# SYNTHESIS OF CARBON NANOTUBES AND THEIR BIOMEDICAL APPLICATION

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Since from the discovery of carbon nanotubes, researches are doing their level best for exploring the potential in biological and biomedical applications. Carbon nanotubes (CNTs) are allotropes of carbon with a nanostructure that can have a length-to-diameter ratio greater than 1,000,000. These cylindrical carbon molecules have novel properties that make them potentially useful in many applications in nanotechnology. Their unique surface area, stiffness, strength and resilience have led to much excitement in the field of pharmacy. Carbon nanotubes belong to the family of fullerenes which consists of graphite sheets rolled up into tubular form. These structures can be obtained either single or multi – walled nanotubes. Carbon nanotubes can also be made water soluble by surface functionalization. Molecular and ionic migration occurs through carbon nanotubes, thus offering novel opportunities for fabrication of molecular sensors and electronic nuclei acid sequencing. The modification of a carbon nanotube on a molecular level using biological molecules is essentially an example of the 'bottom-up' fabrication principle of bio nanotechnology. This article provides an overview about carbon nanotubes, synthesis, functionalization, their toxicity as well as their use for mediated target drug delivery.

(Received June 2, 2010; accepted June 23, 2010)

*Keyword:* CNT, Drug Delivery, Functionalization, Toxicity of CNT,Biomedical application, Synthesis of CNT, SWNTs, MWNTs.

## 1. Introduction

The discovery of carbon nanotube (CNT) has become the subject of intense investigation because their remarkable behavior likes electrical, chemical, mechanical and structural properties [1]. Carbon nanotubes based drug delivery has great promise for cancer ablation [2]. Functionalization of carbon nanotubes are primary step for novel chemical and biological applications [3 -7]. In the carbon nanotubes (CNTs), intense interest has been generated because it can display metallic, semiconducting and superconducting electron transport, possess a hollow core suitable for storing guest molecules and have the largest elastic modulus of any known materials [8]. Pharmaceutical nanotechnology focuses on formulating therapeutically active agents in biocompatible nanoforms such as nanoparticles, nanocapcules and conjugates. These systems offer many advantages in drug delivery mainly focusing on improved safety and efficiency of the drugs for example providing targeted delivery of drugs, improving bioavailability, extending drug or gene effect of drugs, tissue and improving the stability of therapeutic agents against chemical/enzymatic degradation [9-10]. As a consequence, the compatibility of CNT with other materials such as polymers, is also expected to improve. In addition, once properly functionalized CNT become soluble in many solvents, so that their solubility properties can be studied. Many functionalized carbon nanotubes may find useful applications in the field of materials science and technology, including photovoltaics. Also in medicinal chemistry carbon nanotubes are set to play an important role. Their use as drug delivery scaffolds and substrates for vaccines has already been demonstrated. CNT functionalized with bioactive moieties are particularly suited for targeted drug delivery. In fact, not only they become less toxic but also exhibit a high propensity to cross cell membranes.

