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Review Article

CARBON NANOTUBE: NOVEL APPROACHES

M. N. Kale*, R. S. Wanare[†], A. M. Tayade[††], P. A. Pangarkar[†††]
*S. N. Institute of Pharmacy, Pusad-445204, Dist - Yavatmal, Maharashtra, India.
Email: kalemeenan@gmail.com

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Abstract

This review on carbon nanotube (CNTs) in drug delivery covers the full calendar from their discovery in 1991 till the present (dec. 2012 , when the last draft of this review was present). This review is focused in overview of CNT in drug delivery. Carbon nanotube have largest no. of analytical application such as solid phase extraction, biosensors, voltammetry, stripping voltammetry, gas sensors and chromatographic application. Carbon nanotube holds good for desired drug delivery systems for the treatment of cancer , gene transfer and DNA application.

Keywords: Carbon nanotube CNT; solid phase extraction, sensors, voltammetry, stripping voltammetry, cancer, gene transfer.

Introduction

Carbon nanotubes (CNTs) were discovered in 1991 by the Japanese electron microscopist sumio Iijima who was studying the material deposited on the cathode during the arc- evaporation synthesis of fullerenes[1]. Carbon nanotube(CNTs) are allotropes of carbon with a cyclindrical nanostructure.

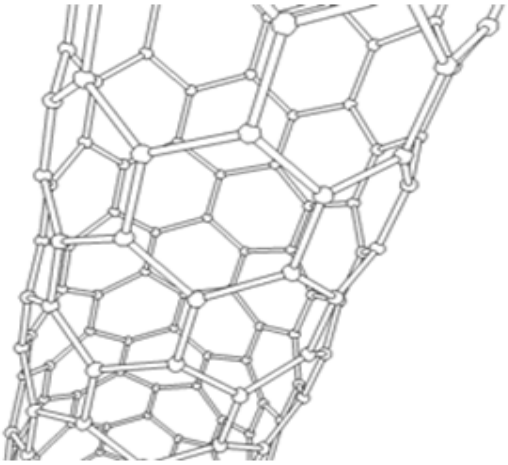

Fig.1. Spinning of carbon nanotube

Nanotubes have been constructed with length to diameter ratio of upto 132,000,000:1[2]. Nanotubes are members of the fullerenes structural family. Their name derived from their long hollow structure with the walls formed by one-atom – thick sheets of carbon, called grapheme.

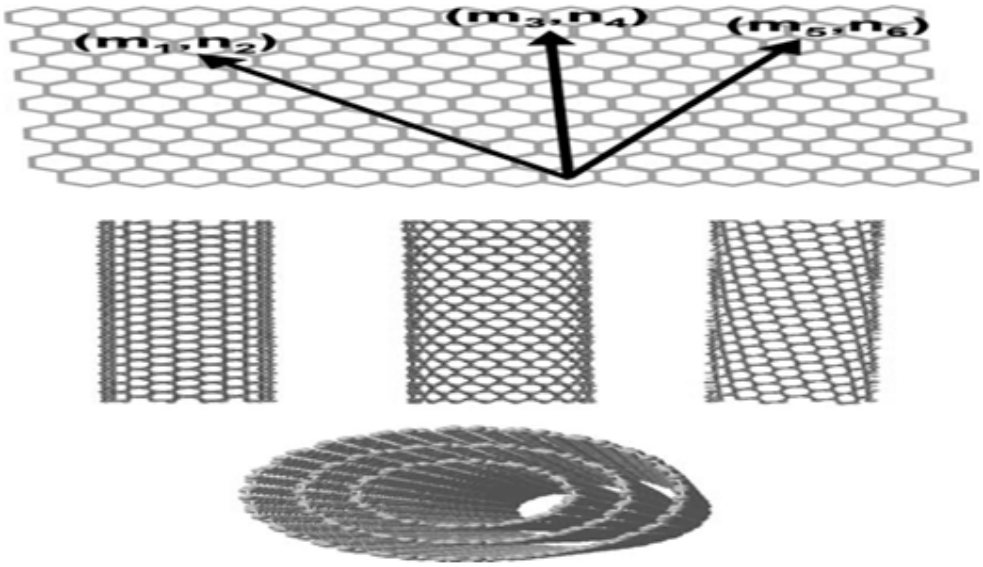

Fig.2. Schematic of the honeycomb structure of a graphene sheet.

Graphene is made up of benzene – type hexagonal rings of carbon atoms. Carbon nanotube ranges from 1to100nm in diameter. Carbon nanotube's diameter can be measured under the electron microscope using nanoscale.

Fig.3. Powder of carbon nanotube.

The chemical bonding of nanotube is composed entirely of sp^2 bonds. These bonds, which are stronger than the sp^3 bonds found in alkanes and diamonds provide nanotubes with their unique strength. Nanotubes are categorized as single-walled nanotube (SWCNTs) and multiwalled nanotube (MWCNTs). Nanotubes have the simplest chemical composition and atomic-bond configuration, but of the nanochemicals, they exihibit the most extreme diversity in

structure and structure – dependent properties [3,4]. Depending on their chirality (i.e. the chiral angle between carbon hexagons and the tube axis), SWCNTs can be metal or semiconductors. CNTs also exhibit mechanical and thermal properties.

Types of carbon nanotubes

Carbon nanotube are divided into two types

1) Single – walled carbon nanotube: (SWCNTs)

SWCNTs is formed by rolling a sheet of graphene into a cyclinder along an (m,n) lattice vector in the graphene plane . These can be imagined perfect graphene sheets in which graphene being the same poly- aromatic mono-atomic layer made of hexagonal display of sp^2 hybridized carbon atoms, rolled up into a cyclinder , with the hexagonal rings put in contact to join seamlessly[5,6,7]

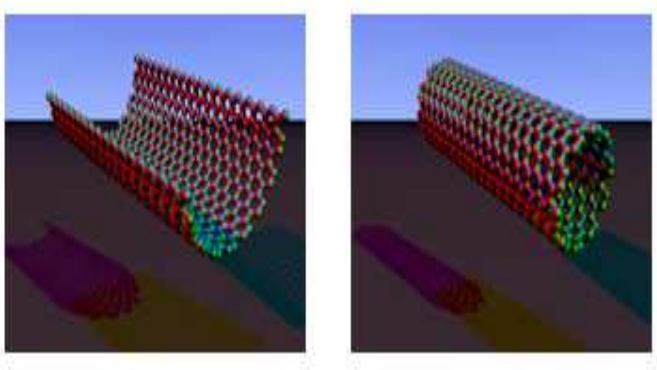

Fig.4. single walled CNTs

The (m,n) indices determine the diameter and chirality, which are key parameter of a nanotube . Strength and stifness it's depends upon the diameter of nanotube. The ideal diameter of the ideal nanotube can be calculated by following formula.

$$d = \frac{a}{\pi}\sqrt{(n^2 + nm + m^2)}.$$

Where,

d- diameter

a-const.(o.246)

n,m- indices

The typical diameter of 1.5nm SWCNTs have a diameter of close to 1 nanometer , with a tube length that can be many millions of times longer . The structure of SWCNTs can be by wrapped a one – atom – thick layer of graphite called graphene into sealess cyclinder.

