



# A Review on Carbon Nanotubes on Cancer Therapy

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## Abstract

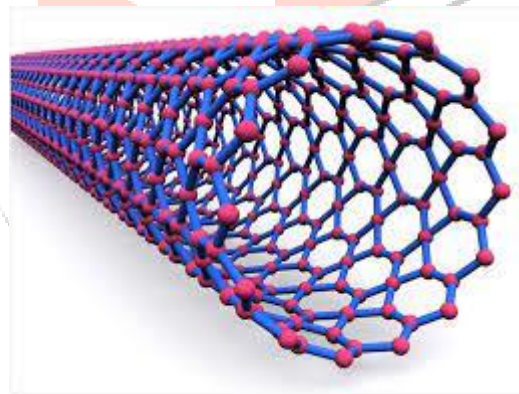
Carbon nanotubes (CNTs) have received increasing attention in medicine fields owing to their distinctive structures and properties, together with high side ratios, massive surface areas, made surface chemical functionalities, and size stability on the nanoscale. notably, they're engaging as carriers and mediators for cancer medical aid. Through acceptable functionalization, CNTs are used as nanocarriers for antitumor medication together with antibiotic, camptothecin, carboplatin, cisplatin, paclitaxel, Pt (II), and platinum (IV), and genes together with inclusion body polymer, tiny busybodied ribonucleic acid, oligonucleotides, and RNA/DNA aptamers. CNTs also can deliver proteins and therapy elements. victimization combos of sunshine energy, they need conjointly been applied as mediators for photothermal medical aid and photodynamic medical aid to directly destroy cancer cells while not severely damaging traditional tissue. If limitations like a long toxicity within the body, lack of size uniformity throughout the artificial method, loading deviations for drug–CNT complexes, and unharness controllability at the target purpose square measure overcome, CNTs can become one in every of the strongest tools that square measure out there for numerous different medicine fields similarly as for cancer medical aid.

**Keywords:** carbon nanotubes, cancer, therapy, carrier, mediators

## Introduction

Carbon nanotubes will be represented as C sheets that area unit rolled up into cylindrical shapes. Carbon nanotubes composed of interlocking carbon atoms hexagonally formed arrangements that are rolled into tubes. These little straw – like cylinders of pure carbon have helpful electrical properties. They have already went to build little transistors & one dimensional copper wire. The length of CNTs is within the type of micrometers with a diameter of

regarding a hundred nm. Carbon nanotubes (CNTs) area unit thought of as a spinoff of each carbon fibers and C with molecules composed of sixty atoms of carbons organized particularly muffled tubes.<sup>1</sup>The structure of a nanotube possess numerous fascinating chemical and physical functionalization strategies of properties, are extensively employed in biomedicine.

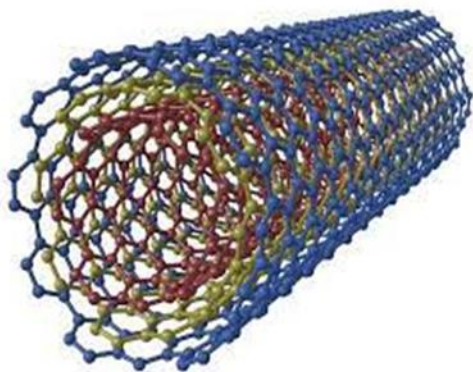


**Fig 1 single walled nanotube**

Functionalized carbon nanotubes with water solubility and biocompatibility area unit able to cross cell membranes, shuttling a large vary of biologically active molecules as well as medication, proteins, deoxyribonucleic acid and RNA into cells. The toxicity of carbon nanotubes is essentially hooked in to their surface functionalization, with bottom toxic effects for well functionalized, serum-stable nanotubes<sup>2</sup>.

CNTs is one in all carbon allotropes like diamond, graphite, graphene, C and amorphous carbon. But, it's the one-dimensional carbon kind which may have a side magnitude relation bigger than a thousand makes it fascinating. The bonding in carbon nanotubes is  $sp^2$ , with every atom joined to a few neighbours, as in C. CNTs area unit folded graphene sheets (graphene is a private C layer).<sup>3</sup> this sort of structural bonding, that is stronger than the  $sp^3$  bonds found in diamond, provides the molecules with their

distinctive strength. below air mass, nanotubes will merge along, commerce some  $sp^2$  bonds for  $sp^3$  bonds, giving the likelihood of manufacturing sturdy, unlimited length wires through air mass carbon nanotube linking. The properties of nanotubes depend upon atomic arrangement (on however the sheets of C area unit 'rolled'), the diameter and length of the tubes, and morphology or nanostructure.



**Fig a 2 of Multi walled carbon nanotubes**

## Cancer:

Life threatening malady, cancer continues to extend with increasing age of the population & urbanization.

