IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ON CARBON NANOTUBES APPLICATIONS IN DRUG DELIVERY SYSTEMS

T. SRI LAKSHMI, T. RAMA RAO, G. BHAVANI, G. YASHASWINI

CMR COLLEGE OF PHARMACY, Kandlakoya(V), Medchal-501401

ABSTRACT

Nanotechnology in recent years is most commonly used technology in the field of medicine. Carbon nanotubes are one of the specialisations of the nanotechnology. Carbon nanotubes are now used in various applications which includes cancer treatment, gene therapy, vaccine preparation drug delivery, genetic engineering, tissue engineering and numerous diseases. The concept of carbon nanotubes was introduced in 21st century in the field of pharmacy. The discovery of carbon nanotubes is the most adequate in the drug delivery system and it is the alternative way in transporting the drugs to the target site. Because of the low toxicity and nonimmunogenic, carbon nanotubes have the greater capacity in the nano field and nanomedicine. Carbon nanotubes are small sized particles and they exhibit amazing properties like optical, electric, and magnetic. They are used alone or in combination with the metals. carbon nano tubes are often described as graphene sheets rolled up into the cylindrical shape. It is expected that there are many applications of carbon nanotubes are going to be explored for future medical use.

Key words: nanotechnology, carbon nanotube, drug delivery, non-immunogenic genetic engineering

INTRODUCTION

Nanotechnology is widely using technology for future drug delivery. Through nanotechnology, scientists are gaining the knowledge and ability to understand and manipulate materials on a global scale of atoms and molecules, with the following key properties[1].

Nanostructures are the molecules with at least one dimension of about 1–100 nm. They are designed using methods that demonstrate fundamental control over physical and chemical properties. Considered structures can be produced by the combination of the nanostructures. "There's a lot of room downstairs" was the title of a 1959 lecture by Richard Feynman, who introduced the concept nanotechnology is an important area for future scientific research[1]

Since their discovery in 1991, carbon nanotubes have generated a great deal of interest for their potential use in variety of industries, including drug delivery and cancer treatment Sumio Ijima's theory of carbon nanotubes,

which are composed of carbon allotrope graphing, explain how they possess brilliant electrical mechanical, optical and synthetic properties.[2]

Carbon nanotubes are used by many researchers as one of the most used nano materials in the field of science. Carbon nanotubes are built as hollow cylindrical tubes which are composed of carbon (graphite) with the ratio ~1000 and sp2 hybridisation. These carbon nanotubes are classified into two types are single walled nanotubes (SWNTs), double walled nanotubes (DWNTs) based on the number of graphite layers. CNTs possess remarkable properties at the atomic level, rendering them exceptionally suited for diverse applications spanning electronics, photonics, renewable energy drug delivery, and biomedicine. Chemical modification aimed at enhancing their dispersion are also a key focus.

Carbon nanotubes has generated a significant interest within the biomedical field. This is due to favourable characteristics such as a high surface area, needle- like structures, substantial strength, adaptable interaction with cargo, substantial drug loading capacity exceptional optical and electrical properties, strong stability, biocompatibility, and the capability to release therapeutic agents at precise locations However, CNTs also possess negative attributes, most notably their lack of biodegradability and toxicity. Despite these drawbacks, CNTs continue to demonstrate remarkable performances in various medical applications, including drug delivery systems, gene therapy, gene delivery bioimaging, diagnostic applications, biosensors, vaccine delivery.[4]

While performing the experiments on the graphite electrodes used in electric arc discharge unfortunately the carbon nanotubes are discovered by the Iijima. This accidental discovery of the carbon nanotubes made a base for the researchers to develop a nanomaterial for the carbon research[5].

STRUCTURE AND MORPHOLOGY

Carbon nanotubes are the hexagonal arrangement of carbon atoms coiled up into the elongated hollow shaped cylinder. It is known for its shape, size, and physical properties. They can be used physically, chemically, for their purpose in material science, electronics, energy management, biomedical applications and others. Carbon nanotubes are made up of carbon materials. Their diameter ranges in a nano meter scale. The end of the carbon nanotubes are curved ends with pentagons.[5]

When the carbon nanotubes are placed under high pressure, they combine together for converting the sp2 bonds to sp3 bonds, to strengthen the wire under high-pressure carbon nanotube connection.[6]

The sp2 bonds present in the carbon nanotubes are much stronger than the sp3 bond present in the diamond. The length-diameter ratio of carbon nanotube present in the ratio of 132,000:1 than any other nano material. Due to their high loading and cell penetration ability allow the CNT to deliver to the target cancer cell and decreasing the cell toxicity.[7]

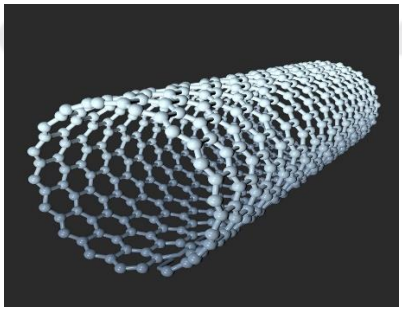

Fig-1: Structure of CNT[27]

CLASSIFICATION

There are 2 types of carbon nanotubes

Based on presence of layers

1.Single walled carbon nanotubes

It contains component of a single layer of graphene. It requires a catalyst for synthesis. Bulk synthesis is difficult due to control over growth and environment conditions. Typically lower purity, It was more susceptible to defects during functionalisation . It has low accumulation in the body . Easily twisted and more flexible. It was relatively easy to characterize and evaluate[21].