2) Multi -walled carbon nanotube (MWCNTs) :

The MWCNTs consists of multi walled graphene sheet rolled up in concentric CNTs , filling each other's inner cavities to end up with nanotube. The intertube distance is in a MWCNTs is approximately that of inter- graphene distance in turbostratics poly aromatic solids and hence these MWCNTs are more stronger in their strength in comparisons to SWCNTs . SWCNTs are graphene sheet rolled up into a tube with nanodimensions[8,9].

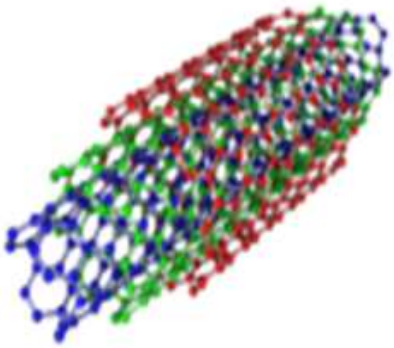

Fig.5. Multiwalled carbon nanotube.

MWCNTs tends to have diameter in the range 2-100nm.

Method of production of CNTs

There are three method for production of carbon nanotube

1) Arc discharge :

Arc discharge initially used to produce C60 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. Adirect current of between 50 and 700mbar, After applying a dc arc voltage between two separated graphite rods by modifying SiC powder production apparatus, the evaporated anode generates fullerenes in the form of soot in the chamber, and apart of the evaporated anode is deposited on the cathode.When a graphite rod that contains metal catalyst(Fe, Co, etc.) is used as the anode, being the cathode pure graphite, SWCNT [10] have been generated instead of MWCNT. Large-scale synthesis of MWCNT by arc-discharge was achieved in helium atmosphere. The arcdischarge evaporation of pure graphite rods have been carried out not only in ambient gases like helium or argon but also in methane 39. It was found that methane is the best gas for the synthesis of MWCNTs. This is due to the thermal decomposition of methane producing hydrogen ($2CH_4C_2H_23H_2$) that achieves higher temperature and activity compared to inert gases such as He or Ar. The effectiveness of hydrogen in the synthesis of MWCNT was reported [11]Fig 6.

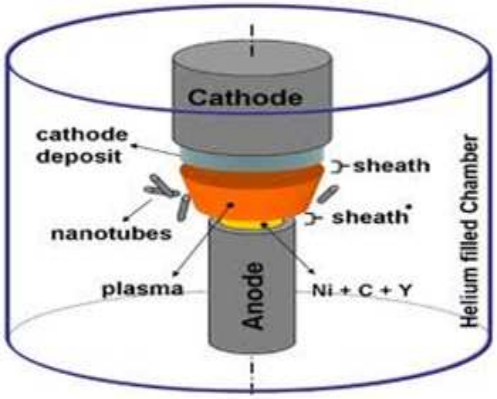

Fig.6.Diagrammatical representation of arc discharge setup for synthesis and growth of nanotube.

Advantage : This method is easy once.

Disadvantage: Soot is form

Drawback : Method is the purification of CNTs . Removal of non-nanotube carbon and metal catalyst material is much more expensive than production it's self.

The yield for this method is up to 30% by weight and it produces both single- and multi-walled nanotubes with lengths of up to 50 micrometers with few structural defects.[12]

2) Laser ablation

This method developed for production of fullerene and CNTs. This method is widely used for production of SWCNTs. The laser is suitable for material with a high boiling temp. such as carbon as the energy density of laser is much higher than that of other vaporization devices. A laser beam of CO_2 is passed onto the target located in the centre of a quartz tube furnace. Then target is vaporized in high temp. and then large size CNTs are formed , it breaks in small particles SWCNTs are formed and it collect in special collector. The material is produced by this method appears as a mat of ropes , 10-20nm in diameter and upto 100um or more in length.

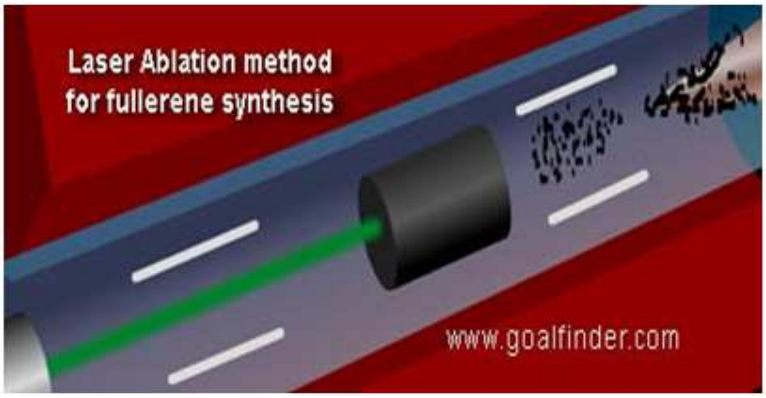

Fig.7. Digrammatical representation of laser ablation setup for synthesis and growth of nanotube.

Advantages : High quality of SWCNTs regarding the diameter growth control.

The change the temp. of the furnance , catalytic metal and flow rate directly affects the SWCNTs diameter [13].

The laser ablation method yields around 70% and produces primarily single-walled carbon nanotubes with a controllable diameter determined by the reaction temperature. However, it is more expensive than either arc discharge or chemical vapor deposition.[12]

3) Chemical vapour deposition

The first two method , arc discharge and laser ablation have the drawback that they do not allow the location and alignment of the synthesized CNTs to be controlled . This method can be avoided by the chemical vapour deposition (CVD) which is another popular method using hydrocarbon vapour (eg. Methane) which is thermally decomposed in the presence of a metal catalyst. The method is also known as thermal or catalytic CVD. Chemical vapour deposition (CVD) utilizes hydrocarbon gases as sources for carbon atoms and metal catalyst particles as ''seeds'' for nanotube growth that takes place at relatively lower temperatures (500–1000 _C) [14]. CVD is a simple and economic technique for synthesizing CNTs at the cost of crystallinity. In fact, CVD has been used for producing carbon filaments and fibers since 1959. The process involves passing a hydrocarbon vapour through a tube furnace in which a catalyst material is present at sufficiently high temperature to decompose the hydrocarbon. CNTs grow over the catalyst and are collected upon cooling the system to room temperature. CNTs have been successfully synthesised also using organometallic catalyst precursors. The three main parameters for CNT growth in CVD are type of hydrocarbon, type of catalyst and growth temperature. Apart from large scale production, CVD also offers the possibility of the production of single CNT for use as probe tips in atomic force microscopy (AFM) . The tips produced are smaller than mechanically assembled ones, thus significantly improving resolution of AFM. Fig.8.

Fig.8. Digrammatical representation of chemical vapour decomposition setup for synthesis and growth of CNTs.

