Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Suppl 4, 2012

Review Article

CARBON NANOTUBES: AN EMERGING DRUG DELIVERY TOOL IN NANOTECHNOLOGY

DHEERAJ T. BAVISKAR*[1], CHETAN M. TAMKHANE[1], AJIM H. MANIYAR[1], DINESH K. JAIN[2]

[1]Department of Pharmaceutics, Institute of Pharmaceutical Education, Boradi, Tal-Shirpur, Dist-Dhule 425428 (MS), [2]College of Pharmacy, IPS Academy, Rajendra nagar, Indore 452012 MP India. Email: baviskar@sancharnet.in

Received: 23 Mar 2012, Revised and Accepted: 30 Apr 2012

ABSTRACT

Carbon nanotubes (CNTs) are allotropes of carbon with a cylindrical nanostructure and shows outstanding mechanical, electrical, magnetic properties. These are having nanometer scale diameter and high aspect ratio that give advantage for preparation of high strength polymer composites. There are many methods have been used to make dispersion of carbon nanotubes in polymer matrix like electrospinning, solution mixing, in-situ polymerization, melt mixing and chemical functionalization. The efficient techniques for achievement of better carbon nanotubes dispersion are done with carbon nanotubes functionalization by click chemistry. Carbon nanotube functionalization by employing click chemistry and the preparation of carbon nanotubes composites with higher branched polymers are noticed as potential techniques in achieving good carbon nanotubes dispersion. With the help of various methods like wetting method, spectroscopic method, force microscopic method it is possible to characterize the interaction of carbon nanotubes with different polymers. The review describes some of the methods and preparation technique of better efficient CNT-polymer composites. The review report that carbon nanotubes show some of the adverse effect when accumulated in major organs like lungs, liver, and spleen. Carbon nanotubes have wide application in photodynamic therapy, thermal therapy and in delivering therapeutic gene. The carbon nanotubes are consider to be most important tool in detection of neoplastic cells and delivering drugs to those cells.

Keywords: Carbon Nanotubes, Functionalization, Preparations, Cancer, Toxicity, Applications.

INTRODUCTION

Iijima discovered carbon nanotubes in 1991[1] and thereafter it have been gained much attention for their many applications such as photovoltaic devices[2], nanoelectronics, superconductors[3], electromechanical actuators[4], electrochemical capacitors[5], nanowires[6], and nanocomposite materials.[7,8] Carbon nanotubes can be classified into three categories as single-walled carbon nanotubes (SWNTs) [9, 10], double-walled carbon nanotubes (DWNTs)[11,12] or multi-walled carbon nanotubes (MWNTs).[1] SWNT and DWNT consist of cylinders of one or two graphene sheets, while MWNT consists several concentric cylindrical shells of graphene sheets. CNTs are prepared in a variety of ways, with the help of arc discharge, laser ablation[13], high pressure carbon monoxide (HiPCO)[14], and chemical vapour deposition (CVD).[15,16] CNTs display excellent mechanical, electrical, thermal and magnetic characteristics.[17,18] Ajayan et al.[19] mentioned the first polymer nanocomposites using CNTs as a filler. The number of articles and patents in polymer composites containing CNTs is increasing everyday.[20] A wide range of polymer matrices are used for composites, including thermoplastics[21], thermosetting resins[22], liquid crystalline polymers[23] water-soluble polymers and conjugated polymers, amongst others. Purification of nanotubes is a necessary step to take away metallic and amorphous carbon impurities, while avoiding severe damage to the nanotubes.[24] The interaction properties of carbon nanotube nanocomposites have been investigated at three different levels between different shells of a multi-walled carbon nanotube (MWNT), between different nanotubes in a bundle, and between carbon nanotubes and polymer matrix.[25]

Carbon nanotubes

Carbon nanotubes [26] are consisting of thin sheets of benzene ring carbons rolled up into the shape of a seamless tubular structure. The ideal structure of CNTs belongs to the fullerenes, the third allotropic form of carbon with graphite and diamond. The outer diameter of these MWNT is about several tens of nanometers, and they have a length of 10–100 μm.[27] Depending on the rolling, CNTs can be further classified as armchair, zigzag and chiral types (Fig 1). Elemental carbon in sp^2 hybridization can made a variety of amazing structures such as, graphite, graphene, CNTs and fullerene.[28] CNTs[29] can be regarded as a unique inner hollow tubular structure of nanometer diameter rolled with graphite plates with large length/diameter ratios and without any aperture in the tube wall.