2.Multi walled carbon nanotubes

It was composed of multiple layers of graphene. It can be produced without a catalyst. The bulk synthesis is easier as it doesn't require strict control over growth conditions. It has higher purity. It is less prone to defects, but difficult to improve if defects occur. It has greater accumulation in the body. It has a complex structure. It is less flexible and not easily twisted. [21]

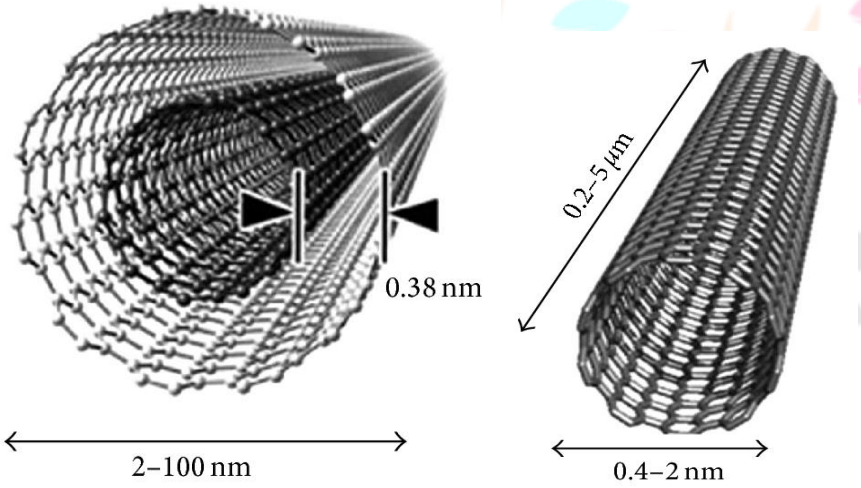

Fig-2 : MULTIWALLED CARBON NANOTUBE[25] SINGLEWALLED CARBON NANOTUBE[25]

PROPERTIES:

Carbon nanotubes possess many excellent properties that inspired many researchers to develop new researches in drug delivery. They possess Mechanical, electrical, thermal, chemical, biological properties. Other than these properties size of the nanotubes also consists numerous advantages.[10]

1.Mechanical properties. Carbon nanotubes consists greater stiffness with axial strength that gives carbon-carbon sp2 bonding. These are the rigid fibres measuring the young's modulus of 1.4 TP a. The capacity to elongate fails in 20-30% by the combination with rigids produces a tensile strength greater than 100 GP a. Due to the greater flexibility of carbon nanotubes they possess long length.[10]

Elastic modulus of the carbon nanotubes is of 1Tpa.

For MWCNTs the young's modulus is 1.7-2.4 TP a, where the SWCNTs is 2.8-3.6.

When the carbon nanotubes are performed under the TEM these are strong and do not break upon ending[9].

2.Electrical properties. The carbon nanotubes have the definite electrical properties that are obtained from the dimensional characteristics and the complex structure of graphite. Electrical resistance is low, by the inclusion

they have the greater current density, as high as 1 10^9 A Cm^{-2}. They show good conductance at low temperatures. These distinctive properties are used for the fabricating field emission display (FEDs). The fourth electron in the valence electrons are alone and these are delocalised in all the atoms and give the electrical nature of CNT.[10]

Carbon nanotubes are either semiconducting or metallic based on their on their chiral vector[9]. The variation is caused due to the molecular structures, thus producing the different band and band gap. The experiments determined that (n, m=3i), here is the integer, n and m the defining the nanotube.[8]

By the presence of sp2 bonds between the carbon atoms they are conducting nature of the carbon nanotubes. Single walled nanotubes electrical conductance ranges up to 10GHz.[5]

3.Thermal properties. Different types of carbon nanotubes contain different conductivities, it was found that the thermal conductivity of MWCNT was 3000W/K at room temperature, whereas the thermal conductivity of SWCNT was 200W/K.[9]

Due to presence of low temperature and thermal conductivity, they show one dimensional quantization of the phonon band structure in CNT.

Carbon nanotubes exhibits double the thermal conductivity than that of diamond. CNTs are good thermal conductors. They can overcome the high temperature; stability is found to be 28000_0 C and 750_0 C in air. Observations shown that the transmittance was 15 times quantity of watt per minute than copper wires[5].

4.Chemical reactivity. Carbon nanotubes are chemically stable with no defects. the surface is large to the volume ratio so that it can store the hydrogen.

In the contrast to the graphene sheet the chemical reactivity of the carbon nanotubes is increased which gives curvature of CNT surface. The reactivity is directly associated with the pi orbital mismatch obtained by increased curvature. For this reason, the comparisons should be made to the sidewall and the nanotube end caps[8].

5.Optical properties. The size of the nanotube influences the optical activity. When the size of the nanotube is larger the optical activity of the chiral nanotube disappears. Because of this the other physical properties get effected. Carbon nanotube has a major role in the optical activity.[8]

6.Size. Carbon nanotubes exhibits the greater benefits, as the size of the carbon nanotubes are very small that they attach to the AFM tips to enhance their resolving capacity. In SWCNTs the small size is make it to understand the chemical binding with the receptor or target pair. Electron emission is the of use in the size of the SWCNTs. Different types of emitters to extract electrons they are light, visible, x-ray[10].