Purification of CNTs:[15]

Nanotubes usually contain a large amount of impurities such as metal particles, amorphous carbon , and multishell . There are different steps in purification of nanotube

1) Air oxidation

The carbon nanotubes are having less purity,the average purity is about 5- 10%. So purification is needed before attachment of drugs onto CNTs. Airoxidation 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.

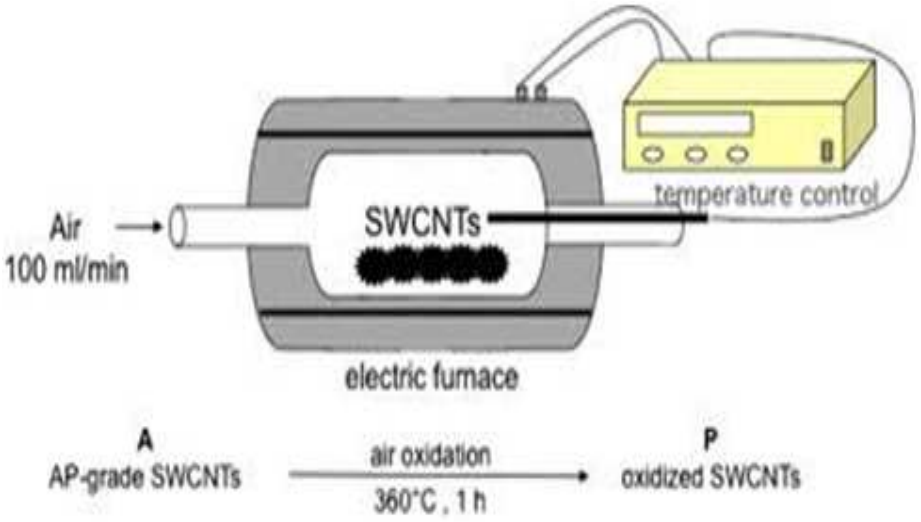

Figure 9. Air oxidation (5-10%, at 673 k for 40 min.)

Acid Refluxing

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

Figure 10. Acid refluxing (HCl,HNO3,H2SO4)

Surfactant aided sonication, filtration and annealing

After acid refluxing, the CNTs were purer but,tubes were 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 was carriedout. 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. The sample was then filtered with an ultra filtration unit and annealed at 1273 k in N_2 for 4 h. Annealing is effective in optimizing the CNT structures. It was proved the surfactant-aided sonication is effective to untangle CNTs, thus to free the particulate impurities embedded in the entanglement.

Solubilization of CNTs

Before application to (bio)analytical assays the produced CNTs must be first modified so as to be transformed to a soluble product. The preparation of homogeneous dispersions of CNTs, suitable for processing into thin films or for other applications is of a great importance. Various methods can be use for this purpose . End [16]and=or sidewall functionalization[17], use of surfactants with sonication[17] , and protonation by superacids[18] have been reported. Althoughthese methods are quite successful, they often indicate cutting the CNTs into smaller pieces (sonication and=or functionalization), thus partly

Losing the high aspect ratio of SWCNTs. An example of CNT solubilization is the work of Kim et al.[19] They developed a simple and efficient process for the solubilization of CNTs with amylase in dimethyl sulfoxide-H2O (DMSO-H2O) mixture as well as in pure water. This process requires two important conditions, presonication of CNT in water and subsequent treatment of the fine CNT dispersion with amylose in a specified DMSO-H2O mixture, followed by a postsonication. The former step disaggregates the CNT bundles, and the latter step maximizes cooperative interactions between CNTs andand amylose, leading to the immediate and complete solubilization. The best solvent composition was found to be 10–20% DMSO, in which amylose assumes an interrupted loose helix. The resulting colloidal solution was stable and exhibited no precipitation over several weeks. CNT solubilization by covalent modification is reported by Luong et al[20] . MWCNTs were solubilized in a mixture of 3-aminopropyltriethoxysilane (APTES) and Nafion-perfluorinated ion-exchange resin and ethanol. A uniformly dispersed MWCNT was obtained after 20min sonication and used for sensor applications. The interactions between CNTs and amino- terminated organic species are complex and dependent on the functionalization reaction conditions. Haddon et al[21]. , presented a study on the electronic behaviour of films of as-

prepared and purified SWCNTs and demonstrate the important role that chemical functionalization plays in modifying their electronic properties, which in turn throws further light on the mechanism of action of SWCNTbased sensors. They used octadecylamine (ODA) functionalized and poly (maminobenzene sulfonic acid) (PABS) functionalized SWCNTs provided by Carbon Solutions. Polymer wrapping of nanotubes[22] , or a noncovalent scheme involves _-stacking of 1-pyrenebutanoic acid succinimidyl ester onto the sidewalls of SWCNTs are also reported[23] . The anchored pyrene moieties on SWCNTs are highly stable against desorption in aqueous solutions, leading to functionalization of SWCNTs with succinimidyl ester groups. The mechanism of protein immobilization on nanotubes, then, involves the nucleophilic substitution of N-hydroxy succinimide by an amine group on the protein, resulting in the formation of an amide bond.

Analytical application of CNTs:

1) Soild phase extraction

The highly developed hydrophobic surface of CNTs exhibits strong sorption properties towards various compound Strong adsorption of small gas molecules on SWCNTs undergoing charge transfer is employed in constructing gas sensors, whose sensitivity is based on changes in the electrical properties of SWCNTs. The desorption of molecules from SWCNTs can be achieved by heating or UV illumination.

There are several examples in the literature of the use of CNTs for preconcentrating trace analytes. MWCNTs have been characterized as superior sorbents for removing dioxins for environmental protection[25]. The strong binding is attributed to the interaction of two benzene rings of dioxin and the surface of CNTs. The amount of dioxin adsorbed on the CNT is 1014 times greater than that on activated carbon, and dioxins can be removed from the sorbent by temperature programmed desorption. In several other works in micro-column systems, sorption on MWCNTs has been examined for different analytes, such as bisphenol A, 4-n-nonylphenol and 4-tert-octylphenol, several phthalate esters and chlorobenzenes . In , different solvents were used as eluents , different sorbents were compared and the highest recoveries were found for MWCNTs.

Another analytical application of CNTs based on their surface properties is as the matrix for matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) [26]. The function of the CNTs is to trap analytes (e.g., peptides and cyclodextrin) deposited on their surface and to act as energy receptacles for laser radiation. The desorption/ionization of CNTs simplifies sample preparation and eliminates interference from

background ions in the matrix. Fig. 6 shows a favorable comparison of the MS spectrum obtained with CNTs and that obtained with a conventional organic matrix of a-cyano-4-hydrocinnamic acid.

