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Emerging applications of carbon quantum dots in pharmaceutical sciences: A Paradigm shift in drug delivery and diagnostics

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Abstract

Background: Carbon quantum dots are a new type of glowing, tiny material that is safe for living things, not harmful to the environment, dissolves well in water, and stays stable when exposed to light.
Objectives: To synthesized carbon quantum dots quickly and easily while adhering to green chemistry principles. CQDs have easily adjustable optical properties and have found use in bioimaging, nanomedicine, drug delivery, solar cells, light-emitting diodes, photocatalysis, electrocatalysis, and other fields.
Materials and Methods: This article presents several methods for the synthesis of CQDs utilizing various precursors and synthesis techniques. Using natural resources to synthesize carbon quantum dots (CQDs) is both cost-effective and environmentally sustainable.
Conclusion: This article gives a detailed look at the structure of carbon quantum dots, how they are made, recent developments, how adding different materials and changing their surfaces affect their light properties, and related models of light emission. The challenges and potential for these nanomaterials are reviewed, with a focus on the use of carbon quantum dots to improve the performance of photovoltaics and white light-emitting diodes.

Keywords: Carbon quantum dots, Nanoparticles, Light emitting diodes, Drug delivery, Nanomedicine.

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1. Introduction

In 2004, carbon quantum dots (CQDs) were first discovered during the washing of single-walled carbon nanotubes. Carbon quantum dots (CQDs) exhibit high efficiency and tunability, facilitating their application in biomedicine, optoelectronics, catalytic sensors, and various other fields. It is highly appropriate for pictorial photostability, small-scale applications, highly tunable photoluminescence (PL), biocompatibility, and electrochemiluminescence. These products exhibit reduced harm and biological inertness, allowing for functionalization with biomolecules, thereby serving as effective carriers for drugs and bioimaging agents. Carbon quantum dots (CQDs) demonstrate potential applications in sensors, optronics, and electrochemical luminescence.[1-4] Carbon quantum dots (CQDs) have traditionally been synthesized through the superficial activity of organic and polymeric molecular nanoparticles in carbon. The preparation processes utilized the carbonization of carbon-containing precursors.[5-6] (**Figure 1**)

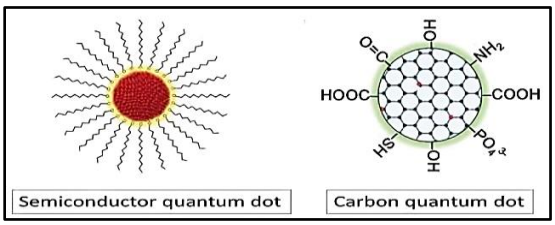

Figure 1: Illustrates the basic structure of carbon quantum dots[27]

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The method synthesized with CQD exhibits significant variability and lacks a degree of control. Carbon quantum dots (CQDs) were synthesized through the carbonization of diverse fruit juices, watermelon and pomelo peels, as well as various food items, herbs, and plant leaves.[7-9] tosan serves as a precursor in the hydrothermal carbonization synthesis of carbon quantum dots. Researchers have reported several techniques for synthesizing carbon quantum dots, such as ultrasonic methods, hydrothermal treatment, graphite laser ablation, and microwave-assisted synthesis.[11-13] Other methods include strong acidic and electrochemical[14] glycerol pyrolysis,[15] modified exfoliation of graphite in organic solvents, BBQ thermal annealing, thermal carbonization,[17] and atmospheric plasma-based synthesis,[18-19] Various precursors include sweet pepper,[20] capsicum,[21] watermelon peel,[22] and synthetic polymer.

