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*Review Article*

# Navigating the Nanoscale: Advancements in Carbon Nanotube-Based Drug Delivery Systems

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Carbon nanotubes (CNTs) are gaining attention as exciting options for drug delivery nanocarriers, thanks to their unique physicochemical properties. These include a high surface area, customizable functionalization, and excellent biocompatibility. Their knack for crossing biological barriers, zeroing in on specific cells, and enabling controlled drug release positions them as strong candidates for enhancing therapeutic effectiveness while minimizing systemic toxicity. In this review, we'll explore the latest developments in CNT-based drug delivery systems, diving into functionalization techniques, targeted delivery methods, and their applications in treating cancer, neurological disorders, and fighting infections. While carbon nanotubes (CNTs) have incredible potential, there are still hurdles to overcome, like cytotoxicity, biodegradability, and regulatory challenges, before they can be used in clinical settings. The combination of CNTs with artificial intelligence and personalized medicine techniques offers exciting possibilities for precise drug delivery. Future studies should prioritize safety and improving biocompatibility to ensure these technologies can be widely adopted in healthcare. By exploring the unique nanoscale properties of carbon nanotubes, researchers can create innovative drug delivery systems that significantly improve patient care and treatment outcomes.



## Introduction

Nanotechnology has really transformed the field of medicine, paving the way for cutting-edge diagnostic tools, therapies, and drug delivery. When we consider materials at the nanoscale, they exhibit some remarkable properties such as increased surface area, improved reactivity, and the ability to interact with biological systems in a highly specific manner [1]. These unique traits have been utilized to great effect in developing ground-breaking solutions for disease detection, delivering drugs right where they're needed, advancing regenerative medicine, and improving imaging technologies. Nanoparticles including carbon nanotubes, liposomes, dendrimers, and quantum dots have been extensively investigated for their potential to boost drug efficacy, reduce side effects, and enhance overall treatment outcomes. Nanotechnology is particularly crucial in the treatment of cancer, the management of neurodegenerative diseases, and the prevention of infections because it allows the release of drugs at the targeted site while minimizing adverse effects on the rest of the body [2]. As research advances, we can anticipate even greater developments as nanotechnology converges with artificial intelligence and personalized medicine to provide more personalized and effective treatment for patients.

CNTs are drawing attention as one of the most exciting nanocarriers for drug delivery, owing to their unique structural and physicochemical properties. With high surface area, excellent mechanical strength, and the ability to be tailored with varied biomolecules, they're ideal for loading drugs effectively and delivering them exactly where they are needed. CNTs can penetrate biological barriers, such as cell membranes, and deliver drugs, genes, and biomolecules directly into cells with impressive accuracy [3-5]. Their hollow tubular shape is ideal for encapsulating therapeutic agents, shielding them from degrading too early and increasing their efficacy. Additionally, CNTs can be engineered to release drugs in controlled and responsive ways, which improves the effectiveness of treatment while limiting side effects [6-11]. These attributes render CNTs highly desirable for the treatment of cancer, neurodegenerative diseases, and infectious disease, where there is a need for precise delivery of drugs. With continuous improvements in functionalization methods and regulatory guidelines, CNT-based drug delivery systems have the potential to transform

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modern medicine by improving treatment accuracy and patient outcomes [8, 9].

This review provides a comprehensive analysis of CNT-based drug delivery systems, focusing on their unique properties, functionalization strategies, drug delivery mechanisms, and medical applications. It explores how CNTs enhance therapeutic efficacy through targeted and controlled drug release while addressing key challenges such as biocompatibility, toxicity, and regulatory hurdles. The review highlights recent advancements in CNT-based drug delivery for cancer, neurological disorders, and infectious diseases, offering insights into their clinical potential [10]. It also examines emerging trends, including the integration of CNTs with artificial intelligence and smart drug delivery systems. While emphasizing the promising applications of CNTs, this paper critically evaluates their limitations and the steps needed for clinical translation. By presenting a balanced overview, this review serves as a valuable resource for researchers, healthcare professionals, and policymakers interested in the future of nanotechnology-driven medicine [12, 13].

## Properties of Carbon Nanotubes for Drug Delivery

Carbon nanotubes (CNTs) have emerged as a revolutionary nanomaterial in the field of drug delivery due to their exceptional physicochemical properties. Their unique hollow cylindrical structure, high surface area, and ability to be chemically functionalized make them highly effective carriers for therapeutic agents. CNTs offer several advantages such as efficient drug loading, controlled and sustained release, and targeted delivery, enhancing the bioavailability of drugs while minimizing side effects. Additionally, their mechanical strength, flexibility, and ability to penetrate biological membranes enable efficient intracellular drug transport [14]. The optical and electrical properties of CNTs further contribute to applications like photothermal therapy (PTT) and electrically triggered drug release. However, careful surface modifications are essential to improve their solubility, biocompatibility, and safety for biomedical applications. Understanding the essential properties of CNTs is crucial for optimizing their potential as advanced drug delivery systems in modern medicine [15]. The essential properties of CNTs for drug delivery is shown in figure 1.