Cancer arises once a gaggle of cells begin to grow abnormally disregard the division rules of traditional cells. owing to their uncontrolled growth and proliferation, these cancer cells establish associate degree autonomous tumor tissue. Metastasis, the spreading of malignant tumor cells, is that the main reason behind cancer deadliness. Cancer could be a leading reason behind morbidity and mortality worldwide.<sup>4</sup>

In cancer medical aid, beyond any doubt the primary and also the most significant step is designation. it's obvious that the sooner the cancer designation, the lot of probability for fortunate treatment and survival. within the case of solid tumors, the primary step of treatment is sometimes removal of the first cancer cells by surgery. Then the realm round the location ought to be irradiated to destroy any attainable remnants of the tumor. Next, or at constant time, cytotoxic medication will be wont to kill residual cancer cells and attainable metastases.<sup>5</sup> Since cytotoxic medication area unit typically kill all cells, it's necessary to guide the metastatic tumor medication toward the cancer cells victim tumor-targeted drug delivery systems. Recently, CNT-polymer hybrid nano-materials are effectively used to deliver biologically active therapeutic agents into the tumor website for the needs of cancer designation and medical aid.<sup>6</sup>

Nanomedicine in oncology- Main concentrate on the event of safer and additional economical techniques for speedy nosology and sensible drug delivery in cancer therapy<sup>7</sup>. the good superiority of nanomedicines against typical medicines is their potential to deliver medicine into tumors because of the leaky tumor vasculature that provides higher tissue penetration. The delivery of quite one therapeutic agent for higher therapeutic effectualness together medical care is another advantage. the opposite vital edges of nanomedicines

are often the particular binding of medicine to the targeted cancer cells, concurrent mental image of tumors via novel imaging techniques, accumulated drug circulation times, controlled drug unharness mechanics, and higher dose planning for compliance of improved patients.<sup>8</sup>

The most necessary characteristic of delivery systems supported nanomaterials and nanostructures is their high potential to boost the delivery of antineoplastic medicine to the tumors by means that of active targeting. as a result of the poor diffusion of some medicine and therefore the random nature of passive targeting, it's typically troublesome to deliver medicine controllably to the inside cells of a tumor. This lack of management might result in an unsuccessful therapy treatment because of multiple-drug resistance (MDR). Over-expressing of transporter proteins that expel medicine on the surface of cancer cells has been delineate as a serious reason of MDR. because it could also be expected, emission processes inevitably lower the therapeutic result of medicine and therefore, cancer cells are ready to develop resistance to a spread of medicine.<sup>9</sup>The passive strategy is more restricted as a result of sure tumors don't indicate the improved porousness and retention (EPR) result, and therefore the porousness of vessels might not be a similar throughout one tumor.

One approach to beat these drawbacks is style of nanocarriers that actively ready to bind to specific cells when extravasations. This binding could also be achieved by attaching targeting agents to the surface of the nanocarrier by a spread of conjugation ways. Then, nanocarriers can acknowledge and bind to focus on cells through ligand-receptor interactions. a large style of ligands will doubtless use to focus on cellular biomarkers together with antibodies, different proteins, Peptides and polysaccharides<sup>10</sup>. Improved targeting of nanoparticles (NPs) to tumors is crucial as a result of larger tumors exhibit poor organic process, notably within death areas, resisting the localization of NPs within the tumor. Although, of these properties create this a perfect technique for drug delivery, by selection targeted drug delivery systems are still facing challenges together with improvement of specificity, stability, control bioavailability, and developing targeted carriers with lower toxicity.

Carbon nanotubes in nanomedicine- in an exceedingly victorious therapy, therapeutic agents ought to pass a series of biological barriers together with internal organ and urinary organ clearance, enzymolysis and chemical reaction, additionally as cellular uptake and lysosomal degradation. within the case of antineoplastic medicine, the potency are often additionally laid low with their poor solubility, low stability and high toxicity for traditional tissues and cells. In spite of of these difficulties, nanomaterial carriers ar ready to improve the biodistribution and prolonged blood circulation of medical specialty, that considerably increase the pharmaceutical effectualness, and reduce the usage dose. they're notably promising candidates for early diagnosing of tumor cells. many categories of nanomaterials, together with nerve fiber and supramolecular polymers, CNT- and graphene-based materials, nanoparticles, and gold nanostructures have shown tremendous ability to acknowledge and destroy cancer cells in vivo.

Nanotechnology collectively branch of engineering, that deals with the manipulation of individual molecules and

atoms. With the event of applied science, several nano-materials were developed and applied into business. Carbon nanotubes (CNTs) are one among the nano-materials that are widely employed in such space in recent years. They need got additional and additional attention as a result of their distinctive properties.<sup>11</sup>

CNTs are additional dynamic compared with different nano-materials in their biological applications, and that they are one among the foremost fascinating nanocarriers in scientific studies. CNTs have displayed obvious prospect that they'll cross the biological barriers as novel delivery systems. Compared with quantum dots that are in the main employed in neoplastic cell imaging, CNTs may be applied in drug delivery and current ablation. They need the flexibility to enter cells, and this behavior is freelance of cell sort and useful cluster at their surface. Presently the careful mechanisms of learning (endocytosis or needle like penetration) haven't been fully explained. The high space of CNTs will give multiple sites for attachment of various molecules, that makes polyvalent derivatization attainable. Additionally, supported the in vitro and in vivo results obtained from various analysis teams, a spread of with chemicals functionalized CNTs have the flexibility of biocompatibility with the biological surroundings.

