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Biomedical applications and future perspectives of carbon dots and their hybrid nanomaterials

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Carbon dot-based hybrid nanomaterials are becoming more popular in the biomedical field because they are safer, work well with living things, and are simple to make. Researchers have come up with different ways to control the shape and features of carbon dots, graphene quantum dots, and carbon nanodots, and have improved their abilities by combining them with metals, polymers, or other substances. These materials are being studied for uses like imaging inside the body, detecting diseases, fighting bacteria, and delivering drugs to specific places, as well as for new treatments that use light or sound. Even so, there are still problems with making sure they are safe, reliable, and easy to produce in large amounts. This review looks at the latest progress in making and using carbon dots and their hybrids, and talks about how they might be used in medicine in the future.

Introduction

Carbon dots (CDs) are significant materials that have garnered recent interest in biomedical research.[1] Their compatibility with biological systems, low toxicity, and optical properties set them apart from conventional semiconductor quantum dots.[2] The synthesis of CDs has been significantly simplified, facilitating a broad array of experiments. The size-dependent luminescence properties, favorable water compatibility, and stable chemical behavior of these nanoparticles indicate significant potential for various applications. Chemically customizable surfaces have diverse applications.[3] These encompass medical imaging, targeted diagnostics, drug and gene delivery, therapies including photodynamic therapy and photothermal therapy, and antimicrobial strategies.[4] Building on this foundation, a multifunctional "chemical toolbox" perspective has emerged, emphasizing pre-/post-synthetic control, heteroatom doping, and surface engineering to precisely tune emission, quantum yield, and interfacial states for improved tissue penetration and signal-to-background ratio *in vivo*.[5] Complementarily, surface engineering frameworks consolidate ligand exchange, polymer/small-molecule passivation, and targeted functionalization strategies to enhance aqueous stability, colloidal robustness, and biointeractions across imaging, sensing, and delivery applications.[6] Seminal overviews have also positioned CDs as low-toxicity alternatives to heavy-metal QDs, while underscoring unresolved needs around robust long-wavelength emission, mechanistic clarity, and reproducible manufacturing as prerequisites for translation.[7] In early antimicrobial use-cases, photoactivated combinations of CDs with other sensitizers/materials achieved synergistic killing *via* boosted ROS generation, foreshadowing hybrid platforms that integrate photodynamic, photothermal, and chemical mechanisms.[8] Barriers that continue to be challenges encompass the stability of long-term *in vivo* behavior, the regulation of physicochemical properties during manufacturing, and the technical difficulties associated with integrating multiple functions onto a single platform.[9]

Investigating hybridizing technologies aims to exceed present limitations and increase CD applicability. Integrating metal nanoparticles, polymers, and organic molecules into CDs allows many applications within a single nanoscale system.[10] Hybrid systems exhibit improved optical performance, enhanced stability, controlled drug release profiles, and synergistic therapeutic effects.[11] Hybridized CDs greatly increase sensitivity and selectivity in biosensor applications.[12] To offer combined therapeutic effects, they combine photothermal, photodynamic, and chemical techniques and show great spatial and temporal resolution. Thus, a basic first step towards using these benefits and developing their clinical applications is the study of CD hybrid nanomaterials.[13]

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This review focuses on biomedical applications based on a detailed overview of the most recent advancements in carbon dots and their hybrid nanomaterials. We investigate basic synthesis techniques, surface modification approaches, and interactions between the structure and the properties needed to match the functionality of CDs with biological surroundings. Furthermore, emphasized in their part in multimodal bioimaging, enhanced biosensing capabilities, targeted drug and gene delivery systems, combined phototherapy methods, and antibacterial and antiviral uses are recent developments in the integration of CDs with other nanostructures. Finally, we go over the primary challenges that CD-based nanomaterials now encounter: biosafety, repeatability, and scalability. We also suggest directions for further investigation aimed at addressing these issues and facilitating the clinical translation of CDs and their hybrid nanostructures.

Structural features and physicochemical properties of carbon dots (CDs)

Core–shell structure in CDs and its impact on optical properties

Usually displaying a core–shell architecture, CDs have a nanocrystalline core mostly composed of sp^2-hybridized carbon clusters surrounded by shells enriched with functional groups, usually including sp^3-hybridized carbons or other surface modifications.[14] The shell passivates surface flaws, thereby lowering non-radiative recombination; it also increases water solubility and offers many available sites for functionalization. This structural arrangement essentially defines the optical properties and stability of CDs since the core produces strong photoluminescence *via* quantum confinement effects.[15] Under irradiation, core–shell CDs generated using levofloxacin and arginine exhibited significant up-conversion fluorescence and nitric oxide release, indicating their suitability for simultaneous bioimaging and photodynamic therapy.[16] By means of their ability to prevent core aggregation and self-quenching, polymer-based core–shell CDs exhibit excellent and amazing fluorescence stability over a broad range of pH levels and solvents. The fundamental core–shell structural design of CDs greatly increases their possible applications in the biomedical domain, including bioimaging and cancer treatment.[17] Further studies are necessary to explore the incorporation of CDs into hybrid nanomaterials, aiming to enhance therapeutic efficacy and achieve precise, controllable functionalities, thus emphasizing their relevance and effectiveness in precision medicine and biomedical applications.[18]

Optical and electronic properties of carbon dots

Their increasing relevance in optoelectronic and biomedical domains is mostly due to their unique optical and electronic characteristics.[19] CDs usually exhibit strong UV absorption in the range of 200–300 nm as well as significant luminescence mostly in the blue-green spectrum (420–565 nm). Techniques for surface functionalization, precursor choice, and synthetic parameters help to control these optical properties. The emission wavelengths and quantum yields are significantly influenced by the type and density of surface functional groups, such as amino, carboxyl, and hydroxyl groups.[20] The fundamental mechanism of photoluminescence is radiative transitions between discrete energy levels driven by surface functionalities and quantum confinement effects in the carbon core.[21] The photoluminescence properties of carbon dots are well-known to be strongly influenced by their size distribution. As the particle diameter decreases, quantum confinement effects become increasingly evident, typically resulting in a blue shift of the fluorescence emission peak. Conversely, larger carbon dots tend to emit at longer wavelengths, often in the green or red spectral regions, which is attributed to an expanded π-conjugation system and a reduced energy gap between the highest occupied molecular orbital and the lowest unoccupied molecular orbital. Incorporating a schematic illustration (see Fig. 1) that visualizes this relationship would greatly enhance comprehension. This figure depicts representative size ranges corresponding to blue, green, and red emissive carbon dots, alongside modulations in the core–shell structural architecture. Many carbon dots exhibit excitation-dependent emission, where varying the excitation wavelength produces distinct emission colors. This property, while useful for multicolor imaging, can complicate quantitative measurements in multiplexed assays. In contrast, some specialized carbon dots maintain stable, excitation-independent emission profiles, which are preferable for rigorous biological imaging and diagnostics. Table 1 summarizes select carbon dot types, their synthesis methods, and their representative biomedical applications.[22] The excitation-dependent emission of CDs enables multicolor fluorescence. Furthermore, CDs exhibit a spectrum of optical phenomena including surface-enhanced Raman scattering (SERS), phosphorescence, chemiluminescence, electrochemiluminescence, and near-infrared (NIR) fluorescence, which greatly extends their applications in biosensing and multimodal imaging.[23] The optical characteristics and electronic structure of CDs are much influenced by precisely tuned surface chemistry. Thus, the addition of heteroatoms such as nitrogen or sulfur together with different functional groups can significantly increase quantum yields, alter emission wavelengths, and improve stability.[24] Advanced surface functionalization methods and strategic integration of CDs into hybrid nanomaterials should be the main focus of future studies, enhancing their practical application potential and enabling clinical translation in precision medicine and advanced biomedical applications.[25] However, the introduction of surface functionalization to carbon quantum dots (CQDs) can pose a risk of reduced photoluminescence quantum yield. Recent studies investigating the optical properties of nitrogen-doped carbon quantum dots (N-CQDs) have elucidated that surface functional groups contribute to the formation of surface states, which enhance nonradiative recombination pathways. This, in turn, leads to a decline in photoluminescence efficiency, manifesting as decreased quantum yield. Notably, the research highlights a correlation whereby increasing densities of surface defects and

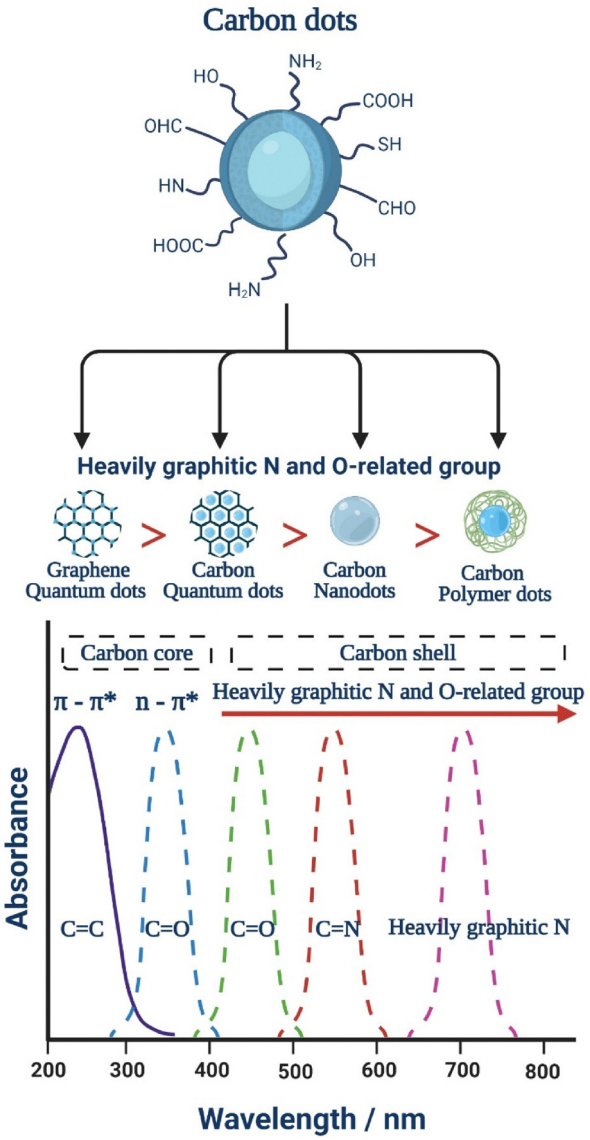

Fig. 1 A schematic illustration of the relationship between absorption spectra and electronic transitions for different types of CDs. Created with Biorender.com.

dopants amplify nonradiative decay processes, thereby exacerbating quantum yield reduction. While surface functionalization plays a vital role in tuning emission wavelengths and improving stability, excessive surface modification may inadvertently induce detrimental effects on quantum yield. Consequently, careful design and optimization of surface chemistry are imperative to balance emission enhancement against potential quenching phenomena associated with increased surface defect states.[26]

Influence of structural properties and surface chemistry of CDs on biocompatibility and cytotoxicity

Recent studies highlight the significant biocompatibility and low cytotoxicity of CDs, particularly in the field of biomedicine.[34] CDs utilized in drug delivery, bioimaging, and optoelectronics exhibit several advantageous properties, including excellent photostability, biocompatibility, adaptability, low cytotoxicity, high chemical inertness, straightforward synthesis methods, eco-friendliness, ease of functionalization, non-blinking photoluminescence, and improved water solubility.[35] *In vivo* studies demonstrate that fluorescence in gut tissues of *Caenorhabditis elegans* (*C. elegans*) remains consistent without toxic effects. Furthermore, safe clearance from the body in mice indicates that CDs derived from natural sources are biocompatible, photostable, and non-toxic in animal models. The structural properties and surface chemistry of CDs significantly affect their biocompatibility and cytotoxicity. For instance, carbonized polymer dots derived from various precursors exhibit varying levels of cytotoxicity in both standard and tumor cell lines, suggesting that the observed cytotoxicity is primarily linked to the specific carbon nanoparticle species rather than the precursors used. Despite their favorable safety profile, the synthesis and structural property analysis of CDs must be conducted carefully to ensure optimal biocompatibility for biomedical applications.[36]

Classification of CDs based on structural properties and their biomedical application perspectives

Among the several subtypes of carbon-based nanomaterials, CDs are systematically classified according to their structure, composition, and formation mechanism as CQDs, GQDs, CNDs, and CPDs.[37] CQDs are quasi-spherical, crystalline nanoparticles composed of mixed sp^2 and sp^3 hybridized carbon atoms, exhibiting strong quantum confinement effects and high photoluminescence quantum yields.[38] Due to their anisotropic structure and abundant surface functional groups, GQDs, small disk-shaped fragments of single or few-layer graphene sheets, exhibit notable quantum confinement and edge effects.[27] CNDs are amorphous or quasi-spherical nanoparticles characterized by a high degree of carbonization, lacking the crystalline or polymeric structure and quantum confinement effects observed in CQDs and GQDs.[39] As cross-linked nanohybrids, CPDs possess unique optical properties and enhanced stability due to their carbonized core being enveloped by polymer chains or functional groups. Recent studies have increasingly focused on the diverse biomedical applications of carbon dots (CDs) based on their distinct structural and chemical characteristics. Carbon quantum dots (CQDs) and graphene quantum dots (GQDs), owing to their high crystallinity and strong quantum confinement effects, exhibit exceptional photoluminescence properties, making them well-suited for high-resolution bioimaging and single-particle tracking. Notably, modulation of surface functional groups enables enhanced biocompatibility and targeted delivery capabilities, facilitating their use as precise bioimaging and biosensing platforms. In contrast, carbon nanodots (CNDs), characterized by their amorphous structure and abundant surface states, display photoluminescence that is highly sensitive to environmental factors such as solvent polarity, pH, and ionic strength. This responsiveness renders them ideal candidates for environmentally sensitive sensors and multiplexed signal detection systems.[40] Carbonized polymer dots (CPDs), benefiting

