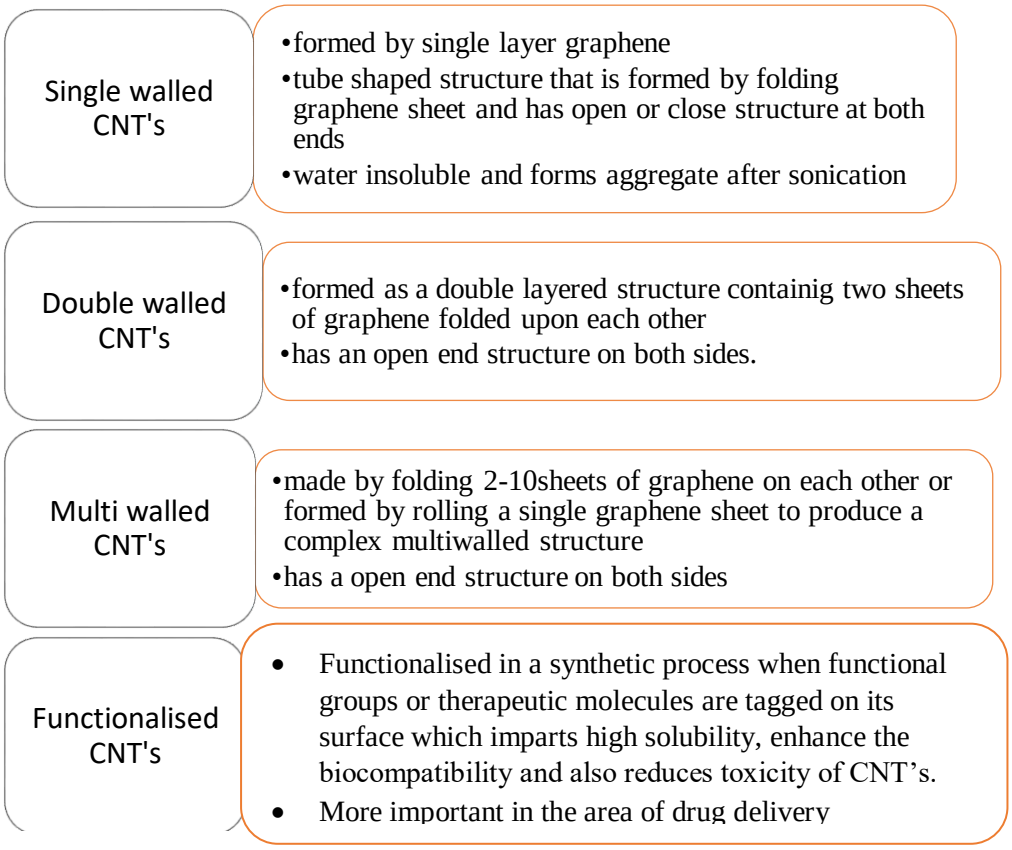

Fig 1: a) Structure of (a) SWCNT, (b) DWCNT, and (c) MWCNT. Note: SWCNT, single-walled carbon nanotubes; DWCNT, double-walled carbon nanotubes; MWCNT, multiwalled carbon nanotubes. (Image source [28])

METHOD OF PREPARATION OF CARBON NANOTUBES:

Previously CNT's were prepared by high heating of carbon black and graphite at specified temperature conditions but thus produced CNT's had uneven physical properties which lead to development of advanced methods like chemical vapour deposition, laser ablation method etc..Among these for bulk production and laboratory scale preparation, CVD is the most used method. Some other advanced techniques for production include plasma-enhanced CVD, laser assisted CVD and high pressure CVD [6].

PROPRETIES OF CARBON NANOTUBES:

- Carbon nanotubes are large cylindrical molecules consisting of a hexagonal arrangement of sp2 hybridized carbon atoms with a diameter ranging from few nanometres to millimetres [7].
- There has been a considerable wide spread interest in the conductivity property of CNT's which has been shown to be the function of their chirality as well as diameter [8].
- Another interesting property of carbon nanotubes is their electrical resistance which changes significantly when other molecules attach themselves to the carbon atoms [9].
- Nanotubes have larger inner volume compared to the diameter of nanotubes for entrapment of drugs or bio molecules for targeted delivery
- They have high elasticity which enhances the chances of intracellular drug delivery [10,11].
- They are excreted 96%by urine and 4% by faeces [12].