CNTs possess some characters, together with a high surface space with cellular membrane and distinctive capability to include multiple functionalization's. At a similar time, CNTs even have the compatibility and transportability in biological fluids. These options create them a great tool for all types of diagnosing and therapeutic additionally as drug delivery application.<sup>12</sup>

The major aim of developing Nano carrier drug delivery systems is to boost the therapeutic result or cut back toxicity of therapeutically active materials. This can be conventionally achieved victim spherically formed cyst nano carriers like liposomes. Instead, carbon nanotubes (CNTs) are primarily cylindrical molecules fabricated from carbon atoms. CNTs are graphene sheets rolled into a seamless cylinder that may be open concluded or capped, having a high ratio with diameters as little as one nm and a length of many micrometers. CNTs made up of one graphene sheet ends up in a single-walled nanotubes whereas many graphene sheets form up multiwall carbon nanotubes. There are 2 broad classes of CNTs, namely, single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs). SWCNTs are created of single graphene layer wrapped into a hexangular shut packed cylindrical structure whose diameter varies from zero.4 to 3.0 nm and length ranges from twenty to one thousand nm. They're control along by Vander Waals forces, that makes them simply twistable and additional pliable. SWCNTs are made by the electrical arc, optical maser ablation, chemical vapor deposition and gas-phase chemical process processes.<sup>13</sup>

## Properties of carbon nanotubes:

1. Ordered structure with high ratio
2. Ultralight weight
3. High mechanical strength
4. High electrical physical phenomenon

5. High thermal physical phenomenon

6. Argentiferous or semi-metallic behavior &

7. High area

8. Strength -

- Carbon nanotubes have a better lastingness than steel and Kevlar.

- The strength comes from the  $sp^2$  bonds between the individual carbon atoms. This bond is even stronger than the  $sp^3$  bond found in diamond.

- Beneath high, individual nanotubes will bond along, mercantilism some  $sp^2$  bonds for  $sp^3$  bonds. This provides the likelihood of manufacturing long carbon nanotube wires.

- Carbon nanotubes aren't solely robust, they're additionally elastic. One will continue the tip of a {nanotube carbon, carbon nanotube fullerene} and cause it to bend while not damaging to the nanotube, and also the carbon nanotube can come back to its original form once the force is removed.

- A nanotube's snap will have a limit, and beneath terribly robust forces, it's attainable to for good deform to form of a carbon nanotube

- A carbon nanotube's strength is weakened by defects within the structure of the nanotube.

- Defects occur from atomic vacancies or a arrangement of the carbon bonds. Defects within the structure will cause a tiny low section of the carbon nanotube to become weaker, that successively causes the lastingness of the complete carbon nanotube to weaken.

- The lastingness of a carbon nanotube depends on the strength of the weakest section within the tube just like the approach the strength of a series depends on the weakest link within the chain.

9. Hardness -

- commonplace single-walled carbon nanotubes will face up to a pressure up to 25 GPa while not [plastic/permanent] deformation. They then endure a change to super hard section nanotubes.

- Most pressures measured victim current experimental techniques square measure around fifty five GPa.

- However, these new super hard section nanotubes collapse at a good higher, albeit unknown, pressure.

- The majority modulus of superhard section nanotubes is 462 to 546 GPa, even over that of diamond (420 GPa for single diamond crystal). Electrical properties

- The structure of a {carbon, carbon nanotube, nanotube fullerene} determines however semiconducting the nanotube is.

- Once the structure of atoms during a nanotube minimizes the collisions between conductivity electrons and atoms, a nanotube is very semiconducting.

- The robust bonds between carbon atoms additionally permit carbon nanotubes to resist higher electrical currents than copper.

- negatron transport happens solely on the axis of the tube.
- Single walled nanotubes will route electrical signals at quickens to ten Gc once used as interconnects on semiconductive devices.
- Nanotubes even have a continuing ohmic resistance.<sup>14</sup>

#### 10. Thermal Properties-

- The strength of the atomic bonds in carbon nanotubes permits them to resist high temperatures. owing to this, carbon nanotubes are shown to be excellent thermal conductors.
- in comparison to copper wires, that square measure normally used as thermal conductors, the carbon nanotubes will transmit over fifteen times the number of watts per meter per Kelvin.
- The thermal physical phenomenon of carbon nanotubes relies on the temperature of the tubes and also the outside atmosphere.

#### 11. Wettability-

- The surface wettability of CNT is of importance for its applications in varied settings.
- though the intrinsic contact angle of carbon is around  $90^\circ$ , the contact angles of most as-synthesized CNT arrays square measure over  $160^\circ$ , exhibiting a superhydrophobic property.<sup>15</sup>
- By applying an occasional voltage as low as one.3V, the intense water repellent surface is switched into super hydrophilic.

#### 12. Field Emission-

- beneath the applying of robust force field, tunneling of electrons from metal tip to vacuum leads to emission development.
- emission results from the high ratio and tiny diameter of CNTs.
- the sector emitters square measure appropriate for the applying in flatpanel displays.
- For MWNTs, the sector emission properties occur thanks to the emission of electrons and light-weight.
- while not applied potential, the luminescence and light-weight emission happens through the negatron emission and visual a part of the spectrum, severally.