Table 1 Summary of synthesis methods, photoluminescence characteristics, and main application areas of excitation-dependent and excitation-independent carbon dots with supporting literature

CD type	Representative system	Synthesis and precursors	Emission behavior/mechanism	Key application	Ref.
Excitation-dependent CDs	Amorphous CDs and GQDs with surface-state emission	Bottom hydrothermal/solvothermal/microwave from citric acid, glucose; heteroatom doped; also top-down exfoliation/oxidation	Broad surface/defect-state manifold causes wavelength-tunable PL with excitation, enabling multi-color but risking spectral overlap	Multiplexed imaging, chemical sensing, photocatalysis, and optoelectronics	27
Excitation-independent CDs	Molecular-state/edge-state dominated CDs with narrow bands	Molecular precursors; controlled thermal decomposition; edge amine protonation strategies for high color purity	Single dominant emissive state yields fixed emission with changing excitation and narrow FWHM; improved color stability	Single-color bio-labeling, *in vivo* imaging, and display color conversion	28
Biomass-derived CDs	Glucose/cellulose/food-waste derived CDs	Green hydrothermal or microwave carbonization; scalable routes; optional heteroatom doping	Mixed behaviors depending on surface chemistry; biocompatible and photostable	Sensors, bioimaging, drug delivery, and energy devices	29
Polymer-embedded CDs	CDs dispersed or formed in polymer matrices	*In situ* formation or blending within polymers	Matrix interactions modulate surface states; excitation dependence often persists	Color-conversion films and polymer optoelectronics	30
Continuous-flow CDs	Flow reactors for CDs	Continuous-flow hydrothermal/microwave for reproducibility and scalability	Tunable PL *via* controlled residence time/temperature; behavior determined by surface chemistry	Scalable sensing/photocatalysis and material inks	31
Top-down GQDs	Laser ablation, arc discharge, and electrochemical exfoliation	Graphite, CNTs, and graphene oxide precursors	Size/edge and functional groups dictate PL; often excitation-dependent due to heterogeneous states	Bioimaging, electronics, and sensing	32,33

from strong interactions with polymeric matrices, offer advantages in drug loading and stimulus-responsive release. Their inherent stability and versatility in functionalization make them particularly suitable for complex biomedical applications, including drug delivery, photodynamic therapy, and theranostics. This nuanced understanding of the relationship between structural features and functional performance underscores the potential of CDs as versatile nanomaterials in advancing next-generation biomedical technologies.[41] Carbon dots (CDs) have been extensively studied for their hybridization with metals, metal oxides, ceramics, and heteroatom doping to maximize the efficiency of photothermal, photodynamic, and sonodynamic therapies. Additionally, surface functionalization strategies have been employed to enhance *in vivo* stability and targeting specificity. Recent advances include sulfur doping of carbon dots, which has improved their photoluminescence quantum yield (PLQY) from 18% to 42%, while maintaining fluorescence stability across a temperature range of 15 to 95 °C. These properties offer significant advantages for anti-counterfeiting applications, including the protection of products, official documents, passports, barcodes, and currency from replication.[42] The structural diversity and tunable characteristics of CDs thus facilitate their broad applicability across various fields.[43]

Synthesis strategies and functional tailoring of CDs

Top-down synthesis methods for CDs

Top-down synthesis methods for CDs typically integrate physical and chemical approaches to convert bulk carbon precursors into nanoscale CDs.[9] Methods such as arc discharge, laser ablation, electrochemical oxidation, chemical oxidation, ultrasonic treatment, and plasma treatment facilitate the cleavage or exfoliation of precursors, including graphite, graphene oxide, carbon nanotubes, carbon fibers, and carbon black, into smaller carbon nanoparticles.[44] Chemical and electrochemical oxidation methods alter carbon structures through the application of strong oxidants or electrochemical reactions, whereas arc discharge and laser ablation utilize high-energy techniques to fragment bulk carbon sources.[2] GQDs are produced from layered carbon precursors through ultrasonic synthesis and chemical exfoliation, employing either ultrasonic energy or chemical agents. Top-down approaches produce CDs characterized by well-defined crystalline cores and intact graphitic domains. However, these methods often require challenging reaction conditions, extended processing durations, and costly equipment.[45] Furthermore, quantum efficiencies are sometimes lower compared to those of bottom-up approaches. Top-down methods are particularly advantageous when precise control over specific optical and structural characteristics of CDs is necessary.[44]

Bottom-up synthetic methods for CDs

Bottom-up synthetic routes for CDs have drawn interest because of their low cost, simplicity, and environmentally friendly precursors.[35] Thermal approaches using basic carbon sources such as candle soot treated with oxidants like HNO_3 or H_2O_2/AcOH produced fluorescent CDs displaying enhanced quantum yields (0.8–1.9%). Microwave-assisted synthesis rapidly produces CDs with broad emission spectra and high biocompatibility *via* electromagnetic energy-induced bond cleavage. For instance, CDs synthesized from phthalic acid and trimethylenediamine hexahydrate exhibited strong green fluorescence within one minute. CDs and their hybrids show

significant potential for biomedical applications, including bioimaging, diagnostics, and therapeutics. However, further improvements in surface functionalization and synthesis reproducibility are required to address existing limitations, such as photostability and toxicity, thereby increasing their clinical applicability.[18]

Enhancing biomedical functionality of CDs through surface engineering and heteroatom doping

Their biomedical potential has been significantly expanded by customizing surface properties and doping heteroatoms into CDs.[46] Crucially, for targeted therapeutic delivery, altering surface chemistry *via* covalent bonding or electrostatic and hydrogen interactions improves biocompatibility and biomolecule conjugation. Heteroatoms such as nitrogen, boron, sulfur, or metals strongly influence photophysical properties; nitrogen doping, for instance, enhances quantum yields and provides pH-responsive fluorescence, whereas boron doping enhances nonlinear optical properties. Microwave-synthesized CDs co-doped with boron and nitrogen exhibited quantum yields of approximately 33%, demonstrating significantly enhanced radiative efficiency. Hybrid nanosystems combining CDs with magnetic nanoparticles (*e.g.*, Fe_3O_4) facilitate targeted therapy and multimodal imaging.[45]

Comparative evaluation of CD synthesis strategies and rational selection

The synthesis of carbon dots (CDs) is commonly divided into two main approaches: top-down and bottom-up methods. Top-down techniques, such as arc discharge, laser ablation, chemical oxidation, and electrochemical exfoliation, involve breaking down bulk carbon sources into nanoscale particles. These methods are prized for retaining structural features of the original materials, including crystalline domains and specific edge configurations, but they often require harsh reaction conditions, specialized equipment, and significant energy input. They also tend to produce CDs with broad size distributions and lower quantum yields, leading to issues with batch-to-batch reproducibility and challenges for scalability and regulatory approval, especially where stringent control over surface chemistry and biocompatibility is essential for biomedical applications.[47] Bottom-up synthesis methods like hydrothermal processing, microwave-assisted pyrolysis, thermal decomposition, and template-directed assembly, build CDs from molecular precursors, offering flexibility to tune particle size, surface functional groups, and optical properties. The versatility in precursor choice from simple organics to biomass enables more sustainable and cost-effective production routes. However, such methods often produce heterogeneous populations requiring extensive purification to remove residual byproducts, which can hinder reproducibility and raise concerns over clinical scalability. Moreover, the connection between synthesis methods and key translational factors such as manufacturing consistency, *in vivo* stability, and regulatory compliance is seldom explicitly addressed in current research. To truly advance translational CD applications, evaluations must go beyond descriptions of synthesis strategies to critically assess how each route meets the practical demands for industrial and biomedical implementation.[48] Emerging technologies such as continuous flow reactors, automation, hybrid synthesis techniques, and AI-driven process optimizations are beginning to address productivity, uniformity, and scalability hurdles. Future research should focus on systematically correlating synthesis parameters with translation-related performance metrics instead of concentrating solely on compositional or photophysical properties. Ultimately, the rational choice of synthesis strategy for CDs should be guided by scalability, reproducibility, biosafety, and applicability rather than traditional conventions or ease of laboratory demonstration. This paradigm shift is crucial to overcoming persistent challenges and fully leveraging the potential of carbon dots in cutting-edge biomedical, energy, and sensing technologies.[49]

Biomedical applications of single carbon dots

Bioimaging and optical sensing

Due to their photoluminescence properties, chemical stability, and low toxicity, individual CDs are highly regarded in optical sensing and biomedical imaging.[50] Owing to their tunable emission wavelengths, these fluorescent nanoparticles offer enhanced contrast in diagnostic imaging, thereby enabling precise visualization of biological tissues and cellular structures.[47] Their stable fluorescence emission also facilitates continuous monitoring of dynamic biological processes, ranging from tracking intracellular pathways to highlighting pathological alterations. Additionally, optical detection represents another important application area for single CDs, leveraging their sensitivity to environmental variations for real-time monitoring of biomolecules, ions, and metabolic markers. For instance, selective interactions between CDs modified with specific functional groups and targeted analytes produce distinct optical signals, significantly enhancing detection sensitivity and specificity, thus contributing to early disease diagnosis and precise biomedical research. Nevertheless, achieving consistent and reproducible sensing outcomes necessitates precise management of surface chemistry, particle homogeneity, and synthesis standardization.[51] Furthermore, rigorous biological evaluations under clinically relevant conditions are critical to establish comprehensive safety and efficacy profiles for these nanoparticles. Engineering single CDs toward red/near-infrared windows and ratiometric or lifetime-based readouts can further mitigate tissue autofluorescence and scattering while improving quantitative robustness in complex biological milieus. Such design choices, together with assay standardization and cross-laboratory benchmarking, will be pivotal for translating single-CD imaging and optical sensing from proof-of-concept studies to clinically actionable diagnostics.[52] In recent work, platforms that combine antifouling surface layers with lifetime-encoded or ratiometric readouts and red/NIR emission have demonstrated higher matrix tolerance, fewer false positives, and better inter-laboratory transferability, moving single-CD assays closer

to clinical practice.[53] Consequently, advancing single CD-based imaging and optical sensing technologies from laboratory research to clinical diagnostics and practical biomedical applications relies heavily on continued refinement of synthesis methodologies alongside thorough biological validations.[54]

Biosensing mechanisms of CDs and their biomedical significance

Due to their distinctive optical characteristics and excellent chemical stability, carbon dots (CDs) have become attractive materials for various biosensing applications, which mostly rely on fluorescence-based detection methods.[51] Typically, these carbon-based nanostructures identify biological analytes *via* mechanisms such as fluorescence resonance energy transfer (FRET), inner filter effects (IFE), or simpler phenomena like fluorescence quenching and enhancement. For instance, modifying CDs with specialized receptors or targeted functional groups enables selective recognition of specific analytes, causing noticeable shifts in fluorescence intensity or emission spectra. Alternatively, enzyme-driven reactions occurring directly on the nanoparticle surface can yield measurable spectral variations, thus allowing precise tracking of enzymatic activities or metabolite levels even within complex biological media. Consequently, these versatile nanoprobes are capable of detecting pH fluctuations, metal ions, proteins, nucleic acids, and diverse metabolites, showing broad utility spanning clinical diagnostics to environmental monitoring.[55] Nevertheless, significant obstacles persist, such as precisely controlling surface modifications, achieving reproducible CD synthesis, and ensuring high sensitivity in complicated biological conditions. Thus, rigorous validation of biosensing efficacy under physiological scenarios, along with ongoing refinement of synthetic techniques, remains critical for successful translation into clinical settings. Additionally, combining CDs with other nanomaterials could further enhance sensitivity and selectivity, underscoring the relevance of multifunctional composite platforms for advanced biomedical diagnostic technologies.[56]

Therapeutic applications of CD

Photothermal therapy (PTT). Photothermal therapy (PTT) is a technique that employs photothermal agents to achieve targeted accumulation within tumor sites, enabling the non-invasive eradication of cancer cells. Since its therapeutic efficacy largely depends on selective accumulation, an ideal photothermal agent should exhibit high photothermal conversion efficiency (PCE) and excellent biocompatibility, and should be nontoxic.[57] In PTT, carbon dots (CDs) utilize their near-infrared (NIR) light absorption capability to effectively convert radiation into localized heat, selectively eliminating cancer cells. Unlike conventional therapies, this approach achieves targeted ablation of tumor tissues while preserving healthy areas. Due to their biocompatibility and ease of functionalization, CDs enable precise delivery to tumor sites, enhancing therapeutic efficacy.[58] For example, asphaltene-derived carbon dots (ACD) enriched with oxygen- and nitrogen-containing functional groups were synthesized, and their *in vitro* photothermal

