CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.883131

**Available online at:** http://www.iajps.com *Review Article*

# EMERGING TREND IN NANOMEDICINE: CARBON NANOTUBES-A REVIEW

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**Abstract:**

*CNTS are basically allotrope of carbon with one or more grapheme sheets rolled to form hollow cylindrical tubular structures. CNTs possess various novel properties. Their unique surface area, stiffness, strength and resilience have led to much excitement in the field of Pharmacy. The important features of these structures are their electronic, mechanical, optical and chemical characteristics, which open a way to future applications. These properties can even be measured on single nanotubes. 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.*

**Keywords:** *CNT'S, SWCNTs), Nanomedicines Graphene sheets, ballistic conduction.*

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*Please cite this article in press as Pawar Kirteebala Pravin et al,* ***Emerging Trend in Nanomedicine: Carbon Nanotubes-A Review****, Indo Am. J. P. Sci, 2017; 4(08).*

## INTRODUCTION:

The term 'nanotechnology' is derived from a Greek word 'nano' meaning 'dwarf', hence it relates to materials of very small size ranges (0.1–100 nm). [1] Nanomaterials are larger than individual atoms/molecules but smaller than bulk materials. They have characteristic properties that neither completely obey quantum- nor classical-physics. Nanoparticles can be zero-, one-, or two-dimensional. Nanoparticles with low dimentions results in large surface-to-volume ratios, and enhanced electronic and optical properties when compared with bulk samples of the same material.[2-6] Among the entire range of the nanoparticles, carbon nanotubes i.e. CNTS have been evolved which has wide varieties of applications based on its property of nanocarrier system. CNTS were discovered by Japanese scientist Ijima in 1991. [7]

CNTS are basically allotrope of carbon with one or more graphene sheets rolled to form hollow cylindrical tubular structures. CNTs possess various novel properties. They are nanometers in diameter and several millimeters in length. Their impressive structural, mechanical, and electronic properties are due to their small size and mass, their incredible mechanical strength, and their high electrical and thermal conductivity. These properties vary with kind of nanotubes defined by its diameter, length, chirality or twist and wall nature. Their unique surface area, stiffness, strength and resilience have led to much excitement in the field of Pharmacy.[8-10]

They have high surface area, chemical stability, rich electronic polyaromatic structure and are able to bind or conjugate with different theraupetic substances like antineoplastic drugs , antibiotics, different biomolecules like genes, vaccines, proteins, antibodies etc. Also CNTS had been proven as excellent and efficient vehicle for drug delivery.[9-17] The hexagonal structure formed due to arrangement of sp2 hybridized carbon atoms in a specific pattern provides CNTS with higher C-C bond stiffness, tensile strength of 150 Gpa and youngs modulus of approximately 1 which gives the measure of nanotube stiffness. Chemically, CNTs originate from synthetic graphites on exposure to an electric arc or laser beam source.[18-20]

Variations in physical properties of CNT's are due to variation in atomic structure, since current synthesis methods cannot yet generate monochiral nanotubes. The inconsistency can be due to difference in length , diameter, chirality, no. of walls of typical sample. Other reason can be the different methods of preparation which results in different byproducts and different levels of defects. The electrical properties of a CNT are determined by the tube helicity and diameter.[30] If a CNT is imagined as a rolled-up graphene sheet, the helicity of the tube depends on the angle at which it is rolled-up, and can be described by its chiral vector, **C**h = n**a**1 + m**a**2 (where **a**1 and **a**2 are unit vectors of the hexagonal lattice and, n and m are integers) . The direction of **C**h is perpendicular to the axis of the nanotube. The chiral angle (q) is the angle between vectors **Ch** and **a1**. The n, m and q values for a particular CNT, determine the electronic behavior of the tube. If n - m is a multiple of 3 the tube is metallic otherwise, the tube is semiconducting. [31]