7.Strength. Compare to the steel and Kevlar carbon nanotubes exists stronger tensile strength because of the presence of the sp2 hybrid bonds between the carbon atoms and these are elastic in nature. They are flexible that it can it can gain its original shape by the applying and removing the force. Carbon nanotubes have restriction, by the strong forces they change their shape permanently. If there are any faults in the structure carbon nanotubes become so weak in return the tensile strength gets weak[5].

Methods

Different Methods used for preparing carbon nanotubes are:

ARC discharge, Laser ablation and CVD (chemical vapour deposition)[21], Flame synthesis method, Saline solution method, Nebulized spray pyrolysis method[9]

1.Arc discharge method

The method is employed to produce large quantities of carbon nanotubes. It is commonly used for generating C60 fullerene and is the simplest approach to produce carbon nano tubes. A direct current of 50A to 100A, powered by approximately 20V, generates a high temperature discharge between the 2 electrodes[21]

2. Laser ablation method

In this method at high temperature and inert atmosphere by using the laser method graphite is vapourised and also at high temperature laser produce carbon species water cooled copper collector from metals like Ni, CO and Fe the small carbon nanotubes are obtained when these metals are given in small quantities. This method is totally relaying on temperature. Based on these parameters like growth temperature, catalyst composition, nature of gases and gas pressure the total nanotube diameter and size distribution can differentiate. These are mainly used in SWCNTs because it is expensive.[6]

3.Chemical vapour deposition

In this method large scale production of CNTs will takes place. They have two methods to synthesis CNTs

1. Thermal CVD
2. Plasma enhanced CVD

CVD serves as a primary procedure for bulk production of CNTs. The energy source used in the thermal CVD are carbon sources such as methane, carbon monoxide, acetylene in the gaseous phase. These processes involves 2 steps

In the first step the catalyst is prepared by physical vapour deposition sputtering or dip coating then the resulting substrate in the presence of carbon rich gaseous environment undergoes heating at 500-1000 degree Celsius as a result of thermal annealing cluster formation takes place on which nanotube will grow nanotube when transition metals like Fe, Ni are added to the system.

In this method, the temperature of the flame is maintained high so that it is suitable for the preparation of flow, scalable method with possible production and lower cost for the nanotube preparation. Flame synthesis process gives special characterize which are not recognized in the presence synthesis methods. These gases are rich in carbon such as CO_2, CH_4, C_2H_2, C_2H_4, C_2H_6 which are present after production of flame in given region. The exothermic reaction promotes endothermic reaction carbon deposition reactions by releasing chemical energy inform of heat in the flame-in order to deposit solid black carbon, grow[21]

4.Flame synthesis method

In this method, the temperature of the flame is maintained high so that it is suitable for the preparation of nanotube when transition metals like Fe, Ni are added to the system. There process is a continuous flow, scalable method with possible production and lower cost for the nanotube preparation. Flame synthesis process gives special characterize which are not recognized in the presence synthesis methods.

These gases are rich in carbon such as CO_2, CH_2, C_2H_2, C_2H_4, C_2H_6 which are present after production of flame in given region. The exothermic reaction promotes endothermic reaction carbon deposition reactions by releasing chemical energy inform of heat in the flame-in order to deposit solid black carbon, catalyst must also supply reaction site.[9]

5.Saline solution method

CNTs were created using the saline solution method, which involved immersing a substrate - such as carbon paper or stainless-steel mesh -in a saline solution of a metal catalyst, preferably Co: Ni in a 1:1 ratio. The substrate was then exposed to a feedstock gas containing a carbon source, such as ethylene, and the catalyst was deposited there while the substrate was heated by electrical current[9]

6.Nebulized spray pyrolysis method

The main component of this technique is a nebulized spray, which is produced by a specialized ultrasonic atomizer. Using this method, MWCNTs with aligned bundles and fairly consistent diameters have been produce ferrocene and catalyst. They have uniform diameters which are aligned in bundles as such MWCNTs are obtained. MWCNTs are produced on high growth surfaces.[9]

PURIFICATION OF CNT

Purification is accomplished after synthesis by removing undesirable components such as amorphous carbon, carbon nano particles, left over catalyst, other graphite impurities. Metal nano-particles, fullerenes, nano-crystalline graphite, an amorphous carbon that are coating the nano tube dividers contaminate the tubes while they are being manufactured. Where possible, utilize gentle purification techniques that does not hurt the carbon to get rid of contaminants[22].