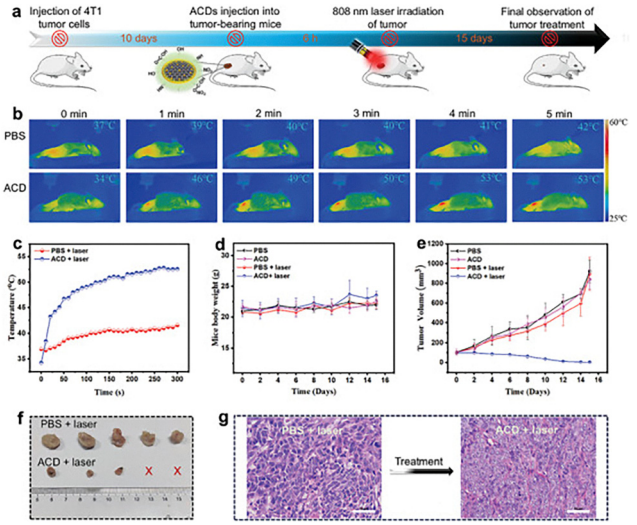

Fig. 2 (a) Schematic illustration of the timeline of mice PTT with the ACDs. (b) Time-course NIR photothermal images of whole mice revealing the tumor region upon laser irradiation (800 nm; 1.5 W cm^{-2}) of the ACDs. PBS served as a control. (c) Temperature elevations induced by the ACDs and PBS (control) in mice tumors during laser irradiation. (d) Mice body weight and (e) tumor volume changes monitored for 15 days post-treatment with PBS and ACDs without and with laser exposure. Data are expressed as mean ± standard deviation. (f) Representative digital images of the tumors excised from mice at 15 days post-treatment with ACDs and PBS with laser exposure in each case (n = 5). (g) H&E staining micrographs of tumors excised at 15 days post-treatment with ACDs and PBS (control). Scale bar = 50 μm. Reproduced under terms of the CC-BY license.[59] Copyright 2024, Akakuru, O. U., Li, X., Wang, Y., Chen, J., Zhang, Q., Liu, Z., and Zhao, H., published by Wiley-VCH GmbH.

therapeutic performance was evaluated using an MTT assay. Under 808 nm laser irradiation (1.5 W cm^{-2}), the photothermal therapeutic effect was significantly enhanced with increasing ACD concentration, demonstrating a corresponding increase in cancer cell ablation[59] (Fig. 2). However, issues such as particle uniformity, long-term biosafety, and reproducibility in synthetic protocols still require attention. Importantly, refining synthesis methods and performing rigorous biological validation under clinically relevant conditions remain critical. Such advancements may facilitate clinical translation of CD-based PTT as an efficient, minimally invasive cancer therapy option.[60]

Photodynamic therapy (PDT). Photodynamic therapy (PDT) is a non-invasive therapeutic modality that specifically targets and destroys cells through the interaction of photosensitizers, particular wavelengths of light, and molecular oxygen.[61] It has been successfully applied in the clinical treatment of various cancers and several non-neoplastic conditions.[62] Conventional photosensitizers exhibit considerable limitations, such as insufficient target selectivity, hydrophobicity, and limited optical efficiency, restricting their widespread clinical utility. Recently, carbon-based nanomaterials, including CQDs and GQDs, have been extensively explored as alternative photosensitizers due to their enhanced aqueous solubility, superior photostability, and excellent biocompatibility, which collectively improve therapeutic outcomes. Typically, PDT involves

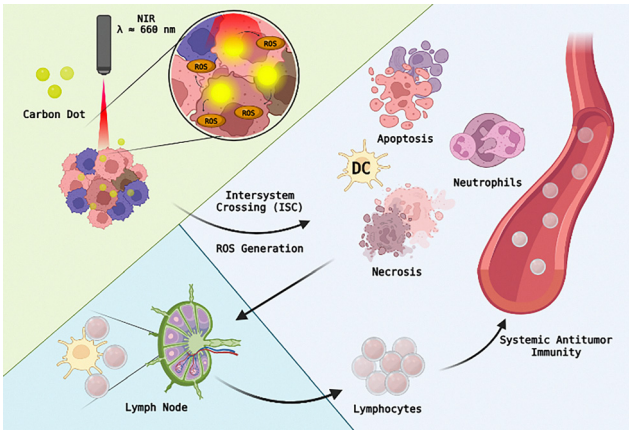

Fig. 3 Photodynamic therapy (PDT) involves the light-mediated activation of photosensitizers (PS) within tumor cells. Upon photoexcitation, reactive oxygen species (ROS) are generated intracellularly, leading to tumor cell death primarily through apoptosis and necrosis. Damage to the surrounding tumor microvasculature further disrupts oxygen and nutrient supply, thereby amplifying cytotoxic effects. Tumor cell destruction is accompanied by the release of proinflammatory cytokines and rapid recruitment of neutrophils, macrophages, and dendritic cells (DCs). The dying tumor cells are phagocytosed by professional phagocytes, including DCs, which subsequently migrate to the draining lymph nodes and differentiate into antigen-presenting cells. This antigen presentation promotes clonal expansion of tumor-specific lymphocytes that home to the tumor site and destroy remaining malignant cells. Created with Biorender.com.

administering a photosensitizer followed by irradiation at a specific wavelength of light to selectively initiate photochemical reactions within target tissues. Upon irradiation, reactive oxygen species (ROS) are generated *via* Type I (radical-mediated) or Type II (singlet oxygen-mediated) pathways, subsequently inducing apoptosis, necrosis, autophagy, vascular damage, and immune activation, all of which contribute to tumor suppression[63] (Fig. 3). Recent studies have reported the development of nanohybrids combining phenylboronic acid-modified carbon dots (PCDs) with proteinase K (PK) to overcome the limitations of photodynamic therapy (PDT). These nanohybrids serve as carbon dot-based photosensitizers exhibiting superior aqueous solubility and stability, with surface modification significantly enhancing singlet oxygen ($^1O_2$) generation efficiency. The phenylboronic acid groups facilitate covalent bonding with key components of both Gram-positive and Gram-negative bacterial cell walls, thus enabling strong bacterial adhesion. Proteinase K enzymatically degrades the extracellular polymeric substances (EPS) of bacterial biofilms, promoting the deep penetration of PCDs within the biofilm matrix and thereby maximizing reactive oxygen species (ROS)-mediated photodynamic bactericidal effects. Optical characterization demonstrated that PCDs exhibit efficient $^1O_2$ generation upon near-infrared light irradiation at 660 nm, and electrochemical analyses confirmed markedly improved electron–hole separation efficiency. Fluorescence staining assays distinguishing viable from dead bacteria revealed strong bactericidal effects in PCD-treated groups, corroborated by scanning electron microscopy observations showing bacterial membrane deformation and disruption. Biofilm eradication assays indicated that PCD-PK nanohybrids have superior efficacy compared to either the photosensitizers or enzyme treatment alone, suggesting enhanced therapeutic potential at infected sites *in vivo*. Furthermore, *in vivo* evaluations combining PCD-PK nanohybrids with 660 nm laser irradiation demonstrated significantly accelerated wound healing relative to controls and monotherapies, with histopathological analyses confirming reduced inflammation and enhanced dermal regeneration. Collectively, these findings highlight that the strategic conjugation of phenylboronic acid-modified carbon dot photosensitizers with biofilm-degrading enzymes effectively overcomes the intrinsic shortcomings of conventional PDT sensitizers, substantially elevating their clinical translational feasibility.[64] This approach delineates a promising direction for next-generation photosensitizer development that simultaneously augments biocompatibility and photodynamic efficacy, underscoring the necessity of continued preclinical and clinical investigation to realize its therapeutic potential.[65]

Drug delivery and nanocarriers

CDs are nano-carriers that exhibit excellent biocompatibility, low toxicity, small particle size, water solubility, and unique photophysical properties.[66] Their usefulness has been consistently demonstrated through various drug delivery studies.[67] In particular, drug delivery systems utilizing CDs in cancer therapy simultaneously satisfy the two goals of achieving efficient therapeutic effects and ensuring safety.[68] For example, doxorubicin (DOX), a widely used anticancer agent, has been loaded onto CD-based carrier systems in various studies. The process of loading drugs onto CD surfaces can be divided into covalent and non-covalent bonding. In covalent bonding, structures that can be cleaved by specific enzymes or redox environments, such as hydrazone and disulfide bonds, are utilized to regulate drug release. On the other hand, non-covalent binding utilizes reversible bonds such as electrostatic forces (van der Waals forces and hydrogen bonds), hydrophobic–hydrophilic interactions, and π interactions to regulate the reversible loading and release of drugs. These diverse drug loading strategies and controllable release mechanisms of CDs are expected to overcome the limitations of existing drug delivery systems and meet the clinical demands for enhancing the efficacy of anticancer therapy and minimizing side effects.[69] Nevertheless, further research is essential to address issues such as the reproducibility of drug delivery efficiency, the *in vivo* dynamics of nano-carriers, and long-term safety evaluation.[70]

Antimicrobial and antiviral applications

Microbes responsible for infectious diseases include *Escherichia coli*, *Salmonella typhimurium*, *Streptococcus pneumoniae*, *Bacillus cereus*, *Mycobacterium tuberculosis*, *Clostridium perfringens*, and *Staphylococcus aureus*. Human antibiotic resistance has evolved from the indiscriminate use of antibiotics in response to the diseases caused by these microbes.[71] It is imperative to develop alternative drugs to current antibiotics since antibiotic-resistant

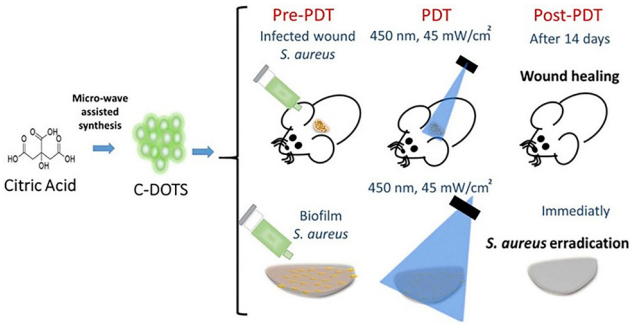

Fig. 4 *In vivo* and *in vitro* antibacterial photodynamic therapy (aPDT) studies, where aPDT mediated by CDs and blue LED light against *S. aureus* was evaluated. Reproduced under terms of the CC-BY license.[72] Copyright 2021, Romero, M. P., Alves, F., Stringasci, M. D., Buzzá, H. H., Ciol, H., Inada, N. M., and Bagnato, V. S., published by Frontiers Media S. A.

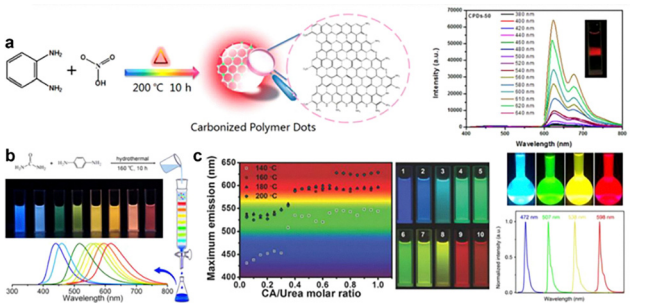

Fig. 5 Synthesis mechanism and optical characteristics of CDs. (a) Synthesis method and PL spectrum of red emissive type CPDs as well as (b) multicolor type CPDs. Optical characteristics of (c) multicolor emissive CPDs as well as CQDs. Synthesis method and PL spectrum of deep red emissive type CPDs. Reproduced under terms of the CC-BY license.[76] Copyright 2024, Khansili, N., published by Elsevier.

bacteria can turn minor infections into fatal ones. Owing to their simple synthesis methods, low toxicity, excellent photostability, high water solubility, and easy surface functionalization, CDs have recently attracted attention as promising nanomaterials for PDT.[51] The antibacterial mechanism of CDs mainly involves electrostatic interactions between positively charged CDs and negatively charged bacterial cell walls, causing structural damage and ultimately cell death[72] (Fig. 4). CDs have also been suggested as effective materials for bacterial detection and optical inactivation of multidrug-resistant (MDR) pathogens. Recent studies demonstrated the effectiveness of PDT employing citric acid-based CDs in significantly reducing microbial loads in *S. aureus* suspensions, biofilms, and infected wounds, indicating their suitability for treating Gram-positive bacterial infections. However, further *in vivo* safety evaluations and detailed mechanistic studies are necessary before the practical application of CD-based antimicrobial photodynamic therapy.[73]

Hybridization of carbon dots with other nanomaterials

Concepts and principles of CD hybridization

Combining external functional nanomaterials with carbon dots (CDs) creates hybrid systems that merge their distinct optical and chemical characteristics.[74] With dimensions of 10 nm or less, carbon dots (CDs) are zero-dimensional carbon nanomaterials distinguished by different functional groups, such as –OH, –COOH, and $–NH_2$. Effective building of composite structures is made possible by electrostatic interactions, hydrogen bonding, π–π stacking, and covalent bonding with different materials. By controlling their surface state, charge distribution, and doping elements, this hybridization aims to improve the luminescence properties, stability, and reactivity of carbon dots (CDs).[75] Combining CDs, which possess quantum confinement effects and surface defect states, with other nanomaterials enhances the photonic transport, energy transfer, and photoreactivity of the resulting hybrid system. Co-growth methods allow hybridization either in post-processing or during the synthesis phase. Composites with a variety of materials, including metals, metal oxides, polymers, and biomolecules, can be made from carbon dots (CDs). From optoelectronic devices and catalysts to biosensors, CD hybrid systems provide a flexible platform suitable for many applications[76] (Fig. 5).

