









Review Article

Fabrication, Characteristics, and Therapeutic Applications of Carbon-Based Nanodots

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Carbon nanodots are a recently discovered sort of carbon nanoparticles, demonstrating excellent fluorescence and physical-chemical properties that make them appealing for diagnostics and chemotherapeutics, including biosensing, bioimaging, and nanocarriers for drug delivery ground-breaking therapeutic agents in photothermal and photodynamic therapy. This critical review strongly focuses on the varied sorts of processes involved in the synthesis of carbon nanodots alongside the benefits and shortcomings. Furthermore, the multiple applications of carbon nanodots are established and used to develop potential theranostic nanoarchitectures. This review paper analyses with a discussion focusing on the discovery, synthesis processes, and diverse biomedical applications.

1. Introduction

Carbon quantum dots (CQDs), also known as carbon nanodots, are a class of carbon nanoparticles. Carbon nanodots were discovered by Xu et al. [1] accidentally while attempting to purify single-walled carbon nanotubes (SWCNT). Carbon nanodots are less than 10 nm in size, and since their discovery, extensive research has been conducted on their unique properties, such as fluorescence, making it an exceptional discovery [2].

The process of synthesis of carbon nanodots, its analytical applications in oxygen reduction, plant cell imaging, and

more have been studied throughout the years. The fluorescent properties of carbon nanodots make them essential for studying several chemical and biological processes, as previously mentioned [3]. Reviewing the existing literature and the research conducted on this particular domain would enable researchers to focus on the gaps in the literature and evaluate further research carried out in this context.

2. Carbon Nanodot Discovery and Structure

Xu et al. [1] had been engaged in purifying single-walled carbon nanotubes when they accidentally discovered these

particles. Synthetic methods have been implemented in their extraction and discovery. In this context, it needs to be stated that the carbon nanodots exhibit various structures responsible for the demonstration of multiple properties of the particles [4]. According to Roy et al. [5], the carbon nanodots are usually quasispherical or spherical shaped, generally from 4 nm to 8 nm in diameter, produced from natural soot, with lattice spacing almost equal to graphite. Additionally, carbon dots developed from natural ingredients such as glycerine and coffee exhibited crystalline and monodisperse structures [3, 6]. The presence of particular functional groups on the carbon dots can be determined through XPS analysis or FTIR spectroscopy. Additionally, carbon dots have been noted to be more stable as compared to nanodots of metals such as Ag and Au [7].

3. Synthesis Processes of Carbon Nanodots

Carbon nanodots can be broadly classified into two categories for the purpose of synthesis, namely, top-down approaches and bottom-up approaches.

3.1. Top-Down Approaches. Arc-discharge method: this method provides approximately 1.6% quantum yield (QY) of carbon nanodots from the crude material oxidizing process. The oxidation was carried out by using HNO_3 (3.3N); then, the oxidized crude carbon nanodots were extracted with alkaline solution (pH 8.4), and purification was done by conducting gel electrophoresis. This particular process was used by Roy et al. [5] during the discovery of carbon nanodots and is considered cost-effective. However, adequate growth conditions are necessary for this method to ensure success (Figure 1) [8]. An electrical discharge around two graphite electrodes bathed in octane was used to make luminous carbon nanodots in a single-step method [9]. The arc-discharge method was also used by Andhika et al. [10] in the toluene environment for the production of carbon nanoparticles. Direct current arc-discharge plasma was used to make SnO_2 /carbon nanotube nanonests (SnO_2 /CNT NNs) composites in one step [11].

Electrochemical method: the QY of the nanodots produced through this method is usually around 2.8%–2%. The size of the carbon nanodots can be maintained by keeping 20–180 mA cm^2 as the range of the current density [12]. Therefore, caution is to be exercised for maintaining a particular size of carbon dots. The easy single-step electrochemical production of CQDs with diameters ranging from 1.2 to 3.8 nm was synthesized that shows size-dependent photoluminescence (pl) and outstanding upconversion luminescence capabilities [13].

Laser ablation: the use of Nd:YAG laser at a frequency of 10 Hz and 1064 nm may yield carbon dots from graphite powder. According to Hsu and Chang [14], the use of citric acid is also noted to enhance hydrophilic properties in CQDs. This is supported by Zhu et al. [15], where soy milk is used to synthesize carbon dots. Nguyen et al. [16] reported the synthesis of ultrasmall CQDs by double-pulse femtosecond laser ablation. CQDs, also prepared by a pulsed laser ablation method with no posttreatments, have been devel-

oped by Yang et al. [17]. Laser pyrolysis of two typical volatile chemical precursors, toluene and pyridine, yielded monodisperse carbon nanodots with controllable pl [18].

3.2. Bottom-Up Approaches. Hydrothermal and aqueous-based methods: several methods established for the synthesis of carbon nanodots can be attributed to various natural substances. For instance, this method implements ground coffee or green tea, as carbon nanodots can be synthesized from organic compounds [12]. Aslan and Eskalen used a single-step hydrothermal approach to make water-soluble carbon nanodots from tangerine juice [19]. Under blue light illumination, fluorescent nitrogen-doped CQDs generated using a single-pot hydrothermal process using multiple isomers, displaying exceptionally intense fluorescence [20], while Chen et al. [21] synthesized spherical CQDs ranging 3–7 nm from the plant material and agriculture waste.

Microwave-assisted methods: synthesis of carbon nanodots has also been found to be effective using PEG₂₀₀ saccharides, such as sucrose, by developing an aqueous transparent solution of the same to extract carbon nanodots. There are three prime examples of modified carbon nanodots synthesized with the help of microwave-assisted method, namely, N, S-carbon nanodots (N,S-doped carbon quantum dots, N, S-CND), N-carbon nanodots-1 (N-CNDs-1), and N-carbon nanodots-2 (N-CNDs-2). N-CNDs-1 and N-CNDs-2 are strongly agglomerated and highly hydrophilic, respectively. Thiol and carboxylic groups are present on N, S-CND [22]. These particles are useful in studying lung and pulmonary diseases in humans.

Carbon nanodots with 30 nm dimensions synthesized by an efficient route by using coffee grounds to the precursor followed the microwave-assisted hydrothermal method where the 10 g spent coffee grounds were soaked in dilute H_2SO_4 solution (50 mL of 0.01 g/mL) heating in the microwave for two hours. The precursor was oxidized in HNO_3 (10%, 20 mL), then sonicated for 0.5 h at 45°C, and then kept on magnetic stirring for 0.5 h at 90°C. The reaction mixture was then cooled down then diluted by cold water to obtain light-yellow carbon nanodot powder [6].

Thermal routes: carbon soot has been primarily considered as the fundamental substance for the production of carbon nanodots. Treatment with an oxidant, namely, HNO_3 and H_2O_2 /AcOH, results in the formation of carbon nanodots [23]. However, the QY values are quite low, ranging between 0.8% and 1.9%.

The stages primarily carried out to synthesize carbon nanodots are dehydration, polymerization, carbonisation, and finally, passivation, as depicted in Figure 2. The use of various compounds has been noted in the synthesis of C-dots. For instance, APTMS or (3-Aminopropyl) trimethoxysilane and glycine, along with other substances like urea, sucrose, and alanine, have been a crucial precursor for the synthesis of carbon nanodots [24]. As formerly stated, there are broadly two major processes involved in synthesizing carbon dots: the bottom-up approach and the top-down approach. As previously discussed, the significant advantages of using carbon dots include low toxicity, the property of being chemically inert, outstanding biocompatibility,

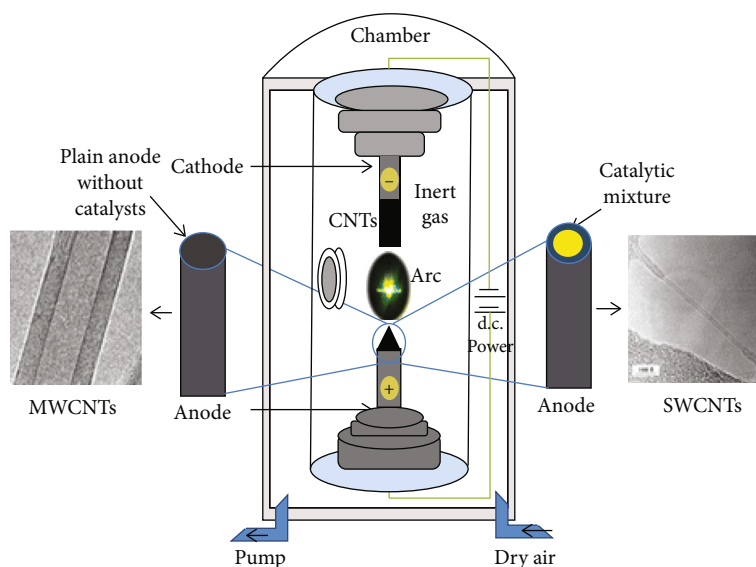


FIGURE 1: Arc discharge apparatus for the synthesis of CNT or carbon dots (reproduced from Das et al. 2016).

