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Review Article

Carbon Nanotubes: An Impending Carter in Therapeutics.

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ABSTRACT

Carbon nanotubes (CNTs) have been under scientific investigation for more than fifteen years because of their unique properties that predestine them for many potential applications. The field of nanotechnology and nanoscience push their investigation forward to produce CNTs with suitable parameters for future 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 and other branches of life science. Their unique surface area, stiffness, strength and resilience have led to much excitement in the field of pharmacy. Nanotubes are categorized as single-walled nanotubes and multiple-walled nanotubes. Techniques have been developed to produce nanotubes in sizeable quantities, including arc discharge, laser ablation, chemical vapor deposition, silane solution and flame synthesis methods. The properties and characteristics of CNTs are still being researched heavily and scientists have barely begun to tap the potential of these structures. CNTs can pass through membranes, carrying therapeutic drugs, vaccines and nucleic acids deep into the cell to targets previously unreachable. Overall, recent studies regarding CNTs have shown a very promising glimpse of what lies ahead in the future of medicines.

Keywords: Carbon nanotubes, Single and multiple walled nanotubes, Preparation Methods, Nano-medicines.

INTRODUCTION

Carbon nanotubes (CNTs) are allotropes of carbon, tubular in shape, made of graphite. CNTs possess various novel properties that make them useful in the field of nanotechnology and pharmaceuticals. These have diameter in nanometers, length in several millimeters and have a very broad range of electronic, thermal and structural properties. 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. The last few years have witnessed number of discoveries, development and in some cases, large-scale manufacturing and production of novel materials that lie within the nanometer scale. Such novel nanomaterials consist of inorganic or organic matter.

Carbon nanotubes are one of the most commonly mentioned building blocks of nanotechnology. With one hundred times the tensile strength of steel, thermal conductivity better than all but the purest diamond and electrical conductivity similar to copper. In fact nanotubes come in a variety of flavors: long, short, single-walled, multi-walled, open, closed, with different types of spiral structure etc.

Carbon nanotubes are expected to become a key material in ultrafine devices of the future, because of their unique electrical characteristics and their extraordinarily fine structure on a nanometer scale. Other merits offered by carbon nanotubes are light weight, extremely high mechanical strength, ability to withstand extreme heat of about 2000°C in the absence of oxygen[1-4].

History and Origin: The discovery of fullerenes[5] provided exciting insights into carbon nanostructures and how architectures built from sp^2 carbon units based on simple geometrical principles can result in new symmetries and structures that have fascinating and useful properties. Carbon nanotubes represent the most striking example. About a decade after their discovery[6], the new knowledge available in this field indicates that nanotubes may be used in a number of practical applications. There have been great improvements in synthesis techniques, which can now produce reasonably pure nanotubes in gram quantities. Studies of structure–topology–property relations in nanotubes have been strongly supported and in some cases preceded, by theoretical modelling that has provided insights for experimentalists into new directions and has assisted the rapid expansion of this field[7-12].

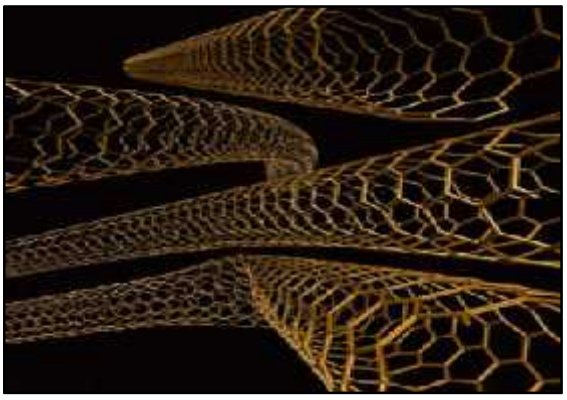

Fig. 1: Schematic diagram of SWCNTs.

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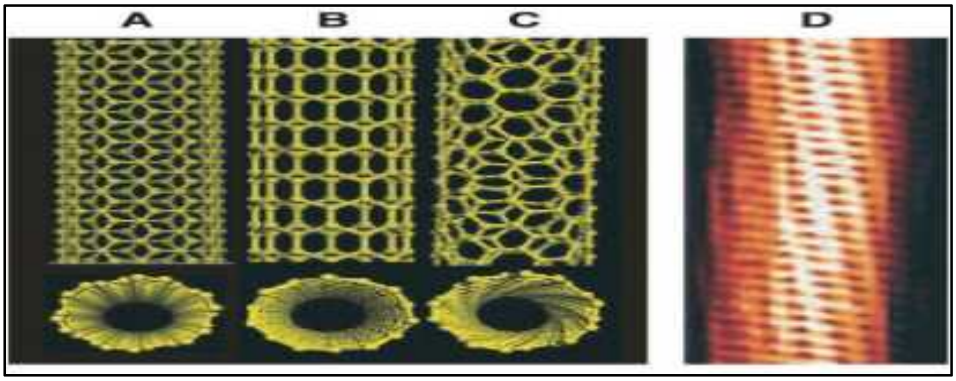

Fig. 2: Schematic illustrations of the structures of (A) armchair, (B) zigzag and (C) chiral SWNTs. Projections normal to the tube axis and perspective views along the tube axis are on the top and bottom, respectively. (D) Tunneling electron microscope image showing the helical structure of a 1.3-nm-diameter chiral SWNT.

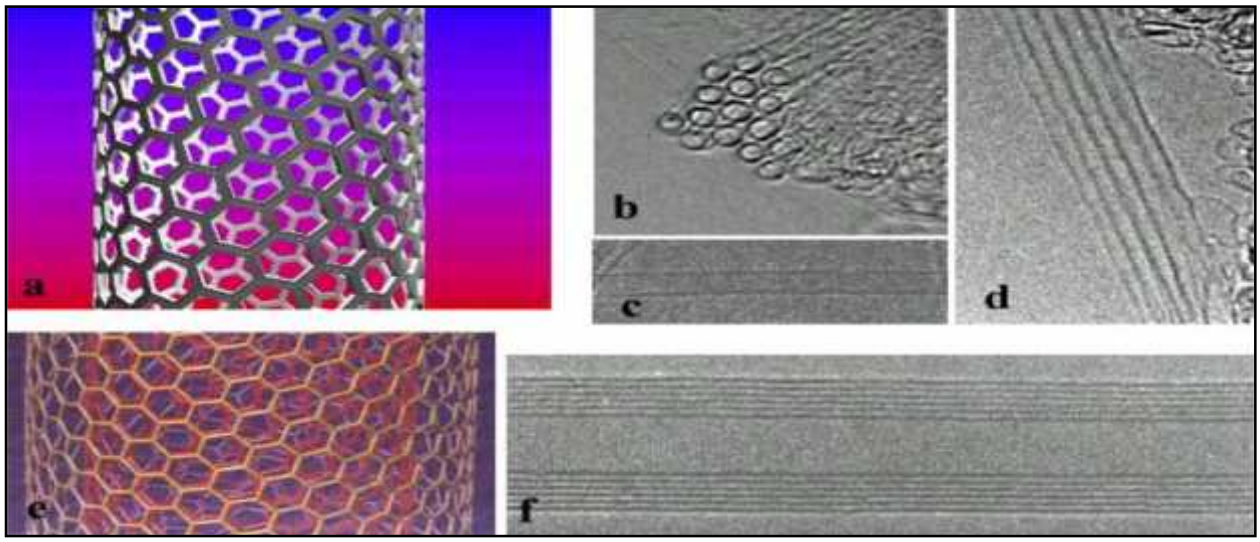

Fig. 3: Structure of Single-Walled (SWNT) (a-d) and Multi-Walled (MWNT) carbon nanotubes (e,f). (a) Shows a schematic of an individual helical SWMT. (b) Shows a cross-sectional view (TEM image) of a bundle of SWNTs [transverse view shown in (d)]. Each nanotube has a diameter of ~1.4 nm and the tube-tube distance in the bundles is 0.315 nm. (c) Shows the high-resolution TEM micrograph of a 1.5 nm diameter SWNT. (e) Schematic of a MWNT and (f) Shows a high resolution TEM image of an individual MWNT. The distance between horizontal fringes (layers of the tube) in (f) is 0.34 nm (close to the interlayer spacing in graphite).