Types of hybridized carbon dot structures

Metal-based carbon dot hybrids. Through surface functional groups, metal-based carbon dot hybrids as composite nanostructures combine the outstanding optical characteristics of carbon dots with the catalytic and electrochemical properties of metals and metal oxides, thus enabling efficient binding with metal ions and nanoparticles.[77] Metal doping modifies the electronic structure of carbon dots, thus regulating the HOMO–LUMO energy gap, improving luminescence characteristics, broadening the light absorption spectrum, and increasing charge transfer efficiency.[78] Silver, copper, iron, zinc, and magnesium are among the metal ions that alter the electron density distribution, thus improving catalytic active sites and photocatalytic reaction efficiency. By acting as reducing agents and stabilizers, carbon dots enable *in situ* synthesis of composites including Ag@CDs, Fe_3O_4@CDs, and CeO_2-CDs.[77] These composites demonstrate outstanding performance in applications such as antibacterial treatments, redox reactions, photothermal therapy, and ROS-based photodynamic therapy. When complexed with carbon dots, metal oxides such as Fe_3O_4, MnO_2, and CeO_2 particularly reduce electron–hole recombination and function as electron storage mediators, thus achieving exceptional photocatalytic activity. Hydrothermal and sol–gel techniques are the primary methods for metal doping and hybridization. The structure and properties of the resulting composites vary depending on the synthesis conditions and precursor types, which enables precise control over quantum yield and photostability. Effective expansion of these nanocomposites into several biomedical uses is expected, including bioimaging, drug delivery systems, antimicrobial platforms, and magnetic-based medical imaging technologies[79] (Fig. 6).

Polymer-based carbon dot hybrids. Polymer-based carbon dot hybrids are composite nanostructures that integrate the exceptional light-emitting capabilities of carbon dots with the

Fig. 6 Schematic representation of various methods used for synthesizing the metal-doped and hybrid CDs. Reproduced with permission.[79] Copyright 2025, Elsevier.

structural flexibility of polymers. Polymers serve as precursors for carbon dots and composite matrices, enhancing structural stability and light-emitting efficiency.[80] Synthetic polymers such as PEG and PCL, together with natural polymers like chitosan, augment the luminous characteristics and physical stability of carbon dots. Polymers enhance biocompatibility and dispersion stability while minimizing the aggregation of carbon structures at the nanoscale and preserving size homogeneity. Polymer–CD hybrids are primarily fabricated using *in situ* synthesis, chemical grafting, and physical mixing techniques. Simple and economical physical mixing may result in mechanical degradation and agglomeration. Chemical grafting enhances mechanical strength and optical properties by covalent bonding; it requires complex production procedures and may require organic solvents. Carbon dots are synthesized directly *in situ* inside the polymer matrix, enhancing environmental sustainability and structural integrity. CD–PCL, CD–PU, and CD–chitosan composites are used in tissue engineering and bioimaging probes. They demonstrate highly stable cellular adhesion and luminous efficacy. Diverse polymer architectures enable the regulation of surface imperfections, photonic transport pathways, and fluorescence emissions, thereby enabling optimization for various applications. Polymer-based carbon dot hybrids emerge as essential nanomaterials in several domains, including biological diagnostics, bioimaging, and therapeutic systems. Further research is required on structural stability and *in vivo* functionality for accurate material design.[74]

Organic–inorganic hybrid nanostructures. Organic–inorganic hybrid nanostructures combine the photoluminescence and surface functionalization of CDs with the physical stability of organic and inorganic matrices, thus providing ideal structures for achieving complex performance in many applications. Common inorganic materials include silica, metal oxides, carbon nitride (g-C_3N_4), MOFs, small molecules, silanes, and gel networks.[3] Particularly, Ormosil glass based on silane-functionalized carbon dots (SiCDs) offers exceptional mechanical stability, light transmittance, and homogeneous dispersion. By silane pretreatment, the carbon dots are covalently bound inside the silica matrix, thus preventing aggregation and exhibiting strong optical stability. High transmittance of over 90% in the visible and near-infrared regions (400–1350 nm) and a maximum quantum yield of 88% characterize gel glasses containing SiCDs. Through organic–inorganic hybridization, one can tune different fluorescence emission wavelengths, charge transfer efficiency, thermal stability, and photostability.[81] In MOF-CDs, for example, carbon dots enhance catalytic activity by acting as electron transfer mediators in a porous structure connecting metal nodes and organic ligands. In silica or oxide-based structures, they effectively prevent high-concentration self-quenching. Besides physical mixing, chemical bonding, and *in situ* techniques, the synthesis of these nanocomposites requires precise control of surface functional groups and synthesis conditions such as pH and temperature optimization. Thus, organic–inorganic hybrid carbon dot composites are expected to emerge as advanced nanomaterials with great functionality in many fields, including biosensors, optical films, catalysts, and environmental pollution detection and removal[3] (Fig. 7).

Biomaterial-integrated carbon dot hybrids. CDs have a structure suitable for bonding with biopolymers due in large part to their excellent biocompatibility and the presence of many surface functional groups. Combining carbon dots with naturally occurring polymers, including DNA, gelatin, and chitosan, enhances physical stability and biological responsiveness.[79] Simple mixing, cross-linking reactions, polymerization, and thermal treatment techniques are the common methods used to fabricate these composites.[82] This process generates a structure characterized by mechanical strength, photo-stimulus responsiveness, and thermal stability; reduces carbon dot aggregation; and increases surface stability. Polymers create internal spaces that enable regulated release in response to external stimuli and help drugs or bioactive compounds to stabilize[25] (Fig. 8). This capability enables complexes, such as hydrogels based on chitosan, to be used as delivery systems for bioactive molecules such as dopamine. To enable the selective elimination of cancer cells, polymers such as PEG and PEI increase the passivation of carbon dot surfaces, thus improving water solubility and inducing photothermal reactions. Additional interactions with external biomaterials are facilitated by retaining the –COOH and –OH functional groups on the surface. Moreover, one can optimize electron transport channels and broaden the spectrum of light absorption through composite structure design. Several next-generation biomedical applications, including tissue regeneration, nanodiagnostics, and precision therapy, fundamentally depend on carbon dot composites coupled with biomaterials. These applications require both biocompatibility and responsiveness, thereby enabling precise functions including drug release control, gene delivery, and cellular targeting.[83]

Advanced biomedical applications of carbon dot hybrids

Hybrid carbon dots for multimodal bioimaging

Based on ultra-small size, excellent water solubility, high biocompatibility, and strong photobleaching resistance, fluorescent metal-doped/hybrid CDs clearly outperform conventional

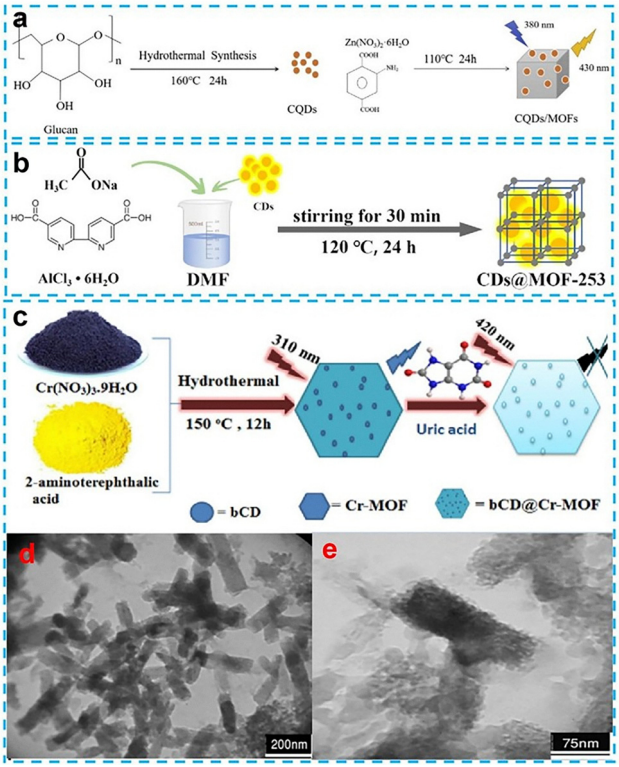

Fig. 7 (a)–(c) Synthetic route for CQDs/MOFs, CDs@MOF-253 and bCD@Cr-MOF. (d) and (e) TEM images of bCD@Cr-MOFs. Reproduced with permission.[3] Copyright 2025, Elsevier.

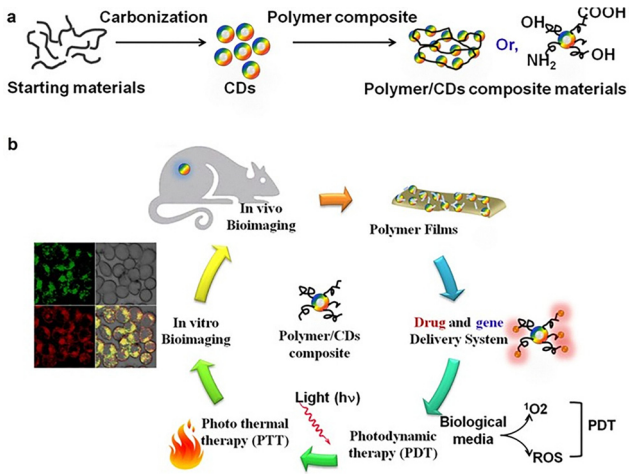

Fig. 8 (a) Schematic diagram of the synthesis of CDs from starting materials (first) and fabrication of CD/polymer composite materials (second). (b) The proposed biomedical application of CD/polymer composite materials. Reproduced under terms of the CC-BY license.[25] Copyright 2022, Adam, G, O., Sharker, S. M., and Ryu J. H., published by MDPI.

inorganic and organic fluorophores in cellular and bioimaging applications. Particularly, their emission characteristics in the NIR spectrum enable deep tissue imaging using long-wavelength light capable of penetrating skin and tissues. The fluorescence mechanism of CDs differs from that of graphene due to the presence of a bandgap.[79] This phenomenon is explained by surface-state luminescence in conjunction with the quantum confinement effect (QCE). The phenomenon known as QCE refers to the widening of the bandgap due to decreasing nanoparticle size, generating light emission at specific wavelengths.[84] Concurrently, surface energy levels produced by functional groups such as –COOH and –NH_2 on the CD surface, or doped atoms (*e.g.*, oxygen), absorb and re-emit light, thus producing surface-state luminescence. Importantly, surface chemical structure primarily determines CD emission wavelength rather than particle size. For example, as the oxygen doping level increases, the surface oxidation state rises and the bandgap progressively narrows, thus producing a red shift. Recent studies have experimentally demonstrated that metal (rhodium)-doped or hybrid carbon quantum dots (CQDs) exhibit superior near-infrared (NIR) fluorescence properties optimized for deep tissue imaging compared to conventional inorganic and organic fluorophores. This enhancement is attributed to the hybrid architecture of CQDs coupled with rhodium nanoparticles, which simultaneously achieves high aqueous solubility, excellent biocompatibility, and strong photobleaching resistance. Notably, the chemical composition, including controlled surface functional groups and optimized oxygen doping levels, was confirmed to directly influence the CQD bandgap modulation and red-shift emission control, allowing facile tuning of multicolor and NIR fluorescence emission within the 450–900 nm range[85] (Fig. 9). Furthermore, another recent study successfully developed bismuth (Bi) and gadolinium (Gd) co-doped carbon quantum dots (Bi,Gd-CQDs) exhibiting dual green and red fluorescence emissions. These nanoprobes demonstrated promising potential as multifunctional imaging agents capable of simultaneous computed tomography (CT) and T1-weighted magnetic resonance imaging (MRI). The Bi,Gd-CQDs possess high attenuation capability and short T1 relaxation times, effectively integrating optical fluorescence imaging with other diagnostic modalities on a single platform. Cellular and *in vivo* imaging experiments verified the excellent biocompatibility and deep tissue-penetrating red fluorescence of Bi,Gd-CQDs, underscoring their utility as highly promising materials for multimodal biomedical diagnostics.[86] Moreover, recently reported iodine-doped carbon dots (IDCs) exhibit significant advantages due to their facile synthesis method and enhanced computed tomography (CT) contrast capabilities. These IDCs effectively mitigate the toxicity and sensitivity limitations found in conventional CT contrast agents. They provide superior contrast enhancement in CT imaging as well as stable fluorescence imaging, making them highly promising candidates for multimodal biomedical imaging applications.[87] As discussed, this precise modulation of the emission wavelength between blue (450 nm) and red (650 nm) by simply altering surface functional groups offers a significant advantage.[88] Moreover, optimizing emission in the near-infrared (NIR) spectrum (700–900 nm) is anticipated to facilitate advances in precision biomedical diagnostics, including tumor microenvironment tracking and real-time blood flow monitoring. These characteristics underscore the potential of

