ISSN–2230-7346
Journal of Global Trends in Pharmaceutical Sciences

CARBON NANOTUBES: A REVIEW

Trinadha Rao. M, Bhavani. U*, Bhanu. M., Kamala Kumari. P.V

Department of Pharmaceutics, Vignan Institute of Pharmaceutical Technology, Duvvada, Visakhapatnam-530049, India.

*Corresponding Author E-mail: trinadh_81@rediffmail.com.

ARTICLE INFO

Key Words
Carbon nanotubes, Single and multi walled nanotubes, drug delivery, Nano technology.

Access this article online
Website:
https://www.jgtps.com
Quick Response Code:

ABSTRACT

Carbon nanotubes (CNTs) were first discovered by lijima and coworkers in 1991. Since then, they become the strongest candidates in various fields such as biomedical engineering .The field of nanotechnology and nanoscience push further investigation of CNTs to produce them with suitable parameters for future applications. Carbon nanotubes (CNTs) are allotropes and can exist in different forms with a nanostructure that have a length-to-diameter ratio greater than 1,000,000. These cylindrical carbon molecules have novel properties which make them useful in many applications in nanotechnology and other branches of life science. They have been applied in the field of pharmacy because of their unique surface area, stiffness, strength and resilience. Nanotubes have been categorized into single-walled nanotubes and multiple-walled nanotubes. Methods of production of carbon nanotubes include arc discharge, laser ablation, chemical vapor deposition, silane solution, flame synthesis methods, nebulized spray dialysis method etc. CNTs can carry therapeutic drugs, vaccines and nucleic acids into the cell to targets that are previously unreachable because of their ability to cross membrane.

INTRODUCTION

Carbon nanotubes (CNTs) are tubular in shape, allotropic form of carbon and are made of graphite. These have diameter in nanometers, length in several millimeters and have a very broad range of electronic, thermal and structural properties [1]. Nanomaterials consist of inorganic or organic matter. Carbon nanotubes are one of the most prominent building blocks of nanotechnology and have hundred times the tensile strength of steel, thermal conductivity better than all but the purest diamond and electrical conductivity similar to copper [2]. In fact nanotubes are available in a variety of forms: long, short, single-walled, multi-walled, open, closed, with different types of spiral structure etc [3]. Carbon nanotubes are tending to become a key material in ultrafine devices for the future, because of their unique properties and their extraordinarily fine structure on a nanometer scale. Other advantages of carbon nanotubes are they are light in weight, posses' high mechanical Strength, able to withstand extreme heat of about 2000°C in the absence of oxygen [4].

Classification of nanotubes: Carbon nanotubes are broadly classified into two types.

1. Single walled carbon nanotubes (SWCNTs)

They consist of carbon atoms which are bonded into a tube shape with a single wall hence they are called as single-wall carbon nanotubes as shown in Fig 1. Single walled carbon nanotubes (SWCNTs) are considered as a single long wrapped graphene sheet [5]. They possess length which is 1000 times more to diameter and hence considered nearly one-dimensional structures. SWCNTs possess some unique properties which make them most suitable candidate for miniaturizing electronics to replace the micro electromechanical systems which are currently the basis of modern electronics. SWCNTs are excellent electric conductors. They posses

Thermal conductivity which has the range of 6000 W/m·K5. Along with their wide potential in diverse nanotechnological applications, SWCNTs are still very expensive for production. Single walled carbon nanotubes synthesis requires catalyst [6].

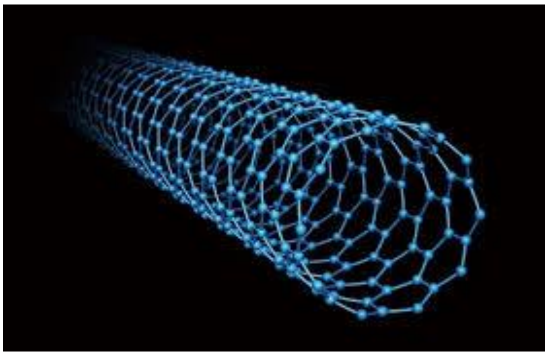

Fig 1: Single walled carbon nanotubes

2. Multiple walled carbon nanotubes (MWCNTs) They consist of carbon atoms bounded into a tube shaped, with multiple walls thus called as multiwall carbon nanotubes as shown in Fig 2. Multiwalled carbon nanotubes (MWCNTs) consist of multiple layers of graphite rolled over co-axially to form a tubular shape. These are invariably produced with high chances of structural defects. MWCNTs are structurally quite sound, though they frequently contain regions of structural imperfection, properties of CNTs, such as structural rigidity and flexibility made us to generate considerable interest. CNTs are very stronger than steel which is one-sixth the weight of CNTS. Depending on their chirality CNTs can also act as either conductors or semiconductors and possess an intrinsic superconductivity. Thermal conductivity in the range of 3000 W/m·K. These are not only ideal thermal conductors, but also behave as field emitters.we can minimize the chances of defects by using arc discharge method [7,8].

