



A comprehensive review on carbon quantum dots

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Abstract

Over the past few decades, carbon quantum dots (CQDs) gained remarkable attention due to their distinctive properties and wide-ranging applications. Usually, CQDs are nano-sized materials, showcase of outstanding optical, electronic, and chemical characteristics. Their synthesis involves the controlled carbonization of diverse carbon-rich precursors, such as organic molecules or waste materials. Their optical properties, including adjustable fluorescence, make them ideal for implementation in bioimaging, sensors, and optoelectronic devices. Their diminutive size, biocompatibility, and minimal toxicity enhance their suitability for applications in biology and medicine. Furthermore, researchers have delved into exploring the potential of CQDs in energy-related domains, such as photo-catalysis, solar cells, and super-capacitors, leveraging their unique electronic structure and catalytic capabilities. Ongoing research continues to uncover their synthesis and fascinating applications due to low toxicity. This review provides comprehensive information on CQDs, including their synthesis, characteristics, and attractive applications.

Keywords: Carbon quantum dots, bio-imaging, photo-catalyst, nano-medicine, chemical sensor

1. Introduction

From the past few decades, researches on carbon quantum dots have significantly increased due to their dramatic and fascinating applications [1]. Carbon quantum dots are a novel class of fluorescent materials from the nano-carbon family with a dimension of less than 10nm that include carbon as one of their constituent parts [2]. Due to their unique properties, such as biocompatibility, ease of surface modification, good photoluminescence, exceptional water+ solubility, and low toxicity, carbon quantum dots have recently emerged as a possible rival for inorganic quantum dots. For example, applications like photo-catalysis in vitro and in vivo bio-imaging, light emitting diodes (LEDs), organic solar cells (OSCs), DSSCs (dye-sensitized solar cells), drug carriers in biomedicine, chemical and biological sensors, as well as photodynamic and photothermal therapies, all utilize CQDs [3]. However, the search for low-cost synthesis/fabrication materials that are also non-toxic, eco-friendly, and biocompatible has been ongoing for some time. C-dots can be made using two different approaches: top-down and bottom-up. For example, laser ablation, electrochemical syntheses, and electric discharges are all top-down techniques [4]. Meanwhile, bottom-up methods include

carbonization of sugars like glucose and sucrose, ascorbic acid, and citric acid [5]. To improve water solubility and luminescent properties, additional synthetic procedures, techniques, stages/levels, hazardous agents, and equipment are required [6]. An urgently needed one-step, facile approach with economic chemistry is required to produce self-passivated photo luminescent C-dots. In particular, it is possible to control the size, shape, and physical properties of the carbon nanoparticles by careful selection of the carbon source and surface modifier [7]. However substantial production of C-dots with tailored composition, structure, morphology and size by a simple and cheap method remains still challenging.

2. Semiconductor Quantum Dots

Semiconductor nanocrystals are the latest developed nanomaterial, also known as QDs, that has piqued many people's curiosity [8]. A broad range of studies have been conducted on semi-conductor quantum dots, which have found them durable, tunable-fluorescence-emission, high productivity, and with new visual characteristics [9]. The most often utilized fluorescent

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compounds are organic dyes, CdSe, and ZnS quantum dots (QDs). These are some of the most frequently utilized fluorescent compounds [8], which use heavy toxic metals (either with low concentrations). Therefore, these QDs are not considered useful in biomedical applications [10]. The disadvantages arise due to photobleaching, quenching of dye molecules, and the toxicity of QDs [11].

Photo-luminescent materials have gained popularity due to their auspicious, diversified, and broad range of uses [12]. Because excitons are restricted in spatial dimensions, QDs exhibit the characteristics that fall between bulk semiconductors and discrete molecules [13]. When stimulated by photons and/or an electric field with greater energy than the band gap, quantum dots produce photons to release the absorbed energy [14]. Furthermore, because of the quantum confinement phenomenon, the emission energy can be adjusted by varying the composition and particle size of quantum dots.

3. Carbon Quantum Dots

Researchers have conducted a broad range of studies for investigating nanotechnology and creating nanomaterials. These nanomaterials are the particles that have been reduced to the nanoscale size and display significantly different characteristics than what they do on a large scale. For example, when the system size decreases, the "quantum size effect" becomes more apparent, causing the electrical characteristics of solids to change [15]. Meanwhile, increasing the exterior part to capacity proportion dramatically alters the mechanical, thermal, and catalytic characteristics of constituents [16]. Nanomaterials' specific characteristics allow for novel uses [7]. Carbon nanotubes, along with fullerenes, as well as nanoparticles composed of different materials such as silver, gold, silica, zinc, and titanium, are usually employed in a variety of goods in the market [17].

The systematic studies and the combination of both nanotechnology and biotechnology are quite appealing for the provision of analytical tools and techniques, and provide an efficient platform for the studies and/or research in biological sciences [18]. Quantum dots have been utilized as strong fluorescent probes for imaging biological targets [19], illness diagnosis and prognosis, tracking cell/protein interactions, and cell viability [20]. Traditional organic dyes have a restricted excitation range, poor fluorescence intensity, and a short lifespan [16]. QDs, on the other hand, have broad emission spectra but a limited, powerful, and modified emission range [21]. With their brilliant emission and exceptional

photostability, they allow a real-time monitoring of particles [17].

Because of their simplicity of functionalization and low cost of synthesis, carbon nanomaterials have shown significant promise in applications such as optoelectronics, bioimaging, and catalysis [22]. However, chemical changes frequently result in unwanted consequences such as low water solubility, limiting their potential in a variety of applications [23].

Carbon QDS, or CQDs, are not very old, and a type of carbon-nanomaterial which has intrinsically high-water solubility, photoluminescent quantum yield, and size-dependent fluorescence, has demonstrated even more potential in these applications [24]. Chemical treatment retains or even improves these characteristics, elevating CQDs above many carbon nanomaterials [24].

3.1. Discovery of CQDs

Xu et al. (2004) [25] unintentionally discovered CQDs during the process of the disintegration and filtration of the SWCNTs (carbon nanotube) [26]. This prompted further research to harness CQD fluorescence characteristics and produce a new class of very small sized practical fluorescent nanomaterials [27].

C-dots particles are found to be very interesting among researchers due to their uniqueness in integration of bright-light photoluminescence, high water solubility, easy functional activity, lower toxicity values, and photostability with higher values [12]. The simple synthesis processes achievable by several methods from a range of initiating materials [28, 29]. Unlike nanodiamonds, which emit light owing to point defects found in the sp^3 hybridized carbon structures due to differences in carbon atom arrangement, energy emission from C-dots exhibits several characteristics along with fully recharged electrons and carbon materials [30].

3.2. Optical Properties of CQDs

The most fascinating element of CQDs is their variable photoluminescence (PL) properties, which are produced by the quantum confinement phenomena. The excited electron transfers from the conduction band towards the valence band of the absorbed photon's wavelength [31]. Light emitted by QDs can have wavelengths ranging from ultraviolet to infrared [32].

The major distinguishing feature of fluorescent CQDs or FCQDs is that the hue of fluorescence varies with size [31]. Quantum dots of various sizes produce high-energy light (Blue). Furthermore, large quantum dots produce light with a low energy (Red) [33].

3.3. Quantum Confinement Effect

Bulk semiconductor materials contain a fully occupied valence band and also a conduction band, which is

separated by relatively small band gap distance (less than 4 eV), acting like insulators at ambient temperature and displaying electrical conductivity when triggered externally [34]. The valence band receives energy through the conduction band when the energy is higher than the band gap, and it also allows electric current to flow. The valence and conduction bands in nanoparticles are divided into different energy levels, with the energy difference between the closest feasible valence and conduction levels increasing with particle size [35,36].

A dot is formed when a bulk substance is reduced to 1nm-10nm in all three dimensions [14]. The band gap between the conduction band and the valence band grows as the number of atoms decreases from bulk material to quantum dots. The number of electrons that jump from the conduction band to the valence band is determined by the energy gap between the conduction and valence bands, which is directly proportional to the number of atoms present in the material [37].