Typically, CNT's have more impurities such as metal constituent part, multi shells and amorphous carbon(soot) which affects the characteristics. It has been found that the CNT;'s produced by the CVD are typically between 5 and 10% pure. Therefore prior to the usage in biochemical applications considerable purification is necessary. A nano particulate system contains several residual metals including Co, Ni, Mo, Fe as well as certain organic contaminants. Nanotubes generally contain a large amount of impurities such as metal particles, amorphous carbon and multi shell. There are different stages in purification of nanotubes.[23]

1. Oxidative treatment

A good technique to get rid of carbonaceous impurities or to clean the metal surface of the SWNTs is to oxidize them. The main drawbacks of oxidation are the oxidization of SWNTs as well as contaminants. Fortunately, SWNTs sustain less damage than contaminants do. These contaminants are more open or have more flaws than other impurities. The fact that these impurities are frequently bonded to the metal catalyst, which also serves as an oxidizing catalyst, is another reason why impurity oxidation is favoured. Overall, many variables, including metal content, oxidation period, atmosphere, oxidizing agent, and temperature, have a significant impact on the procedure's efficiency and yield. Due of its role as an oxidizing catalyst, metal. When examining the oxidizing time, content should undoubtedly be taken into account. SWNTs, for instance, will also oxidize at temperatures exceeding 600 °C, even in the absence of a catalyst60. This is true for the oxidations of thermal54, fixed air, and pure oxygen. The temperature and the duration should be under good control because these can easily oxidize all the components.[24]

2.Acid treatment

The metal catalyst will often be eliminated by the acid treatment. The metal surface must first be made visible through oxidation or sonification. The metal catalyst is then solvated after being subjected to acid. The SWNTs' suspended status continues. When HNO3 is used for the treatment, the acid only affects the metal catalyst. The SWNTs and other carbon atoms are unaffected by it. The acid has a considerable impact on SWNTs and other carbon particles when HCl is employed as a treatment. HCl is therefore regarded as the best refluxing acid.[28]

3.Magnetic Purification

This technique involves mechanically separating ferromagnetic (catalytic) particles from their graphitic outer shells. To eliminate the ferromagnetic particles, the SWNT solution is combined with inorganic nanoparticles (mostly ZrO2) in an ultrasonic bath. Permanent magnetic poles are then used to capture the particles. A highly pure SWNT material will be created after further chemical processing. This method allows for the manufacturing of laboratory-sized quantities of SWNTs devoid of magnetic contaminants without the need for expensive machinery.[24]

4.Ultrasonication

Ultrasonic waves in this method separate the particles. Different nanoparticle aggregations will be compelled to vibrate and spread more widely. The surfactant, solvent, and reagent utilized have a significant impact on how the particles are separated. The stability of the system's scattered tubes is affected by the solvent. The SWNTs are more stable in weak solvents if they are still bonded to the metal. However, mono distributed particles are relatively stable in some solvents, such as alcohols.

The purity of the SWNTs relies on the exposure period when an acid is applied. Only the metal dissolves when the tubes are subjected to acid for a brief period of time; but, after a longer exposure, the tubes also undergo chemical cutting.[28]

FUNCTIONALIZATION OF CNTs

Functionalisation is the process of introduction of functional groups onto the walls of carbon nanotubes for the various uses giving the functionalised carbon nanotubes. (f-CNT). There are various types of functionalization are present[11].

1.Covalent Functionalization

By the covalent bonding between the carbon nanotubes gives strength to them. Oxidation, carboxy based coupling comes under covalent functionalisation, they are steady in bio-environment as they produce Robust attachment, because tube cap openings are formed and functional groups which are present in the covalent bond are safe. By the addition of strong acids, reduction and production of group of carboxylic groups results in the increasing of dispersibility which cause the covalent functionalization of carbon nanotubes. Methotrexate, reactions to 1,3-cycloaddition are the examples of common covalent functionalisation of carbon nanotubes. With this approach, the combination of various functional groups takes place, specifically bonding with right groups. Carbon nanotubes gets dissolved in aqueous or organic solvents. The presence of carboxylic group on the sidewalls of carbon nanotubes decreases the van der walls forces which allows the detachment of nanotube bundles into single, separate tubes. 1,3 dipolar cycloaddition is the most used for functionalization because the depending on the reaction of amino acids, aldehydes produce azomethine yield adduct which further react on the carbon nanotubes side walls, which leads to the generation of pyrrolidine ring[2]. Reaction of HNO_3 with H_2SO_4 are one of the most used processes for functionalization[12].

2.Oxidation

When the carbon nanotubes are exposed to the acidic conditions by the oxidation process the functionalization takes place on the surface by breaking the bond network between the carbon-carbon of the nanolayers. Oxygen groups are introduced into the carbon nanotubes in the form of carboxyl, phenolic, and lactone groups. For the liquid phase reaction nanotubes are reacted with the oxidizing solutions of nitric acid or combination of nitric acid and sulfuric acid[5].

3.Esterification

Carboxylic groups are used for the functionalization that acts as a precursor to the esterification and amidation reactions. By the thionyl or oxalyl chloride as a catalyst the acyl chloride is obtained from the carboxyl group which further produces required amide, amine or alcohol. Reaction between the acyl chloride and the highly branched molecules like poly (amino diamine), the alteration of the carbon nanotubes occurs, by the reduction of formaldehyde using silver ions. Amino-modified carbon nanotubes are produced by the treatment of ethylenediamine with acyl chloride functionalized carbon nanotubes.[5]

4.Non covalent functionalization

Non covalent bonding is the most preferred drug delivery system. This type of functionalization is performed by covering the molecules with either amphiphilic surfactant molecules or polymers. Other type of functionalization is pie-pie bonding that is obtained with the attaching of pyrene molecules on the surface of the carbon nanotubes[9]. The non covalent bonding involves the distribution of carbon nanotubes that provides the conservation their aromatic structure along with their electronic features. The dispersion process includes ultrasonication, centrifugation and filtration. Surfactants, polymers, biopolymers are commonly used for the dispersion process[8]. The adsorption of the pie system on the graphene sheets takes place with no disruption on the CNT surface, pie-pie, CH-pie and other possible interactions takes place through the van der wall interactions with the hydrophobic part of the adsorbed drug preparation of aqueous and organic solutions[10].