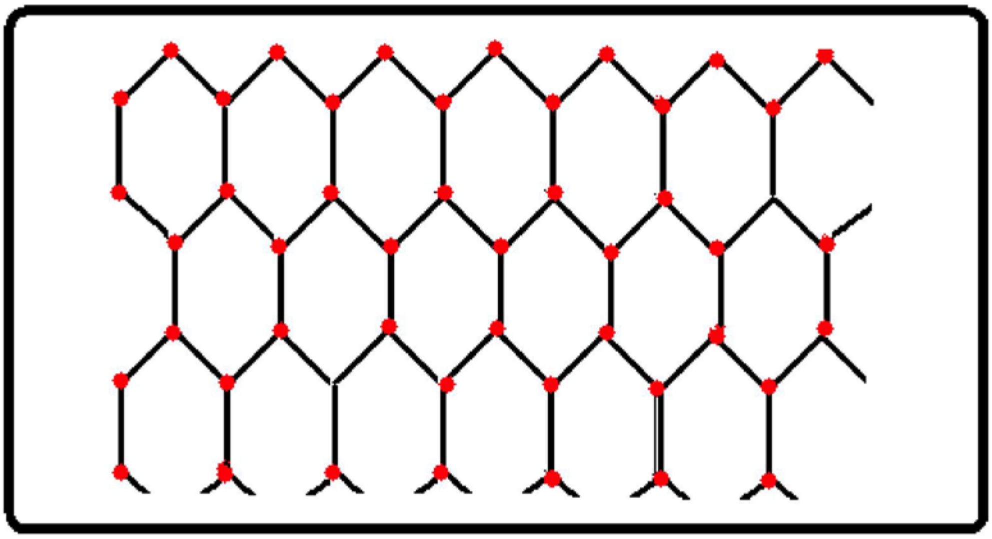

*Fig. 1. Single sheet of Graphene.*

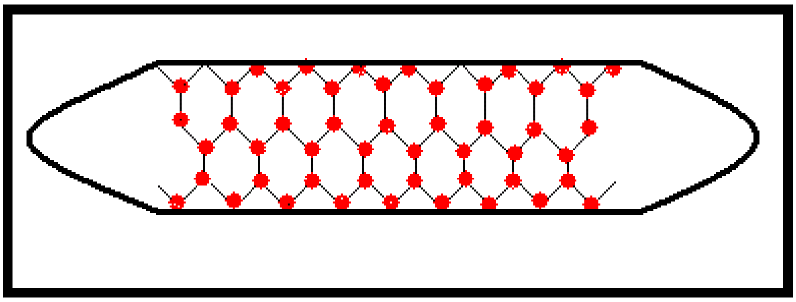

*Fig. 2- General representation of carbon nanotubes having ends close with some functional groups of hemi fullerenes.*

However, the organic modification of CNT is not yet a well established field. The intrinsic low chemical reactivity of CNT coupled with the difficulty in characterizing and purifying the reaction products, makes this discipline difficult and fascinating at the same time. Among the many ways available, several strategies have been devised to solubilise nanotubes. Among these, the most successful are: 1) the covalent functionalization of *sp*2 carbons at the sidewalls with organic pendant groups and 2) the non-covalent functionalization through supra-molecular interactions (e.g., π-π stacking interactions) which allows the formation of stable suspensions.

**2. Carbon Nanotube**

Carbon occurs in many forms, and the dependence of the properties of each form on its special structure makes carbon a truly unique building block for nanomaterials. Carbon can bond to itself to form extremely strong two dimension sheets, if these sheets are rolled and folded into diverse range of three dimension structure, of which the most famous are the ball-shaped fullerenes and cylindrical nanotubes for this reason carbon has been investigated from more than half a century. Since their discovery in 1991 by Iijima [11] and coworkers, carbon nanotubes have been investigated by many researchers all over the world .Perhaps the most interesting nanostructure with large application are carbon nanotubes. Carbon nanotubes are graphene sheets (figure 1) which are rolled into tubes and are closed at their ends by semi-fullerene like structure [12] (figure 2).There are two types of carbon nanotubes i.e. single and multi walled nanotubes. Multi walled nanotubes (MWNTs) are essentially Single walled nanotubes (SWNTs) of different diameters. SWNTs may be divided into three different categories, each of which is pair of fullerene caps connected by a tube that is a rolled up seamless graphene sheet. The first of the three structural categories is zigzag, which is named for the pattern of hexagon as one moves circumferentially around the body of the tubule. The second form is known as chiral and is believed to be the most commonly occurring SWNT. The name chiral means handedness and indicates that the tubes may twist in either direction. Third of these nanotubes structures is termed as armchair which describe one of the two conformers of cyclo-hexane, hexagon of carbon atoms and describe the shape of the hexagons as one moves around the body of the tubules.