Because QDs have broad absorption spectra, they may be excited by a wide variety of wavelengths. This feature may be used to concurrently stimulate several colored QDs with a single wavelength. The emission spectra of QDs are narrow. This can be easily adjusted by making changes to the size, composition, and surface coating [36]. When quantum dots are produced, the number of atoms in each cluster of material may vary, resulting in fluorescent carbon quantum dots of varying sizes displaying distinct colors [17]. Color of QDs depends on size, decreasing size from 6nm to 2nm, energy bandgap increases and color changed red>yellow>green>blue (decreasing size order) [38]. This is caused by the quantum confinement effect.

- i) As the nanoparticle's size shrinks, the exciton (electron-hole pair) becomes more restricted.
- ii) As the exciton is restricted further, the recombination energy increases. This is caused by the quantum confinement effect.

During the synthesis process, the size of quantum dots may be adjusted [33].

3.4. Review on Various Synthetic Methods

Carbon dots can be synthesized from different materials including lemon juice [5], wheat straws [39], milk [40], apple juice [41], aspirin [42], coffee grounds [43], egg yolk [44], and chocolate [45]. There are two basic approaches to the synthesis of carbon dots [15]; top-down methods, and bottom-up methods.

In the top-down method, the carbon particles (bulk material) are usually broken down, which results in different products, such as carbon soot, graphite, graphite oxide, nanodiamonds, and/or nanotubes. These materials are produced by using different processes such

as the laser ablation, electrochemical oxidation, and/or electrochemical oxidation [46]. Unlike the top-down method, the bottom-up method involves the carbonization of tiny organic molecules to produce CDs, which are frequently manufactured utilizing combustion/thermal/hydrothermal, supported synthesis, microwave/ultrasonic-aided processes in which CQDs usually generated from molecular precursors [47].

3.4.1. The Top-down Approaches

3.4.1.1. The Arc-discharge Methods

C-dots were discovered by Xu et al. while purifying arc-discharge dust-derived single-walled nanotubes (SWCNTs). Carbonaceous materials were divided into a number of components with varying degrees of fluorescence based on their size. The researchers used 3.3 M HNO₃ to add carboxyl-functional groups to the arc soot, which improves the substance's hydrophilicity. They then extracted the dust/soot using a NaOH solution (pH 8.4) to create a stable black suspension. Gel electrophoresis was used to separate the suspension into SWCNTs, short tubular carbons, and fluorescent Carbon dots. Lack of poly aromatic hydrocarbon (PAH) characteristic C-H bond out of plane bending modes in the FTIR spectrum showed that the PL was not derived from PAH sources [25].

3.4.1.2. The Electrochemical Oxidation

For the first time, electrochemical synthesis of C-dots in a solution was shown by Zhou et al. (2007). They grew multiwall carbon nanotubes (MWCNTs) on carbon paper made from scrolled grapheme layers using chemical vapor deposition. A degassed acetonitrile solution with 0.1 M tetrabutylammonium perchlorate (TBA+ClO₄) served as the electrolyte, and the nanotubes were used as the working electrode in an electrochemical cell along with a Pt wire counter electrode and an Ag/AgClO₄ reference electrode, as well as a Pt wire counter electrode and a reference electrode. When developed, they were spherical and emitted photoluminescence. When no MWCNTs were used in the carbon paper, no C-dots were generated. Chi and colleagues also created C-dots in phosphate buffer solution (pH 7.0) using a Pt mesh counter electrode and an Ag/AgCl reference electrode assembly by electrochemically oxidizing graphite rods [48].

3.4.1.3. Laser-Ablation Methods

Argon was used to heat-press a mixture of graphite powder and cement, which was then baked, cured, and annealed at 900°C and 75 kg/cm². To enhance C-Dot fluorescence, different non-toxic polymeric agents [47] such as poly(ethylene glycol) diamine (PEDG), poly(propionyl ethylene-imine-ethyleneimine) (PEIE) [49],

terminated polyethylene glycol diamine [50], and poly(propionyl-ethylenimine-coethylenimine) (PEIE-EI) [49]. After dialysis against water, followed by centrifugation, a highly fluorescent product was obtained from the fluorescently pure C-dots [51]. It was necessary to design and execute a slightly modified technique utilizing ^{13}C powder and more rigorous control in order to produce C-dots with a high quantum yield of 20% [52]. For 2 hours, the authors of the study used a pulsed Nd:YAG laser to irradiate graphite or carbon black mixed in diamine hydrate, diethanolamine, or PEG200N, which acted as a surface passivating agent.

3.4.2. Bottom-up Approaches

3.4.2.1. Combustion/Thermal/Hydrothermal Methods

Unscented candle soot and natural gas burner soot are also excellent sources of C-dots. To make multicolor luminous C-dots from candle combustion soot, Mao et al. used an oxidative acid treatment to the C-dot surfaces, adding -OH and -COOH groups [53]. Polyacrylamide gel electrophoresis (PAGE) fractionation was employed to clean up the particles after they had been separated.

Thermally degrading low-temperature melting molecular precursors were used to produce surface passivated C-dots in a single procedure [54]. Careful selection of the carbon source and surface modification increased control over the C-dots' form and physical properties. The EDTA salts were converted using a one-step pyrolytic process into extremely blue luminous C-dots with a PL QY of 31.6–40.6%. Chemical oxidation of carbohydrates was a significant technique for generating C-dots [55]. To increase water solubility and other PL properties, most synthesis methods call for a number of steps, a strong acid, and further treatment with other compounds. Wu et al. created hydrophilic C-dots with a high yield via controlled carbonization of sucrose, as reported in *Science* [55]. Green luminescent C-dots were differentiated from non-luminous C-dots that emitted blue fluorescence after being functionalized with PEG, and this was accomplished effectively. The hydrothermal technique was also utilized by other researchers for the production of C-dots with a high quantum yield from chemical precursors including glucose, fructose, saccharide, and ascorbic acid as compared to others [56]. We recently synthesized huge quantities of highly photoluminescent C-dots on a massive scale using hydrothermal treatment of cheap orange juice that is readily available. Because of their high photo-stability and low toxicity, these C-dots have shown to be excellent probes for cellular imaging. Using hydrothermal treatment of soya milk, Zhu et al. created bi-functional fluorescent C-dots with strong electro-catalytic activity for oxygen reduction [57].

3.4.2.2. Microwave/Ultrasonic Synthesis

To make C-dots with electro-chemiluminescence properties, Yang says he used a microwave pyrolysis approach by mixing PEG200 with a saccharide (such as glucose or fructose) in water to make a transparent solution, which was then heated for 2–10 min in a 500 W microwave oven to produce electro-chemiluminescence [58]. The length of the microwave heating influences the size and PL properties of these C-dots (5 minutes in this case). Kang et al. created C-dots that showed vividly colored PL from glucose or active carbon in the visible to near-infrared spectral region using an ultrasonic treatment method [59]. Also, using hydrogen peroxide as a catalyst, the same group devised a one-step ultrasonic treatment to generate water-soluble bright C-dots from active carbon [56]. It was found that these C-dots generated bright and colorful photoluminescence throughout the whole visible to near-infrared spectral range, despite their up-conversion fluorescent properties. One-pot ultrasonic synthesis was utilized in a recent research to produce photocatalytically active fluorescent N-doped C-dots (NCDs), which were then used in the visible light photo degradation of methyl orange [60]. Figure 2.5 depicts the photodegradation of methyl orange utilizing fluorescent N-doped C-dots (NCDs) with photocatalytic activity [60].

