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CARBON NANOTUBE: ITS FUNCTIONALIZATION AND APPLICATIONS IN TARGETED DRUG DELIVERY SYSTEM

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Abstract

Nanomedicine is having a great potential for introducing new generation of targeted drug delivery system in the field of pharmaceutical sciences. Amongst new generation of nano-vectors are carbon nanotubes, which can be manufactured as single or multi-walled. Multi-walled carbon nanotubes can be fabricated as biocompatible nanostructures of cylindrical bulkytubes. High aspect ratio, unique optical property and the likeness as small molecule make carbon nanotubes (CNTs) an unusual allotrope of carbon element. The insolubility and the manipulation difficulty in any solvents have imposed great limitations to the use of CNT. Functionalization of CNTs is the solution to this problem. Functionalized CNTs showing a variety of medicinal/pharmaceutical applications, including the diagnosis and treatment of cancer, central nervous system disorders and infectious diseases, and applications in tissue engineering. Generally, two types of functionalization approach were reported over the last decades: 1) non-covalent (p-stacking, exohedral or endohedral) and 2) covalent (defect or sidewall) functionalization. Commonly, a covalent bond between the CNTs and functional group is preferred over a non-covalent interaction in terms of thermal and chemical stability of the resulting material. This review article mainly focused on overview of carbon nanotube, functionalization of carbon nanotube and its applications in targeted drug delivery system.

Keywords: Biocompatibility, covalent modification, MWCNTS, solubility

Introduction

In the field of nanotechnology, carbon nanotube (CNTs) represents one of the most unique inventions. CNTs have been studied closely over the last two decades by many researchers around the world due to their

potential application in different fields. CNTs shows extraordinary strength as well as unique mechanical, electrical and thermal properties. CNTs was first discovered by Japanese electron microscopist Sumio Iijima in 1991. [(1)]

Carbon exists in 3 allotropic forms such as diamond, graphene, and fullerenes (C_{60}). Carbon nanotubes also known as buckytubes which belongs to the fullerene family of carbon allotropes with a cylindrical nanostructure. The length of the CNTs is in the size of micrometers with diameters up to 100 nm. CNTs consist of hexagonally arranged sp^2 hybridized carbon atoms with C-C distance is about 1.4 Å.

There are two types of CNTs on the basis of the number of graphene sheet:

A. Single walled carbon nanotubes (SWCNT)

SWCNTs are formed by rolling up of single sheet of graphene with a diameter of 1–2 nm. The length can vary depending upon the methods of preparations.

B. Multiwalled carbon nanotubes (MWCNTs)

MWCNTs are formed by rolling up of more than one graphene sheets or made by SWCNTs with additional graphene tubes around the core of SWCNTs.

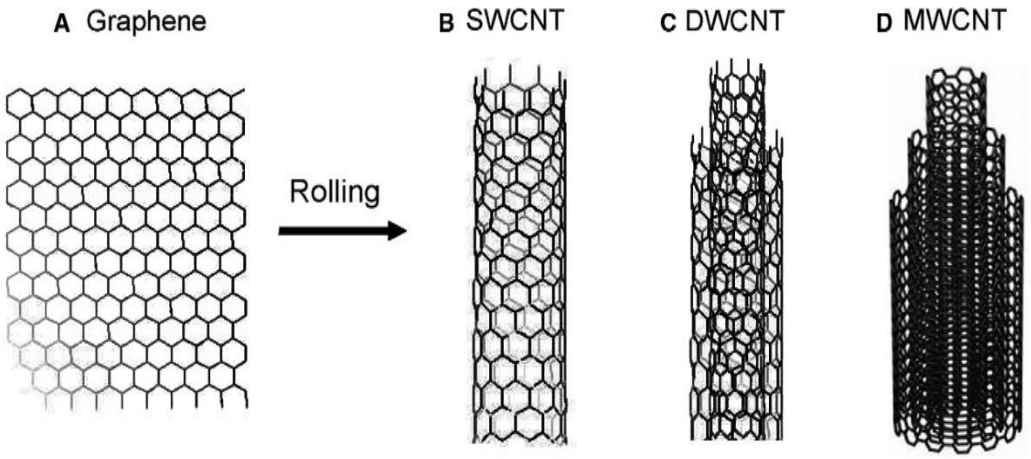

Figure 1: illustration of graphene (A), single (B), double (c) and multi walled carbon nanotubes (D).

The both ends of the CNTs are capped by a hemispherical arrangement of carbon networks called fullerenes warped up by the graphene sheet. The interlayer separation of the graphene layers of MWCNTs measures approximately 0.34 nm on average, and thereby each layers forming an individual tube, with all the tubes having a larger outer diameter (2.5 to 100 nm) than SWCNTs (0.6 to 2.4 nm). SWCNTs have a well-defined wall, whereas MWCNTs are more likely to have structural defects, resulting in a less stable nanostructure.