**Classification of Carbon Nanotubes:**

Depending upon the number of layers, CNT'S structures has been classified as

1. Single-walled carbon nanotubes (SWCNTs)
2. Multi-walled carbon nanotubes (MWCNTs) [20]

Single-walled carbon nanotubes consist of a single graphene cylinder with diameter varying between 0.4 and 2 nm, and usually occur as hexagonal close-packed bundles.[12,32]. The SWNTs are closed at both ends with cap-like structures during the process of synthesis and the rings form ends by C–C bonds.[33] The growth of SWNTs with a narrow diameter distribution by the arc-discharge [34] and the laser-ablation techniques [35] requires and critically depends on the composition of the catalyst. MWNTs are of few layers of graphene sheets (2–10), more than one atom thick. [36, 37].

MWCNTs consist of two to several coaxial cylinders, which are 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 $\mu$m.[12,32]

Multi-walled carbon nanotubes grow both lengthening and thickening, and at some stage the nanotubes tend to close.[38] SWNTs are structurally different from MWNTs by having different basic arrangements of the carbon atoms to give three different structural configurations.[36,37] The way the graphene sheet is wrapped is represented by a pair of indices (n,m) called the chiral vector. If m = 0, the Nanotubes are called "zigzag, which is named for the pattern of hexagons as we move on circumference of the tube. If n = m, the Nanotubes are called "armchair", which describes one of the two confirmers of cyclohexene a hexagon of carbon atoms. Otherwise, they are called "chiral", in which the m value lies between zigzag and armchair structures.[39,40]

**Comparision Of SWNT And MWNT: [41]**

| SWNT | MWNT |
|---|---|
| 1. Single layer of grapheme | 1. Multiple layer of grapheme |
| 2. Catalyst is required for synthesis | 2. Can be produced without catalyst |
| 3.Good electrical conductivity | 3.Bad conductors of electricity |
| 4.Bulk synthesis is difficult as it requires atmospheric condition | 4.Bulk synthesis is easy |
| 5.Purity is poor | 5.Purity is high |
| 6.More defection during Functionalization | 6.Less defection, but difficult to Improve |
| 7.Less accumulation in body | 7.More accumulation in body |
| 8.Easy characterization and Evaluation | 8.Difficult characterization and Evaluation |
| 9.Easily twisted | 9.Difficult to twist |

**Properties of Carbon Nanotubess:**
Mechanical properties: Carbon nanotubes are the strongest and stiffest materials yet discovered in terms of tensile strength and elastic modulus respectively. This strength results from the covalent $sp^2$ bonds formed between the individual carbon atoms. The modulus of a SWNT depends on the diameter and chirality. However, in the case of MWNT, it correlates to the amount disorder in the sidewalls.[52]
**Electrical properties:** Carbon nanotubes can be metallic or semiconducting depending on their structure. This is due to the symmetry and unique electronic structure of graphene. For a given (n,m) nanotube, if n = m, the nanotube is metallic; if n − m is a multiple of 3, then the nanotube is semiconducting with a very small band gap, otherwise the nanotube is a moderate semiconductor.[53] It has been demonstrated that the introduction of pentagon–heptagon pair of defects into the hexagonal network of a carbon nanotube can change the chirality of the tube and change its electronic properties .[54-57] A set of electrical properties — resistance, capacitance and inductance — which arise from the intrinsic structure of the nanotube and its interaction with other objects can be used to characterize individual nanotubes, like macroscopic structures.[58,59]

**Thermal properties**: All nanotubes should have very good thermal conduction property along the tube, exhibiting a property known as "ballistic conduction". It is expected that low-defect CNTs will have very low coefficients of thermal expansion. [60,61] Phonons are used to derermine the specific heat and thermal conductivity of carbon nanotube systems primarily.

**Optical properties**: Optical properties of SWNT are related to their quasi one- dimensional nature. The optical activity of chiral nanotubes disappears if the nanotubes become larger.[62] CNTs have been shown to exhibit strong optical absorbance in certain spectral windows such as NIR (near-infrared) light.