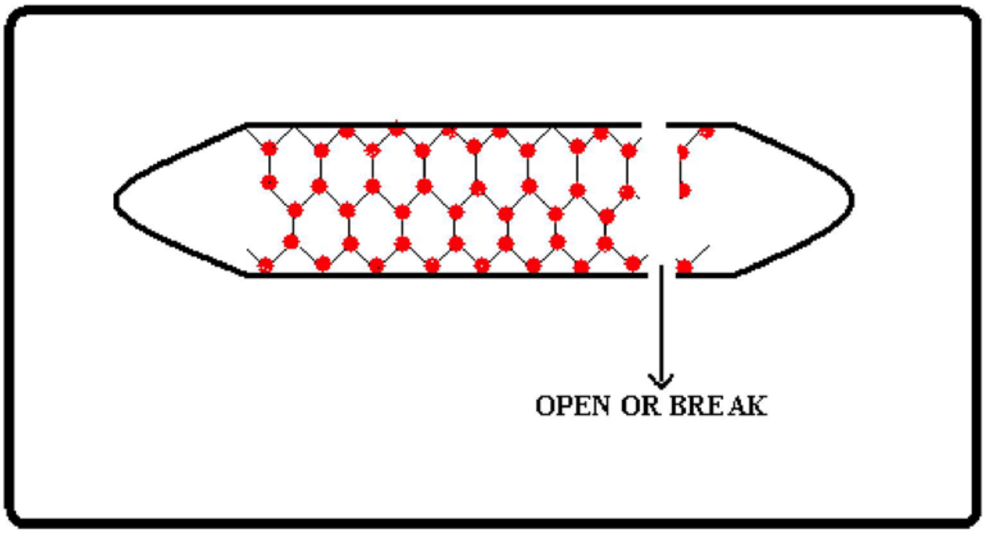


*Fig. 3. General representation of Open Carbon Nanotube by action of acid.*

Carbon nanotubes (CNTs) possess high specific surface areas, electrical conductivities, chemical stability etc which is possible with the treatment of CNT with acid [13-15] (figure3) which is known as refluxing. It has also been demonstrated that CNTs enhance the electron transfer rate of many redox reactions [16]. These unique properties make CNTs very useful for supporting noble-metal nanoparticles, and metal-nanoparticle/ CNT nano hybrid have many potential applications ranging from advanced sensors to highly efficient fuel cells [17].

### 3. Synthesis of CNT

CNTs are generally produced by three main techniques, arc discharge [18], laser ablation [19] and chemical vapor deposition [20]. Arc discharge, initially used to producing $C_{60}$ fullerenes, is the most common and easiest way to produce CNTs. This method creates CNTs through arc-vaporization of two carbon rods placed end to end, separated by approximately 1mm, in an enclosure that is usually filled with inert gas at low pressure. A direct current of 50 to 100 A, driven by a potential difference of approximately 20 V creates a high temperature discharge between the two electrodes. The discharge vaporizes the surface of one of the carbon electrodes and forms a small rod-shaped deposit on other electrode (figure 4).