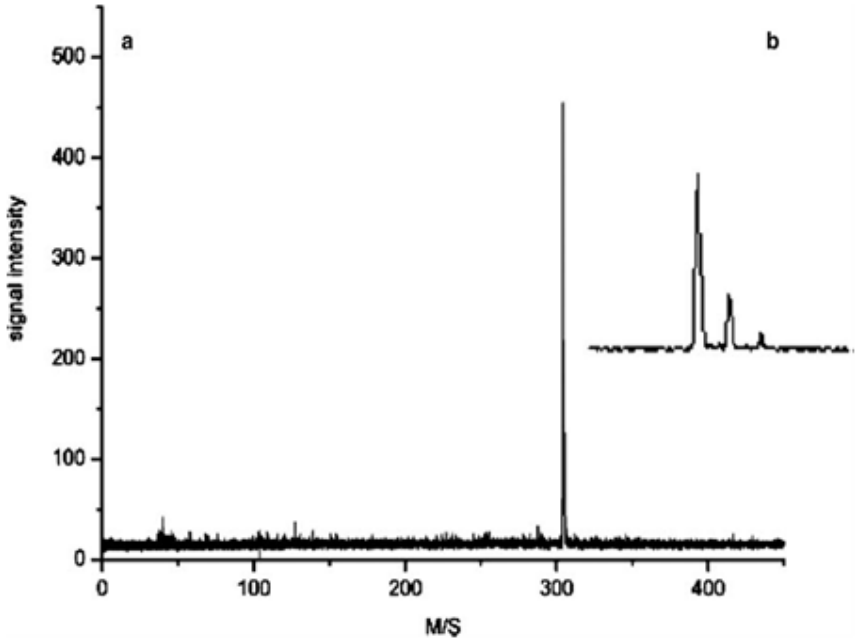

Fig.11. Mass spectra of Na-benzoyl-L-arginine ethylester hydrochloride (3 mg/mL) at m/z 307.87 [M - Cl]+ obtained for laser desorption/ionization time-of-flight mass spectrometry by using matrixes of (a) CCA and (b) carbon nanotubes (CNTs). 50 pulsed laser shots were applied with laser power of 195 lJ.

2) Stripping voltammetry :

Because of the strong sorption properties of CNTs, their application on the surface of working electrode has allowed several original methods of stripping voltammetry to be developed. In stripping measurements of several organic analytes, the first step of determination (sorption of analytes) has been carried out at open circuit on electrodes modified with CNTs. In the next step, the electrochemical oxidation or reduction of accumulated analyte is carried out. These procedures have been developed for anodic determination of xanthine[27], 6 benzylpurine and fluphenazine , as well as for determination of 4-nitrophenol based on a very sensitive well-defined reduction peak at the SWCNT-modified GCE[28]. In the first stage of voltammetric stripping determination of transition metal cations with electrodes modified with MWCNTs, cations have been adsorbed from solution containing iodide, then reduced at _0.6 V (Hg^{2+}) or _1.2 V (Cd^{2+} and Pb^{2+}), and, in the last step, anodic stripping has been employed. Such methods are alternatives to conventional anodic stripping voltammetry using thin-film mercury electrodes. Fig. shows a stripping voltammogram recorded in mercury-free system. Stripping voltammetry of Cd(II) was also reported using a GCE modified with an MWCNT/Nafion composite film[29] .

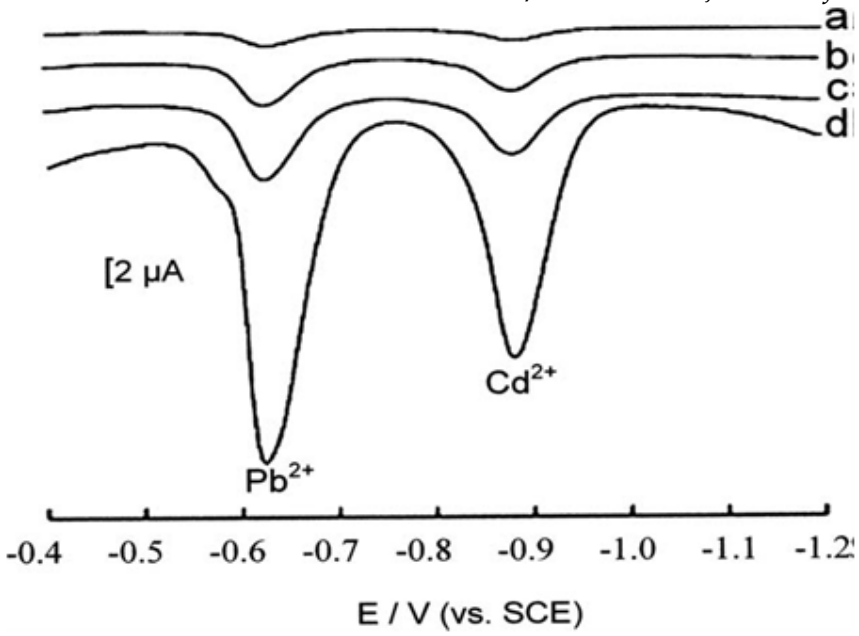

Fig. 12. Differential pulse voltammograms recorded for mercuryfree simultaneous determination of 0.5 lM Cd and Pb at a glassy carbon electrode (GCE) modified with MWCNTs . Curves (a) and (c): bare GCE and MWCNT-modified GCEs in acetate buffer of pH 4.5. Curves (b) and (d): analogous measurements in acetate buffer containing 20 mM KI, which induces adsorption of metal ions at the electrode surface.

3) Voltammetry

Especially large number of applications can be found in the literature on applications of CNTs as electrode materials or modifiers of conventional working electrodes in analytical voltammetry. These applications, pioneered by work of Britto et al[30]. On reversibility in the oxidation of dopamine using CNTs as electrodes, concerned both amperometric and voltammetric determinations, as well as the electrochemical biosensors mentioned below and the voltammetric stripping methods discussed separately below. These applications have already been reviewed, indicating the advantages of CNTs in electrochemical measurements, such as the large active surface at electrodes of small dimensions, the enhanced electron transfer or the often indicated electrocatalytic properties. A particular advantage is the possibility of fabrication and electroanalytical applications of nanoelectrode arrays based on vertically-aligned MWCNTs [31]. Nanoelectrodes and nanoelectrode arrays can be integrated with microelectronics and microfluidic chips. Nanoelectrodes can also be fabricated from a single CNT attached to sharpened Pt wire [32].

However, used most often are various ways of modifying the surfaces of conventional working electrodes with CNTs. This can be achieved by evaporationon the surface of working electrode a suspension of CNTs in bromoform, ethanol , or N,N dimethylformamide. The N,N-dimethylformamide method was also successfully

employed for modifying the surface of graphite screen-printed electrodes [32] . Carbon-fiber electrodes were modified by SWCNTs by suspension in dodecyl sulfate [33]. Successful solubilization of CNTs was reported with perfluorosulfonated polymer Nafion [34-36].

A general advantage of modified working electrode CNTs is improvement in the reversibility of the electrode process, which was observed for dopamine[37] and other neurotransmitters.

Electrocatalytic activity of CNTs was observed in oxidizing homocysteine , brucine , hydrazine and carbohydrates , and also in reducing nitrite . Electrocatalytic behavior of CNT was observed toward hydrogen peroxide, which can be very useful in design of biosensors based on oxidases . Fig. 2 shows effect of modification with MWCNT on cyclic voltammogram of hydrogen peroxide.