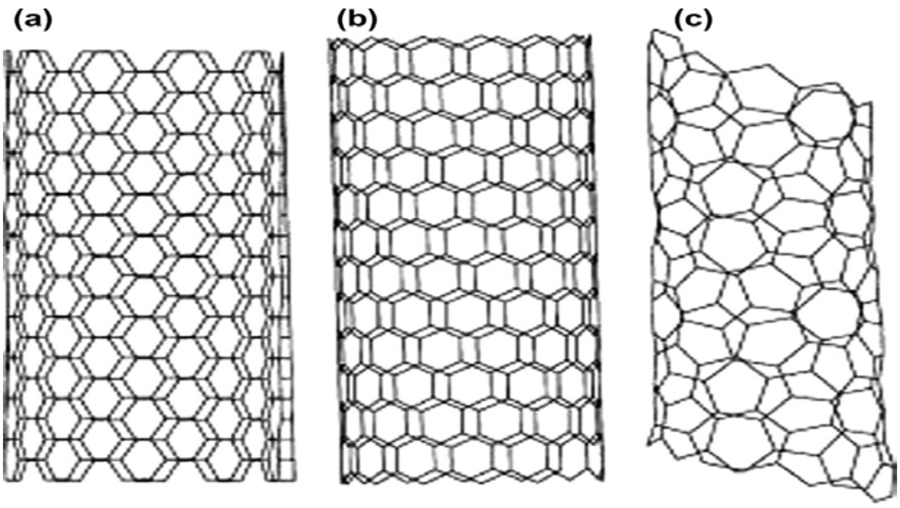

Fig. 1: Scheme of different SWNTs: armchair (a); zigzag (b); and chiral (c)

SWNT made up of a seamless graphene sheet rolled up into a cylinder of a small number of nanometers diameter and several microns length. A MWNT is an arrangement of numerous, up to tens and hundreds of concentric tubes of graphite sheets with adjacent shells. Armchair nanotubes are really metallic[30], whereas other tubes zigzag and chiral 1/3 are narrow gap and 2/3 wide-gap semiconductors. Crystallinity and structural perfection of arc produced CNTs are higher in comparison to other methods. Arc growth was the first method for the production of macroscopic amounts of MWNTs.[31] CVD (chemical vapour deposition) of hydrocarbon gases over catalysts is one of the most simplest and versatile techniques to synthesize CNTs. This method involves catalyst-assisted decomposition of hydrocarbons (commonly benzene, ethanol, acetylene, propylene, methane, ethylene, CO, etc.) and growth of CNTs over the catalyst (usually transition metals such as Ni, Fe, Co, etc.) in a temperature range of 300–1200 °C.[32,33] Comparing with the other methods, CVD can produce mass and relatively high purity CNTs. The by-product in CNTs production by CVD is usually aromatic carbon, amorphous carbon, polyhedral carbon, metal particles etc. In SWNT synthesis using arc discharge and laser ablation method side products formed as, C60, fullerenes, graphite particles, and graphitic polyhedrons. Several purification methods have been reported like dilute HNO_3 reflux/air oxidation procedure, dispersion by sonication in a surfactant, filtration and high temperature heating under neutral or lightly oxidizing conditions[34, 35], bromination and infrared irradiation in air.[36] Techniques for the purification of CNTs have been reviewed in detail, with an emphasis on their purification principles by Pillai et al.[37]

Funtionalization methods of CNTs

Since CNTs generally agglomerate due to Van der Waals forces, they are extremely hard to disperse and arrange in a line into a polymer matrix. Hence, a major challenge in developing matrix in order to achieve better dispersion and alignment and strong interfacial interactions, to improve the load transfer across the CNT-polymer matrix interface. There are a number of approaches for functionalisation of CNTs together with defect functionalisation, covalent functionalisation and non-covalent functionalisation.[38]

Defect functionalization method

The purification of CNTs is done with the help of oxidative methods in order to eliminate metal particles or amorphous carbon from raw material.[39] The oxidized carbon atoms in the form of

–COOH group is present in purified SWNTs. In this oxidizing method, SWNTs are broken down to very short tubes of lengths 100–300 nm. Mawhinney et al.[40] mentioned surface defect site density on SWNTs by measuring the evolution of CO_2 (g) and CO (g) heated at 1273 K. The results showed that about 5% of the carbon atoms in the SWNTs are localized at defective sites.