The details of such essential properties of CNTs that contribute to their effectiveness in drug delivery applications are described below as

### Morphology and dimensional characteristics

*i. Cylindrical nanostructure*: One or more sheets of graphene are rolled up into a long cylindrical tube to form CNTs. They are highly efficient for drug loading and functionalization for use in biological applications due to their characteristic tubular structure, providing an enormous surface area [16]. In addition, CNTs can also have their ends kept open or capped with hemispherical structures approximating fullerene, and this influence the extent to which they interface with biological systems and release drugs.

*ii. Size and aspect ratio:* Due to their large length-to-diameter (aspect) ratio normally ranging from 10 to 10,000 CNTs are very versatile for a large number of applications. Depending on the variety, they possess varied dimensions. Multi-walled CNTs (MWCNTs) possess larger diameters ranging from 2 to 100 nm with proportionally larger lengths, while single-walled CNTs (SWCNTs) possess diameters ranging from 0.4 to 2 nm with lengths measuring up to a few micrometres. They are particularly useful in biomedical applications such as targeted drug delivery and gene therapy due to their ultra-thin nature, which allows deep tissue penetration [16, 17].

### Atomic structure and bonding

*i. Hexagonal carbon lattice:* CNTs have remarkable structural integrity because they consist of sp2 hybridized carbon atoms, arranged in the hexagonal shape like graphene. The structural covalent bond of such an arrangement increases its mechanical strength and thermal stability and thus renders CNTs incredibly durable and fit for applications as varied as drug delivery and nanomedicine [18].

*ii. Chirality and structural types:* CNT's chirality, or twisting angle, is defined by the way the graphene sheet is rolled up in a tube, and this has a direct influence on their electrical properties. Chiral CNTs (n "' m, n "' 0, m "' 0) tend to be semiconducting, Armchair CNTs (n = m) are metallic with high electrical conductivity, and Zigzag CNTs (n = 0 or m = 0) may either be metallic or semiconducting. Depending on their chirality indices (n, m), CNTs are classified.

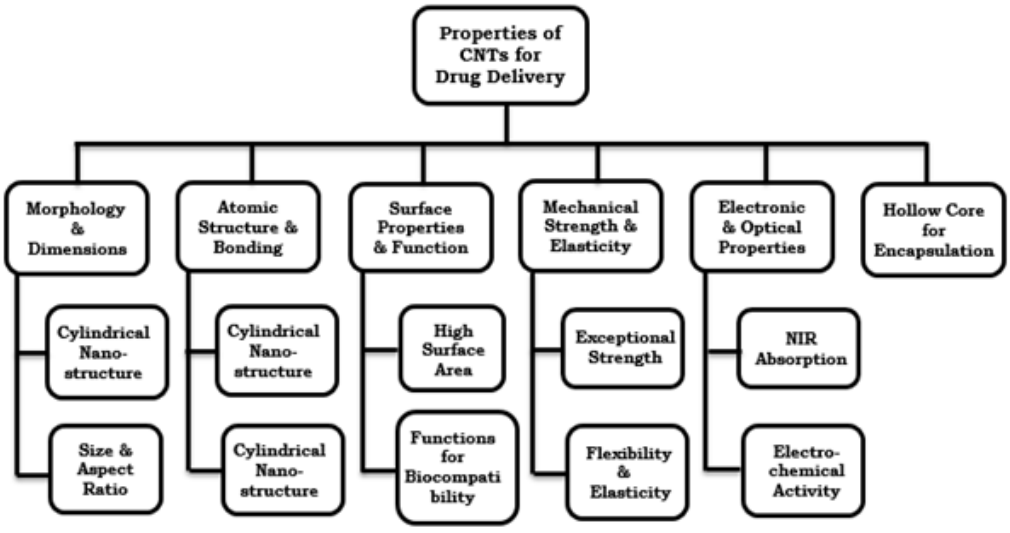


**Figure 1: Essential properties of CNTs for drug delivery depicted in tree pattern**

Due to the tunability of their electronic characteristics, carbon nanotubes (CNTs) are of the utmost importance for applications in targeted drug delivery, biosensors, and nanoelectronics [18].

### Surface properties and functionalization

*i. High surface area*: Owing to their exceedingly high surface area (~1000 $m^2/g$ for SWCNTs), CNTs can adsorb effectively drugs, biomolecules, and targeting molecules with a high loading efficiency, which significantly enhances their application in controlled drug delivery. CNTs are extremely helpful in biomedical applications owing to their enormous surface area, enabling immense drug-loading capacity and ease in functionalization towards targeted therapy.

