International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

© International Scientific Organization

# Advancements in Nanomedicine: Carbon Quantum Dots for Drug Delivery

***Harinath Sankar, Sangeetha. S*, N. Damodharan***

[1]*Postgraduate, Department of Pharmaceutics, SRM College of Pharmacy, SRM Institution of Science and Technology, Kattankulathur, Chengalpattu, India*

[2]*Professor, Department of Pharmaceutics, SRM College of Pharmacy, SRM Institution of Science and Technology, Kattankulathur, Chengalpattu, India*

[3]*Professor & Head, Department of Pharmaceutics, SRM College of Pharmacy, SRM Institution of Science and Technology, Kattankulathur, Chengalpattu, India*

**Abstract**

Carbon quantum dots (CQDs) are a unique family of fluorescent carbon nanoparticles and nanomaterials with remarkable properties, including feasible methods of manufacture, minimal toxicity, soluble in water, biological compatibility, and ecological friendliness. Over the past 10 years, these have garnered attention from all over the world and have been used in various sectors. The development of bio analysis and biosensors has recently advanced, and we have evaluated such developments in this paper with an emphasis on their synthesis techniques. CQDs are used in biomedicine for a variety of purposes, such as fluorescent tracers, drug carriers, and drug release regulators, thanks to their nontoxicity and biocompatibility. As an example, CQDs are used as photosensitizers in photodynamic treatment to kill cancer cells. Solvents containing CQDs can be injected into an active body to produce images in vivo for detection or diagnosis. Carbon quantum dots are generating a lot of research because of their strong and controlled fluorescence emission properties. These characteristics make applications in biology, catalysis, and sensing possible.

**Keywords:** CQDs, Chemotherapy, Cancer, fluorescence, Bio-imaging, Bio-sensing, Emission, Doxorubicin.

**Full-length article** **Corresponding Author*, e-mail: *sangeets2@srmist.edu.in* Doi # https://doi.org/10.62877/110-IJCBS-24-25-19-110

## 1. Introduction

Carbon quantum dots (CQDs), often referred to as carbon dots (CDs or C-dots) or carbon nanodots (CNDs), are a brand-new class of carbon nanomaterials with noticeable fluorescence composed of discrete, quasi-spherical carbon nanoparticles with ultrafine diameters under 10 nm [1-4]. Using gel electrophoresis, CQDs were accidentally found while purifying single-walled carbon nanotubes [5]. While synthesizing carbon nanomaterials of various sizes, he gave the substance the moniker CQDs [6-8]. Semiconductor quantum dots have considerable problems since the heavy metals utilized in their manufacture are extremely poisonous. Clinical research may be impossible to conduct because heavy metals are known to be exceedingly hazardous, even in low quantities. CQDs were designed to replace semiconductor quantum dots due to their low toxicity, biocompatibility, low cost, chemical inertness, and similar fluorescence properties [7]. The hazardous heavy metals used in the production of semiconductor quantum dots cause several issues. Because heavy metals are known to be extremely dangerous, even in small amounts, clinical studies may not be practical.

Due to their comparable fluorescence characteristics, low toxicity, biocompatibility, affordability, and chemical inertness, CQDs were developed to replace semiconductor quantum dots [9]. Compared to other carbon-based nanoparticles, CQDs are currently seen as a particularly useful asset of nanotechnology. Aside from CQDs, carbon nano-lights are another name for them because of their intense luminous properties [6]. CQDs have high amounts of epoxy, hydroxyl, and carboxyl groups at their surfaces and basal planes. The O concentration might be between 5% and 50% of the total weight, depending on the synthesis method [5]. Since then, CQDs have been the subject of considerable and expanding research in a variety of domains, such as bio-sensing, bio-imaging, drug delivery, photo catalysis, photovoltaic devices, and optoelectronics [1]. Currently, significant advancements have been made in the synthesis

and advantages of CQDs. Top-down and bottom-up synthesis of CQDs will be covered. Although CQDs' properties, application, and drug delivery of carbon quantum dots (CQDs) [10].

## 2. Synthesis of Carbon Quantum Dots (CQDs)

Since the discovery of carbon quantum dots (CQDs), a wide range of efficient, affordable, large-scale, and size-controlled manufacturing methods have been developed. The two primary types of methodologies utilized for the synthesis of CQDs are top-down and bottom-up techniques (Figure 1). The process of making CQDs is straightforward, but various challenges must overcome, including the aggregation of nanomaterials, the control of size and homogeneity, and the tuning of surface properties.

### *2.1. Top-Down Synthesis*

The top-down approach, which mostly uses physical techniques like arc discharge, electrochemical oxidation, chemical oxidation, laser ablation, etc., produces carbon dots by fracturing or pealing larger carbon material structures. The top-down approach has many advantages and is ideal for the microsystems industry, but it also has some disadvantages, such as the inability to produce pure nanomaterials from the substantial carbon precursor, the cost of distillation, and the inability to precisely manage the CQDs' shape and size distribution [1].

#### *2.1.1. Laser ablation*

Sun and colleagues first presented a laser ablation strategy in 2006. In this method, CQDs are produced by exposing a targeted surface to excessive energy from a laser pulse [6]. Pulsed laser ablation (PLA), a novel and promising technique, has been used to prepare nanomaterials, particularly CQDs, because of its ease of use and quick processing time. It is possible to directly cut a target into micro particles or nanoparticles without leaving any residues when using a laser to ablate it [11]. High-purity nanoparticles can be prepared in a liquid solution using the quick, easy, and environmentally friendly laser ablation process [12]. Fluorescent CQDs were created using nanoscale carbon as the carbon source and an organic solvent as the liquid medium. This procedure involved dissolving 0.02 g of nanoscale carbon material in 50 mL of an organic solvent, such as water, acetone, or ethanol. 4 mL of the produced suspension was transported to a cell after ultra-sonication, where it was subjected to 532 nm laser radiation. The mixture was then centrifuged at 6000 rpm to separate the supernatant, which contains CQDs, from the solution [13-14]. The created CQDs exhibited photoluminescence (PL) emission at two wavelengths. Later, Ren's team improved the preparation by developing an ultrafast method for producing homogenous CQDs using dual-beam pulsed laser ablation.

#### *2.1.2. Arc discharge*

The initial discovery of fluorescent carbon quantum dots was made by accident while using the arch discharge approach to separate and purify a single-wall carbon nanotube. Nitric acid was employed in this procedure as an oxidizing agent to oxidize arch ash, resulting in the formation of various surface functional groups and an increase in water solubility. At an excitation wavelength of 366 nm, the QYs were 1.66% [15]. Another experiment proved that hydrophilic carboxyl groups were linked to the surface of CQDs. Different-sized carbon particles are created throughout the discharge process (Figure 3). The CQDs produced by this process have a wide range of particle sizes and are extremely water-soluble [16-17]. CQDs are produced by arc discharge in water, with up-conversion fluorescence and carbon by-products from arc synthesis [18-19].

#### *2.1.3. Chemical oxidation*

One of the techniques for creating CQDs is chemical oxidation, which uses powerful oxidants like nitric acid, sulfuric acid, and hydrogen peroxide to treat carbon compounds. With its ease of use, speed, and great repeatability, this method makes it possible to construct CQDs on a large scale. Using chemical oxidation, one may make fluorescent CQDs with QYs between 0.8, 1.8%, and diameters under 2 nm [20]. The study's customizable fluorescent CQDs offer a fresh method for creating multicolor luminous CQDs. By heating and refluxing citric acid and polyethyleneimine (PEI), we produced PEI-CQDs with a size variation of 1–7 nm that were used for the inner filter effect (IFE)-based detection of Cu2+ and H2S [21]. The benefit of the refluxing process is the ability to produce CQDs with a uniform particle size distribution and a longer emission wavelength without arduous passivation and purification stages. Meng and his coworkers developed many CQDs. Size: 3-5 nm, quantum yield: 5.4–10.1%, produced by chemically combining coal pitch powder, formic acid, and H2O2 without the use of heat or energy [22]. The creation of N-CQDs using ammonia and petroleum coke (Figure 4) The petroleum coke was first oxidized using H2SO4 and HNO3 and then functionalized using hydrothermal ammonia treatment.