There are two models which can be used to describe the structures of multi-walled carbon nanotubes:

(1) In the Russian Doll model, many graphene layers are rolled up and arranged in concentric cylindrical fashion that means a single-walled nanotube within a larger single-walled nanotube.

(2) In the Parchment model, a single graphene layer is rolled in around itself, resembling a scroll of parchment or a rolled newspaper. The interlayer distance in MWCNTs is close to the distance between graphene layers in graphite, approximately 3.4 Å (330 pm). [2, 3, 4]

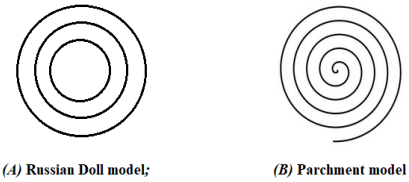

Figure 2: illustration of two different models of MWCNTs.

(A) Russian Doll model; (B) Parchment model.

Double-walled carbon nanotubes (DWCNTs) are a special case of MWCNTs, consist of just two concentric cylinders. DWNTs resemble SWNTs with respect to their length, small diameter and ability to form bundles, but their mechanical stability is much greater than that of the SWNTs, chiefly when covalently functionalized. In addition, the outer wall of DWNTs can be functionalized without affecting the mechanical and electrochemical properties of the innertube, just like MWNTs. [5]

Functionalization

Raw carbon nanotubes are not soluble in aqueous solutions due to the presence of highly hydrophobic surfaces whereas pristine CNTs are insoluble in all organic solvents and aqueous solutions. Pristine CNTs can be dispersed in some solvents by sonication, but precipitation immediately occurs when this process is interrupted. Functionalization of CNTs is the solution to this problem. Functionalization of CNTs is a process of chemical synthesis where desired functional groups can be introduced onto the walls of CNTs producing functionalized carbon nanotubes (f-CNT).

The formation of supramolecular complexes permits a better processing of CNT toward the fabrication of innovative nanodevices. Additionally, CNT can undergo chemical reactions that make them more soluble for their integration into inorganic, organic, and biological systems. The functionalized-CNTs have greater entrapment efficiency due to the availability of high surface area. Functionalized carbon nanotubes have remarkable advantages over cancer treatment, by enhancing the biocompatibility within the body, improving

the encapsulation tendency and the solubility. Functionalization of CNTs can be divided into two categories; covalent and noncovalent approaches. [6, 7]

Non-covalent functionalization

In the non-covalent method (Physical modification), interaction is attained without disturbing the system of graphene sheets. The major advantage of non-covalent functionalization is that it does not destroy the conjugated system of the CNTs sidewalls, and as a result it does not affect the final structural properties of the material. This kind of modification is an alternative method for tuning the interfacial properties of CNTs. The CNTs are non-covalently modified by aromatic compounds, surfactants, and polymers, employing π-π stacking or hydrophobic interactions for the most part. By these approaches, the CNTs can do much to preserve their desired properties, while improving their solubilities quite remarkably. It will conclude as followed: aromatic small molecule absorption, polymer wrapping, biopolymers, surfactants and endohedral method. [7,8]

M. Eguilaz et al (2016), reported the non-covalent functionalization (dispersion) of MWCNTs with cytochrome c (Cyt c), the direct electron transfer (DET) after drop-coating deposition of MWCNTs-Cyt c dispersion on glassy carbon electrodes (GCE), and the analytical applications for the highly sensitive quantification of hydrogen peroxide. The drastic treatment for dispersing the MWCNTs (5.0 min sonication in water with ultrasonic tip) produces a partial denaturation that enables the interaction of Cyt c with the MWCNTs and makes possible an efficient electron transfer between the electrode and heme group. The Cytochrome c that supports MWCNTs retained its electrocatalytic activity towards hydrogen peroxide. GCE/MWCNT-Cyt c demonstrated to be a highly sensitive sensor for H_2O_2 quantification and also used for the quantification of H_2O_2 in real samples. [9]

Tunckol et al (2013), demonstrated non covalent functionalization of MWCNTs with various imidazolium-based polymerized ionic liquids (PILs). The method is based on the free-radical polymerization of the imidazolium-based IL monomers containing a vinyl group to obtain a PIL coating on the MWCNT surface. The resulting hybrid materials, synthesised both by in situ polymerization and solution mixing methods. The in situ method permits a homogeneous coating of the MWCNT surface and as a result a better dispersion of the nanotubes. The solution mixing method, for which diffusion limitations of the PILs into nanotubes aggregates should exist, does not permit a uniform surface functionalization. Finally, with protic IL

monomers displaying a tendency for hydrogen bonding and a stable CNT/PIL organo- or hydrogel composites were produced. (10)

Covalent functionalization.