*ii. Functionalization for biocompatibility:* The hydrophobic nature of pristine CNTs and their tendency to aggregate in wet conditions limit their usage in biomedicine. Surface modification is employed to enhance solubility, dispersion, and biocompatibility and reduce cytotoxic effects in an effort to bypass this issue. Covalent modification such as oxidation, amination, and carboxylation may be employed to modify a material and introduce a stable chemical bond with drugs or targeted ligands. As an alternative, non-covalent changes which enhance CNTs' compatibility with biomedical purposes without damaging their structure are the adsorption of polymers, surfactants, or proteins [19].

### Mechanical strength and elasticity

*i. Exceptional strength:* Owing to their excellent mechanical strength, which is a result of their sp2 carbon-carbon bonding, CNTs are more than twice as strong as steel. They are ideal for use where high strength and durability are required, such as in drug delivery systems and biomedical engineering, due to their tensile strength, which can be 50–100 times that of steel but is still surprisingly light.

*ii. Flexibility and elasticity:* CNTs are best suited for biomedical use since they can be twisted, bent, and stretched without fracturing. Their high flexibility makes it easy for them to penetrate cells, which enhances the delivery of drugs intracellularly and enhances the effectiveness of treatment [16, 20].

### Hollow core for encapsulation

CNTs can encapsulate drugs, genes, or imaging probes due to their hollow cylindrical structure, which shelters sensitive therapeutic entities and retards their degradation. This nano-confinement stabilizes and optimizes the loaded payload. Further, the internal volume of CNTs is modifiable to release drugs in response to stimuli. This maximizes targeted therapy and minimizes side effects by allowing controlled delivery through temperature- or pH-responsive triggers [18-20].

### Electronic and optical properties

*i. Near-infrared (NIR) absorption:* CNTs take up NIR light and are thus very effective for photo-thermal treatment (PTT) for cancer therapy. They produce localized heat when irradiated with NIR, which not only facilitates targeted drug release but also leads to the ablation of cancer cells, promoting the efficacy of the treatment without causing damage to healthy tissue.

*ii. Electrochemical activity:* CNTs' outstanding conductivity makes them perfectly suited for biosensors and bioelectronics, allowing real-time monitoring of drugs and controlled release [21, 22].

## Functionalization Strategies of Carbon Nanotubes

Although carbon nanotubes (CNTs) possess excellent drug-loading capabilities, their use in biomedicine is limited by their hydrophobicity and tendency to agglomerate in aqueous environments. To enhance their solubility, stability, biocompatibility, and efficacy of targeted drug delivery, functionalization is a critical strategy [23]. Covalent and non-covalent modifications are the two broad functionalization categories, and both have distinct advantages for drug delivery.

### Covalent functionalization

Covalent functionalization involves chemically modifying CNTs by forming strong covalent linkages with drug molecules or functional groups. Even though the CNT framework can be altered to some extent, this method ensures stable anchorage [24-27].

*a) Oxidation (carboxylation & hydroxylation):* By introducing carboxyl (-COOH) and hydroxyl (-OH) groups onto the surface of carbon nanotubes, oxidation significantly enhances their water solubility and reduces aggregation in biological fluids. Through the creation of ester, amide, or peptide bonds, this modification enhances the efficiency of drug conjugation and allows stable and efficient drug attachment. In targeted therapeutics, oxidized CNTs are extremely useful for the delivery of proteins, genes, or anticancer drugs. For example, doxorubicin (DOX), an anticancer drug, has been successfully loaded onto carboxylated carbon nanotubes, enhancing its targeted delivery and therapeutic efficacy while minimizing side effects [26].

*b) Amination (-NH, Functionalization):* Through the addition of amine (-NH, ) groups to carbon nanotubes (CNTs), amination enhances their solubility and cellular uptake, making them more appropriate for application in biomedical fields. Aminated CNTs can bind to negatively charged biomolecules such as DNA and siRNA with high efficiency, making it simpler for them to penetrate target cells safely and efficiently. Because CNTs are used as carriers of genetic material in gene therapy, their functionalization is particularly useful [24]. For example, plasmid DNA has been effectively delivered into cells through aminated carbon nanotubes (CNTs) and used for gene silencing and therapeutic applications in various genetic diseases.