During the hydrothermal process in ammonia, they noticed that the QY and fluorescence eternity of CQDs significantly increased from 8.7 to 15.8% and 3.86 to 6.11 nm, respectively. Both CQDs and N-CQDs had homogenous particle distributions, strong luminescence, and great sensitivity to pH between 2.0 and 12.0. They were also both soluble in water. The nitrogen doping and homogenous size variation of CQDs improved the radical interaction and, subsequently, the fluorescence characteristics [23]. The yield of CQDs from this study was 49%, providing a strong base for CQD mass production. By using nitric acid reflux to exfoliate carbon fiber fragments, varying the crystallization duration, and molecular weight screening, it is possible to create CQDs with a range of sizes and levels of surface oxidation [24]. With the reduction of the energy band, the fluorescence emission of the produced CQDs draped the visible spectrum from blue to red, allowing for a variety of multi-color imaging applications. Chemical reagents used in chemical oxidation are extremely caustic and necessitate controlled experimental settings. Therefore, a key research area for the chemical oxidation-based synthesis of CQDs is the quest for a mild oxidant [25].

#### *2.1.4. Electrochemical oxidation*

The redox theory of the efficient functioning electrode in the electrolyte allows the electrochemical method of CQDs at normal temperatures and pressures. Hydrophilic groups (OH, COOH, NH2, etc.) on the surface of CQDs can be altered by directing the elements of the electrolyte and the electrochemical oxidation-reduction process [26-27].

Various excitation wavelengths are frequently required for emission spectra; however, it is very challenging to generate and maintain the white-light spectrum [28]. Joseph and his colleagues successfully produced white-light CQDs with a QY of 11.51%, which they subsequently employed as light-emitting components in illumination systems, by electrochemically reacting two graphite rod electrodes in a battery arrangement [29]. The wide emission spectrum, size and functional group heterogeneity, and white luminescence of CQDs are all contributing factors. When compared to other studies, this one has made significant strides in understanding how fluorescent QY and illuminant color work.

By electrochemical deposition, they obtained N-CQDs and N-CQDs/Cu2O composites, which they then used to detect ASA (a non-steroidal anti-inflammatory medication) in berries in a sensitive and targeted manner [30]. A three-electrode setup comprised of an Ag/AgCl reference electrode, a platinum foil counter electrode, and a graphite electrode-working electrode was used for CQD preparation (Figure 5). To create the electrolyte, ethanol (35 mL), water (8 mL), and NaOH (0.03 g) were combined. The working electrode was placed in a nitrogen atmosphere and subjected to a 5 V potentiostatic voltage for three hours. It was possible to create a homogenous CQD dispersion by centrifuging the excess NaOH precipitate. Based on the mass reduction of the graphite electrode and the amount of remaining dispersion, the starting level of the CQDs (500 g mL-1) was determined. At 4 °C, or if suitable, at ambient temperature, the dispersion was maintained [31].

#### *2.1.5. Ultrasonic synthesis*

Due to the powerful energy of ultrasonic waves, big carbon materials can be broken down into smaller CQDs [32-33]. CQDs were created using an ultrasonic process and the carbon source D-fructose, together with PEG for surface passivation. By having the target analyte present during synthesis, CQDs have a greater chance of acting as fluorescent probes. CQDs were roughly 2.6 nm in size when they were first made, making them acceptable for analysis with a portable fluorospectrometer. The ultrasound technique was used by Dang and his coworkers to create CQDs from an oligomer polyamide resin [34]. The created CQDs displayed low crystallinity, excellent dispersion, and functional group-rich surfaces [35].

### *2.2. Bottom-Up Synthesis*

The bottom-up technique is according to the creation of the nanostructures from organic molecule precursors, as was already indicated [2]. The hydrothermal method, microwave irradiation method, pyrolysis method, combustion method, and template method are the techniques for creating CQDs.

#### *2.2.1. Hydrothermal method*

To create the CQDs through chemical reactions, hydrothermal synthesis is a straightforward, economical, non-toxic, and environmentally benign synthetic approach. In this procedure, after transferring the chemical composition and solvent to an autoclave, a stainless steel chamber lined with Teflon is used to heat solutions above room temperature and pressure [36-37]. By adjusting the temperature and the organic precursors, one may tailor the optical and electrical properties of these CQDs, but one has little control over the CQDs' size [2]. In the straightforward hydrothermal method utilized to make the CQDs, L-lysine functioned as the carbon source and thiourea as the source of sulphur and nitrogen. The mixture was first ultrasonically sonicated for 20 minutes with 20 ml of ultrapure water, 0.5 g of L-lysine, and 0.5 g of thiourea. Then, the mixture put into a 60-ml Teflon-lined hydrothermal autoclave and heated to 220 °C for 5 hours. It gradually became a pale yellow mixture when it reached room temperature. To obtain the supernatant, this yellow mixture was then centrifuged at 10,000 rpm for 10 minutes. This supernatant underwent further filtration using a 0.22-micron syringe filter to create clear CQDs [38]. Hydrothermal synthesis of amorphous CQDs in 2020 using the shells of extinct passion fruit Spheres should have a width of less than 5 nm and 1.8% QY, which are characteristics of CQDs. For the resource utilization of ruined fruit, their study generated cutting-edge concepts and patterns [39]. CQDs are created via hydrothermal means from citric acid and EDA.

#### *2.2.2. Microwave irradiation method*

The microwave irradiation process can be stopped at any point to prevent excessive heating of the sample and is quicker than hydrothermal synthesis, which also demands a higher temperature [40]. Even though this synthetic technology is quick, affordable, easily scalable, energy-efficient [41], and environmentally benign [42], it is challenging to accurately regulate the size of CQDs using this approach [2]. This process involves heating an aqueous solution of carbon precursors in a microwave until CQDs are created. Polar molecules can be heated by microwave radiation because they have an electric dipole moment. The polar molecules rotate due to an oscillating external electric field, a phenomenon known as dipole rotation, dipole polarization, or dielectric rotation. Because of these revolving molecules' pushing, pulling, or colliding with nearby molecules, heat is generated throughout the material. This is due to the correlation between molecules' kinetic energy and temperature. This process of heating is called dielectric heating [3]. Glu and the MPD's amino groups were used as precursors for the nitrogen-doped CQDs, which were made utilizing a microwave-assisted process with ethylene glycol serving as the solvent at 120 C for 5 minutes (Figure 6).

When subjected to ultraviolet (UV) light having a 365 nm wavelength, the CQD is made in the manner of fluorescing green. Similar to this, Lopez used ultrasonic mixing to combine concentrated hydrochloric acid and lactose solutions in a polytetrafluoroethylene reaction vessel. The solution was heated hydrothermally in a microwave oven at 160 °C for 15 minutes to produce fluorescent CQDs [43-44]. The microwave-assisted approach opens up a novel pathway for the creation of CQDs, offers the benefits of efficient and controlled performance, as well as the ability to quickly, and uniformly heat reactions while shortening reaction times and increasing CQD yield and quantum yield [45]. A research team created CQDs in 2020 by combining citric acid and urea and heating them for various amounts of time. When exposed to UV light (365 nm), the majority of the CQDs emitted blue light that was independent of stimulation. It was found that the heat duration had an impact on the band gap and stability of the CQDs that were produced. In our study, the lowest heat duration needed for CQD synthesis was 165 seconds. CQDs synthesized in this time frame had the maximum stability, but at the expense of a lower PL [40].

#### *2.2.3. Pyrolysis method*

This procedure involves the organic molecules being broken down under pressure, at a high temperature (often above 430 °C), and without oxygen. A strong acid or alkali may also be employed occasionally; this acts as a catalyst. It an irreversible process that simultaneously alters the chemical composition and physical phase. The use of pyrolysis to create CQDs from zero a brand-new method for creating CQDs by pyrolysis. The carrier, surfactant-modified silica spheres, and the carbon precursor, resol, were used to create the CQDs. CQD synthesis is a multi-step process, although it does not call for expensive machinery. Once PEG is used to passivity, the produced CQDs (blue emission) have a quantum yield of 14.7% and are amorphous, measuring 1.5 to 2.5 nm in diameter. Additionally, the photoluminescence QY of the CQDs only slightly decreased for a group of pH values of 5–9, with 11.0% and 12.1%, respectively, for pH 5 and 9 [46]. The efficient one-step synthesis approach for extremely fluorescent CQDs using the low-temperature pyrolysis of ethylenediamine-tetraacetic acid (EDTA) salts CQDs generated intense blue fluorescence with PL quantum yields (QYs) higher than 40% and 6%, which was a significant increase above the QYs of 15% that had previously been reported. CQDs have an optimum diameter of roughly 6 nm. Furthermore, they discovered that pH, solvent, spin, and emission spectrum all had a significant impact on the PL properties [47]. CQDs in pyrolyzing citric acid at 180 C The prepared CQDs had a QY of 2.3% and an average diameter of roughly 6 nm (excitation at 360 nm) [48].