3.4.2.3. Supported Synthetic Methods

With this method, the C dots may be made to have a monodisperse structure while still being synthesized using a supported synthetic approach. The support helps to keep the C-dots separate during high-temperature treatment, which prevents nanoparticle aggregation. For C-dot formation, Li and colleagues used surfactant-modified silica spheres as supports; the silica spheres were then removed using a 2 M NaOH solution etched with a diamond pen [61]. Using 3M HNO_3 , the surface was passivated and oxidized to produce hydrophilic photoluminescent C-dots. When developing C-dots, Giannelis and colleagues used an ion-exchanged version of NaY zeolite [54]. To make hydrophilic C-dots, Zhu et al. utilized mesoporous silica (MS) spheres as nanoreactors. After calcination and support removal, MS spheres were impregnated with a complex salts and citric acid solution, resulting in monodisperse, hydrophilic C-dots [62].

3.5. Applications of CQDs

3.5.1. The Chemical sensing

CQDs have proven useful in chemical sensing, e.g., mercury (Hg^{2+}) must be identified as soon as possible since it poses a major hazard to both the environment and human health. CQDs have been used in chemical sensing applications because of their low toxicity, water

solubility, high photostability, and remarkable chemical stability. The selective detection of Hg^{2+} in aqueous solutions and live cells was one of the first successful attempts to utilize CQDs in chemical sensing [6]. Fluorescence emissions from both CQD solution and CQDs immobilized in sol-gel were found to be Hg^{2+} -dependent, as shown by Goncalves and colleagues in their study. Fluorescent probes included laser-ablated CQDs, NH_2 -PEG200, and N-acetyl-L cysteine-passivated CQDs. The team of Goncalves and associates used micromolar quantities of Hg^{2+} with a Stern–Volmer constant of 1.3105 M^{-1} . Barman and Sadhukhan (2012) found that fluorescence intensity in CQDs could be successfully reduced. This means that the quenching induced by Hg^{2+} is most likely due to static quenching as a consequence of the formation of a stable non-fluorescent complex between CQD and Hg^{2+} , given the high value of the Stern–Volmer constant. Substituting N-CQDs for the laser-ablated CQDs led to a substantial improvement in sensitivity down to nanomolar levels, as later found. Again, it is speculated that static quenching is responsible for the loss of fluorescence; but this time, the value of the Stern–Volmer constant is two orders of magnitude higher: 1.4107 M^{-1} . The significantly improved Hg^{2+} sensing ability of N-CQDs has been attributed to the presence of nitrogen element, most likely in the form of $-\text{CN}$ groups on the N-CQD surface [63]. The Hg^{2+} -CQD system, developed more recently by Yan and colleagues, enables the selective detection of Hg^{2+} in aqueous solution and in live cells. When compared to conventional synthesis methods, the authors were able to achieve quantum yields of 65.5 and 55.4 percent using citric acid and 1,2-ethyldiamine (CQD-1 and CQD-2, respectively). These quantum yields were much higher than those of the usual technique. They looked into the influence of Hg^{2+} on CQD-1 and CQD-2's fluorescence emission quenching effectiveness and selectivity. Both CQDs served as selective and sensitive fluorescence probes, respectively, for the detection of mercury levels in aqueous solutions and live cells. After injecting 20 mM of Hg^{2+} , the fluorescence became more intense.

The intensity of CQD-1 was reduced by 80% in the first hour, whereas the intensity of CQD-2 was reduced by 55% in the first hour and stayed constant afterwards. This shows that CQD-1 and CQD-2 may be used as Hg^{2+} chemical sensing probes in a wide range of applications [64]. The Hg^{2+} selectivity of CQD-1 and CQD-2 was then determined by measuring the quantity of fluorescence quenching produced by different metal ions added to the cells at 20 mM concentrations. Using Hg^{2+} , the most potent metal ion tested, scientists were able to significantly reduce the fluorescence of the CQD-1 and CQD-2 fluorescent materials. Reversible quenching of

fluorescence was shown in these CQDs, making them useful as reversible fluorescent probes. This was demonstrated in the studies. The detection of Hg^{2+} in growing cells was also made with efficient and successful efforts [64].

Some of the additional elements identified by CQDs in chemical sensing include Cu^{2+} [65], Fe^{3+} [66], Pb^{2+} [20], Cr^{4+} [67], and Ag^+ [68]. The bulk of the methods proposed are based, as previously mentioned, on the fluorescence quenching produced by metal ions, similar to the Hg^{2+} sensing approach. Cu^{2+} was discovered to be selectively detected utilizing CQDs modified with lysine and bovine serum albumin in aqueous samples such as tap water described by Liu et al (CQDs-BSA-Lys). Sensitive detection of Cu^{2+} in solution was achieved using the coordination reaction of Cu^{2+} with the $-\text{COOH}$ and $-\text{NH}_2$ groups of the CQDs-BSA-Lys [69]. CQD-based fluorescent probes with higher sensitivity were developed by covering them with more sensitive metal-organic frameworks (ZIF-8 – zinc imidazolate frameworks) and silica nanoparticles rather than polymeric materials [70]. A new class of ultrasensitive nanocomposite fluorescence probes has been developed by Lin and colleagues by using CQDs coated with b-PEI and encapsulated in ZIF-8. It was discovered that by using the synergistic effects of the strong fluorescence of the CQDs and the selective accumulation action of ZIF-8 hosts, CQD-ZIF-8 nano composite probes could detect Cu^{2+} concentrations down to 80 parts per million (ppm) [52]. To make more CQD-metal-organic framework probes, the same method may be employed, which would enable very sensitive and selective detection for many analytes like concentration of metal ions, detect pH, citrate ion concentration in a single experiment.

A few examples of reactive oxygen species are CN^- [71], S^{2-} [72], ClO^- [73], and I^- [74]. Instead of using the fluorescence quenching method to measure metal ions, many anion assays use the fluorescence rise (also known as fluorescence recovery) of previously quenched CQD-metal complexes. CQD fluorescence was recovered by creating more stable complexes between I^- and metal ions in the I^- assay, which displaced the CQDs from the CQD-metal complexes. The authors, Z. Yang et al. (2013), state that Ascorbic acid, 4-nitrophenol, quercetin, 2,4-dinitrophenol, and APTS-GO were also tested for chromium [67], as were other minor inorganic substances [75]. Variations in the synthesis of CQDs have serious consequences because studies suggest that the fluorescence characteristics of CQDs are strongly dependent on the composition of CQDs and residue chemical groups on their surface; different starting materials and procedures invariably result in CQDs with significantly different physicochemical properties overall, and optical properties specifically. CQDs must

be standardized, and their performance must be evaluated, as soon as possible [13].

3.5.2. Biosensing

CQDs were used in immunoassays and biomarker studies in addition to biosensing using antibodies and their gene-recombinant fragments [76]. In immunoassays, CQDs are mainly employed as fluorescent labels. Posthuma-Trumpie and colleagues studied the utilization of CQDs in lateral flow and microarray immunoassays [77]. Because they are less costly, more stable, and more sensitive, CQDs were chosen for this study over other commonly used fluorescent markers. CQDs have been found to be more sensitive as labels in lateral flow tests than gold or latex nanoparticles (LFA). As recently as 2019, researchers discovered that the pico-molar range was capable of accurately detecting CQDs.