**Chemical properties:** The chemical reactivity of a CNT is, compared with a graphene sheet, enhanced as a direct result of the curvature of the CNT surface which causes the mixing of the π and σ orbital, which leads to hybridization between the orbitals. As the diameter of a SWNT gets smaller, the degree of hybridization becomes larger. Hence, carbon nanotube reactivity is directly related to the π-orbital mismatch caused by an increased curvature. [63]

**Synthesis of Carbon Nanotubes:**
The CNTs produced for pharmaceutical use, must be of good quality, free from impurities and carbonaceous matter and should not have damaged structures.[7] All known production techniques involve a carbon feedstock, a metal catalyst, and heat. Three main techniques used for CNTs synthesis are as follows:

1) Electric arc discharge method (EAD)
2) Laser ablation technique (LA)
3) Catalytic chemical vapor deposition (CVD)

Other methods employed for synthesis of CNTs are plasma enhanced chemical vapour deposition (PE-CVD) and high pressure carbon monoxide disproportionation process (HiPCO) technique.

1) **Electric arc discharge:** Basically it involves use of arc vaporization of two carbon rods. It produces best quality of nanotubes. The carbon arc discharge uses two graphite electrodes through which a direct current is passed in an inert He atmosphere. The anode is consumed and a cigar-like deposit forms on the cathode.[64] SWNTs may also be obtained but require mixed metal catalysts, such as Fe:Co, Ni:Y that are inserted into the anode.[65] It produces SWNTs with a diameter of 1.2 to 1.4nm.Replacing He by H2 results in MWNTs with a very thin innermost tube of <0.4 nm. The length of the MWNTs can be increased by introducing B into the anode. Boron also appears to favor the formation of zigzag MWNTs.[66-68]
Efficacy of SWNT production using arc discharge method is improved with inert gas like argon, optical plasma control, catalysts like Co and Mo, open air synthesis with welding arc torch.[69-71]

2) **Laser ablation technique:** A pulsed or continuous laser is used to vaporize a 1.2 at. % of cobalt/nickel with 98.8 at.% of graphite composite target that is placed in a 1200°C quartz tube furnace with an inert atmosphere of ~500 Torr of Ar or He. [72] Two different laser sources, as primary laser and secondary laser beam are used in this method. The initial bombardment is done with the primary laser followed by a secondary laser beam to finally produce CNTs of high quality. However, this method has the drawback of being time consuming and costly.[73-75] Arc discharge and laser ablation are similar methods, as both use a metal impregnated graphite target (anode) to produce SWNTs, and both produce MWNT and fullerenes when pure graphite is used instead. But, the length of MWNT produced through arc discharge is much larger than that produced by laser ablation. Two new developments in this field are ultra fast Pulses from a free electron laser method the continuous wave laser-powder method.

3) **Catalytic chemical vapor deposition:** The feed material used is present in the form of a mixed vapour phase (vaporized carbon along with an inert gas). This feed material is passed through a hot furnace where it decomposes to give CNTs deposited on the surface of a substrate. The substrate is made by embedding nanometre-sized nickel or cobalt particles, or a combination of both, as a catalyst on its surface and is generally heated to approximately 700°C.[73, 76,77] For commercial production, the nano-sized metal particles are mixed with MgO or Al2O3 to increase catalyst support and increase the surface area for higher yield.[78] MWNTs are mainly produced at lower temperatures (300-800°C) in an inert gas atmosphere, whereas SWNTs require higher temperatures (600-1150°C) and a mixture of H2 and an inert gas such as Ar.[79]

The HiPCO technique can be used for the catalytic production of SWNTs in a continuous-flow gas phase, using carbon monoxide (CO) as the carbon feedstock and Fe(CO)5 (iron pentacarbonyl) as the iron-containing catalyst precursor. The size and diameter distribution of the nanotubes can be roughly selected by controlling the pressure of the CO. This process is promising for bulk production of CNTs.[80]
Plasma-enhanced chemical vapor deposition (PECVD) systems have been used to produce both SWNTs and MWNTs. The carbon for PECVD synthesis comes from feedstock gases such as CH4 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 C2, CH, and other reactive carbon species (CxHy) to facilitate growth at low temperature and pressure. 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, SiO2, or glass substrate using thermal CVD or sputtering.