In covalent functionalization, interaction is attained by disturbing the graphene system. The CNTs can be oxidized with strong acids such as concentrated sulfuric acid (H_2SO_4) or nitric acid (HNO_3) and this oxidation reaction generates -COOH, - OH on the CNT surface, which facilitates the esterification, amidation, bromination and Diels Alder reaction essential for functionalization. The covalent functionalization done on the surface tends to increases the dispersibility of CNTs without disturbing its mechanical and electric properties. (11)

X. Zhao et al (2018) carried out the synthesis of PEGylated multi-walled carbon nanotubes (PEG-MWCNTs) through PEGylation of carboxylated multi-walled carbon nanotubes (CMWCNTs) with PEG-NH_2 via amidation reaction with controllable length and PEGylation degree. By adjusting oxidation time, the length and surface carboxyl groups of the carboxylated multi-walled carbon nanotubes (CMWCNTs) were easily tailored. The longer CMWCNTs or those with high carboxyl group content showed noticeable cytotoxicity, while the PEG-MWCNTs ≤ 300 nm showed enhanced cytocompatibility. The PEG-MWCNTs-3 of about 300 nm was selected as drug delivery vector, holding a high drug-loading capacity of 0.55 mg/mg. The cumulative DOX release rate reached 57% within 24 h, whereas the premature leakage under the simulated physiological condition was only 10%. The WST-1 assays demonstrated the DOX-loaded PEG-MWCNTs-3 showed the enhanced inhibitory efficiency against HepG2 cells, in comparison with free DOX. (12)

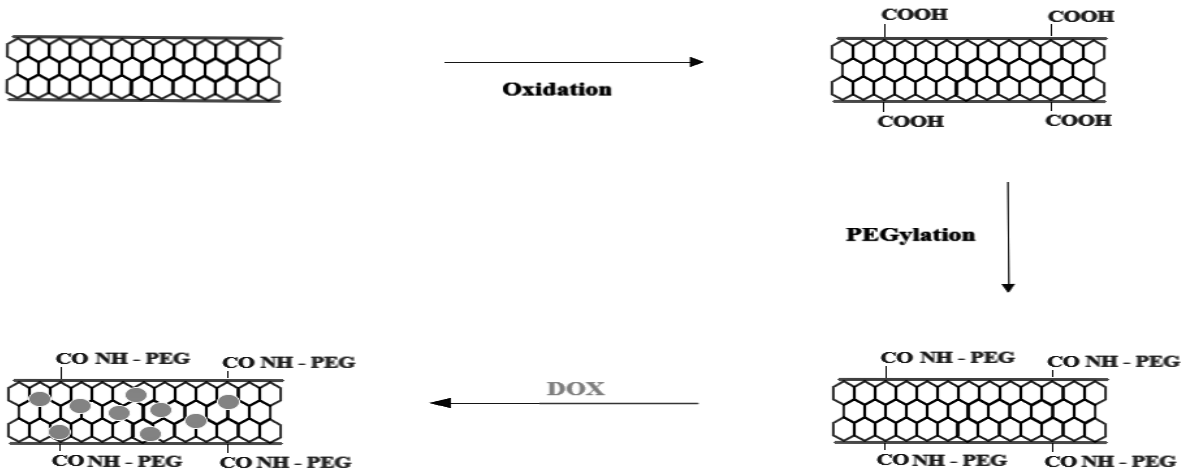

Figure 3: schematic illustration of functionalization and loading of DOX in MWCNTs.

Jafari et al (2016) investigated folic acid, polyethylene glycol and Fe_3O_4 nanoparticles multifunctionalized short multiwalled carbon nanotubes (PEG-FA-conjugated SMWCNT@Fe_3O_4) which could be used as multi-targeted drug nano-carrier for delivering an anticancer agent to cancer cells with the assistance of an external magnetic field. [13]

Mehra et al (2014) compared the in vitro and in vivo cancer targeting property of doxorubicin (DOX) loaded folic acid (FA), and estrone (ES) anchored PEGylated MWCNTs employing tumor bearing Balb/c mice. The in vitro, ex vivo and in-vivo studies were performed on MCF-7 cell line for assessing the anticancer activity. The ligand anchored surface engineered MWCNTs shows high loading efficiency, anticancer activity and improved biocompatibility profile along with increased pharmacokinetic parameter as compared to free DOX solution. The results of cancer targeting efficacy of various MWCNTs formulations utilizing MCF-7 cells ranked in the following order: DOX/ES-PEG-MWCNTs > DOX/FA-PEG-MWCNTs > DOX/PEG-MWCNTs > DOX/ox-MWCNTs > DOX/MWCNTs > free DOX > control. Thus estrone anchored MWCNTs shows superior targetability as compared to FA-anchored, oxidised (*ox*), plain MWCNTs and free DOX solution. [14]