NALFA serves as a good generic example of nucleic acid LFA. The amplicons' distinguishing tags are recognized by the appropriate antibodies, and the CQDs attached to the amplicons generate fluorescence signals [78]. For the rapid and specific detection of 4,4'-dibrominated biphenyl (PBB15), a persistent organic pollutant that has been shown to disrupt the endocrine system, Bu and colleagues developed an immune-sensor based on the principles of Forrester resonance energy transfer (FRET) and homogenous immunoassay. Gold nanoparticles (AuNPs) functionalized with anti-PBB15 antibody have been used as fluorescence acceptors, whereas PBB15 antigens have been CQD-labeled have been used as donors. Because of the FRET phenomena, the AuNPs were able to reduce the CQDs' fluorescence. Fluorescence recovery happened when the CQD-labeled antigens were competitively immune-reacted off of AuNP's surface with PBB15 added to the solution. Using antibodies and antigens specific to the analyte, this immunosensor may be used as a model for the future creation of immunoassays for the detection of other analytes [79]. The fluorescence dye was successfully quenched by the addition of single-stranded DNA to the CQDs, and this technique was used to identify nucleic acids with such great selectivity that even a single base mismatch could be detected first. The newly generated cs-DNA desorbed from the CQD surface when single-stranded DNA (ss-DNA) hybridized with its matching target to make a double-stranded DNA (ds-DNA). This allowed the fluorescence to return [80]. Single-nucleotide polymorphisms may be detected using this technology's ability to detect changes in fluorescence intensity. The use of nucleic acid binders called aptamers, selected from a large nucleic acid library, has also been shown in another CQD application [13]. Most of the time, aptamers are linked to a conformational

change in the target that can be detected in the radiometric response. When used in conjunction with thrombin-functionalized CQDs, this technique creates a sandwich-structure with aptamer-functionalized silica nanoparticles by creating a specific interaction between thrombin and a particular aptamer [80]. With a detection limit of 1.0 nM, this thrombin assay was shown to be one of the most sensitive fluorescence assays available for thrombin. Stable fluorescent CQDs made using a one-step microwave pyrolysis method previously reported were used to identify the proteins after they were separated using gel electrophoresis. Protein staining was a breeze with these CQDs since they worked so well.

Conventional staining agents like Coomassie Brilliant Blue and Ag⁺ work extremely well or even better in terms of sensitivity than [80]. According to the researchers, water-soluble CQDs made from rice straws thermally burned in a furnace with insufficient air flow were used to rapidly identify and count bacteria cells in sewage water. These CQDs engaged with the receptors only when they came into touch with the bacterial cell membrane [81]. In addition to macro-biomolecules, CQDs have shown promise as fluorescent probes for the detection of small bio-analytes such as anti-bacterial drugs. This was clearly shown by Niu and Gao's experiments. Luminescent N-CQDs were initially synthesized from glutamic acid using a one-step pyrolysis method. These N-CQDs were utilized in a number of applications for the detection of amoxicillin, a popular antibiotic used to treat bacterial infections. The researchers found that amoxicillin molecules effectively separate N-CQDs from one another, decreasing the frequency of non-radiative transitions, which ultimately led to an increase in fluorescence intensity [82]. CQDs were also utilized to detect previously undetectable small bio-analyte including dopamine, ascorbic acid, and glucose. Some of these CQD-based methods utilize dopamine as a carbon source and generate highly fluorescent CQDs, which may be used to detect dopamine without the need of labelling chemicals. Using dopamine, researchers were able to restore the fluorescence of a previously quenched Fe³⁺ CQD complex in a manner similar to the anion sensing described earlier. In the range of 0.1–10 mM, the increase in fluorescence was shown to be proportional to an increase in dopamine concentration, with a detection limit of just over 68 nM. [71]. Dopamine, on the other hand, was shown to be an efficient quencher in another study. The differences in the techniques and carbon sources used to make CQDs likely account for this discrepancy. Consistency in CQD synthesis is crucial to prevent data misunderstanding of data [70].

3.5.3. Bio-imaging

CQDs provide numerous advantages over semiconductor quantum dots due to their comparable optical properties and outstanding chemical and photochemical durability [12]. First and foremost, carbon does not pollute the environment in any way. These features make CQDs an appealing technology as an alternative to semiconductor quantum dots for studying biological systems both *in vitro* and *in vivo* [72]. Cytotoxicity is caused by surface passivating chemicals on the CQD surface, not by the carbon core of the CQDs [83]. Surface passivating compounds with low cytotoxicity have been proven to be safe at high dosages for *in vivo* imaging. Mice were given 8–40 mg/kg (CQD/weight) of PEGylated CQDs intravenously, and no adverse effects could be detected up to 28 days later for the evaluation of toxicity [84]. To test whether CQDs are detrimental at exposure levels and durations beyond what is typically used in *in-vivo* imaging studies, researchers gave mice various dosages of CQDs or NaCl as a control. Physiological indicators were all similar. Despite liver and spleen CQD levels being higher than those reported in the other organs, no abnormalities were seen in the tissues. Additionally, the health of cells exposed to various doses of CQDs was evaluated. Cell viability was reported to be more than 95% at CQD dosages up to 1.8 mg/ml. As a result of these results, CQDs have been shown to be much more biocompatible than semiconductor quantum dots as a result of these results [85]. Even at low concentrations and/or short incubation times, it is feasible to use CQDs modified with high cytotoxicity agents for *in vivo* applications. It has been shown that organic dye-conjugated CQDs are effective fluorescent H₂S probes. When organic dye-conjugated CQDs were exposed to residues of H₂S, a FRET reaction took place, changing the blue emission into a green emission [12]. H₂S has already been shown to cross cell membranes through simple diffusion [84]. A fluorescence microscope was used to investigate the ability of organic dye-conjugated CQDs to detect changes in physiologically relevant H₂S levels in live cells. Additionally, CQDs synthesized using N-(β -aminoethyl)- γ -aminopropyl methyl-dimethoxysilane as a carbon source interacted preferentially with Cu²⁺ owing to the presence of ethylenediamine residues on their surface [85]. RhB-doped silica nanoparticles were coated with these CQDs to produce dual-emission Cu²⁺ probes. Cu²⁺ significantly reduced the fluorescence of CQDs but had no effect on RhB. These probes worked well for imaging Cu²⁺ in live cells [85]. The images taken by Hsu et al. showed that the cytoplasm and membrane were the primary locations of CQDs. Passivated PPEI-EI water-soluble CQDs have been shown to label MCF-7 cells' cell membrane and cytoplasm, but not their nucleus [86]. COS-7 cells' membranes and cytoplasm

were labelled with CQDs produced from activated carbon alone [84]. Only cells treated with silica-encapsulated CQDs exhibited the highest light in the cytoplasm [81]. Fowley and colleagues created CQDs that passed the membrane of Chinese hamster ovary cells and landed in the cytoplasm using a biocompatible amphiphilic polymer [86]. Researchers led by Hu have created CQDs with a 54.3% quantum yield b-PEI coating that are uniformly dispersed throughout the cytoplasm [63].

Surface passivating chemicals and surface passivation mode influence CQDs localization, as shown by these examples. It is common practice to apply CQDs to cells before imaging to enable uptake by the cells and utilization within them. When CQD internalization was tested at 481°C, no CQDs were found within the cells. As reported, CQDs enter cells through endocytosis [87, 88]. One possible way to enhance CQD absorption is by coupling them with membrane translocation peptides to facilitate this process [89]. CQDs are unique labelling agents due to their variety of emission colors. Consequently, researchers can now select and control the excitation and emission wavelengths more easily [65]. The multicolor emissions they produce when stimulated at different wavelengths were also observed when folic acid passivated CQDs were used in HepG2 cells [84]. Bacteria and yeast cells utilized several excitation modes to stimulate green CQDs produced from sugar cane juice [90]. The strong fluorescence intensity required for cell imaging [89]. Even without any surface passivating compounds, thermally combusted soot CQDs treated with acid efficiently translocated into Ehrlich ascites carcinoma cells. If the excitation wavelength is sufficiently red-shifted, CQDs may emit in the near infrared (NIR). Despite their low NIR emission, CQDs have great potential for *in vivo* fluorescence tracking studies [91]. This is due to the fact that the animal's body is almost transparent in the near-infrared spectrum. Yang's team was the first to use CQDs in live mice as a contrast agent [91]. PEG1500N-passivated CQDs were administered subcutaneously into mice, and the animals continued to emit bright fluorescence for 24 hours after the injection. This study found that intravenously administered CQDs mostly exit the body through urine extraction. The same group observed lymph vessel movement using ZnS-doped CQDs [92].