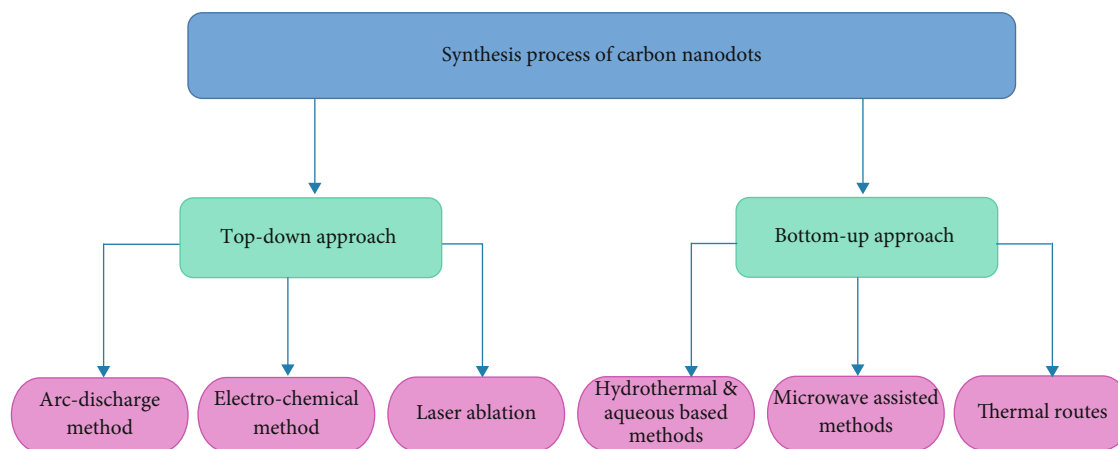


FIGURE 2: Synthesis process of carbon nanodots.

good water solubility, and multiphoton excitation, as well as excellent pl properties. Additionally, the physicochemical, electronic, optical, and electrochemical properties of carbon nanodots have been noted to be unique features and environment-friendly. Electrochemical properties were used to observe the energy gap of the carbon nanodots and Hückel level calculations of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO).

There are certain limitations identified for each of the approaches. For instance, it has been evident that synthesis steps are monotonous and occur at extremely high temperatures, utilizing toxic or harmful substances such as alkali or acids [25]. Hence, it becomes evident that Karfa et al. [25] contradict the existing idea or concept that C-dot synthesis is inexpensive. Apart from the statement that carbon dot synthesis has high costs, Karfa et al. [25] state that special equipment and nonpolar organic solvents are used in the process.

4. Properties of Carbon Nanodots

Modification is a process that is integrated into the overall mechanism of the formation of carbon nanodots. As noted previously, though carbon nanodots have a profound impact in biosensing or bioimaging, carbon dots face extreme competition in terms of their applications [26]. In this context, it must be noted that a high QY must be achieved to compete with other similar compounds effectively. Though there have been instances for producing carbon nanodots with a quantum yield of ~80%, most of the carbon nanodots synthesized through various methods have exhibited QY, less than 10%. To improve the quantum yield for the synthesized nanodots, surface passivation and other doping methods are implemented for modifying the same. Figure 3 illustrated the water-soluble carbon nanodot of the size range 20 to 50 nm [26].

Another significant property illustrated by the carbon nanodots is the reduced levels of cytotoxicity compared to

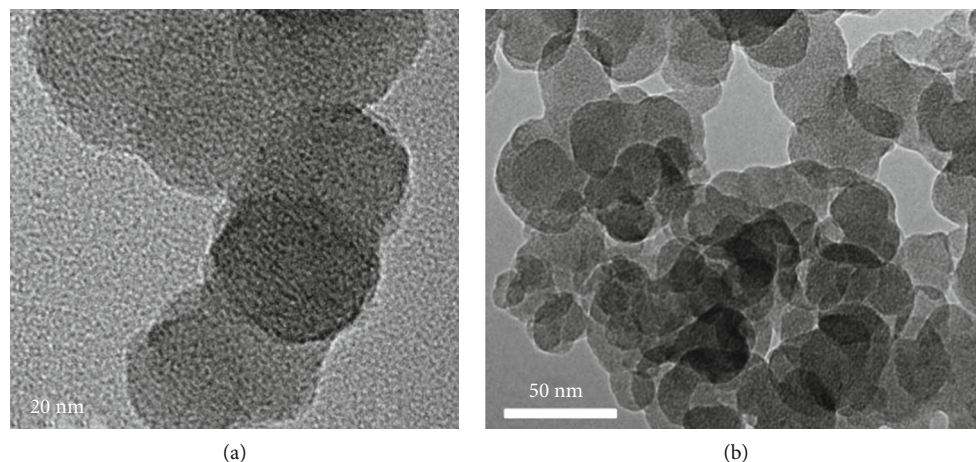


FIGURE 3: (a, b) TEM images of carbon nanodots (reproduced from Tripathi et al. 2017).

other carbon nanoparticles. The enhanced stability, biocompatibility, and hydrophilicity have been considered to contribute to the lower levels of cytotoxicity in carbon nanodots. Carbon nanodots continue to draw attention in biomedical applications, though their therapeutic efficacy becomes conceded due to rapid clearance from the human body. However, rapid clearance of carbon nanodots is advantageous in terms of cytocompatibility, but it is a significant restraint for their prolonged utilization as imaging and therapeutic agents, and this clearance depends on the surface charge on carbon nanodots [27–29]. Goryacheva et al. [30] state that they are cheap to produce and demonstrate bright light emissions, demonstrating the potential to completely replace the inorganic quantum dots for their applications in photocatalysis, solar cells, and more. Other physicochemical properties include absorption, variant morphology, surface properties, pl, and stability as a compound.

The property of pl of carbon nanodots has been used for several applications in biosensing and bioimaging [31]. According to Nguyen et al. [32], certain surface functional groups in carbon nanodots are responsible for the exhibition of this particular property. C-dots were utilized as agents for multicolor labelling to detect bacteria *Staphylococcus aureus* and *Escherichia coli* [19]. Hence, the pl property is increased as the conditions mentioned above serve as an excitation energy trap [33]. The impact of an extreme environment containing hydrogen peroxide, a potent oxidizing agent, has been tested, where the Zn-CDs manifested steady fluorescence and high stability against highly oxidizing H_2O_2 [33].

In addition, Himaja et al. [34] mention that synthesizing highly fluorescent carbon nanodots from kitchen waste is a thriving green process. Furthermore, the color of light emissions has been noted to be primarily yellow. Contradictory evidence illustrates that the carbon nanodots produced exhibited green and blue color emissions when synthesized with the help of controllable flame reactors, which are essentially fuel-rich [35]. Laser ablation has been regarded as a potentially effective procedure for synthesizing carbon nanodots, mainly when produced in ionic fluids [36]. Furthermore, it has been evident with the help of bioimaging that

agglomeration behavior is strongly demonstrated by the particles, N-CND-1 or N, S-CND. Agglomeration property could be due to successful construction and doping with nitrogen/sulfur and nitrogen. Positively charged N-CNDs-1, bearing amide groups at the surface, displayed a highly amorphous profile [37].

In order to further illustrate the impact of exposure to the modified carbon nanodots, a 3D human lung had been exposed to these particles over a period of 24 hours. With the help of the pseudo-air-liquid interface, by maintaining a concentration of $100 \mu\text{g/mL}$, alveolar epithelial cells, primarily the A549 cell line as well as the two primary immune cells, namely, dendritic cells and macrophages, were exposed to the carbon nanodots [37]. Utilizing the property of pl, researchers were able to identify that after 1 hour, approximately 80% of the N, S-CND and N-carbon dots-1 were left on the apical surface of the lungs [22]. It has been previously mentioned that the properties of the surface functional groups play a critical role in studying the overall behavior exhibited by carbon nanodots. In this case, amide groups and amino acids have been noted to be present on the surface of the nanodots, which enhanced the uptake properties of the N-carbon dots, as compared to the ones, which bore carboxylic acid groups, as the surface functional groups [22].