Non-covalent functionalization method

Non-covalent functionalization of nanotubes is use frequently because it does not compromise the physical properties of CNTs, but help to improve solubility and process ability. It mainly involves surfactants, biomacromolecules or wrapping with polymers. The nanotubes are enclosed by the hydrophobic components of the related micelles and polymers can wrap around CNTs, forming supramolecular complexes. Coleman and co-workers[41] prepared a nanotube-polymer hybrid by suspended SWNTs in organic solvents poly (p-phenylenevinylene-co-2, 5-dioctyloxy-m-phenylenevinylene) to enclose the copolymer around the nanotubes. This encapsulation significantly enhanced the dispersion of SWNTs into a wide variety of polar and non-polar solvents and polymer matrices as the copolymer shell was permanently fixed. Thus, encapsulated SWNTs may be stabilized with respect to typical polymer processing and recovery from the polymer matrix. Nativ-Roth et al.[42] recommended that the block copolymers adsorbed to the nanotubes by a non-wrapping mechanism, and the solvophilic blocks act as a steric barrier that leads to formation of stable dispersions of individual SWNTs and MWNTs above a threshold concentration of the polymer.

Covalent functionalization method

In covalent functionalization, the translational symmetry of CNTs is interrupted by changing sp2 carbon atoms to sp3 carbon atoms, and the properties of CNT, such as electronic and transport are changed.[43] Normally, functional groups such as –COOH or –OH are created on the CNTs during the oxidation by oxygen, air, concentrated sulfuric acid, nitric acid, aqueous hydrogen peroxide, and acid mixture.[44] The number of –COOH groups on the surface of CNT depends on acid treatment temperature and time, increasing with increasing temperature. The extent of the induced -COOH and –OH functionality also depends on the oxidation procedures and oxidizing agents.[45] Fu et al[46] reported functionalization of CNTs with the help of “grafting to” method. They refluxed CNTs containing carboxylic acid groups with thionyl chloride to convert acid groups to acylchlorides. Then, the CNTs with surface-bound acylchloride moieties were used in the esterification reactions with the hydroxyl groups of dendritic poly(polyethylene glycol) polymer. Zeng et al.[47] reported “grafting from” approach developed due to in-situ ring-opening polymerization o**Ɛ** -caprolactone to covalently graft biodegradable poly(Ɛ-caprolactone) onto CNT surfaces.

Functionalization method by click chemistry

Huisgen coined the term “Click” chemistry, for the dipolar cycloaddition reaction[48], is an ideal reaction for material synthesis and modification and also for self assembly of nanomaterials. Cho and co-workers[49] prepared gold nanoparticles functionalized SWNTs using click chemistry approach. Gold nanoparticles containing octanethiol were synthesized by the reduction of tetrachloroauric acid using sodium borohydride in presence of alkanethiol. Li and co-workers[50] introduced an alkyne functionalized nanotube surface using a carbamate linkage. The azide moiety containing a thermoresponsive diblock copolymer composed of N, N dimethylacrylamide (DMA) and poly (N-isopropylacrylamide) (NIPAM) was covalently attached with alkynated MWNTs.

Preparation techniques of polymer/CNT nanocomposites

The dispersion of CNTs in polymer matrices is a critical issue in the preparation of CNT/polymer composites. Now days there are many methods used to improve the dispersion of CNTs in polymer matrices such as solution mixing, melt blending, and in-situ polymerization method.

Solution mixing technique

In this approach, a dispersion of CNTs in a suitable solvent and polymers are mixed in solution. It is done by precipitation or with evaporation of the solvent. A high power ultrasonication process is more efficient in forming a dispersion of CNTs. Ultrasonic irradiation has been extensively used in dispersion, emulsifying, crushing, and activating the particles. Chemical effects of ultrasound are associated with the rapid, violent collapse of cavitation bubbles created as the ultrasonic waves pass through a liquid medium.[51]

Melt blending technique

Melt mixing is useful for thermoplastic polymers. In melt processing, CNTs are mechanically dispersed into a polymer matrix with a high temperature and high shear force mixer. Shear forces assist to break nanotube aggregates or prevent their formation. Bocchini et al.[52] fabricated MWNTs/linear low density polyethylene (LLDPE) nanocomposites via melt-blending using a Brabender Plasticorder internal mixer. MWNTs dispersed in LLDPE delay thermal and oxidative degradation with respect to that for virgin LLDPE. Melt mixing has been successfully applied for the preparation of different polymers-CNT composites such as polypropylene/CNT, high density PE/CNT, polycarbonate/CNT, PMMA/CNT,polyoxymethylene/CNT, polyimide/CNT,PA6/CNT, etc.