3.5.4. Nano-medicine

CQDs are an ideal alternative to other fluorescent nanomaterials since they are tiny fluorescent nanoparticles that can be synthesized rapidly and inexpensively using various synthetic methods [93]. As CQDs show no apparent signs of toxicity in animals,

they hold great promise for application in nano-medicine [94]. CQDs were administered intravenously to mice in vivo and used in photodynamic treatment to treat transdermal tumors with no effect on thrombin activity or blood coagulation [95]. The production of singlet oxygen species, which leads to cell death, and the localization and concentration of photosensitizers in cancer tissue are induced using a specific wavelength of irradiation. The strong tumor-to-background fluorescence contrast and the low fluorescence levels in other tissues and organs indicate that CQDs might be used as photosensitizers due to their ability to selectively concentrate within tumors [96].

PPEI-EI functionalized small CQDs (PPEI-CQDs) showed a significant photodynamic impact on Du145 and PC3 cells when exposed to UV light. The observed photodynamic impact was caused by the photo-induced production of singlet oxygen (Type II process) and other reactive oxygen species and radicals (Type I mechanism) [97]. Due to the size of its bandgap, TiO₂ is a typical semiconductor photo-catalyst that can only be activated by UV light [98]. CQDs also used to treat deep-seated tumors like colon and bladder cancer [99]. CQDs combined with conventional photosensitizer (protoporphyrin IX). The up-conversions activated the photosensitizer without causing any negative side effects thanks to FRET. Fluorescence emission is produced by excitation of the CQDs at 800 nm. In comparison to clinical photodynamic treatment, the excitation light at 800 nm from the phototherapeutic window may penetrate four times deeper into human tissue than clinical photodynamic therapy [100].

CQDs significantly used for radiotherapy as well as phototherapy. Silver-coated PEG-CQDs (C-Ag-PEG CQDs) were employed as radiosensitizers in Du145 cells. To enhance their therapeutic selectivity, low-energy X-ray exposure generated electrons that damaged cancer cells around the CQDs but did not affect healthy cells [101]. bPEI-coated CQDs efficiently used as nanocarriers for gene delivery to the retinal cells due to high number of amino groups on their surfaces. The bPEI was successfully delivered into cells without any issues. Because of its high positive charge density and proton-sponge activity, biotin gathers and condenses genetic material to form toroidal complexes that cells can easily uptake through endocytosis [102].

Zheng & coworkers used chemical coupling to attach an anticancer Pt⁴⁺-based pro-drug – oxidized oxaliplatin (Oxa(VI)-COOH) to CQD surfaces [103]. When exposed to light, the quinoline molecules on the CQDs' surfaces serve as release triggers, allowing researchers to monitor the dispersion of drug-CQDs conjugates. In addition to pH-triggered drug release, several mechanisms for the

release of medicines have been investigated [104]. Folic acid was used as a navigation molecule on the CQDs surface because of its association with almost all types of cancer cells. CQDs were used to evaluate the loading capacity of DOX, and the release kinetics were found to follow first order kinetics at a physiological pH, providing for a good release profile.

Interestingly, the DOX-loaded CQDs killed cancer cells more quickly and were less harmful to normal cells than free DOX because of the better targeting ability of the folic acid molecule [105].

4. Conclusion

In conclusion, CQDs represent a fascinating class of nano-sized carbon-based materials that have garnered significant scientific interest in recent decades. Their distinct qualities, including optical, electrical, and chemical characteristics, make them ideal candidates for a variety of applications. The controllable fluorescence and biocompatibility of CQDs have led to their utilization in domains such as bioimaging and sensors, highlighting their promise for medical and technological advancements. Furthermore, the study of CQDs in energy-related applications, such as photocatalysis and solar cells, demonstrates their potential importance in sustainable technology. As new synthesis methods are discovered, the multifarious nature of CQDs presents them as exciting and valuable materials with far-reaching ramifications in a various scientific technological field. This comprehensive review highlights the synthesis, properties, and applications of CQDs, which will serve as an informative foundation for future research.

References

- [1] P. Kumar, S. Dua, R. Kaur, M. Kumar, G. Bhatt, A review on advancements in carbon quantum dots and their application in photovoltaics, *RSC Advances* 12 (8), 4714-4759, 2022.
- [2] M. Farshbaf, S. Davaran, F. Rahimi, N. Annabi, R. Salehi, A. Akbarzadeh, Carbon quantum dots: recent progresses on synthesis, surface modification and applications, *Artificial Cells, Nanomedicine, and Biotechnology* 46 (7), 1331-1348, 2018.
- [3] M. Pourmadadi, E. Rahmani, M. Rajabzadeh-Khosroshahi, A. Samadi, R. Behzadmehr, A. Rahdar, L. F. R. Ferreira, Properties and application of carbon quantum dots (CQDs) in biosensors for disease detection: A comprehensive review, *J Drug Deliv Sci Tec* 80 104156, 2023.
- [4] T. J. Pillar-Little, N. Wanninayake, L. Nease, D. K. Heidary, E. C. Glazer, D. Y. Kim, Superior photodynamic effect of carbon quantum dots through both type I and type II pathways: Detailed comparison study of top-down-synthesized and bottom-up-synthesized carbon quantum dots, *Carbon* 140 616-623, 2018.
- [5] A. Tadesse, D. Rama Devi, M. Hagos, G. Battu, K. Basavaiah, Facile green synthesis of fluorescent carbon quantum dots from