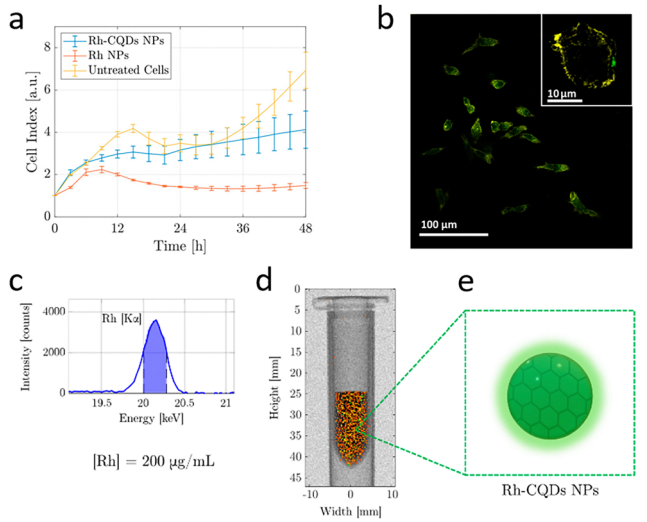

Fig. 9 RTCA assay on RAW 264.7 cell lines with Rh and Rh-CQDs NPs (a), while keeping [Rh] = 100 µg mL^{-1}. The cell index is normalized (CI = 1) at the time when NPs were added (t = 0). Confocal microscopy images (b) of fixed and stained RAW264.7 Macrophages incubated for 24 h with Rh-CQDs (100 µg mL^{-1}, in green), at 20× (63× in the inset). Alexa 555 Phalloidin (yellow) is used to visualize the plasma membrane. X-ray fluorescence (XRF) experiment on Rh-CQD NPs at 200 µg mL^{-1}. XRF spectrum recorded for 3 min at the central position of the vial (c); projection image of the vial with absorption and XRF signals (d); schematic representation of Rh-QD NPs, contained in the vial (e). Reproduced under the terms of the CC BY 4.0 license.[85] Copyright 2021, Giovanni M. Saladino, Nuzhet I. Kilic, Bertha Brodin, Bejan Hamawandi, Idris Yazgan, Hans M. Hertz, and Muhammet S. Toprak, published in Nanomaterials.

carbon dots as integral components in the development of multimodal bioimaging platforms.[89]

Hybrid CDs for enhanced biosensing

Due to their high sensitivity and rapid analysis capability, CDs and GQDs have attracted increasing interest as materials for electrochemical biosensors targeting DNA mutation and pathogen detection.[90] Reduced background signals and improved signal amplification enable fluorine- and nitrogen-doped CD-based ECL sensors to exhibit higher sensitivity and stability than conventional sensors, thereby enhancing the detection of HIV-DNA fragments. GQDs enable precise identification of HBV-DNA at low concentrations through changes in potassium ferricyanide ion current. GQDs utilize current variations in electrochemically active materials induced by interactions with targets. In contrast, variations in electron transfer efficiency or ECL signal amplification upon target DNA binding constitute the primary detection mechanism of CD sensors[91] (Fig. 10). Integration of carbon-based quantum dot biosensors with the CRISPR-Cas12a system significantly reduces analysis time to about thirty minutes compared to conventional PCR methods.[92] Cancer-related genes (miRNA-21), viruses (HIV, HBV), and bacteria (*E. coli*) are among the various analytical targets covered by this method.[93] Technological developments redefine paradigms in early disease diagnosis and pathogen monitoring, as continuous performance improvements for clinical applications

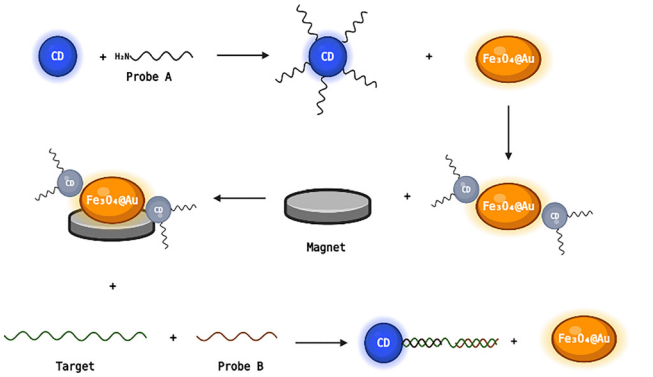

Fig. 10 Schematic illustration of the detection steps of DNA target. Created with biorender.com.

combined with cost-saving advantages enhance their practical prospects.[94]

Hybrid CDs in drug and gene delivery systems

Since gene therapy offers new approaches to treat genetic diseases including Parkinson's disease and immunodeficiency diseases, it has attracted considerable attention over the past ten years. However, conventional virus-based vector systems still have limitations such as low gene delivery efficiency, high manufacturing costs, and potential induction of immune responses. Due to their excellent biocompatibility, high solubility, and capacity to bind with both organic and inorganic materials, CDs have recently emerged as promising alternatives to viral vectors for gene delivery, overcoming these limitations[95] (Fig. 11). CDs efficiently deliver plasmid DNA or siRNA into cells through clathrin and caveolae-mediated endocytosis, showing higher gene expression efficiency than the micropinocytosis pathway.[96] Furthermore, inhibitor assays (DMA) have clarified the precise internalization pathway of CDs, providing essential information for the design of targeted delivery systems.[95] Optimizing CD properties is expected to enable non-invasive and highly effective gene therapy, as physicochemical parameters such as particle size, surface charge, and shape determine cellular uptake efficiency. Thus, in the field of gene therapy, CD-based gene delivery systems are anticipated to overcome the limitations of viral vectors and develop into effective and stable therapeutic platforms.[97]

Hybrid CDs for synergistic cancer therapy

Nanoplatforms for combined PDT and PTT. Phototherapy is a topic of ongoing investigation in cancer treatment due to its low toxicity, minimal invasiveness, reduced side effects, and reduced incidence of drug resistance, providing several advantages over radiation therapy, chemotherapy, and surgery.[98] However, limited light penetration lowers its effectiveness in treating deep tumors. Recently proposed solutions for this issue rely on X-ray radiation, NIR light, self-emitting nanoparticles and other light sources. Phototherapy, including PDT and PTT, utilizes light at specific wavelengths.[99] PTT removes cancer cells *via* heat generated by photothermal agents (PAs), while PDT kills tumor cells through ROS generated by irradiating photosensitizers (PSs).

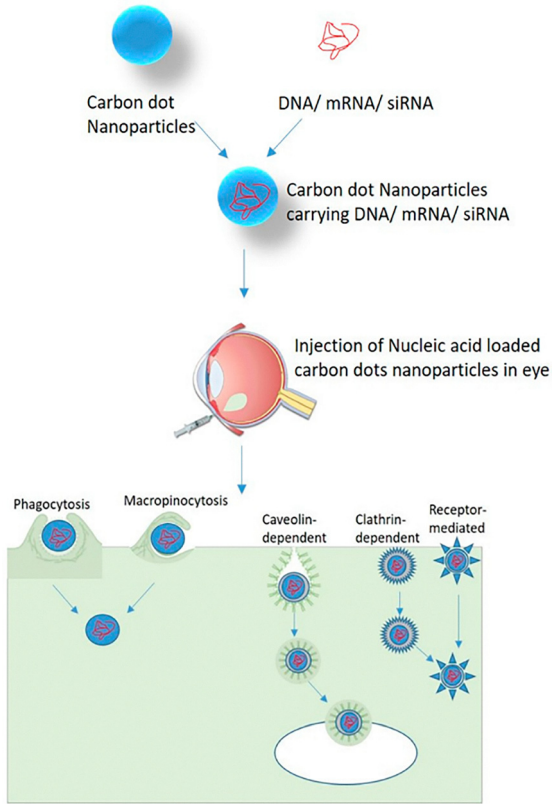

Fig. 11 Nucleic acid delivery in retinal cells using CD nanoparticles. Reproduced under terms of the CC-BY license.[95] Copyright 2021, Khiev, D., Mohamed, Z. A., Vichare, R., Paulson, R., Bhatia, S., Mohapatra, S., Volo, G. P., Valapala, M., Kerur, N., Passaglia, C. L., *et al.*, published by MDPI.

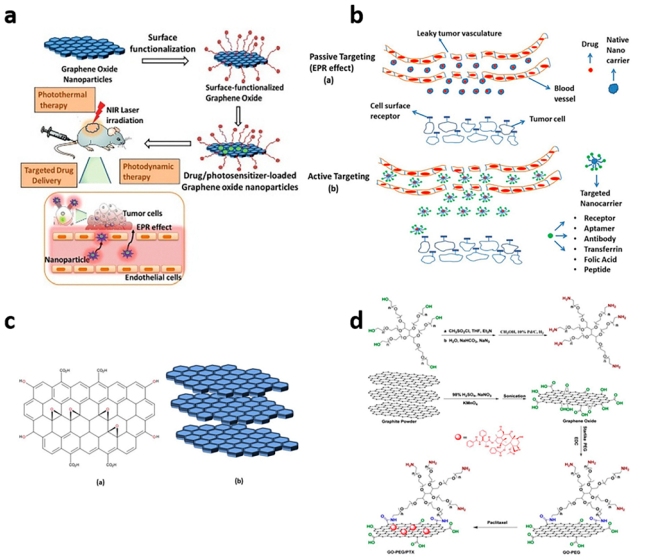

Fig. 12 (a) Surface functionalization of graphene oxide (GO) nanoparticles (NPs) and loading of drug and photosensitizer on the surface-modified GO–metal NPs. Finally, the application of GO nanocomposites for targeted drug delivery and *in vivo* photodynamic therapy using the near-infrared (NIR) laser irradiation is shown. (b) The figure shows passive enhanced permeability and retention (EPR) effect. (c) Chemical structure of graphene oxide (GO) and multilayered planar structural arrangement of GO. (d) Preparation of graphene oxide (GO)-polyethylene glycol (PEG)/paclitaxel (PTX) nanoscale drug delivery system.[100] Copyright 2020, Khan, I., Saeed, K., Khan, I., published by MDPI.

Both treatments require active agents to satisfy specific physicochemical criteria including excellent photoresponsiveness, low toxicity toward healthy cells, and high specificity[100] (Fig. 12). Current studies primarily aim to combine PDT and PTT to generate a synergistic therapeutic effect surpassing either treatment alone. Recently, several nanocomposite materials, especially graphene oxide-based platforms, have attracted interest for achieving PDT/PTT synergy. Graphene oxide composites combined with amino-functionalized hybrid nanoparticles (*e.g.*, Yb^{3+}/Er^{3+}@$NaGdF_4$:Nd^{3+}/Yb^{3+}), PEG, and Ce6 demonstrate significant ROS-generating capability and enhanced photothermal conversion efficiency. Under 808 nm wavelength irradiation, simultaneous PDT/PTT application in a mouse liver cancer (U14) model significantly reduced the relative tumor volume (V/V) to half its original level after 14 days, demonstrating remarkable therapeutic efficacy.[101] These results confirm that nanocomposites combining both therapies provide superior cancer treatment strategies compared to conventional monotherapies. Thus, future development and optimization of phototherapy-based nanomaterials are anticipated to greatly increase cancer treatment efficiency and overcome current penetration depth limitations.[102]

Targeted drug release and smart delivery

Due to their excellent fluorescence characteristics, biocompatibility, and multifunctionality compared to conventional semiconductor QDs, carbon dots (CDs) have attracted interest as a nanoplatform for early diagnosis and targeted cancer treatment.[103] Strategies targeting specific cellular organelles, such as mitochondria, are particularly promising since they can increase the sensitivity of chemotherapy and radiation treatment, although current treatment approaches have major disadvantages including pharmacokinetic limitations and systemic toxicity.[104] Recent extensive development of targeted nanocomposites based on CDs has overcome these constraints. Confocal microscopy studies, for instance, confirmed that the Hep-CDs/DOX complex firmly binds and efficiently internalizes into A549 lung cancer cells. Heparin appears to enhance blood–cell interactions, thereby improving delivery efficiency[105] (Fig. 13). Moreover, CDs offer advantages for non-invasive treatment monitoring and accurate cancer therapy compared to conventional solid lipid nanoparticles or liposomes through precise targeting and real-time fluorescence tracking *via* surface functionalization. Enhanced intracellular absorption, improved drug loading efficiency, and anticancer efficacy were observed in CDs-DOX complexes, synthesized by a hydrothermal synthesis technique combining citric acid and ethylenediamine, compared to basic DOX. Excellent biocompatibility and pharmacological efficacy of CDs were confirmed by evaluating cell toxicity on L929 and MCF-7 cell lines.[106] These results suggest that CD-based nanocomposites will be significantly important in targeted therapy and cancer diagnosis, as they appear capable of overcoming the limitations of conventional cancer treatments, such as low drug delivery efficiency and systemic toxicity.[107]

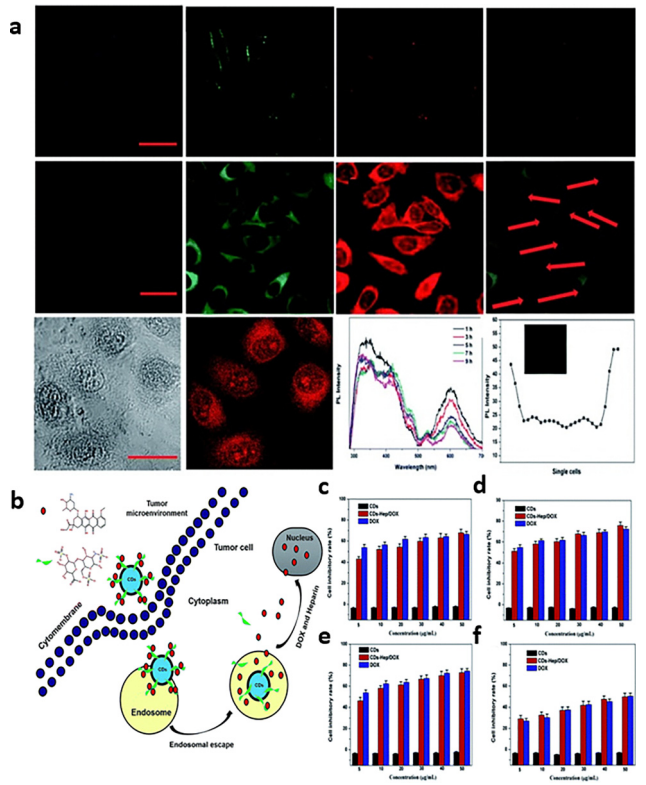

Fig. 13 (a) LSCM images of HeLa cells incubated with CDs-Hep for 3 h, A549 cells incubated with CDs-Hep/DOX for 5 h, and LSCM images of A549 cells incubated with DOX for 5 h. (b) Schematic of intracellular release behavior of DOX from the CDs-Hep/DOX drug delivery system. The cell inhibitory rate of MCF-7 (c), HeLa (d), A549 (e) and NIH3T3 cells (f) after incubation with CDs and CDs-Hep/DOX or free DOX for 48 h. Reproduced under terms of the CC-BY license.[105] Copyright 2017, Wang, Y., Li, Y., Han, X., Zhang, X., Zhang, Y., Liu, Y., published by Royal Society of Chemistry.