In-situ polymerization technique

In this polymerization method, the CNTs are dispersed in monomer and then subjected to polymerization. Hu et al.[53] synthesized MWNT-reinforced polyimide nanocomposites by in-situ polymerization of monomers in the presence of acylated MWNTs. The final MWNT-polyimide nanocomposite films were obtained by imidization of MWNT-poly-(amic acid) at 350 °C for 1 h under vacuum. In this method, the CNTs were uniformly dispersed in polymer matrix. Conducting polymers are attached to CNTs surfaces by in-situ polymerization to improve the processability, and electrical, magnetic and optical properties of CNTs. They showed that the conductivity of nanocables increased with increasing nanotube weight percentage. In-situ polymerization method has also been used for the preparation of polyurethane/CNT nanocomposites.

Preparation of CNT nanocomposites using dendritic polymers

CNTs have three-dimensional globular and sphere like structural architectures, dendritic polymers (DP) such as dendrimeric and hyperbranched polymers, have generated great excitement in polymer research, owing to their wide range of applications from drug delivery to chemical sensors. Dendrimers have unique size, controlled and symmetric structure with ideally branching units without any structural defects, but require multi-step synthesis reaction, while the Hyperbranched polymers exhibit a randomly branched structure, with a single step synthesis process. [54]

Interaction characterisation technique

Wetting method

Wetting measurements are typically reported in terms of contact angle, surface tension, and Hamaker constant.[55] Surface tension is usually reported in mN/m, for liquids, and mJ/m^2, for solid surfaces. In macroscopic wetting experiments, liquid polymer is placed on top of a carbon nanotube sample (or polymer powder is heated on the sample to melt) to check whether the polymer is absorbed by the surface or forms a spherical bead. Laplace– Young model is typically used and the results are presented in the form of contact angle.[56] A surface tension in the range of 40–45 mJ/m^2 was reported for MWNT, which agrees with the value of 40–80 mJ/m^2 reported elsewhere.

Spectroscopic method

Spectroscopy techniques, including Raman and Fourier Transform infrared spectroscopy (FTIR) are powerful techniques for material characterisation. Unlike MWNTs Raman and infrared spectra of SWNT are significantly different from those obtained from single crystal graphite Furthermore, Raman and infrared spectra of pristine and functionalized nanotubes are different. Therefore, spectroscopy techniques are used not only to detect the functionalization but also to distinguish different types of functionalization. A typical Raman spectrum of SWNTs shows three main features. The first features are the radial breathing modes (RBM), which are related to the nanotube diameter and are located in the range of 100– 400 cm^{-1}. The second features in the range of 1000–1700 cm^{-1} are the G and D bands that are related to the nanotube structure and tangential vibration modes (TM). The last spectral range is between 1700 and 3000 cm^{-1} and features the second order Raman spectrum. The most significant peaks in this range are the ones located at approximately twice the wavenumbers of the G and D bands.

Force microscopic method

Atomic force microscopy is a great technique with extremely high accuracy in force–displacement measurement, which gives it atomic resolution. Two different approaches have been considered to employ AFM for interaction measurement studies in carbon nanotube nanocomposites: (a) attach a nanotube to the AFM tip and use a polymer substrate and (b) coat the AFM tip with polymer and use a nanotube substrate.[57]

Drug delivery using CNTs

Conventional administration of chemotherapeutic agents is often compromised by their systemic toxicity due to lack of selectivity. In addition, limited solubility, poor distribution among cells, inability of drugs to cross cellular barriers[58], and especially a lack of clinical procedures for overcoming multidrug resistant (MDR) cancer, all limit the clinical administration of chemotherapeutic agents. f-CNT has potential of being used as for the delivery of small drug molecules as it penetrates into cells.[59] Researchers have found that functionalized CNTs can cross the mammalian cell membrane by endocytosis or other mechanisms. With the help of specific peptides or ligands on their surface to distinguish cancer-specific receptors on the cell surface, CNTs can carry therapeutic drugs more safely and effectively into the cells that are previously unreachable, which makes them ideal candidates for drug delivery.