Quasi-one-dimensional carbon whiskers or nanotubes are perfectly straight tubules with diameters of nanometer size and properties close to that of an ideal graphite fiber (Figure 1). Carbon nanotubes were discovered accidentally by Sumio *Iijima* in 1991, while studying the surfaces of graphite electrodes used in an electric arc discharge[6]. His observation and analysis of the nanotubes structure started a new direction in carbon research, which complemented the excitement and activities then prevalent in fullerene research. These tiny carbon tubes with incredible strength and fascinating electronic properties shortly leaved behind fullerenes in the race.

Structure and Morphology: Structurally, SWNTs can be compared to ‘‘rolled up’’ one atom thick sheets of graphite called graphene (Fig. 1). The way the graphene is wrapped along the honeycomb graphene structure is given by chiral vector ~C which is a result of a pair (n,m) of integers that correspond to graphene vectors ~a1 and ~a2. The principle of SWNT construction from a graphene sheet along the chiral vector ~C is shown in Fig. 2. There are two standard types of SWNTs constructions from a single graphene sheet according to integers (n, m). The (n, 0) structure is called ‘‘zigzag’’ and the structure where n ¼ m (n, n) is called ‘‘armchair’’. The third non-standard type of CNTs construction, which can be characterized by the equation where n > m > 0, is called ‘‘chiral’’.

The chirality predestinates the electrical, mechanical, optical and other properties of CNTs. For example Dresselhaus et al. reported how the chiral vector and the corresponding pairs of integers influence the electrical properties of CNTs[13].

The bonding in carbon nanotubes is sp^2, with each atom joined to their unique strength. Under high pressure, nanotubes can merge together, trading some sp^2 bonds for sp^3 bonds, giving the possibility of producing strong, unlimited length wires through high-pressure nanotube linking. Structure of nanotubes is as shown in Figure 2 and 3.

Classification of Carbon Nanotubes**:** Carbon nanotubes are broadly classified into following two types[14]:

1) Single walled carbon nanotubes (SWNTs): These consist of carbon atoms bonded into a tube shape with a

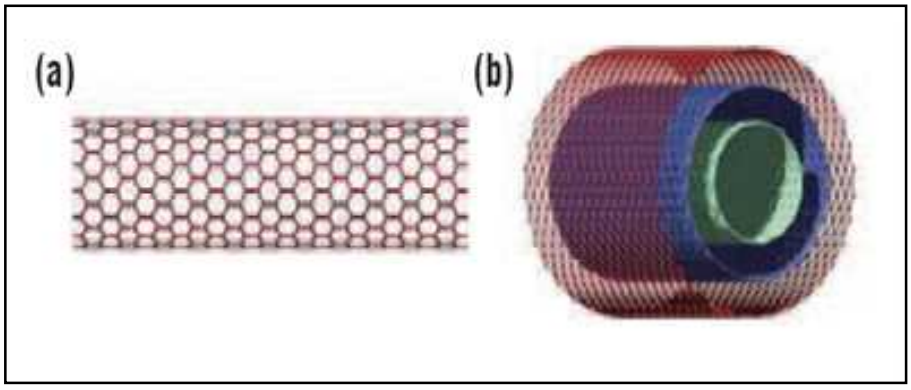

Fig. 4: Computational image of single and multi-walled nanotubes.

Table 1: Comparison between SWNTs and MWNTs.

Sr. No.	SWNTs	MWNTs
1.	Single layer of graphene.	Multiple layers of graphene.
2.	Catalyst is required for the synthesis.	Can be produced without catalyst.
3.	Bulk synthesis is difficult as require control over growth and atmospheric conditions. Poor purity.	Bulk synthesis is easy.
4.	Less body accumulation.	High purity.
5.	Chance of defect is more during functionalization.	More body accumulation.
6.	Due to simple structure characterization and evaluation is easy.	Chance of defect is less but once occurred it's difficult to overcome.
7.	Can be easily twisted and are more pliable.	Due to complex structure characterization and evaluation is quite difficult. These can't be reformed easily.

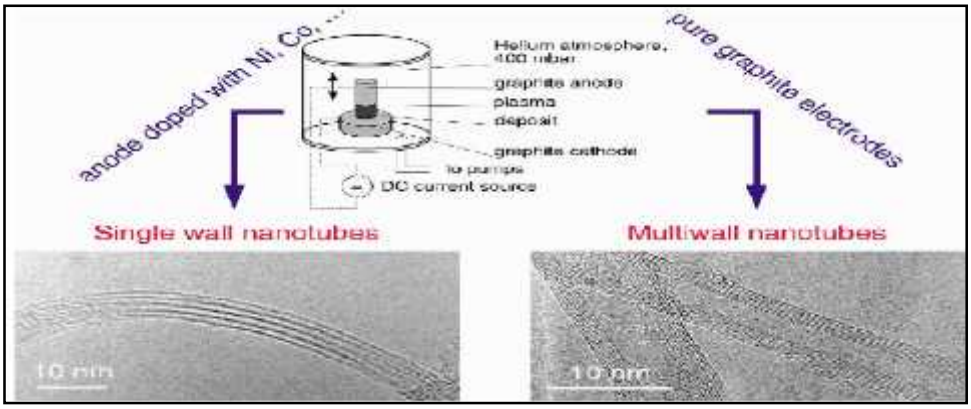

Fig. 5: Experimental set-up of an arc discharge apparatus.

single wall called single-wall carbon nanotubes (Figure 4a).

2) Multiple walled carbon nanotubes (MWNTs): These consist of carbon atoms bounded into a tube shaped, with multiple walls called as multiwall carbon nanotubes (Figure 4b).

Some differential points amongst SWNTs and MWNTs are listed in Table 1.

Methods of Productions of CNTs:

1) ARC Discharge Method[15-17]: The carbon arc discharge method, initially used for producing C60 fullerenes, is the most common and perhaps easy way to produce carbon nanotubes as it is rather simple to undertake.

However, it is a technique that produces a mixture of components and requires separating nanotubes from the soot and the catalytic metals present in the crude product. This method creates nanotubes 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 (helium, argon) at low pressure (between 50 and 700 mbar). Recent investigations have shown that it is also possible to create nanotubes with the arc method in liquid nitrogen[18]. A direct current of 50 to 100 A driven by approximately 20 V creates a high temperature discharge between the two electrodes. The discharge vaporizes one of the carbon rods and forms a small rod shaped deposit on the other rod. Producing nanotubes in high yield depends on the uniformity of the plasma arc and the temperature of the deposit form on the carbon electrode. These properties affect the speed with which the carbon and catalyst molecules diffuse and cool affecting nanotube diameter in the arc process. This implies that single-layer tubules nucleate and grow on metal particles in different sizes depending on the quenching rate in the plasma and it

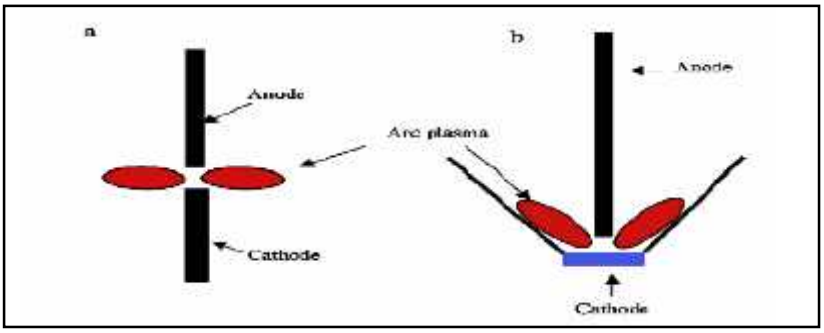

Fig. 6: Schematic drawings of the electrode set-ups for (a) conventional and (b) new arc discharge electrodes.