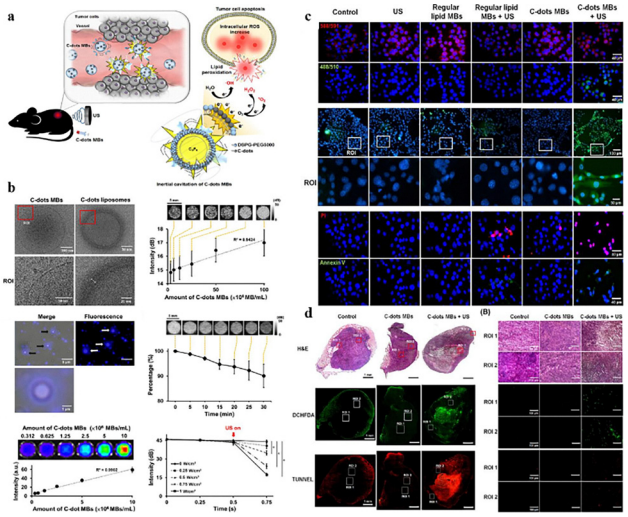

Fig. 14 (a) Illustration of SDT for anti-tumor application using CD MBs with US. (b) The properties of CD MBs. (c) Cell experiments to determine the mechanism of cell death induced by CD MBs + US. (d) Histological images of H&E staining, DCFDA staining, and TUNEL staining revealing tissue damage, ROS level, and apoptosis, respectively, after different treatment protocols, and enlargement of ROIs. Reproduced under terms of the CC-BY license.[110] Copyright 2023, Fan, C.-H., Wu, N., Yeh, C.-K., published by Elsevier.

Sonodynamic therapy (SDT) with hybrid CDs

SDT is a non-invasive cancer treatment using ROS generated by sonosensors triggered by ultrasonic waves.[108] As possible SDT platforms, the excellent biocompatibility and ROS-generating capacity of CD-based hybrid systems have recently attracted significant interest. Particularly, RB-CDs@RGD, with αvβ3 integrin targeting capability, displayed selective accumulation in glioblastoma cells and strong ROS-generation capability, causing cell death and validating the efficacy of SDT.[109] Furthermore, even under low-energy ultrasonic waves, the C-dot MBs system combining liposomes, perfluoropropane gas, and CDs demonstrated outstanding ROS-generating efficiency, optimizing tumor therapeutic effects. TEM analysis confirmed this hybrid system's monolayer lipid structure; it also demonstrated significant contrast enhancement in 7.5 MHz ultrasonic imaging and maintained over 90% stability at 37 °C. *In vitro* studies revealed a 50.1% cell death rate in TRAMP cells treated with C-dot MBs combined with ultrasonic waves, a result that clearly demonstrates strong anticancer activity. *In vivo* solid tumor models also confirmed excellent therapeutic efficacy; tumor volume decreased by 70% and apoptotic cell count increased by 2.8-fold following ultrasonic irradiation. Injected C-dot MBs naturally degraded in 400 seconds, thus reducing long-term toxicity[110] (Fig. 14). The future of non-invasive tumor treatment using CD-based SDT platforms looks bright, focusing on combining selective tumor cell death efficacy, long-term toxicity evaluation, and large-scale production technology development.[111]

Antibacterial and antimicrobial properties of CD hybrids

CD-based hybrid systems are increasingly valuable as effective therapeutic approaches in antimicrobial treatment through structural disruption, biochemical damage, and synergistic interactions among multiple mechanisms.[112] Carbon dots (CDs), utilizing the various functional groups and photothermal properties of their surfaces, have recently been shown to exhibit effective antibacterial activities against antibiotic-resistant strains.[113] Targeting MurD ligase specifically on bacterial cell walls, D-glutamic acid-based CDs increase membrane permeability through electrostatic interactions with negatively charged surfaces. Moreover, near-infrared irradiation disrupts cell walls and denatures bacterial membrane proteins, thus significantly enhancing antimicrobial properties in combination with conventional treatments. Competitive analyses confirmed that positively charged guanidinium-functionalized CDs specifically interact with lipid A, disrupting the outer membrane of Gram-negative bacteria. For targeting drug-resistant bacterial infections, results indicate that CDs could effectively serve as biocompatible coatings, drug delivery systems, and nanomedicines[114] (Fig. 15). Still under investigation, however, are mechanisms of multidrug resistance, manufacturing process standardization, and long-term toxicity assessment. Thus, hybrid systems based on CDs exhibit great potential as

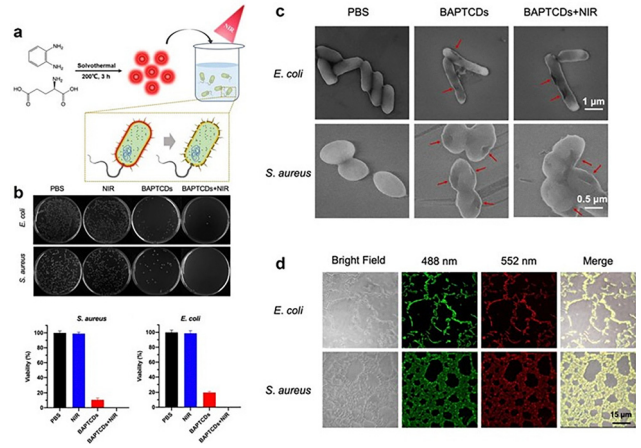

Fig. 15 (a) Schematic illustration of synthesis of the BAPTCD mechanism of bacterial targeting and photothermal ablation of BAPTCDs upon laser irradiation. (b) Photographic images of the colonies, and bacterial viability of *E. coli* ATCC 700926 and *S. aureus* ATCC 29213. (c) SEM images of *E. coli* ATCC 700926 and *S. aureus* ATCC 29213 treated using BAPTCDs at 200 μg mL^{-1} with or without NIR (the red arrow shows where the bacterial cell wall has broken). (d) Confocal microscopy images of *E. coli* ATCC 700926 and *S. aureus* ATCC 29213 treated with BAPTCDs. Reproduced under terms of the CC-BY license.[114] Copyright 2022, Qie, X., Zan, M., Gui, P., Chen, H., Wang, J., Lin, K., Mei, Q., Ge, M., Zhang, Z., Tang, Y., Dong, W.-F., Song, Y., published by Frontiers Media S. A.

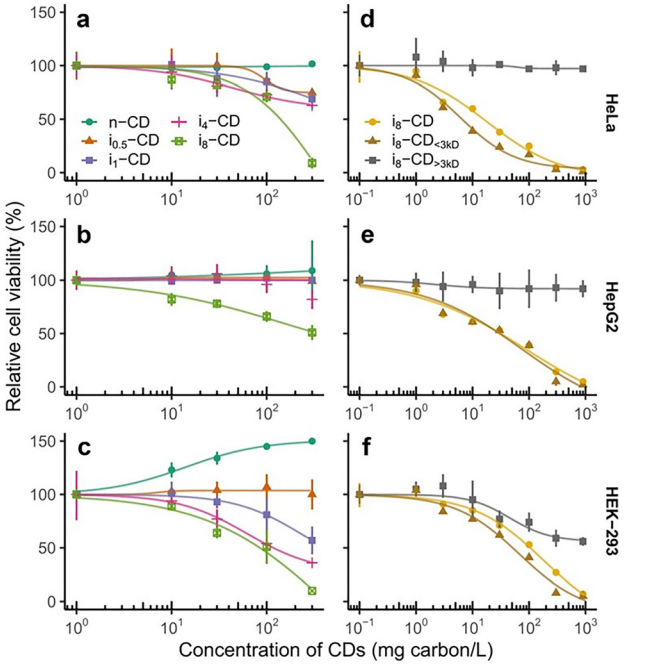

Fig. 16 Cell viability testing of laboratory-synthesized CDs (a)–(c) Dose–response data showing that the cytotoxicity of CDs to HeLa, HepG2, and HEK-293 cells increased with irradiation time. (d)–(f) Dose–response data showing that the photolyzed products in the <3 kD fraction contributed substantially to the photo-induced cytotoxicity of CDs to HeLa, HepG2, and HEK-293 cells. Reproduced under terms of the CC-BY license.[117] Copyright 2021, Liu, Y.-Y., Yu, N.-Y., Fang, W.-D., Tan, Q.-G., Ji, R., Yang, L.-Y., Wei, S., published by Springer Nature.

targeted antibacterial treatments capable of overcoming limitations of current methods.[115]

Challenges and future perspectives

Toxicity and biocompatibility considerations

Although the toxicity profile of CDs generally shows excellent biocompatibility and low cellular toxicity, notable variations may occur depending on specific environmental conditions and surface functionalization.[116] Recent studies revealed that CDs under continuous illumination degrade into low-molecular-weight compounds, producing byproducts including polyethylene glycol and aromatic compounds, which have been confirmed to induce cellular toxicity. In HEK-293, HeLa, and HepG2 cells, light-exposed CDs particularly showed time-dependent toxicity; undegraded CDs had minimal effect. High concentrations of CDs in zebrafish embryo models also induced physiological toxic reactions. Moreover, particle size and chemical characteristics of surface functional groups influence the intensity of toxicity[117] (Fig. 16). Furthermore, tissue distribution analyses revealed that CDs primarily accumulated in the liver and heart, a finding that indicates possible organ toxicity. Thus, to accurately evaluate the biocompatibility of CDs, consideration of particle size, synthesis routes, surface functional groups, photostability, toxic byproduct generation due to degradation, and assessments at the tissue and organism levels is essential.[118]

Stability and scalability of hybrid carbon dots

The practical application of hybrid CDs requires the development of technologies for ensuring stability and enabling mass production. CDs are structurally susceptible to degradation, so they must maintain stability under various environmental conditions.[119] To address this, recent strategies include embedding carbon structures within silica or salt crystals or combining them with polymer matrices to improve fluorescence stability and reduce photobleaching under oxidative conditions. In terms of mass production technology, diverse synthesis methods including hydrothermal synthesis have been suggested. One-step methods that simultaneously achieve solid-state solvent-free synthesis and carbonization with surface functionalization contribute to process simplification and increased production efficiency.[120] For the practical use of hybrid CDs, solutions that concurrently address process-related factors such as reproducibility, uniformity, and purification, as well as ensuring stability, are required.[121] Therefore, if hybrid CDs can simultaneously fulfill optical performance, stability, and productivity, they are expected to serve as key materials in various fields such as biosensors, diagnostic technologies, and energy conversion devices.[122]

Emerging trends and potential clinical applications

CDs are attracting attention as potential next-generation diagnostic and therapeutic tools due to their diverse applications and biocompatibility.[123] Recent studies have focused on possible applications of these nanoparticles as photothermal therapy agents generating heat in response to external stimuli or as

drug carriers. Furthermore, they are suitable for photodynamic therapy, which generates reactive oxygen species in response to light. They can also function as gene delivery systems.[124] Excellent tissue penetration of CDs emitting near-infrared (NIR) light makes them ideal for heat-based treatments and tumor-targeted imaging.[66] Composite nanostructures loaded with anticancer drugs or genetic materials are currently under development for theragnostic systems that integrate diagnosis and treatment, with their efficacy assessed in various animal models.[125] Lesion sites are tracked in real time using CD-based technologies; pathways of drug action are observed; and biological responses are recorded.[126] Regarding long-term accumulation and tissue degradation rates, preclinical data provide a basis for evaluating clinical relevance.[127] Recent work has shown that a DOX-loaded hybrid system (ICG-loaded HA-CD@p-CBA-DOX) achieved roughly an 80% tumor inhibition rate in 4T1 tumor-bearing mice compared with free DOX, and in a hepatocellular carcinoma model (HepG2 xenografts), CDs–DOX led to about a 50% reduction in tumor volume within 24 hours and more than 72% inhibition by day 20, providing clear quantitative benchmarks. In addition, surface-modified CDs exhibited robust ROS generation under 635 nm irradiation together with high photothermal conversion efficiency (on the order of 70%), demonstrating suppressed tumor growth in 4T1 mouse models as a multifunctional photo-theranostic platform.[128] Another study engineered gold–silver-doped carbon nanocomposites to enhance photothermal therapy against colorectal cancer; leveraging the brightness increase from the gold surface plasmon resonance effect yielded strong NIR absorption, and the resulting *in vitro*/*in vivo* data substantiated photothermal anticancer efficacy, thereby strengthening prospects for clinical translation.[129] Collectively, these advances have extended into multi-spectral imaging modalities, enabling a single probe to capture detailed physiological information.[130] This, in turn, supports early detection of infectious diseases, precise delineation of tumor margins, and long-term monitoring of therapeutic responses.[131]