5. Applications of Carbon Nanodots

5.1. Imaging Applications. To date, many specific and novel methods have been discovered to identify bacterial species for instant and precise microorganism detection. CQDs have been innovative for imaging numerous microorganisms [38]. The carbon dots had tunable pl that empowered the identification of *Escherichia coli* through multicolor imaging after three hours of incubation with the carbon dots and the imaging-based attachment of the carbon dots to the surface of the bacterial cell [39]. Yu et al. [40] synthesized N-doped carbon dots by creating a combination of curcumin and polyethyleneimine hydrothermally. The synthesized carbon dots were kept incubated for three hours that have been utilized for the multicolor imaging of *Staphylococcus aureus* and *E. coli* [41].

Furthermore, the tested carbon dots no longer display antibacterial activity against the tested bacteria, permitting the identification and labelling of live bacteria. Baig and Chen [33] produced carbon dots from the white portion of the egg that was suitable for multicolor pl identification of *S. aureus* and *E. coli*, despite the fact that these carbon dots were fabricated at a much higher QY i.e., 45%, and used for identification and labeling bacteria upon 10 minutes of incubation, allowing them to be viable and lower quantity of carbon dots used for faster labeling of microorganisms. In another study, N, S-codoped carbon dots have been produced using a microwave irradiated method and a combination of thiourea and tris-acetate-ethylenediamine. The QY of the produced carbon dots was higher, making them feasible for multicolor labelling of microorganisms. Multicolor labelling demonstrates against four microorganism species, including *E. coli*, *Pseudomonas aeruginosa*, *S. aureus*, and *Klebsiella pneumoniae*. The bacterial species can efficiently be identified as endocytosis of the carbon dots has to be observed, except pneumonia bacteria which have no longer exhibited fluorescence after incubation. The equal conditions due to the catabolic pathway expresses for fragrant compounds could devastate the carbon dots [33]. Wang et al. [42] utilized a urea, sodium citrate, and thiourea to produce carbon dots with a QY of 37% that emitted blue fluorescence and, therefore, enable the utilization of labelling of *Xanthomonas axonopodis* with incubation of three hours which exhibits blue fluorescence under UV light; here, microorganism was found alive, and no distraction in shape and morphology observed [42].

Aside from microorganism cells, the potential of carbon dots for imaging purposes has conjointly been explored in other cells. Applications of carbon dots are overemphasized and exploited for imaging of cells of mammals. Most of the manufactured carbon dots accomplish the needs for a composite that could be used as an imaging agent. They showed a stable fluorescent signal and did not show adverse effects on cells' physiology [43]. Many reports on imaging revolve around cell imaging that is incredibly giant and not prudent or sensible to include all individual findings. Several properties of manufactured carbon dots created from citrus sinensis, apple seeds, and citrus limon, were observed when they were utilised to label A549, MDA-MB-231, HeLa, and HEK-293 cells for imaging purposes. Carbon dots are also synthesized from human fingernails that exhibit various pl properties [44].

The carbon dots produced with oil of vitriol from microwave irradiation exhibit an associated degree emission at 380 nm, whereas those produced from pyrolysis showed a dual emission at 450 nm and 380. Besides the different pl features, these carbon dots produce the 42.8% QY with microwave treatment and 81.4% QY from pyrolysis that efficiently utilizes four different cell lines [45]. Furthermore, carbon dots produced from pyrolysis after forty-eight hours of incubation will promote HEK-293 cell proliferation by up to 18 hrs. These findings were thus vital that could be utilized for additional advanced clinical applications [41].

Du et al. [46] synthesized carbon dots from the hydrothermal treatment of glycine and glucose that effectively

label MTEC1 and Sh-y5y cells in which the carbon dots localized within the membrane and protoplasm, while the nucleus pl was not strong. Pal et al. [47] produced polyethyleneimine carbon dots from the hydrothermal method of polyethyleneimine and curcumin used for microorganism labelling. These carbon dots were also utilized for labelling of NIH 3T3, A549, and HCT-15 cells and exhibited multicolored pl. Though differences in the pl intensity were recorded in all tested cells. Cancer cells HCT-15 and A549 showed high pl as compared to fibroblasts NIH3T3 cells due to the higher rate and uptake by cancer cells [48]. Carbon dots formed by irradiated microwave method by using a mixture of acid and ethylenediamine exhibited excitation-dependent red pl that was helpful for labelling of animal tissue cells, retinal, lens, and CHO cells to exhibit multicolored pl [49].

Furthermore, the red pl was significantly helpful as cells became ready to emit pl once excited at 635 nm. This way, the fluorescence was reduced, resulting in the quantitative ratio of signal to background which was amplified. Carbon dots produced by the irradiated microwave method by using aspirin-hydrazine were used to imaging HeLa, RAW246.7, KB, and BMSC cells. Notably, the carbon dots will enter the cell organelle and label it with the cytoplasmic space [50].

In another study, carbon dots made from histidine and cotton were ready to enter the organelle of AD-293 cells used to label organelle of A193 cells, respectively [51]. In this regard, it needs to be mentioned that there are several widespread applications of carbon nanodots, and most of the applications can be attributed to its property of pl.

Bioimaging is one of the significant applications of carbon dots, which can be attributed to its fluorescent property. Carbon dots have been noted to emit lights of varying wavelengths in their excited state. Kim et al. [52] mention that dual-color emitting carbon dots have been used in gaining optogenetic control of ion channels and multicolor bioimaging. According to Mishra et al. [53], targeted drug delivery is another option being considered for medical purposes of carbon nanodots. Despite the potential applications of carbon nanodots in advanced medicine, Atchudan et al. [54] mention that carbon dots can be synthesized conveniently from *Malus floribunda*, commonly known as Japanese crab or purple chokeberry, illustrating and supporting the former views of driving carbon dots from natural sources [5].

5.2. Biosensing Applications. The detection of various biological and chemical compounds can be performed with the help of carbon nanodots. In addition, Bui and Park [55] further mention the use of carbon nanodots in the screening of cholesterol as a part of biosensing. It has been formerly discussed that the detection of carbon nanodots in the human lung has been measured owing to their fluorescence property [56]. The biosensor mentioned above comprises primarily of haemoglobin complex and C-dot components, respectively.

Another critical application of carbon dots in biosensing is the detection of gene mutation [57]. Additionally, Yu et al. [58] mention that *Saccharomyces* or yeast may aid in the

production of carbon nanodots, which has been noted to be effective in detecting vitamin B₁₂ and pH. Hong et al. [59] further illustrate that multimodal carbon dots act as effective biosensors. Moreover, it has been stated that the use of carbon dots may influence and even enhance the provision of therapeutic functionalities and trigger the development of theranostic materials (Figure 4) [59].

5.3. Antibacterial Potential. Carbon nanodot's bactericidal potential is due to oxidative stress persuaded by reactive oxygen species produced by carbon nanodots that act as a signalling particle inside the cells in response to the pathogen. Oxidative stress progresses when the reactive oxygen species production surpasses the usual defense of antioxidant in bacterium that induces oxidative injury to biomolecules such as nucleotides, lipids, and proteins resulting in damage to the cell wall and bacterial death. Heteroatoms present in functionalized carbon dots improve the production of reactive oxygen species due to free-electron integration in carbon dots [60–63]. The life of reactive oxygen species is usually short that depends upon the type of reactive oxygen species. For instance, hydrogen peroxide has an elongated life of about 1 ms compared to other reactive oxygen species, while other types of reactive oxygen species have a short life that measures in microsecond range [64]. As a consequence, reactive oxygen species can diffuse over very short distances to several 100 nm allowing diffusion around the lipid bilayer, which is required for the generation of reactive oxygen species in the close locality of its target to show effective bactericidal potential. Nitrogen atoms in carbon dots produce groups, which are positively charged results in augmenting the electrostatic interaction to cell surface, which are negatively charged resulting in reactive oxygen species production which leads to target pathogens and exhibits antibacterial effects [62].