#### 13. ratio –

- one in all the exciting properties of CNTs is that the high ratio, inferring that a lower CNT load is needed compared to alternative semiconducting additives to attain similar electrical physical phenomenon.
- The high ratio of CNTs possesses distinctive electrical physical phenomenon as compared to the standard additive materials like sliced carbon fiber, smut, or stainless-steel fiber.<sup>15</sup>

#### 14. Absorbent –

- Carbon nanotubes and CNT composites are rising as perspective engrossing materials thanks to their lightweight weight, larger flexibility, high mechanical strength and superior electrical properties.
- CNTs emerge out as ideal candidate to be used in gas, air and water filtration.
- The absorption frequency vary of SWNT-polyurethane composites broaden from half-dozen.4–8.2 (1.8 GHz) to seven.5–10.1 (2.6 GHz) and to twelve.0–15.1 GHz (3.1 GHz) (Wang et al. 2013).
- a great deal of analysis has already been administered for commutation the C with CNTs for sure ultrahigh purity applications.

the mixture of those characteristics build CNT a singular material with the potential for numerous applications, including medicine.<sup>16</sup>

## Techniques of Functionalization of Carbon Nanotubes-

Despite of the benefits of CNTs in targeting varied varieties of cancer cells, varied constraints are created on the biological and medicine applications of CNTs because of their lack of solubility in liquid medium yet as their toxicity caused by the hydrophobic surface. These limitations of CNTs may be overcome by a method known as Functionalization.

CNT while not surface modification, are cytotoxic to sure class cells, as an example, pure MWCNTs will injure cell wall of human macrophages thus, methods for surface functionalization as well as valency and noncovalent functionalization are disbursed on the synthesized CNTs. the method of functionalization is additionally useful in conjugating the therapeutic molecule or the ligands to the CNTs either on the surface or on the ends of CNTs to render them active against cancer cells.<sup>17</sup>

1. valency functionalization
2. Noncovalent functionalization

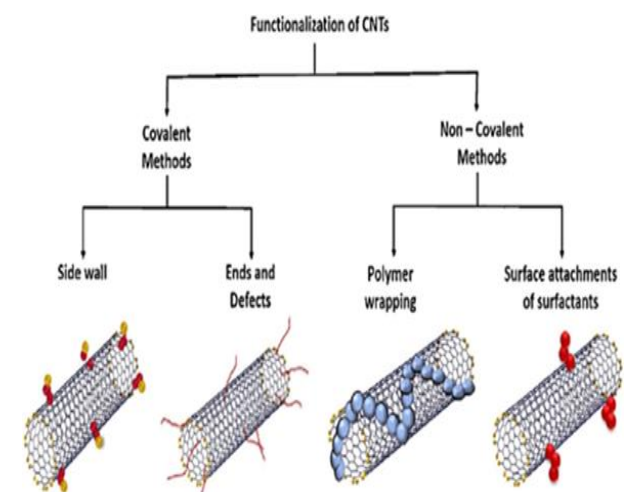


Fig 3

## 1. Covalent functionalization-

valency functionalization of CNTs with the therapeutically active molecule or the biocompatible surfactants is ruled by the reaction of CNTs mistreatment sturdy acids (conc. H<sub>2</sub>SO<sub>4</sub> or conc. HNO<sub>3</sub>) that generates substitutable deliquescent useful teams like COOH and OH on the Carbon nanotubes that then more endure into the chemical reactions like esterification, amidation, chlorination, bromination, chemical process, and Diel's-Alder reaction.

so as to urge functionalized with these active molecules, CNTs permit side-wall valency attachment of useful teams by the addition of radicals, nucleophilic carbenes, nitrenes, nucleophilic cyclopropanation, and electrophiles. the tactic of reaction ends up in the gap of the CNT finish caps, generating radical teams appropriate for enhancing the solubility of the CNTs with improved biocompatibility.

extremely charge developed as a results of the carboxylation will increase the hydrophilicity of CNTs. valency linkage of polythene glycols will increase the hydrophilicity and also the solubility of CNTs in liquid media yet as increasing the dimensions that reduces the speed of clearance of CNTs through the kidneys and tends to extend the circulation time within the plasma.

The valency functionalization of CNTs may be achieved via the functionalization of "ends and defects" and "side walls." The ends and defects technology has high specificity and reaction compared with the perform of facet walls. The valency functionalization of CNTs can also be finished via the bond between the surfaces of CNTs and also the biocompatible teams. The surface reaction treatment may be a typically method of originating valency bonding.<sup>18</sup>

The surface of CNTs may be cut via treatment with sturdy acid solutions so cause chemical {group} group being exposed at the defect purpose, predominately on the open ends. CNTs in focused element and aqua fortis are treated and heated by supersonic wave. The facet wall valency functionalization may be achieved via this method, and acid cluster will attach to CNTs so create CNTs become soluble. CNTs may be cut and oxidised to supply a particular range of radical teams so be later derivatized with differing types of molecules.<sup>19</sup>