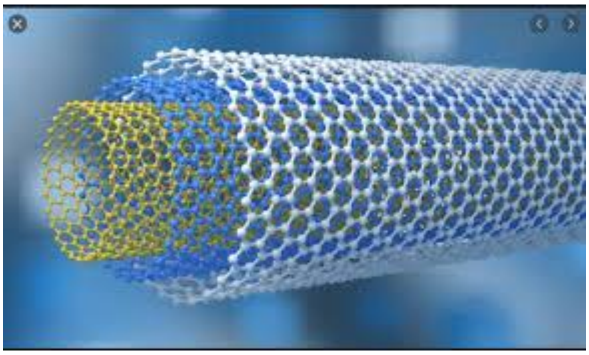

Fig 2: Multiple walled carbon nanotubes

Functionalization of carbon nanotubes

Raw CNTs have highly hydrophobic surfaces which are not soluble in aqueous solutions. Functionalization of CNTs is a solution to this problem. Functionalization is a process of chemical synthesis where desired functional groups can be introduced onto the walls of CNTs for various applications, producing functionalized carbon nanotubes (f-CNT). There are two methods of functionalization.

1. Covalent bonding: Strong chemical bonds between nanotubes and the attached molecule results due to covalent chemical bonding of polymer chains onto CNTs as depicted in the Fig 3. There are various covalent reactions to graft molecules based on their varying properties, which can be further classified as grafting from or grafting to reactions, which involve the polymerization of monomers from surface-derived initiators on CNTs or the addition of preformed polymer chains, respectively. Both methods involve functionalization reactions to the surface of the CNT. There are three main methods used to attach molecules covalently: molecules or polymer chains reacting with the surface of pristine, pre functionalized, or oxidized CNTs. Oxidation of CNTs is one of the most common modifications that uses oxidizing agents such as concentrated nitric acid. Covalent bonding gives a robust attachment that is generally stable in a bioenvironment. Covalently PEGylated SWCNTs synthesized by this strategy are now used for both *in vitro* and *in vivo* applications.However, the major disadvantage of this is intrinsic physical properties of CNTs such as photoluminescence and Raman scattering are reduced because of disruption of CNT structure associated with covalent bonding. For this reason covalent bonding cannot be used to functionalize CNTs for the use in photothermal ablation.

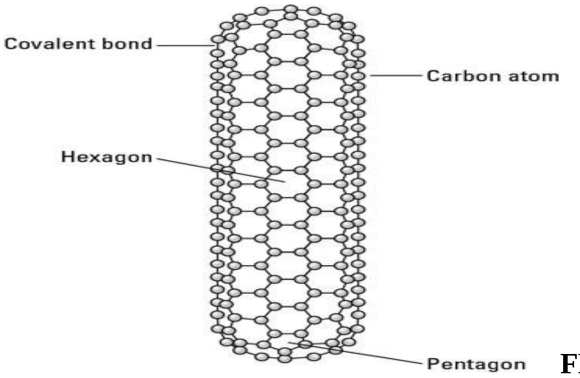

FIG.3: Covalent functionalization of carbon nanotubes

2. Non covalent bonding: Noncovalent bonding is the most widely used method for drug delivery. As compared to covalent functionalization, noncovalent functionalization of CNTs can be carried out by coating CNTs with amphiphilic surfactant molecules or polymers [9]. A carbon nanotube which is noncovalently functionalized should have specific properties; the more it is closely matched, the greater will be its usefulness in biologic roles [10]. This process can be carried out by creating micelle-type structures where amphiphilic molecules are coated to the CNT. This type of bonding can also be applied to single strands of DNA by virtue of the aromatic DNA base units as shown in Fig 4. Another type of functionalization is p-p bonding that can be achieved by the stacking of pyrene molecules onto the surface of the CNT.

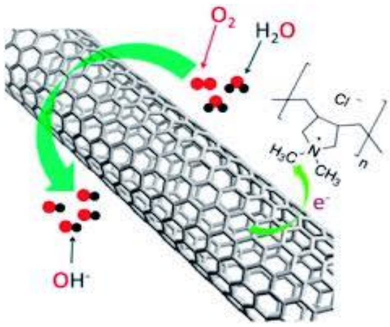

Fig 4: Non covalent functionalization of carbon nanotubes

Method of preparation

1. **ARC DISCHARGE METHOD**:

This is one of the best methods to prepare large amounts of nanotubes. This method is commonly used for producing C60 fullerence, it is one of the most common and the easiest way to produce carbon nanotubes. This method results in the production of a mixture of components and separation of nantubes catalytic metals present in the crude product. This method involves the vaporization of two carbon rods placed end to end, which are separated by approximately 1mm, in an enclosure filled with inert gas (helium of argon) at low pressures i.e. between 50 to 700 mbar. A direct current of 50 to 100A driven by approximately 20V creates a high temperature discharge between these two electrodes as shown in Fig 5. The discharge created vaporizes one of the carbon rods and forms a small shaped deposit on the other rod [11]. Depending on this technique it is possible to grow SWCNTs or MWCNTs and the typical yield is up to 30 to 90%.