CNTs in cancer treatment

Amongst all cancer treatment choices like surgery, radiotherapy, immunotherapy, thermotherapy and chemotherapy etc., surgery plays important role in primary stage cancer. Patients with advanced cancer and those received palliative operation procedures, chemotherapy and radiotherapy are required. Although these modalities are successful in some cases, systemic toxicity may develop at the same time due to lack of selectivity for these treatments. Capabilities of carbon nanotubes combined with appropriate surface modifications and their unique physicochemical properties can lead to a new kind of nanomaterials for cancer therapy.

Toxicity of CNTs

So far, many studies have been performed to evaluate the toxicological effects of CNTs both *in vitro* and *in vivo*. After cells were exposed to CNTs *in vitro*, different degrees of toxicity on cell viability were observed. It is likely that CNT toxicity might depend on many other factors rather than concentration alone such as their physical form, degrees of functionalisation and agglomeration state etc. CNTs have also been administrated to mice and rats by different routes in several studies[60]. Most of them reported adverse effects resulting from accumulation of CNTs in major organs, such as lung, liver and spleen. Therefore, toxicity of CNTs might be relevant to the route of administration.

Application of CNTs

Carbon nanotube-based diagnosis

Conventional clinical cancer diagnostic techniques, such as X-ray, CT scan and MRI, do not acquire satisfactory spatial resolution for early detection of the disease. Fluoro-desoxy-glucose (FDG), is widely used PET tracer in clinical oncology is not a specific tracer for malignant diseases.[61] Hence, it is necessary to established new tools for early cancer diagnosis. Hong et al.[62] reviewed molecular imaging with single walled carbon nanotubes. When Gd^{3+}functionalized SWCNTs was applied to MRI, high resolution and better tissue penetration were achieved. Similarly, medium resolution, high sensitivity and good tissue penetration were obtained from radioisotopes labelled SWCNTs with radionuclide based imaging techniques.

CNTs in thermal therapy applications

CNTs are also useful in the field of thermal therapy and considered to be a non-invasive, harmless, and highly efficient technique. Biris et al.[63] demonstrated that infrared photothermal (PT) radiometry, combined with recent advances in time-resolved infrared imaging techniques, was a very useful tool for determining the temperature dynamics in scattered individual cancer cells or their small clusters labelled with carbon nanotubes, which was helpful in determining the appropriate dose regimens for laser PT therapy using relatively long laser pulses.

CNTs-mediated photodynamic therapy

The use of CNTs as a new photosensitizer for photodynamic therapy (PDT) is another area of research currently under investigation. It is well known that the most common cancer treatments, including surgery, radiation therapy and chemotherapy, all tend to be immunosuppressive. In contrast, PDT could potentially be an ideal cancer treatment, a confined therapy capable of efficiently destroying tumors while at the same time sensitizing the immune system to seek out and destroy metastases. Currently, the knowledge of CNTs-based photodynamic therapy is limited and further research is needed in this area. Zhu et al.[64] engineered a novel molecular complex of a photosensitizer, an ssDNA aptamer, and single-walled carbon nanotubes, which efficiently control and regulate singlet oxygen generation, whereby more efficient, reliable and selective PDT (Photodynamic therapy) could be guaranteed.

Delivery of therapeutic gene by CNTs

Gene therapy is the most promising method in cancer treatment and is expected to be an alternative method to traditional chemotherapy. Generally, the development of new vectors for therapeutic gene transfer requires protection of DNA from degradation, good membrane penetration and low immunogenicity.[65] In this context, CNTs seem to be very suitable due to their capability of crossing the mammalian cell membrane easily by endocytosis as we mentioned above. Moreover, functionalized CNTs can provide a safe nonviral vehicle for the delivery of DNA molecules into mammalian cells, since these DNA–CNT structures are inorganic and produced under strict conditions in a cell free manner. They found that the CNT-gene structure led to a higher level of gene expression compared to the naked DNA alone.

CONCLUSION

From last two decades carbon nanotubes have been under extensive investigations and have shown outstanding mechanical, thermal and electrical properties. However, their full potential has not been reached when combined with polymer matrices in nanocomposites. The difficulty arises in the development of methods to improve the dispersion of CNTs in a polymer matrix because their enhanced dispersion in polymer matrices greatly improves the mechanical, electrical and optical properties of composites. Despite various methods, as melt processing, solution processing, in situ polymerization, and chemical functionalization, there are some more opportunities and challenges to be found in order to improve dispersion and modify interfacial properties. Also detailed understanding of the toxicological properties of carbon nanotubes and a balanced evaluation of risk/benefit ratio are required before they can be recommended for routine clinical use.