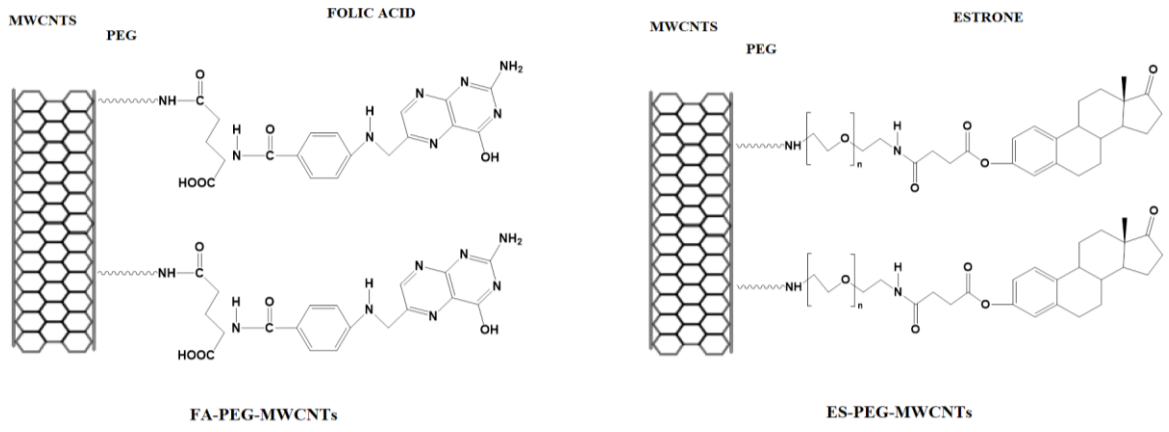

Figure 4: Conjugation scheme of FA-, and ES-PEG conjugated MWCNTs.

Sobhani et al (2011) studied on multiwalled carbon nanotubes functionalized with hyper branched polycitric acid (MWNT-g-PCA) and conjugated to the paclitaxel (PTX, a potent chemotherapeutic agent) to produce MWNT-g-PCA-PTX conjugate. PCA facilitates high drug loading capacity because of large number of carboxylic functional groups and it also provides decreased hydrophobicity of MWCNTs due to the hydrophilic behaviour of PCA. The rate of release in degradation was decreased due to steric hindrance of PCA. PTX can be released from the conjugate more rapid at pH 6.8 and pH 5.0 than at pH 7.4 which was

suitable for the release of drug in tumour tissues. Invitro cytotoxicity studies of MWNT-g-PCA-PTX conjugate in the A549 and SKOV3 cell lines shows increased cytotoxicity of drug than a free drug over a shorter incubation time. This conjugation helps the PTX to reach the tumour site via enhanced permeability and retention effect. [15]

Mallakpour et al (2014) reported an efficient electrophilic addition reaction for the covalent modification of MWCNTs which is easy to scale up without any kind of pollutions and at a low cost. MWCNTs were functionalised by a natural polymer S-valine amino acid by the rapid microwave assisted process. This process remarkably increased the reaction rates compared to conventional heating. The surface modified nanotubes resulted in significant debundling of the MWCNTs which offer better chemical stability in common organic solvent such as N-N-dimethyl acetamide (DMAc).The functionalization of multiwalled carbon nanotubes is a simple and green approach, which means less toxic and environmentally friendly alternative. The attached amino acid group are likely to improve the interaction between the modified MWCNTs and polymer chain and the terminal hydrophilic carboxyl group can be available for covalent binding with the variety of monomer and polymer matrices. With the aid of amino acid base poly (amide-imides)s (PAI) a stable MWCNTs-val dispersion were effectively prepared and lead to enhancement of both mechanical and thermal properties at low CNTs content (5%).[16]

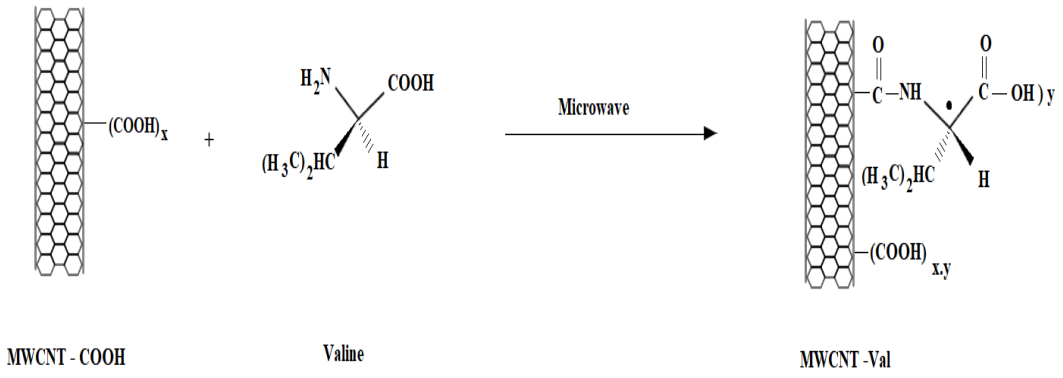

Figure 5: Schematic illustration of functionalization of MWCNTs with S-valine amino.