#### *2.2.4. Combustion method*

CQDs were produced using combustion in 2007. By using oxidative acid treatments, this method can make CQDs from carbon sources that are not as common, make them more soluble in water, and change how they fluoresce. According to Liu and colleagues, candle ashes are created by first partially combusting a candle using aluminum foil and then refluxing it in a nitric acid solution. The candle ashes were dissolving into an equal substance; the mixture centrifuged; and finally, a dialysis method was used to create the pure CQDs [20]. Despite having a low QY, the CQDs made using the combustion technique displayed high fluorescence without the requirement for doping [49-50].

#### *2.2.5. Template method*

First, Bourlinos and associates created fluorescent CQDs utilizing the template method [4]. It contains two stages: Making CQDs using calcinations in the proper template or silicon sphere. To get rid of the supporting materials, etching is used. The simplicity, accessibility of the equipment, suitability for CQD surface passivation, ability to prevent particle agglomeration, and control over CQD size are some of the advantages of the template approach. The difficulty in separating the CQDs from the template is a drawback of the template approach, which may have an impact on the pureness, size of the particles, fluorescence, and quantum yield [1].

## 3. Characterization of CQDs

Multiple methods of analysis used to characterize the synthesized CQDs. They are nuclear magnetic resonance (NMR), Transmission electron microscope (TEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), Raman spectroscopy, and Zeta potential measurement.

#### *3.1. Transmission electron microscope*

It is possible to determine the sample's ultrastructure using TEM, which has a high resolution of up to 0.1–0.2 nm. As a result, the method might be used to study the NPs' morphology and provide information about their sizes, shapes, dispersion, and other characteristics. One of the methods used to describe CQDs is TEM, which has been employed extensively. The high-resolution TEM can be utilized for CQDs' fine structural details. CQDs are structurally unique and exhibit their post-surface modification structure [5-7].

#### *3.2. Fourier transform infrared spectroscopy*

Studies have also shown that oxygen, hydrogen, and carbon frequently found in CQDs. Given that carbon-based QDs produced by significantly oxidizing the precursor composed of carbon and that the outermost layer of CDs is covered in hydroxyl, epoxy, ether, carboxylic acid, or carboxyl groups, the FTIR has also been regarded as a reliable tool for analyzing above-mentioned oxygen-containing groups. Before using FTIR, CQDs mainly required adjustments for stabilizing the potential wells on the energy surface, enhancing the fluorescence QY, and decreasing cytotoxicity. An effective technique for examining the functional groups found on the surface of Carbon Quantum Dots (CQDs) is Fourier Transform Infrared Spectroscopy (FTIR). It offers important details regarding the surface chemistry and biological composition of CQDs [8-9].

#### *3.3. Nuclear magnetic resonance*

Nuclear magnetic resonance is frequently utilized to identify different forms of carbon atoms in the crystalline structure and the various kinds of interactions between the carbon atoms, which provides additional structural information regarding CQDs [8].

#### *3.4. X-ray diffraction*

The XRD technique is primarily used to characterize CQDs and other associated data, such as particle size, phase purity, and structure of the crystal. Additionally, the crystalline phases of the CQDs were identified by this technique [8].

#### *3.5. Raman spectroscopy*

Raman spectroscopy is a quick, non-destructive, and high-resolution (HR) method for characterizing the lattice structure, electronic, optical, and phonon properties of carbon materials, such as three-dimensional (3d) diamond and graphite, two-dimensional (2d) graphene, one-dimensional (1d) carbon nanotubes, and 0d fullerenes and CQDs. The structure and bonding of CQDs have been extensively studied through Raman spectroscopy [10].

#### *3.6. Zeta potential measurement*

CQD is a colloidal nanoparticle, it is important to quantify the electrical charge (or zeta potential) surrounding the CQD NPs to determine whether they adhere. With zeta's potential as far away as zero, NPs become more stable. In this instance, it has proposed that zeta potential, a type of surface charge, is also influencing the effectiveness of encapsulation.