Positively charged carbon dots are synthesized from spermidine or quaternary ammonium salts. These carbon dots firmly adhere to proteins, porins, and peptidoglycan of the bacterial cell wall resulting in inhibition of cell wall synthesis of Gram-positive and Gram-negative bacteria, indicating their enhanced antibacterial activity [65–67]. Carbon dots entered into the bacteria interior result in oxidative damage to biomolecules, including DNA content which leads to damaging the cell wall [61].

Additionally, synergistic utilization of carbon dots with antibiotics or photosensitizers shows better efficacy; for instance, photoactivated carbon dots combined with photosensitizers like toluidine blue and methylene blue achieve higher reactive oxygen species generation than photosensitizers or carbon dots alone under the illumination of visible light, thus resulting in enhanced killing of bacteria [68, 69].

Carbon is usually nontoxic and showed no apparent side effects and toxicity in treating infected wounds in rats and pneumonia in tested mice [70, 71]. A biosafety evaluation of photoluminescent carbon dots produced by nitric acid oxidation found no acute toxicity, genotoxicity, or abnormalities or lesions in the organs of mice [72]. No cytotoxicity of cadmium-selenide quantum dots was observed, which was improved by a coating of polyethylene glycol [73].

5.4. Cancer Diagnosis. The higher sensitivity, including spatial and temporal resolution of fluorescence imaging, makes carbon dots the most auspicious agent in cell sensing, targeting, and imaging [74]. For instance, Song et al. [75] produced carbon dots coupled with folic acid to distinguish folate receptor-positive from folate receptor-negative cells that were utilized to identify and label and analyse HeLa and NIH-3T3 cells. Lee et al. [75] synthesized carbon dots coupled with maleimide-terminated TTA1 aptamer expressed highly in C6 rat glioma cell line and HeLa cell line and not expressed in normal healthy CHO Chinese hamster ovary cell line cells. The incubation of the carbon dots conjugated with maleimide-terminated TTA1 aptamer exhibits a strong fluorescence and selectively along with cancer cells and is only very less absorbed in normal cells. Zhang et al. [76] synthesized carbon dots coupled with folic acid that were able to selectively recognise cancer cells in a combination of PC12 and HepG2 by showing a bright green luminescence after incubation of 2 hours. In another study, Li et al. [74] revealed a new tumor therapy that depends on autophagy by combining the folic acid and biocompatible N-doped carbon dots that possess a broad range of high ability of targeted including 26 kinds of tumor cell and distress the metabolism which results in autophagy. Bhunia et al. [77] synthesized functionalized fluorescent carbon dots with folate or TAT peptide and incubated them with folate receptor-positive cancerous cells and folate receptor-negative normal cells that enhanced cell labelling and uptake.

5.5. Cancer Therapy. Photodynamic therapy is of utmost promising and noninvasive cancer therapeutic approaches with fewer side effects that could be utilized unaided or in amalgamation with ionizing radiation, surgery, and chemotherapy and can be utilized to abolish cancerous cells, which are undetected [78]. Photodynamic therapy employed photosensitizing drugs as these are inactive pharmacologically till a specific wavelength of light irradiates that generates reactive oxygen species resulting in induced cell death and necrosis [78–81]. For instance, photosensitizing drugs such as porphyrin and phthalocyanine and their derivatives have potential in cancer imaging and therapeutic approved for medical applications [82, 83]. Their utilization is limited due to cutaneous photosensitivity enhancement, water solubility reduction, low photostability, and selectivity [84]. For this cause, many other approaches have been examined. For instance, Huang et al. [85] revealed an innovative theranostic method that depends on chlorin e6-conjugated carbon dots which exhibit good solubility, stability, low cytotoxicity, enhanced photosensitizer fluorescence detection, good biocompatibility, and outstanding photodynamic efficacy as compared to utilization of Ce6 alone. Furthermore, in another study, in vitro or in vivo utilization of a carbon dot-chlorin e6-hyaluronate coupled, which is transdermal, was successfully utilized for the photodynamic therapy in skin cancer that showed significant photodynamic outcomes on cancer cells as compared to Cdot-Ce6 and Ce6 alone [86]. Li et al. [87] synthesized porphyrin-containing carbon dots

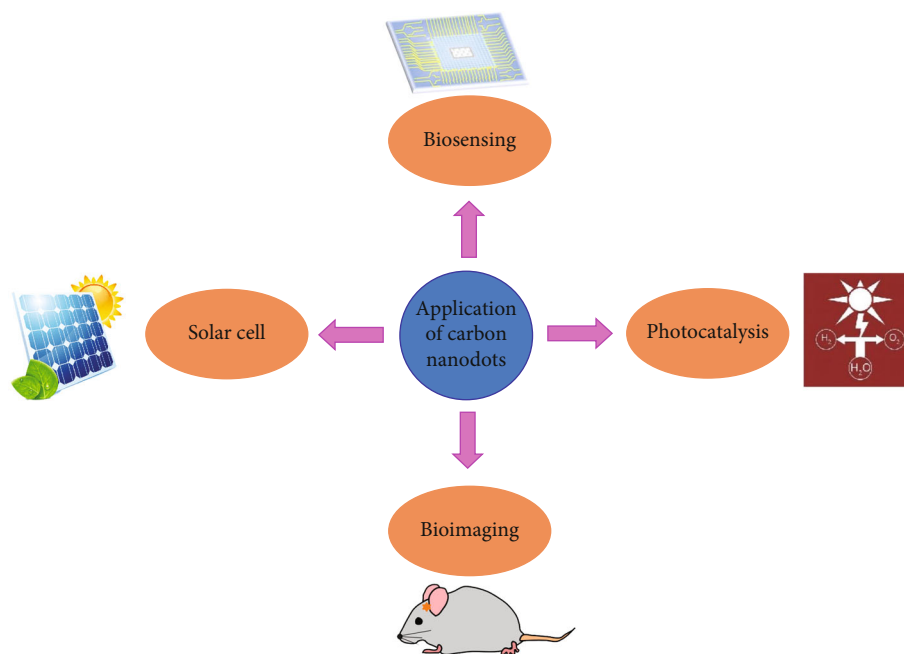


FIGURE 4: Applications of carbon nanodots.

utilized in the effective photodynamic therapy in hepatoma treatment and showed good photostability, cellular uptake, biocompatibility, and potent cytotoxicity which leads to suppress the tumor.

Recently, carbon dots have also been utilized as photosensitizing chemicals as they possess substantial temperature variations upon irradiation. Sun et al. [88] revealed red emissive carbon dots and utilized them quickly and efficiently that convert laser energy into heat resulting in reduction of the viability of MCF-7 cells. Geng et al. [89] synthesized near-infrared absorbing nitrogen and oxygen codoped carbon dots that generate high efficiency under laser irradiation results in attaining 100% of ablation of tumor tissue without any harm or side effects. Zheng et al. [90] produced near-infrared fluorescent hydrophobic cyanine dye and polyethylene glycol-doped carbon dots that exhibit superior uptake and accumulation in tumors with high photothermal conversion efficiency. Ge et al. [91] synthesized carbon dots using polythiophene benzoic acid that shows photodynamic and photothermal effects under laser irradiation of 635 nm. Lan et al. [92] synthesized S, Se-codoped carbon dots by utilizing polythiophene and diphenyl diselenide that utilized new multifunctional phototheranostic reagents. Wang et al. [23] synthesized near-infrared-emissive boron and nitrogen-doped carbon dots to induce higher penetration into tissue that exhibits a photothermal therapeutic effect and kills cancer cells entirely to suppress tumor growth in vivo.

5.6. Other Applications

5.6.1. Solar Cells. Margraf et al. [93] mention that carbon nanodots can be actively used in mesoscopic solar cells as sensitizers, since these particles are environment-friendly and relatively inexpensive. Furthermore, Chatzimitakos

and Stalikas [94] state that carbon nanodots can be easily produced or generated from the most common natural resources, making their availability abundant and production cost cheaper. This can be further substantiated by Marinovic et al. [95], who mention that carbon nanodots have been noted to have the highest recorded solar PCE or solar power conversion efficiency, attributing to approximately 0.36%. L-arginine carbon dots had been used for this purpose as sensitizers. On the contrary, the use of lobster shells in hydrothermal carbonisation resulted in the generation of PCE of 0.22%. Loading CQDs into perovskite precursor solution results in a superior hybrid $\text{Cs}_{0.15}\text{FA}_{0.85}\text{PbI}_3$ thin film. The productivity of the associated ITO/PTAA/ $\text{Cs}_{0.15}\text{FA}_{0.85}\text{PbI}_3$ /PC₆₁BM/BCP/Ag inverted planar perovskite solar cells increased from 17.36 percent to 20.06 percent [96]. Wang et al. [97] reported that to enhance the productivity of the associated perovskite solar cells, CQDs were added to the CsPbI_2Br photoactive layer. Upon incorporating CQNDs in an ideal amount, it is discovered that the trap density may be significantly reduced and crystallinity can be improved. Riaz and Park [98] used freeze-dried urea and CQD precursors to make nitrogen-rich CQDs that were implanted in CN nanotubes. The CN nanotubes that had been synthesized were utilized as efficient light harvesters.