Domagala et al (2019) set a novel two-step process for the functionalization of MWCNTs. First the purification process has been done by non-oxidative treatment with dilute HCl in order to remove catalyst impurities which remain after the synthesis process. As a result, 90 wt% of the catalyst (Fe/Ni) was successfully removed. Secondly the surface of MWCNTs functionalized with COOH group by using an oxidation process with hot concentrated HNO_3. Functionalization thus facilitated the enhanced

hydrophilicity and other better chemical reactivity. The functionalized MWCNTs showed a lower degree of agglomeration and shorter tubes. Finally concluded that strong oxidation conditions of MWCNTs tube results in breaking and shortening. [17]

Zhao et al (2013) carried out a simple multi functionalization method. Introducing carboxyl and amino group on to the surface of MWCNTs. The multi functionalization of MWCNTs achieved by the treatment with mixed acid and the diazonium reaction. The MWCNTs – $COOH/NH_2$ could be a new versatility platform for further functionalization in material science and biological applications. [18]

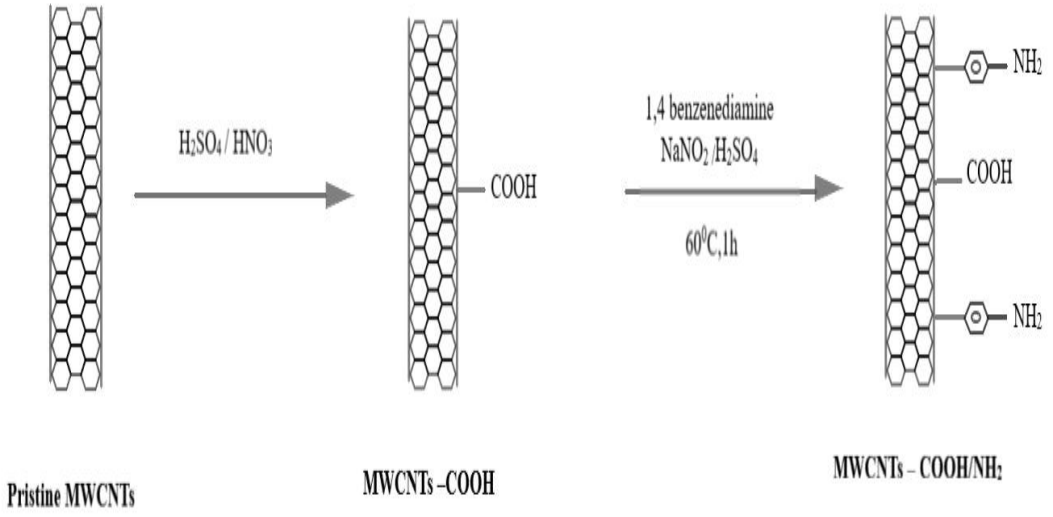

Figure 6: schematic illustration of multi-functionalization of MWCNTs.

Ngoy et al (2011) carried out the coupling of the MWCNTs with folic acid; and essential biocompatible water soluble B-complex vitamin which can be used as a biocompatible molecule in the improvement cancer treatment. The covalent functionalization of MWCNTs with phenol and carboxyl group by the reaction of MWCNTs with sulphuric acid and nitric acid (3:1) at room temperature (RT), 50 ^{0}C, and 100 ^{0}C. In addition, aspartic acid at 230 ^{0}C was used to generate the carboxyl f-MWCNTs group. The increase in temperature from RT to 100 ^{0}C causes decreased mol ratio (COOH/OH) of the f-CNTs from 80 to 20 nm which was characterised with the aid of transmission electron microscopy. The solubility of f- CNT covered with the OH and COOH are more water soluble as compared to f-CNT covered COOH. The f-CNTs carboxyl were attached to 3-(N, N-dimethylamino) propylamine (DMP) and folic acid (FA) through 2-(1H-benzotrial -1-yl)- 1,1,3,3 tetramethylurium hexaflurophosphate (HBTO) to produce f-CNTs-FA. Thus f-MWCNT-FA moiety have a greater versatility and can be used for cancer treatment and restoration of noeplasma cell. [19]

Datsyuk et al (2008), investigated the effect of oxidation on the structural integrity of MWCNTs through acidic (nitric acid and a mixture of sulfuric acid and hydrogen peroxide) and basic (ammonium hydroxide/hydrogen peroxide) agents. For the purification of the received material (MWCNTs synthesized by CCVD) a non-oxidative treatment (with hydrochloric acid) was also applied. Results of electron microscopy and thermogravimetric analysis clearly revealed that the nitric acid treated material under reflux conditions suffered the highest degree of degradation, such as nanotube shortening and additional defect generation in the graphitic network. Basic oxidative treatment directed to the complete removal of amorphous carbon and metal oxide impurities but the structural integrity was found to be intact. [(20)]

Ahmed et al (2013), investigated the functionalization of MWCNTs with two different agents such as concentrated nitric acid and olive oil via ultra-sonication technique. The investigation aimed to functionalize the MWCNTs with less structure disruption and to obtain stable MWCNTs colloidal suspension. Result of scanning electron microscopy shows CNTs treated with strong oxidizing agents (nitric acid 65%) causes severe engraving of the graphitic surface of CNTs leading to tubes of shorter length. No structural damages occurred for the treatment of MWCNTs with olive oil. Finally a well dispersed and stable MWCNTs colloidal system was successfully obtained with less structure collision due to the generation of the (OH, C=O, and COOH) groups on the surface of the CNTs. [(21)]