REFERENCES

1. Iijima S. Helical microtubules of graphitic carbon. Nature 1991; 354:56–58.
2. Bachtold A, Hadley P, Nakanishi T, Dekker C. Logical circuits with carbon nanotube transistors. Science 2001; 294:1317–20.
3. Kasumov AY, Deblock R, Kociak M, Reulet B, Bouchiat H, Khodos I, et al. Supercurrents through single-walled carbon nanotubes. Science 1999; 284:1508–11.
4. Baughman RH, Cui C, Zakhidov AA, Iqbal Z, Barisci JN, Spinks GM, et al. Carbon nanotube actuators. Science 1999; 284:1340–4.
5. Niu C, Sichel EK, Hoch R,MoyD, Tennet H. High power electrochemical capacitors based on carbon nanotube electrodes. Appl Phys Lett 1997; 70:1480–2.
6. Ajayan PM, Iijima S. Capillarity-induced filling of carbon nanotubes. Nature 1993; 361:333–4.
7. Xie XL, Mai YW, Ping X. Dispersion and alignment of carbon nanotubes in polymer matrix: a Review. Mater Sci Eng Rep 2005; 49:89–112.
8. Andrews R, Weisenberger MC. Carbon nanotube polymer composites. Curr Opin Solid State Mater Sci 2004; 8:31–7
9. Iijima S, Ichihashi T. Single-shell carbon nanotubes of 1-nm diameter. Nature 1993; 363:603
10. Bethune DS, Kiang CH, Devries MS, Gorman G, Savoy R, Vazquez J, et al. Cobalt- catalyzed growth of carbon nanotubes with single atomic- layer walls. Nature 1993; 363:605–7.
11. Sugai T, Yoshida H, Shimada T, Okazaki T, Shinohara H. New synthesis of high-quality double-walled carbon nanotubes by high temperature pulsed arc discharge. Nano Lett 2003; 3:769–73.
12. Bandow S, Takizawa M, Hirahara K, Yudasaka M, Iijima S. Raman scattering study of Double-wall carbon nanotubes derived from the chains of fullerenes in single-wall carbon nanotubes. Chem Phys Lett 2001; 337:48–54.
13. Guo T, Nikolaev P, Thess A, Colbert DT, Smalley RE. Catalytic growth of single-walled nanotubes by laser vaporization. Chem Phys Lett 1995; 243:49–54.
14. Nikolaev P, Bronikowski MJ, Bradley RK, Rohmund F, Colbert DT, Smith KA, et al. Gas phase catalytic growth of single-walled carbon nanotubes from carbon monoxide. Chem Phys Lett 1999; 313:91–7.
15. Joseyacaman M, Mikiyoshida M, Rendon L, Santiesteban JG. Catalytic growth of carbon microtubules with fullerene structure. Appl Phys Lett 1993; 62:657–9.
16. Huang SM, Woodson M, Smalley RE, Liu J. Growth mechanism of oriented long single walled carbon nanotubes using fast-heating chemical vapor deposition process. Nano Lett 2004; 4:1025–8.
17. Treacy MM, Ebessen TW, Gibson JM. Exceptionally high Young's modulus observed for individual carbon nanotubes. Nature 1996; 381:678–80.
18. Saito R, Dresselhaus G, Dresselhaus MS. Physical properties of carbon nanotubes. London:Imperial College Press; 1998.
19. Ajayan P M, Stephan O, Colliex C, Trauth D. Aligned carbon nanotube arrays formed by cutting a polymer resin-nanotube composite. Science 1994; 265:1212–4.