*c) Polymer Functionalization (PEGylation):* By affixing biocompatible polymers, such as polyethylene glycol (PEG), to carbon nanotubes (CNTs), functionalization of polymers significantly increases the biocompatibility and stability of the CNTs. PEGylation extends the duration that CNTs are in the bloodstream and reduces early clearance by inhibiting recognition by the immune system. This modification also minimizes toxicity without altering the high drug-loading potential of the CNTs, making them effective drug carrier therapeutic agents. PEG-functionalized CNTs, for example, are most commonly used in cancer treatment to facilitate the transport of drugs better along with reducing deleterious side effects and maximizing treatment outcomes [27].

### Non-covalent functionalization

Although facilitating attachment of drugs or biomolecules by weak forces (ð-ð stacking, van der Waals forces, electrostatic interactions, or hydrophobic forces), non-covalent functionalization preserves the integrity of the carbon nanotube structure.

*a) Surfactant functionalization:* By employing substances like sodium dodecyl sulphate (SDS) or pluronic, surfactant functionalization effectively disperses CNTs in water by lowering aggregation and enhancing their stability in biological fluids. Due to this modification, CNTs exhibit much greater bioavailability, thus rendering them more suitable for application in biological fields.

Surfactants also enable hydrophobic drugs to be loaded effectively, enhancing therapeutic outcomes and enabling custom drug delivery. For example, surfactant-coated CNTs are often used for the delivery of hydrophobic anticancer medicines, enhancing solubility in the blood and ensuring better distribution of the drugs within the body [28-31].

*b) ð-ð Stacking and hydrophobic interactions:* Through ð-ð stacking interactions between the drug and aromatic rings of the CNTs, drug molecules can be attached to CNTs non-covalently, enabling efficient drug loading without altering the structure of the CNT. This method preserves the integrity and conductivity of CNTs, making it ideal for targeted therapies with controlled drug release. The ð-ð interactions which the doxorubicin (DOX) exploits to bind onto CNTs, for example, facilitate high drug-loading efficiency and pH-sensitive release in cancer cells, ensuring precise drug delivery with minimum adverse effects on healthy tissues [30].

*c) Biomolecule functionalization (peptides, antibodies, ligands):* By binding to specific cells or receptors, biomolecules such as transferrin, folic acid, peptides, and antibodies can be functionalized onto CNTs to provide targeted drug delivery. By enhancing cell-targeted drug delivery, this functionalization reduces toxicity in healthy tissues and reduces off-target effects. Folic acid-functionalized CNTs, for example, are designed to target cancer cells specifically, increasing medication concentration at tumor sites and improving the efficacy of cancer therapy while decreasing undesirable side effects [32].

### Dual Functionalization for smart drug delivery

Stimuli-responsive CNT-based drug delivery devices can be created by hybridizing covalent and non-covalent methods:

*a) pH-responsive CNTs:* Under acidic environments, such as those found in lysosomes and tumors, pH-sensitive polymers coated functionalized CNTs permit controlled drug release. By minimizing drug release in normal tissues, this targeted approach significantly reduces side effects and enhances therapeutic efficacy. pH-sensitive polymers-coated doxorubicin-loaded CNTs, for instance, improve cancer therapy while minimizing systemic toxicity due to their ability to selectively release the drug in the acidic tumor environment but remain stable under physiological conditions [33-35].

*b) Light-triggered release:* Near-infrared (NIR) light is absorbed by CNTs, generating localized heat that can be utilized to trigger medication release on demand. This property is widely applied in photothermal therapy (PTT), a cancer therapy technique that employs precisely controlled heat to destroy cancer cells with minimal damage to surrounding healthy tissues. For example, gold nanoparticle-coated CNTs enhance NIR absorption and release drugs upon exposure to radiation, delivering therapeutic drugs to cancer sites effectively and inducing hyperthermia that kills cancer cells [36-38].

*c) Temperature-responsive drug release:* Temperature-sensitive polymer-coated CNTs can release drugs at elevated temperatures, making them suitable for the treatment of localized hyperthermia or diseases associated with fever. At specific temperature levels, such polymers structurally change in response to temperature, enabling controlled drug release. To ensure targeted and responsive drug release while restricting early release under normal physiological conditions, CNTs functionalized with poly(N-isopropylacrylamide) (PNIPAM), for instance, release drugs when the temperature of the body rises above 37°C [39].

## Mechanisms of CNT-Based Drug Delivery

Drug delivery systems based on carbon nanotubes (CNTs) employ a number of techniques for efficient delivery of therapeutic drugs to targeted sites.

The structural properties of CNTs, their functionalization, and the nature of the medication being delivered are the primary factors that determine these pathways. Among the major mechanisms are:

### Passive diffusion and endocytosis

Due to their hydrophobic cell membrane interactions and nanoscale dimensions, CNTs are capable of entering cells by passive uptake, allowing efficient drug delivery. For further enhanced intracellular drug delivery, they are also internalized via endocytosis via the clathrin-mediated, caveolae- mediated, and macropinocytosis routes. CNTs are highly effective carriers for drug delivery applications with targeted delivery due to their multiplicity of entry pathways, which also enhance the bioavailability of medicinal compounds [40, 41].