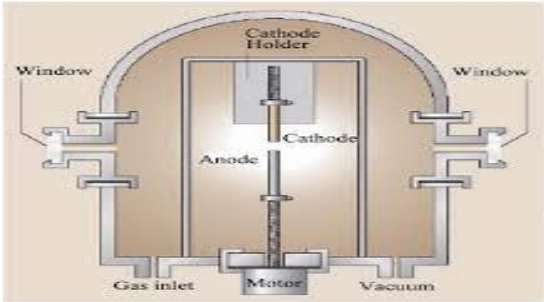

Fig 5: ARC discharge method

2. LASER ABLATION METHOD: This type of synthesis was first reported in 1995, by Smalley's group at Rice University. There are two types of lasers used to vaporize graphite at a specific temperature. They are Pulsed type and Continuous type. The main difference between continuous and pulsed laser is that: pulsed laser demands a much higher light intensity (100KW/cm^2) as compared with continuous type 12KW/cm^2.The oven is filled with helium or argon gas in order to keep the pressure at 500 Tor. This leads to the formation of very hot vapour plume forms which expands and cools rapidly. As the vaporized species cool, small carbon molecules and atoms quickly condense to form larger forms, possibly fullerences. The catalyst also begins to condense and attach to carbon clusters and prevents their further closing into cage structure. The SWCNTs formed in this case are bundled together by Vander walls forces as shown in Fig 6.

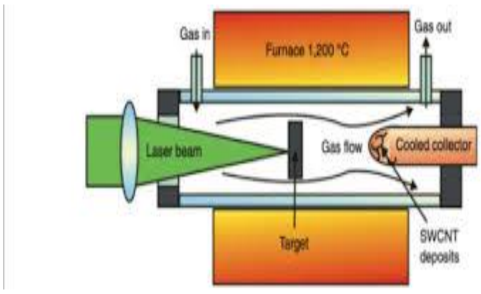

FIG.6: Laser Ablation method

3. Chemical vapour deposition method (CVD)

This method involves putting a carbon source such as methane, carbon monoxide and acetylene in the gas phase and using an energy source, such as plasma or a resistively heated coil, we can transfer energy to a gaseous carbon molecule as shown in Fig 7. The energy source is used to break the molecule into reactive atomic carbon. Then Ni, Fe & CO where it wills bind CVD synthesis is a two step process which includes catalyst preparation and the actual synthesis of CNT. The catalyst is prepared by inclining transition metal onto a substrate and by means of thermal annealing we can induce catalyst particle nucleation. Thermal annealing results in agglomeration on the substrate, which leads to the growth of nanotubes.

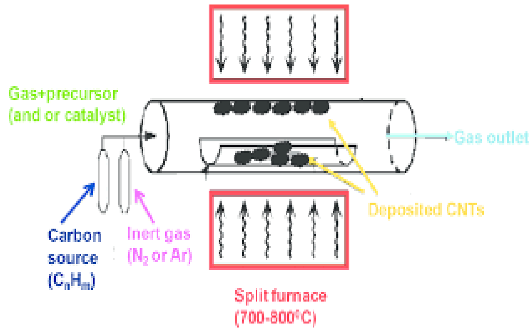

Fig 7: Chemical Vapour Deposition Method

4. FLAME SYNTHESIS METHOD

A fuel-rich flame is a high-temperature, carbon-rich environment that can be suitable for nanotube formation when transition metals like Fe or Ni are introduced into the system as shown in Fig 8. Flame synthesis is a continuous-flow, scalable method with potential for considerable lower cost of nanotube production than other methods [12]. Flame synthesis of CNTs provides unique features not realized in current synthetic methods. The most significant aspect of the flame synthesis approach is the very short residence times realized for catalyst inception and nanotube growth [13]. Gases such as CO, CH_4, C_2H_2, C_2H_4, and C_2H_6 Catalysts, which are present in the post flame area, are rich sources of carbon. The reaction is exothermic, and chemical energy released in the form of heat in the flame supports endothermic carbon deposition reactions.

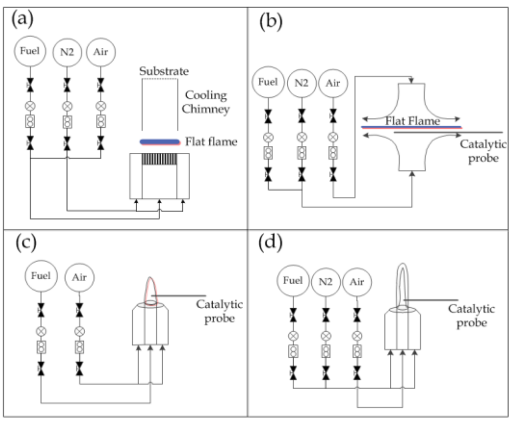

FIG.8: Flame synthesis method

5. Silane solution method

It is one of the common method in which a substrate such as carbon paper or stainless-steel mesh was immersed in a silane solution of a metal catalyst, preferably Co: Ni in a 1:1 ratio. A feedstock gas that have a carbon source such as ethylene was inserted through the substrate and the catalyst deposited thereon while the substrate was heated by applying an electrical current as shown in Fig 9.