The synthesis methods discussed in this article are preferable to physical and chemical processes. Chemical, electrochemical, or physical techniques typically synthesize boron quantum dots, using both top-down and bottom-up approaches. Carbon nanotubes, and nanodiamonds are categorized into carbohydro-quantum points through methods such as laser ablation, arc discharge, and electrochemical techniques employed in the synthesis of carbon quantum dots (CQD). The synthesis of carbon quantum dots (CQDs) using a bottom-up approach includes processes such as hydrothermal treatment, thermal treatment, chemical agent treatment, plasma treatment, and microwave systems, which utilize large precursor molecules like carbohydrates, organic acids such as citrates, and natural products. (**Figure 2**)

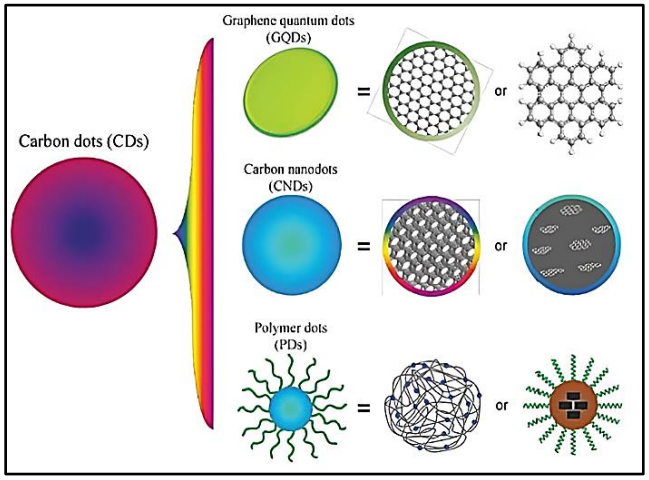

Figure 2: Carbon quantum dots[26]

This review aims to examine the sources and rationale of non-communicable diseases (NCDs), along with their synthesis pathways and modifications. We examine the mechanisms that enhance the efficacy of naturally produced carbon dots for drug delivery, taking into account their luminescence properties. Our analysis informs NCDs, drawing on recent studies regarding the operational mechanisms that enhance drug supply, including quantum yield and toxicological profiles, specifically biosafety and biodistribution. A study examines the advantageous effects of NCD-based drug delivery systems, specifically in relation to sensing and monitoring sensors, antimicrobials, anticancer agents, and neurodegenerative treatments. Researchers may link these benefits to their vision, multifunctionality, and adaptability in surface modification. Clarify the boundaries and requirements for clinical trials, both in vitro and in vivo, during the upcoming period.

1.1. Source and rationale behind NCDs

Their numerous origins and environmentally sustainable characteristics have intrigued researchers in the field of natural products.[23-24] NCDs are composite materials composed of economic, non-toxic, predominantly renewable, and easily synthesized natural raw materials. These NCDs can be prepared using water solubilities instead of organic solvents. necessitate external energy for their synthesis. The ongoing availability of raw materials and their reduced production costs have established NCD Synthesis as a protocol specific to the industry. Recent studies have focused on the preparation and investigation of lemon juice for future applications in bioimaging.[25] Various materials have been used to make NCDs, such as carrot roots, egg yolk oil, chitosan, sucrose, raw cashew gum, lotus root, konjac flour, curcumin from mangosteen peel, and N-acetyl-L-cysteine. It is frequently utilized in the preparation of non-communicable diseases (NCDs). Additionally, due to significant environmental concerns, experts are currently concentrating on the recycling of wood waste. Recyclable sources are cost-effective, environmentally sustainable, and safe and contribute to the reduction of societal environmental burdens.

1.2. NCDs: synthesis method and modifications

The selection of a synthesis method is critical, considering both the specific application and the controlled, desirable characteristics of NCDs. Nair et al. identified two primary methods for the synthesis of NCDs, categorized as 'bottom up' and 'top down.'

The 'Bottom-up' approach employs methods such as microwave, thermal pyrolysis, hydrothermal, or solvothermal decomposition to partially dry and lose hydrogen from small organic molecules.

The 'Top-down' method involves fragmenting larger particles into smaller molecules or nanoparticles through techniques such as laser ablation, arc discharge, ultrasonic treatment, or chemical oxidation.[25]

Both methods necessitate external energy for the synthesis process. This segment aims to provide an overview of the preparation of NCDs, including various synthesis approaches, with a focus on the advantages and disadvantages of each method and the modifications involved.

