



“Carbon Based Nanodots: Recent Advances in Fabrication, Functional Properties, and Drug Delivery for Cancer Therapy”

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Abstract:

Carbon-based nanodots (CNDs) are a promising family of nanomaterials that have drawn interest due to their unique physicochemical properties, remarkable biocompatibility, and tunable optical features. These nanostructures, typically smaller than 10 nm, are perfect for biomedical applications due to their high surface area, strong photoluminescence, and ease of functionalization. Over the past ten years, a lot of research has been done on the development of flexible manufacturing techniques, including bottom-up strategies like pyrolysis, hydrothermal, and microwave-assisted procedures, as well as top-down strategies like arc discharge and laser ablation. Utilizing natural biomass, green synthesis has also surfaced, providing environmentally friendly alternatives with comparable structural and functional characteristics” intrinsic qualities such as their small size, surface functional groups, and high solubility allow for controlled release and efficient drug loading, which has significant advantages for targeted cancer treatment. Functionalization methods like ligand conjugation and PEGylation further enhance their stability, biocompatibility, and tumor-targeting potential. CNDs facilitate passive targeting via the enhanced permeability and retention (EPR) effect and active targeting via receptor-mediated pathways. Stimuli-responsive designs have enhanced therapeutic effects and decreased systemic toxicity by allowing precise spatiotemporal medication release that is triggered by light, temperature, or pH.

Apart from conventional chemotherapy, CNDs have shown remarkable potential in gene transfer, theragnostic applications, photodynamic therapy, photothermal therapy, and the integration of imaging and therapy on a single platform. Reproducibility, long-term stability, large-scale production, and comprehensive in vivo safety assessment remain challenges despite these positive advancements. The potential of carbon-based nanodots as efficient and adaptable drug delivery vehicles for cancer treatment is emphasized in this review, which also highlights recent advancements in their production, structural and functional characterization, and biomedical applications. More research focusing on clinical translation, hybrid nanostructures, and tailored treatment strategies is expected to improve the utility of CNDs and create new opportunities for precision oncology.

Keywords: Carbon Nanodots, Drug Delivery, Cancer Therapy, Nanomedicine, Photoluminescence, Surface Functionalization, Theragnostic.

Introduction:

Nanotechnology has revolutionized biomedical research by offering versatile platforms for imaging, diagnostics, and drug delivery. Among the various nanomaterials, carbon-based nanodots (CNDs) have attracted a lot of attention due to their unique structural and optical properties. Because of their strong photoluminescence, remarkable water solubility, chemical inertness, and low toxicity, CNDs are perfect for biomedical applications. Usually, they are smaller than 10 nm. Unlike traditional inorganic quantum dots, CNDs are environmentally benign and biocompatible, addressing the primary safety concerns associated with heavy-metal-based nanomaterials. Using both top-down and bottom-up approaches, the production of CNDs has advanced dramatically over the past ten years. Arc discharge, laser ablation, and electrochemical methods are examples of top-down strategies that rely on breaking down larger carbon structures. In contrast, pyrolysis, hydrothermal, and microwave-assisted processes are examples of bottom-up techniques that combine carbon sources into nanoscale dots.

Recently, green synthesis methods that employ renewable resources and natural biomass have emerged as environmentally friendly alternatives, producing CNDs with modifiable properties suitable for biological applications. Given that conventional therapeutic approaches usually have shortcomings like poor solubility, systemic toxicity, and lack of selectivity, one of the most promising applications for CNDs is cancer therapy. Because of their small size, high surface area, and versatile surface chemistry, CNDs can efficiently load therapeutic agents, target tumor tissues, and release drugs in a controlled manner. Functionalization with polymers, ligands, or targeting moieties enhances their stability, biocompatibility, and tumor-specific accumulation. In addition to drug delivery, CNDs have shown promise in theragnostic applications, which combine therapy and imaging on a single platform. Their intrinsic fluorescence allows for real-time tracking of drug distribution, and stimuli-responsive designs allow for precise spatiotemporal release, improving therapeutic efficacy and minimizing off-target effects. This study aims to provide a comprehensive overview of recent advancements in the synthesis, functionalization, and therapeutic applications of carbon-based nanodots, with a focus on their use as multifunctional drug delivery vehicles for the treatment of cancer. The challenges, limitations, and prospects are also discussed, highlighting the potential of CNDs in the next generation of precision oncology.