20. Moniruzzaman M, Winey KI. Polymer nanocomposites containing carbon nanotubes. Macromolecules 2006; 39:5194–205.
21. Jamal A, Ali R, Somayeh M. Preparation and characterization of linear low density Polyethylene/carbon nanotube nanocomposites. J Macromol Sci Part B: Phys 2007; 46:877–89.
22. Gryshchuk O, Karger-Kocsis J, Thomann R, Konya Z, Kiricsi I. Multiwall carbon nanotube modified vinylester and vinylester-based hybrid resins. Compos Part A 2006; 37:1252–9.
23. Bliznyuk VN, Singamaneni S, Sanford RL, Chiappetta D, Crooker B, Shibaev PV. Matrix mediated alignment of single wall carbon nanotubes in polymer composite films. Polymer 2006; 47:3915–21.
24. Kingston CT. Efficient laser synthesis of single-walled carbon nanotubes through laser heating of the condensing vaporization plume. Carbon 2004; 42(8–9):1657.
25. Qian D. Load transfer and deformation mechanisms in carbon nanotube– polystyrene composites. Appl Phys Lett 2000; 76(20):2868.
26. Chae HG, Liu J, Kumar S. Carbon nanotubes properties and applications. In: O'Connell MJ, editor. Carbon nanotube-enabled materials. Boca Raton: Taylor & Francis Group, LLC; 2006.
27. Zhang H, Fu X, Chen Y, Yi S, Li S, Zhu Y, et al. The electrochemical hydrogen storage of multi-walled carbon nanotubes synthesized by chemical vapor deposition using a lanthanum nickel hydrogen storage alloy as catalyst. Physica B 2004; 352:66–72.
28. Dodziuk H, Dolgonos G. Molecular modeling study of hydrogen storage in carbon nanotubes. Chem Phys Lett 2002; 356:79–83.
29. Darkrim FL, Malbrunot P, Tartaglia GP. Review of hydrogen storage by adsorption in carbon nanotubes. Int J Hydrogen Energy 2002; 27:193–202.
30. Jamal Y, Wyszynski JL. On-board generation of hydrogen-rich gaseous fuels, a review. Int J Hydrogen Energy 1994; 19:557–72.
31. Pettersson L, Sjostrom K. Onboard hydrogen generation by methanol decomposition for the cold start of neat methanol engines. Int J Hydrogen Energy 1991; 16:671–6.
32. Li W, Wang H, Ren Z, Wang G, Bai J. Co-production of hydrogen and multiwall carbon nanotubes from ethanol decomposition over Fe/Al_2O_3 catalysts. Appl Catal B Environ 2008; 84:433–9
33. Maruyama S, Kojima R, Miyauchi Y, Chiashi S, Kohno M. Low-temperature synthesis of high- purity single-walled carbon nanotubes from alcohol. Chem Phys Lett 2002; 360:229– 34.
34. Kruger P. Electric power requirement for large-scale production of hydrogen fuel for the world vehicle fleet. Int J Hydrogen Energy 2001; 26:1137–47.
35. Wang G, Wang H, Tang Z, Li W, Bai J. Simultaneous production of hydrogen and multi- walled carbon nanotubes by ethanol decomposition over Ni/Al_2O_3 catalysts. Appl Catal B: Environ 2009; 88:142–51.
36. Dillon AC, Gennett T, Jones KM, Alleman JL, Parilla PA, Heben MJ et al. A simple and complete purification of single-walled carbon nanotube materials. Adv Mater 1999; 11:1354–8.