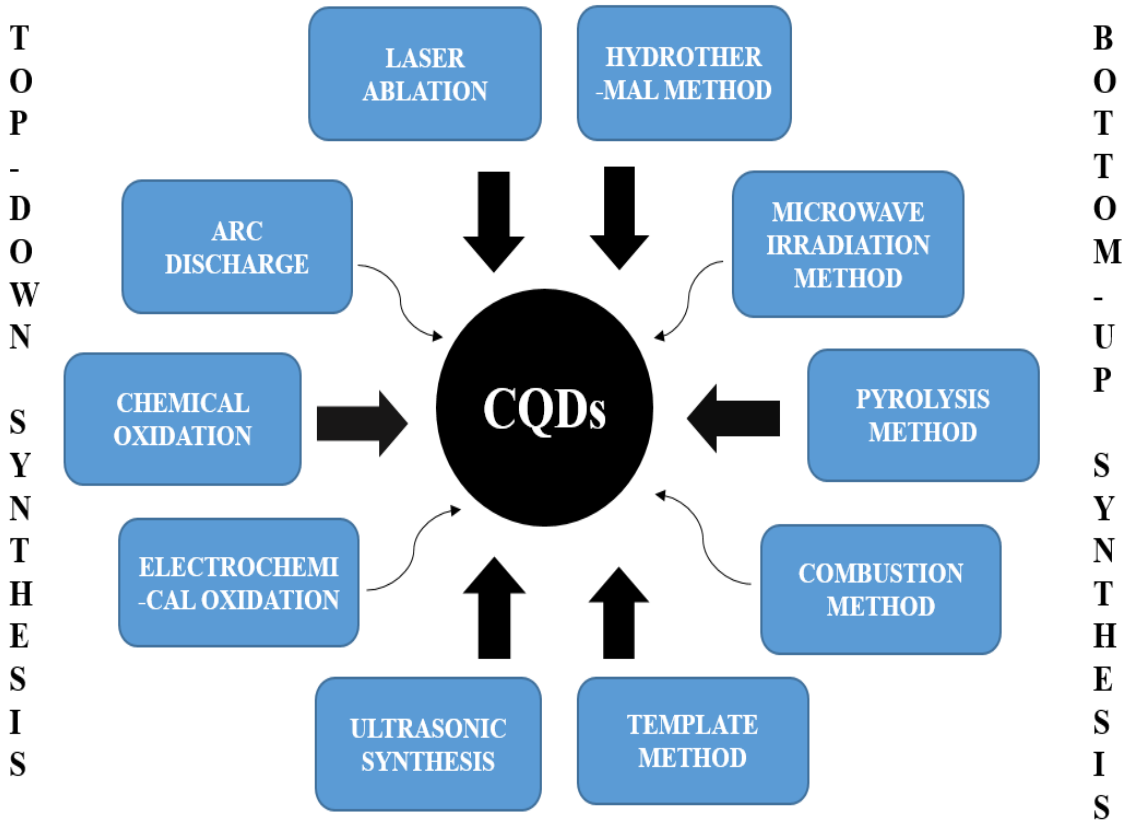


**Figure 1:** Synthesis of CQDs flowchart

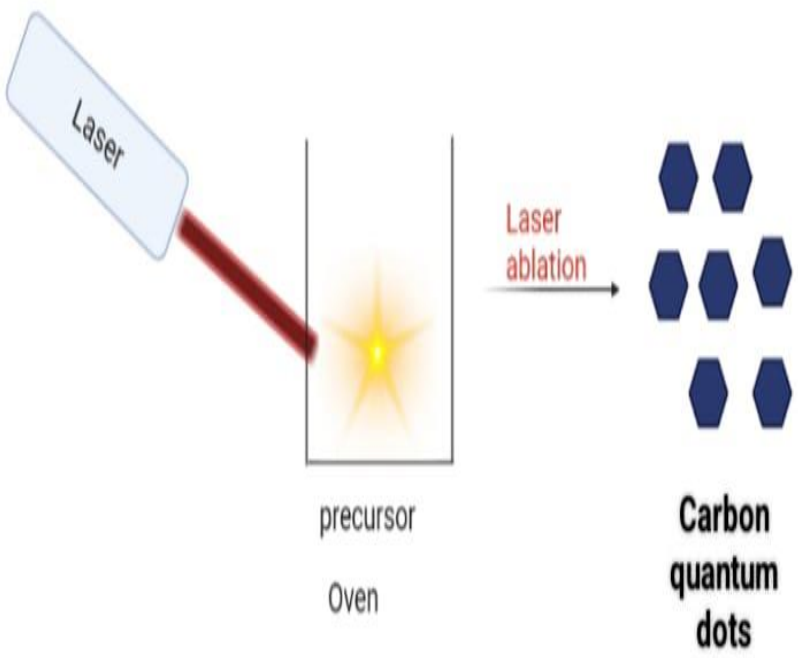


**Figure 2:** Synthesis of CQDs by laser ablation

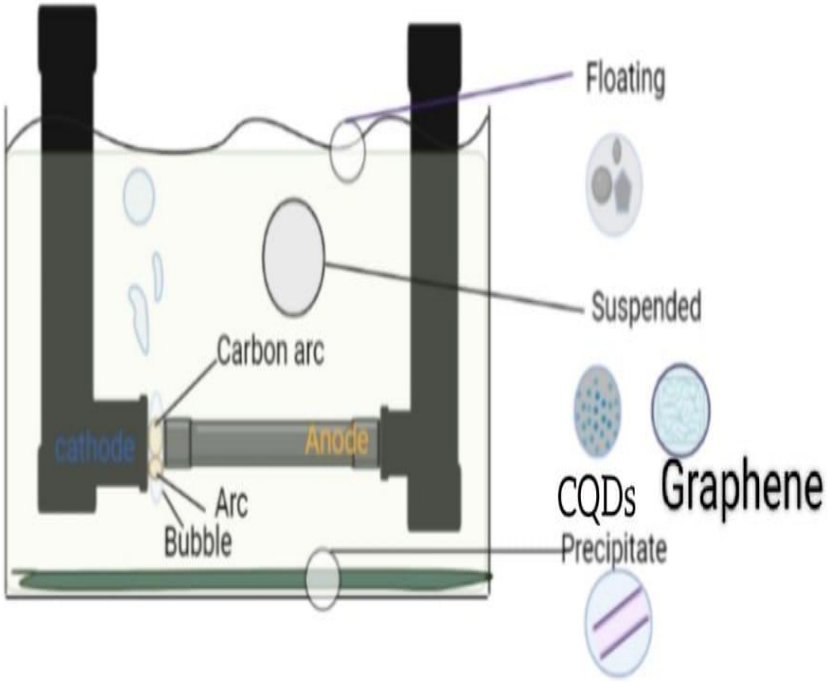


**Figure 3:** Synthesis of CQDs by arc discharge method

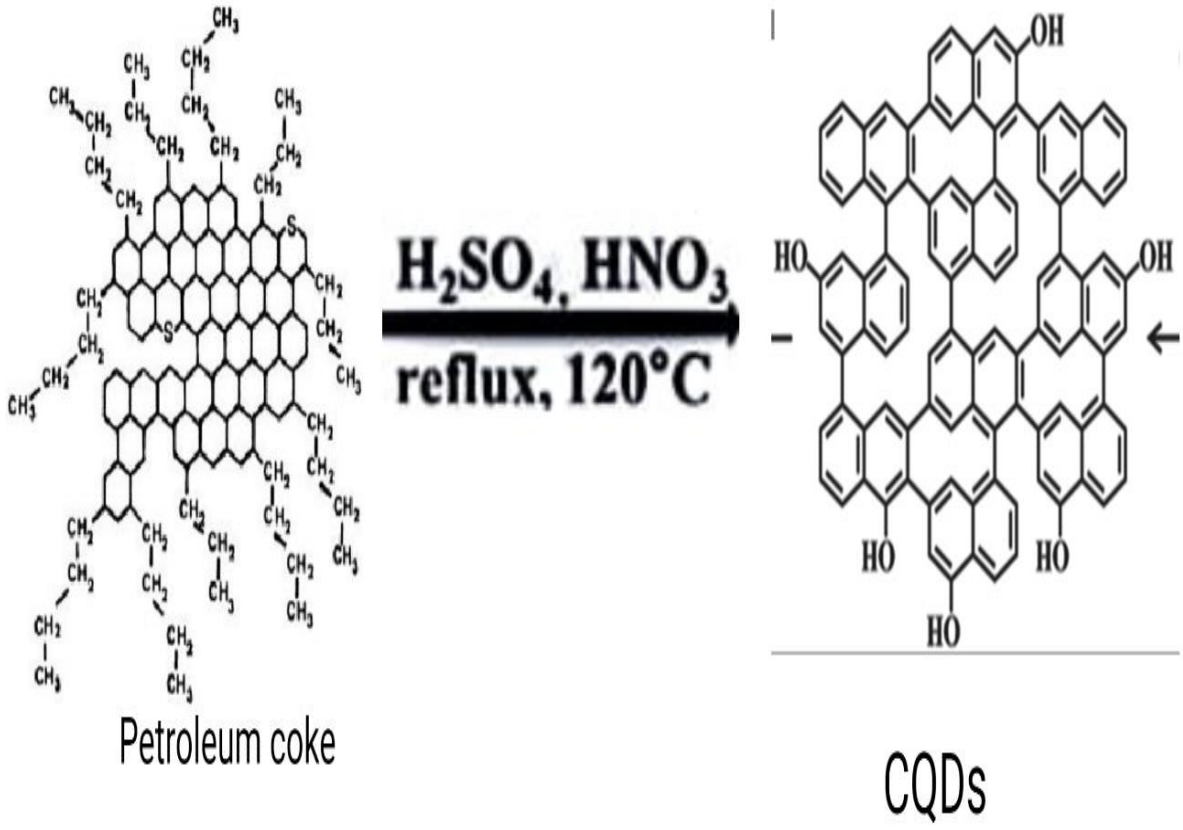


**Figure 4:** Synthesis of carbon quantum dots from petroleum coke

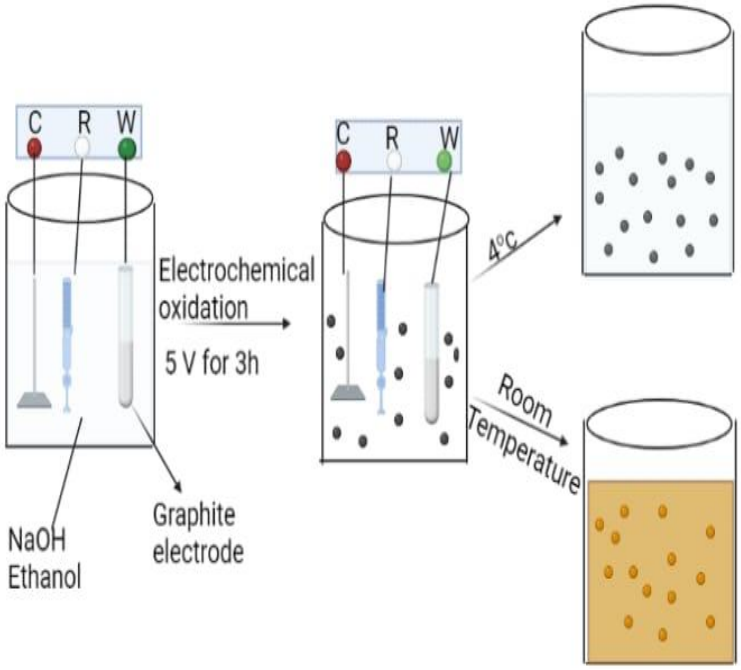


**Figure 5:** Synthesis of CQDs by electrochemical oxidation method

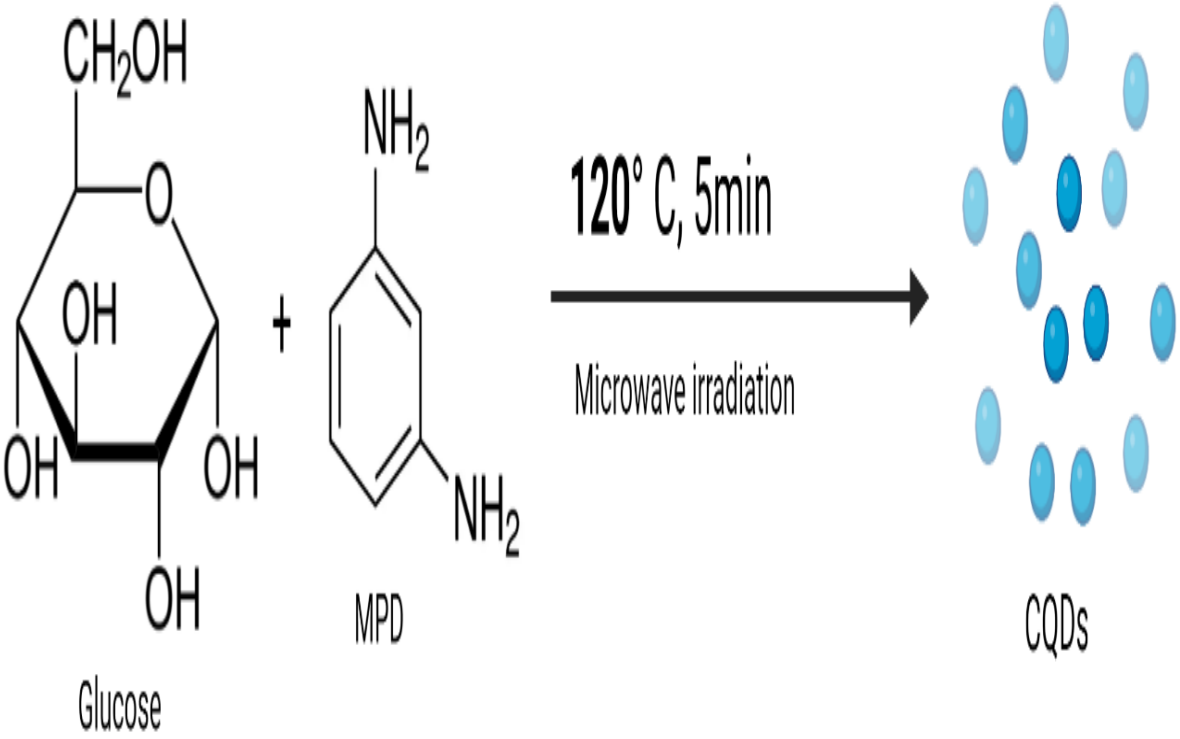


**Figure 6:** Synthesis of CQDs by microwave irradiation method

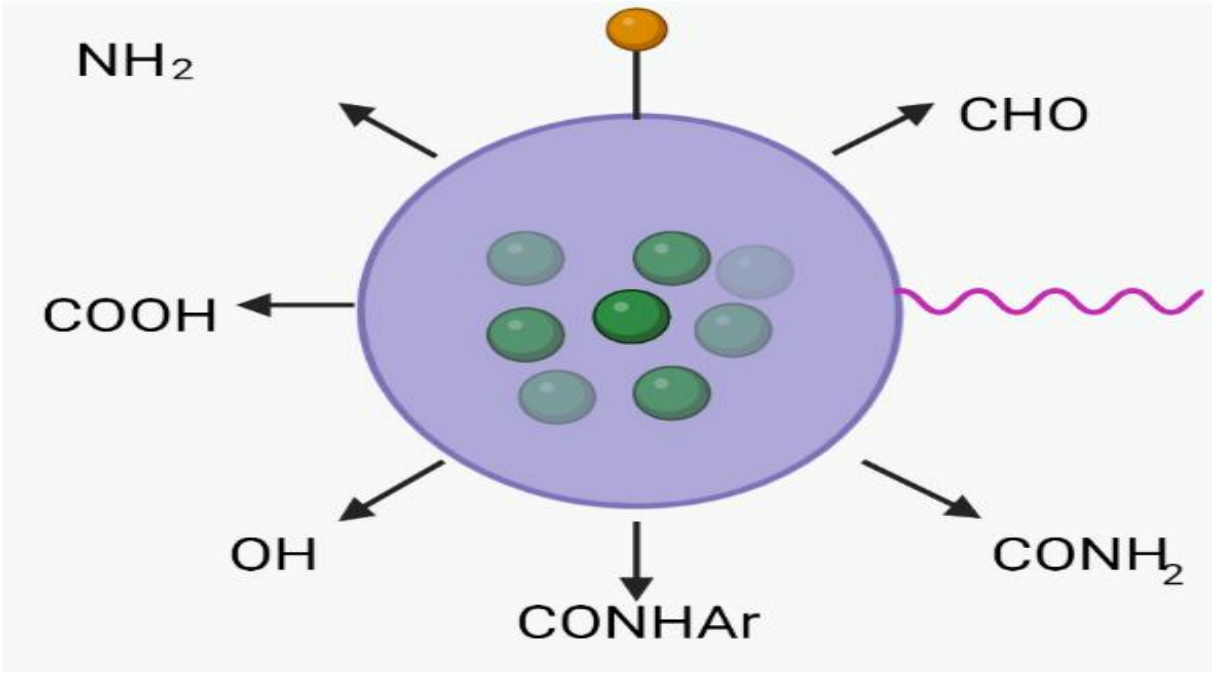


**Figure 7:** Structure of CQDs

**Table 1:** Emission characteristics of CQDs and their application

| **Methods** | **QY (highest %)** | **Emission characteristics** | **Emission (Band, surface, states, etc.)** | **Doping (or) surface passivation** | **Application of prepared CQDs** | **Ref.** |
|---|---|---|---|---|---|---|
| Pyrolysis | 14.70% | Excitation of blue emission at 365 nm Excitation-dependent emission: As the excitation, wavelength grows from 320 to 500 nm, the emission intensity changes, and the emission peak moves towards the red. | Quantization and surface conditions | Surface passivation | bio imaging | [28] |
| Microwave irradiation | 14% | Excitation of blue emission at 365 nm | - | - | A fluorescent probe that can detect glutathione when it activated. | [29] |
| Electrochemical carbonization | 15.9% | Excitation of blue emission at 365 nm | Quantization and surface conditions | Surface passivation is not necessary when undoped. | Bio-imaging of HeLa cells | [30] |
| Hydrothermal-l | CQDs(7.5 V):5.0%~35% | Excitation at 365 nm produces blue, green, yellow, and red emissions. | Surface states | N-Doping | In-vivo bioimaging | [31] |

| | | | | | | |
|---|---|---|---|---|---|---|
| Hydrothermal | 77.07% | Excitation of blue emission at 360 nm (for Et-EDA CQDs) | Molecular states are also referred to as molecular fluorescence and fundamental states. | N-Doping | Bio-application | [32] |
| Hydrothermal | 84.8% | Excitation of blue emission at 365 nm. When the excitation wavelength is extended from 300 to 500 nm, the emission intensity reduces. | Surface states | N-Doping and surface passivation | Silicone-nanowire solar cells | [33] |
| Pyrolysis | ~36% | Excitation of blue emission at 365 nm. Excitation-dependent emission: as the excitation wavelength is increased from 300-500 nm | Surface states | N-Doping | QDSC | [34] |