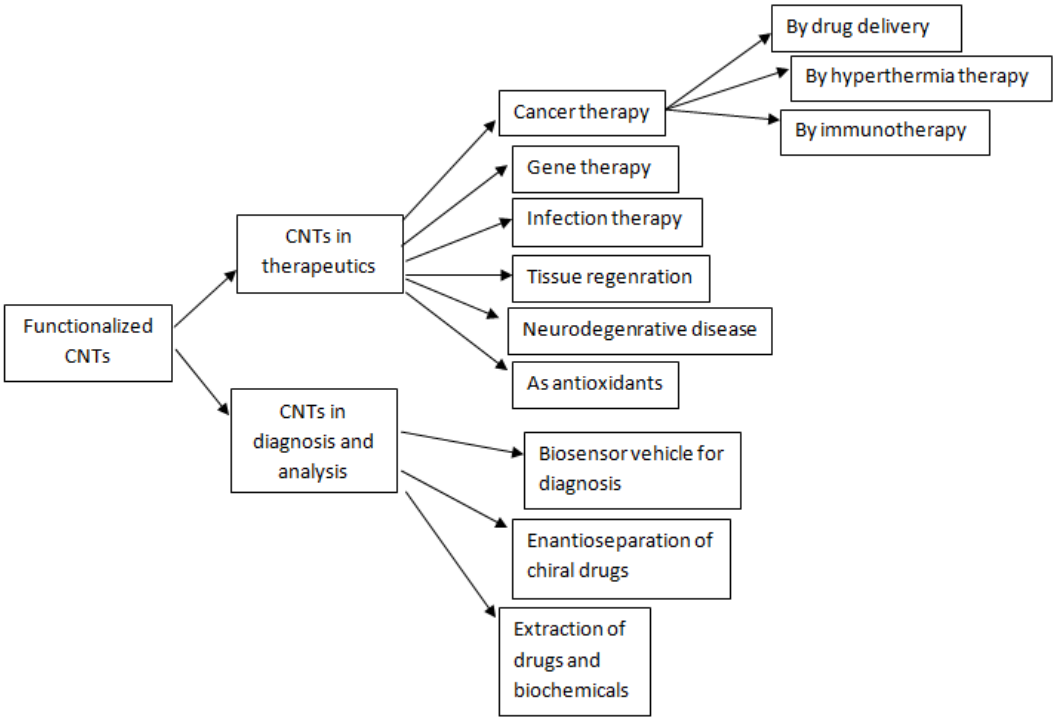
**Purification of Carbon Nanotubes:**
After preparation, CNTs are submitted to purification in order to eliminate impurities such as amorphous carbon, fullerenes, and transition metals introduced as catalysts during the synthesis. Various methods used for purification of carbon nanotubes are acid refluxing, surfactant aided sonication, air oxidation. [81]
**Air oxidation:** Purification is needed before attachment of drugs onto CNTs. Air oxidation is useful in reducing the amount of amorphous carbon and metal catalyst particles (Ni, Y). Optimal oxidation condition at 673 k for 40 min are found..

**Acid refluxing:** For reducing the amount of metal particles and amorphous carbon, refluxing the sample in strong acid is effective. The ideal refluxing acids are hydrochloric acid (HCl) nitric acid (HNO3) and sulphuric acid (H2SO4).