Drug delivery

Drug delivery in a specific manner explains about the physiological and the therapeutic activity of a drug molecule. The bigger size of the inner volume of the carbon nanotube permits the encapsulation of the high and the low size molecules of the drug along with the hydrophillic and the lipophillic drugs. Multiple number of drugs can be loaded in the carbon nanotubes in the multiple drug therapy. They provide the controlled drug release system dy allowing the to release along the period of time[13].For particular drug delivery various

techniques and routes are used for administration of drugs. Nanocomposites and polymers are the vectors used in various drug delivery methods. There are few drawbacks to these medication delivery techniques. For example, since the polymers in polymer hydrogel formulations containing erythropietin are biodegradable, a surgical excision is necessary following the drug administration. In stomach rate of dissolution is very rapid when the drug is orally administered due to acid attack. Different methods are used for the drug loading so that the drug can transport to the cytoplasm and nucleus. There are various entities which are used in tube such targeting molecules, drugs, contrast agents, or reporter molecules. These are also considered as CNTs chemical properties. There are some limitations in therapeutic rate which involve low bioavalability, low water solubility, low inherent disssolution rate. There are 2 types of drug delivery which include active and passive targeting drug delivery.[12]

1.Passive targeting.

Drug targeting is well known concept the endothelium of blood vessels becomes more porous during inflammation and hypoxia, engulfing pre-existing blood vessels and growing new vessels these vessels facilitate macromolecules greater than 40KDa's selective penetration. Abnormal lymphatic drainage can lead to the retention of CNTs, but it doesn't apply to the tiny molecules with rapid circulation.[11]

2.Active targeting.

Active targeting is a targeting of the tumour cells with particular binding sites and functionalization. drugs used for the active targeting are not consumed by RES. compared to free or passively targeted drugs, it enhances the amount of drug supplied. Active targeting was discovered in 1980 through the liposomal surface of the grafted antibodies it improves the medication, penetration and affinities of cancer cells [11]

In vivo studies

In vivo studies include absorption, distribution, metabolism, excretion.

1.Absorption

The medicine must be absorbed from the administration site to the target site in order to exert its effects. It may be given orally or parentrally, such as through intravenous, subcutaneous, or abdominal injections. These travel through the circulatory systems of the blood and lymph. There are numerous processes by which CNTs are absorbed, and study into these mechanisms is ongoing. Erythropoietin is loaded into carbon nanotubes, and a surfactant is added to improve absorption. This leads to the study of the impact of fibre length, including both long and short fibre length. According to ELISA data, CNTs can absorb themselves, and short fibre CNTs deliver more erythropoietin. Transmission Physically shortened CNTs are absorbed through columnar channels when consumed when given orally, according to an electron microscope.[26]

Carbon nanotubes (CNTs) enter the lymphatic system and local tissues because of the openings in the endothelial cells of blood vessels, which are around 30nm-50nm wide. In contrast, the lymphatic vessels have larger openings, over 100nm in diameter, which facilitates quicker and easier absorption into the lymph. These CNTs are utilized for delivering anti-cancer drugs to combat metastatic cancer cells. Gemcitabine was effectively transported to lymph nodes using magnetically-guided multi-walled carbon nanotubes (MWCNTs) through the lymphatic route. When CNTs are administered through veins, they directly enter the bloodstream and are distributed throughout the body. The clearance of CNTs from the blood is primarily influenced by their surface modifications. The most widely accepted strategy for prolonging the circulation time of CNTs in the bloodstream is PEGylation, which involves coating the surface with polyethylene glycol. PEGylation reduces immunogenicity and prevents their no specific uptake by the reticuloendothelial system.[26]

2.Distribution

Distribution is the reversible movement of a substance from one part of the body to another. To ascertain the in vivo and ex vivo bio distributions of SWCNTs as well as their capacity to target cancer numerous investigations had been conducted. This covers the diameter, length, and non- covalently PEG-phospholipid functionalized functionalization. PEG chain lengths, such as PEG-5400- has 0.5h, can also be used to determine the bio

distribution and circulation of CNTs. The absorption of RES is decreased when PEG and SWCNTs are combined. Through intravenous injection, further functionalization of SWCNTs with PEG branches lengthens the blood circulation period.[26]