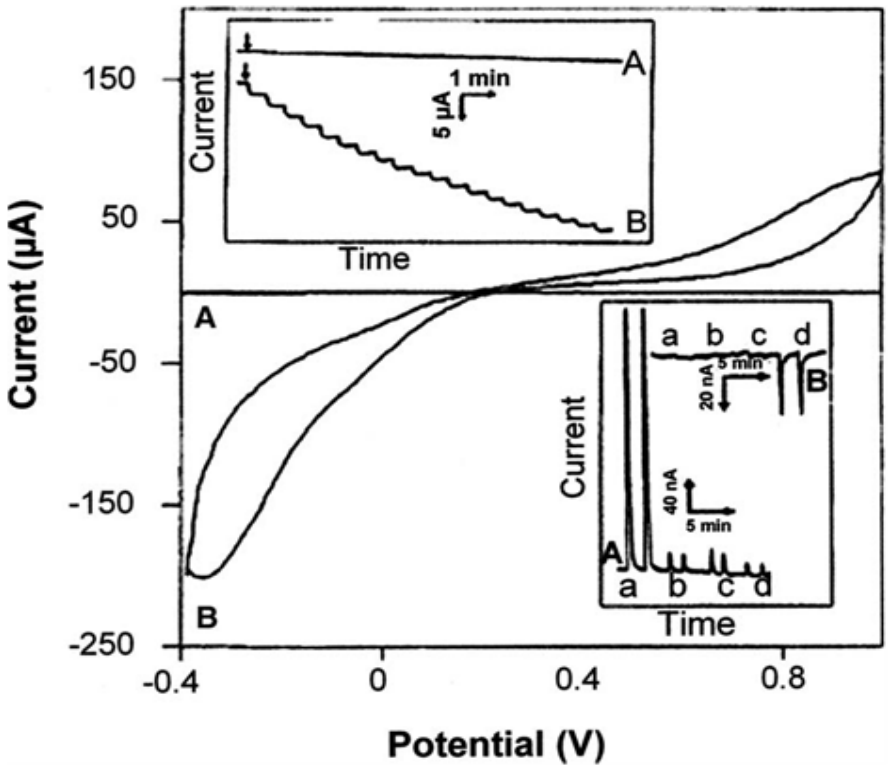

Figure 13. Cyclic voltammograms obtained for 5 mM hydrogen peroxide at unmodified (A) and multi-walled carbon nanotube (MWCNT)-modified (B) glassy carbon electrodes (GCEs) in 50 mM phosphate buffer of pH 7.4 at scan rate 50 mV/s [45]. In the upper insert, amperometric response is shown for increasing hydrogen peroxide in 1 mM steps for both electrodes held at 0.0 V. The lower insert shows flow-injection signals for 0.2 mM acetominophen (a), 0.2 mM ascorbic acid (b), 0.2 mM uric acid (c) and 10 mM glucose (d) at the Nafion-coated GCE (A) at 0.8 V, and using the MWCNT-modified GCE (B) at _0.05 V. Flow-rate 1.25 ml/mi.

4) Biosensors

The analytical applications of CNTs in developing electrochemical biosensors have already been partly reviewed [38,39] . Most favorable is direct attachment (e.g., of proteins) to CNTs, already mentioned in immobilizing cytochrome c and hemoglobin. In both these cases, the direct transfer of electrons between electrodes and proteins was observed.

Non-covalent functionalization of CNTs has been reported for binding of specific proteins and detection of clinically important biomolecules such as antibodies associated with human autoimmune diseases [40].

Among the various reported designs of CNT-based enzymatic biosensors, the simplest are those where enzyme was entrapped in the MWCNT paste, as described for glucose oxidase [41], or where enzyme was physically adsorbed on the electrode surface modified with MWCNT, as reported for a screen-printed biosensor with organophosphorus hydrolase .

On the surface of electrodes modified with CNTs, enzyme has also been placed encapsulated in a sol-gel composite [42] by casting the enzyme solution in a Nafion layer onto the CNT-modified GCEs [43] or in an electrodeposited poly(o-phenylenediamine) film [44].

Enzymes can also be covalently immobilized to SWCNTs functionalized with carboxylic groups, cast on platinum electrodes, as reported for glucose oxidase [45], or to the ends of vertically oriented SMCNT forest arrays,as reported for myoglobin and horseradish peroxidase[46].

In designing a biosensor immobilized with uricase, differential pulse voltammetric measurements showed that a biosensor with enzyme immobilized on MWCNTs functionalized with tin-oxide nanoparticles had much greater electrocatalytic oxidation than non-functionalized or carboxylate-functionalized MWCNTs [47]. The covalent attachment was also employed for immobilizing glucose dehydrogenase, where enzyme was attached to a film of a polysaccharide biopolymer chitosan-containing CNT [48].

In another design, where SWCNTs were placed together with Pt nanoparticles in a Nafion layer, the enzyme solution was evaporated on the surface of the Nafion layer and enzyme was cross-linked with glutaraldehyde [49].

Fig. 4 shows the effect of the presence of particular components in the layer modifying the electrode surface on cyclic voltammograms obtained for hexacyanoferrate with carbon-fiber microelectrodes.