Cao et al (2015) developed a green approach for the functionalization of multifunctional MWCNTs which is covalently modified with polyethyleneimine (PEI) followed by sequential modification with fluorescein isothiocynate (FI, an imaging dye) and hyalouronic acid (HA, a targeting ligand). Even after further modification of the PEI amines with acetyl group or polyethylene glycol moieties, the water dispersibility and biocompatibility of PEI- modified MWCNTs can be improved significantly. HA-modified MWCNTs/PEI-FI-HA/DOX complex can afford the target delivery of DOX into cancer cell overexpressing CD44 receptors. This new carrier system provides pH responsive DOX release with a faster release rate under an acidic pH condition. [(22)]

Liu et al (2010) proposed the use of ozone which is an effective agent for modification of polymers and thereby formation of hydroperoxide and peroxide groups, chain scissions, and intramolecular rearrangements. These groups thermally decompose into oxygen radicals, which can initiate the radical polymerizations for the preparation of graft copolymers. Nonreactive polymers such as poly (vinylidene

fluoride) (PVDF, vinyl polymer), polysulfone (PSF, engineering plastic), poly (2,6- dimethylphenylene oxide) (PPO, engineering plastic), and poly(phthalazinone ether ketone) (PPEK, heterocyclic polymer), are used for the functionalization of MWCNTs and preparation of corresponding MWCNT–polymer hybrids. The MWCNT–polymer hybrids are then used for the preparation of PVDF/MWCNT composites. Compared to unmodified MWCNTs and PSF-modified MWCNTs, PVDF-modified MWCNTs are more efficient additives to improve the mechanical strength and electrical conductivity of PVDF. Hence, matrix–polymer-modified MWCNTs are relatively attractive in the preparation of high performance polymer/MWCNT composites. [(23)]

Shen et al (2007), carried out the preparation of four different amino functionalized carbon nanotubes by carboxylation, acylation and amidation. The four different MWCNTs such as e-MWNT, h-MWNT, p-MWNT, c-MWNT were preaperd with four different amino groups [(Ethylenediamine), (1, 6-Hexanediamine),(4,4' –Diaminodiphenylmethane), (4,4' -Diamino-dicyclohexylmethane)]. The amino-functionalized carbon nanotubes offer a pathway to a wide spectrum of nanotube derivatives suitable for various applications, and can be promising in applications such as polymer/carbon nanotube composites and coating. Different amino groups on surface of the MWCNTs have a greater effect on their dispersibility in different solvent and thereby it open up new perspective of functionalization by selecting different amines to functionalize MWCNTs. [(24)]

Rathod et al (2019), Carried out dual functionalization of MWCNTs with ethylenediamine (EDA, cationic units) and phenyl boronic acid (PBA, lectin mimetic) followed by encapsulation of paclitaxel (PTX). A ligand-target interaction is mediated through charge based interaction and formation of diol-phenyl boronate complex. Hence the functionalization improves the aqueous dispersibility and biocompatibility which was confirmed by FT-IR and Raman spectra. [(25)]

Murugan et al (2011), carried out the preparation two MWCNTs-dendrimer based hybrids. First, covalent functionalization of MWCNTs with amphilic poly(propyleneimine) dendrimer (APPI) to form MWCNTs-APPI complex. Secondly, silver nanoparticles deposited over the chemically modified MWCNTs (MWCNTS-APPI-AgNPs). By thermal gravimetry analysis the amount of APPI functionalised on MWCNTs was found to be 67% which facilitates an effective dispersibility in aqueous and organic solvents without sonication and these solution were stable for 6 months without enduring aggregation of MWCNTs.

Raman studies shows that the electronic properties of the hybrid material does not disrupted because of functionalization. The order of in-vitro antimicrobial properties of 2 MWCNTs dendrimer based hybrids and MWCNTs-COOH against Bacillus subtilis, Staphylococcus aureus, and Escheriachia coli in terms of percentage of kill were MWCNTs-APPI-AgNPs > MWCNTs-APPI > MWCNTs-COOH. Hence MWCNTs-APPI-AgNPs shows greater antimicrobial effect due to the cooperative effects of AgNPs deposition on to MWCNTs-APPI. [(26)]

Chowdhry et al (2019), established the defect functionalization methodology, in which the walls of MWCNTs were covalently bonded with carboxy and amino group. When compared to pristine MWCNTs, the functionalization facilitate MWCNTs solubilisation also significantly enhanced the cytotoxicity and the prooxidant potential in HEK 293 cell while zebra fish, as a model system remained refractory to MWCNTs toxicity. Hence the results showed MWCNTs –COOH fared better than MWCNT-NH_2 in reducing MWCNTs toxicity to the cell. [(27)]