2. Fabrication of Carbon Nanodots:

The synthesis process has a significant impact on the size distribution, optical properties, surface chemistry, carbon core structure, and biocompatibility of carbon nanodots, or CDs. The literature categorizes these into three general groups: top-down, bottom-up, and increasingly green/biomass-derived techniques.(1,2)

2.1 Top-Down Approaches:

Top-down methods are used to break down larger carbon allotropes, including graphite, graphene, carbon soot, and carbon nanotubes, into nanoscale fragments.

a) Chemical oxidation / oxidative “cutting”:

Strong oxidants (like HNO_3 , H_2SO_4 , and KMnO_4) are used on bulk graphitic or carbonaceous materials to break down carbon skeletons. Furthermore, during oxidation, oxygenated functional groups ($-\text{COOH}$, $-\text{OH}$) are added, which enhances water dispersion and permits surface modifications afterwards.(2) The severe conditions, however, may cause a broad size distribution, require extensive purification, and introduce structural flaws.(3)

b) Laser ablation / arc discharge:

Pulsed laser ablation of a carbon target in a liquid or gas phase produces vaporized carbon clusters that condense into nanoparticles, much like arc discharge between graphite electrodes vaporizes carbon, which then recondenses into soot, from which nanodots are separated.(4) Although they offer comparatively pure carbon cores, these have limited scalability and high instrumentation costs.(5)

c) Electrochemical etching / exfoliation:

Carbon electrodes, like graphite rods, are electrochemically oxidized in electrolyte media; the resulting carbon fragments nucleate to form CDs. The method offers control over current, potential, electrolyte, and additives to modify size and surface states. Recent technologies like “resculpting” (post-etch electrochemical trimming) enable size refinement and quantum yield enhancement.(6)

d) Mechanical / sonication fragmentation:

Bulk carbon (like graphite or carbon black) can be sheared, ultrasonically sonicated, or milled to break bonds; moderate oxidation is often added to improve dispersibility. However, such methods can lead to a large size spread if they are not properly regulated.(7) Despite the fact that top-down methods can yield strong graphitic cores and are helpful for starting from well-defined carbon sources, their frequent low conversion yield, wide size dispersion, structural damage, and difficult purification limit their applicability in precise biomedical contexts.(8)

2.2 Bottom-Up Approaches:

Bottom-up strategies build CDs from small molecular or polymeric precursors, involving processes such as condensation, nucleation, carbonization, and surface passivation.(7)

a) Hydrothermal / solvothermal methods:

Organic precursors, including polymers, citric acid, glucose, and amino acids, are heated and sealed under pressure. With the aid of surface chemical groups to stabilize them, carbon nuclei undergo dehydration, polymerization, and aromatization to form nanodots. Reaction parameters, such as temperature, duration, precursor ratios, and pH, control dot size, doping, and optical properties.(4) A recent review on hydrothermal synthesis emphasizes the impact of precursor and reaction conditions on the shape of carbon dots and PL behavior.(9)

b) Microwave-assisted synthesis:

Microwave irradiation speeds up reaction kinetics and enables very rapid volumetric heating, allowing CDs to form in a matter of minutes. This method often results in narrower distributions and is believed to be energy efficient.(10) Bottom-up microwave-based methods are commonly used in large-scale synthesis reviews.(7)

c) Thermal pyrolysis / carbonization:

Thermal breakdown of organic precursors creates nanoscale domains from the carbon nuclei in inert or controlled atmospheres. Some variations use ionic liquids or molten salts to influence doping or surface states.(8) For instance, the review "Large Scale Synthesis of Carbon Dots and Their Applications" classifies solid-phase carbonization and pyrolysis as scalable techniques.(11)

d) One-pot condensation / polymerization → CDs:

Some methods involve direct condensation or polymerization of small molecules (sometimes solvent-free), forming carbonaceous polymer networks that evolve into fluorescent nanodots with in situ surface passivation.(12)

e) Sono chemical bottom-up routes:

Ultrasonic energy may aid in the creation, mixing, and fragmentation of radicals during bottom-up synthesis, potentially assisting in the regulation of nucleation and growth.(13) Bottom-up approaches usually allow for more precise control over size, heteroatom doping (N, S, and P), and surface passivation, often leading to higher fluorescence quantum yields. However, challenges include removing small molecule by-products, batch repeatability, and strict purification.(14)

2.3 Green / Biomass-Derived Synthesis:

There is growing interest in sustainable, biocompatible synthesis using natural or waste carbon sources rather than pure chemical reagents.

a) Biomass / waste precursors:

Initial carbon sources have included proteins, polysaccharides, shells, fruit peels, leaves, and agricultural waste. Intrinsic heteroatoms (phosphorus, sulfur, and nitrogen) in biomass may facilitate self-doping during synthesis. A review of biomass-derived CD strategies, doping effects, and applications is provided.(4)

b) Mild aqueous, one-pot processing:

Reactions in water without strong acids or dangerous solvents simplify purification and reduce risks under mild conditions; these environmentally friendly hydrothermal or microwave methods are attractive for scale-up.(15)

c) Solvent-free / minimal reagent methods:

By pyrolyzing or catalytically carbonizing dried biomass or precursor solids without the use of solvents or other reagents, certain designs minimize waste. Batch variability, size homogeneity, and nucleation are challenging to control, though.(8)

d) Hybrid green strategies:

Numerous methods employ templating, catalytic aid, or mild post-treatment (like passivation or size reduction) to lessen biomass heterogeneity to combine the benefits of green feedstocks with performance and control.(16) Despite its appeal because of its low cost, safe processing, and biological compatibility, green synthesis frequently leads to less stringent size control, lower maximal quantum yields, and batch-to-batch variability when compared to carefully calibrated chemical bottom-up approaches.(2)

3. Comparative Observations: Yield, Size, PL, Scalability:

A comparative evaluation of synthesis techniques highlights how each approach uniquely influences the yield, particle size uniformity, photoluminescence (PL) behavior, and scalability of carbon-based nanodots. The interplay between process parameters and precursor chemistry largely determines these performance metrics.

3.1 Yield & scalability:

Bottom-up hydrothermal and microwave techniques are more scalable (gram scale or greater) and frequently yield higher carbon conversion than many top-down methods. Solid-state or electrochemical methods also show promise for scalability.(17) In electrochemical pathways, scalability and tunability are balanced.(18)

3.2 Size control & uniformity:

Microwave-assisted and controlled hydrothermal syntheses often result in narrower size distributions; electrochemical adjustments, like resculpting, further enhance homogeneity. Top-down fragmentation typically results in broader distributions.(19)

3.3 Photoluminescence / quantum yield (QY):

Both the type of surface states (defects, dopants, and functional groups) and the conjugated carbon core have an impact on PL. Usually, bottom-up methods employing passivating agents or heteroatom sources yield higher QYs. Post-treatment techniques such as electrochemical etching (resculpting) have been shown to significantly raise QY in top-down generated dots.(20) The PL process includes quantum confinement, surface defect states, fluorophore emission from molecules, and cross-chain enhanced emission states.(21)

3.4 Purity & reproducibility:

Well-defined chemical bottom-up syntheses generally exhibit higher repeatability than biomass approaches, even though rigorous purification (dialysis, chromatography, centrifugation) is required in every scenario.(22)

3.5 Trade-offs:

In biological or drug delivery contexts, the objective is often to achieve high fluorescence efficiency, monodispersed, high purity, and customizable surface functionalization rather than maximizing yield. As a result, a technology that provides high control, but low yield is commonly used. A few innovative studies employ hybrid or integrated methods to optimize yield, homogeneity, and performance. For example, a bottom-up synthesis employing biomass and mild electrochemical or thermal post-treatment, or combining templating and passivation stages.(23) A comparative summary of various fabrication methods for carbon-based nanodots, highlighting their yield, scalability, size uniformity, photoluminescence properties, and reproducibility aspects.

Table 1: Comparative Summary of Carbon Nanodot Fabrication Techniques (18-23)

Parameter	Top-Down Methods	Bottom-Up	Green / Biomass-Derived Synthesis	Remarks
Yield & Scalability	Moderate to low yield; limited scalability	High yield (gram-scale possible); scalable	Variable yield; depends on feedstock composition	Bottom-up preferred for mass synthesis
Size Control & Uniformity	Broader size distribution	Narrower, more uniform sizes	Broader distribution; influenced by natural precursor heterogeneity	Hydrothermal & microwave give consistent nanosized
Photoluminescence / Quantum Yield	Moderate QY; improved by post-treatment	Typically, high QY (passivation, doping)	Moderate QY; may require passivation or doping to improve	PL influenced by surface states and core structure
Purity & Reproducibility	Variable; depends on precursor	High reproducibility; requires purification	Low reproducibility; varies with biomass source	Chemical synthesis > biomass in consistency

Trade-offs	Simpler setup, less control	High control but sometimes lower yield	Eco-friendly and cost-effective but less controllable	Hybrid or green modifications can balance yield and purity
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4. Structural and Functional Properties:

Shape, optical behavior, surface chemistry, and biological stability are some of the structural and functional properties of carbon nanodots (CNDs or CDs) that determine their suitability for imaging, sensing, and drug delivery applications,(24)

4.1 Morphology and size:

Transmission electron microscopy (TEM), the main technique for evaluating the core size, crystallinity, and lattice fringes of CDs, often reveals near-spherical particles with sizes of less than 10–15 nm and occasional graphitic lattice fringes at high resolution.(25) Scanning electron microscopy (SEM) complements transmission electron microscopy (TEM) by revealing particle aggregation, surface roughness, and larger-scale morphology on substrates. SEM is particularly useful for assessing film or composite samples that contain CDs.(23)

Atomic force microscopy (AFM) often reports heights consistent with TEM diameters when particles are widely dispersed. Additionally, AFM offers three-dimensional topography and height profiles that help with thickness/height measurements (useful for graphene quantum dot variants) and the separation of individual dots from tiny aggregates.(18) Crystalline domains or amorphous carbon shells within single dots can be seen using high-resolution transmission electron microscopy (HRTEM), which is frequently used to connect structural domains with optical properties.(26)