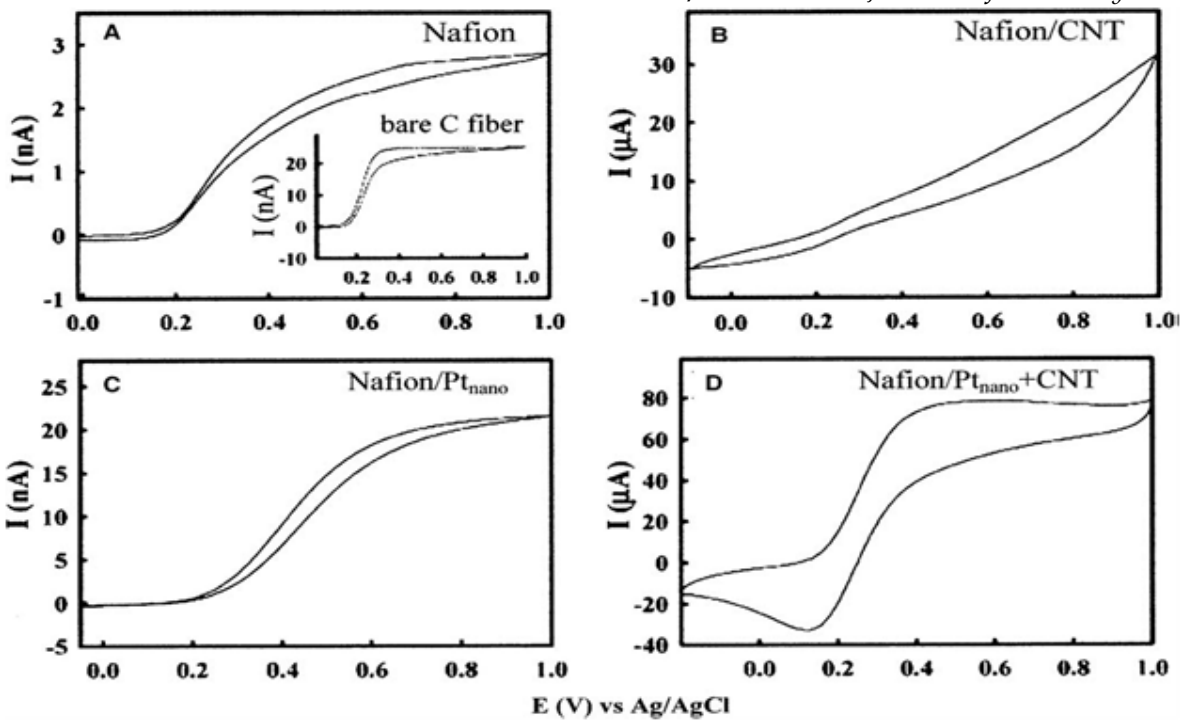

Figure 14. Cyclic voltammograms recorded for unmodified and modified carbon-fiber microelectrodes in 20 mM hexacyanoferrate and 0.2 M KCl at 20 mV/s vs. Ag/AgCl (3 M NaCl) [78]. (A) carbon fiber electrode modified with Nafion (insert shows bare electrode), (B) carbon-fiber electrode modified by single-walled carbon nanotube (SWCNT)/Nafion, (C) Ptnano/Nafion-modified fiber electrode, and (D) Ptnano/SWCNT/Nafionmodified microelectrode.

Based on the use of CNTs, an electroluminescent immunosensor for a-fetoprotein was developed, where streptavidin was immobilized by covalent coupling to carboxylic acid and biotinylated antibodies were then attached [50].

5) Gas sensors:

In the design of gas sensors, some unusual electronic, mechanical and thermal properties of CNTs are utilized, as already reviewed [51]. The sensors developed so far have used different mechanisms of interacting analytes with CNTs, as well as different modes of preparing CNTs in sensors.

In constructing gas sensors, changes in the electrical properties of CNTs, as result of their interaction with analytes, are used most often. Changes in the resistance of the CNT layer have been used for detection of nitrogen dioxide, ammonia , hydrogen , and inorganic vapor generally .

In sensors with CVD-produced CNTs arranged across prefabricated electrode arrays, polymers have been used to impart high sensitivity and selectivity [52]. With polyethyleneimine coating, NO2 was detected without interference by NH3, while, with Nafion coating, selective sensing of NH3 was observed (Fig. 1).

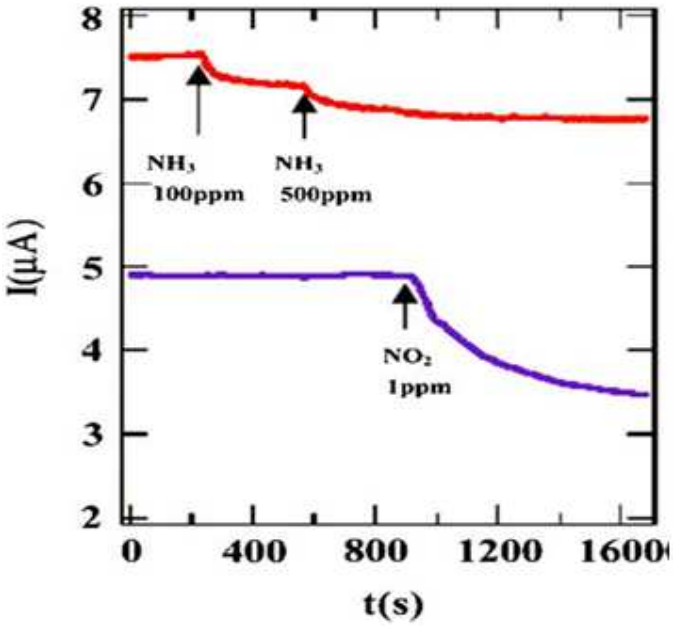

Figure 15. Response curves recorded for gas sensor comprising multiple single-walled carbon nanotubes (SWCNTs) functionalized with Nafion for NH_3 sensitivity (upper curve) and with polyethyleneimine coating for NO_2.

The detection of carbon monoxide with sensors based on MWCNTs was attributed to strong catalytic effect toward the electrochemical oxidation of CO [53]. A MWCNT sensor fabricated on silicon wafer exhibited Schottky behavior with marked sensitivity or current changes in the presence of hydrogen [54]. Increasing detection sensitivity in hydrogen sensing was observed with increasing operating temperature.

Changes of electrode impedance were used as analytical signal for detection employing MWCNTs. With CNTs trapped in an interdigitated microelectrode gap, NH3 was detected [55]. Increasing impedance was observed also for MWCNT sensors with increasing humidity or partial pressure of NH_3, CO and CO_2 [56]. Humidity sensing was also reported for Nafion-coated SWCNT field-effect transistors (FETs) and for sensors with carboxylated MWCNTs modified with lithium perchlorate . For studying the gas-sensing properties of CNTs, a circular disk resonator was also employed to detect the presence of gases based on changes in the dielectric constant rather than the electrical conductivity [57]. Noticeable shifts in resonant frequency to both polar (NH_3, CO) and non-polar gases (He, Ar, N_2, O_2) were observed.

Gas-ionization microsensors have also been reported, featuring the electrical breakdown of a range of gases and gas mixtures at CNT tips[58]. The sharp tip of CNTs generate high electric fields at relatively low voltage, lowering breakdown voltages and enabling operation of such microsensors to be battery-powered.

6) **Chromatographic application :**

In spite of the extraordinary sorption properties of CNTs, chromatographic applications have been limited to improving electrochemical detection in high performance liquid chromatography (HPLC) methods. Amperometric detection with a GCE modified with MWCNTs has been satisfactory employed for determining monoamine neurotransmitters, their metabolites[58,59] , and selected aromatic amines[60] . It was also employed in ion chromatography of oxidizable amino acids[61] , and thiosulfate, sulfite, thiocyanate and iodide[62] . As was demonstrated in detecting the neurotransmitters, modification of a working GCE with MWCNTs allowed a 10-fold increase in signal magnitude with detection limits at the sub-nanomolar level, which can be then applied for determinations in cerebrospinal fluid. Fig. 7 shows chromatograms obtained with amperometric detection with unmodified and modified GCEs. The modification in this case was carried out by evaporating MWCNTs suspended in dimethylformamide (DMF) on the electrode surface.