Surfactant aided sonication, filtration and annealing**:** After acid refluxing, the CNTs were
purer but, tubes were entangled together, trapping most of the impurities which were difficult to remove with filtration. So surfactant-aided sonication was carried out. Sodium dodecyl benzene sulphonate (SDBS) aided sonication with ethanol (or methanol) as organic solvent were preferred because it took the longest time for CNTs to settle down, indicating an even suspension state was achieved. The sample was then filtered with an ultra filtration unit and annealed at 1273 k in N2 for 4 h.

**Functionalisation of Carbon Nanotubes:**
For biological and biomedical applications, the lack of solubility of carbon nanotubes in aqueous media has been a major technical barrier. Surface fuctionalization is required to solubilize CNTs, and to render biocompatibility and low toxicity for their medical applications.[82]
With different molecules it is achieved by adsorption, electrostatic interaction or covalent bonding of different molecules and chemistries that render them more hydrophilic. Through such modifications, the water solubility of CNT is improved and their biocompatibility profile is completely transformed. Moreover, the bundling/aggregation of individual tubes through vander Waals forces are also reduced by the fuctionalization of their surface.[83]
With different molecules it is achieved by adsorption, electrostatic interaction or covalent bonding of different molecules and chemistries that render them more hydrophilic. Through such modifications, the water solubility of CNT is improved and their biocompatibility profile is completely transformed. Moreover, the bundling/aggregation of individual tubes through vander Waals forces are also reduced by the fictionalization of their surface.[84] The fictionalization procedure of CNTs can be divided into two main approaches, depending on the nature of the biomolecule linked to carbon nanotube, that is, covalent attachment (chemical bond formation) and noncovalent attachment (physioadsorption).
The covalent functionalization of CNTs is generally obtained by oxidation with strong acids (HNO3). Then on covalent fuctionalization of CNTs can be carried out by coating CNTs with amphiphilic surfactant molecules or polymers (polyethyleneglycol).[10,85]

**Applications of Carbon Nanotubes:**
The various applications of carbon nanotubes are summarized as follows:



**1.CNTs in cancer therapy:** Anticancer drug Polyphosphazene platinum given with nanotubes had enhanced permeability, distribution and retention in the brain due to controlled lipophilicity of nanotubes. [86] Chemotherapeutic agents delivered with CNTs help in achieving better uptake by malignant cells without affecting collateral tissues.[87]

2**.CNTs as biosensors:** A biosensor is an analytical device, used for the detection of an analyte that combines a biological component twith a physicochemical detector. The use of CNTs in biosensing nanotechnology is recent and represents a most exciting application area for therapeutic monitoring and in vitro and in vivo diagnostics. CNTs have been coupled with glucose oxidase biosensors and dehydrogenease biosensors [88,89] Sotiropoulou and Chaniotakis used CNTs as an immobilization matrix for the development of an amperometric biosensor. The biosensor was developed by growing aligned MWNTs on platinum substrates. CNT-based nanobiosensors are now used to detect DNA sequences in the body and help in the detection of very specific pieces of DNA related to cancer production, and identification of genes and biomolecules such as antibodies associated with human autoimmune diseases.[90-93]

**3.In genetic engineering :** In genetic engineering, CNTs and CNHs are used to manipulate genes and atoms in the development of bioimaginggenomes, proteomics and tissue engineering.[86]
The use of CNTs as gene therapy vectors has shown that these engineered structures can effectively transport the genes inside mammalian cells and keep them intact because the CNT-gene complex has conserved the ability to express proteins.[94]

**4.CNTs in solubility enhancement:** The functionalized nano carriers are able to deliver several hydrophobic biomolecules (proteins, peptides, nucleic acids, enzymes) to the target site. [95]