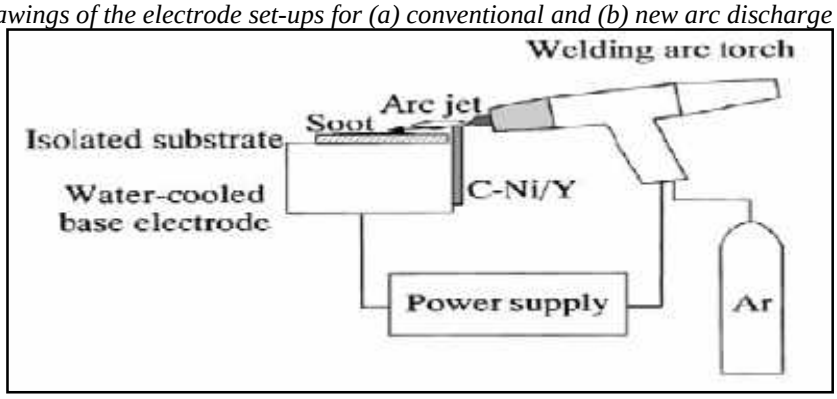

Fig. 7: Experimental set-up of the torch arc method in open air.

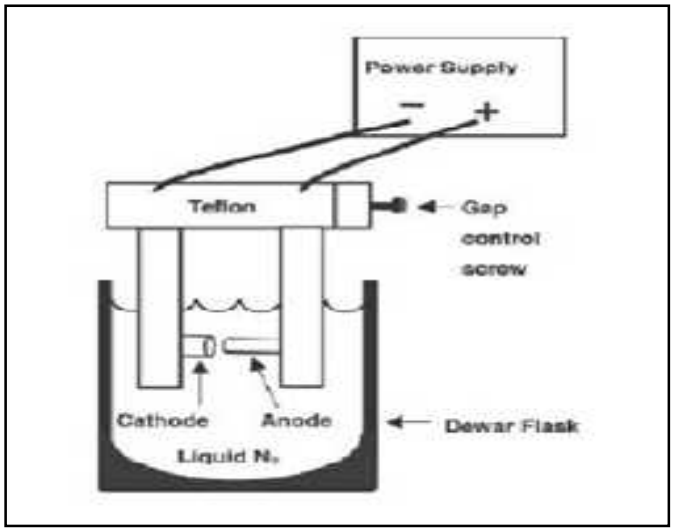

Fig. 8: Schematic drawings of the arc discharge apparatus in liquid nitrogen.

suggests that temperature, carbon and metal catalyst densities affect the diameter distribution of nanotubes. Depending on the exact technique, it is possible to selectively grow SWNTs or MWNTs, which is shown in Figure 5. Two distinct methods of synthesis can be performed with the arc discharge apparatus.

A) Synthesis of SWNTs: If SWNTs are preferable, the anode has to be doped with metal catalyst such as Fe, Co, Ni, Y or Mo. A lot of elements and mixtures of elements have been tested by various authors and it is noted that the results vary a lot, even though they use the same elements. This is not surprising as experimental conditions differ. The quantity and quality of the nanotubes obtained depend on various parameters such as the metal concentration, inert gas pressure, kind of gas, the current and system geometry. Usually the diameter is in the range of 1.2 to 1.4 nm. A couple of ways to improve the process of arc discharge are as stated below:

a) Inert gas: The most common problems with SWNTs synthesis are that the product contains a lot of metal catalyst, SWNTs have defects and purification is hard to perform. On the other hand, an advantage is that the diameter can slightly be controlled by changing thermal transfer, diffusion and hence condensation of atomic carbon and metals between the plasma and the vicinity of the cathode can control nanotube diameter in the arc process. This was shown in an experiment in which different mixtures of inert gases were used. It appeared that argon, with a lower thermal conductivity and diffusion coefficient, gave SWNTs with a smaller diameter of approximately 1.2 nm. A linear fit of the average nanotube diameter showed a 0.2 nm diameter decrease per 10 %

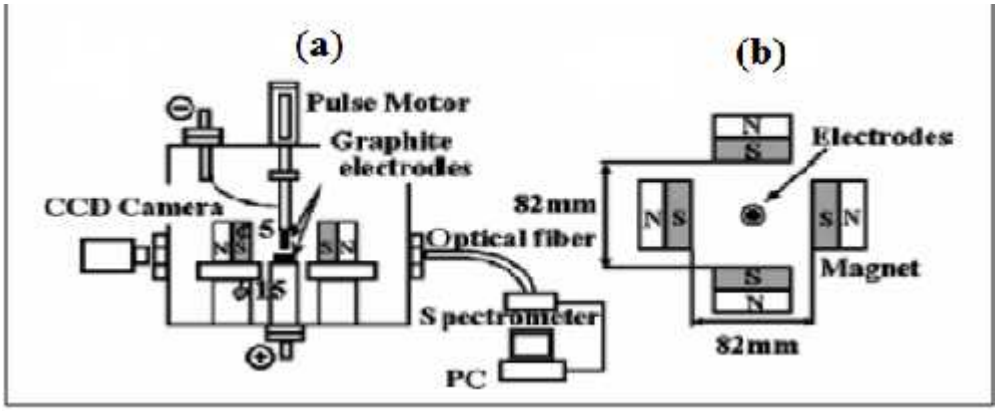

Fig. 9: Schematic diagram of synthesis system for MWNTs in a magnetic field, side view (a) and top view (b).

increase in argon helium ratio, when nickel/yttrium was used(C/Ni/Y was 94.8:4.2:1) as catalyst.

b) Catalyst: Knowing that chemical vapour deposition (CVD) could give SWNTs with a diameter of 0.6–1.2 nm; researchers tried the same catalyst as used in CVD on arc discharge. Not all of the catalysts used appeared to result in nanotubes for both methods. But there seemed to be a correlation of diameter of SWNTs synthesized by CVD and arc discharge. As a result, the diameter can be controllably lowered to a range of 0.6-1.2 nm with arc-discharge. Use of mixture of Co and Mo in high concentrations as catalyst, resulted in this result. These diameters are considerably smaller than 1.2-1.4 nm, which is the usual size gained from arc discharge.

c) Improvement of oxidation resistance: There is also progress in developing methods to improve the oxidation resistance of the SWNTs, which is a consequence of the defects present in nanotubes. A strong oxidation resistance is needed for the nanotubes if they have to be used for applications such as field emission displays. Recent research has indicated that a modified arc-discharge method using a bowl-like cathode (Figure 6) decreases the defects and gives cleaner nanotubes and thus improves the oxidation.