37. Pillai SK, Ray SS, Moodley M. Purification of multi-walled carbon nanotubes. J Nanosci Nanotechnol 2008; 8:6187–207.
38. Hirsch A. Functionalization of single-walled carbon nanotubes. Angew Chem Int Ed 2002; 41:1853–9.
39. Nalwa HS, editor. Handbook of nanostructured materials and nanotechnology, vol. 5. New York: Academic Press; 2000.
40. Mawhinney DB, Naumenko V, Kuznetsova A, Yates JT, Liu J, Smalley RE et al. Surface defect site density on singal walled carbon nanotubes by titration. Chem Phys Lett 2000; 324:213–6.
41. Coleman JN, Dalton AB, Curran S, Rubio A, Davey AP, Drury A, et al. Phase separation of carbon nanotubes and turbostratic graphite using a functional organic polymer. Adv Mater 2000; 12:213–6.
42. Nativ-Roth E, Shvartzman-Cohen R, Bounioux C, Florent M, Zhang D, Szleifer I, et al. Physical adsorption of block copolymers to SWNT and MWNT: a non wraping mechanism. Macromolecules 2007; 40:3676–85.
43. Park H, Zhao J, Lu JP. Effects of sidewall functionalization on conducting properties of single wall carbon nanotubes. Nano Lett 2006; 6:916–9.
44. Liu J, Rinzler AG, Dai H, Hafner JH, Bradley RK, Boul PJ, et al. Fullerene pipes. Science 1998; 280:1253–6.
45. Datsyuk V, Kalyva M, Papagelis K, Parthenios J, Tasis D, Siokou A, et al. Chemical oxidation of multi-walled carbon nanotubes. Carbon 2008; 46:833–40
46. Jin Z, Sun X, Xu G, Goh SH, Ji W. Nonlinear optical properties of some polymer/multi-walled carbon nanotube composites. Chem Phys Lett 2000; 318:505–10.56.
47. Zeng HL, Gao C, Yan DY. PolyƐ(-caprolactone) functionalized carbon nanotubes and their biodegradation properties. Adv Funct Mater 2006; 16:812–8.
48. Huisgen R. 1, 3-Dipolar cycloadditions-introduction, survey, mechanism in 1, 3-dipolar cycloaddition chemistry. In: Padwa A, editor. 1, 3-Dipolar cycloaddition chemistry, vol. 1.New York: Wiley; 1984. p. 1–176.
49. Cho JW, Rana S. Synthesis and characterization of polyurethane functionalized carbon nanotubes with shape memory effect using click chemistry. Proceed intern confer intelligent textiles 2007, Seoul, Korea; 2007. p. 142–3.
50. Li C, Pang XJ, Qu MZ, Zhang QT, Wang B, Zhang BL, et al. Fabrication and characterization of polycarbonate/carbon nanotubes composites. Compos Part A 2005; 37:1485-9.
51. Xia H, Wang Q, Qiu G. Polymer-encapsulated carbon nanotubes prepared through ultrasonically initiated in situ emulsion polymerization. Chem Mater 2003; 15:3879–86.
52. Bocchini S, Frache A, Camino G, Claes M. Polyethylene thermal oxidative stabilisation in carbon nanotubes based nanocomposites. Eur Polym J 2007; 43:3222–35.
53. Hu N, Zhou H, Dang G, Rao X, Chen C, Zhang W et al. Efficient dispersion of multi-walled carbon nanotubes by in situ polymerization. Polym Int 2007; 56:655–9.
54. Gao C, Yan D. Hyperbranched polymers: from synthesis to applications.Prog Polym Sci 2004; 29:183–275.
55. Maeno Y, Ishikawa A, Nakayama Y. Adhesive behavior of single carbon nanotubes. Appl Phys Express 2010; 3(6):065102 (2 pp.).
56. Dujardin E. Wetting of single shell carbon nanotubes. Adv Mater 1998; 10(17):1472.
57. Li X. Direct measurements of interactions between polypeptides and carbon nanotubes. J Phys Chem B 2006; 110(25):12621.
58. Heister E, Neves V, Carmen T.Triple functionalisation of single-walled carbon nanotubes with doxorubicin, a monoclonal antibody, and a fluorescent marker for targeted cancer therapy, Carbon 2009;47: 2152–60.
59. Mali N, Jadhav S, Manisha K, Kadam V. Carbon nanotubes as carrier for delivery bioactive and therapeutic agent: an overview. Int J Pharm Pharm Sci 2011; 3(3): 4552.
60. Schipper ML, Nakayama-Ratchford N, Davis CR, A pilot toxicology study of single-walled carbon nanotubes in a small sample of mice, Nat. Nanotechnol. 2008; 3: 216–221.
61. Bhirde AA, Patel V, Gavard V. Targeted killing of cancer cells *in vivo* and *in vitro* with EGF-directed carbon nanotube-based drug delivery, ASC NANO.2009;3: 307–316.
62. Hong H, Gao T, Cai WB, Molecular imaging with single-walled carbon nanotubes, Nano Today. 2009;4: 252–261.
63. Biris AS, Boldor D, Palmer J. Nanophotothermolysis of multiple scattered cancer cells with carbon nanotubes guided by time-resolved infrared thermal imaging, J. Biomed. Opt. 2009; 14: 021007.
64. Zhu Z, Tang ZW, Phillips JA, Regulation of singlet oxygen generation using single-walled carbon nanotubes, J. Am. Chem. Soc. 2008;130: 10856–10857.
65. Shun-rong J, Chen L, Zhang B, Feng Y, Jin X, Jiang L et al. Carbon nanotubes in cancer diagnosis and therapy. Biochimica e m t Biophysica Acta. 2010;1806: 29–35.