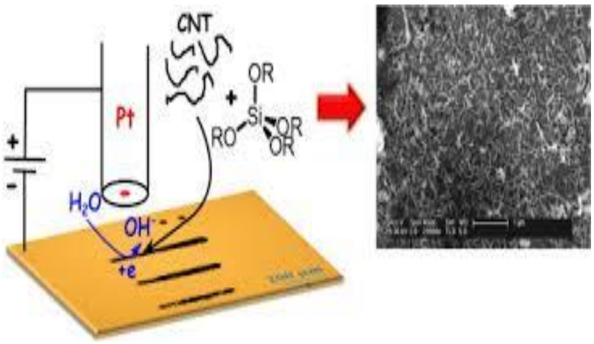

Fig 9: Silane solution method

6. Nebulized spray pyrolysis method

A nebulized spray as shown in Fig 10 is the key factor in this method which is generated by a special ultrasonic atomizer. Ferrocene (catalyst) and ethanol (as solvent and carbon source) are sprayed into a tubular furnace by means of ultrasonic nebulizer at a fixed temperature of 80^0C under an argon flow of 1 L/min. Ethanol is used as a solvent as well as a carbon source due to its nonpolluting nature, low cost, harmless byproducts (e.g., CO), and ease of handling. High growth of MWCNTs on a surface can be produced [14,15].

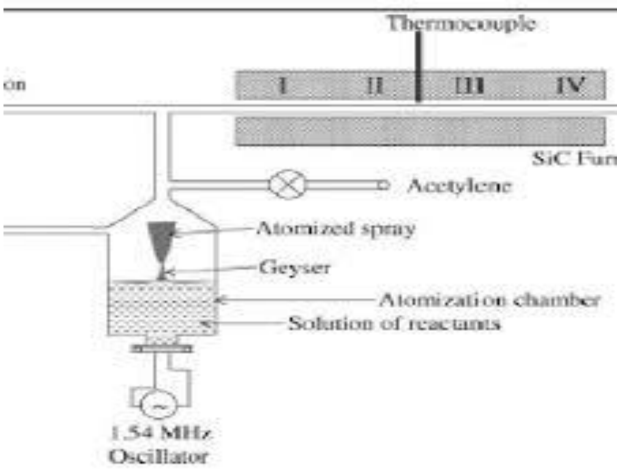

Fig 10: Nebulized spray pyrolysis method

Characteristics of carbon nanotubes: CNTs are endowed with exceptionally high material properties, such as electrical and thermal conductivity, strength, stiffness, toughness, and low density. The tensile strength of CNTs is a hundred times greater than that of steel, and the electrical and thermal conductivities approaches those of copper [16].

A. **Mechanical properties:** CNTs are characterized both by the high tensile strength and by a surprising elasticity under axial compressive forces. These properties tied to their intrinsic stability and structural flexibility have direct applications for drug delivery because they can penetrate and/or perforate cells as needles [17,18].

B. Thermal properties: Owing to their exceptionally high thermal conductivity, CNTs can be manipulated in complex tissues or media or serve as imaging probes, alone or combined with specific compounds. Light- or magnetic-mediated heating of these CNTs can lead to the killing of both cancer and healthy cells [19]. Note also that semiconducting CNTs can be used to improve and control drug release with near-infrared (NIR) lasers [20].

C. Electrical and optical properties: Depending on their rolling up, CNTs are metallic when n¼m s 0, semimetallic (i.e., with a very small band gap) when nm is a multiple of 3, and semiconducting for the other values of the two integers n and m. Semiconducting CNTs also allow fluorescence emission in the NIR region, which, by using video rate imaging, can reveal the tumor location through the enhanced permeability and retention of the tissues [21,22]. The fluorescence Raman technique can also track the CNTs in tissues [23].

D. Hydrophilicity and solubility: The hydrophobicity of CNTs has wide industrial applications. It is used specifically to create arrays of tubes, becomes highly unsuitable for biomedical applications. Separation of the CNTs is a prerequisite for medical applications. Dispersibility can be achieved by the addition of surfactants, polymers, or other colloidal particles functionalization with the carboxylic acid group makes CNTs water soluble and easily dispersible into the solvent [24].