The Raman spectrum of the newly synthesized nanotubes shows that the nanotubes formed are cleaner and less defective compared with those synthesized by conventional methods. The anode rod contained Ni and Y catalyst (C /Ni/Y is 94.8:4.2:1). No information is given about the diameter size.

d) Open air synthesis with welding arc torch: Only a couple of years ago, researchers discovered that it was possible to form MWNTs in open air. A welding arc torch was operated in open air and the process was shielded with an argon gas flow. The anode and cathode were made of graphite containing Ni and Y (Ni/Y is 4.2:1 at. %). This method was modified for preparing SWNTs. A plate target made of graphite containing metal catalyst Ni and Y (Ni/Y is 3.6:0.8 at. per cent), was fixed at the sidewall of a water cooled, steel based electrode. The torch arc aimed at the edge of the target and the soot was deposited on the substrate behind the target (Figure 7). The arc was operated at a direct current of 100 A, and shielding argon gas flowed through the torch, enhancing the arc jet formation beyond the target. In the soot, carbon nanohorns (CNHs) and bundles of SWNT with an average diameter of 1.32 nm were found. However, the yield was much lower than for the conventional low-pressure arc discharge method. There are two reasons for this fact. At first, because of the open air, the lighter soot will escape into the atmosphere. Secondly, the carbon vapour might be oxidized and emitted as carbon dioxide gas. In order to improve the yield in this method, contrivances for collecting soot and development of an appropriate target are required. This method promises to be convenient and inexpensive once the conditions for higher yield are optimized.

B) Synthesis of MWNT: If both electrodes are graphite, the main product will be MWNTs. But next to MWNTs a lot of side products are formed such as fullerenes, amorphous carbon and some graphite sheets. Purifying MWNTs led loss of structure and disorders the walls. However scientists are developing ways to gain pure MWNTs in a large-scale process without purification. Typical sizes for MWNTs are inner diameter of 1-3 nm and an outer diameter of approximately 10 nm. Because no catalyst is involved in this process, there is no need for a heavy acidic purification step. This means, the MWNTs, can be synthesized with lesser defects.

a) Synthesis in liquid nitrogen: A first, possibly economical route to produce highly crystalline MWNTs is the arc-discharge method in liquid nitrogen (Figure 8); with this route mass production is also possible. For this option low pressures and expensive inert gasses are not needed. The content of the MWNTs can be as high as 70% of the reaction product. Analysis with Auger spectroscopy revealed that no nitrogen was incorporated in the MWNTs. There is a strong possibility that SWNTs can be produced with the same apparatus under different conditions[16].

b) Magnetic field synthesis: Synthesis of MWNTs in a magnetic field gives defect-free and high purity MWNTs that can be applied as nanosized electric wires for device fabrication. In this case, the arc discharge synthesis was controlled by a magnetic field around the arc plasma. Extremely pure graphite rods (purity > 99.999 %) were used as electrodes. Highly pure MWNTs (purity>95%) were obtained without further purification, which disorders walls of MWNTs (Figure 9, 10).

c) Plasma rotating arc discharge: A second possibly economical route to mass production of MWNTs is synthesis by plasma rotating arc discharge technique

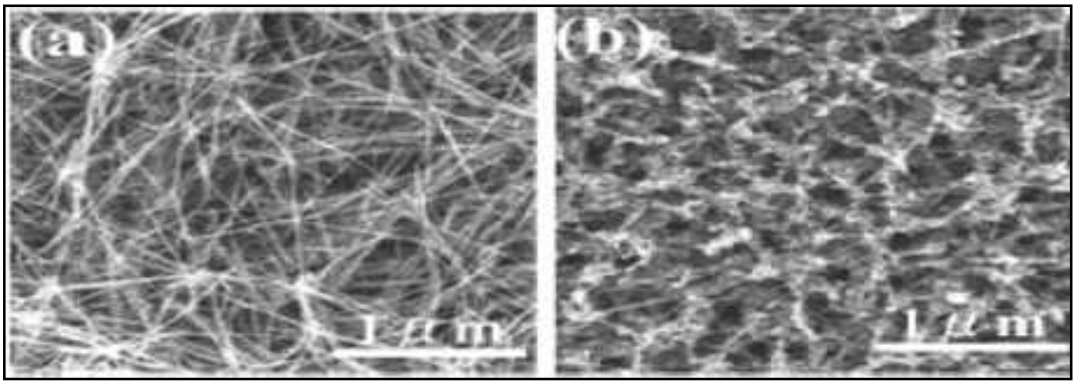

Fig. 10: SEM images of MWNTs synthesized with (a) and without (b) magnetic field.

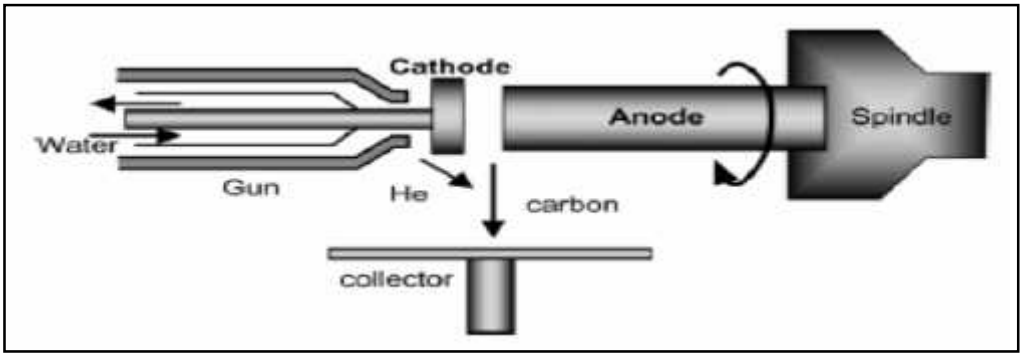

Fig. 11: Schematic diagram of plasma rotating electrode system.

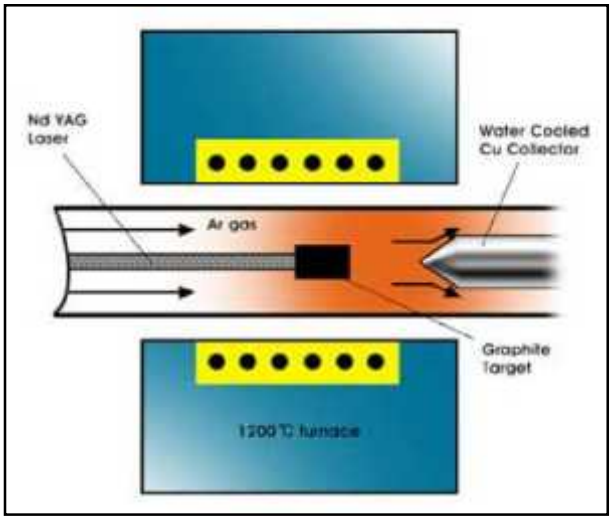

Fig. 12: Schematic drawing of a laser ablation apparatus.

(Figure 11). The centrifugal force caused by the rotation generates turbulence and accelerates the carbon vapour perpendicular to the anode. In addition, the rotation distributes the micro discharges uniformly and generates stable plasma. Consequently, it increases the plasma volume and raises the plasma temperature.

At rotation speed of 5000 rpm a yield of 60% was found at formation temperature of 1025 °C without use of a catalyst. The yield increases up to 90% after purification if the rotation speed is increased and the temperature is enlarged to 1150 °C[16-18].

2) Laser Ablation Method[15-18]**:** In 1995, Smalley's group at Rice University reported the synthesis of CNTs by laser vaporisation. The laser vaporisation apparatus used by Smalley's group is shown in **Figure 12**. A pulsed or continuous laser is used to vaporise a graphite target in an oven at 1200 °C. The main difference between continuous and pulsed laser, is that the pulsed laser demands a much higher light intensity (100 kW/cm^2 compared with 12 kW/cm^2). The oven is filled with helium or argon gas in order to keep the pressure at 500 Torr. A very hot vapour plume forms, then expands and cools rapidly. As the vaporised species cool, small carbon molecules and atoms quickly condense to form larger clusters, possibly including fullerenes. The catalysts also begin to condense, but more slowly at first, and attach to carbon clusters and prevent their closing into cage structures. Catalysts may even open cage structures when they attach to them. From these initial clusters, tubular molecules grow into SWCNTs until the catalyst particles become too large, or until conditions have cooled sufficiently that carbon no longer can diffuse through or over the surface of the catalyst particles. It is also possible that the particles become that much coated with a carbon layer that they cannot absorb more and the nanotube stops growing. The SWNTs formed in this case are bundled together by van der Waals forces.