## 2. Non valency functionalization-

Noncovalent functionalization involves Van der Waals interactions,  $\pi$ - $\pi$  interactions, and hydrophobic interactions of biocompatible useful teams with the surface of the CNT. one amongst the most benefits of this kind of bonding is that the token harm caused to the CNT surface. it's been prompt that noncovalent attachment preserves the aromatic structure and therefore the electronic character as compared to pristine CNTs.

this kind of functionalization may be done by the addition of deliquescent polymers, biopolymers, and surfactants to the walls of CNTs through weak bonds.<sup>20</sup> A series of anionic, cationic, and nonionic surfactants are already planned to disperse nanotubes in liquid media.

metal dodecyl salt (SDS) and benzylalkonium chloride ar alternative smart samples of surfactants that non covalently aggregative to the fullerene facet walls and facilitate the

dissolution of CNTs in water. The adhesion between wetters and {nanotube|carbon fullerene|fullerene} walls becomes terribly sturdy because of because of stacking interactions resulted from the attachment of aromatic teams of the amphiphile surfactant within the aromatic network of the nanotube facet walls, as proven within the case of adhesion of N-succinimidy-1-pyrenebutanoate.<sup>20</sup>

## Mechanism of Carbon nanotubes penetration into the cell –

Both sorts of pure CNTs, the one walled and therefore the the} multiwalled carbon nanotubes have no affinity for cells and also no to cancer cells. meaning they need to be functionalized so as to form them able to cross the membrane of the conventional cells and even a lot of specifically for targeting them to cancer cells.<sup>21</sup> For this reason, they're essentially similar carriers like liposomes, dendrimers, or nanoparticles. However, the benefits of SWCNTs and MWCNTs over different carriers are important to their polygonal shape compact cylindrical structure and sp<sup>2</sup> coupling that renders them to urge simply functionalized with the various substance or therapeutic moiety.

These functionalized CNTs have a capability to cross cell membranes. Hence, to grasp the acquisition method, CNTs may be tracked by labelling them with a fluorescent agent (such as fluoresceine isothiocyanate) then observance the uptake by mistreatment epifluorescence, confocal research, and flow cytometry studies. in addition, detection of CNTs by nonlabelling strategies like transmission {electron research, microscopy} (TEM) or atomic force microscopy has conjointly been conducted by several researchers.<sup>22</sup>

To conclude concerning the precise cellular uptake pathway of CNTs is advanced and it's believed that there are 2 doable pathways to cross the cellular membrane. the primary is endocytosis dependent pathway which can be either receptor mediate or non receptor mediate and also the second relies on endocytosis freelance pathway which has diffusion, membrane fusion, or direct pore transport of the animate thing material into the cell.<sup>23</sup>

the method of acquisition of CNTs depends on many parameters like the scale, length, nature of practical teams, property, Associate in Nursingd surface chemistry of CNTs Endocytosis dependent pathway is an energy and temperature dependent transport method that involves engulfing of animate thing materials inside a phase of the cell wall to make a sacculus or a sac (hence conjointly referred to as somatic cell or sac transport) that is then pinched off intracellularly into the protoplasm of the cell.<sup>24</sup> what is more, acquisition endocyte formation was shown to be clathrin mediate, caveolin-driven endocytosis, and thru macropinocytosis.

just in case of receptor mediate endocytosis, substance conjugated-drug loaded CNT binds to the complementary transmembrane receptor proteins then enters the cell as receptor-ligand complexes in clathrin coated vesicles. once acquisition vesicles are shaped that were called early endosomes and thanks to come by pH, the substance dissociates from the receptor. once the receptors are free, the vesicles carrying the animate thing particle fuses with lysosomes and therefore trigger the discharge of the drug particle by the action lysozymes on the endosomes and at the

same time the free receptors therefore shaped are being recycled to the semipermeable membrane for conjugating with different substance conjugated CNTs.<sup>25</sup>

Associate in Nursing example from the antiangiogenetic space is that the targeting of integrin  $\alpha v \beta 3$ , that are epithelium cell receptors for animate thing matrix proteins possessing the RGD sequence (arginine-glycine-aspartic acid) and are extremely expressed on neovascular epithelium cells.<sup>26</sup> Conjugation of RGD peptides to nanovectors will cause higher levels of cellular acquisition and what is more have an effect on tube-shaped structure epithelium protein receptor-2 (VEGFR-2) signalling thanks to intrinsic association with this signalling pathway, resulting in downregulation of the receptor and at last to reduced.