4.2 Optical properties:

The emission mechanisms of carbon dots, which show strong photoluminescence (PL) ranging from the blue to the near infrared depending on size, surface chemistry, and degree of conjugation, are believed to be a combination of quantum confinement, surface/defect states, and molecular fluorophore contributions.(19) The inhibition of non-radiative recombination pathways, heteroatom doping (such as N or S), and surface passivation all have a significant impact on photoluminescence quantum yield (PLQY). In optimized, passivated, or heteroatom-doped systems, it can range from a few percent to over 60 percent, with significant variation across syntheses.(27) Excitation-dependent emission is commonly observed in many CDs and is often ascribed to heterogeneous emissive traps or multiple emissive centers, whereas excitation-independent (narrowband) emission is linked to more homogeneous surface states or well-defined molecular fluorophores.(19) The creation of red and near-infrared emission CDs through surface engineering, targeted heteroatom insertion, and prolonged conjugation has made deeper tissue imaging and phototherapy applications feasible.(26)

4.3 Surface functionalization:

Several synthesis pathways depend on carboxyl, hydroxyl, and amino surface functional groups, which also act as anchors for additional chemical conjugation and colloidal stability.(28) Through electrostatic interactions, amine functionalization ($-NH_2$) may simultaneously enhance cellular absorption and promote covalent attachment to carboxylate medications, peptides, or targeted ligands through standard carbodiimide chemistry (e.g., EDC/NHS).(29) Carboxylate CDs facilitate straightforward bioconjugation and water dispersibility, and carboxyl groups are commonly added directly by oxidative or bottom-up synthesis to streamline linker chemistry for drug loading.(28) Polyethylene glycol (PEG) grafting (PEGylation) on CDs is a common technique to improve pharmacokinetics and biocompatibility for drug-delivery formulations because it reduces immune recognition in vivo, increases blood circulation, and decreases protein adsorption.(30) Other surface engineering methods include cleavable linkers for stimuli-responsive drug release, peptide/antibody ligands for active targeting, and zwitterionic coatings. These methods are used to modify biodistribution by emphasizing specificity and controlled cargo release.(31)

4.4 Stability and biocompatibility:

The colloidal stability of CDs in physiological media is influenced by surface charge, ionic strength, and steric stabilization (such as PEG); properly functionalized CDs sustain their fluorescence and dispersion in serum-containing solutions for prolonged periods of time in vitro.(32) Many CDs have relatively low acute toxicity at standard imaging or distribution concentrations, according to in vitro cytotoxicity studies; however, toxicity is highly composition- and surface-dependent, and repeated dosage of oxygen-rich CDs or functional motifs can worsen cellular stress.(33) The importance of size, surface chemistry, and PEGylation for beneficial biodistribution is demonstrated by in vivo studies that demonstrate that large, aggregated, or poorly passivated CDs can accumulate in the liver and spleen, while small, hydrophilic CDs are often rapidly removed by renal excretion.(34)

Because long-term and repeated-dose toxicity data are still scarce and inconsistent across studies, a thorough biocompatibility assessment (including immunotoxicity, genotoxicity, and chronic exposure investigations) is still required before clinical translation. Well-designed surface chemistry (e.g., PEGylation, neutral or slightly negative charge, and customized ligands) enhances stability, reduces off-target accumulation, and boosts in vivo tolerance of CDs for drug-delivery applications when combined with careful physical evaluation.(35)

5. Mechanisms of Drug Delivery:

The effectiveness of carbon nanodots (CNDs) as cancer treatments depends on how they interact with biological barriers and their ability to transport drugs to tumor tissues. CNDs can employ both passive and active targeting strategies, which are governed by physicochemical properties such as size, charge, and surface chemistry. Understanding these systems is essential for improving treatment efficacy, decreasing off-target toxicity, and optimizing biodistribution. (36,38)

5.1 Passive targeting - EPR effect:

Because of leaky tumor vasculature and insufficient lymphatic drainage, the enhanced permeability and retention (EPR) effect, which is primarily in charge of nanoparticle passive targeting to solid tumors, permits preferential extravasation and retention of nanoscale carriers in the tumor interstitium.(36) Carbon nanodots (CDs) with hydrodynamic diameters in the typical ~5–100 nm window can use the EPR effect to passively accumulate in a range of experimentally generated tumors, increasing local drug concentration relative to free drug.(37) However, without additional techniques (such as size/shape tuning, vascular modulation, or active targeting), EPR-mediated accumulation alone frequently falls short of providing therapeutic doses in human tumors. Furthermore, different tumor types and patients have different EPR effect magnitudes and clinical significance.(36)