3.Metabolism and Excretion

The inability to biodegrade and the persistent presence in the body offer the potential for their effective utilization in clinical applications. Functionalized SWCNTs are metabolized within the animal body, with surface carboxylation facilitating their gradual degradation over a 90-day period when exposed to phagolysosome stimulants. This process leads to a reduction in length and the accumulation of extremely fine carbonaceous residue. In contrast, non-functionalized CNTs remain unchanged under similar conditions. CNT metabolism involves acid carboxylation, resulting in modifiable COOH groups on the CNT surface. Research suggests that CNTs can remain in the body for up to 5 months after administration by evading SWCNTs are catalysed by hypochlorite neutrophil enzymes. Macrophage-mediated CNT metabolism is observed to a lesser extent. Molecular modelling reveals further insights into CNT metabolism, highlighting the interaction between amino acid residues on enzymes backbones and carboxyl groups at catalytic sites. CNTs can enter cells through two distinct pathways: receptor-mediated or non-receptor- mediated. The latter includes endocytosis-independent pathways such as diffusion, membrane fusion, or direct pore transport of extracellular material into the cell. The choice of CNTs is crucial because they can interact with cells effectively. Thanks to their shape, CNTs can traverse cellular membranes and enter cellular components without harming neighbouring cells. A nano-injector system was created using an atomic force microscope (AFM) tip with functionalized MWCNTs, allowing cargo delivery via disulfide linkages. Results demonstrate the successful delivery of CNTs into the cytosol by breaking the disulfide bond. It revealed that nanotubes are taken up by cells through endocytosis, confirmed by attaching fluorinated proteins to SWCNT biotin. Epi-fluorescence and con focal microscopy showed SWCNTs in endosomes, penetrating the cytoplasm and nucleus of fibroblast.[26]

APPLICATIONS OF CARBON NANOTUBES

1.In transdermal patch.

The tans dermal patch is the modern drug delivery system which are applied in the skin use. The drug is present in the form of adhesive patch which consist of drug component that is attached to the adhesive layer of the skin. This is the most preferable delivery as it is used in the comfortably[4]. The transdermal drug delivery contains very low quantity of the drug as the drug is released in very low concentration from the matrix with low permeability of the drug under the skin. In general, in optimizing the drug therapy requires accurate control over the drug amount and release rate. This can be achieved by when the drug shows its effect and activates under internal and the external conditions like electric field, PH, and temperature. By using external stimulus for external stimulus is the effective method that successfully employed to increase the amount of released drug applying the voltage.[14]

2.In cancer lymph node metastasis treatment.

In earlier researches there was a substantiation that poly (acrylic acid) which is functionalised multi walled carbon nanotube which are covered with the magnetite nanosubstance can be effectively absorbed by the lymphatic vessels and supplied to the lymph nodes region in vivo through little toxicity. Along with this, the instructions given by the magnetic field, gemcitabine (GEM) by magnetic lymphatic target system is carried to the lymph nodes inside the body. Many cancers disease like pancreatic cancer, small cell lung cancer, germ cell tumour, head and neck squamous cell cancer and others like bladder, breast, ovary, cervix, biliary tumours and blood cancers are treated by the GEM as it shows its therapeutic activity.[15]

3.In treatment of Mycobacterium tuberculosis

In the anti-TB multi drug delivery, many experiments are made to ensure that the nanoparticles are good substances for the treating the TB in the form of nano vehicles. The researches made successful by nanoparticles. They show less toxicity, greater bioavailability, control release. Introduction of carboxyl, chlorine in MWCNTs

improves the carrying ability and lower the problematic symptoms on active cells. Administration of the drug in the right way and the timely observation increase the capacity to decrease the disease.[16]

4.Carbon nanotubes in peptide delivery

The studies explain CNT applications is a platform for the introducing the bio active peptides in the immune system. To this ground to the amine group on the CNT by the bifunctional linker a B-cell epitope of the foot and mouth disease (FMDV) was covalently attached. CNTs surrounding the peptides gets acclimatized to the possible secondary molecule to identify the particular monoclonal and polyclonal antibodies. Then the immunogenic characters of peptide CNT conjugates are observed.[17]

5.Carbon nanotubes in cellular uptake

Cellular uptake is the main property of functionalized-CNT is their natural behaviour to cross cell membrane. Fluorescent agents are placed inside the carbon nanotube so that they are tracked in the cytoplasm or nucleus of fibroblast by epifluorescence and confocal microscopy. This method of f-CNT does not depend on passive and endocytosis.[17]

6.Carbon nanotube in nucleic acid delivery

Many cationic systems are experimented to nucleic acid delivery to the cells. The main objective is to increase the gene transfer, and expressions as the penetration of plasmid DNA into the cells to enter the nucleus is a complex process. In these electrostatic interactions were studied by forming a super molecular complex with ammonium-f-CNT with nucleic acid[17]

7.In target and control release

In target drug delivery the drug is transported to the targeted site or specific part of the body and released for a prolong period. Passive targeting and the active targeting are the two methods for targeting the site in nanoscale. Depending on the size and the growth behaviour of the cancer passive targeting takes place. The endothelial cells are kept far away from the normal cells in the malignant cells, so that they permit the enhanced permeability of the drugs carrying to the cancer cells. CNT are hydrophobic in nature which allows to remain the blood circulation for prolonged time. In the active mechanism the drugs are actively carried to the cancer cells or diseased part of the body.[18]

8.Carbon nanotubes in tissue engineering

In the Orthopaedic mechanical loading, it was found that the implants made of hydroxyapatite and MWCNTs filled with iron when used in the patients improves the bone tissue formation, which was developed in tissue engineering. By the young's modulus of HA-Ag/MWCN +Fe was found to be 740 and compressive strength was 168MPa, with these values for male cortical femur bone was 141 and 338 MPa and for female it was found to be 118 and 404MPa. It is found that the composite made with Alg /MWCNT +Fe can cure the bone defects[4].