Another example for active targeting supported ligand-receptor interactions relevant to the current space of cancer medical specialty is that the interaction of vitamin B complex with its receptors. B-complex {vitamin B complex, vitamin B complex, vitamin B} may be a vitamin and necessary for the synthesis of nucleotides, the deoxyribonucleic acid building blocks. Its counterpart, the vitamin B complex receptor, is considerably upregulated by a broad spectrum of human cancers, in some cases by 2 orders of magnitude, facilitating cellular acquisition of folate conjugated nanovectors by receptor-mediated endocytosis, angiogenesis.<sup>27</sup>

Folate-conjugated nanovectors loaded with antitumour medication have shown large potential in overcoming the matter of multidrug resistance by evading P-glycoprotein-mediated effluence, that is taken into account to be a typical downside in cytotoxic drug administration. In general, the long CNTs ( $>1 \mu\text{m}$  in length) were obsessed by the method of body process (a part of endocytosis) that was primarily conducted by the macrophages, monocytes, and neutrophils, whereas the shorter CNTs<sup>28</sup> (length from some to many hundred nanometers) were primarily internalized by bodily function.

it had been found that neutering the property of the CNTs by conjugating them with phospholipids considerably alters the uptake of CNTs by the cells as discovered by Kapralov et al. They compared the acquisition of the chemical agent (phosphatidylcholines and phosphatidylglycerols) conjugated SWCNT with pristine SWCNT within the murine RAW 264.7 cells and also the knowledge obtained from flow cytometric analysis clearly states that the adsorbate phospholipids considerably increased the uptake of SWCNTs via body process as phospholipids are proverbial to greatly escort the phospholipids head cluster of the cellular membrane as compared to pristine or uncoated SWCNT. just in case of nonreceptor mediate endocytosis, a little portion of the semipermeable membrane surrounds the drug loaded CNTs then pinches off intracellularly as Associate in Nursing endocyte sac. the method is ruled by the intrinsic property of the CNTs still as practical teams gift on that. The endosomes therefore shaped are eventually reborn into the lysosomes and ultimately end in the drug unharness.<sup>29</sup>

In endocytosis freelance pathway there's an immediate translocation of CNT through the semipermeable membrane into the protoplasm that has been termed by some researchers because the "nanoneedle" mechanism. This pathway includes processes like diffusion, membrane fusion, and direct pore transport. one by one spread CNTs in liquid solutions are by experimentation incontestible to be able to enter the protoplasm of cells by directly crossing the cell wall. Such cellular uptake of CNT, that isn't influenced by the presence of endocytosis matter (such as Na azide), advises the endocytosis freelance pathway of acquisition.<sup>30</sup>

## Drug delivery By CNTs

Nowadays, many novel CNT-based tumour-targeted drug delivery systems are developed by analysis teams everywhere the planet. These delivery systems usually accommodates 3 parts: functionalized-CNTs, tumor-targeting ligands, and antitumour medicine.<sup>31</sup> once NDDSs move with cancer cells, they might acknowledge cancer-specific receptors on the surface of the cells and so induce receptor-mediated endocytosis. it's been incontestible that the complicated is obsessed with efficiency and specifically by cancer cells with resultant animate thing unleash of chemotherapeutical agents, that suppress proliferation of cancer cells a lot of effectively than untargeted controls containing identical drug.<sup>32</sup>

1. Gene delivery systems -In a sequence medical care treatment technique, the genetic materials (DNA or RNA) square measure delivered as pharmaceutical agents to assist target cells to recover missing or defective genes and generate their own therapeutic proteins with tokenish toxicity to cure a malady.<sup>33</sup> This technology may be a promising treatment possibility particularly in cancer and is predicted to be an alternate methodology to ancient therapy. many genes are studied for this kind of medical care, together with suicide genes (genes that cause cellular death once expressed), anti-angiogenesis genes and cellular stasis genes.<sup>34</sup>

2. basic categories of materials are accustomed deliver these genes into the cells: biological NPs (viral vectors) and nonviral vectors. infectious agent techniques square measure a lot of less complicated and extremely economical pathways that utilize varied categories of viruses as a tool in sequence medical care however the most drawbacks of infectious agent

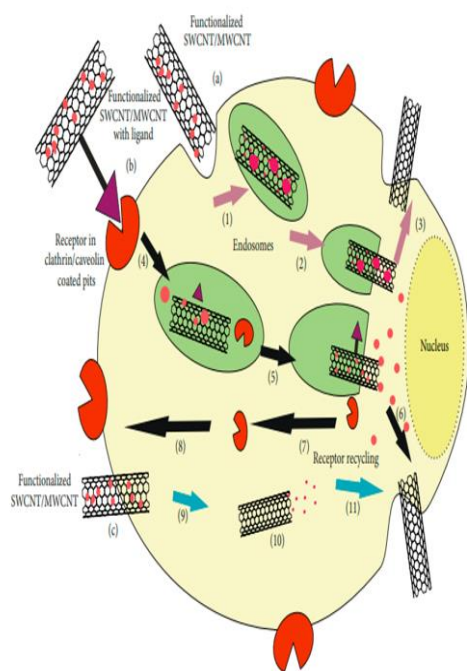
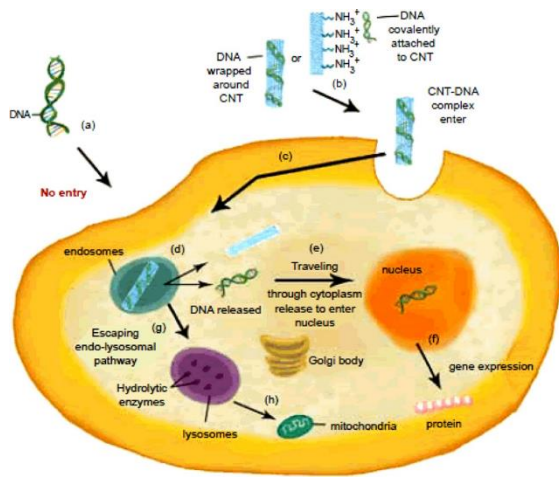