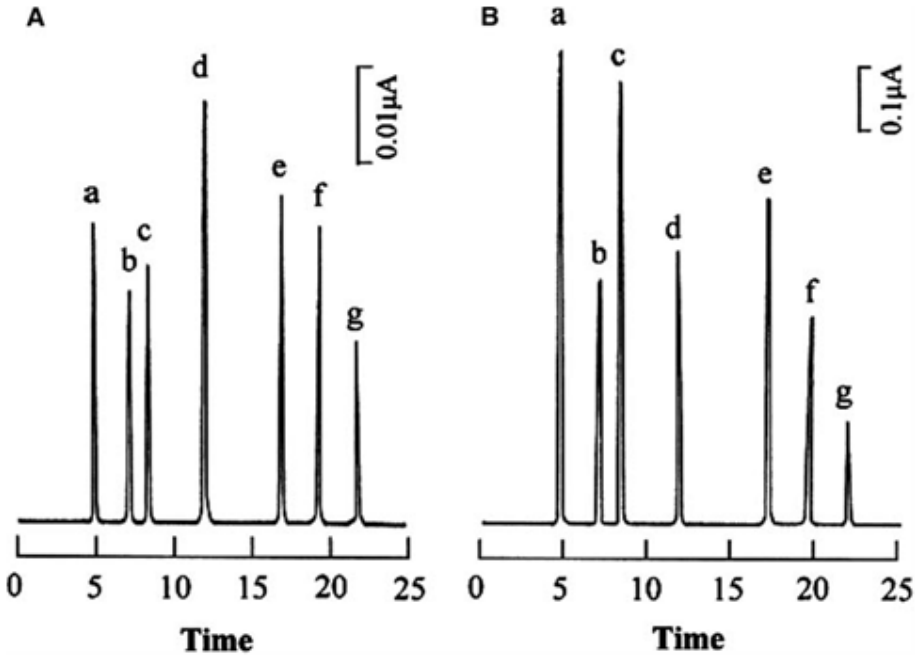

Figure 16. Chromatograms of 1.0 Æ 10_6 mol/l: (a) NE; (b) MHPG; (c) DA; (d) DOPAC; (e) 5-HT; (f) 5-HIAA; and, (g) HVA at (A) the bare glassy carbon electrode (GCE) and (B) the multi-walled carbon nanotube (MWCNT)-COOH chemically modified electrode (CME). Applied potential: +0.70 V.

Recent use of carbon nanotube in drug delivery:

1) Carbon nanotube for transdermal drug delivery

The CNT patch represents a major step forward in developing a programmable, transdermal delivery system that can usefully treat a variety of syndromes and be tailored to an individual patient's needs in a manner that will both improve therapeutic administration and efficacy.

Dr. Hinds and his colleagues have developed a novel skin patch device for delivering nicotine based on an active layer of aligned carbon nanotubes (CNT) approximately 1.5-7 nm in diameter crossing through a solid polymer film [56].

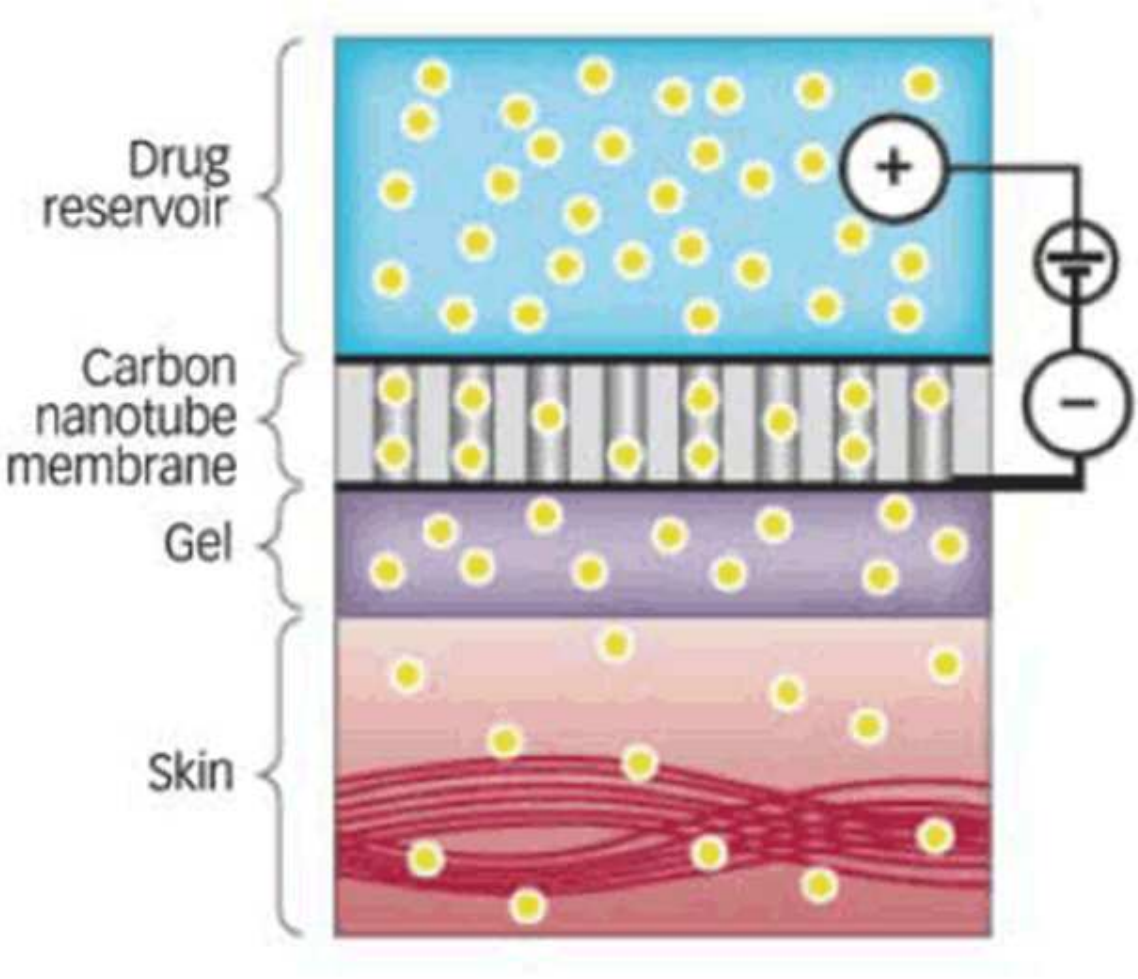

Figure 17. Transdermal drug delivery

2) Carbon nanotube for cancer treatment

Though the current treatments of cancer by surgery, radiation and chemotherapy are successful in several cases, these curative methods also kill healthy cells and cause toxicity to the patient. The spread of cells between organs, a process known as, is the cause of most cancer death. CNT's can be considered as antitumor agents and when in with conventional drugs, can significantly enhance their chemotherapeutic effect with the help of the advanced drug

delivery system. It has been reported that Paclitaxel loaded PEG--CNT's are promising for cancer therapeutics. Aqueous solutionof functionalized SWCNTs on exposure to radiofrequency (RF) field experiences efficient heating and this property has been exploited by Gannon et al for a noninvasive and selective thermal destruction of human cancer cells with minimal or no toxic effects to human cells. This demonstrates that carbon nanotubes are capable of leading to new exciting directions and approaches in therapeutic oncology. A photo-thermal effect can be employed to induce thermal cell death in a noninvasive manner, provides important information on potential therapeutic targets for pancreatic cancer treatment. There are three key features of this nanoscale drug delivery system (DDS):

i) Use of functionalized SWCNTs as a biocompatibleplat form for the delivery of therapeutic drugs or diagnostics,

ii) Conjugation of prodrug modules of an anti canceragent that is activated to its cytotoxic form inside the tumor cells upon internalization and in situ drug release,

iii) Attachment of tumor-recognition modules to thenanotube surface [57,58].