5.6.2. Photocatalysis. Liu et al. [99] have stated that carbon nanodots act as efficient catalysts for oxidation as well as reduction reactions. Furthermore, the surface modifications have been found to play a critical role in the same. On the other hand, it has been mentioned previously that Margraf et al. [93] mention the use of carbon dots in mesoscopic solar cells, mostly carried out with the bottom-up microwave approach, deploying resources such as urea, citric acid, and formic acid. However, despite expecting PCE of 0.24%, it

has been evident from research and experimentation that the PCE deteriorates, and the lower performance rates can be attributed to photovoltage decay [93].

Other key applications of carbon nanodots include the detection of luminescence or fluorescence of hydrazine hydrate and such compounds [100]. Furthermore, Sai et al. [101] mention that carbon nanodots may effectively utilize UV light by acting as light conversion material. In this regard, it needs to be mentioned that the fundamental advantages or benefits of using carbon nanodots are the environment-friendly nature and the easy generation process from various natural sources, making it relatively inexpensive compared to other types of carbon nanoparticles [102, 103]. In addition to that, it has been established that carbon dots are quite effective in biosensing as they are relatively sensitive and efficient, rapid, and selective in their mode of action [104, 105].

Graphene quantum dots have the potential to be utilized as surfactants in miniemulsion polymerization for various vinyl monomers, which were employed for hybrid nanocomposite synthesis [106]. The Ag/CQDs microspheres displayed excellent catalytic activity [107]. Carbon dot-stabilized Pickering emulsions were effectively used to load hydrophobic and hydrophilic pharmaceuticals into poly-lactide-co-glycolide (PLGA) drug delivery systems [108]. Carboxylated graphene quantum dots were used as effective surfactants in miniemulsion polymerization employed of novel hybrid nanocomposite synthesis [109].

The coaxial electrosprayed nanoparticles and carbon dot composites showed a fluorescence “on-off” behavior due to the volume phase transition of the poly(*N*-isopropylacrylamide) shell. These composite in Pickering emulsions exhibits the motions of coaxial electrosprayed NPs in response to changes in temperature [110]. Fluorescent carbon nanodots derived from mandarin peel can be used to detect micromolar amounts of hydrazine hydrate solution with exceptional sensitivity [100].

6. Conclusion

Carbon dots have shown a promising future, especially in biomedical applications that exhibit alternatives to traditional quantum dots based on heavy metal. This review stated various methods of synthesizing carbon dots and their recent applications as diagnosis and therapy. Primarily, we studied physical and chemical properties, including optical and stability, then biological properties including cytotoxicity, internalization at the cellular level, biocompatibility, and distribution that could be exploited in various biomedical applications such as antibacterial, diagnosis, and therapy bioimaging including in vitro and in vivo studies on functionalized carbon dots that show impressive results in reference to their cytotoxicity, photostability, biocompatibility, and anticancer effects. All these applications represent that carbon dots could be a promising method for biomedical applications, cancer diagnosis, and cancer therapy and have potential medical uses in the near future.

Data Availability

The authors can also make data available on request through a data access committee, institutional review board, or the authors themselves. In this case, they can contact the corresponding author to request the data.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Supplementary Materials

Graphical Abstract. (*Supplementary Materials*)

References

- [1] X. Xu, R. Ray, Y. Gu et al., “Electrophoretic analysis and purification of fluorescent single-walled carbon nanotube fragments,” *Journal of the American Chemical Society*, vol. 126, no. 40, pp. 12736–12737, 2004.
- [2] Z. Wang, Y. Qu, X. Gao, C. Mu, J. Bai, and Q. Pu, “Facile preparation of oligo(ethylene glycol)-capped fluorescent carbon dots from glutamic acid for plant cell imaging,” *Materials Letters*, vol. 129, pp. 122–125, 2014.
- [3] C. W. Lai, Y. H. Hsiao, Y. K. Peng, and P. T. Chou, “Facile synthesis of highly emissive carbon dots from pyrolysis of glycerol; gram scale production of carbon dots/mSiO₂ for cell imaging and drug release,” *Journal of Materials Chemistry*, vol. 22, no. 29, pp. 14403–14409, 2012.
- [4] D. Kukreja, J. Mathew, R. Lakshmiopathy, and N. C. Sarada, “Synthesis of fluorescent carbon dots from mango peels,” *International Journal of ChemTech Research*, vol. 8, no. 5, pp. 61–64, 2015.
- [5] P. Roy, P. C. Chen, A. P. Periasamy, Y. N. Chen, and H. T. Chang, “Photoluminescent carbon nanodots: synthesis, physicochemical properties and analytical applications,” *Materials Today*, vol. 18, no. 8, pp. 447–458, 2015.
- [6] H. Xu, L. Xie, and M. Hakkarainen, “Coffee-ground-derived quantum dots for aqueous processable nanoporous graphene membranes,” *ACS Sustainable Chemistry & Engineering*, vol. 5, no. 6, pp. 5360–5367, 2017.
- [7] A. Sciortino, A. Cannizzo, and F. Messina, “Carbon nanodots: a review—from the current understanding of the fundamental photophysics to the full control of the optical response,” *C—Journal of Carbon Research*, vol. 4, no. 4, p. 67, 2018.
- [8] R. Das, Z. Shahnava, M. Ali, M. M. Islam, and S. B. Abd Hamid, “Can we optimize arc discharge and laser ablation for well-controlled carbon nanotube synthesis?,” *Nanoscale Research Letters*, vol. 11, no. 1, pp. 1–23, 2016.
- [9] A. Nevar, N. Tarasenko, M. Nedelko, and N. Tarasenko, “Carbon nanodots with tunable luminescence properties synthesized by electrical discharge in octane,” *Carbon Letters*, vol. 31, no. 1, pp. 39–46, 2021.
- [10] I. F. Andhika, T. E. Saraswati, and S. Hastuti, “The structural characteristics of carbon nanoparticles produced by arc discharge in toluene without added catalyst or gases,” *Evergreen Joint Journal of Novel Carbon Resource Sciences & Green Asia Strategy*, vol. 7, no. 3, pp. 417–428, 2020.
- [11] D. Zhang, Y. Tang, C. Zhang, Q. Dong, W. Song, and Y. He, “One-step synthesis of SnO₂/carbon nanotube nanonests