E. Toxicity: CNTs' intrinsic toxicity depends on their geometry, size, and purity, their nature (SWCNT vs. MWCNT) As a matter of fact, extrinsic toxicity can also rely on the nature of the grafted chemicals or proteins however, and adequate functionalization of the CNTs can reduce inherent toxicities related to these devices. The perfect CNTs (called also pristine nanotubes) are inert by nature, because of the saturation of their backbone. But, the presence of defects, such as pentagonal arrangement instead of hexagonal, to the tube end, and still to dangling bonds, makes CNTs reactive to many chemical groups. This happens, for instance, with carbonyl, hydroxyl, and carboxylic chemical bonds, which make the CNTs dispersible and thus suitable for different applications in biological media.

APPLICATIONS OF CARBON NANOTUBES IN VARIOUS FIELDS

A. Genetic engineering

CNTs are used to manipulate genes and atoms in the development of bioimaging genomes, proteomics, and tissue engineering. Gene therapy is an approach to correct a defective gene that causes some chronic or hereditary diseases by introducing a DNA molecule into the cell nucleus . The unwound DNA winds around the SWCNT by connecting its specific nucleotides and causes change in its electrostatic property. Wrapping of CNTs by single-stranded DNA was found to be sequence dependent, so it can be used in DNA analysis. Nanotubes, due to their unique cylindrical structure and properties, are used as carriers for genes to treat cancer and genetic disorders [25].

B. Biomedical imaging: For the past few years, carbon-based nanomaterials have been important agents for bioimaging applications due to their unique mechanical, electronic, optical, and chemical properties. The basis of this application is successful surface modification [26]. Roy *et al.*, prepared carbon nanoparticles with different dimensions and variable fluorescence quantum efficiency and used these as high brightness fluorescent probes for staining human blood platelets with very high target specificity [27]. In another study, a new imaging technology used CNTs as an electron emitter for the X-ray tube. Here CNT-enabled X-ray sources proved ideal for repetitive imaging that was used to capture 3-D information. This has been further utilized for the development of a gated microcomputed tomography scanner, which can acquire images in specific points in cardiac and respiratory cycles, as well as a stationary tomosynthesis that captures information from depth [28]. Recently, functionalized SWCNTs decorated with gold nanoparticles induced an excellent surface-enhanced Raman scattering effect to the nanoparticles, which was further utilized for cell imaging [29].

C. Infection therapy:CNTs have found application in this case because of the resistance of infectious agents against numerous antiviral and antibacterial drugs or due to certain vaccine inefficacy in the body. Functionalized CNTs have been demonstrated to be able to act as carriers for antimicrobial agents such as the antifungal amphotericin B. CNTs can attach covalently to amphotericin B and transport it into mammalian cells, and this conjugate has reduced the antifungal toxicity about 40%, as compared to the free drug [30]. Functionalized CNTs also have a role in antigen delivery and in the field of vaccination [31]. There is an induced antibody response with a right specificity, as the linkage of a bacterial or viral antigen with CNTs permits keeping an intact.

D.Artificial implantation and tissue regeneration: CNTs possess exceptional thermal, mechanical, and electrical properties, facilitating their use as reinforcements in various materials to improve the properties of the materials. The aim behind tissue engineering is the substitution of damaged or diseased tissue with biologic alternates that can ultimately repair normal and original function of the tissue.Major advances in this area have supported the promising progress of tissue regenerative engineering and medicine. Due to post administration pain, the body often shows rejection for implants, whereas because of miniature size, nanotubes and nanohorns easily get attached with other amino acids and can be used for implanting artificial joints without rejection reaction by the host [32]. Biomaterials that contain polymers are often placed adjacent to bone. CNTs are also incorporated in these biomaterials applied to bone, mainly to improve their overall mechanical properties, and they are expected to act as scaffolds to guide and promote bone tissue regeneration [33].

E. Catalyst: A catalyst at the molecular level can be incorporated into nanotubes in large amounts and can be released at a required rate at a particular time, as nanohorns offer a large surface area. Many researchers have proved this application. Shi et al. synthesized graphene-encapsulated Fe3C embedded in CNTs with direct pyrolysis of renewable biomass, and this catalyst proved very active for selective hydrogenation of C]C bond in several compounds [34]. In a similar research, nitrogen-doped CNT platinum-based catalyst supports were prepared, which were synthesized using a self-degraded template method. It was concluded that using the graphene-encapsulated Fe3C CNTs as support greatly reduces the loading of noble metal platinum, further promoting the commercialization process of proton exchange membrane fuel cells [35]. So, CNTs have an application as a catalyst.

F. Waste water treatment: The tangled sheets of CNTs oxidize the organic contaminants electrochemically [36]. It also works for viruses and bacteria. Commercialization of the water purification filter containing CNTs has reduced the cost of desalination by reverse osmosis by enhancing the permeability [37].

G. Agriculture application: The unique properties of nanomaterials such as small size, large surface area, and reactivity provide excellent opportunities for its use in the agricultural sector. The foremost applications of CNTs in the agricultural field include seed germination, early plant growth. The potential toxicity of nanomaterials has not yet been widely investigated [38,39]. Here, we described the potential utilization of CNTs in the agricultural sector by considering some selected, but significant works [40].