- citrus lemon juice for live cell imaging, *Asian Journal of Nanoscience and Materials* 1 (1), 36-46, 2018.
- [6] Y. Guo, Z. Wang, H. Shao, X. Jiang, Hydrothermal synthesis of highly fluorescent carbon nanoparticles from sodium citrate and their use for the detection of mercury ions, *Carbon* 52 583-589, 2013.
- [7] K. Dimos, Carbon Quantum Dots: Surface Passivation and Functionalization, *Curr Org Chem* 20 (6), 682-695, 2016.
- [8] M. Bangal, S. Ashtaputer, S. Marathe, A. Ethiraj, N. Hebalkar, S. W. Gosavi, J. Urban, S. K. Kulkarni, Semiconductor Nanoparticles, in: D. R. S. Somayajulu, K. P. Lieb (Eds.) *IWNMS 2004*, Springer Berlin Heidelberg, Berlin, Heidelberg, 2005, pp. 81-94.
- [9] W. Zhou, J. J. Coleman, Semiconductor quantum dots, *Curr Opin Solid St M* 20 (6), 352-360, 2016.
- [10] A. M. Wagner, J. M. Knipe, G. Orive, N. A. Peppas, Quantum dots in biomedical applications, *Acta Biomater* 94 44-63, 2019.
- [11] A. Gour, S. Ramteke, N. K. Jain, Pharmaceutical Applications of Quantum Dots, *AAPS Pharm Sci Tech* 22 (7), 233, 2021.
- [12] H. Li, Z. Kang, Y. Liu, S.-T. Lee, Carbon nanodots: synthesis, properties and applications, *J Mater Chem* 22 (46), 24230-24253, 2012.
- [13] S. Y. Lim, W. Shen, Z. Gao, Carbon quantum dots and their applications, *Chem Soc Rev* 44 (1), 362-381, 2015.
- [14] K. J. Mintz, Y. Zhou, R. M. Leblanc, Recent development of carbon quantum dots regarding their optical properties, photoluminescence mechanism, and core structure, *Nanoscale* 11 (11), 4634-4652, 2019.
- [15] P. Anilkumar, X. Wang, L. Cao, S. Sahu, J.-H. Liu, P. Wang, K. Korch, K. N. Tackett II, A. Parenzan, Y.-P. Sun, Toward quantitatively fluorescent carbon-based "quantum" dots, *Nanoscale* 3 (5), 2023-2027, 2011.
- [16] P. Namdari, B. Negahdari, A. Eatemadi, Synthesis, properties and biomedical applications of carbon-based quantum dots: An updated review, *Biomed Pharmacother* 87 209-222, 2017.
- [17] A. S. Barnard, S. P. Russo, I. K. Snook, Size dependent phase stability of carbon nanoparticles: Nanodiamond versus fullerenes, *J Chem Phys* 118 (11), 5094-5097, 2003.
- [18] J. M. Klostranec, W. C. W. Chan, Quantum Dots in Biological and Biomedical Research: Recent Progress and Present Challenges, *Adv Mater* 18 (15), 1953-1964, 2006.
- [19] S. C. Ray, A. Saha, N. R. Jana, R. Sarkar, Fluorescent Carbon Nanoparticles: Synthesis, Characterization, and Bioimaging Application, *J Phys Chem C* 113 (43), 18546-18551, 2009.
- [20] X. Wang, K. Qu, B. Xu, J. Ren, X. Qu, Multicolor luminescent carbon nanoparticles: Synthesis, supramolecular assembly with porphyrin, intrinsic peroxidase-like catalytic activity and applications, *Nano Research* 4 (9), 908-920, 2011.
- [21] P. Koutsogiannis, E. Thomou, H. Stamatis, D. Gournis, P. Rudolf, Advances in fluorescent carbon dots for biomedical applications, *Advances in Physics: X* 5 (1), 1758592, 2020.
- [22] D. L. Zhao, T.-S. Chung, Applications of carbon quantum dots (CQDs) in membrane technologies: A review, *Water Research* 147 43-49, 2018.
- [23] Y. Zhang, D. Petibone, Y. Xu, M. Mahmood, A. Karmakar, D. Casciano, S. Ali, A. S. Biris, Toxicity and efficacy of carbon nanotubes and graphene: the utility of carbon-based nanoparticles in nanomedicine, *Drug metabolism reviews* 46 (2), 232-46, 2014.
- [24] A. Truskewycz, S. Beker, A. S. Ball, I. Cole, Photoluminescence measurements of carbon quantum dots within three-dimensional hydrogel matrices using a high throughput 96 well plate method, *MethodsX* 6 437-441, 2019.
- [25] X. Xu, R. Ray, Y. Gu, H. J. Ploehn, L. Gearheart, K. Raker, W. A. Scrivens, Electrophoretic analysis and purification of fluorescent single-walled carbon nanotube fragments, *J Am Chem Soc* 126 (40), 12736-7, 2004.
- [26] P. K. Yadav, S. Chandra, V. Kumar, D. Kumar, S. H. Hasan, Carbon Quantum Dots: Synthesis, Structure, Properties, and Catalytic Applications for Organic Synthesis, *Catalysts* 13 (2), 422, 2023.
- [27] X. Liu, J. Hao, J. Liu, H. Tao, Green synthesis of carbon quantum dots from lignite coal and the application in Fe³⁺ detection, *IOP Conference Series: Earth and Environmental Science* 113 (1), 012063, 2018.
- [28] R. Wang, K.-Q. Lu, Z.-R. Tang, Y.-J. Xu, Recent progress in carbon quantum dots: synthesis, properties and applications in photocatalysis, *J Mater Chem A* 5 (8), 3717-3734, 2017.
- [29] R. Das, R. Bandyopadhyay, P. Pramanik, Carbon quantum dots from natural resource: A review, *Mater Today Chem* 8 96-109, 2018.
- [30] M. J. Molaei, Principles, mechanisms, and application of carbon quantum dots in sensors: a review, *Anal Method* 12 (10), 1266-1287, 2020.
- [31] T. Takagahara, K. Takeda, Theory of the quantum confinement effect on excitons in quantum dots of indirect-gap materials, *Physical Review B* 46 (23), 15578-15581, 1992.
- [32] H.-L. Yang, L.-F. Bai, Z.-R. Geng, H. Chen, L.-T. Xu, Y.-C. Xie, D.-J. Wang, H.-W. Gu, X.-M. Wang, Carbon quantum dots: Preparation, optical properties, and biomedical applications, *Mater Today Adv* 18 100376, 2023.
- [33] T. Yuan, T. Meng, P. He, Y. Shi, Y. Li, X. Li, L. Fan, S. Yang, Carbon quantum dots: an emerging material for optoelectronic applications, *J Mater Chem C* 7 (23), 6820-6835, 2019.
- [34] A. M. Smith, H. Duan, M. N. Rhyner, G. Ruan, S. Nie, A systematic examination of surface coatings on the optical and chemical properties of semiconductor quantum dots, *Physical chemistry chemical physics : PCCP* 8 (33), 3895-903, 2006.
- [35] D. Ozyurt, M. A. Kobaisi, R. K. Hocking, B. Fox, Properties, synthesis, and applications of carbon dots: A review, *Carbon Trends* 12 100276, 2023.
- [36] Z. Liu, H. Zou, N. Wang, T. Yang, Z. Peng, J. Wang, N. Li, C. Huang, Photoluminescence of carbon quantum dots: coarsely adjusted by quantum confinement effects and finely by surface trap states, *Sci China Chem* 61 (4), 490-496, 2018.
- [37] Y. K. Chang, H. H. Hsieh, W. F. Pong, M. H. Tsai, F. Z. Chien, P. K. Tseng, L. C. Chen, T. Y. Wang, K. H. Chen, D. M. Bhusari, J. R. Yang, S. T. Lin, Quantum Confinement Effect in Diamond Nanocrystals Studied by X-Ray-Absorption Spectroscopy, *Phys Rev Lett* 82 (26), 5377-5380, 1999.
- [38] O. D. Neikov, N. A. Yefimov, Chapter 9 - Nanopowders, in: O. D. Neikov, S. S. Naboychenko, N. A. Yefimov (Eds.), *Handbook of Non-Ferrous Metal Powders (Second Edition)*, Elsevier, Oxford, pp. 271-311, 2019.
- [39] M. Yuan, R. Zhong, H. Gao, W. Li, X. Yun, J. Liu, X. Zhao, G. Zhao, F. Zhang, One-step, green, and economic synthesis of water-soluble photoluminescent carbon dots by hydrothermal treatment of wheat straw, and their bio-applications in labeling, imaging, and sensing, *Appl Surf Sci* 355 1136-1144, 2015.
- [40] D. Wang, L. Zhu, C. McCleese, C. Burda, J.-F. Chen, L. Dai, Fluorescent carbon dots from milk by microwave cooking, *RSC Advances* 6 (47), 41516-41521, 2016.
- [41] S. Borna, R. E. Sabzi, S. Pirsia, Synthesis of carbon quantum dots from apple juice and graphite: investigation of fluorescence and structural properties and use as an electrochemical sensor for measuring Letrozole, *J Mater Sci: Materials in Electronics* 32 (8), 10866-10879, 2021.
- [42] X. Xu, K. Zhang, L. Zhao, C. Li, W. Bu, Y. Shen, Z. Gu, B. Chang, C. Zheng, C. Lin, H. Sun, B. Yang, Aspirin-Based Carbon Dots, a Good Biocompatibility of Material Applied for Bioimaging and Anti-Inflammation, *ACS Appl Mater Inter* 8 (48), 32706-32716, 2016.
- [43] L. Wang, W. Li, B. Wu, Z. Li, S. Wang, Y. Liu, D. Pan, M. Wu, Facile synthesis of fluorescent graphene quantum dots from