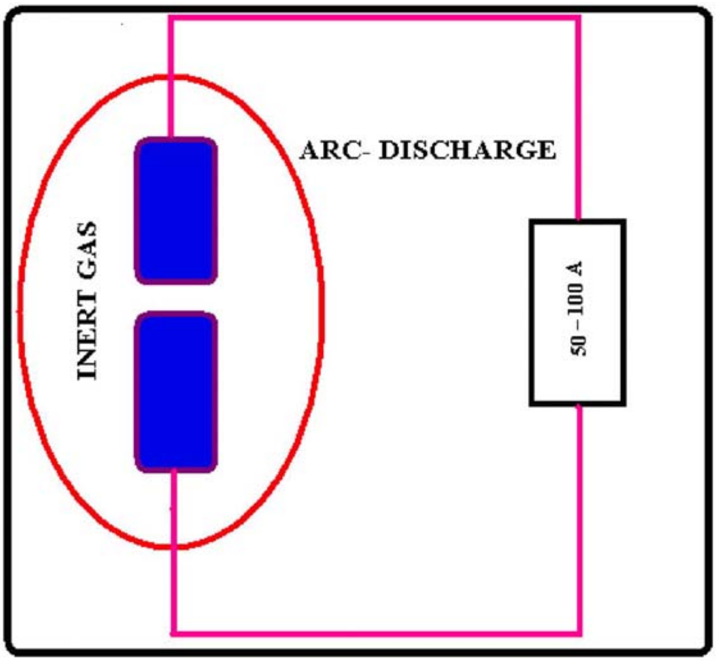


*Fig. 4. Diagrammatical representation of Arc Discharge setup for Synthesis and growth of nanotube.*

In Laser ablation laser vaporization pulses were followed by a second pulse, to vaporize the target more uniformly. The use of two successive laser pulses minimizes the amount of carbon deposited as soot. The second laser pulse breaks up the larger particles ablated by the first one, and feeds them into the growing nanotubes structure (figure 5). The material produced by this method appears as a mat of "ropes", 10-20 nm in diameter and upto 100µm or more in length.

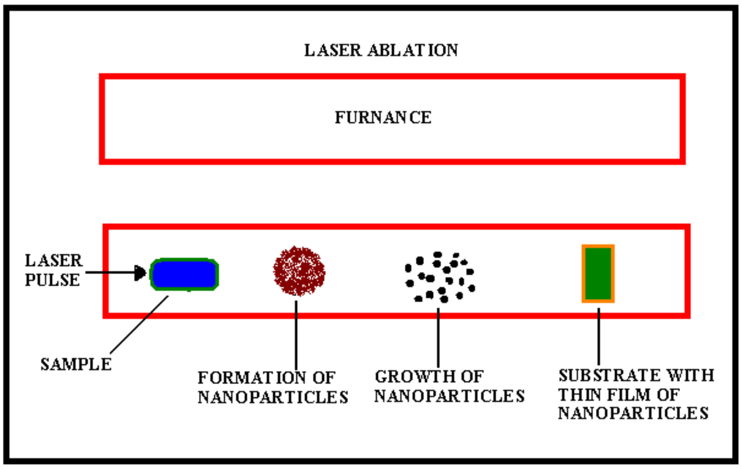


*Fig. 5. Diagrammatical representation of Laser Ablation setup for nanotube synthesis and growth.*

Chemical Vapor Deposition of hydrocarbons over a metal catalyst is a classical method that has been used to produce various carbon materials like carbon fibers and filaments. Large amount of CNTs can be formed by catalytic CVD (figure 6) of acetylene over cobalt and iron catalysts supported on silica or zeolite. High yields of single walled nanotubes have been obtained by catalytic decomposition of $H_2/CH_4$ mixture all over well dispersed metal particles such as cobalt, nickel and iron on magnesium oxide at

$1000^0$C.The reduction produces very small transition metal particles at a temperature of usually $>800^0$C. The decomposition of $CH_4$ over the freshly formed nanoparticles prevents their further growth and thus results in a very high proportion of SWNTs and few MWNTs.

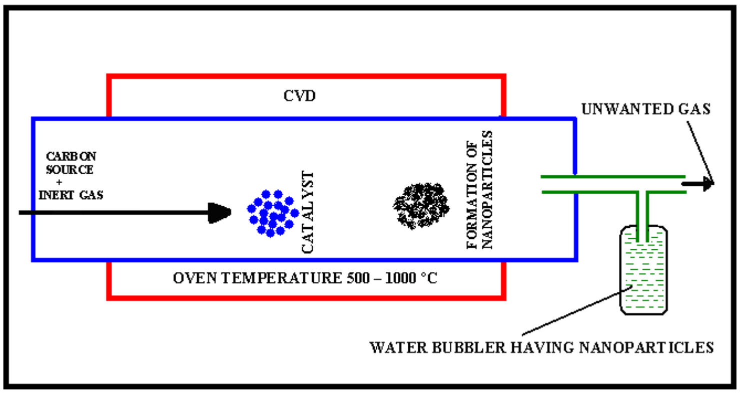


*Fig. 6. Diagrammatical representation of Chemical vapor deposition (CVD) setup for nanotube synthesis and growth.*