There are some striking, but not exact similarities, in the comparison of the spectral emission of excited species in laser ablation of a composite graphite target with that of laser-irradiated C60 vapour. This suggests that fullerenes are also produced by laser ablation of catalyst-filled graphite, as is the case when no catalysts are included in the target. However, subsequent laser pulses excite fullerenes to emit C2 that adsorbs on catalyst particles and feeds SWNT growth. However, there is insufficient evidence to conclude this with certainty laser ablation is almost similar to arc discharge, since the optimum

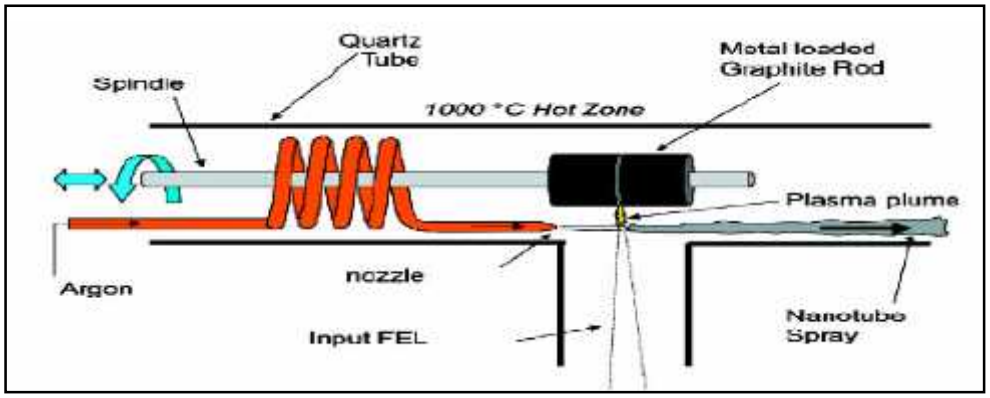

Fig. 13: Schematic drawings of the ultra fast-pulsed laser ablation apparatus.

background gas and catalyst mix is the same as in the arc discharge process. This might be due to very similar reaction conditions needed, and the reactions probably occur with the same mechanism.

Large scale synthesis of SWNT: Because of the good quality of nanotubes produced by this method, scientists are trying to scale up laser ablation. However the results are not yet as good as for the arc-discharge method, but they are still promising. In the next two sections, two of the newest developments on large-scale synthesis of SWNTs will be discussed. The first is the 'ultra fast Pulses from a free electron laser' method, the second is 'continuous wave laser-powder' method. Scaling up is possible, but the technique is rather expensive due to the laser and large amount of power required.

a) Ultra fast Pulses from a free electron laser (FEL) method: Usually the pulses in an Nd: YAG system has width of approximately 10 ns, in this FEL system the pulse width is ~ 400 fs. The repetition rate of the pulse is enormously increased from 10 Hz to 75 MHz. To give the beam the same amount of energy as the pulse in an Nd:YAG system, the pulse has to be focused. The intensity of the laser bundle behind the lens reaches ~5 x 1011 W/cm^2, which is about 1000 times greater than in Nd: YAG systems. A jet of preheated (1000 °C) argon through a nozzle tip is situated close to the rotating graphite target, which contains the catalyst. The argon gas deflects the ablation plume approximately 90° away from the incident FEL beam direction, clearing away the carbon vapour from the region in front of the target. The produced SWNT soot is collected in a cold finger. This process can be seen in Figure 13. The yield at this moment is 15 g/h, which is at 20 % of the maximum power of not yet upgraded FEL. If the FEL is upgraded to full power and is working at 100 % power, a yield of 45 g/h could be reached since the yield is not limited by the laser power.

b) Continuous wave laser-powder method: This method is a novel, continuous, highly productive laser-powder method of SWNT synthesis based on the laser ablation of mixed graphite and metallic catalyst powders by a 2kW continuous wave CO_2 laser in an argon or nitrogen stream. Because of the introduction of micron-size particle powders, thermal conductivity losses are significantly decreased compared with laser heating of the bulk solid targets in known laser techniques. As a result, more effective utilization of the absorbed laser power for material evaporation is achieved. The set-up of the laser apparatus is shown in Figure 14.

The established yield of this technique is 5 g/h. A Ni/Co mixture (Ni/Co is 1:1) is used as catalyst and the temperature 1100 °C. In the soot a SWNT abundance of 20-40% is found with a mean diameter of 1.2-1.3 nm. An HRTEM-picture of sample is also shown in Figure 14.

3) Chemical Vapour Deposition[18,19]: Chemical vapour deposition (CVD) synthesis is achieved by putting a carbon source in the gas phase and using an energy source, such as plasma or a resistively heated coil, to transfer energy to a gaseous carbon molecule. Commonly used gaseous carbon sources include methane, carbon monoxide and acetylene. The energy source is used to "crack" the molecule into reactive atomic carbon. Then, the carbon diffuses towards the substrate, which is heated and coated with a catalyst (usually a first row transition metal such as Ni, Fe or Co) where it will bind. Carbon nanotubes will be formed if the proper parameters are maintained. Excellent alignment; as well as positional control on nanometer scale, can be achieved by using CVD. Control over the diameter, as well as the growth rate of the nanotubes can also be maintained. The appropriate metal catalyst can preferentially grow single rather than multi-walled nanotubes. CVD carbon nanotube synthesis is essentially a two-step process consisting of a catalyst preparation step followed by the actual synthesis of the nanotube. The catalyst is generally prepared by sputtering a transition metal onto a substrate and then using either chemical etching or thermal annealing to induce catalyst particle nucleation. Thermal annealing results in cluster formation on the substrate, from which the nanotubes will grow. Ammonia may be used as the etchant. The temperatures for the synthesis of nanotubes by CVD are generally within the 650–900^{0}C range. Typical yields for CVD are approximately 30%. These are the basic principles of the CVD process. In the last decennia, different techniques for the carbon nanotubes synthesis with CVD have been developed, such as plasma enhanced CVD, thermal chemical CVD, alcohol catalytic CVD, vapour phase growth, aero gel-supported CVD and laser assisted CVD.

a) Plasma enhanced CVD method: 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. Figure 15 shows a schematic diagram of a

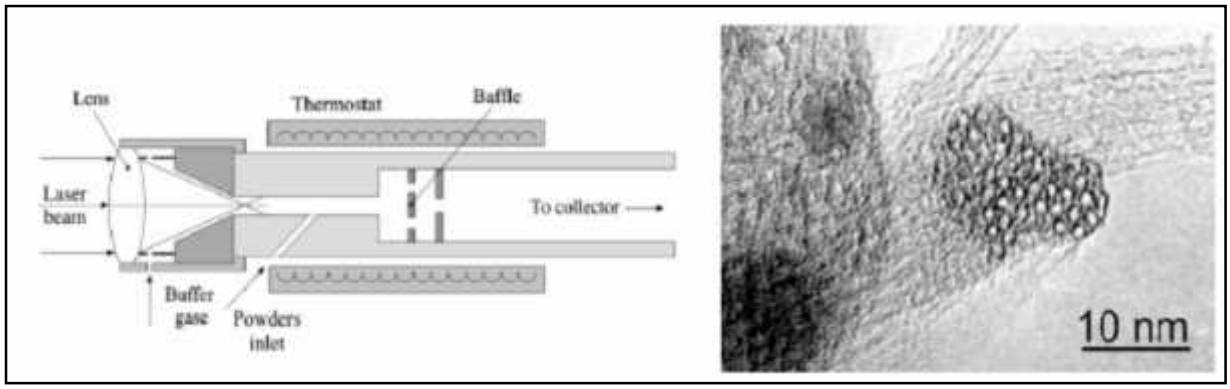

Fig. 14: (Left) The principle scheme of the set-up for SWNTs production by continuous wave laser powder method, (Right) HRTEM of a SWNT-bundle cross-section.