Fig 4

vectors square measure considerations concerning their safety, together with immunogenicity, oncogenicity and inflammatory properties. Effective nonviral vectors ought to with success cross totally different biological barriers, shield polymer from degradation and move with alternative biological molecules and build low immunogenicity. Nonviral materials embody cationic lipids, liposomes, polyethylenimine (PEI), polyamidoamine, nanoparticles and alternative cationic polymers that use naked polymer or polymer.<sup>35</sup>



**Fig 5**

Functionalized-CNTs (f-CNTs) appear to be terribly appropriate for sequence medical care as a result of they're simply able to cross cell membranes and deliver genes into cells. In several reports, polymer and polymer are covalently and noncovalently hooked up to f-CNTs. It's been found that not solely polymer molecules is joined to the ideas and walls of f-CNTs, however can also be encapsulated within the structure. Unleash of polymer molecules from CNTs-based delivery systems exploitation thermal properties of CNTs has been investigated and it's been found that DNAs is free from f-CNTs transporters to the nucleus once the optical maser pulses.<sup>36</sup>

2. Photothermal therapy- though the idea of exploitation heat in cancer treatment contains a long background as early because the late 1800s, these days, photothermal medical care continues to be recognized as a unique developing methodology for cancer medical care.<sup>44</sup> these days, photothermal medical care is being employed as a noninvasive, harmless and economical therapeutic technique that heats the growth location and cancer cells by a skin penetrating near-infrared (NIR) irradiation and later destroys them while not making significance facet effects for the opposite elements of body. Among many active nanomaterials and nanostructures in photothermal medical care like gold nanorods, gold nanopyramids, gold nanoshells, gold nanocages, and gold-CNT hybrid nanomaterials, CNT-based ones have received explicit interest as a result of they need sturdy optical absorption throughout NIR optical maser and frequency (RF) irradiation. Optical coupling of sunshine with CNTs is expected to be highest once the length of the nanotubes is over  $[\lambda_{fr}]$  the wavelength of the incident light as determined by the antenna theory. Moreover, the length of fullerenes has been found to be a significant determinant of ability of the nanotube to transfer heat and kill the growth.<sup>37</sup>

one in every of the foremost vital blessings of CNT-based photothermal medical care systems, is their ability to mix with therapy and sequence medical care techniques for treating cancer in an exceedingly a lot of economical manner. so as to lift the property of treatment and diminish undesirable effects to traditional cells, CNTs are covalently and noncovalently joined to cell binding ligands like peptides or being antibodies (MAbs).<sup>38</sup>

However, the most downside of valence functionalization of CNTs is feasible harm to the CNT structure and interference with their electronic and optical properties. additionally, photothermal medical care exploitation the absorption properties of antibody-conjugated nanomaterials has incontestible selective killing of cancer cells whereas departure healthy cells unaffected.<sup>39</sup>

## Toxicity of Carbon Nanotubes

For profitably applying a replacement generation of nanomaterials as biomedicine, it's essential to manipulate their medicine and pharmacological medicine profiles. though the biological toxicity of NPs has been evaluated by many teams, more investigations area unit still necessary for achieving comprehensive info concerning the toxicity of nanomaterials. it's been at one time discovered that nanoparticle chemistry properties like size, pure mathematics (shape), surface charge, surface chemistry, property, roughness, rigidity and degree of composition will have an effect on on differential uptake and targeting to sure organs, tissues or cells and should be optimized through the effective style of NPs.<sup>40</sup>

though the molecular and cellular mechanisms for the toxicity and also the coming into of CNTs into cells haven't been utterly understood and their biocompatibility continues to be receptive question, f-CNTs area unit with success able to cross cell membranes via AN endocytosis pathway or endocytosis freelance mechanism.<sup>41</sup> Toxicity and immunogenicity of CNTs in each in vivo and in vitro studies has been attributed to numerous factors like variety of walls, length and ratio, area, degree of aggregation, extent of oxidation, property, surface topology, methodology of administration, dispersibility, kind and degree of functionalization, and methodology of manufacture (which will leave catalyst residues and turn out impurities).<sup>42</sup>

Toxicity of CNTs is additionally addicted to their concentration, dose, length and methodology that cells or organisms area unit exposed to them and even the utilised dispersant to solubilize the nanotubes. The length and form of CNTs influence however well they cross the membrane of macrophages and confirm the ensuing response. as an example, shorter CNTs (B0.2 millimetre in length) were found to possess higher immunogenic responses than longer ones (larger than zero.8 mm).<sup>150</sup> A complementary study has additionally been showed similar results when injection of long and short length CNTs into mice.<sup>43</sup>