Azari et al (2019) investigated the individual and combined toxicity of carboxylic acid functionalized MWCNTs (F-MWCNTs) and benzo a pyrene (BaP) in human lung adenocarcinoma A549 cell. The modified MWCNTs and BaP reduces cell viability individually and produce ROS, apoptosis and 8-OHdG in exposed cells. [(28)]

Santos et al (2003) carried out the in situ polymerization for the incorporation of chemically modified MWCNTs into the polymer matrix in order to improve the transfer of mechanical load through a chemical bond. In comparison with unfunctionalised MWCNTs (u-MWCNTs), the functionalised MWCNTs (f-MWCNTs) composite shows excellent mechanical and thermal properties. These composite shows higher storage modulus (E′) and tensile strength than existing similar composites, with only 1 % weight of functionalized nanotubes. The storage modulus at 90 °C is increased by an outstanding 1135% and the glass transition temperature is exceptionally raised by =40°C. Therefore, truly a synergetic composite materials with CNTs could be able to produce through chemical functionalization in combination with in situ polymerization. [(29)]

Cui et al (2013) carried out the functionalization of MWCNTs by grafting carboxyl group and amino groups on to the MWCNTs to produce COOH-MWCNTs and amino-MWCNTs. Epoxy based composites filled with those MWCNTs were prepared. The introduction of MWCNTs decreases the activation energy of the

reaction and promoted the cure reaction. The addition of MWCNTs especially the amino- functionalized MWCNTs enhanced the tensile strength. For different MWCNT/epoxy composites, the tensile strengths of composites attained maximum values at MWCNT loadings of 0.2 wt %, 0.6 wt % and 1.0 wt % and increased by 24.27%, 35.33% and 57.61% for pristine MWCNTs, COOH–MWCNTs and amino MWCNTs compared with the neat epoxy, respectively. The functionalized MWCNTs enhanced the interfacial bonding and made the dispersion of MWCNTs homogeneous in the matrix, making composite present better mechanical properties. (30)

Wu H.X et al (2007) carried out the 'grafting to' method in which linear polystyrene (PS) was grafted onto the convex surfaces of MWCNTs. Bromine-terminated polystyrene (Br-PS-Br or PS-Br) synthesized by atom transfer radical polymerization (ATRP) was directly reacted with MWCNTs under ATRP conditions using CuBr/2,20 -bipyridine as catalyst. Polystyrene was chemically bonded with MWCNTs, and the grafting amount of three products was 40%, 50% and 55%, respectively. The PS-grafted MWCNTs can dissolve in organic solvents such as 1,2-dichlorobenzene, tetrahydrofuran and chloroform to form well-dispersed solutions. The optical limiting property measurement of these PS-grafted MWCNTs samples was carried out at 532 nm using the open-aperture z-scan technique and the samples preserved optical limiting properties. (31)

Wang et al (2006), introduced an acid –thionyl chloride route in which MWCNTs were functionalized with amino group by grafting tri-ethylene tetraamine (TETA) on the surface of MWCNTs. An enhanced compatibility was showed by the amino-functionalized MWCNTs with epoxy resin. Thus more homogeneous dispersion in the matrix will accomplished. The f-MWCNTs/epoxy composite could increase the charpy impact strength, glass transmission temperature (Tg) and initial decomposing temperature of cured epoxy resin. (32)

Chinh et al (2019), established a new method of preparation of gold nanoparticles (AuNPs) decorated MWCNTs by using cysteaminium chloride via the formation of a Zwitterionic acide-base bond. The synthesis is done by avoiding the use of dangerous and toxic chemical agents such as thionylchloride ($SOCl_2$) or carbodiimide hydrochloride (EDAC). The grafting process consists of 3 mains steps such as oxidation, thiolation and decoration of AuNPs on the surface of MWCNTs. The acidic treatment benefited by removing the impurities resulted from the residual metallic catalysts during production process of

MWCNTs and also to cut down the MWCNTs into shorter open-ended pipes with the presence of large amounts of carboxylic and oxygen-containing groups at the open-end. Preparation of new thiol-functionalized MWCNTs by using covalent ionic bonds approach in which the strong electrostatic attractions between negatively charged oxi-MWCNTs and positively charged cysteamine were reacted to form stable covalent chemical bonds. Further decoration of functionalized MWCNTs with gold nanoparticles was attained by a simple reaction of thiol groups in the cysteamine with Au cation. Gold nanoparticles (AuNPs) decorated MWCNTs opens new platform for photocatalytics and biosensors (DNA, proteins, glucose). [33]