| Hydrothermal | ~75% | Excitation at 365 nm produces blue, green, yellow, orange, and red emissions. | Quantum confinement | N-Doping, surface passivation | LED | [35] |
| Hydrothermal | F-CQD: 31% Undoppe d CQD 28% | Emission that is excitation-dependent in both CQDs. At 360 nm excitation, F-CQD emits a yellow color. The range of the emission is 550–600 nm, while the range of the excitation is 360–580 nm. Green emission from undoped-CQD at excitation of 360 nm. By the excitation wavelength range of 360–500 nm, the emission ranges from 480–550 nm. | Surface states | F-CQD: F-doping, N-doping | Red cell imaging and sensitive intracellular Ag+ detection | [36] |
| Microwave irradiation | 5.4% | Excitation of blue emission at 400 nm. | Molecular fluorescence | Surface passivation | White LED | [37] |
| Microwave irradiation | 1.8% | Excitation of blue emission at 265 nm. | - | Undoped, surface passivation is not required | Determination of Fe3+ ions | [38] |
| Microwave irradiation | 85% | Excitation of blue emission at 355 nm. | Surface states | Surface functionaliz | | [39] |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | ation while synthesis | Dopamine fluorescence probe and cellular imaging | |
| Chemical oxidation | 0.43% | Excitation of blue emission at 310 nm. | Surface states | Surface functionalization | no | [40] |
| Laser ablation | >10% | Excitation of blue emission at 400 nm. | Quantization and surface conditions | Surface passivation | No | [41] |

**Table 2:** Advantages and disadvantages of synthetic methods

| **Synthetic Methods** | **Advantages** | **Disadvantages** | **ref.** |
|---|---|---|---|
| Chemical oxidation | Most readily available, numerous sources. | Harsh circumstances, extreme procedures, numerous steps, and poor size control. | [42-45] |
| Laser ablation | Quick, powerful, and extremely adjustable. | Low quantum yield, inadequate size control, and the need for modification. | [46-48] |
| Ultrasonic synthesis | Easy operation | Instrumental wastage, high-energy cost. | [49-50] |
| Microwave synthesis | Quick, scalable, affordable, and environmentally friendly. | inadequate control of sizes | [29-51-52] |
| Hydrothermal | Cheap, environmentally friendly, and non-toxic. | inadequate control of sizes | [53-55] |
| Pyrolysis | Simple operation, absence of solvents, low price, and mass production. | A not-equivalent size distribution | [56-58] |
| Electrochemical oxidation | Size and nanostructure are stable, one-step, and adjustable. | Only a few precursors of tiny molecules. | [59] |