#### 4. Toxicity of CNT

Harmful effect of nanoparticles arises due to high surface area and intrinsic toxicity of the surface [21]. CNT, in the context of toxicology, can be classified as 'nanoparticles' due to their nanoscale dimensions, therefore unexpected toxicological effects upon contact with biological systems may be induced. The nanometer-scale dimensions of CNT make quantities of milligrams possess a large number of cylindrical, fbre-like particles with a concurrent very high total surface area. The intrinsic toxicity of CNT depends on the degree of surface functionalisation and the different toxicity of functional groups. Batches of pristine CNT (non-purified and/or non-functionalised) readily after synthesis contain impurities such as amorphous carbon and metallic nanoparticles (catalysts: Co, Fe, Ni and Mo) which can also be the source of severe toxic effects [22]. On the basis of recent studies with carbon derived nanomaterials showed that platelet aggregation was induced by both single and multi-wall carbon nanotube but not by the $C_{60}$-fullerenes that are used as building blocks for these CNT [23, 24].

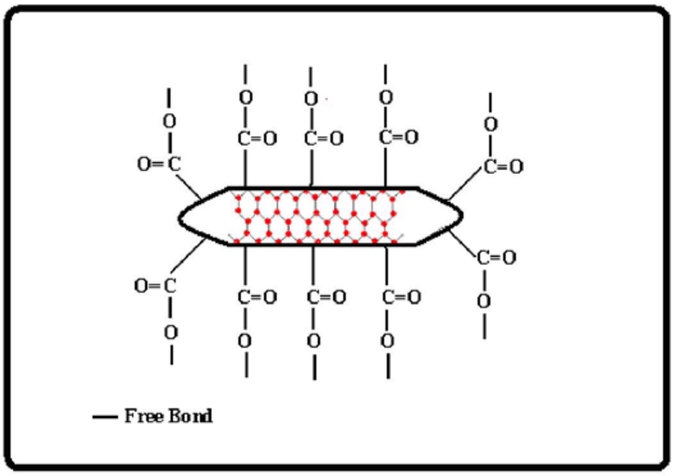


*Fig. 7. The Carbon nanotubes are functionalized with carboxylic acid.*

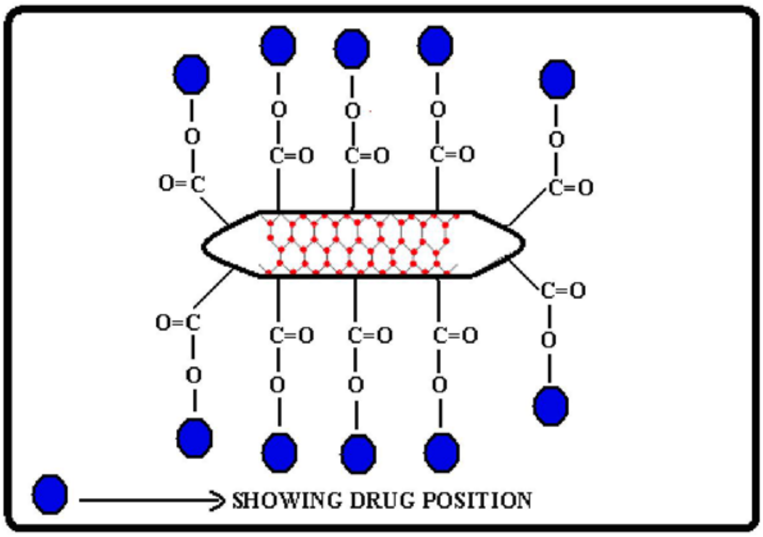


*Fig. 8. Drug uploaded with functionalized carbon nanotube (CNT).*

**5. Functionalization of CNT**

Single walled carbon nanotubes (SWCNTs) consisting of a single graphite plane (so-called graphene) rolled up into a cylinder behave as either a metal or a semiconductor depending on their wrapping angle of graphene sheet and its diameter while MWCNTs are reported to be always electrically conductive and to have an electrical conductivity approximately 1.85 x 103 S/cm [25-27]. CNTs polymeric composites are aimed at the exploitation of the high electrical conductivity of CNTs coupled to high mechanical properties, thermal properties and others unique properties [28-29]. However, high molecular weight and strong intertube forces keep CNT together in bundles, making their manipulation, characterization and analytical investigation very difficult. The organic functionalization offer the great advantages of producing soluble and easy-to- handle CNT. Consequently, compatibility of CNT with other material, such as polymer should be strongly improved. Functionalization methods such as chopping, oxidation and wrapping of the CNT in certain polymer can be created more active bonding sites on the surface of the nanotubes. For, biological uses, CNTs can be functionalized by attaching biological molecules such as lipids, proteins, biotins etc to them, through this it is possible to solubilise and disperse carbon nanotubes in water, thus opening the path for their facile manipulation and processing in physiological environments. Then they can usefully mimic certain biological functions, such as gene therapy and drug delivery. In biochemical and chemical applications such as the carboxylic acid (figure 7), poly-amino benzoic sulfonic acid, poly vinyl alcohol has been used to functionalize CNTs, as have amino acid derivatives, halogens and compounds (figure 8).