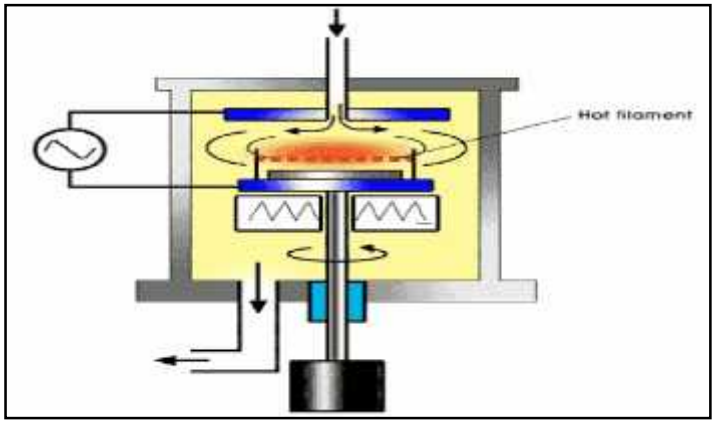

Fig. 15: Schematic diagram of plasma CVD apparatus.

typical plasma CVD apparatus with a parallel plate electrode structure.

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 for example a Si, SiO_2, or glass substrate using thermal CVD or sputtering. After nanoscopic fine metal particles are formed, CNTs will be grown on the metal particles on the substrate by glow discharge generated from high frequency power. A carbon containing reaction gas, such as C_2H_2, CH_4, C_2H_4, C_2H_6, CO is supplied to the chamber during the discharge. The catalyst has a strong effect on the nanotube diameter, growth rate, wall thickness, morphology and microstructure. Ni seems to be the most suitable pure-metal catalyst for the growth of aligned MWNTs. The diameter of the MWNTs is approximately 15 nm. The highest yield of CNTs achieved here is about 50% and is obtained at relatively low temperatures (below 330^o C)[18].

b) Thermal CVD method: In this method Fe, Ni, Co or an alloy of the three catalytic metals is initially deposited on a substrate. After the substrate is etched in a diluted HF solution with distilled water, the specimen is placed in a quartz boat. The boat is positioned in a CVD reaction furnace, and nanometer-sized catalytic metal particles are formed after an additional etching of the catalytic metal film using NH_3 gas at a temperature of 750 to 1050^{o}C. As carbon nanotubes are grown on these fine catalytic metal particles in CVD synthesis, forming these fine catalytic metal particles is the most important process. Figure 16 shows a schematic diagram of thermal CVD apparatus in the synthesis of CNTs. When growing carbon nanotubes on a Fe catalytic film by thermal CVD, the diameter range depends on the thickness of the catalytic film. By using a thickness of 13 nm, the diameter distribution lies between 30-40 nm. When a thickness of 27 nm is used, the diameter range is between 100-200 nm. The CNTs formed are multiwall[18,19].

c) Liquid pyrolysis: The aerosol pyrolysis process is a catalytic CVD-based method involving pyrolysis of mixed liquid aerosols composed of both liquid hydrocarbon and catalyst precursor. Byeon and colleagues developed a new aerosol assisted chemical vapour deposition (AACVD) process to synthesize vertically aligned CNTs arrays with outstanding height (4.38 mm) with very low metal contents in a short time (20 min) without supporting materials and water-assistance. An essential part of this technique was in-situ formation of metal catalyst nanoparticles via pyrolysis of ferrocene–ethanol aerosol right before CNTs synthesis[20].

d) Solid state pyrolysis: Nowadays, solid state pyrolysis for CNTs synthesis is less frequently used compared to previously mention ones. Kucukayan and colleagues synthesized MWNTs through pyrolysis of the sulfuric acid-carbonized by product of sucrose. They observed the presence of sulfur in catalyst particles trapped inside nanotubes, but no sulfur was present in the side-walls of the CNTs[21]. Clauss *et al* thermally decomposed two nitrogen-rich iron salts, ferric ferrocyanide (Prussian Blue, ‘‘PB’’) and iron melonate (‘‘FeM’’) in a microwave oven,

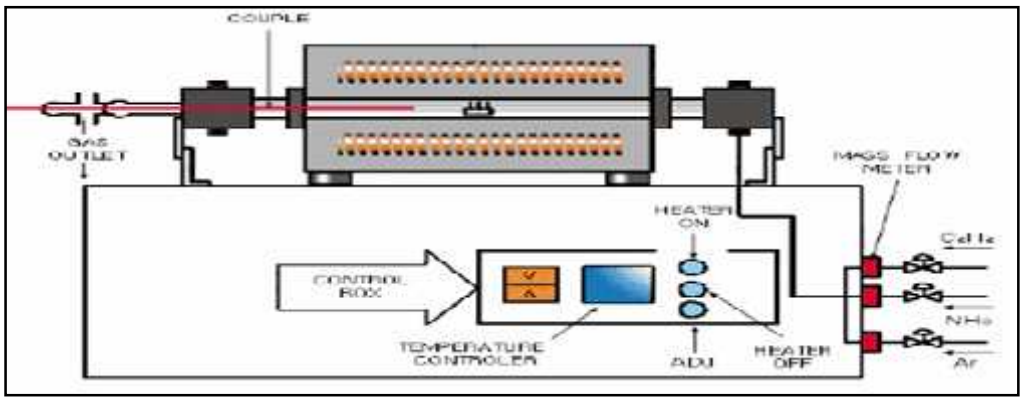

Fig. 16: Schematic diagram of thermal CVD apparatus.

which was used to heat a molybdenum wire after being coated with the precursor and protected from ambient atmosphere. While the PB-precursor did not give any nanotube containing products, the FeM-precursor furnished tubular carbon nanostructures in a reproducible manner. This result may be due to the graphite-like nature of the melonate anions presented in FeM[22]. Kuang *et al* synthesized straight CNTs in large scale through thermal CVD by pyrolysis of two mixed metal phthalocyanines with a certain amount of S at 800–950 ^{0}C. The as-synthesized CNTs were 15–35 nm in diameter and 200–800 nm in length, quite straight and well-graphitized with nearly no defects.

4) Bottom-Up Organic Approach: The bottom-up approach to integrate vertically PECVD grown MWNTs into multilevel interconnects in silicon integrated circuit manufacturing from patterned catalyst spot was reported first by Li *et al*[23]. More recently, Jasti and Bertozzi described in their frontier article the potential advantages, recent advances and challenges that lie ahead for the bottom-up organic synthesis of homogeneous CNTs with well-defined structures[24]. Current synthetic methods used for CNTs fabrication produce mixtures of structures with varying physical properties. Jasti and Bertozzi demonstrated the CNTs synthesis with control of chirality, which relies on utilizing hoop-shaped carbon macrocycles, i.e. small fragments of CNTs that retain information regarding chirality and diameter as templates for CNTs synthesis (Figure 17). Their strategy lies in two basic areas: the synthesis of aromatic macrocyclic templates and the development of polymerization reactions to extend these templates into longer CNTs. This approach is particularly attractive because it can be used for synthesis of both zigzag and armchair CNTs of different diameters, as well as of chiral CNTs with various helical pitches. For example, a (5, 5) armchair CNT can be constructed by fusing additional phenyl rings to cycloparaphenylene (Fig. 17a). In similar fashion, a (10, 0) zigzag CNT can be constructed from cyclacene (Fig. 17b).