Conclusions

Due to their excellent optical properties, high biocompatibility, and simplicity of surface functionalization, carbon dots (CDs) have become promising next-generation biomedical nanomaterials. Based on quantum confinement effects and surface functional groups, CDs exhibit distinct luminescence characteristics; their simple synthesis methods and high solubility have shown promise in bioimaging, biosensing, drug and gene delivery, and phototherapy. Combining CDs with materials such as metal nanoparticles, polymers, and organic–inorganic hybrid structures enhances their functional properties and environmental stability, enabling the expansion into multifunctional nanosystems. Hybrid CD composites integrating therapeutic modalities, including photothermal, photodynamic, and ultrasonic responses, are developing into theragnostic technologies for simultaneous diagnosis and treatment. Clinical application of these technologies requires biological safety verification through *in vivo* distribution analysis, immune response evaluation, and tissue-specific metabolic tracking. Additionally, precise medical applications depend on integration with AI-based tailored treatment platforms. Addressing biocompatibility, structural reproducibility, and large-scale production standardization will position CDs and their hybrid materials as essential components in future medical technologies for precision cancer treatment and infectious disease control. This review shows that carbon dots (CDs) and their hybrid nanostructures can realize integrated theranostics—diagnosis and therapy on a single platform. Hybridization and spectral engineering elevate CD signal fidelity and stability, bringing clinical use closer. We first summarized structure and synthesis principles. Hybridization with metals, inorganic matrices, or polymers reduces photobleaching and improves colloidal stability. Surface functionalization and heteroatom doping tune electron/energy transfer. As a result, quantum yield and the signal-to-noise ratio increase. These material advances translate into higher analytical sensitivity and better reproducibility across applications. In diagnostics, fluorescence/NIR imaging and SERS/MRI-augmented systems achieved higher target selectivity and *in vivo* signal stability. Lower limits of detection were reported for nucleic acids, ions, proteins, and metabolites, with real-time monitoring in complex media. Mechanistic designs that control distance-dependent quenching/recovery and charge/energy transfer pathways lowered false positives and improved accuracy. In therapy, PTT and PDT work alone or in combination. PTT converts NIR absorption into localized heat for minimally invasive ablation. PDT leverages aqueous compatibility, photostability, and biocompatibility to address the limitations of hydrophobic photosensitizers. Together, these modes trigger complementary death pathways—thermal damage, ROS generation, vascular effects, and immune activation. Hybrid designs increase $^1O_2$ yield, tumor accumulation, and photothermal synergy, improving tumor eradication and safety margins. Carbon-based emitters with red/near-infrared (R/NIR) emission improve tissue penetration and reduce autofluorescence. A large Stokes shift, low scattering, and long lifetimes further strengthen imaging reliability and enhance PDT efficiency. Such spectral engineering is achieved by controlling the sp^2 domain size, surface oxidation/defects, heteroatom doping, and precursor/reaction/post-treatment conditions. These levers provide the physical basis for the diagnostic and therapeutic gains mentioned above. Manufacturing and safety remain pivotal. For scale-up, solid-state or low-solvent processes and one-step carbonization–passivation simplify production and increase throughput. Stability is improved through silica/salt or polymer encapsulation and surface passivation. Next steps require systematic assessment of toxicology, biodistribution, excretion, and photolysis by-products, along with standardized synthesis–characterization–preclinical protocols and clear QC metrics. In sum, CD–hybrid platforms can unify (i) mechanism-driven surface chemistry and doping, (ii) R/NIR-centric spectral engineering, and (iii) multimodal therapy (PTT, PDT, and SDT) to deliver

precision diagnosis and targeted therapy in one nanosystem. The immediate priorities are standardization and scale-up, deeper mapping of immune–microenvironment interactions, and clinical readiness validation. With these in place, CD hybrids can mature into practical theranostic platforms.

Author contributions

Gyeongsu Seo and Byoung-su Kim: writing – original draft and writing – review and editing. Hyeongu Lim: investigation. Jaewon Choi: data curation. Minse Kim: investigation. Hyungseok Lee: supervision and funding acquisition. Hyun-Ouk Kim: supervision, writing – review and editing and funding acquisition.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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Notes and references

1 N. Rabiee, S. Iravani and R. S. Varma, *Molecules*, 2022, **27**(19), 6186.
2 B. D. Mansuriya and Z. Altintas, *Nanomaterials*, 2021, **11**(10), 2525.
3 X. Meng, F. Shen, D. Wang, S. Zhang, J. Hou, L. Ding and J. Sun, *Chem. Eng. J.*, 2025, **503**, 158278.
4 K. Singh, T. Mandal, U. P. Pandey and V. Singh, *ACS Biomater. Sci. Eng.*, 2025, **11**, 742–773.
5 L. Đordevic, F. Arcudi, M. Cacioppo and M. Prato, *Nat. Nanotechnol.*, 2022, **17**, 112–130.
6 W. Liu, C. Li, Y. Ren, X. Sun, W. Pan, Y. Li, J. Wang and W. Wang, *J. Mater. Chem. B*, 2016, **4**, 5772–5788.
7 C. J. Shearer, A. Cherevan and D. Eder, *Adv. Mater.*, 2014, **26**, 2295–2318.
8 X. Dong, A. E. Bond, N. Pan, M. Coleman, Y. Tang, Y.-P. Sun and L. Yang, *Int. J. Nanomed.*, 2018, 8025–8035.
9 T. Bhattacharya, G. H. Shin and J. T. Kim, *Pharmaceutics*, 2023, **15**(3), 1019.
10 A. M. Diez-Pascual, *Int. J. Mol. Sci.*, 2021, **22**(14), 7726.
11 J. Li and X. Gong, *Small*, 2022, **18**, e2205099.
12 K. J. Lagos, H. H. Buzza, V. S. Bagnato and M. P. Romero, *Int. J. Mol. Sci.*, 2021, **23**(1), 22.
13 Y. Li, Z. Xu, Z. Qi, X. Huang, M. Li, S. Liu, Y. Yan and M. Gao, *Int. J. Nanomed.*, 2024, **19**, 10899–10915.
14 W. Zajac, A. Rozycka and A. Trenczek-Zajac, *Inorg. Chem.*, 2023, **62**, 10955–10964.
15 H. B. A. Sousa, C. S. M. Martins and J. A. V. Prior, *Nanomaterials*, 2021, **11**(3), 611.
16 S. R. Lodha, J. G. Merchant, A. J. Pillai, A. H. Gore, P. O. Patil, S. N. Nangare, G. G. Kalyankar, S. A. Shah, D. R. Shah and S. P. Patole, *Heliyon*, 2024, **10**, e41020.
17 L.-N. Wu, Y.-J. Yang, L.-X. Huang, Y. Zhong, Y. Chen, Y.-R. Gao, L.-Q. Lin, Y. Lei and A.-L. Liu, *Carbon*, 2022, **186**, 452–464.
18 L. Cui, X. Ren, M. Sun, H. Liu and L. Xia, *Nanomaterials*, 2021, **11**(12), 3419.
19 Y. Zhou, W. Zhang and R. M. Leblanc, *J. Phys. Chem. B*, 2022, **126**, 10777–10796.
20 A. Nzihou, K. C. Hui, N. H. Zainal Abidin, N. S. Sambudi, R. Boopathy, M. Nasef, S. Yusup, D. C. W. Tsang, N. A. Amran and B. Abdullah, *E3S Web Conf.*, 2021, **287**, 02002.
21 H. Ding, X.-H. Li, X.-B. Chen, J.-S. Wei, X.-B. Li and H.-M. Xiong, *J. Appl. Phys.*, 2020, **127**, 231101.
22 T. Mandal, S. R. Mishra, K. Singh, H. Agarwalla, R. E. Masto, M. Kumar and V. Singh, *J. Nanopart. Res.*, 2023, **25**(6), 125.
23 M. Liu, *Nanoarchitectonics*, 2020, **1**, 1–12.
24 N. Javed and D. M. O'Carroll, *Part. Part. Syst. Charact.*, 2021, **38**(4), 2000271.
25 G. O. Adam, S. M. Sharker and J. H. Ryu, *Appl. Sci.*, 2022, **12**(10), 10565.
26 S. D. Dsouza, M. Buerkle, P. Brunet, C. Maddi, D. B. Padmanaban, A. Morelli, A. F. Payam, P. Maguire, D. Mariotti and V. Svrcek, *Carbon*, 2021, **183**, 1–11.
27 D. Ozyurt, M. Al Kobaisi, R. K. Hocking and B. Fox, *Carbon Trends*, 2023, **12**, 100276.
28 M. G. Giordano, G. Seganti, M. Bartoli and A. Tagliaferro, *Molecules*, 2023, **28**, 2772.
29 H. Liu, X. Zhong, Q. Pan, Y. Zhang, W. Deng, G. Zou, H. Hou and X. Ji, *Coord. Chem. Rev.*, 2024, **498**, 215468.
30 S. Dua, P. Kumar, B. Pani, A. Kaur, M. Khanna and G. Bhatt, *RSC Adv.*, 2023, **13**, 13845–13861.
31 A. Kumar, D. Kumar and M. Saikia, *Mater. Adv.*, 2023, **4**, 3951–3966.
32 H. Kaurav, D. Verma, A. Bansal, D. N. Kapoor and S. Sheth, *Front. Chem.*, 2023, **11**, 1227843.
33 C. Campalani and D. Rigo, *Next Sustainability*, 2023, **1**, 100001.
34 W. Su, H. Wu, H. Xu, Y. Zhang, Y. Li, X. Li and L. Fan, *Mater. Chem. Front.*, 2020, **4**, 821–836.
35 H. F. Etefa, A. A. Tessema and F. B. Dejene, *C*, 2024, **10**(3), 60.
36 H. Kaurav, D. Verma, A. Bansal, D. N. Kapoor and S. Sheth, *Front. Chem.*, 2023, **11**, 1227843.