- coffee grounds for bioimaging and sensing, *Chem Eng J* 300 75-82, 2016.
- [44] Y. Zhao, Y. Zhang, X. Liu, H. Kong, Y. Wang, G. Qin, P. Cao, X. Song, X. Yan, Q. Wang, H. Qu, Novel carbon quantum dots from egg yolk oil and their haemostatic effects, *Scientific Reports* 7 (1), 4452, 2017.
- [45] Y. Liu, Q. Zhou, J. Li, M. Lei, X. Yan, Selective and sensitive chemosensor for lead ions using fluorescent carbon dots prepared from chocolate by one-step hydrothermal method, *Sensor Actuator B: Chem* 237 597-604, 2016.
- [46] F. Limosani, E. M. Bauer, Top-Down N-Doped Carbon Quantum Dots for Multiple Purposes: Heavy Metal Detection and Intracellular Fluorescence, 11 (9), 2021.
- [47] L. Cao, X. Wang, M. J. Mezzani, F. Lu, H. Wang, P. G. Luo, Y. Lin, B. A. Harruff, L. M. Veca, D. Murray, S.-Y. Xie, Y.-P. Sun, Carbon Dots for Multiphoton Bioimaging, *J Am Chem Soc* 129 (37), 11318-11319, 2007.
- [48] L. Zheng, Y. Chi, Y. Dong, J. Lin, B. Wang, Electrochemiluminescence of Water-Soluble Carbon Nanocrystals Released Electrochemically from Graphite, *J Am Chem Soc* 131 (13), 4564-4565, 2009.
- [49] A. Khayal, V. Dawane, M. A. Amin, V. Tirth, V. K. Yadav, A. Algahtani, S. H. Khan, S. Islam, K. K. Yadav, B.-H. Jeon, Advances in the Methods for the Synthesis of Carbon Dots and Their Emerging Applications, *Polymers* 13 (18), 3190, 2021.
- [50] [50] Z.-A. Qiao, Y. Wang, Y. Gao, H. Li, T. Dai, Y. Liu, Q. Huo, Commercially activated carbon as the source for producing multicolor photoluminescent carbon dots by chemical oxidation, *Chem Commun* 46 (46), 8812-8814, 2010.
- [51] H. B. Ahmed, H. E. Emam, Environmentally exploitable biocide/fluorescent metal marker carbon quantum dots, *RSC Adv* 10 (70), 42916-42929, 2020.
- [52] Y.-P. Sun, X. Wang, F. Lu, L. Cao, M. J. Mezzani, P. G. Luo, L. Gu, L. M. Veca, Doped Carbon Nanoparticles as a New Platform for Highly Photoluminescent Dots, *J Phys Chem C* 112 (47), 18295-18298, 2008.
- [53] C. H. Lei, X. E. Zhao, S. L. Jiao, L. He, Y. Li, S. Y. Zhu, J. M. You, A turn-on fluorescent sensor for the detection of melamine based on the anti-quenching ability of Hg²⁺ to carbon nanodots, *Anal Method* 8 (22), 4438-4444, 2016.
- [54] A. B. Bourlinos, A. Stassinopoulos, D. Anglos, R. Zboril, V. Georgakilas, E. P. Giannelis, Photoluminescent Carbogenic Dots, *Chem Mater* 20 (14), 4539-4541, 2008.
- [55] M. J. Krysmann, A. Kellarakis, P. Dallas, E. P. Giannelis, Formation Mechanism of Carbogenic Nanoparticles with Dual Photoluminescence Emission, *J Am Chem Soc* 134 (2), 747-750, 2012.
- [56] X. He, H. Li, Y. Liu, H. Huang, Z. Kang, S.-T. Lee, Water soluble carbon nanoparticles: Hydrothermal synthesis and excellent photoluminescence properties, *Colloid Surface B* 87 (2), 326-332, 2011.
- [57] C. Zhu, J. Zhai, S. Dong, Bifunctional fluorescent carbon nanodots: green synthesis via soy milk and application as metal-free electrocatalysts for oxygen reduction, *Chem Commun* 48 (75), 9367-9369, 2012.
- [58] H. Li, R. Liu, W. Kong, J. Liu, Y. Liu, L. Zhou, X. Zhang, S.-T. Lee, Z. Kang, Carbon quantum dots with photo-generated proton property as efficient visible light controlled acid catalyst, *Nanoscale* 6 (2), 867-873, 2014.
- [59] H. Li, X. He, Y. Liu, H. Huang, S. Lian, S.-T. Lee, Z. Kang, One-step ultrasonic synthesis of water-soluble carbon nanoparticles with excellent photoluminescent properties, *Carbon* 49 (2), 605-609, 2011.
- [60] Z. Ma, H. Ming, H. Huang, Y. Liu, Z. Kang, One-step ultrasonic synthesis of fluorescent N-doped carbon dots from glucose and their visible-light sensitive photocatalytic ability, *New J Chem* 36 (4), 861-864, 2012.
- [61] R. Liu, D. Wu, S. Liu, K. Koynov, W. Knoll, Q. Li, An Aqueous Route to Multicolor Photoluminescent Carbon Dots Using Silica Spheres as Carriers, *Angew Chem Int Edit* 48 (25), 4598-4601, 2009.
- [62] J. Zong, Y. Zhu, X. Yang, J. Shen, C. Li, Synthesis of photoluminescent carbogenic dots using mesoporous silica spheres as nanoreactors, *Chem Commun* 47 (2), 764-766, 2011.
- [63] L. Lu, R. Helgeson, R. M. Jones, D. McBranch, D. Whitten, Superquenching in Cyanine Pendant Poly(L-lysine) Dyes: Dependence on Molecular Weight, Solvent, and Aggregation, *J Am Chem Soc* 124 (3), 483-488, 2002.
- [64] F. Yan, Y. Zou, M. Wang, X. Mu, N. Yang, L. Chen, Highly photoluminescent carbon dots-based fluorescent chemosensors for sensitive and selective detection of mercury ions and application of imaging in living cells, *Sensor Actuator B-Chem* 192 488-495, 2014.
- [65] S. Zhang, Q. Wang, G. Tian, H. Ge, A fluorescent turn-off/on method for detection of Cu²⁺ and oxalate using carbon dots as fluorescent probes in aqueous solution, *Mater Lett* 115 233-236, 2014.
- [66] Y.-L. Zhang, L. Wang, H.-C. Zhang, Y. Liu, H.-Y. Wang, Z.-H. Kang, S.-T. Lee, Graphitic carbon quantum dots as a fluorescent sensing platform for highly efficient detection of Fe³⁺ ions, *RSC Advances* 3 (11), 3733-3738, 2013.
- [67] M. Zheng, Z. Xie, D. Qu, D. Li, P. Du, X. Jing, Z. Sun, On-Off-On Fluorescent Carbon Dot Nanosensor for Recognition of Chromium(VI) and Ascorbic Acid Based on the Inner Filter Effect, *ACS Appl Mater Inter* 5 (24), 13242-13247, 2013.
- [68] Z. Qian, J. Ma, X. Shan, H. Feng, L. Shao, J. Chen, Highly Luminescent N-Doped Carbon Quantum Dots as an Effective Multifunctional Fluorescence Sensing Platform, *Chem – A Eur J* 20 (8), 2254-2263, 2014.
- [69] J.-M. Liu, L.-p. Lin, X.-X. Wang, L. Jiao, M.-L. Cui, S.-L. Jiang, W.-L. Cai, L.-H. Zhang, Z.-Y. Zheng, Zr(H₂O)₂EDTA modulated luminescent carbon dots as fluorescent probes for fluoride detection, *Analyst* 138 (1), 278-283, 2013.
- [70] X. Lin, G. Gao, L. Zheng, Y. Chi, G. Chen, Encapsulation of Strongly Fluorescent Carbon Quantum Dots in Metal-Organic Frameworks for Enhancing Chemical Sensing, *Anal Chem* 86 (2), 1223-1228, 2014.
- [71] X. Hou, F. Zeng, F. Du, S. Wu, Carbon-dot-based fluorescent turn-on sensor for selectively detecting sulfide anions in totally aqueous media and imaging inside live cells, *Nanotechnology* 24 (33), 335502, 2013.
- [72] S.-L. Hu, K.-Y. Niu, J. Sun, J. Yang, N.-Q. Zhao, X.-W. Du, One-step synthesis of fluorescent carbon nanoparticles by laser irradiation, *J Mater Chem* 19 (4), 484-488, 2009.
- [73] B. Yin, J. Deng, X. Peng, Q. Long, J. Zhao, Q. Lu, Q. Chen, H. Li, H. Tang, Y. Zhang, S. Yao, Green synthesis of carbon dots with down- and up-conversion fluorescent properties for sensitive detection of hypochlorite with a dual-readout assay, *Analyst* 138 (21), 6551-6557, 2013.
- [74] Z. Yang, Z. Li, M. Xu, Y. Ma, J. Zhang, Y. Su, F. Gao, H. Wei, L. Zhang, Controllable Synthesis of Fluorescent Carbon Dots and Their Detection Application as Nanoprobes, *Nano-Micro Letters* 5 (4), 247-259, 2013.
- [75] Y. Zhou, Z.-b. Qu, Y. Zeng, T. Zhou, G. Shi, A novel composite of graphene quantum dots and molecularly imprinted polymer for fluorescent detection of parantrophenol, *Biosens Bioelectron* 52 317-323, 2014.
- [76] C. Ji, Y. Zhou, R. M. Leblanc, Z. Peng, Recent Developments of Carbon Dots in Biosensing: A Review, *ACS Sensors* 5 (9), 2724-2741, 2020.
- [77] X. Terzapulo, A. Kassenova, R. Bukasov, Immunoassays: Analytical and Clinical Performance, Challenges, and Perspectives of SERS Detection in Comparison with Fluorescent Spectroscopic Detection, *Int J mol sci* 25 (4), 1-33, 2024.