- composites by direct current arc-discharge plasma and its application in lithium-ion batteries," *Nanomaterials*, vol. 11, no. 11, p. 3138, 2021.
- [12] P. C. Hsu, Z. Y. Shih, C. H. Lee, and H. T. Chang, "Synthesis and analytical applications of photoluminescent carbon nanodots," *Green Chemistry*, vol. 14, no. 4, pp. 917–920, 2012.
- [13] H. Li, X. He, Z. Kang et al., "Water-soluble fluorescent carbon quantum dots and photocatalyst design," *Angewandte Chemie International Edition*, vol. 49, no. 26, pp. 4430–4434, 2010.
- [14] P. C. Hsu and H. T. Chang, "Synthesis of high-quality carbon nanodots from hydrophilic compounds: role of functional groups," *Chemical Communications*, vol. 48, no. 33, pp. 3984–3986, 2012.
- [15] C. Zhu, J. Zhai, and S. Dong, "Bifunctional fluorescent carbon nanodots: green synthesis via soy milk and application as metal-free electrocatalysts for oxygen reduction," *Chemical Communications*, vol. 48, no. 75, pp. 9367–9369, 2012.
- [16] V. Nguyen, N. Zhao, L. Yan, P. Zhong, and P. H. Le, "Double-pulse femtosecond laser ablation for synthesis of ultrasmall carbon nanodots," *Materials Research Express*, vol. 7, no. 1, article 015606, 2020.
- [17] M. J. Yang, J. X. Shi, Y. Yin, and C. G. Shi, "Preparation of carbon nanodots with ultraviolet emission by pulsed laser ablation," *Physica status solidi (b)*, vol. 258, no. 10, article 2100110, 2021.
- [18] N. Mas, J. L. Hueso, G. Martinez et al., "Laser-driven direct synthesis of carbon nanodots and application as sensitizers for visible-light photocatalysis," *Carbon*, vol. 156, pp. 453–462, 2020.
- [19] M. Aslan and H. Eskalen, "A study of carbon nanodots (carbon quantum dots) synthesized from tangerine juice using one-step hydrothermal method," *Fullerenes, Nanotubes, and Carbon Nanostructures*, vol. 29, no. 12, pp. 1026–1033, 2021.
- [20] P. C. Yang, Y. X. Ting, S. Gu, Y. A. Gandomi, and C. T. Hsieh, "Fluorescent nitrogen-doped carbon nanodots synthesized through a hydrothermal method with different isomers," *Journal of the Taiwan Institute of Chemical Engineers*, vol. 123, pp. 302–309, 2021.
- [21] Y. Y. Chen, W. P. Jiang, H. L. Chen et al., "Cytotoxicity and cell imaging of six types of carbon nanodots prepared through carbonization and hydrothermal processing of natural plant materials," *RSC Advances*, vol. 11, no. 27, pp. 16661–16674, 2021.
- [22] E. Durantie, H. Barosova, B. Drasler et al., "Carbon nanodots: opportunities and limitations to study their biodistribution at the human lung epithelial tissue barrier," *Biointerphases*, vol. 13, no. 6, p. 06D404, 2018.
- [23] H. Wang, Q. Mu, K. Wang et al., "Nitrogen and boron dual-doped graphene quantum dots for near-infrared second window imaging and photothermal therapy," *Applied Materials Today*, vol. 14, pp. 108–117, 2019.
- [24] A. Roy, S. Kim, P. Paoprasert, S. Park, and I. in, "Preparation of biocompatible and antibacterial carbon quantum dots derived from resorcinol and formaldehyde spheres," *RSC Advances*, vol. 5, no. 40, pp. 31677–31682, 2015.
- [25] P. Karfa, S. De, K. C. Majhi, R. Madhuri, and P. K. Sharma, *Functionalization of carbon nanostructures*, Academic Press, 2019.
- [26] K. M. Tripathi, T. S. Tran, T. T. Tung, D. Losic, and T. Kim, "Water soluble fluorescent carbon nanodots from biosource for cells imaging," *Journal of Nanomaterials*, vol. 2017, 10 pages, 2017.
- [27] J. Yan, S. Hou, Y. Yu et al., "The effect of surface charge on the cytotoxicity and uptake of carbon quantum dots in human umbilical cord derived mesenchymal stem cells," *Colloids and Surfaces. B, Biointerfaces*, vol. 1, no. 171, pp. 241–249, 2018.
- [28] L. N. Ramana, L. N. Dinh, and V. Agarwal, "Influence of surface charge of graphene quantum dots on their uptake and clearance in melanoma cells," *Nanoscale Advances*, vol. 3, no. 12, pp. 3513–3521, 2021.
- [29] L. Dong, W. Li, L. Yu, L. Sun, Y. Chen, and G. Hong, "Ultra-small Ag₂Te quantum dots with rapid clearance for amplified computed tomography imaging and augmented photonic tumor hyperthermia," *ACS Applied Materials & Interfaces*, vol. 12, no. 38, pp. 42558–42566, 2020.
- [30] I. Y. Goryacheva, A. V. Sapelkin, and G. B. Sukhorukov, "Carbon nanodots: mechanisms of photoluminescence and principles of application," *TrAC Trends in Analytical Chemistry*, vol. 90, pp. 27–37, 2017.
- [31] S. C. Ray, A. Saha, N. R. Jana, and R. Sarkar, "Fluorescent carbon nanoparticles: synthesis, characterization, and bioimaging application," *The Journal of Physical Chemistry C*, vol. 113, no. 43, pp. 18546–18551, 2009.
- [32] V. Nguyen, J. Si, L. Yan, and X. Hou, "Direct demonstration of photoluminescence originated from surface functional groups in carbon nanodots," *Carbon*, vol. 108, pp. 268–273, 2016.
- [33] M. M. F. Baig and Y. C. Chen, "Bright carbon dots as fluorescence sensing agents for bacteria and curcumin," *Journal of Colloid and Interface Science*, vol. 501, no. 501, pp. 341–349, 2017.
- [34] A. L. Himaja, P. S. Karthik, B. Sreedhar, and S. P. Singh, "Synthesis of carbon dots from kitchen waste: conversion of waste to value added product," *Journal of Fluorescence*, vol. 24, no. 6, pp. 1767–1773, 2014.
- [35] C. Russo, B. Apicella, and A. Ciajolo, "Blue and green luminescent carbon nanodots from controllable fuel-rich flame reactors," *Scientific Reports*, vol. 9, no. 1, pp. 1–8, 2019.
- [36] H. P. Castro, V. S. Souza, J. D. Scholten et al., "Synthesis and characterisation of fluorescent carbon nanodots produced in ionic liquids by laser ablation," *European Journal*, vol. 22, no. 1, pp. 138–143, 2016.
- [37] C. Wang, Z. Xu, and C. Zhang, "Polyethyleneimine-functionalized fluorescent carbon dots: water stability, pH sensing, and cellular imaging," *ChemNanoMat*, vol. 1, no. 2, pp. 122–127, 2015.
- [38] X. Su, Y. Xu, Y. Che, X. Liao, and Y. Jiang, "A type of novel fluorescent magnetic carbon quantum dots for cells imaging and detection," *Journal of Biomedical Materials Research*, vol. 103, no. 12, pp. 3956–3964, 2015.
- [39] N. Puvvada, B. Kumar, S. Konar, H. Kalita, M. Mandal, and A. P. Mahanty, "Synthesis of biocompatible multicolor luminescent carbon dots for bioimaging applications," *Science and Technology of Advanced Materials*, vol. 13, no. 4, article 045008, 2012.
- [40] T. Yu, H. Wang, C. Guo, Y. Zhai, J. Yang, and J. Yuan, "A rapid microwave synthesis of green-emissive carbon dots