**Table 3:** Information on several drug delivery applications utilizing CQDs and different synthesis techniques

| **Carbon Materials** | **Precursor** | **Synthesis method** | **Drug loaded** | **Ligand attached** | **Targeted cells** | **Reference** |
|---|---|---|---|---|---|---|
| MF-CQDs | Crab shell | One-pot microwave-assisted pyrolysis | Dox | Folic acid at Gd-CQDs | HeLa cells | [67] |
| TF-CQDs | Citric acid (CA) | Hydrothermal | Dox | Transferrin (TF) | MCF-7 cells | [68] |
| CQDs | CA and EDA | Hydrothermal | | Quinic acid | Breast cancer cells | [69] |
| Arg-Ag/Cu-CQDs | L-arginine | Hydrothermal | Dox | - | 4T1 and HUVEC | [70] |
| N-CQDs | CA and EDA | Tube furnace thermal synthesis | Dox | D-biotin | HeLa cells | [71] |

In addition to preserving colloidal stability and improving particle interactions with cells and surroundings. An instrument called a Zeta Potential Analyzer is frequently used to detect zeta potential [11]. The zeta potential and dynamic light scattering (DLS) of particles in a solution, including Carbon Quantum Dots (CQDs), are commonly measured using a zeta sizer. The Zeta Sizer integrates zeta potential analysis and DLS measurements to produce insightful data on the size distribution and colloidal stability of CQDs.

## 4. CQDs' Structure

The core-shell architectures of CQDs can be either mixed sp2/sp3 (amorphous) or sp2 (graphitic crystalline), depending on the quantity of sp2 carbon in the core [12]. Multiple researchers have observed the presence of graphitic crystalline (sp2) cores [13-15]. Cores are quite tiny (2–3 nm) and typically have a 0.2 nm lattice spacing [16]. The synthesis process, additional factors (such as time, temperature, pH, etc.), and the precursors utilized are all taken into account when classifying the cores [17]. Unless sp2/sp3-hybridized carbon is present in the precursor, undefined cores are normally generated at reducing temperatures, but reaction temperatures exceeding 300 °C are usually required to produce the graphitization (sp2) structure [18]. Various instrumental techniques, including X-ray diffraction (XRD), Scanning Electron Microscopy (SEM), Raman spectroscopy, and Transmission Electron Microscopy (TEM) or High Resolution (HR) TEM, are used to ascertain the fundamental structure of CQDs. TEM or SEM measurements are made to determine the CQDs' size and shape [19]. Amorphous or crystalline CQDs can be identified by their selected area electron diffraction (SAED) patterns [20]. The XRD pattern of CQDs can also be used to determine their crystal structure.

While the wide peak at 2 and 22 exposes the unstructured character of CQDs, the appearance of the two wide peaks at 2 and 24, and 44, respectively, suggests a carbon lattice with less graphite comparable to that of (002) and (100) diffraction [21]. Fourier transforms infrared (FT-IR) spectroscopy, elemental analysis, X-ray photoelectron spectroscopy, and nuclear magnetic resonance (NMR) are used to Analyze the overall makeup of the CQDs and whether or not various functional categories are present [22-23]. It is possible to calculate the carbon nanoparticles' surface area using nitrogen sorption analysis [22]. The optical properties and qualitative information on the presence of C=C and C=O in CQDs are determined using UV-Vis absorption spectroscopy [24]. The degree of the electrostatic contact between CQDs and their surface charge, as well as their positive or negative charge, are both determined by zeta potential [25-26]. The typical structure of carbon quantum dots (CQDs) shows that the surface of CQDs contains a variety of functional groups, such as carboxyl, carbonyl, hydroxyl, and amino. These functional groupings' existence was validated by instrumental methods like FTIR and XPS [27].

### *4.1. CQDs-guided drug delivery system*

Chemotherapy is frequently employed for treating cancer and other conditions, however, it is inaccurate, related to toxicity, and related to resistance to multiple drugs, therefore targeted drug administration has been selected as a strategy to maximize drug bio-availability effectiveness and lowering side effects [60]. However, because of this, the medication leaks till it gets to its destination. To integrate bio imaging and targeted medication administration with the least amount of cytotoxicity, effective target agents like CQDs are required [61]. Functionalized CQDs can reduce the cytotoxicity brought on by drug leakage into healthy cells [62]. The surfaces of functionalized CQDs have amino groups that can crosslink with tumor theranostics] [63]. Citric acid is microwave-pyrolysis to produce CQDs, which are subsequently PEGylated oxidized alginate cross-linked with the theranostic drug doxorubicin (DOX) via an acid-labile Schiff base connection. In the laboratory, it was demonstrated that theranostic nanoparticles may release drugs into the tumor's acidic microenvironment in a pH-dependent manner [64]. Cancer cells can be distinguished from ones that have already gone into apoptosis using CQDs' brightness and the location of their emission [65].

Using fluorescence microscopy, CQDs included in the hydrogel were detected by A549 cells and released green light. The level of CQD concentration in the gel was correlated with the amount of green light that was emitted. The anticancer drug (DOX) was delivered to the targeted area using CQDs made using hydrothermal techniques in a drug delivery system. A different study found that drug-loaded CQDs had better localization than DOX alone [64]. The effect of conjugated CQDs on the body was investigated using HepG2 and MCF-7 cells. Cancer cells were shown to have higher lethal doses of the DOX-conjugated CQDs than normal cells. Because of insufficient brain permeability, limited medication persistence in the brain, and the barrier between the blood and the brain, it is challenging to utilize in brain cancers and neurological diseases. As a result, accurate diagnosis and prognosis depend on trustworthy cancer cell imaging. CQDs were also employed to target brain malignancies in addition to peptides that can penetrate tumors [66].

## 5. Conclusion

Carbon quantum dots (CQDs) have become a potential nanomaterial with numerous uses, including medicine delivery. Size-controlled and surface-functionalized nanoparticles are produced when CQDs are synthesized utilizing various techniques, such as bottom-up and top-down procedures. These nanoparticles exhibit unique properties, including high photoluminescence, excellent biocompatibility, and stability. CQDs are useful for a wide range of applications due to their characteristics. Since they are small, have a large surface area, and have different chemical compositions, CQDs can be used as carriers for the targeted administration of therapeutic molecules in drug delivery. They can encapsulate drugs, protect them from degradation, and facilitate controlled release at the desired site. Additionally, the photoluminescence property of CQDs enables them to act as imaging agents for real-time monitoring of drug release and distribution in the body. CQDs have also been used in different industries, including catalysis, energy storage, sensing, and bio imaging. Scientists are looking into new ways to make nanomaterials, change their surfaces, and mix them with other nanomaterials to make them better at carrying drugs, finding their targets, and releasing them slowly. Compared to un-doped CQDs, the fluorescence quantum yield of doped and co-doped CQDs is

higher. In doped and co-doped CQDs, the fundamental fluorescence mechanism may thus \realized in the future. A majority of doped and co-doped CQDs glow blue. This makes it challenging scientists to produce multicolored emission CQDs and employ them in other applications in the future.

**References**


[1] P.K. Yadav, S. Chandra, V. Kumar, D. Kumar, S.H. Hasan. (2023). Carbon quantum dots: synthesis, structure, properties, and catalytic applications for organic synthesis. Catalysts. 13(2): 422.

[2] S. Dua, P. Kumar, B. Pani, A. Kaur, M. Khanna, G. Bhatt. (2023). Stability of carbon quantum dots: a critical review. RSC advances. 13(20): 13845-13861.

[3] P. Kumar, G. Bhatt, R. Kaur, S. Dua, A. Kapoor. (2020). Synthesis and modulation of the optical properties of carbon quantum dots using microwave radiation. Fullerenes, Nanotubes and Carbon Nanostructures. 28(9): 724-731.

[4] A.B. Bourlinos, A. Stassinopoulos, D. Anglos, R. Zboril, V. Georgakilas, E.P. Giannelis. (2008). Photoluminescent carbogenic dots. Chemistry of Materials. 20(14): 4539-4541.

[5] S. Tajik, Z. Dourandish, K. Zhang, H. Beitollahi, Q. Van Le, H.W. Jang, M. Shokouhimehr. (2020). Carbon and graphene quantum dots: a review on syntheses, characterization, biological and sensing applications for neurotransmitter determination. RSC advances. 10(26): 15406-15429.

[6] X. Ke, C. Bittencourt, G. Van Tendeloo. (2015). Possibilities and limitations of advanced transmission electron microscopy for carbon-based nanomaterials. Beilstein journal of nanotechnology. 6(1): 1541-1557.