H. Pesticide analysis:The high adsorption properties of CNTs are utilized for extraction techniques such as solidphase extraction (SPE) and solid-phase micro-extraction (SPME) [41]. SPE technology is one of the most widely used extraction methods for environmental, food, and biological sample pre treatment.

IN DRUG DELIVERY

The various properties of CNTs such as physical and chemical with easy modification have led to a number of applications in the drug delivery field. CNTs are promising drug carriers in the target drug delivery systems for cancer and other therapies [42]. CNTs can easily pass through different biologic barriers, can pass through the plasma membrane and enters the cytoplasm through a “tiny nanoneedle” mechanism, which provides the transport and delivery of the cargo molecules or therapeutics into the target tissue

[43]. CNTs are considered as promising candidates because of their acceptable biocompatibility levels, needlelike structure, and high surface area that is responsible for extensive modification and molecular cargo binding [44].

1. Transdermal drug delivery: The main objective of a transdermal drug delivery system is to deliver drugs into systemic circulation through the skin at a predetermined rate with minimal inter- and intra patient variation [45]. CNTs are not directly incorporated inside the organism, but in these systems, those are applied outside the stratum corneum, and only the active pharmaceutical ingredient is intended to cross the body barriers [46]. Thermo conductive CNT molecules hybridized with chitosan, and they concluded that membranes indicating highly effective drug-loading/-releasing characteristics could have a potential use as a skin heat signale responsive patch type transdermal drug delivery system in the medicinal field [47]. A major step in the development of a programmable transdermal drug delivery system was the CNT patch. A novel skin patch device for delivering nicotine based on an active layer of aligned CNTs approximately 1.507 nm in diameter crossing through a solid polymer film was developed and proved effective.

2. CNTs for cancer treatment: CNTs are tubular materials with nanometer-sized diameters and axial symmetry has a wide role in the in the diagnosis and treatment of cancer. To overcome drawbacks like limited solubility and poor nonselective biodistribution, scientists started to use CNTs in targeted drug delivery to treat cancer cells. In addition, CNTs have the potential to deliver drugs directly to targeted cells and tissues [48]. There are three key features of this nanoscale drug delivery system.use of single walled carbon nanotubes as a platform for the delivery of therapeutic drugs or diagnostics, conjugation of prodrug modules of an anticancer agent that is activated to its cytotoxic form inside the tumor cells upon internalization and in situ drug release, attachment of modules which recognise tumour to the nanotube surface. CNTs have multiple applications in this areafor example, diagnostic imaging, hyperthermia (inducing cell death in the region of cancer cells by an increase in temperature, and photodynamic therapy (a minimally invasive technique that exploits special photosensitizers that, upon illumination, generate reactive oxygen species (ROS) [49,50].

3. CNTs for platelet activation :A study was conducted to characterize the effects of diesel, titanium dioxide rutile, and CNTs nanoparticles on platelet activation, and it was found that SWCNTs induced platelet activation [51].In another study it is found that CNTs have been activate the blood platelets, so they are known to potentiate arterial thrombosis [52]. In a recent study, surface-modified SWCNTs known to induce in vitro platelet activation, aggregation, and platelet granulocyte complex formation [53].

4. CNTs for bioactive substances: The ability of the CNT’s to penetrate the cell membranes, which allows their use in the transportation of drugs into the cells. CNTs have already found many applications in delivery of therapeutic agents and bioactive substances [54].

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. Single and multiple walled carbon nanotubes have been proven to serve as most effective alternatives to previous drug delivery methods. They are able to carry therapeutic drugs, vaccines and nucleic acids to the target cells because of their ability to pass through the membrane. 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.

Acknowledgement: We express our sincere thanks to Dr.Y.Srinivasa Rao and the management of Vignan Group of Institutions for providing necessary facilities to carry out the above review.

REFERENCES

1. Harris PJ: Carbon Nanotubes and Related Structures. Cambridge University Press, Cambridge1999; 1-13.
2. Dresselhaus MS, Dresselhaus G, Ecklund PC: Science of Fullerenes and Carbon