### Conjugation and functionalization-based delivery

Drugs may be functionalized on the surface or within the hollow structure of carbon nanotubes via covalent or non-covalent


**Figure 2: Key mechanisms of CNT-based drug delivery**

methods, enhancing the efficacy of drug delivery. Functionalized CNTs enhance therapeutic potency by facilitating controlled drug release, reducing systemic toxicity, and enhancing solubility and stability [42]. Due to these modifications, CNTs find application in many drug delivery mechanisms, ensuring targeted and controlled care.

### pH-responsive and stimuli-triggered release

On exposure to external stimulants such as light, heat, or ultrasound, or pH changes like those in the tumor microenvironment, CNTs may be designed to release drugs. Through targeted delivery of these drugs to a specific site, this controlled release reduces systemic toxicity and enhances therapeutic effectiveness. CNT-based drug delivery devices that respond to specific biological or external stimuli offer a more effective and safer means of treatment [43].

### Nuclear and mitochondrial targeting

Due to their high aspect ratio, CNTs are able to deliver drugs directly to subcellular sites for enhanced therapeutic impact by penetrating deep into the mitochondria or cell nucleus. This precise intracellular delivery reduces side effects but enhances therapeutic efficiency. Through these mechanisms, CNTs are very efficient carriers for precision drug delivery purposes, promising much in individualized and customized therapy [44,45].

## Applications of Carbon Nanotube Drug Delivery Systems

With their extraordinary aspect ratio, modifiable surface chemistry, and impressive ability to penetrate cells, carbon nanotubes (CNTs) have been turned into the nanocarriers of the next generation for exact and controlled drug delivery [46,47]. These carbon nanotubes, which can be single-walled (SWCNT) or multi-walled (MWCNT), offer the loading of one medicinal compound in a high manner through covalent bonding or non-covalent interactions like hydrophobic adsorption and ð–ð stacking [48]. Their surfaces may be functionalised with polymers, biomolecules, ligands, or antibodies, to facilitate their solubility, targeted delivery, and biocompatibility. CNT-based drug delivery systems (CNT-DDS) have drawn substantial interest in the pursuit of translation to the clinic in precision medicine, given their remarkable potential [49]. Cancer treatment, antimicrobial treatment, gene silencing, neuroprotection, immunomodulation therapies, cardiovascular therapies, and tissue regeneration are all areas where existing CDT-DDS research has limitations [50,51].

### Cancer chemotherapy and targeted therapy

Carbon nanotubes (CNT-DDS) are the leading platform that researchers have examined for delivery of chemotherapeutic drugs to improve the therapeutic efficacy of various drugs, including doxorubicin, paclitaxel, cisplatin, gemcitabine, and methotrexate, via improvements in biodistribution, cellular uptake, tumor retention, and reductions in systemic toxicity [52,53]. Furthermore, carbon nanotubes (CNT) are able to demonstrate both a passive targeting step via the EPR effect and display active targeting step with tumor specific ligands (folic acid, hyaluronic acid, transferrin, RGD peptides, and HER2 antibodies) to localize selectively to tumor sites [54,55]. Once inside the cell via receptor-mediated endocytosis or direct membrane diffusion, the small size of CNTs can be a means of intracellular controlled drug release as lysosomes have an acidic environment [56]. In addition, CNTs currently allow combined modalities in cancer therapy by providing chemotherapy with photothermal or photodynamic effects resulting in tumor death at a site-sensitive level and giving normal tissue less risk of damage. For example, hyaluronic acid functionalized MWCNTs loaded with gemcitabine are a specific and effective route to targeting the CD44 receptor in colon cancer [57-59].

### Photothermal and photodynamic therapy

Carbon nanotubes (CNTs) strongly absorb light over the near-infrared (NIR) region (650–900 nm), thus allowing very efficient energy transformation that can then be used for cancer treatments [60]. Essentially, a major part of the function of CNTs in photothermal therapy (PTT) is to act as nano-heaters. By the conversion of NIR light into localized thermal energy, tumor cells are made apoptotic or necrotic in a targeted way with the least possible collateral damage of healthy tissues [61]. Moreover, CNTs are a very effective therapeutic delivery module for photodynamic therapy (PDT), which involves the delivery of photosensitizers (e.g., porphyrins or indocyanine green) via CNTs [62]. These photosensitizers generate dilapidating intracellular reactive oxygen species (ROS) when light-activated and use CNTs to gain access to cancerous tissue [63]. In addition to these single modalities, CNTs are now being rapidly explored in the literature for their use in synergistic combination of chemo-photothermal therapy protocols in which heating to a maximum temperature provides permeability to the cells allowing improved drug penetration into the tumor, with the result being an increased therapeutic effect with a lower resistance to the drug.