5.2 Active targeting - ligand conjugated CNDs:

Active targeting improves cell- or tissue-specific uptake by enhancing receptor-mediated endocytosis and intracellular cargo delivery by encasing CDs with targeting ligands (peptides, antibodies, aptamers, or small molecules) that attach to overexpressed receptors on cancer cells.(38) Common ligands used to reroute CDs to tumors include folic acid (which targets folate receptors), RGD peptides (which target integrins), transferrin, and antibodies against tumor-associated antigens; conjugation typically uses click-chemistry for stable attachment or covalent linkers (like EDC/NHS chemistry to couple carboxyl and amine groups).(39) According to research, ligand-conjugated CDs perform better than their non-targeted counterparts in preclinical models in terms of cellular uptake, tumor accumulation, and therapeutic efficacy when ligand density, linker stability, and nanoparticle size are optimized.(28)

5.3 Stimuli-responsive release - pH, redox, light, temperature:

Stimuli-responsive CDs use endogenous (pH, redox gradients, enzymes) or exogenous (light, heat, magnetic field) cues to start site-specific drug release, increasing on-site potency and reducing off-target exposure. pH-responsive CDs are designed to release cargo in the mildly acidic tumor microenvironment or the acidic endo/lysosomal compartments; acid-labile linkers or protonatable surface groups enable accelerated drug detachment or nanoparticle swelling under low pH, enabling tumor-selective payload release.(40) Redox-responsive mechanisms use disulfide or diselenide linkages that are stable extracellularly but broken by high intracellular glutathione (GSH) concentrations in cancer cells to release drugs attached to or encapsulated within CDs intracellularly.(41) Light-triggered CDs can be used as either photothermal agents, which generate heat under NIR irradiation to promote thermally induced drug release, or photosensitizers for photodynamic therapy (PDT), which generate reactive oxygen species, when an external light source is applied. Therapy can be controlled spatiotemporally through light activation.(42) In temperature-sensitive designs, CDs are combined with thermo-labile polymers or phase-change materials to enable controlled drug discharge and improved carrier dispersion or breakdown in response to mildly generated external heat.(42) Combining stimuli that minimize premature leakage and maximize intracellular release in the tumor microenvironment, such as pH + redox or light + redox, can result in synergistic control.(41)

6. Applications in Cancer Therapy:

Carbon nanodots (CNDs) have garnered significant interest in the treatment of cancer due to their remarkable photoluminescence, variable surface functionality, biocompatibility, and ease of drug conjugation. Their nanoscale size allows for better tumor penetration, and surface modification allows for more individualized delivery and less systemic toxicity. These versatile characteristics have enhanced their potential in the areas of phototherapy, gene therapy, chemotherapy, and theragnostic applications, as discussed in the following subsections.

6.1 Chemotherapy Delivery:

Carbon nanodots (CNDs) have emerged as appealing delivery systems for chemotherapeutic drugs due to their biocompatibility and ability to increase drug solubility.(22) Studies have successfully loaded chemotherapeutic compounds, like doxorubicin, onto CNDs, increasing therapeutic efficacy and reducing side effects in the treatment of cancer.(43) CNDs can be functionalized with targeting ligands to achieve selective delivery to tumor cells, which would further increase the specificity and effectiveness of chemotherapy.(44)

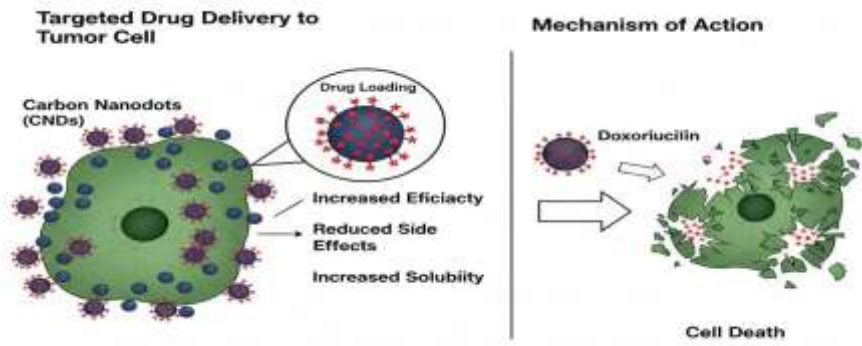


Figure 1: Chemotherapy Delivery

6.2 Gene Therapy:

Particularly for microRNA (miRNA) and small interfering RNA (siRNA), CNDs are effective gene delivery vehicles.(45) Their small size and surface modification enable targeted gene silencing and cellular absorption, offering a potential therapeutic option for genetic disorders and cancer.(42) Additionally, CNDs can be engineered to release their payload in response to specific stimuli, such as pH changes or the presence of specific enzymes, to create regulated gene delivery systems.(45)