Nanotubes. Associated Press, New York.1996.
3. Iijima S, Helical: Microtubules of Graphitic Carbon. Nature1991; 354:56-58.
4. Iijima S, Ichihashi T:Single-shell carbon nanotubes of 1-nm diameter. Nature.1993; 363:603-605.
5. Abrahamson, P G Wiles, and B. L. Rhoades:"Structure of carbon fibres found on carbon arc anodes," *Carbon*, 1999; 37(11):1873–1874.
6. Hirlekar, M. Yamagar, H. Garse, V. Mohit, and V. Kadam: "Carbon nanotubes and its applications: a review," *Asian Journal of Pharmaceutical and Clinical Research*. 2009; 2(4): 17–27.
7. Meyyappan, L. Delzeit, A. Cassell, and D. Hash: "Carbon nanotube growth by PECVD: a review," *Plasma Sources Science and Technology*, 2003; 12(2):205–216.
8. He, H.; Pham-Huy, L.; Dramou, P.; Xiao, D.; Zuo, P.; Pham-Huy, C: Carbon Nanotubes: Applications in pharmacy and medicine. BioMed Res. Int. 2013; 1–12.
9. Ugnivenko AP, Perepelitsina OM, Sydorenko MV, Ostapchenko LI: Carbon nanotubes in delivery of bioactive substances. J Bionanoscience .2017; 11(6):531-47.
10. Sharma P, Mehra NK, Jain K, Jain NK: Biomedical applications of carbon nanotubes. Curr Drug Deliv. 2016;13(6):796-817.
11. Srinivasulu Doddaga, Ashima Srivastava, Roli Verma: Textbook of Engineering. parshva publishers private limited, first edition 2011.
12. 12.He ZB, Maurice JL, Lee CS, Cojocaru CS, Pribat D: Nickel catalyst faceting in plasma-enhanced direct current chemical vapor deposition of carbon nanofibers. Arabian J Sci Eng 2010; 35:11-19.
13. Ebbesen TW, Ajayan PM: Large-scale synthesis of carbon nanotubes. Nature 1992; 358(6383):220-222.
14. Liu Z, Fan AC, Rakha K, Sherlock S, Goodwin A, Chen X: Supramolecular stacking of doxorubicin on carbon nanotubes for in vivo cancer therapy. Angew Chem Int Ed Engl .2009;48:7668-7772.
15. Zhang W, Zhang Z, Zhang Y: The application of carbon nanotubes in target drug delivery systems for cancer therapies. Nanoscale Res Lett. 2011; 6(1):555.
16. Guven A: Carbon nanotube capsules enhance the *in vivo* efficacy of cisplatin. Acta Biomater 2017;58:466-478.
17. Chakrabarti M: Carbon nanomaterials for drug delivery and cancer therapy. J Nanosci Nanotechnol. 2015;15:5501-11.
18. Burlaka OM, Pirko YV, Yemets AI, Blume YB: Plant genetic transformation using carbon nanotubes for DNA delivery. Cytol Genet. 2015.
19. Bhunia T, Giri A, Nasim T, Chattopadhyay D, Bandyopadhyay A: Uniquely different PVA-xanthan gum irradiated membranes as transdermal diltiazem delivery device. Carbohydr Polym .2013; 95:252-261.
20. Madani SY, Naderi N, Dissanayake O, Tan A, Seifalian AM: A new era of cancer treatment: carbon nanotubes as drug delivery tools. Int J Nanomed .2011; 6:2963-2979.
21. Bihari P, Holzer M, Praetner M, Fent J, Lerchenberger M, Reichel C, Rehberg M, Lakatos S, Krombach F: Single-walled carbon nanotubes activate platelets and accelerate thrombus formation in the microcirculation. Toxicology. 2009;269: 148-54.
22. Fent J, Bihari P, Vippola M, Sarlin E, Lakatos S: Invitro platelet activation, aggregation and plateletegranulocyte complex formation induced by surface modified singlewalled carbon nanotubes. Toxicol Vitro. 2015; 29(5):1132-39.
23. He H, Pham HLA, Dramou P, Xiao D, Zuo P, Pham HC: Carbon nanotubes: applications in pharmacy and medicine. 2013.
24. Srinivasa Rao Y, Kamala Kumari,P.V: Biodegradable Nanospheres:Current Status. Indian Drugs. 2020; 57 (5): 7-18
25. Wen J, Xu Y, Li H, Lu A, Sun S: Recent applications of carbon nanomaterials in fluorescence biosensing and bioimaging. Chem Commun Camb. 2015;51(57): 11346-58.
26. Roy S, Korzeniowska B, Dixit CK, Manickam G, Daniels S, McDonagh C: Biocompatibility and bioimaging application of carbon nanoparticles