**7. Biological application**

The search for new and effective drug delivery systems is rapidly expanding. Many different delivery systems and methodologies are currently available. They have been developed according to the different classes of bioactive molecules to be delivered (e.g. peptides, proteins, nucleic acids and small organic molecules) and the characteristics of the target tissues. Liposome's, emulsions, cationic polymers, micro and nanoparticles are the most commonly studied vehicles. A drug delivery system is generally designed to improve the pharmacological and therapeutic profile of a drug molecule [30-31]. Problems associated with the administration of free drugs, such as limited solubility, poor bio distribution, lack of selectivity, unfavourable pharmacokinetics, healthy tissue damage, can be overcome and/or ameliorated by the use of a drug delivery system. The exploration of CNTs in biomedical application is just underway but has been significant potential [32]. Since large part of the human body consists of carbon, it is generally thought of as a very biocompatible material. Cells have been shown to grow on CNTs so they appear to have no toxic effect. The cells also do not adhere to the CNTs, potentially giving rise to application such as coatings for prosthetics. The ability to functionalize the sidewalls of CNTs also leads to biomedical application such as vascular stents [33] and neuron growth and regeneration.

## 8. Conclusions

The properties and characteristics of CNTs are still being researched heavily and scientists have barely begun to tap the potential of these structures. Single and multiple walled carbon nanotubes have already proven to serve as safer and more effective alternatives to previous drug delivery methods. 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. Carbon nanotubes are one of the most important materials under investigation for nanotechnology applications. Their unique properties, ranging from ultra high strength through unusual electronic behaviour and high thermal conductivity to an ability to store nanoparticles inside the tubes themselves has suggested potential applications in many different fields of scientific and engineering endeavour. As was the case with silicon transistor technology, these applications will grow in time as the capacity for industrial production and manipulation of CNT is created and as understanding of the physics of CNT continues to improve.

## Acknowledgement

I would like to express my heartfelt thanks to Dr. Naveen Prakash, Director-MRCE and Prof.S.K.Chakarvarti, Director Research & Development; Admissions, Manav Rachna International University (MRIU) India, for their continuous support and cooperation.

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