2. Hydrothermal/ Solvothermal Synthesis

The hydrothermal method is one of the most common ways to make colloidal quantum dots because it is simple to set up and produces nearly uniform particles that have a high quantum yield. In a typical procedure, small organic molecules and polymers are dissolved to create a precursor for the reaction and subsequently transferred to a Teflon-lined stainless steel autoclave, utilizing either water or an organic solvent. At elevated temperatures, organic molecules and polymers aggregate to form carbon seed centers, subsequently developing into carbon quantum dots (CQDs) with particulate sizes under 10 nm. These CQDs exhibit fluorescence characteristics and can achieve up to approximately 80% of the maximum quantum yield (QY). The CQDs were synthesized utilizing carbon and nitrogen sources derived from citric acid and ethylene diamine.[17] Quantum Dots exhibit high hydrothermal yields, making them effective biosensors for the detection of Fe^{3+} in living cells.

3. Ultrasound-Assisted Method

Ultrasound necessitates high wavelength intensity to produce NCDs via chemical modifications and is predominantly utilized in a 'top-down' approach. In an acidic or basic environment, glucose underwent ultrasound treatment, which resulted in the successful synthesis of PL CQDs with a diameter of less than 5 nm and a quantum yield of 7%.[18] This method for making carbon quantum dots (CQDs) uses strong ultrasound waves to break down carbon materials into tiny particles in the presence of acid, base, or oxidants. The application of high-energy ultrasound waves eliminates the dynamic post-phase, which facilitates the synthesis of small-sized CQDs. Carbon quantum dots (CQDs) are synthesized for the sensitive and selective detection of Zn^{2+} in aqueous solutions, serving as an effective fluorescent sensing probe. The material with significant applications in sensing and catalytic areas can alter the oxygen-rich groups on the surface of CQD.

Non-conventional diamonds (NCDs) can be improved by adding elements like nitrogen (N), sulfur (S), and boron (B) to make them shine brighter, which helps them be used in more ways. Additionally, one can modify NCDs by adding, removing, or converting their functional groups. Face modifications and passivation enhance the quantum performance of nanocrystalline diamonds (NCDs) by introducing abundant functional groups that interact with ligands such as DNA, proteins, polymers, and organic molecules through electrostatic, amidation, and coordination interactions. NCDs made from the chemical treatment of sugarcane bagasse are treated with organic solvents like toluene, which leads to better compatibility with biological systems, stable light emission, excellent quantum performance, and crystal sizes of 4.1 ± 0.17 nm with a roughness of 5 nm, as shown by various analysis methods including UV–vis absorption, fluorescence microscopy, X-ray photoelectron microscopy (XPS), X-ray diffraction (XRD), high-resolution transmission electron microscopy (HR-TEM), and atomic force microscopy (AFM). Surface passivation is a repetitive and challenging method; therefore, heteroatomic doping is recommended as a direct and efficient strategy. Heteroatomic doping can be done using metal or non-metal materials, which change how electrons are arranged and the surface structure of carbon dots (CDs) and nitrogen-doped carbon dots (NCDs) by adjusting the gap between the conduction band and the valence band, thus enhancing their fluorescent properties.

Non-metallic dopants like nitrogen or silicon increase the amount of carbon dots (CDs), control metallic dopants such as manganese or copper, and change the structure of CDs through processes like carbonization or dehydration that involve chemical groups and metal ions, using carboxyl or amino groups from the starting materials. Various studies indicate enhancements in the quantum yield of nitrogen-doped carbon dots (NCDs), particularly through the synergistic effects that improve fluorescence by chelating the amino group to several functional NCDs. Hylocereus undatus nitrogen-doped carbon dots (H. undatus) emit strong blue light at 400 nm, and their light changes depending on the type of light used to excite them, which was done using hydrothermal methods.

Nitrogen doping using aqueous ammonia was confirmed through energy dispersive spectroscopy (EDS) and FT-IR, while the size was verified by HR-TEM. The fluorescent nitrogen-doped carbon dots (N-CDs) showed lower toxicity to human breast cancer cells (MCF-7) and Lymphoblastoid (L-929) cells, as shown by the MTT assay, and they also demonstrated strong catalytic activity in reducing methylene blue with sodium borohydride.