### Gene and RNA delivery

SWCNTs are considered as gene vectors as among the most effective non-viral delivery vehicles due to their unique structural and physicochemical properties [64]. In principle, CNTs can be used as a single platform to deliver many different types of genetic material including siRNA, miRNA, shRNA, mRNA, CRISPR–Cas9 plasmids, and antisense oligonucleotides [65]. Besides, they can shield nucleic acids from being degraded by enzymes in the circulation. CNTs are generally less immunogenic than viral vectors since they can effortlessly translocate across the membrane and thus many nucleic acids are able to be taken up by the cells [66,67]. The nucleic acids can bind with the carbon nanotube surfaces mainly through electrostatic interactions and ð–ð stacking, thereby allowing a comparatively controlled cellular genetic material release.

An essential application was the delivery of siRNA by CNTs for the purpose of silencing VEGF that cardinally inhibited angiogenesis in lung cancer models and thus provides the therapeutic practice of great value for a vast range of gene silencing applications [68-70].

### Neurological disorders

The ability of carbon nanotubes (CNTs) to breach the blood-brain barrier (BBB), a crucial barrier inhibiting the care of neurodegenerative diseases, makes them an interesting strategy for treating conditions of the CNS. When functionalized and paired with targeting ligands such as transferrin or Apo-E peptides, CNTs are able to deliver neuroactive medications to the brain and permits delivery to have a higher degree of targeting and control with minimal systemic side effects [71,72]. There is new evidence for the utility of CNTs as carriers for CNS-targeted therapeutic delivery for glioblastoma chemotherapeutic drugs, acetylcholinesterase inhibitors for the treatment of Alzheimer's disease, and dopamine or selegiline for the treatment of Parkinson's disease [73-75].

### Antimicrobial and antiviral therapy

CNTs are primarily attributed to a more accurate delivery of

antibiotics and antiviral drugs, representing a potential application as a nanocarrier for antimicrobial therapy [76]. Functionalised CNTs could penetrate bacterial biofilms more effectively and potentially improve the targeted delivery of treatments such as vancomycin, tetracycline, and ciprofloxacin and allow targeted treatment of osteomyelitis, tuberculosis, and other disorders involving oral biofilms [77]. To breathe oxidative stress into bacteria and disrupt their membranes, CNTs being one of the most potent weaponries in the fight, do not only serve as carriers but also have an inherent antimicrobial effect. Besides, they are also being considered for the delivery of antiviral drugs such as remdesivir and acyclovir which, when administered, provide better therapeutic results against resistant infections, prolonged release, and increased bioavailability [78].

### Cardiovascular diseases

Carboxylated carbon nanotube drug delivery systems (CNT-DDS) utilizing functionalised carbon nanotubes (CNTs) as a method of delivering anti-inflammatory and anti-proliferative drugs in a safe and targeted manner, also represents one of the most exciting therapeutic options for patients suffering cardiovascular ailments [79]. As such, intervention with functionalized CNTs improves the therapeutic effectiveness and reduces complications like restenosis after the procedure of angioplasty [80]. CNTs enable the ability to specifically deliver siRNAs and nitric oxide donors to the damaged endothelium and promote tissue regeneration while also decrease atherosclerotic plaques [81]. Lastly, CNT stents will permit continuous drug release and more effective vascular healing and management of thrombus.

### Imaging and theranostics

Carbon nanotubes (CNTs) are a single entity capable of both therapy and diagnosis due to their theranostic properties. CNTs deliver ultra-high-resolution imaging of living systems by being employed as contrast agents in MRI, Raman spectroscopy, photoacoustic, and fluorescence imaging which take advantage of their unique optical and magnetic properties [82]. They can provide the same visualization in vivo of the drug release and biodistribution during the therapy hence the multifunctional platform they are [83]. To achieve treatment accuracy, a single-walled CNT–doxorubicin compound that is NIR (near-infrared) light-activated can not only localise chemotherapy be tumour imaging but also visualise tumour accumulation [84].

### Vaccine delivery and immunotherapy

Functionalised carbon nanotubes (CNTs) as part of vaccine delivery systems are the most suitable candidates for antigen transporters and efficient nano-adjuvants [85]. Being at the nanoscale, they make the absorption by dendritic cells easy, while their huge surface area allows effective binding of peptide or protein antigens [86]. Moreover, carbon nanotubes (CNTs) enhance vigorous T-cell activation and prolonged immunological memory. In a variety of non-human studies, such as the case of the carbon nanotubes (CNTs) conjugated with melanoma peptide antigens, a very strong anti-tumor immunity was elicited, thereby pointing to their dual potential application in infectious disease vaccines as well as in cancer immunotherapy [87].