Properties of CNTs

Electrical Properties: The Unique Electrical Properties of carbon nanotubes are to a large extent derived from their 1-D character and the peculiar electronic structure of graphite. They have extremely low electrical resistance. Resistance occurs when an electron collides with some defect in the crystal structure of the material through which it is passing. The defect could be an impurity atom, a defect in the crystal structure, or an atom vibrating about its position in the crystal. Such collisions deflect the electron from its path. But the electrons inside a carbon nanotube are not so easily scattered. Because of their very small diameter and huge ratio of length to diameter, a ratio that can be up in the millions or even higher. In a 3-D conductor, electrons have plenty of opportunity to scatter, since they can do so at any angle. Any scattering gives rise to electrical resistance. In a 1-D conductor, however, electrons can travel only forward or backward. Under these circumstances, only backscattering (the change in electron motion from forward to backward) can lead to electrical resistance. But backscattering requires very strong collisions and is thus less likely to happen. So the electrons have fewer possibilities to scatter. This reduced scattering gives carbon nanotubes their very low resistance. In addition, they can carry the highest current density of any known material, measured as high as 109 A/cm^2. One use for nanotubes that has already been developed is as extremely fine electron guns, which could be used as miniature cathode ray tubes (CRTs) in thin high-brightness low-energy low-weight displays. This type of display would consist of a group of many tiny CRTs, each providing the electrons to hit the phosphor of one pixel, instead of having one giant CRT whose electrons are aimed using electric and magnetic fields. These displays are known as Field Emission Displays (FEDs). A nanotube formed by joining nanotubes of two different diameters end to end can act as a diode, suggesting the possibility of constructing electronic computer circuits entirely out of nanotubes. Nanotubes have been shown to be superconducting at low temperatures[25-28].

Mechanical Properties: The carbon nanotubes are expected to have high stiffness and axial strength as a result of the carbon–carbon sp^2 bonding. The practical application of the nanotubes requires the study of the elastic response, the inelastic behavior and buckling, yield strength and fracture. Efforts have been applied to the experimental and theoretical investigation of these properties. Nanotubes are the stiffest known fiber, with a measured Young's modulus of 1.28 TPa. They have an expected elongation to failure of 20-30%, which combined with the stiffness, projects to a tensile strength well above 100 GPa (possibly higher), by far the highest known. For comparison, the Young's

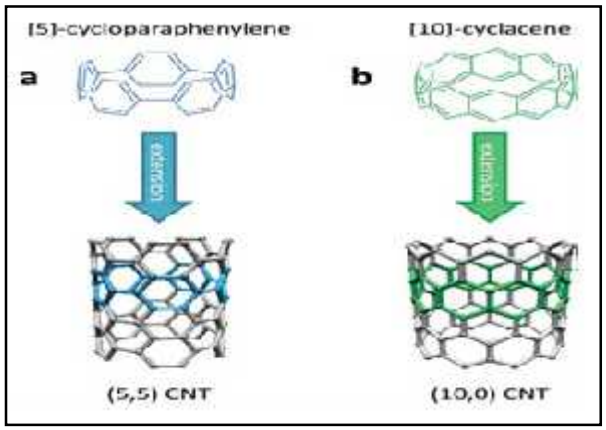

Fig. 17: Bottom-up, organic synthesis approach to CNTs with discrete chirality.

modulus of high-strength steel is around 200 GPa and its tensile strength is 1-2 GPa[29-32].

Thermal Properties: Prior to CNTs, diamond was the best thermal conductor. CNTs have now been shown to have a thermal conductivity at least twice that of diamond[33]. CNT have the unique property of feeling cold to the touch, like metal, on the sides with the tube ends exposed, but similar to wood on the other sides. The specific heat and thermal conductivity of carbon nanotube systems are determined primarily by phonons. The measurements yield linear specific heat and thermal conductivity above 1 K and below room temperature while a T0.62 behavior of the specific heat was observed below 1 K. The linear temperature dependence can be explained with the linear k-vector dependence of the frequency of the longitudinal and twist acoustic phonons. The specific behaviour of the specific heat below 1 K can be attributed to the transverse acoustic phonons with quadratic k dependence. The measurements of the thermoelectric power (TEP) of nanotube systems give direct information for the type of carriers and conductivity mechanisms[27-29]. Young's modulus, tensile strength, density and some parameters for CNTs are given in Table 2 and Table 3.

Characterisation of CNTs: CNTs have very interesting physicochemical properties such as ordered structure with high aspect ratio, ultra light weight, high mechanical strength, high electrical conductivity, high thermal conductivity, metallic or semi metallic behavior and high surface area.

Raman Spectroscopy is suitable for the quick and reliable screening of presence of SWCNTs.

Transmission Electron Microscopy (TEM) allows the assessment of detailed structures.

Scanning Electron Microscopy (SEM) provides overviews of sample structures; while less sensitive to sample preparation and homogeneity than TEM.

Thermo-gravimetric Analysis (TGA) gives information about relative abundance of catalyst particles, nanotubes and other carbonaceous structures.

Purification of CNTs: Nanotubes usually contain a large amount of impurities such as metal particles, carbonaceous impurities such as amorphous carbon, fullerenes, nanoparticles, and transition metals introduced as catalysts during the synthesis. There are different steps in purification of nanotubes.

1) Air Oxidation: The CNTs are having less purity; the average purity is about 5-10%. So 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 is found to be at 673 k for 40 min.

2) Acid Refluxing: Refluxing the sample in strong acid is effective in reducing the amount of metal particles and amorphous carbon. Different acids used are hydrochloric acid (HCl), nitric acid (HNO_3) and sulphuric acid (H_2SO_4), but HCl was identified to be the ideal refluxing acid.

3) Surfactant Aided Sonication, Filtration and Annealing: After acid refluxing, the CNTs became purer but tubes get entangled together, trapping most of the impurities such as carbon particles and catalyst particles, which were difficult to remove with filtration. So surfactant aided sonication is carried out. Sodium dodecyl benzene sulphonate (SDBS) aided sonication with ethanol (or methanol) as organic solvent are preferred because it took the longest time for CNTs to settle down, indicating an even suspension state is achieved. The sample is then filtered with an ultra filtration unit and annealed at 1273 k in N_2 for 4 h. Annealing is effective in optimizing the CNTs structures. It is proved that surfactant-aided sonication is effective to untangle CNTs, thus to free the particulate impurities embedded in the entanglement[34].

Functionalization of CNTs**:** For biological and biomedical applications, the lack of solubility of carbon nanotubes in aqueous media has been a major technical barrier. To overcome this problem modification of the surface of CNTs i.e. functionalization is done[35]. 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. The recent expansion in methods to chemically modify and functionalize carbon nanotubes has made it possible to solubilize and disperse carbon nanotubes in water, thus opening the path for their facile manipulation and processing in physiological environments. Equally important is the recent demonstration that biological and bioactive species such as proteins, carbohydrates and nucleic acids can be conjugated with carbon nanotubes[36]. These nanotube bioconjugates will play a significant role in the research efforts towards bioapplications of CNTs. Concerning the intrinsic toxicity, *in-vitro* studies had indicated that SWNT functionalized by a covalent method with phenyl-SO_3H or phenyl-$(COOH)_2$ groups produced less cytotoxic effects than aqueous dispersions of pristine SWNT stabilized with a surfactant 1% of Pluronic F108. Moreover, in the same study, the cytotoxicity of covalently modified SWNT has been reported to be further decreased with the increase in the degree of sidewall functionalization[35,37].