Aqueous ammonia, utilized as a doping nitrogen, has proven beneficial for the synthesis of carbon dots from Phyllanthus emblica (P. emblica). Triple properties were analyzed: energy-dispersing X-ray spectroscopy (EDX) and FTIR doping of NCDs were confirmed; HR-TEM measurements indicated a value of 4.08 nm; an intensive blue fluorescence at approximately 320 nm was observed, corroborated by NaBH4 for EDS, Raman spectroscopy, and catalytic properties; and the reduction of fiber effluents is advantageous for these findings.[15] Nitrogen-doped NCDs are effectively synthesized using extracts from unripe Prunus mume (P. mume) through hydrothermal carbonization, modified with 25% aqueous ammonia. The resulting products exhibit distinct pH-dependent properties, characterized by high fluorescence at pH 9, as observed through HR-TEM, which reveals an interlayer gap of approximately 9 nm, confirmed by UV-vis and fluorescence spectroscopy measurements. They have demonstrated efficacy as a staining test for minimal cytotoxicity in fluorescence cell imaging.

4. Physical and Chemical Properties

Absorbance refers to the measure of the amount of light absorbed by a substance when light passes through it. This property is critical in various scientific fields, including chemistry and biology, for analyzing the concentration of solutes in a solution. Substances generally exhibit noticeable optical absorption in the UV-visible region.[15] Aqueous CQDs exhibit an absorption range of 260–323 nm, independent of their synthesis method. In certain instances, the n–p transition of C1⁄4O or the p–p transformation of C1⁄4C bonds may cause absorption shoulders in the absorption spectrum. Certain molecules exhibit passive behavior on surfaces, leading to a shift in absorption toward longer wavelengths.

Photoluminescence refers to the emission of light from a material after it has absorbed photons. This phenomenon is significant in various fields, including materials science and optoelectronics, as it offers clues about the electronic and optical properties of substances. Optical absorption or photoluminescence, a classical indicator of quantum confinement, represents one of the most intriguing properties of colloidal quantum dots. Due to the varied and conflicting results of studies on the optical properties of CQD, additional clarification is required regarding dependable PL mechanisms. Dependency on the emission wavelengths and the strength of kex is a notable characteristic of the photoluminescence of carbon quantum dots, attributed to either the varying sizes of nanoparticles or the diverse forms of emission traps present on the surface of these dots. Dispersion of emissive trap sites on the surface of CQDs contributes to the diverse photoluminescence emission, alongside the variation in sizes of CQDs. Surface passivation is essential for attaining photoluminescence properties in colloidal quantum dots with sizes ranging from 1.5 to 2 nm.[16]

Fluorescence quenching of NCDs or CDs exhibits excitation-dependent emissions, which are beneficial for analytical applications, bioimaging identification, and drug delivery. The interaction between CDs and analytes affects fluorescence by either enhancing it through the elimination of quenching effects or diminishing it via quenching mechanisms. Energy transfer falls into three categories: dexter energy transfer (DET), surface energy transfer (SET), and Förster resonance energy transfer (FRET). The process can be categorized into a complex static energy transfer mechanism, an internal filter effect (IFE), and photo-induced electron transfer (PET). The investigation of chitosan-based NCDs for fluorescence quenching involved nitroaromatics with diverse ring substitutions, and it demonstrated that the primary quenching mechanism associated with NCDs was FRET quenching.