[7] B. Guo, Y. Zuo, Y. Shi, T. Han, M. Lanza. (2020). Transmission Electron Microscopy-Based Statistical Analysis of Commercially Available Graphene Oxide Quantum Dots. Crystal Research and Technology. 55(4): 1900231.

[8] P. Zuo, X. Lu, Z. Sun, Y. Guo, H. He. (2016). A review on syntheses, properties, characterization and bioanalytical applications of fluorescent carbon dots. Microchimica Acta. 183: 519-542.

[9] D. Barmpakos, A. Segkos, C. Tsamis, G. Kaltsas In *Enhancement Of PEDOT: PSS Seebek Coefficient Using Carbon-Quantum-Dot-Based Nanocomposite Materials: Application To Inkjet Printing On Flexible Substrate*, 2019 20th International Conference on Solid-State Sensors, Actuators and Microsystems & Eurosensors XXXIII (TRANSDUCERS & EUROSENSORS XXXIII), 2019; IEEE: 2019; pp 2515-2518.

[10] J.-B. Wu, M.-L. Lin, X. Cong, H.-N. Liu, P.-H. Tan. (2018). Raman spectroscopy of graphene-based materials and its applications in related devices. Chemical Society Reviews. 47(5): 1822-1873.

[11] S. Samadian, A. Karbalaei, M. Pourmadadi, F. Yazdian, H. Rashedi, M. Omidi, S. Malmir. (2022). A novel alginate-gelatin microcapsule to enhance bone differentiation of mesenchymal stem cells. International Journal of Polymeric Materials and Polymeric Biomaterials. 71(6): 395-402.

[12] L. Tang, R. Ji, X. Cao, J. Lin, H. Jiang, X. Li, K.S. Teng, C.M. Luk, S. Zeng, J. Hao. (2012). Deep ultraviolet photoluminescence of water-soluble self-passivated graphene quantum dots. ACS nano. 6(6): 5102-5110.

[13] K. Hola, A.B. Bourlinos, O. Kozak, K. Berka, K.M. Siskova, M. Havrdova, J. Tucek, K. Safarova, M. Otyepka, E.P. Giannelis. (2014). Photoluminescence effects of graphitic core size and surface functional groups in carbon dots: COO− induced red-shift emission. Carbon. 70: 279-286.

[14] A. Sciortino, E. Marino, B.v. Dam, P. Schall, M. Cannas, F. Messina. (2016). Solvatochromism unravels the emission mechanism of carbon nanodots. The journal of physical chemistry letters. 7(17): 3419-3423.

[15] A. Dager, T. Uchida, T. Maekawa, M. Tachibana. (2019). Synthesis and characterization of mono-disperse carbon quantum dots from fennel seeds: photoluminescence analysis using machine learning. Scientific reports. 9(1): 14004.

[16] W. Zhang, S.F. Yu, L. Fei, L. Jin, S. Pan, P. Lin. (2015). Large-area color controllable remote carbon white-light light-emitting diodes. Carbon. 85: 344-350.

[17] B.C. Martindale, G.A. Hutton, C.A. Caputo, S. Prantl, R. Godin, J.R. Durrant, E. Reisner. (2017). Enhancing light absorption and charge transfer efficiency in carbon dots through graphitization and core nitrogen doping. Angewandte Chemie. 129(23): 6559-6563.

[18] T. Yu, H. Wang, C. Guo, Y. Zhai, J. Yang, J. Yuan. (2018). A rapid microwave synthesis of green-emissive carbon dots with solid-state fluorescence and pH-sensitive properties. Royal Society open science. 5(7): 180245.

[19] H. Li, Z. Kang, Y. Liu, S.-T. Lee. (2012). Carbon nanodots: synthesis, properties and applications. Journal of materials chemistry. 22(46): 24230-24253.

[20] Y. Zheng, D. Yang, X. Wu, H. Yan, Y. Zhao, B. Feng, K. Duan, J. Weng, J. Wang. (2015). A facile approach for the synthesis of highly luminescent carbon dots using vitamin-based small organic molecules with benzene ring structure as precursors. RSC advances. 5(110): 90245-90254.

[21] H. Hou, C.E. Banks, M. Jing, Y. Zhang, X. Ji. (2015). Carbon quantum dots and their derivative 3D porous carbon frameworks for sodium-ion batteries with ultralong cycle life. Advanced materials. 27(47): 7861-7866.

[22] M. Semeniuk, Z. Yi, V. Poursorkhabi, J. Tjong, S. Jaffer, Z.-H. Lu, M. Sain. (2019). Future perspectives and review on organic carbon dots in electronic applications. ACS nano. 13(6): 6224-6255.

[23] D. Briggs. (2005). X-ray photoelectron spectroscopy (XPS). Handb. Adhes. 621-622.

[24] Y. Zhou, S.K. Sharma, Z. Peng, R.M. Leblanc. (2017). Polymers in carbon dots: a review. Polymers. 9(2): 67.

[25] A. Kolanowska, G. Dzido, M. Krzywiecki, M.M. Tomczyk, D. Łukowiec, S. Ruczka, S. Boncel. (2022). Carbon quantum dots from amino acids revisited: Survey of renewable precursors toward high quantum-yield blue and green fluorescence. ACS omega. 7(45): 41165-41176.

[26] S. Qiang, L. Zhang, Z. Li, J. Liang, P. Li, J. Song, K. Guo, Z. Wang, Q. Fan. (2022). New insights into the cellular toxicity of carbon quantum dots to Escherichia coli. Antioxidants. 11(12): 2475.

[27] B. Gayen, S. Palchoudhury, J. Chowdhury. (2019). Carbon dots: A mystic star in the world of nanoscience. Journal of Nanomaterials. 2019(1): 3451307.

[28] R. Liu, D. Wu, S. Liu, K. Koynov, W. Knoll, Q. Li. (2009). An aqueous route to multicolor photoluminescent carbon dots using silica spheres as carriers. Angewandte Chemie International Edition. 48(25): 4598-4601.

[29] Q. Wang, X. Liu, L. Zhang, Y. Lv. (2012). Microwave-assisted synthesis of carbon nanodots through an eggshell membrane and their fluorescent application. Analyst. 137(22): 5392-5397.

[30] J. Deng, Q. Lu, N. Mi, H. Li, M. Liu, M. Xu, L. Tan, Q. Xie, Y. Zhang, S. Yao. (2014). Electrochemical synthesis of carbon nanodots directly from alcohols. Chemistry–A European Journal. 20(17): 4993-4999.

[31] H. Ding, S.-B. Yu, J.-S. Wei, H.-M. Xiong. (2016). Full-color light-emitting carbon dots with a surface-state-controlled luminescence mechanism. ACS nano. 10(1): 484-491.

[32] Y. Song, S. Zhu, S. Zhang, Y. Fu, L. Wang, X. Zhao, B. Yang. (2015). Investigation from chemical structure to photoluminescent mechanism: a type of carbon dots from the pyrolysis of citric acid and an amine. Journal of Materials Chemistry C. 3(23): 5976-5984.

[33] X. Han, S. Zhong, W. Pan, W. Shen. (2015). A simple strategy for synthesizing highly luminescent carbon nanodots and application as effective down-shifting layers. Nanotechnology. 26(6): 065402.

[34] H. Wang, P. Sun, S. Cong, J. Wu, L. Gao, Y. Wang, X. Dai, Q. Yi, G. Zou. (2016). Nitrogen-doped carbon dots for "green" quantum dot solar cells. Nanoscale research letters. 11: 1-6.

[35] F. Yuan, Z. Wang, X. Li, Y. Li, Z.a. Tan, L. Fan, S. Yang. (2017). Bright multicolor bandgap fluorescent carbon quantum dots for electroluminescent light-emitting diodes. Advanced materials. 29(3): 1604436.

[36] G. Zuo, A. Xie, J. Li, T. Su, X. Pan, W. Dong. (2017). Large emission red-shift of carbon dots by fluorine doping and their applications for red cell imaging and sensitive intracellular Ag+ detection. The Journal of Physical Chemistry C. 121(47): 26558-26565.

[37] V. Hinterberger, W. Wang, C. Damm, S. Wawra, M. Thoma, W. Peukert. (2018). Microwave-assisted one-step synthesis of white light-emitting carbon dot suspensions. Optical Materials. 80: 110-119.

[38] A. Başoğlu, Ü. Ocak, A. Gümrükçüoğlu. (2020). Synthesis of microwave-assisted fluorescence carbon quantum dots using roasted–chickpeas and its applications for sensitive and selective detection of Fe3+ ions. Journal of fluorescence. 30(3): 515-526.