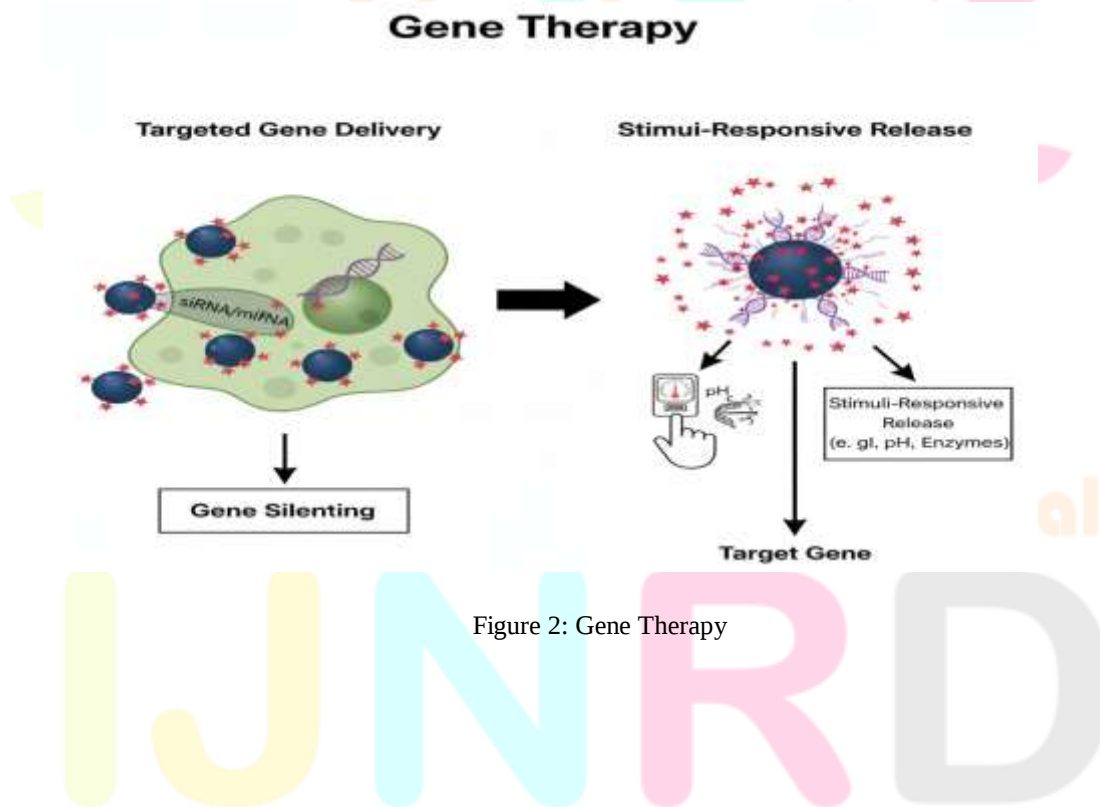


Figure 2: Gene Therapy

6.3 Photodynamic and Photothermal Therapy:

CNDs can be employed as photosensitizers in photodynamic treatment (PDT) due to their high UV-visible absorption.(46) When exposed to light, CNDs release reactive oxygen species, which triggers the death of tumor cells.(47) Moreover, their ability to convert light into heat enables photothermal treatment (PTT), which provides a dual therapeutic approach.(28) Recent advancements have led to the development of CNDs that emit near-infrared (NIR) light, which offers greater tissue penetration and less photodamage to adjacent healthy tissues.(48)

Photodynamic & Photothermal Therapy

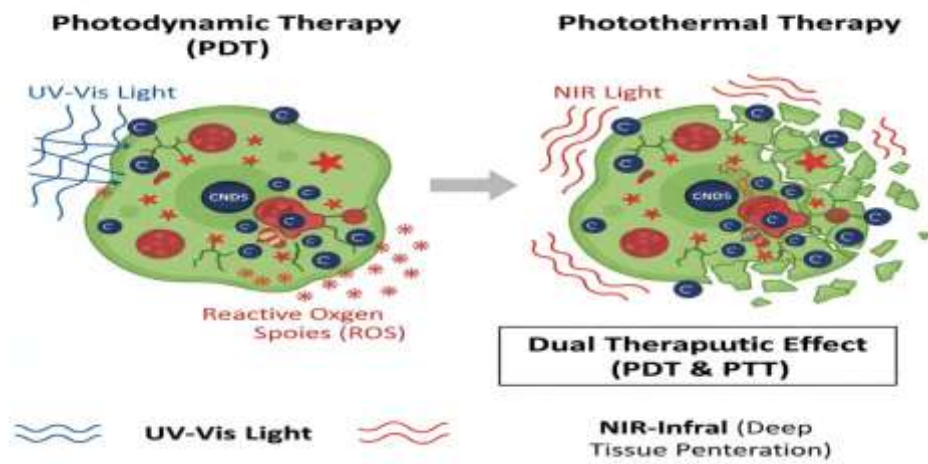


Figure 3: Photodynamic and Photothermal Therapy

6.4 Theragnostic Therapy:

Theragnostic applications, which integrate therapeutic and diagnostic imaging capabilities, can make use of CNDs due to their unique properties.(49) Their fluorescence allows for real-time tumor imaging, and their capacity to disperse therapeutic chemicals allows for simultaneous diagnosis and treatment, increasing the precision of cancer therapy.(23) Furthermore, CNDs can be engineered to respond to specific stimuli in the tumor microenvironment, such as elevated glutathione levels or an acidic pH, enabling more accurate and controlled theragnostic therapies.(50)