Electrochemical luminescence refers to the emission of light resulting from electrochemical reactions.[18] This phenomenon is significant in various applications, including sensors and light-emitting devices. The parameter known as electrochemical luminescence is widely utilized in the investigation of fluorescent emission in semiconductor nanocrystals and has recently attracted the attention of researchers studying colloidal quantum dots (CQDs).[19] 's QD exhibits action comparable to that of CQD, akin to CdSe. The process of CQDs ECL is described as follows: initially, two states, oxidized (R′) and reduced (R) CQDs, are produced through the potential loop. Lowering the electron-transfer process that eliminates the two opposing carriers (Rβ and R), the excited state (R) is generated. Excited CQDs (R-state) return to the ground state via a radiative process through photo. The cathodic ECL power is recognized asgnized to be inferior to the anodic, indicating that Rβ exhibits greater unpredictability compared to R. Furthermore, ECL sensing has demonstrated diverse applications and garnered interest from field researchers due to its stable ECL reaction over time. Elevated ECL emission from CQDs produced via the electrochemical oxidation of graphite was observed within the voltage range of −1.8 to 1.5 V. In semiconductor nanomaterials, surface states predominantly serve as the primary sources for most electroluminescence, which are significantly embedded in contrast to photoluminescence images. The correlation between surface-state transitions and electrogenerated chemiluminescence (ECL) in nanoparticles makes the comparison of ECL and photoluminescence (PL) nanoparticles valuable for identifying the presence of surface up-conversion photoluminescence (UCPL). UCPL is when materials take in low-energy light and then release it as high-energy light, usually seen in specific materials when they are excited in certain ways.

The applications of up-conversion fluorescent materials in biomedical imaging have gained significant importance. Up-conversion photoluminescence (UCPL) of carbon quantum dots (CQDs) has largely remained unchanged. UCPL happens because of a process where two or more photons are absorbed at the same time, causing light to be emitted at a shorter wavelength than the light that was used to excite it. This light is the one used for excitation. UCPL implementation of CQDs offers novel opportunities for cell imaging using a 2-photon light microscope. Carbon quantum dots (CQDs) demonstrate significant emissions in the visible spectrum when stimulated by a femtosecond pulsed laser for two-photon near-infrared excitation (800–840 nm) or an argon-ion laser (458 nm). The typical two-photon light spectrum shows that the UCPL is actually regular fluorescence, which is activated by a part of the second diffraction in the fluorescence response. An FL spectrophotometer can eliminate UCPL by implementing an appropriate long-pass filter in its excitation pathway. Recent studies indicate that UCPL is fundamentally the standard fluorescence (FL) characterized by linear responses, rather than a multiple-photon operation. The standard fluorescence (FL) must be eliminated when the upgraded FL is detected.

Characterization of carbon quantum dots involves the analysis of their structural, optical, and electronic properties. To fully understand how C-dots are made, different methods

can be used, such as nuclear magnetic resonance (NMR), X-ray diffraction (XRD), transmission electron microscopy (TEM), Fourier-transform infrared spectroscopy (FTIR), ultraviolet (UV) spectroscopy, and photoluminescence (PL).

TEM enables the identification of a sample's ultrastructure due to its high resolution of 0.1–0.2 nm. is in high demand across various fields, including science, pharmaceuticals, material science, and other research and development sectors. This technique allows for the study of NP morphology to elucidate information about their shape, size, and dispersion. is widely utilized in the characterization of C-dots. High-resolution TEM can be employed to ascertain the fine structure of C-dots. OTS exhibit a crystalline structure that can be categorized into two types of lattice fringes: interlayer spacing and in-plane lattice spacing. Interlayer spacing is generally approximately 0.34 nm, while in-plane lattice spacing is typically around 0.24 nm. XRD is effectively utilized for the characterization of C-dots, providing insights into particle size, phase purity, and crystal structure. XRD also identifies the crystalline phases of CQDs. 2 synthesis of carbon dots utilizing hexaperihexabenzocoronene as the precursor. Dots about 60 nm wide and 2-3 nm thick were made using high-temperature heating, surface treatment, reduction, and peeling. The resulting C-dots exhibited a fluorescence quantum yield of 3.8%.

Fourier-transform infrared spectroscopy (FTIR) IR has been employed to identify the functional groups present on the surface of C-dots. Ten C-dots primarily consist of oxygen, carbon, and hydrogen. The development of C-dots through the partial oxidation of a carbon precursor results in a surface rich in carboxyl or carboxylic acid groups, hydroxyl groups, and ether/epoxy functionalities. Consequently, Fourier Transform Infrared Spectroscopy (FTIR) serves as an effective tool for investigating these oxygen-containing groups. or to application, modifications were necessary for C-dots to equilibrate potential wells on the energy surface, reduce cytotoxicity, and enhance fluorescence quantum yield. Red C-dots can be characterized through infrared spectroscopy to determine their adequacy of passivation.