[39] H. Lin, J. Huang, L. Ding. (2019). Preparation of Carbon Dots with High-Fluorescence Quantum Yield and Their Application in Dopamine Fluorescence Probe and Cellular Imaging. Journal of Nanomaterials. 2019(1): 5037243.

[40] L. Tian, D. Ghosh, W. Chen, S. Pradhan, X. Chang, S. Chen. (2009). Nanosized carbon particles from natural gas soot. Chemistry of Materials. 21(13): 2803-2809.

[41] Y.-P. Sun, B. Zhou, Y. Lin, W. Wang, K.S. Fernando, P. Pathak, M.J. Meziani, B.A. Harruff, X. Wang, H. Wang. (2006). Quantum-sized carbon dots for bright and colorful photoluminescence. Journal of the American Chemical Society. 128(24): 7756-7757.

[42] P. Zhao, M. Yang, W. Fan, X. Wang, F. Tang, C. Yang, X. Dou, S. Li, Y. Wang, Y. Cao. (2016). Facile one-pot conversion of petroleum asphaltene to high quality green fluorescent graphene quantum dots and their application in cell imaging. Particle & Particle Systems Characterization. 33(9): 635-644.

[43] J. Peng, W. Gao, B.K. Gupta, Z. Liu, R. Romero-Aburto, L. Ge, L. Song, L.B. Alemany, X. Zhan, G. Gao. (2012). Graphene quantum dots derived from carbon fibers. Nano letters. 12(2): 844-849.

[44] H. Liu, T. Ye, C. Mao. (2007). Fluorescent carbon nanoparticles derived from candle soot. Angewandte Chemie. 119(34): 6593-6595.

[45] C. Zhu, S. Yang, G. Wang, R. Mo, P. He, J. Sun, Z. Di, Z. Kang, N. Yuan, J. Ding. (2015). A new mild, clean and highly efficient method for the preparation of graphene quantum dots without by-products. Journal of Materials Chemistry B. 3(34): 6871-6876.

[46] X. Li, H. Wang, Y. Shimizu, A. Pyatenko, K. Kawaguchi, N. Koshizaki. (2011). Preparation of carbon quantum dots with tunable photoluminescence by rapid laser passivation in ordinary organic solvents. Chemical Communications. 47(3): 932-934.

[47] S.-L. Hu, K.-Y. Niu, J. Sun, J. Yang, N.-Q. Zhao, X.-W. Du. (2009). One-step synthesis of fluorescent carbon nanoparticles by laser irradiation. Journal of materials chemistry. 19(4): 484-488.

[48] S.H. Kang, S. Mhin, H. Han, K.M. Kim, J.L. Jones, J.H. Ryu, J.S. Kang, S.H. Kim, K.B. Shim. (2016). Ultrafast method for selective design of graphene quantum dots with highly efficient blue emission. Scientific reports. 6(1): 1-7.

[49] S. Zhuo, M. Shao, S.-T. Lee. (2012). Upconversion and downconversion fluorescent graphene quantum dots: ultrasonic preparation and photocatalysis. ACS nano. 6(2): 1059-1064.

[50] L. Cui, X. Ren, J. Wang, M. Sun. (2020). Synthesis of homogeneous carbon quantum dots by ultrafast dual-beam pulsed laser ablation for bioimaging. Materials Today Nano. 12: 100091.

[51] L.L. Li, J. Ji, R. Fei, C.Z. Wang, Q. Lu, J.R. Zhang, L.P. Jiang, J.J. Zhu. (2012). A facile microwave

avenue to electrochemiluminescent two-color graphene quantum dots. Advanced Functional Materials. 22(14): 2971-2979.

[52] N.R. Pires, C.M. Santos, R.R. Sousa, R.C.d. Paula, P.L. Cunha, J.P. Feitosa. (2015). Novel and fast microwave-assisted synthesis of carbon quantum dots from raw cashew gum. Journal of the Brazilian Chemical Society. 26(6): 1274-1282.

[53] R.M. Sendão, D.M. Crista, A.C.P. Afonso, M.d.V.M. de Yuso, M. Algarra, J.C.E. da Silva, L.P. da Silva. (2019). Insight into the hybrid luminescence showed by carbon dots and molecular fluorophores in solution. Physical Chemistry Chemical Physics. 21(37): 20919-20926.

[54] Y. Liu, Y. Zhao, Y. Zhang. (2014). One-step green synthesized fluorescent carbon nanodots from bamboo leaves for copper (II) ion detection. Sensors and Actuators B: Chemical. 196: 647-652.

[55] R. Bandi, B.R. Gangapuram, R. Dadigala, R. Eslavath, S.S. Singh, V. Guttena. (2016). Facile and green synthesis of fluorescent carbon dots from onion waste and their potential applications as sensor and multicolour imaging agents. RSC advances. 6(34): 28633-28639.

[56] H. de Waard, H.W. Frijlink, W.L. Hinrichs. (2011). Bottom-up preparation techniques for nanocrystals of lipophilic drugs. Pharmaceutical research. 28: 1220-1223.

[57] S.S. Wee, Y.H. Ng, S.M. Ng. (2013). Synthesis of fluorescent carbon dots via simple acid hydrolysis of bovine serum albumin and its potential as sensitive sensing probe for lead (II) ions. Talanta. 116: 71-76.

[58] M. Sun, Y. Han, X. Yuan, P. Jing, L. Zhang, J. Zhao, Y. Zheng. (2020). Efficient full-color emitting carbon-dot-based composite phosphors by chemical dispersion. Nanoscale. 12(29): 15823-15831.

[59] L. Cui, X. Ren, M. Sun, H. Liu, L. Xia. (2021). Carbon dots: Synthesis, properties and applications. Nanomaterials. 11(12): 3419.

[60] M.J. Molaei. (2019). Carbon quantum dots and their biomedical and therapeutic applications: a review. RSC advances. 9(12): 6460-6481.

[61] Z. Qian, X. Shan, L. Chai, J. Ma, J. Chen, H. Feng. (2014). Si-doped carbon quantum dots: a facile and general preparation strategy, bioimaging application, and multifunctional sensor. ACS applied materials & interfaces. 6(9): 6797-6805.

[62] V. Magesh, A.K. Sundramoorthy, D. Ganapathy. (2022). Recent advances on synthesis and potential applications of carbon quantum dots. Frontiers in materials. 9: 906838.

[63] R. Cai, L. Xiao, M. Liu, F. Du, Z. Wang. (2021). Recent advances in functional carbon quantum dots for antitumour. International Journal of Nanomedicine. 7195-7229.

[64] G. Li, M. Pei, P. Liu. (2020). DOX-conjugated CQD-based nanosponges for tumor intracellular pH-triggered DOX release and imaging. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 603: 125258.

[65] I. Singh, R. Arora, H. Dhiman, R. Pahwa. (2018). Carbon quantum dots: Synthesis, characterization and biomedical applications. Turk. J. Pharm. Sci. 15(2): 219-230.

[66] J. Pardo, Z. Peng, R.M. Leblanc. (2018). Cancer targeting and drug delivery using carbon-based quantum dots and nanotubes. Molecules. 23(2): 378.

[67] Y.-Y. Yao, G. Gedda, W.M. Girma, C.-L. Yen, Y.-C. Ling, J.-Y. Chang. (2017). Magnetofluorescent carbon dots derived from crab shell for targeted dual-modality bioimaging and drug delivery. ACS applied materials & interfaces. 9(16): 13887-13899.

[68] M. Mahani, M. Pourrahmani-Sarbanani, M. Yoosefian, F. Divsar, S.M. Mousavi, A. Nomani. (2021). Doxorubicin delivery to breast cancer cells with transferrin-targeted carbon quantum dots: An in vitro and in silico study. Journal of Drug Delivery Science and Technology. 62: 102342.

[69] S. Samimi, M.S. Ardestani, F.A. Dorkoosh. (2021). Preparation of carbon quantum dots-quinic acid for drug delivery of gemcitabine to breast cancer cells. Journal of Drug Delivery Science and Technology. 61: 102287.

[70] C. Han, X. Zhang, F. Wang, Q. Yu, F. Chen, D. Shen, Z. Yang, T. Wang, M. Jiang, T. Deng. (2021). Duplex metal co-doped carbon quantum dots-based drug delivery system with intelligent adjustable size as adjuvant for synergistic cancer therapy. Carbon. 183: 789-808.

[71] W. Bao, H. Ma, N. Wang, Z. He. (2019). pH-sensitive carbon quantum dots− doxorubicin nanoparticles for tumor cellular targeted drug delivery. Polymers for Advanced Technologies. 30(11): 2664-2673.