FILLING OF CARBON NANOTUBES:

Carbon nanotubes are usually end capped and thus for drug loading there are essentially two approaches which include the filling of carbon nanotubes during synthesis or after synthesis. The suitable approach depends on the drug material that is to be inserted into the CNT. The criteria to be considered while filling of CNT's include melting temperature, reactiveness, surface tension and sensitivity of the material. Post-synthesis filling of CNTs implies that the ends of the tube which is closed, needs to be opened .This can be done by passing electric currents through the CNT, through attacking the CNT with acid which corrodes the angled parts of the tube or by oxidization using carbon dioxide [13].

CARBON NANOTUBES FOR DRUG DELIVERY:

CNT's have emerged as an efficient drug delivery system in the field of medicine for targeted delivery of drug molecules to the specific site of action. The large inner volume of CNTs allows enclosing of both low and high molecular weight drugs. It also permits encapsulation of both hydrophilic as well as lipophillic drugs [7].It can also act as a controlled drug delivery system for releasing of drugs for a prolonged period of time. The intrinsic spectroscopic properties of CNTs which include characteristics

such as Raman and photoluminescence provides an additional advantages for tracking as well as real-time monitoring of drug delivery efficacy in human body[14].

CONTROLLED DRUG DELIVERY APPLICATION:

The application of carbon nanotubes has been researched widely as a controlled release drug delivery system owing to their ability to release therapeutic molecules in a controlled manner for a prolonged period of time [15]. Advancement in the research of CNTs has paved way to so called "smart bio-nanotubes" as the next-generation nanomaterial which has supramolecular properties when compared with the conventional nanotubes. These are trilayered structures which has a tubulin layer enclosed by a lipid bilayer. The important formulation variables that regulate the rate of drug release from such bio-nanotubes are the thicknesses of protein lipid as well as protein coats. Recently, several pharmaceutical formulations of CNTs have been developed for use in various controlled drug delivery applications.

TARGETED DRUG DELIVERY APPLICATION:

Functionalized nanotubes have been vastly used for targeted delivery of nucleic acids, proteins, antibodies, drugs, and other therapeutics agents to their respective sites of action. The use of CNT's for targeted delivery is primarily employed in treating various malignant disorders, like choriocarcinoma, carcinoma of cervix, breast cancer, prostate cancer, brain gliomas, and testicular tumors[16]. Functionalization of chitosan on the surface enhances the cell attachment to the sidewalls of the nanotubes, thus resulting in the desired targeted release to the cells with improved drug absorption [17].

- **Cancer-targeting application**: In cancer chemotherapy it is common to destroy the healthy cells along with cancerous cells, thus causing severe side effects. In such cases, CNT's are helpful in treating cancer cells safely without affecting the nearby healthy tissues. CNT's which are loaded with chemotherapeutic agents can effectively deliver them to the malignant cells, due to high cellular uptake. The CNTs provides effective delivery of drugs into the tumors cells, thus enhancing their permeability and retention (EPR) effect [18].
- **Brain-targeting application**: Many disorders of CNS like Alzheimer's disease, dementia, Parkinsonism, mood disorder, AIDS, and meningitis (both viral and bacterial) remain untreated because of restricted entry of therapeutic substances into the blood brain barrier. Drug molecules fail to enter into the brain by crossing the BBB due to their poor lipophilicity. CNTs have been effectively used for the delivery of drug molecules to the brain primarily because of their ability to cross the BBB .MWCNTs are more effective in delivering neuropharmaceutical agents to brain microglial cells compared to the SWCNTs. Also, CNTs are useful in treating neurodegenerative disorders owing to their magnetic properties [19].
- **Lymphatic targeting application**: Drug targeting to lymphatics is important for treating disorders of lymphatic systems and also for targeting drug molecules to the reticuloendothelial system (RES). Magnetic nanotubes can be used for targeting drug molecules to the lymphatic system by selective functionalisation on their surface. MWCNTs can be retained in the lymph nodes for prolonged period of time to facilitate the continuous release of the targeting chemotherapeutics by placing a magnet externally [20].