synthesized by phosphorus pentoxide combustion method. J Nanomater 2015.
27. Puett C, Inscoe C, Hartman A, Calliste J, Franceschi DK, Lu J, Zhou O, Lee YZ: An update on carbon nanotube-enabled X-ray sources for biomedical imaging. WIREs Nanomed Nanobiotechnol. 2017;1939-1941.
28. Ursu EL, Doroftei F, Peptanariu D, Pinteala M, Rotaru A: DNA-assisted decoration of single-walled carbon nanotubes with gold nanoparticles for applications in surface enhanced Raman scattering imaging of cells. J Nanopart Res. 2017;19:181.
29. Rosen Y, Mattix B, Rao A, Alexis F: Carbon nanotubes and infectious diseases. In: Hunter RJ, editor. Nanomedicine in health and disease. (London, UK): Science Publishers; 2011;. 249-267.
30. Gottardi R, Douradinha B: Carbon nanotubes as a novel tool for vaccination against infectious diseases and cancer. J Nanobiotechnol .2013;11:30.
31. Kumar S, Rani R, Dilbaghi N, Tankeshwar K, Kim KH: Carbon nanotubes: a novel material: Asian J Pharm Clin Res 2010; 2:57-6
32. Sahithi K, Swetha M, Ramasamy K, Srinivasan N, Selvamurugan N: Polymeric composites containing carbon nanotubes for bone tissue engineering. Int J Biol Macromol .2010; 46(3):281-83.
33. Shi J, Wang Y, Du W, Hou Z:Synthesis of graphene encapsulated Fe3C in carbon nanotubes from biomass and its catalysis application. Carbon 2016; 99:330-337.
34. Zhang F, Hou PX, Liu C, Wang BW, Jiang H, Chen ML, Sun DM, Li JC, Cong HT, Kauppinen EI, Cheng HM: Growth of semiconducting single-wall carbon nanotubes with a narrow band-gap distribution. Nat Commun 2016; 7:254-261.
35. HirlekarR,YamagarM,GarseH,VijM,KadamV:Carbonnanotubesanditsapplications: aReview. Asian J Pharm Clin Res 2009; 2:17-27.
36. Rahman A, Ellis JT, Miller CD: Bioremediation of domestic wastewater and production of bioproducts from microalgae using waste stabilization ponds. J Bioremediat Biodegrad 2012; 3:113.
37. Holt JK, Park HG, Wang Y, Stadermann M, Artyukhin AB, Grigoropoulos CP, Noy A, Bakajin O: Fast mass transport through sub-2-nanometer carbon nanotubes. Science 2006;312(5776):1034-1037.
38. Lin, D.; Xing, B. Phytotoxicity of nanoparticles: Inhibition of seed germination and root growth. Environ. Pollut. 2007; 150: 243–250.
39. Zaytseva, O, Neumann, G. Carbon nanomaterials: Production, impact on plant development, agricultural and environmental applications. Chem. Biol. Technol. Agric. 2016; 3-17.
40. Juganson, K.,Ivask, A, Blinova, I, Mortimer, M, Kahru, A. NanoE-Tox: New and in-depth database concerning ecotoxicity of nanomaterials. Beilstein J. Nanotechnol. 2015; 6: 1788–1804.
41. Pyrzynska, K: Carbon nanotubes as sorbents in the analysis of pesticides. Chemosphere 2011; 83: 1407–1413.
42. Perla S. Flame synthesis of carbon-nanostructures [LSU Master's Theses]. 2005; 1450.
43. Vander Wal RL, Ticich TM, Curtis VE: Diffusion flame synthesis of single-walled carbon nanotubes. Chem Phys Lett. 2000; 323:217-23.
44. HahmMG,HashimDP,VajtaiR,AjayanPM :Areview:controlledsynthesisofvertically aligned carbon nanotubes. Carbon Lett .2011; 12:185.
45. Rummeli MH, Borowiak-Palen E, Gemming T, Pichler T, Knupfer M, Kalbac M, Dunsch L, Jost O, Silva SRP, Pompe W, Buchner B: Novel catalysts, room temperature, and the importance of oxygen for the synthesis of single-walled carbon nanotubes. Nano Lett .2005; 5(7):1209-15.
46. Huang X, Mclean RS, Zheng M: High-resolution length sorting and purification of DNA-wrapped carbon nanotubes by size-exclusion chromatography. Anal Chem 2005; 77(19):6225-6228.
47. Fabbro C: Targeting carbon nanotubes against cancer. Chem Commun 2012; 48(33):3911-26.
48. Kostarelos K, Bianco A, Prato M: Promises, facts and challenges for carbon nanotubes in imaging and therapeutics. Nat Nanotechnol 2009; 4(10):627-33.

49. Lara.L, Alberto B, Maurizic P, Kostas K: Carbon nano tubes as nanomedicines: from toxicology to pharmacology.Advanced drug delivery reviews 2006; 58(14): 1460-1470.
50. Beik J, Abed Z, Ghoreishi FS, Hosseini-Nami S, Mehrzadi S, Shakeri-Zadeh A, Kamrava SK: Nanotechnology in hyperthermia cancer therapy: from fundamental principles to advanced applications. J Control Release 2016; 235:205-21.
51. Pfeiffer R. Interaction between concentric tubes in DWCNTs. Eur Phys J B 2004; 42(3):345-50.
52. Zheng M: DNA-assisted dispersion and separation of carbon nanotubes. Nat Mater 2003; 2(5):338-42.
53. Lacerda L: Intracellular trafficking of carbon nanotubes by confocal laser scanning microscopy. Adv Mater 2007; 19(14):1789.
54. Sharma P, Mehra NK, Jain K, Jain NK: Biomedical applications of carbon nanotubes. Curr Drug Deliv 2016; 13(6):796-817.