9.Drug delivery carriers

1.CNT consists some special aggregates called carbon nano horns (CNH)which are like horn shape used as prospective carrier in drug delivery.

2.Functionalized carbon nanotubes are used in Amphotericin B to cells activity.

3.The incorporation of the oxidized cisplatin into the SWCNHs gives the measured release of cisplatin the liquid condition. The released has the ability to inhibit the growth of human lung cancer cells.

4.Intracellular penetration is observed in antibiotics, doxorubicin when taken with nanotubes.

5 Due to the denaturation of the drug erythropoietin in gastric condition, the drug is taken in oral route.[9]

10.Genetic engineering

CNTs and CNHs in genetic engineering change the genes and atoms in the discovery of bioimaging genomes, proteomics, and tissue engineering. Uncoiled DNA winds around the SWNT by attaching with certain

nucleotides and makes changes in the electrostatic property. This generates the probability in applications in medication. Depending on the sequence the carbon nanotubes are covered with the single stranded DNA which is used in DNA analysis. Carbon nanotubes by forming a complex with the DNA acts as a defence mechanism and improve transfection notably. They have the antiviral activity in respiratory syncytial virus. In both bronchitis and asthma. The therapy for this was given by the combination of nanoparticles and slicing, technologies[9].

11.Cancer treatment

There are many techniques for the cancer treatment like surgery, radiation, and chemotherapy which had a greater success but CNTs are the anticancer agents when administered in combination with the conventional drugs improves the effectiveness of the drug in curing the cancer. Paclitaxel with the PEG-CNT is the favourable in the cancer treatment. When exposed to a radio frequency (RF) field it exhibits the more heat which was exploited by the Gannon for less harmful and destroying of the tumour cells without any toxic effect to the healthy cells. This reveals that carbon nanotubes are eligible for principle for novel exciting way and advance towards the therapeutic oncology. The important data on prospective drugs in the treatment of pancreatic cancer is provided by the non-invasive thermal cell death that can be caused by a photo thermal action.[20]

12.Detection of chemical substances

Colin et al explained that carbon nanotubes consist of better adsorption properties as they contain distinct surface area and nanoscale arrangement which produce numerous areas where gases in chemical can react. With the help of composite film of SWCNTs mash reacted with alkanethiol monolayer prevented gold cluster, young et al found that NO_2 is tracked by ultrahigh sensitivity detection.[20]

13.Artificial implants

The body when undergoes implantations they show non acceptance reaction because of the pain after the administration of the implants. To reduce this pain, the nano sized carbon nanotubes are incorporated with the proteins and the amino acids. The artificial joints are also prepared by using the nanotubes in the form of implants. Some implants are made in the bone structure by filling with the calcium for the bone substitute[19].

14.Preservative

The special property of the carbon nanotube are they are antioxidant, so to prevent from the oxidation carbon nanotubes are used. Mostly in the cosmetics and preventing from aging. In sunscreen zinc oxide is used to prevent oxidation.[8]

Conclusion

By the many earlier study, it was found that nanotechnology was the important technology used for the development of the many new drugs and treating many diseases. There are wide applications of carbon nanotubes not only in the field of medicine but also in other industries, these exhibit many advantages and disadvantages. Many methods are involved in the preparation carbon nanotubes The carbon nanotubes have many future benefits.

References

[1] Javad safari ,Zohre Zarengar, advanced drug delivery systems :Nano technology of health design A review, Journal of Saudi Chemical Society ,2014, vol 18, Issue 2 , 85-99.

[2]S .Paliwal, K .Pandey, S. Pawar , H. Joshi and N. Bisht, A Review on Carbon Nanotubes :

As a Nano carrier Drug Delivery System, Indian Journal of Pharmaceutical Sciences. 2020 , 82 (5), 766- 772.

[3] Sandeep Kumar , Ruma Rani ,Neeraj Dilbaghi , K. Tank Eshwar and Ki-Hyun Kim , Carbon nanotubes : a novel material for multifaced applications in human healthcare ,chem. Soc. Rev.

2017,vol 46,Issue1, 158-196.

[4] Zare H, Ahmadi S, Ghasemi A, Ghanbari M ,Rabiee N, Bagherzadeh M , Karimi M , Webster TJ, Hamblin MR, Mostafavi E, Carbon Nanotubes, Smart Drug/Gene Delivery Carriers, Int J Nanomedicine, 2021, 16:1681-1706.

[5] Sonia Khanna 1 and Nazmul Islam2 ,Carbon Nanotubes-Properties and Applications, Organic and Medicinal Chemistry International Journal,2018 ,Vol 7, Issue 1.

[6] Rajashree Hirlekar Manohar Yamagar , Harshal Garse, Mohit Vij, Vilasrao Kadam, Carbon nanotubes and its applications, Asian Journal of Pharmaceutical and Clinical Research Review,

2009, vol 2 issue 4.

[7] Anil Kumar Bhardwaj , Amit Kant Pandit, Arvind Rehalia, Vikram Singh and Ruchi Sharma, A Review on nanomaterials for Drug Delivery Systems and Applications of Carbon based Nanomaterials, Engineered Science publisher, 2023; vol 21.