OCULAR DRUG DELIVERY APPLICATION:

CNT's have been useful for ocular delivery of therapeutic molecules as they are helpful in local targeting of drug molecules to the retina. They have the ability to cross the blood retinal barrier [21]. Also it provide the advantage of enhanced retention ability in the retinal site to release the drug molecules ·However this field has not been much researched and thus needs to be further explored for ocular delivery of drugs.

TRANSDERMAL DRUG DELIVERY APPLICATION:

CNTs are effective in transdermal electrophoretic and iontophoretic delivery of drugs through skin. The functionalised CNT membranes facilitate the fast flow of drugs through the CNT cores due to their dramatically high charge density and small pore size [22]. Also CNT membranes are integrated with the drug molecule to obtain switchable transdermal delivery devices. There is minimum skin irritation associated with these devices .These are widely used nowadays for transdermal delivery of nicotine for smoking cessation as well as symptoms associated with opioids withdrawal[23].

VACCINE DELIVERY APPLICATION:

CNT's have high potential for antigen delivery which makes them effective vaccine delivery systems. Both SWCNTs as well as MWCNTs are highly useful in the delivery of vaccines, as they have shown improved performance for complement activation, protein adsorption, and generating the immune response by formation of antibodies [24].

GENE DELIVERY APPLICATION:

Gene delivery suffers from myriad problems in transfection of DNA, mRNA, siRNA, and other nucleic acid carriers across the cell membrane or nuclear membrane. Here CNT's have been widely used for improving gene delivery because of their capability of replacement of damaged or missing genes, and transportation of DNA into cells [1]. Studies have shown that when single-stranded DNA is tagged onto the surface of SWCNTs, it helps in the protection of DNA probes from possible enzymatic cleavage and interference from nucleic acid binding proteins [25]. New conjugate systems provide greater potential for applications in the field of genetic engineering.

TRANSFECTING AGENTS:

Infectious diseases like tuberculosis, leishmaniasis, severe acute respiratory syndrome, and various flu‘s like swine flu, bird flu etc., have always been a major public health issue globally. Nowadays functionalized CNTs have shown favourable outcomes in the treatment of these diseases, because of their ability to easily conjugate with drugs such as amphotericin B, which is shown to have reduced toxicity and enhanced antimycotic efficiency[(26)].

BREAKDOWN OF CARBON NANOTUBES IN HUMAN BODY:

A study conducted by a team of Swedish and American scientists recently has shown that carbon nanotubes can be broken down by an enzyme, Myeloperoxidase (MPO), which is found in white blood cells. This new discovery contradicts the previous belief that carbon nanotubes are not broken down in the body or in nature. The scientists thus hopes that this new understanding of MPO mechanism of converting carbon nanotubes into water and carbon dioxide can be of great importance to medicine and thus reduce adverse effects associated with the persistence of the nanotubes in the body[(27)].

CONCLUSION:

CNT’s as a potential drug delivery system can improve the pharmacological and therapeutic properties of conventional drugs. They have exclusive characteristics like ability to absorb pathogenic molecules and heat conduction that would enhance their use in the medical field. Functionalisation of CNT’s is an area which has opened new outlook in the application of CNTs in advanced drug delivery. The remaining task to the successful practical use of CNT’s as drug carriers is to make clear the mechanisms for their pharmacological as well as toxicological effects as this makes it possible to take the advantage of CNT’s to the maximum and to limit their disadvantages. There needs to be extensive research in this field in the fore coming years in order to explore the potentials of carbon nanotubes as an effective drug delivery system.

CONFLICT OF INTEREST:

The author(s) declared no conflict of interest with respect to the authorship, research or publication of the article.

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