Theragnostic Applications

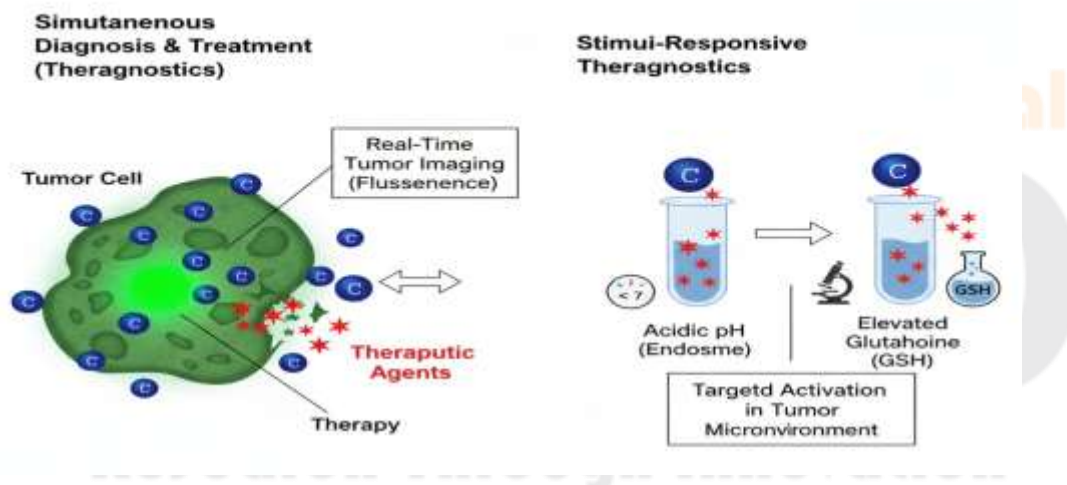


Figure 4: Theragnostic Therapy

7. Challenges and Limitations:

Even though carbon nanodots (CNDs) have demonstrated significant promise in the treatment of cancer, several barriers still stand in the way of their widespread use. Significant issues remain unresolved, such as toxicological uncertainty, reproducibility, scalability, and regulatory uniformity. An in-depth knowledge of these limitations is required to guarantee their safe and effective application in biomedicine. The following subsections discuss the primary problems with CND-based systems.

7.1. Toxicity Concerns:

Despite their promising applications, the potential toxicity of CNDs remains a significant concern.(21) Among the factors influencing CND cytotoxicity are size, surface charge, and functional groups.(51) Studies have shown that certain surface modifications can lessen toxicity, despite the current lack of comprehensive in vivo evaluations.(51) Further studies are needed to ascertain the long-term biocompatibility and clearance mechanisms of CNDs in order to ensure their safety in clinical settings.(52) Studies on the cytotoxicity of carbon dots have shown that they can photodegrade and release toxic compounds that may pose a threat to human cells when exposed to light.(28)

It has also been discovered that the composition of carbon dots has a major impact on their cytotoxic effect.(53) Carbon dots were made from natural precursors, such as orange juice, and demonstrated low cytotoxicity and good biocompatibility.(54) Because of their dose-dependent cytotoxicity, carbon dots kill more cells at higher concentrations.(9) Surfaces can be made more biocompatible and less harmful by adding biocompatible compounds. Moreover, CNDs can serve as active interfaces for controlled drug release and improved tissue integration, enhancing the overall therapeutic performance of implantable devices.(55,56) Research on the specific mechanisms underlying these changes is still ongoing. Concerns about carbon dots' long-term safety and possible environmental effects are raised by their tendency to progressively accumulate in organs and tissues.(57) Therefore, before carbon dots are widely used in biomedical domains, extensive toxicity evaluations are required.(58)

7.2 Large-Scale Production Challenges:

There are a few obstacles to overcome when transferring CND synthesis from the lab to the industrial setting.(59) Current methodologies often lack consistency in product quality and reproducibility.(60) Techniques like hydrothermal methods and microwave-assisted synthesis are effective on a small scale, but they have trouble controlling reaction conditions and maintaining homogeneity on a larger scale.(35) Moreover, the cost-effectiveness and energy consumption of these techniques need to be optimized to enable large-scale production.(59) Structural uncertainty significantly hinders large-scale production, particularly in terms of reproducibility of functional groups, precise control over optoelectronic properties, and batch-to-batch consistency.(61) The scalability of green synthesis methods, which utilize renewable resources, is still being investigated.(62) These methods may not yet be suitable for industrial production, even though they are environmentally friendly.(3) Therefore, developing synthesis processes that are economical, reproducible, and scalable is crucial for real-world applications.(51)