[8] Rohini Chavan, Ujwala Desai, Priti Mhatre, Ruchira Chinchole, A Review: Carbon Nanotube, International Journal of Pharmaceutical Sciences Review and Research, 2021, vol 13, issue 1.

[9] Jashandeep Kaur, Gurlal Singh Gill, Kiram Jeet, Applications of carbon Nanotubes in Drug Delivery: A Comprehensive Review, Science Direct, 2019 , 113-135.

[10] Rama Dubey ,Dhiraj Dutta, Arpan Sarkar and Pronobesh Chattopadhay Carbon nanotubes: synthesis, properties and applications in water purification, drug delivery, and material and biomedical sciences. Royal Society of Chemistry, 2021,5 5722.

[11] Charitha Bandlapalli1, Hima Udaya Sree Gaddam 1, Pavan Kumar Chintmaneni1, S Hari Hara Sudhan1, Reshma Thadipatri2. Carbon nanoparticles: A Complete Review on origin and Medical and Application. Saudi Journal of Medical and Pharmaceutical Sciences, 2021, 7(8), 395-41.

[12] Bhushan O.Murjani1, Parikshit S .Kadu 1, Manasi Bansod, Saloni S. Vaidya1, Manish Kumar D. Yadav, carbon nanotubes in biomedical applications: current status, prmises, and challenges, Springer, 2022, 32:1207-1226.

[13] GP. Bhagath Singh, Chandu Baburao, Vedayas Pispati, Harshavardhan Pathipati, Narsimha Muthv, SRV . Prassana and B .Ganesh Rathod, carbon nanotubes-a novel drug delivery system, international journal of research in pharmacy and chemistry, 2012, issue: 2231-278.

[14] Im JS, Bai BC, Lee YS, The effect of carbon nanotubes on drug delivery in an electrosensitive transdermal drug delivery system. Biomaterials , 2010 Feb 1, 31(6):1414-9.

[15] F .Yang, C . Jin, D. Yang et al, Magnetic functionalised carbon nanotubes as drug vehicles for cancer lymph node metastasis treatment, European Journal of Cancer, vol.47, no.12, pp, 1873-1882, 2011.

[16] Zomorodbaksh, S, Abbasian, Y. Naghinejad, M, and Sheikh pour, M. (2020). The effects study of isoniazid conjugated multi-wall carbon nanotubes nanofluid on mycobacterium Int, J. Nano med, 15, 5901-5909. Doi:10.2147/IJN.S251524.

[17] Bianco A, Kostarelos K, Prato M, Applications of carbon nanotubes in drug delivery. Current opinion in chemical biology. 2005Dec 1;9(6): 674-9.

[18] Kumar S, Rani R, Dilbaghi N, Tankeshwar K, Kim K-H. Carbon nanotubes: a novel material for multifaced applications in human healthcare. Chem Soc Rev, 2017,46:158-196.

[19] Rajashree Hirlekar Manohar Yamagar , Harshal Garse, Mohit Vij, Vilasrao Kadam. Carbon nanotubes and its applications : Asian Journal of Pharmaceutical and Clinical Research 2009, vol 2 issue 4.

[20] M.S. Digge, R.S. Moon, S.G. Gattani, Applications of carbon Nanotubes in Drug Delivery: A Review, International Journal of Pharm Tech Research ,2012, vol 4, No 2.

[21] B.G.P Singh , CH Babu Rao , V. Pispati, H. Pathipati, N. Muthy, S.R.V Prasana, B.G.Rathode. Carbon nanotubes . A novel drug delivery system . International-Journal-of-Research -in -Pharmacy- and-Chemistry, 2012, ISSN: 2231-278.

[22] S.Rathinavel, K.Priyadharshini, Dhananjaya Panda . A review on carbon nanotune: An overview of synthesis, properties, functionalization, characterisation, and the application, Science Direct. 2021, vol 268.

[23] Roopali Jha , Amit Singh, P.K. Sharma, Neeraj Kumar Fuloria. Smart carbon nanotubes for drug delivery system: A comprehensive study. Science Direct, 2020,vol 58.

[24] Harini Kantamneni, Akhila Gollakota, 2013, Carbon Nanotubes Based Systems for Targeted Drug Delivery, A Review , International Journal Of Engineering Research & Technology (IJERT), Volume 02, Issue 02 (February 2013).

[25] Hua He, Lien Ai Pharm-Huy, Pierre Dramou, Deli Xiao, Pengli Zuo , Chiung pharm-Huy, Carbon Nanotubes: Applications in pharmacy and medicine, Bio med research international,2013, vol 2013, Article ID 578290, 12 pages .

[26] Zhang, W, Zhang, Z & Zhang, Y. The application of carbon nanotubes in target drug delivery systems for cancer therapies, Nanoscale Res Lett 6, 555 (2011).

[27] Ren , Guoqiang, Carbon nanotubes , Encyclopedia Britannica, 21 Jul,2023.

[28] Shikha Singh Harshil Patel Manish Govani Pinkisha Patel. Carbon nanotubes- A Novel Drug Delivery system. Multidisciplinary International Research Journal of Gujarat Technological University, 2021, vol 3 issue 1.

.