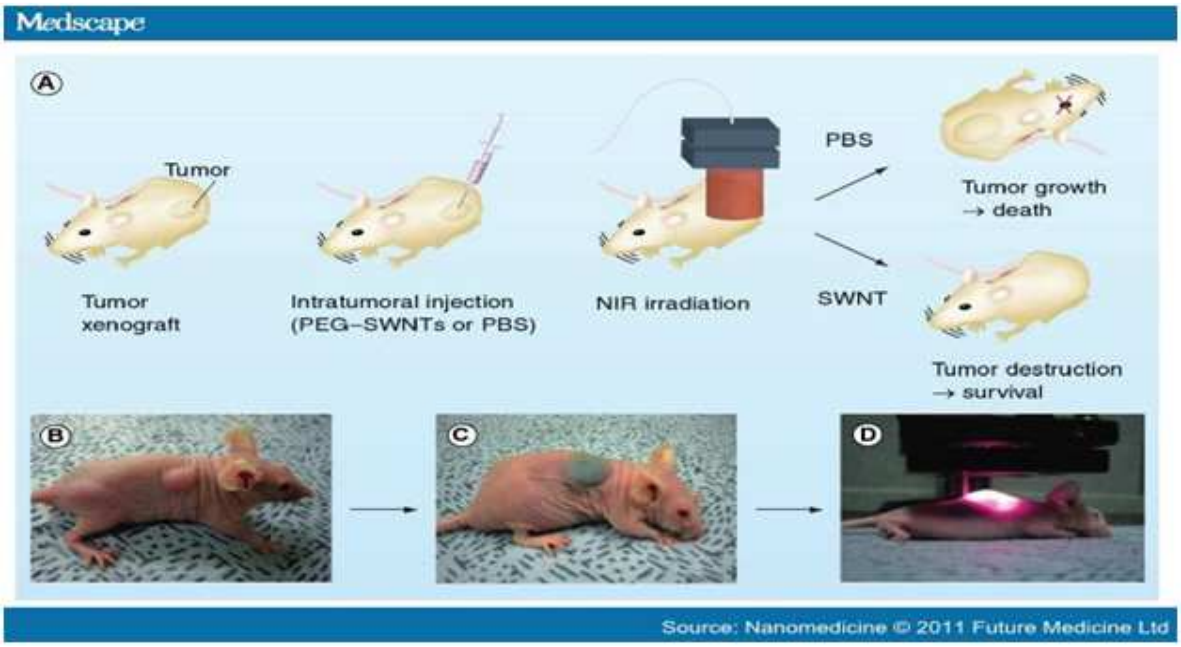

Figure 18. For cancer treatment.

3) CNTs for Cardiac Autonomic Regulation

Single walled carbon nanotubes share physicochemical properties with ultrafine Component may impair cardiovascular autonomic control proved after the study conducted in rats, suggest that SWCNTs may alter the baroreflex function, thus affecting the autonomic cardiovascular control regulation[59].

4) CNTs for platelet activation:

SWCNTs using alongwith platelet P-selectin when injected into anaesthetized mice, light dyeinduced thrombus formation was found and the platelet found to be activated. MWCNTs activate blood Platelet by inducing extracellular Ca2+ influx that could be inhibited by calcium channel blockers SKF 96365 and 2-APB. CNT-induced platelet activation is associated with a marked release of platelet membrane microparticles positive for the granular secretion markers CD62P and CD6356[60].

5) CNT for tissue regeneration:

CNTs are combined with polymers such as poly-l-lactide, Polylactide and poly-D,Llactide- coglycolide copolymer which have been used as a scaffolds in tissue regeneration. MacDonald et al., prepared composite materials comprised of a collagen matrix with embedded CNTs by mixing solubilized collagen with solution having carboxylated SWCNTs[61].

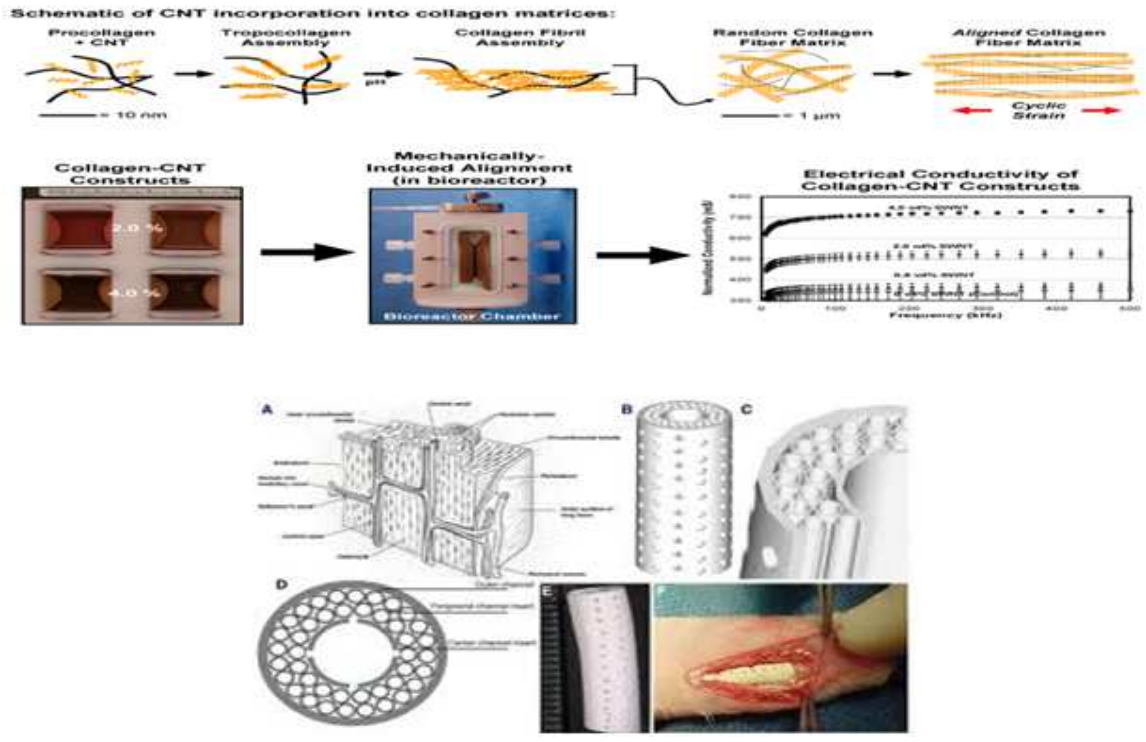

Figure *19.*Tissue regeneration

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Corresponding Author:

Miss. Meena N. Kale*,

Email: *kalemeenan@gmail.com*