Toxicity of CNTs**:** Generally, the harmful effects of nanoparticles arise from the combination of various factors, two of which are particularly important: (a) the

Table 2: Young's modulus, tensile strength and density of carbon nanotubes compared with other materials.

Material	Young's modulus (GPa)	Tensile Strength (GPa)	Density (g/cm^3)
Single wall nanotube	1054.000	150.000	-
Multiwall nanotube	1200.000	150.000	2.600
Steel	208.000	0.400	7.800
Epoxy	3.500	0.005	1.250
Wood	16.000	0.008	0.600

high surface area and (b) the intrinsic toxicity of the surface[38]. In contrast with conventional particles of larger mean diameter, nanoparticles under 100 nm can potentially be more toxic to the lung, can redistribute from their site of deposition, can escape from the normal phagocytic defenses and can modify the structure of proteins. Therefore, nanoparticles can activate inflammatory and immunological responses and may affect the normal tissue functions. CNTs, 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 CNTs make quantities of milligrams possess a large number of cylindrical, fiber-like particles, with a concurrent, very high total surface; depending on degree of bundling and aggregation of nanotubes in solution[36].

Another important factor is the bioavailability of CNTs in the body. The mechanism of CNT metabolism, degradation or dissolution, clearance and bioaccumulation requires attention and study in order to obtain a clearer idea of the limitations of such nanomaterials as components of pharmaceuticals. So far the vast majority of reports published on the administration of CNTs are primarily concerned with the toxicology of CNTs[36].

Applications of CNTs: Carbon nanotubes are expected to become a key material in ultrafine devices of the future because of their unique electrical characteristics and may also bring a revolution in pharmaceuticals due to their extraordinarily fine structure on a nanometer scale obliging for efficient drug delivery. Various applications of CNTs are as follows:

1) Carrier for Drug Delivery: Carbon nanohorns (CNHs) are the spherical aggregates of CNTs with irregular horn like shape. Research studies have proved CNTs and CNHs as a potential carrier for drug delivery system.

2) Functionalised CNTs are reported for targeting of Amphotericin B to Cells[27].

3) Cisplatin incorporated oxidized SWNHs have showed slow release of Cisplatin in aqueous environment. The released Cisplatin had been effective in terminating the growth of human lung cancer cells; while the SWNHs alone did not show anticancer activity[28].

4) Anticancer drug Polyphosphazene platinum given with nanotubes had enhanced permeability, distribution and retention in the brain due to controlled lipophilicity of nanotubes.

5) Antibiotic, Doxorubicin given with nanotubes is reported for enhanced intracellular penetration.

6) The gelatin CNT mixture (hydro-gel) has been used as potential carrier system for biomedicals.

7) CNTs based carrier system can offer a successful oral alternative administration of Erythropoietin (EPO), which has not been possible so far because of the denaturation of EPO by gastric environment conditions and enzymes.

8) They can be used as lubricants or glidants in tablet manufacturing due to nanosize and sliding nature of graphite layers bound with van der walls forces.

9) Carbon nanotubes are strong, flexible, conduct electrical current and can be functionalized with different molecules, properties that may be useful in basic and applied neuroscience reaserch[29].

10) Genetic Engineering: In genetic engineering, CNTs and CNHs are used to manipulate genes and atoms in the development of bioimaging genomes, proteomics and tissue engineering. The unwound DNA (single stranded) winds around SWNT by connecting its specific neucleotides and causes change in its electrostatic property. This creates its potential application in diagnostics (polymerase chain reaction) and in therapeutics[28,29].

11) Artificial Implants: Normally body shows rejection reaction for implants with the post administration pain. 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, CNTs filled with calcium and arranged/grouped in the structure of bone can act as bone substitute[31,32].

12) As Preservative: CNTs and nanohorns are antioxidant in nature. Hence, they are used to preserve drugs formulations prone to oxidation. Their antioxidant property is used in antiaging cosmetics and with zinc oxide as sunscreen dermatological to prevent oxidation of important skin components[29].

13) 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. Hence, reduction in the frequency and amount of catalyst addition can be achieved by using CNTs and CNHs[29,36].

14) In Drug Delivery: For instance, carbon nanotubes have the potential to carry drugs in the organism as they are hollow and much smaller than the blood cells. The methods were developed for attaching DNA and protein molecules to the inside and outside of the nanotubes. This gives one the ability to target and destroy individual cells that may be cancerous or infected by a virus[35,38].

15) In Computer Industry: SWCNTs are excellent conductors, and many computing companies are developing ways to use them in computers. The use of carbon nanotubes will allow the computing industry to

Table 3: Some parameters for CNTs (All values are for SWCNTs unless otherwise stated).

Equilibrium Structure:
Average diameter of SWNTs 1.2-1.4 nm
Distance from opposite carbon atoms (Line 1) 2.830 Å
Analogous carbon atom separation (Line 2) 2.456 Å
Parallel carbon bond separation (Line 3) 2.450 Å
Carbon bond length (Line 4) 1.420 Å
C-C tight bonding overlap energy ~ 2.50 eV
Group symmetry (10, 10) C5V
Interlayer spacing:
(n, n) Armchair- 3.380 Å
(n, 0) Zigzag- 3.410 Å
(2n, n) Chiral- 3.390 Å
Optical Properties:
Fundamental gap:
For (n, m); n-m is divisible by 3 [Metallic]- 0 eV
For (n, m); n-m is divisible by 3 [Semiconducting]- ~0.5 eV
Maximum current density 10^{13} A/m^2
Thermal Transport:
Thermal conductivity (room temperature) ~ 2000 W/m K
Phonon mean free path ~ 100 nm
Relaxation time ~ 10^{-11} s
Elastic Behavior:
Young's modulus (SWNT) ~ 1 TPa
Young's modulus (MWNT) 1.28 TPa

create computers more powerful than those which can be fabricated via the conventional method of photolithography.

16) Gene Delivery by CNTs: Not only are nanotubes practical in the delivery of medicinal molecules, they can also be utilized to deliver genes directly into the cell and across the nuclear membrane. *Gao et al* found that not only can DNA molecules be attached to the tips and walls of CNTs but also it can be encapsulated inside. Currently, viral vectors for gene delivery are in use and achieve high gene expression. However, this method of delivery is far from perfect, as viral vectors can be immunogenic and can cause inflammation and oncogenic effects. Functionalized CNTs can provide a safe non-viral vehicle for the delivery of DNA molecules into mammalian cells, since these DNA-CNT structures are produced under strict conditions in a cell free manner. In one study, *Singh et al* tested the functionality of a SWNT-DNA complex as a non-viral vector to deliver plasmid DNA into an A549 cell. The team used the 7.2 kb plasmid pCMV-Bgal in combination with a single walled nanotube. This research concluded that the CNT-gene structure lead to gene expression levels ten times higher than that of naked DNA alone. Not only was this complex very effective as a vehicle for gene delivery, it was concluded to be of low toxicity, soluble in aqueous solution, stable for long-term storage and highly modifiable for specific gene delivery needs[29,30].

Limitations of CNTs

1) Lack of solubility in most solvents compatible with the biological milieu (aqueous based).

2) The production of structurally and chemically reproducible batches of CNTs with identical characteristics.

3) Difficulty in maintaining high quality and minimal impurities[36].

CONCLUSION

With the prospect of gene therapy, cancer treatments and innovative, new answers for life-threatening diseases on the horizon, the science of nanomedicines has become an ever-growing field that has an incredible ability to bypass all barriers. 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 vehicle, which in some cases increase the solubility of the drug attached, resulting in greater efficacy and safety. Thus, overall recent studies regarding CNTs have shown a very promising glimpse of what lies ahead in the future of medicine.

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