- [78] Y. Yu, C. Li, C. Chen, H. Huang, C. Liang, Y. Lou, X.-B. Chen, Z. Shi, S. Feng, Saccharomyces-derived carbon dots for biosensing pH and vitamin B 12, *Talanta* 195 117-126, 2019.
- [79] Y. Dai, Z. Liu, Y. Bai, Z. Chen, J. Qin, F. Feng, A novel highly fluorescent S, N, O co-doped carbon dots for biosensing and bioimaging of copper ions in live cells, *RSC Advances* 8 (73), 42246-42252, 2018.
- [80] H. Shi, J. Wei, L. Qiang, X. Chen, X. Meng, Fluorescent carbon dots for biolmaging and biosensing applications, *J biomed nanotechnol* 10 (10), 2677-99, 2014.
- [81] T. Sarkar, H. B. Bohidar, P. R. Solanki, Carbon dots-modified chitosan based electrochemical biosensing platform for detection of vitamin D, *Int j biol macromol* 109 687-697, 2018.
- [82] M. Pan, Z. Xu, Q. Jiang, J. Feng, J. Sun, F. Wang, Interfacial engineering of carbon dots with benzenediboric acid for fluorescent biosensing, *1 (2)*, 765-771, 2019.
- [83] Q. Zhang, R. Shi, Q. Li, T. Maimaiti, S. Lan, P. Ouyang, B. Ouyang, Y. Bai, B. Yu, S.-T. Yang, Low toxicity of fluorescent carbon quantum dots to white rot fungus *Phanerochaete chrysosporium*, *J Environ Chem Eng* 9 (1), 104633, 2021.
- [84] V. Sharma, P. Tiwari, S. M. Mobin, Sustainable carbon-dots: recent advances in green carbon dots for sensing and bioimaging, *J Mater Chem B* 5 (45), 8904-8924, 2017.
- [85] F. Du, Y. Ming, F. Zeng, C. Yu, S. Wu, A low cytotoxic and ratiometric fluorescent nanosensor based on carbon-dots for intracellular pH sensing and mapping, *Nanotechnology* 24 (36), 365101, 2013.
- [86] S. Barman, M. Sadhukhan, Facile bulk production of highly blue fluorescent graphitic carbon nitride quantum dots and their application as highly selective and sensitive sensors for the detection of mercuric and iodide ions in aqueous media, *J Mater Chem* 22 (41), 21832-21837, 2012.
- [87] G. Sahay, D. Y. Alakhova, A. V. Kabanov, Endocytosis of nanomedicines, *Journal of controlled release: official journal of the Controlled Release Society* 145 (3), 182-95, 2010.
- [88] L. W. Zhang, N. A. Monteiro-Riviere, Mechanisms of Quantum Dot Nanoparticle Cellular Uptake, *Toxicol Sci* 110 (1), 138-155, 2009.
- [89] X. T. Zheng, A. Ananthanarayanan, K. Q. Luo, P. Chen, Glowing Graphene Quantum Dots and Carbon Dots: Properties, Syntheses, and Biological Applications, *Small* 11 (14), 1620-1636, 2015.
- [90] T. S, R. S. D, Green synthesis of highly fluorescent carbon quantum dots from sugarcane bagasse pulp, *Appl Surf Sci* 390 435-443, 2016.
- [91] K. Qu, J. Wang, J. Ren, X. Qu, Carbon Dots Prepared by Hydrothermal Treatment of Dopamine as an Effective Fluorescent Sensing Platform for the Label-Free Detection of Iron(III) Ions and Dopamine, *Chem – A Eur J* 19 (22), 7243-7249, 2013.
- [92] A. Hamidu, W. G. Pitt, Recent Breakthroughs in Using Quantum Dots for Cancer Imaging and Drug Delivery Purposes, *Nanomater (Basel, Switzerland)* 13 (18), 1-35, 2023.
- [93] P. Devi, S. Saini, K.-H. Kim, The advanced role of carbon quantum dots in nanomedical applications, *Biosens Bioelectron* 141 111158, 2019.
- [94] S. Chaudhary, A. Umar, K. Bhasin, S. Singh, Applications of Carbon Dots in Nanomedicine, *J Biomed Nanotechnol* 13, 591-637 13 (6), 591-637, 2017.
- [95] K. Soumya, N. More, M. Choppadandi, D. A. Aishwarya, G. Singh, G. Kapusetti, A comprehensive review on carbon quantum dots as an effective photosensitizer and drug delivery system for cancer treatment, *Biomed Technol* 4 11-20, 2023.
- [96] H. Wang, S. Yang, L. Chen, Y. Li, P. He, G. Wang, H. Dong, P. Ma, G. Ding, Tumor diagnosis using carbon-based quantum dots: Detection based on the hallmarks of cancer, *Bioact mater* 33 174-222, 2024.
- [97] K. Naik, S. Chaudhary, L. Ye, A. S. Parmar, A Strategic Review on Carbon Quantum Dots for Cancer-Diagnostics and Treatment, *Front Bioeng Biotech* 10 2022.
- [98] V. Etacheri, C. Di Valentin, J. Schneider, D. Bahnemann, S. C. Pillai, Visible-light activation of TiO₂ photocatalysts: Advances in theory and experiments, *J Photoch Photobio C* 25 1-29, 2015.
- [99] S. Masha, O. S. Oluwafemi, Synthesis of blue and green emitting carbon-based quantum dots (CBQDs) and their cell viability against colon and bladder cancer cell lines, *Mater Lett* 283 128790, 2021.
- [100] C. Fowley, N. Nomikou, A. P. McHale, B. McCaughan, J. F. Callan, Extending the tissue penetration capability of conventional photosensitisers: a carbon quantum dot-protoporphyrin IX conjugate for use in two-photon excited photodynamic therapy, *Chem commun (Cambridge, England)* 49 (79), 8934-6, 2013.
- [101] S. Bayda, E. Amadio, Carbon dots for cancer nanomedicine: a bright future, *Nanoscale Adv.* 3 (18), 5183-5221, 2021.
- [102] M. R. Biswal, S. Bhatia, Carbon Dot Nanoparticles: Exploring the Potential Use for Gene Delivery in Ophthalmic Diseases, *Nanomaterials (Basel, Switzerland)* 11 (4), 2021.
- [103] D. Tolan, V. Gandin, L. Morrison, A. El-Nahas, C. Marzano, D. Montagner, A. Erxleben, Oxidative Stress Induced by Pt(IV) Prodrugs Based on the Cisplatin Scaffold and Indole Carboxylic Acids in Axial Position, *Sci Rep.* 6 29367, 2016.
- [104] A. Ray Chowdhuri, S. Tripathy, C. Haldar, S. Roy, S. K. Sahu, Single step synthesis of carbon dot embedded chitosan nanoparticles for cell imaging and hydrophobic drug delivery, *J Mater Chem B* 3 (47), 9122-9131, 2015.
- [105] X. Li, K. Vinothini, T. Ramesh, M. Rajan, Combined photodynamic-chemotherapy investigation of cancer cells using carbon quantum dot-based drug carrier system, *Drug delivery* 27 (1), 791-804, 2020.