**5.Artificial implants:** Normally body shows rejection reaction for implants with the postadministration pain[96].But, miniature sized nanotubes and nanohorns 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 nanotubes filled with calcium and arranged/grouped in the structure of bone can act as bone substitute.[97]
**6.Carbon Nanotubes for Neurodegenerative Diseases andAlzheimer Syndrome:** As a promising biomedical material, CNTs have been used in neurosciences. Because of their tiny dimensions and accessible external modifications, CNTs are able to cross the blood-brain barrier by various targeting mechanisms for acting as effective delivery carriers for the target brain. Yang et al. have observed that SWCNTs were successfully used to deliver acetylcholine in mice brains affected byAlzheimer's disease with high safety range.[98]
**7.As catalyst:** Nanohorns offer large surface area and hence, the catalyst at molecular level
can be incorporated into nanotubes in large amount and simultaneously can be released in required rate at particular time.[99]
**8.Preservative:** Carbon nanotubes and nanohorns are antioxidant in nature. Hence, they are
used to preserve drugs formulations prone to oxidation. [86]
**9.CNTs in vaccine delivery :** Vaccines are biological substances used for imparting immunization
against foreign disease-causing pathogenic microorganisms.[100]
Major problems associated with vaccine delivery include improper absorption, chances of antigen-induced hypersensitivity, anaphylactic reactions and hypersensitivity due to vaccine adjuvants. CNTs have also been tried for vaccine delivery. CNTs, when conjugated with antigenic peptides, can act as a new system for safe and effective delivery of synthetic vaccines.[101]
**10.Carbon Nanotubes for Enantioseparation of Chiral Drugs and Biochemical:** In pharmaceutical industries, 56% of the drugs currently in use are chiral products and 88% of the last ones are marketed as racemates consisting of an equimolar mixture of two enantiomers. [102] Recently, US Food and Drug Administration (FDA) recommended the assessments of each enantiomer activity for racemic drugs in body and promoted the development of new chiral drugs as single enantiomers. Therefore, a wide rangeof new technologies for chiral separation has been developed, among them carbon nanotubes. [103]
**11.Carbon Nanotubes for Solid Phase Extraction of Drugs and Biochemical.** Due to their strong interaction with other molecules, particularly with those containing benzene rings, CNTs surfaces possess excellent adsorption ability . [104]
**Toxicity of CNTs:**
Nanomaterials have unique properties in comparison with bulk materials, such as a high surface area to volume ratio that also leads to unique mechanisms of toxicity from xenobiotics. In general, researchers found that the toxicity originated from the nanomaterial size and surface area, composition and shape. [105] Several invitro and invivo toxicological

studies regarding CNTs are been performed. 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.[106]

MWCNT exposure is associated with oxidative damage, increased apoptosis, chromosome damage, and necrosis.[107]It was concluded from the study that carbon nanomaterials with different geometric structures exhibit quite different cytotoxicity and bioactivity.

## CONCLUSION:

This review on carbon nanotubes involves the overview on structure, morphology, synthesis and purification methods of carbon nanotubes along with their properties, benefits and applications. Carbon Nanotubes have been of great interest, both from a fundamental point of view and for future applications. The important features of these structures are their electronic, mechanical, optical and chemical characteristics, which open a way to future applications. These properties can even be measured on single nanotubes.Large quantities of purified nanotubes are needed for commercial application,. Different types of carbon nanotubes can be produced in various ways. The most common techniques used nowadays are: arc discharge, laser ablation and chemical vapour deposition. Purification of the tubes can be divided into a couple of main techniques: oxidation, acid treatment, annealing, sonication, filtering and functionalisation techniques. Economically feasible large-scale production and purification techniques still have to be developed. Fundamental and practical carbon nanotube researches have shown possible applications in various fields. Real applications are still under development. This report provides an overview of current carbon nanotube technology, with a special focus on synthesis and purification, properties, benefits and applications. The distinct structural properties of carbon nanoparticles, in particular their high aspect ratio and propensity to functional modification and subsequent use as carrier vectors, make them useful for pharmaceutical nanodelivery. Carbon nanotubes have great scope in Nanotecthnology..

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