- with solid-state fluorescence and pH-sensitive properties,” *Royal Society Open Science*, vol. 5, no. 7, article 180245, 2018.
- [41] M. Zhang, C. Chi, P. Yuan, Y. Su, M. Shao, and N. Zhou, “A hydrothermal route to multicolor luminescent carbon dots from adenosine disodium triphosphate for bioimaging,” *Materials Science and Engineering:C*, vol. 76, pp. 1146–1153, 2017.
- [42] J. Wang, X. Liu, G. Milcovich et al., “Co-reductive fabrication of carbon nanodots with high quantum yield for bioimaging of bacteria,” *Beilstein Journal of Nanotechnology*, vol. 9, no. 1, pp. 137–145, 2018.
- [43] M. Hassan, V. Gomes, A. Dehghani, and S. Ardekani, “Engineering carbon quantum dots for photomediated theranostics,” *Nano Research*, vol. 11, no. 1, pp. 1–41, 2018.
- [44] W. Niu, Y. Li, R. Zhu, D. Shan, Y. Fan, and X. Zhang, “Ethylenediamine-assisted hydrothermal synthesis of nitrogen-doped carbon quantum dots as fluorescent probes for sensitive biosensing and bioimaging,” *Sensors and Actuators B: Chemical*, vol. 218, pp. 229–236, 2015.
- [45] G. He, M. Xu, S. Mengjun et al., “Rapid solid-phase microwave synthesis of highly photoluminescent nitrogen-doped carbon dots for Fe^{3+} detection and cellular bioimaging,” *Nanotechnology*, vol. 27, no. 39, article 395706, 2016.
- [46] F. Du, J. Li, Y. Hua et al., “Multicolor nitrogen-doped carbon dots for live cell imaging,” *Journal of Biomedical Nanotechnology*, vol. 11, no. 5, pp. 780–788, 2015.
- [47] T. Pal, S. Mohiyuddin, and G. Packirisamy, “Facile and green synthesis of multicolor fluorescence carbon dots from curcumin: in vitro and in vivo bioimaging and other applications,” *ACS Omega*, vol. 3, no. 1, pp. 831–843, 2018.
- [48] W. Zou, Y. Ji, X. Wang et al., “Insecticide as a precursor to prepare highly bright carbon dots for patterns printing and bioimaging: a new pathway for making poison profitable,” *Chemical Engineering Journal*, vol. 294, pp. 323–332, 2016.
- [49] H. Sadhanala and K. Nanda, “Boron-doped carbon nanoparticles: size-independent color tunability from red to blue and bioimaging applications,” *Carbon*, vol. 96, pp. 166–173, 2016.
- [50] X. Xu, K. Zhang, L. Zhao et al., “Aspirin-based carbon dots, a good biocompatibility of material applied for bioimaging and anti-inflammation,” *ACS applied materials & interfaces*, vol. 8, no. 48, pp. 32706–32716, 2016.
- [51] A. Kasouni, T. Chatzimitakos, and C. Stalikas, “Bioimaging applications of carbon nanodots: a review,” *C*, vol. 5, no. 2, p. 19, 2019.
- [52] H. Kim, Y. Park, S. Beack et al., “Dual-color-emitting carbon nanodots for multicolor bioimaging and optogenetic control of ion channels,” *Advanced Science*, vol. 4, no. 11, p. 1700325, 2017.
- [53] V. Mishra, A. Patil, S. Thakur, and P. Kesharwani, “Carbon dots: emerging theranostic nanoarchitectures,” *Drug Discovery Today*, vol. 23, no. 6, pp. 1219–1232, 2018.
- [54] R. Atchudan, T. N. J. I. Edison, S. Perumal, N. Muthuchamy, and Y. R. Lee, “Eco-friendly synthesis of tunable fluorescent carbon nanodots from *Malus floribunda* for sensors and multicolor bioimaging,” *Journal of Photochemistry and Photobiology A: Chemistry*, vol. 390, article 112336, 2020.
- [55] T. T. Bui and S. Y. Park, “A carbon dot–hemoglobin complex-based biosensor for cholesterol detection,” *Green Chemistry*, vol. 18, no. 15, pp. 4245–4253, 2016.
- [56] Y. Wu, H. Wu, C. Kuan et al., “Multi-functionalized carbon dots as theranostic nanoagent for gene delivery in lung cancer therapy,” *Scientific Reports*, vol. 6, no. 1, p. 21170, 2016.
- [57] T. García-Mendiola, I. Bravo, J. M. López-Moreno et al., “Carbon nanodots based biosensors for gene mutation detection,” *Sensors and Actuators B: Chemical*, vol. 256, pp. 226–233, 2018.
- [58] Y. Yu, C. Li, C. Chen et al., “Saccharomyces-derived carbon dots for biosensing pH and vitamin B 12,” *Talanta*, vol. 195, pp. 117–126, 2019.
- [59] J. Hong, M. Kim, and C. Cha, “Multimodal carbon dots as biosensors,” in *Theranostic Bionanomaterials*, pp. 377–400, Elsevier, 2019.
- [60] P. Sharma, A. B. Jha, R. S. Dubey, and M. Pessarakli, “Reactive oxygen species, oxidative damage, and antioxidative defense mechanism in plants under stressful conditions,” *Journal of Botany*, vol. 2012, 26 pages, 2012.
- [61] W. Bing, H. Sun, Z. Yan, J. Ren, and X. Qu, “Programmed bacteria death induced by carbon dots with different surface charge,” *Small*, vol. 12, no. 34, pp. 4713–4718, 2016.
- [62] N. A. Travlou, D. A. Giannakoudakis, M. Algarra, A. M. Labella, E. Rodríguez-Castellón, and T. J. Bandoz, “S- and N-doped carbon quantum dots: surface chemistry dependent antibacterial activity,” *Carbon*, vol. 135, pp. 104–111, 2018.
- [63] Y. Li, W. Zhang, J. Niu, and Y. Chen, “Mechanism of photo-generated reactive oxygen species and correlation with the antibacterial properties of engineered metal-oxide nanoparticles,” *ACS Nano*, vol. 6, pp. 5164–5173, 2021.
- [64] F.-J. Schmitt, G. Renger, T. Friedrich et al., “Reactive oxygen species: re-evaluation of generation, monitoring and role in stress-signaling in phototrophic organisms,” *Biochimica et Biophysica Acta*, vol. 1837, no. 6, pp. 835–848, 2014.
- [65] Y. J. Li, S. G. Harroun, Y. C. Su et al., “Synthesis of self-assembled spermidine-carbon quantum dots effective against multidrug-resistant bacteria,” *Advanced Healthcare Materials*, vol. 5, no. 19, pp. 2545–2554, 2016.
- [66] H. J. Jian, R. S. Wu, T. Y. Lin et al., “Super-cationic carbon quantum dots synthesized from spermidine as an eye drop formulation for topical treatment of bacterial keratitis,” *ACS Nano*, vol. 11, no. 7, pp. 6703–6716, 2017.
- [67] Z. Song, H. Wang, Y. Wu, J. Gu, S. Li, and H. Han, “Fabrication of bis-quaternary ammonium salt as an efficient bactericidal weapon against *Escherichia coli* and *Staphylococcus aureus*,” *ACS Omega*, vol. 3, no. 10, pp. 14517–14525, 2018.
- [68] X. Dong, A. E. Bond, N. Pan et al., “Synergistic photoactivated antimicrobial effects of carbon dots combined with dye photosensitizers,” *International Journal of Nanomedicine*, vol. Volume 13, pp. 8025–8035, 2018.
- [69] K. Kholikov, S. Ilhom, M. Sajjad et al., “Improved singlet oxygen generation and antimicrobial activity of sulphur-doped graphene quantum dots coupled with methylene blue for photodynamic therapy applications,” *Photodiagnosis and Photodynamic Therapy*, vol. 24, pp. 7–14, 2018.
- [70] C. Zhao, X. Wang, L. Yu et al., *Quaternized carbon quantum dots with broad-spectrum antibacterial activity for treatment of wounds infected with mixed bacteria*, Research Square, 2020.
- [71] C. Zhao, L. Wu, X. Wang et al., “Quaternary ammonium carbon quantum dots as an antimicrobial agent against gram-positive bacteria for the treatment of MRSA-infected pneumonia in mice,” *Carbon*, vol. 163, pp. 70–84, 2020.