### Tissue engineering and regenerative medicine

Carbon nanotubes (CNTs) paired with hydrogels or polymeric scaffolds provide topical and controlled drug release for tissue engineering and regenerative medicine [88,89]. The actual combined use of CNTs and hydrogel or polymeric scaffolds can create regeneration of bone and blood vessels as it enhances the mechanical properties and bioactivity of the scaffold, while also allowing for sustained release of growth factors, i.e., VEGF and BMP-2 [90]. In addition, electrically conductive CNT-based scaffolds can also be used for the recovery of neural tissue and the controlled release of anti-inflammatory agents that can accelerate the wound healing process.

## Challenges and Risks

Carbon nanotube-based drug delivery systems hold incredible promise for advancing precision medicine thanks to their unique structural and physicochemical properties. However, several challenges and risks stand in the way of their clinical use. Key concerns include cytotoxicity, long-term biocompatibility, and the potential for accumulation in essential organs. The safe application of these systems is further complicated by issues related to purity, especially with leftover metal catalysts, and the lack of standardized techniques for functionalization. Additionally, inconsistent drug loading and release profiles, along with unclear mechanisms for biodistribution and clearance, add to the safety worries. On top of that, we need to navigate regulatory challenges, consider the environmental impact, and address public skepticism about nanomaterials to ensure that these technologies are implemented responsibly and effectively. These challenges and risks can be broadly categorized as (**figure 3**).

Here are six major challenges and risks that stand in the way of effectively translating carbon nanotube (CNT)-based drug delivery systems into clinical practice:

*a) Toxicity and biocompatibility:* Unmodified carbon nanotubes (CNTs) can cause harmful effects like oxidative stress, inflammation, mitochondrial damage, and even cell death. The severity of these effects can vary based on factors like size, length, surface area, and purity. Studies in animals have shown that CNTs can accumulate in organs such as the liver, spleen, lungs, and kidneys, raising serious safety concerns about their long-term effects in living organisms. Additionally, multi-walled CNTs (MWCNTs) can provoke immune responses, which may lead to chronic inflammation or the formation of granulomas.

*b) Purity and catalyst contamination:* When carbon nanotubes are produced through chemical vapor deposition (CVD), they often end up with leftover metal catalysts like iron (Fe), cobalt (Co), or nickel (Ni), which can be toxic. Completely eliminating these catalysts is not only difficult but also expensive, yet it's crucial for ensuring that CNTs are safe and compatible for use in biomedical applications.


**Figure 3: Highlighting the major challenges and risks**

**Table 1: Comparison between recent trends and future directions**

| Aspects | Recent Trends | Future Directions |
|---|---|---|
| Functionalization Strategies | Covalent and non-covalent functionalization improve solubility and targeting. | AI-driven, patient-specific functionalization enables personalized delivery. |
| Drug Release Mechanisms | Stimuli-responsive systems (e.g., pH, temperature, redox) for controlled drug release. | Real-time, programmable, feedback-controlled drug release systems. |
| Therapeutic Focus | Focused mainly on cancer and antimicrobial therapies. | Expanding into neurodegenerative, genetic, and autoimmune diseases. |
| Theranostic Capabilities | CNTs enable combined drug delivery and basic imaging (MRI, fluorescence). | Smart theranostics with biosensing and real-time diagnostics. |
| Toxicity and Biocompatibility | Reducing short-term toxicity via surface modifications. | Long-term safety, biodegradability, and regulatory compliance. |
| Manufacturing and Clinical Translation | Lab-scale synthesis with scalability and reproducibility challenges. | Focus on scalable, green manufacturing and GMP-compliant production. |

*c) Inconsistent drug loading and release:* The way drugs are adsorbed or encapsulated on CNT surfaces can be quite uneven, resulting in inconsistent dosages of therapeutic agents and diminished effectiveness. Moreover, achieving controlled drug release is tricky, especially given the varying physiological conditions like pH levels, enzyme activity, and redox states. These challenges call for advanced functionalization techniques to ensure precise, targeted, and reliable drug delivery.

*d) Biodistribution and clearance:* Carbon nanotubes have a long half-life in living organisms and tend to build up in critical organs such as the liver, kidneys, and lungs over time, which raises concerns about long-term toxicity. Furthermore, the pathways through which they are cleared—likely involving the liver and kidneys—are still not well understood and can be inefficient. This slow elimination process raises alarms about bioaccumulation, potentially leading to long-term health risks and complicating clinical safety assessments.