37 Q. Zeng, T. Feng, S. Tao, S. Zhu and B. Yang, *Light: Sci. Appl.*, 2021, **10**, 142.
38 Z. A. Qureshi, H. Dabash, D. Ponnamma and M. K. G. Abbas, *Heliyon*, 2024, **10**, e31634.
39 S. Tajik, Z. Dourandish, K. Zhang, H. Beitollahi, Q. V. Le, H. W. Jang and M. Shokouhimehr, *RSC Adv.*, 2020, **10**, 15406–15429.
40 T. Mandal, S. R. Mishra, M. Kumar and V. Singh, *Sustainable Energy Fuels*, 2024, **8**(24), 5638–5671.
41 H. Singh, M. Razzaghi, H. Ghorbanpoor, A. Ebrahimi, H. Avci, M. Akbari and S. Hassan, *Adv. Drug Delivery Rev.*, 2025, 115644.
42 N. Ahmed, M. Hussain, T. H. Qamar, S. Ul Hassan, P. Xia, L. Ma, X. Gao and L. Deng, *Org. Electron.*, 2025, **139**, 107197.
43 S. Wang, C. P. McCoy, P. Li, Y. Li, Y. Zhao, G. P. Andrews, M. P. Wylie and Y. Ge, *Nanomaterials*, 2024, **14**(15), 1250.
44 Z. Li, L. Wang, Y. Li, Y. Feng and W. Feng, *Mater. Chem. Front.*, 2019, **3**, 2571–2601.
45 V. L. John, Y. Nair and T. P. Vinod, *Part. Part. Syst. Charact.*, 2021, **38**(11), 2100170.
46 X. Miao, D. Qu, D. Yang, B. Nie, Y. Zhao, H. Fan and Z. Sun, *Adv. Mater.*, 2018, **30**(1), 1704740.
47 M. Bartkowski, Y. Zhou, M. Nabil Amin Mustafa, A. J. Eustace and S. Giordani, *Chemistry*, 2024, **30**, e202303982.
48 F. Bruno, A. Sciortino, G. Buscarino, M. L. Soriano, A. Rios, M. Cannas, F. Gelardi, F. Messina and S. Agnello, *Nanomaterials*, 2021, **11**(5), 1265.
49 A. Khayal, V. Dawane, M. A. Amin, V. Tirth, V. K. Yadav, A. Algahtani, S. H. Khan, S. Islam, K. K. Yadav and B.-H. Jeon, *Polymers*, 2021, **13**, 3190.
50 Y. Xue, C. Liu, G. Andrews, J. Wang and Y. Ge, *Nano Convergence*, 2022, **9**, 15.
51 P. Koutsogiannis, E. Thomou, H. Stamatis, D. Gournis and P. Rudolf, *Adv. Phys.: X*, 2020, **5**(1), 1758592.
52 V. Singh, K. S. Rawat, S. Mishra, T. Baghel, S. Fatima, A. A. John, N. Kalleti, D. Singh, A. Nazir and S. K. Rath, *J. Mater. Chem. B*, 2018, **6**, 3366–3371.
53 S. R. Mishra, T. Mandal, S. Sahu, M. Mishra, R. N. Senapati and V. Singh, *ACS Omega*, 2024, **9**, 38916–38924.
54 D. Maiti, X. Tong, X. Mou and K. Yang, *Front. Pharmacol.*, 2018, **9**, 1401.
55 C. L. Shen, H. R. Liu, Q. Lou, F. Wang, K. K. Liu, L. Dong and C. X. Shan, *Theranostics*, 2022, **12**, 2860–2893.
56 M. Ullah, U. A. Awan, H. Ali, A. Wahab, S. U. Khan, M. Naeem, M. Ruslin, A. Z. Mustopa and N. Hasan, *J. Nanotheranostics*, 2024, **6**(1), 1.
57 Y. Li, H. Qi, Y. Geng, L. Li and X. Cai, *Colloids Surf., B*, 2024, **234**, 113743.
58 G. Liu, S. Wang, S. Wang, R. Wu, H. Li, M. Zha, J. Song, Y. Yin, K. Li, J. Mu and Y. Shi, *J. Nanobiotechnol.*, 2023, **21**, 151.
59 O. U. Akakuru, J. Xing, S. Huang, Z. M. Iqbal, S. Bryant, A. Wu and M. Trifkovic, *Small*, 2025, **21**, e2404591.
60 T. Bhattacharya, S. Preetam, S. Mukherjee, S. Kar, D. S. Roy, H. Singh, A. Ghose, T. Das and G. Mohapatra, *Discover Nano*, 2024, **19**, 122.
61 A. Karagianni, N. G. Tsierkezos, M. Prato, M. Terrones and K. V. Kordatos, *Carbon*, 2023, **203**, 273–310.
62 P. Agostinis, K. Berg, K. A. Cengel, T. H. Foster, A. W. Girotti, S. O. Gollnick, S. M. Hahn, M. R. Hamblin, A. Juzeniene, D. Kessel, M. Korbelik, J. Moan, P. Mroz, D. Nowis, J. Piette, B. C. Wilson and J. Golab, *Ca-Cancer J. Clin.*, 2011, **61**, 250–281.
63 A. Chiaviello, I. Postiglione and G. Palumbo, *Cancers*, 2011, **3**, 1014–1041.
64 H. Sun, S. Sun, H. Wang, K. Cheng, Y. Zhou, X. Wang, S. Gao, J. Mo, S. Li, H. Lin and P. Wang, *Acta Biomater.*, 2025, **194**, 352–363.
65 P. Mroz, A. Yaroslavsky, G. B. Kharkwal and M. R. Hamblin, *Cancers*, 2011, **3**, 2516–2539.
66 S. Das, S. Mondal and D. Ghosh, *Front. Bioeng. Biotechnol.*, 2023, **11**, 1333752.
67 G. B. Kharkwal, S. K. Sharma, Y. Y. Huang, T. Dai and M. R. Hamblin, *Lasers Surg. Med.*, 2011, **43**, 755–767.
68 X. Chen and J. Li, *Carbon*, 2020, **158**, 1–23.
69 L. Yang, Z. Wang, J. Wang, W. Jiang, X. Jiang, Z. Bai, Y. He, J. Jiang, D. Wang and L. Yang, *Nanoscale*, 2016, **8**, 6801–6809.
70 T. Feng, X. Ai, G. An, P. Yang and Y. Zhao, *ACS Nano*, 2016, **10**, 4410–4420.
71 F. Cui, Y. Ye, J. Ping and X. Sun, *Biosens. Bioelectron.*, 2020, **156**, 112085.
72 M. P. Romero, F. Alves, M. D. Stringasci, H. H. Buzza, H. Ciol, N. M. Inada and V. S. Bagnato, *Front. Microbiol.*, 2021, **12**, 662149.
73 A. Saravanan, M. Maruthapandi, P. Das, J. H. T. Luong and A. Gedanken, *Nanomaterials*, 2021, **11**(2), 369.
74 R. Pathak, V. D. Punetha, S. Bhatt and M. Punetha, *J. Mater. Sci.*, 2023, **58**, 6419–6443.
75 Y. Xiao, Z. Wang, J. Fu, J. Zhang, Q. He, H. Lu, Q. Zhou and H. Wang, *Water*, 2025, **17**(2), 210.
76 N. Khansili, *Environ. Adv.*, 2024, **16**, 100542.
77 B. Domingo-Tafalla, E. Martinez-Ferrero, F. Franco and E. Palomares-Gil, *Molecules*, 2022, **27**(3), 1081.
78 R. Yu, M. Ou, Q. Hou, C. Li, S. Qu and Z. A. Tan, *Light: Adv. Manuf.*, 2024, **5**, 41.
79 N. Tejwan, A. K. Saini, A. Sharma, T. A. Singh, N. Kumar and J. Das, *J. Controlled Release*, 2021, **330**, 132–150.
80 Y. Zhou, S. K. Sharma, Z. Peng and R. M. Leblanc, *Polymers*, 2017, **9**(2), 67.
81 W. Shi, J. Wang, S. Yang, X. Lin, F. Guo and J. Shi, *J. Chem. Technol. Biotechnol.*, 2020, **95**, 2129–2138.
82 X. Xing, Z. Wang and Y. Wang, *Micromachines*, 2024, **15**(3), 331.
83 S. E. Elugoke, G. E. Uwaya, T. W. Quadri and E. E. Ebenso, *Carbon Dots: Recent Developments and Future Perspectives*, ACS Publications, 2024, pp. 3–42.
84 H. Zhang, H. Liu, X. Liu, A. Song, H. Jiang and X. Wang, *Adv. Healthcare Mater.*, 2025, **14**, e2402285.
85 G. M. Saladino, N. I. Kilic, B. Brodin, B. Hamawandi, I. Yazgan, H. M. Hertz and M. S. Toprak, *Nanomaterials*, 2021, **11**(9), 2165.

86 Q. Meng, Y. Wang, C. Li and X. Hu, *New J. Chem.*, 2022, **46**, 16970–16980.
87 Y. Jeong, M. Jin, K. S. Kim and K. Na, *Biomater. Res.*, 2022, **26**, 27.
88 Y. C. Lin, E. Perevedentseva, Z. R. Lin, C. C. Chang, H. H. Chen, S. M. Yang, M. D. Lin, A. Karmenyan, G. Speranza, L. Minati, C. Nebel and C. L. Cheng, *Sci. Rep.*, 2022, **12**, 5331.
89 L. Cao, X. Wang, M. J. Meziani, F. Lu, H. Wang, P. G. Luo, Y. Lin, B. A. Harruff, L. M. Veca and D. Murray, *J. Am. Chem. Soc.*, 2007, **129**, 11318–11319.
90 B. Wang, H. Cai, G. I. N. Waterhouse, X. Qu, B. Yang and S. Lu, *Small. Sci.*, 2022, **2**, 2200012.
91 M. Zarei-Ghobadi, S. H. Mozhgani, F. Dashtestani, A. Yadegari, F. Hakimian, M. Norouzi and H. Ghourchian, *Sci. Rep.*, 2018, **8**, 15593.
92 M. M. Rahman, L. Wang, Y. Chen, M. M. Rahman, M. O. A. Islam, L. P. Lee and Y. Wan, *Extracell. Vesicles Circ. Nucleic Acids*, 2025, **6**, 72–86.
93 X. Lin, Y. Mei, C. He, Y. Luo, M. Yang, Y. Kuang, X. Ma, H. Zhang and Q. Huang, *Front. Chem.*, 2021, **9**, 769648.
94 R. Garg and D. Prasad, *Biochem. Biophys. Res. Commun.*, 2023, **680**, 93–107.
95 M. R. Biswal and S. Bhatia, *Nanomaterials*, 2021, **11**(4), 935.
96 Y. Wei, X. Jin, T. Kong, W. Zhang and B. Zhu, *Cell Proliferation*, 2019, **52**, e12586.
97 S. Mohammadi, A. Salimi, Z. Hoseinkhani, F. Ghasemi and K. Mansouri, *J. Nanobiotechnol.*, 2022, **20**, 73.
98 Y. Cai, T. Chai, W. Nguyen, J. Liu, E. Xiao, X. Ran, Y. Ran, D. Du, W. Chen and X. Chen, *Signal Transduction Targeted Ther.*, 2025, **10**, 115.
99 Y. Ma, Y. Zhang, X. Li, Y. Zhao, M. Li, W. Jiang, X. Tang, J. Dou, L. Lu, F. Wang and Y. Wang, *ACS Nano*, 2019, **13**, 11967–11980.
100 H. Sharma and S. Mondal, *Int. J. Mol. Sci.*, 2020, **21**(17), 6280.
101 W. Zhang, Z. Guo, D. Huang, Z. Liu, X. Guo and H. Zhong, *Biomaterials*, 2011, **32**, 8555–8561.
102 B. Geng, J. Hu, Y. Li, S. Feng, D. Pan, L. Feng and L. Shen, *Nat. Commun.*, 2022, **13**, 5735.
103 A. Sharma and J. Das, *J. Nanobiotechnol.*, 2019, **17**, 92.
104 T. Feng, X. Ai, H. Ong and Y. Zhao, *ACS Appl. Mater. Interfaces*, 2016, **8**, 18732–18740.
105 M. Zhang, P. Yuan, N. Zhou, Y. Su, M. Shao and C. Chi, *RSC Adv.*, 2017, **7**, 9347–9356.
106 T. Kong, L. Hao, Y. Wei, X. Cai and B. Zhu, *Cell Proliferation*, 2018, **51**, e12488.
107 S. Bayda, E. Amadio, S. Cailotto, Y. Frion-Herrera, A. Perosa and F. Rizzolio, *Nanoscale Adv.*, 2021, **3**, 5183–5221.
108 Y. Zhang, Y. Zhao, Y. Zhang, Q. Liu, M. Zhang and K. Tu, *Front. Pharmacol.*, 2022, **13**, 961725.
109 N. A. Pechnikova, K. Domvri, K. Porpodis, M. S. Istomina, A. V. Iaremenko and A. V. Yaremenko, *Aggregate*, 2024, **6**(3), e707.
110 C. H. Fan, N. Wu and C. K. Yeh, *Ultrason. Sonochem.*, 2023, **94**, 106342.
111 D. Jana, D. Wang, P. Rajendran, A. K. Bindra, Y. Guo, J. Liu, M. Pramanik and Y. Zhao, *JACS Au*, 2021, **1**, 2328–2338.
112 N. H. Hussen, A. H. Hasan, Y. M. FaqiKhedr, A. Bogoyavlenskiy, A. R. Bhat and J. Jamalis, *ACS Omega*, 2024, **9**, 9849–9864.
113 D. I. Abu Rabe, M. M. Al Awak, F. Yang, P. A. Okonjo, X. Dong, L. R. Teisl, P. Wang, Y. Tang, N. Pan, Y. P. Sun and L. Yang, *Int. J. Nanomed.*, 2019, **14**, 2655–2665.
114 X. Qie, M. Zan, P. Gui, H. Chen, J. Wang, K. Lin, Q. Mei, M. Ge, Z. Zhang, Y. Tang, W. F. Dong and Y. Song, *Front. Bioeng. Biotechnol.*, 2022, **10**, 894100.
115 X. Dong, W. Liang, M. J. Meziani, Y. P. Sun and L. Yang, *Theranostics*, 2020, **10**, 671–686.
116 M. Havrdova, K. Hola, J. Skopalik, K. Tomankova, M. Petr, K. Cepe, K. Polakova, J. Tucek, A. B. Bourlinos and R. Zboril, *Carbon*, 2016, **99**, 238–248.
117 Y. Y. Liu, N. Y. Yu, W. D. Fang, Q. G. Tan, R. Ji, L. Y. Yang, S. Wei, X. W. Zhang and A. J. Miao, *Nat. Commun.*, 2021, **12**, 812.
118 H. Kuznietsova, A. Geloen, N. Dziubenko, A. Zaderko, S. Alekseev, V. Lysenko and V. Skryshevsky, *Discover Nano*, 2023, **18**, 111.
119 N. Yadav, K. H. Adolfsson and M. Hakkarainen, *Biomacromolecules*, 2021, **22**, 2211–2223.
120 Z. Huang and L. Ren, *Molecules*, 2025, **30**(4), 774.
121 P. Kumar, S. Dua, R. Kaur, M. Kumar and G. Bhatt, *RSC Adv.*, 2022, **12**, 4714–4759.
122 S. Dua, P. Kumar, B. Pani, A. Kaur, M. Khanna and G. Bhatt, *RSC Adv.*, 2023, **13**, 13845–13861.
123 G. Nocito, G. Calabrese, S. Forte, S. Petralia, C. Puglisi, M. Campolo, E. Esposito and S. Conoci, *Cancers*, 2021, **13**(9), 1991.
124 P. Zhuang, K. Li, D. Li, H. Qiao, Y. E. M. Wang, J. Sun, X. Mei and D. Li, *Nanoscale Res. Lett.*, 2021, **16**, 121.
125 S. Hapuarachchige and D. Artemov, *Front. Oncol.*, 2020, **10**, 1131.
126 J. Liu, R. Li and B. Yang, *ACS Cent. Sci.*, 2020, **6**, 2179–2195.
127 X. Tian, A. Zeng, Z. Liu, C. Zheng, Y. Wei, P. Yang, M. Zhang, F. Yang and F. Xie, *Int. J. Nanomed.*, 2020, **15**, 6519–6529.
128 M. Gonzalez and M. P. Romero, *Int. J. Nanomed.*, 2025, **20**, 7715–7741.
129 F. Liu, X. D. Wang and S. Y. Du, *Sci. Rep.*, 2020, **10**, 7618.
130 H. Lin, J. Huang and L. Ding, *J. Nanomater.*, 2019, **2019**, 1–9.
131 M. Algarra, M. Perez-Martin, M. Cifuentes-Rueda, J. Jimenez-Jimenez, J. C. Esteves da Silva, T. J. Bandosz, E. Rodriguez-Castellon, J. T. Lopez Navarrete and J. Casado, *Nanoscale*, 2014, **6**, 9071–9077.