Also, it's been reported that CNTs would possibly induce mesothelioma-like lesions in mice, in an exceedingly manner like that determined for carcinoma iatrogenic by amphibole.<sup>45</sup> Takagi et al. have shown that intraperitoneally administered multiwalled carbon nanotubes (MWCNTs) induce carcinoma within the mouse carcinogenesis model, in all probability thanks to the MWCNTs' similarity to

amphibole in size and form and to their biopersistency. Moreover, Poland et al. have determined asbestos-like moribific behavior of CNTs related to their needle-like fiber form and established a structure–activity relationship supported the length of the CNTs.<sup>46</sup>

Migliore et al. have indicated that long rigid MWCNTs seem to make fiber-like aggregates or structures that area unit too long to be phagocytosed by phagocyte cells, so leading to reactive atomic number 8 species (ROS) production. additionally, Nagai et al. recommended large-diameter or tangled MWCNTs area unit less deadly, less inflammogenic, and fewer cancer than loosened MWCNTs. In fact, no inflammatory response was determined with short MWCNT, as they were effectively obsessed by macrophages with economical body process.<sup>47</sup>

## Carbon Nanotubes in Cancer Treatment

1. Blood Cancer-An increased targeted delivery of daunorubicin (Dau) to acute lymphocytic leukemia was achieved by Taghdisi et al., they developed a tertiary complicated of Sgc8c aptamer, daunorubicin, and SWCNT named as Dau-aptamer SWCNTs.<sup>48</sup>

2. Brain Cancer-Ren et al. developed a twin targeting PEGylated MWCNTs and loaded with a targeting matter angiopep2 (ANG) and antibiotic, severally, to focus on density macromolecule|compound protein} receptor-related protein receptor that is overexpressed on the blood brain barrier (BBB) and C6 brain tumour cells.<sup>49-55</sup> In vitro animate thing trailing and in vivo light imaging incontestable the perfect twin targeting of the developed system that was earned by the upper transcytosis capability and parenchymal accumulation by the angiopep-2 and may be thought-about a cloth of option to cross blood brain barrier also on specifically recognise their conjugated protein receptors gift on the brain tumour cells for steering the positioning specific unleash of metastatic tumor drug.

3. Breast Cancer-A water soluble SWCNT-Paclitaxel (PTX) conjugate has been developed by conjugating PTX to functionalized polythene glycol SWCNTs via a divisible organic compound bond. SWCNT-PTX has been found to be extremely economical in suppressing tumour growth in comparison with clinical taxol during a murine 4T1 carcinoma cells, that has been attributed to the extended blood circulation (due to PEGylation) and multiple higher tumour PTX uptake by SWCNT delivery, most likely through increased porousness and retention (EPR) impact.

4. Liver Cancer-Polyamidoamine dendrimer changed CNTs (dMWCNTs) were made-up for the economical delivery of antisense c-myc oligonucleotide (asODN) into carcinoma cell line HepG2 cells. asODN-dMWCNTs composites were incubated with HepG2 cells and confirmed to enter into tumour cells at intervals fifteen min by optical device confocal research. These composites inhibited the cell growth in time and dose dependent suggests that and downregulated the expression of the c-myc sequence.<sup>56</sup>

5. Colon Cancer-Triple functionalized SWCNTs were made-up with Associate in Nursing metastatic tumor drug (Doxorubicin), a antibody and a fluorescent marker (fluorescein) at the monopolistic binding sites on the

SWCNTs for targeting the cancer cells.<sup>57</sup> Confocal optical device research reveals the bovine humor albumin-antibody specific receptor mediate uptake of SWCNTs by the human colon glandular cancer cell WiDr cells with resulting targeting of antibiotic intracellularly to the nucleus

6. Lymph Node Metastasis-Yang et al. compared the in vitro and in vivo potential therapeutic impact of gemcitabine (GEM) loaded magnetic MWCNTs (mMWCNTs) therewith of gemcitabine loaded magnetic-carbon particles (mACs). His finding reflects the high antitumour activity in human carcinoma BxPC3 cells of each the systems in comparison at the side of free drug.

7. Kidney Cancer-SWCNTs induce changes within the cell cycle that may be attributed to the decrease within the variety of cells within the S-phase thanks to upregulated expression of P16 that inhibits the cyclin dependent enzyme activity of Cdk2, Cdk4, Associate in Nursing CdkR and thus prevents the cells from getting into an S-phase and later on impressive the cell cycle within the G1 phase<sup>58</sup>

8. Prostate Cancer -Li et al. developed a completely unique targeting SiRNA delivery system by mistreatment SWCNTs that was with chemicals functionalized with polyethylenimine and certain by DSPE-PEG 2000 maleimide for any conjugation with tumour targeting Asn-Gly-Arg (NGR) amide.<sup>59</sup> This novel system with efficiency crosses human glandular carcinoma cell PC-3 cytomembrane in vitro and induces additional severe necrobiosis and suppression within the proliferating cells.<sup>60</sup>

9. Cervical Cancer-Five sorts of CNTs suspensions were ready by Zhang et al., by dispersing SWCNTs, acid-treated SWCNTs, MWCNTs, acid treated MWCNTs, and amylose wrapped SWCNTs, separately in water, and also the influence of those scaffolds on human cervical malignant neoplastic disease.<sup>61</sup>

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