*e) Manufacturing and scalability:* Producing high-purity, reproducible carbon nanotubes (CNTs) on a large scale is a tough nut to crack and can be quite expensive. This challenge could hinder the broader clinical and commercial use of CNT-based drug delivery systems. The technical complexities and high costs associated with large-scale production of these CNTs present significant hurdles that may slow down their adoption in the medical field.

*f) Environmental and occupational risks:* The inhalation of CNTs during their production poses serious health risks to workers, much like asbestos exposure does. Additionally, if CNT-based materials are not disposed of properly, they can lead to environmental toxicity, as their long-lasting nature and interactions with ecosystems can be harmful to biological systems. It's crucial to ensure safe handling, disposal, and regulation to minimize these environmental and health risks.

## Recent Trends and Future Development

Thanks to their unique structural, mechanical, and chemical properties, carbon nanotubes (CNTs) are becoming increasingly popular in drug delivery systems, sparking significant interest in the field of nanomedicine. As research continues to evolve, the latest advancements in CNT-based delivery systems are paving the way for groundbreaking approaches in targeted therapy. To enhance treatment outcomes and facilitate clinical translation, it is vital to bridge the gaps between current methods and the promising future pathways. **Table 1** provides a comparison of recent trends and future directions for CNTs across various aspects.

To enhance accuracy, safety, and therapeutic efficiency, advanced technology must be incorporated in carbon nanotube (CNT)-mediated drug delivery. Important areas of progress consist of:

### Integration with artificial intelligence (AI) for precision medicine

By ensuring precise and efficient drug delivery, predictive models based on AI can enhance drug loading, release kinetics, and carbon nanotube functionalization, enhancing therapeutic efficacy [91]. By optimizing medication dosages and targeting strategies to minimize side effects and maximize efficacy, machine learning algorithms can also analyze patient data to tailor CNT-based therapies [92,93]. Additionally, real-time tracking of CNT dispersion is enabled by AI-powered imaging and tracking systems, enhancing treatment accuracy and providing insightful data regarding drug dynamics in the body [94]. AI-powered CNT-based drug delivery holds vast potential to reshape patient-specific therapeutics and push precision medicine to the next level [95].

### Smart CNT-based drug delivery systems

To improve targeted therapy, scientists are developing stimuli-responsive CNTs that release medication under controlled conditions in response to pH, temperature, light, or magnetic field changes. Additionally, on-demand, real-time treatment is achieved through nanorobotic CNTs coupled with biosensors, which are able to detect disease biomarkers and administer medication autonomously as needed. Moreover, by increasing stability, targeting accuracy, and controlled release mechanisms, hybrid CNTs with hydrogels or nanoparticles can ensure more efficient and precise drug delivery. Precision medicine and personalized treatment protocols might be revolutionized entirely with these advancements in intelligent CNT-based systems [96,97].

### Innovations in biodegradable CNTs for enhanced safety

The synthesis of biodegradable carbon nanotubes that have functionalized coatings enhancing their excretion out of the body and reducing long-term toxicity issues is an area of growing interest [98]. Researchers seek to enhance the biocompatibility and safety profile of CNTs for treatment purposes by having them break down into non-toxic products. In addition, advances in graphene-based and carbon-derived nanomaterials are unveiling the prospect of greener and safer drug carriers by offering innovative alternatives that hold excellent therapeutic performance coupled with minimal side effects [99-101]. These developments could expedite the translation of CNT-based drug delivery devices into clinics and overcome current limitations.

CNT-based drug delivery systems can revolutionize precision

medicine by integrating AI, intelligent nanotechnology, and biodegradable materials to deliver safer, more effective, and more targeted therapeutic options.

## Conclusion

Carbon nanotube -based drug delivery systems have shown enormous promise in transforming nanomedicine through the delivery of precise, effective, and targeted therapeutic interventions. Their remarkable physicochemical characteristics, such as high drug-loading capacity, structural flexibility, and capacity to penetrate biological barriers, have made them promising candidates as carriers for numerous therapeutic agents, ranging from chemotherapeutics, nucleic acids, to proteins [102]. Functionalization methods have greatly enhanced CNT biocompatibility, lowering toxicity issues and improving targeted delivery. Moreover, the integration of CNTs with imaging technologies has facilitated real-time monitoring, enhancing therapeutic monitoring and precision medicine strategies. In the future, CNT-based drug delivery systems possess transformative power in personalized medicine, regenerative therapies, and theranostics [103,104]. Their capacity to increase drug efficacy while reducing side effects may revolutionize cancer therapy, neurodegenerative disease treatment, and antimicrobial uses. With ongoing research and inter-disciplinary interaction, CNTs are likely to revolutionize contemporary medicine in a big way, opening avenues for more effective, safer, and highly specific therapeutic interventions in the times to come [105].

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