7.3 Stability and Reproducibility Issues:

CNDs need to be stable in a range of environmental conditions to be used in practice.(53) Factors such as photobleaching, pH sensitivity, and deterioration over time may affect their efficacy.(33) It can be challenging to guarantee the repeatability of their synthesis because slight modifications to the precursor materials or reaction conditions may produce noticeable differences in properties.(63) Standardized processes and quality control techniques are essential to resolving these issues and ensuring consistent product quality.(64) The structure and content of CQDs are influenced by precursors, solvents, synthesis techniques, and reaction conditions, all of which have an impact on the stability of the particles.(65) Environmental variables such as temperature and concentration also affect the stability of generated CQDs.(11) The type of surface functional groups that CQDs have determines how sensitive they are to environmental influences, which impacts their long-term application .(55) Stability and repeatability issues need to be addressed if carbon dots are to be successfully applied in a range of industries.(56)

8. Future Perspectives:

Carbon nanodots (CNDs) have made significant strides in their production and biomedical applications, but more work is needed to fully realize their clinical potential. Future research should focus on improving structure property correlations, large-scale reproducibility, precise targeted delivery, and long-term biosafety. By combining CNDs with advanced nanostructures and intelligent materials, new possibilities for targeted and precise cancer treatment may become possible. (69,70)

8.1 Hybrid Nanomaterials:

Hybrid nanomaterials with both organic and inorganic components offer enhanced stability, multifunctionality, and targeted delivery in the treatment of cancer.(66) Recent studies have demonstrated their capacity to improve therapeutic efficacy and reduce adverse effects.(67) Researchers have investigated the possible synergistic effects of metal–phenolic networks and metal–organic frameworks in cancer immunotherapy.(68) By fusing therapeutic and diagnostic capabilities, these hybrid systems pave the way for theragnostic applications.(69)

8.2 Personalized Cancer Therapy Applications:

Combining nanotechnology and personalized medicine could lead to more individualized cancer treatments.(68) Customizing nanomaterials to respond to specific biomarkers enables real-time monitoring and precise drug delivery.(66) Advances in nanomaterial-based platforms facilitate the development of customized treatment regimens, leading to better patient outcomes.(28)

8.3 Clinical Translation Opportunities:

The transition of nanomaterials from laboratory research to clinical applications represents a significant turning point in cancer treatment.(68) Clinical trials for a variety of nanoparticle types have already begun, underscoring the importance of addressing concerns like reproducibility, scalability, and regulatory approval. Further research and development are required to get past these obstacles and make the most of nanomedicine in clinical settings.(70)

9. Conclusion:

Carbon-based nanodots (CNDs), including carbon quantum dots (CQDs) and related zero-dimensional carbon nanomaterials, have made significant strides in the treatment of cancer in recent years. Improvements in surface functionalization, doping, and top-down and bottom-up manufacturing techniques have enhanced their physical, optical, and biological properties for drug delivery, imaging, and theragnostic. Variable size, water solubility, good luminescence and photostability, high quantum yield (in many cases), and favorable biocompatibility are important functional advantages. In addition to being effective carriers for anticancer drugs improving targeting, reducing off-target toxicity, and enabling stimuli-responsive or tumor microenvironment (e.g., acidic, redox) triggered release these properties enable CNDs to function as multimodal agents that combine therapy and diagnostics (e.g., bioimaging, photothermal or photodynamic effect), improving treatment specificity and effectiveness. Despite these successes, a few challenges need to be addressed before widespread clinical translation is practical.

Targeting specificity in vivo, including penetration into solid tumors and overcoming biological barriers (e.g. reticuloendothelial system uptake, renal or hepatic clearance); long-term toxicity, biodistribution, clearance, and immunogenicity profiles; large-scale reproducible synthesis with strictly regulated size, surface chemistry, and doping; and stability of drug loading and release kinetics under physiological conditions. Regulatory barriers and manufacturing scale-up are also significant issues. Large-scale production, long-term stability, and extensive toxicity profiles are issues that need to be carefully addressed to allow for the practical translation of CND based treatments. To overcome these challenges, interdisciplinary collaboration, extensive preclinical testing, and regulatory compliance are required. Combining CNDs with other nanomaterials, specialized medical approaches, and advanced imaging techniques holds great promise for the future. These advancements could pave the way for more effective, less invasive, and patient-specific cancer treatments. In conclusion, despite not being a panacea, CNDs have the potential to revolutionize cancer treatment. This raises the prospect of soon-to-be more effective and individualized treatment options.

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