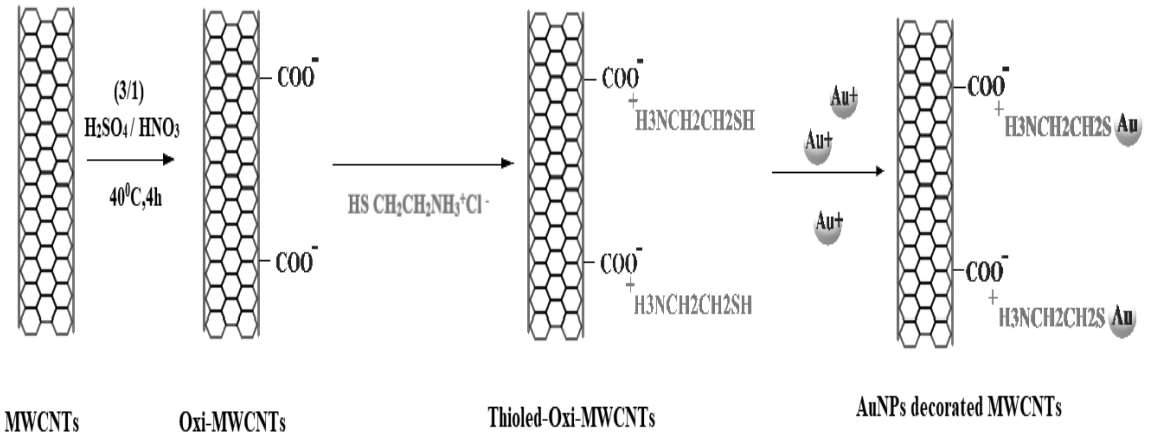

Figure 7: Schematic illustration for the preparation of Au-MWCNTs.

Wulandari et al (2018) conducted the synthesis of carboxyl functionalized MWCNTs (MWCNTs-COOH; to improve the compatibility of CNTs) and amino group functionalized MWCNTs (MWCNTs-NH_2; to improve conductive properties). By functionalization, it can also automatically reduce Fe (an impurity derived from ferrocene source) during its fabrication. [34]

Shanmughara et al (2007), carried out the functionalization of MWCNT with 3-aminopropyltriethoxysilane and investigated its influence on the properties of natural rubber (NR) composites. Chemical modification with silane results in higher polymer-filler interaction because of the formation of excess chemical crosslinks between the silane and NR which thereby restricts the polymer slippage with increasing deformation. Thus NR/silane functionalized MWCNTs modification facilitated higher modulus, tensile strength and elongation at break compared to NR vulcanizates. Rheometric properties like scorch time and optimum cure time increases significantly due to absorption of basic accelerator by acid groups and quinone type oxygen atoms. [35]

Sun et al (2018), carried out the prefunctionalization of MWCNTs by acid oxidation, followed by functionalization with water-soluble silk fibroin (SF). These fillers have the features of low toxicity and eco-friendly in nature. The SF-functionalized MWCNTs exhibited excellent dispersibility in water and methanoic acid. The methyl thiazolyl tetrazolium (MTT) assay revealed that SF-Ms (silk fibroin-functionalized MWCNTs) showed good proliferation. Therefore, SF functionalization of MWCNTs dramatically improved the biocompatibility. [(36)]

Francisco et al (2015) conducted a study on the effect of carboxyl and amino functionalization of MWCNTs on the mechanical property of the epoxy resin filled with modified CNTs. The CNTs were treated with sulfuric and nitric acids and dispersed in hexamethylenediamine. The composites were obtained with the aid of epoxy resin and functionalised MWCNTs. The results of Vickers hardness tests for the composites and neat resin, showed an increase of hardness in the composite synthesized with functionalized carbon nanotubes. This is because of the reason that the chemical interaction between modified CNTs and epoxy resin is much stronger than between pristine CNTs and epoxy resin. [(37)]

Haider et al (2018), carried out the functionalization of MWCNTs with carboxyl groups were produced through treating MWCNTs with Walnut oil using sonication method. The antimicrobial activity of functionalized MWCNTs with oil, thus improved significantly and there were no growth of Escherichia coli, and Staphylococcus aureus at high consecrations. [(38)]

Jurzinsky et al (2019), focused on the covalent functionalization of MWCNTs with indazole groups. Thermogravimetric analysis coupled with a mass spectrometer (TGA-MS) evaluation studies inferred that the indazole-functionalized MWCNTs are thermally stable until a temperature of approximately 300 ^{0}C is reached. The thermal degradation of the functional group was evaluated by monitoring the expulsion of NOX gases. Under gas-phase conditions the electrochemical stability of the novel material was evaluated using high-temperature differential electrochemical mass spectrometry (HT-DEMS). Thus the functionalization leads to slightly increased electrochemical carbon corrosion as compared to unmodified MWCNTs. The functionality tests of the indazole-functionalized CNTs showed a better dispersibility in water and a lower contact angle with concentrated H_3PO_4 (an electrolyte in high-temperature proton-exchange membrane fuel cells) in comparison to unmodified MWCNTs. [(39)]

Conclusion

Chemically modifiable surfaces with a large surface area and tunable length, along with unique physical properties, make CNTs welcome candidates in modern medicine. Tailored modification of CNTs is assumed to open way roads toward real nanotechnology applications. Thus the functionalization enables the enhancement of aqueous solubility, biocompatibility, physical properties (electrical, mechanical and thermal conductivity), target ability and also decreases hydrophobicity of MWCNTs.

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