- [72] K. Wang, Z. Gao, G. Gao et al., "Systematic safety evaluation on photoluminescent carbon dots," *Nanoscale Research Letters*, vol. 8, no. 1, p. 122, 2013.
- [73] D. Painuly, A. Bhatt, and V. K. Krishnan, "Mercaptoethanol capped CdSe quantum dots and CdSe/ZnS core/shell: synthesis, characterization and cytotoxicity evaluation," *Journal of Biomedical Nanotechnology*, vol. 9, no. 2, pp. 257–266, 2013.
- [74] J. Li, S. Yang, Y. Deng et al., "Emancipating target-functionalized carbon dots from autophagy vesicles for a novel visualized tumor therapy," *Advanced Functional Materials*, vol. 28, no. 30, p. 1800881, 2018.
- [75] Y. Song, W. Shi, W. Chen, X. Li, and H. Ma, "Fluorescent carbon nanodots conjugated with folic acid for distinguishing folate-receptor-positive cancer cells from normal cells," *Journal of Materials Chemistry*, vol. 22, no. 25, p. 12568, 2012.
- [76] J. L. Zhang, X. W. Zhao, M. Xian, C. Dong, and S. M. Shuang, "Folic acid-conjugated green luminescent carbon dots as a nanoprobe for identifying folate receptor-positive cancer cells," *Talanta*, vol. 183, p. 47, 2018.
- [77] S. K. Bhunia, A. Saha, A. R. Maity, S. C. Ray, and N. R. Jana, "Carbon nanoparticle-based fluorescent bioimaging probes," *Scientific Reports*, vol. 3, no. 1, p. 1473, 2013.
- [78] M. Kurupparachchi, H. Savoie, A. Lowry, C. Alonso, and R. W. Boyle, "Polyacrylamide nanoparticles as a delivery system in photodynamic therapy," *Molecular Pharmaceutics*, vol. 8, pp. 920–931, 2011.
- [79] M. Korbelik, "PDT-associated host response and its role in the therapy outcome," *Lasers in Surgery and Medicine*, vol. 38, no. 5, pp. 500–508, 2006.
- [80] C. A. Robertson, E. D. Hawkins, and H. Abrahamse, "Photodynamic therapy (PDT): a short review on cellular mechanisms and cancer research applications for PDT," *Journal of Photochemistry and Photobiology B: Biology*, vol. 96, no. 1, pp. 1–8, 2009.
- [81] H. Thomsen, N. Marino, S. Conoci, S. Sortino, and M. B. Ericson, "Confined photo-release of nitric oxide with simultaneous two-photon fluorescence tracking in a cellular system," *Scientific Reports*, vol. 8, no. 1, p. 9753, 2018.
- [82] K. Berg, P. K. Selbo, A. Weyergang et al., "Porphyrin-related photosensitizers for cancer imaging and therapeutic applications," *Journal of Microscopy*, vol. 218, no. 2, pp. 133–147, 2005.
- [83] I. Di Bari, A. Fraix, R. Picciotto et al., "Supramolecular activation of the photodynamic properties of porphyrinoid photosensitizers by calix [4] arene nanoassemblies," *RSC Advances*, vol. 6, no. 107, p. 105573–105577, 2016.
- [84] C. M. Moore, D. Pendse, and M. Emberton, "Photodynamic therapy for prostate cancer—a review of current status and future promise," *Nature Clinical Practice. Urology*, vol. 6, no. 1, pp. 18–30, 2009.
- [85] P. Huang, J. Lin, X. Wang et al., "Light-triggered theranostics based on photosensitizer-conjugated carbon dots for simultaneous enhanced-fluorescence imaging and photodynamic therapy," *Advanced Materials*, vol. 24, no. 37, pp. 5104–5110, 2012.
- [86] S. Beack, W. H. Kong, H. S. Jung et al., "Photodynamic therapy of melanoma skin cancer using carbon dot - chlorin e6 - hyaluronate conjugate," *Acta Biomaterialia*, vol. 26, pp. 295–305, 2015.
- [87] Y. Li, X. Zheng, X. Zhang et al., "Porphyrin-based carbon dots for photodynamic therapy of hepatoma," *Advanced Healthcare Materials*, vol. 6, no. 1, p. 1600924, 2017.
- [88] S. Sun, L. Zhang, K. Jiang, A. Wu, and H. Lin, "Toward high-efficient red emissive carbon dots: facile preparation, unique properties, and applications as multifunctional theranostic agents," *Chemistry of Materials*, vol. 28, no. 23, pp. 8659–8668, 2016.
- [89] B. Geng, D. Yang, D. Pan et al., "NIR-responsive carbon dots for efficient photothermal cancer therapy at low power densities," *Carbon*, vol. 134, pp. 153–162, 2018.
- [90] M. Zheng, Y. Li, S. Liu, W. Wang, Z. Xie, and X. Jing, "One-pot to synthesize multifunctional carbon dots for near infrared fluorescence imaging and photothermal cancer therapy," *ACS Applied Materials & Interfaces*, vol. 8, no. 36, pp. 23533–23541, 2016.
- [91] J. Ge, Q. Jia, W. Liu et al., "Carbon dots with intrinsic theranostic properties for bioimaging, red-light-triggered photodynamic/photothermal simultaneous therapy in vitro and in vivo," *Advanced Healthcare Materials*, vol. 5, no. 6, pp. 665–675, 2016.
- [92] M. Lan, S. Zhao, Z. Zhang et al., "Two-photon-excited near-infrared emissive carbon dots as multifunctional agents for fluorescence imaging and photothermal therapy," *Nano Research*, vol. 10, no. 9, pp. 3113–3123, 2017.
- [93] J. T. Margraf, F. Lodermeier, V. Strauß et al., "Using carbon nanodots as inexpensive and environmentally friendly sensitizers in mesoscopic solar cells," *Nanoscale Horizons*, vol. 1, no. 3, pp. 220–226, 2016.
- [94] T. G. Chatzimitakos and C. D. Stalikas, "Carbon nanodots from natural (re) sources: a new perspective on analytical chemistry," in *Handbook of Nanomaterials in Analytical Chemistry*, pp. 3–28, Elsevier, 2020.
- [95] A. Marinovic, L. S. Kiat, S. Dunn, M. M. Titirici, and J. Briscoe, "Carbon-nanodot solar cells from renewable precursors," *ChemSusChem*, vol. 10, no. 5, pp. 1004–1013, 2017.
- [96] Y. Gao, W. Xu, F. He et al., "Carbon nanodots enhanced performance of Cs_{0.15}FA_{0.85}PbI₃ perovskite solar cells," *Nano Research*, vol. 14, no. 7, pp. 2294–2300, 2021.
- [97] Y. Wang, C. Xie, X. Yao et al., "Improved comprehensive performance of CsPbI₂Br perovskite solar cells by modifying the photoactive layers with carbon nanodots," *Journal of Materials*, vol. 8, no. 2, pp. 358–365, 2021.
- [98] S. Riaz and S. J. Park, "Carbon quantum dots-embedded graphitic carbon nitride nanotubes for enhancing the power conversion efficiency of sensitized solar cells," *Materials Today Chemistry*, vol. 24, article 100763, 2022.
- [99] J. Liu, S. Zhao, C. Li et al., "Carbon nanodot surface modifications initiate highly efficient, stable catalysts for both oxygen evolution and reduction reactions," *Advanced Energy Materials*, vol. 6, no. 9, p. 1502039, 2016.
- [100] P. Suvarnapaet, W. Pinyo, S. Pechprasarn, and N. Albutt, "Fluorescence detection of hydrazine hydrate using carbon nanodots synthesized from mandarin rind," in *Applied Mechanics and Materials*, vol. 891, pp. 71–77, Trans Tech Publications Ltd., 2019.
- [101] L. Sai, S. Liu, X. Qian, Y. Yu, and X. Xu, "Nontoxic fluorescent carbon nanodot serving as a light conversion material in plant for UV light utilization," *Colloids and Surfaces B: Biointerfaces*, vol. 169, pp. 422–428, 2018.

- [102] Y. Wang and A. Hu, "Carbon quantum dots: synthesis, properties and applications," *Journal of Materials Chemistry C*, vol. 2, no. 34, pp. 6921–6939, 2014.
- [103] H. Huang, Y. Liu, and Z. Kang, "Carbon nanodot composites: fabrication, properties, and environmental and energy applications," *Novel Carbon Materials and Composites: Synthesis, Properties and Applications*, pp. 223–273, 2019.
- [104] F. Wang, Z. Xie, H. Zhang, C. Liu, and Y. Zhang, "Highly luminescent organosilane-functionalized carbon dots," *Advanced Functional Materials*, vol. 21, no. 6, pp. 1027–1031, 2011.
- [105] H. Huang, C. Li, S. Zhu et al., "Histidine-derived nontoxic nitrogen-doped carbon dots for sensing and bioimaging applications," *Langmuir*, vol. 30, no. 45, pp. 13542–13548, 2014.
- [106] L. N. Dinh, L. N. Ramana, R. P. Kuchel, V. Agarwal, and P. B. Zetterlund, "Miniemulsion polymerization using carboxylated graphene quantum dots as surfactants: effects of monomer and initiator type," *Polymer Chemistry*, vol. 11, no. 36, pp. 5790–5799, 2020.
- [107] X. Zhai, J. Gao, X. Wang et al., "Inverse Pickering emulsions stabilized by carbon quantum dots: influencing factors and their application as templates," *Chemical Engineering Journal*, vol. 345, pp. 209–220, 2018.
- [108] T. Zhou, Z. Huang, F. Wan, and Y. Sun, "Carbon quantum dots-stabilized Pickering emulsion to prepare NIR light-responsive PLGA drug delivery system," *Materials Today Communications*, vol. 23, article 100951, 2020.
- [109] L. N. Dinh, L. N. Ramana, V. Agarwal, and P. B. Zetterlund, "Miniemulsion polymerization of styrene using carboxylated graphene quantum dots as surfactant," *Polymer Chemistry*, vol. 11, no. 18, pp. 3217–3224, 2020.
- [110] J. Chen, C. Zhu, Z. Yang, P. Wang, Y. Yue, and T. Kitaoka, "Thermally tunable Pickering emulsions stabilized by carbon-dot-incorporated core-shell nanospheres with fluorescence "on-off" behavior," *Langmuir*, vol. 34, no. 1, pp. 273–283, 2018.