Nuclear Magnetic Resonance techniques are frequently employed to acquire structural information regarding C-dots. NMR determines the hybrid types of carbon atoms in the crystalline network and the binding modes between them. Sp2 carbons exhibit resonance in the range of 90-180 ppm, while sp3 aliphatic carbons resonate between 8-80 ppm. The structural characteristics of C-dots are elucidated through NMR measurements, which differentiate sp3 carbons from sp2 carbons. A carbon-13 (13C) NMR spectrum demonstrated the absence of aliphatic carbons, showing no peaks below 120 ppm. A sequence of peaks was observed within the region of 120-150 ppm, predominantly arising from aromatic carbons. NMR spectroscopic analyses confirmed that the C-dots originated from sp2 carbons.

Ultraviolet spectroscopy of the made OTS usually shows strong UV absorption, but the locations of the UV absorption peaks can change a lot based on how it was prepared. 12 C-dots measuring 3.8, 1.5-3, and 1.2 nm exhibit transmission in the NIR, visible (400-700 nm), and UV (350 nm) regions, respectively. 10 maximum emission wavelengths remained constant when activated at different excitation wavelengths.

4.1. Biodistribution and pharmacokinetics

Subcutaneous (s.c.) and intravenous (i.v.) injections represent the primary routes for administering CQDs. On entering the systemic circulation, these quantum dots identify and bind to their target. On attachment to the target, each quantum dot emits light. Fluorescence color is contingent upon the quantum dot size and can be readily detected and identified using various techniques. s, or C-dots, are semiconductor nanocrystals ranging from 1 to 10 nanometers in size, produced through various surface passivation methods, including modification and functionalization. They exhibit low toxicity and high fluorescence, resulting in various applications in bioanalysis, bioimaging, drug delivery, and related fields. It is essential to examine the biosafety studies of C-dots, encompassing biodistribution and pharmacokinetics.

Toxicological assessment of nanocarrier drugs, focusing on biosafety and biodistribution. Ototoxicity presents significant concerns due to its potential to induce severe adverse effects on both diseased and healthy tissues. Consequently, drugs and therapeutic interventions are developed with consideration of cytotoxicity. Quantum dots pose significant concerns regarding cytotoxicity, whereas carbon dots demonstrate greater biocompatibility and reduced toxicity. Different concentrations of CDs, with or without surface passivation or doping, exhibit biocompatibility across various cell lines. The situation is analogous for NCDs, which exhibit biocompatibility with most cell types. To further investigate the cytotoxicity of NCDs, efforts have been made to assess their biocompatibility with MDCK cells, utilizing NCDs prepared with Trapa Bispinosa peel extract. The study demonstrated that cell survival exceeded 80% across all concentrations of these NCDs (1−4 μg/mL). This outcome is likely attributable to receptor-mediated endocytosis and direct binding to cell membranes. Any harmful effects observed may be due to blocking the transporters or channel proteins that help essential substances enter the cells.

The primary aim of a biosafety assessment is to determine the safe doses or concentration ranges for bio-applications, including diagnostics, bio-imaging, therapeutics, and drug delivery, across whole animal systems, organs, integrated organs, and at molecular and cellular levels.[7,2] For global acceptance of NCDs/CDs, these substances must demonstrate efficacy in biological systems and be free from any undesirable or non-specific functions[7,3] Therefore, establishing the biosafety profiles of these

substances is crucial. Numerous evaluations exist both in vivo and in vitro; however, there is a lack of comprehensive comparisons between these two approaches, which are crucial for future biological applications. Additionally, notable differences in response, including species sensitivity (specifically in rats) to these NCDs/CDs, have been observed.[7,4] Li and colleagues examined the biosafety profile of NCDs derived from tender ginger juice. ginger juice NCDs demonstrated superior biosafety and biocompatibility relative to other CDs derived from green tea, EDTA, or glycine. Administration of ginger juice at a concentration of 440 μg demonstrates an inhibitory effect on tumor growth in mice over a period of 14 days. Research indicated that the 50% inhibitory concentration (IC50) of the NCDs on Hepatocellular carcinoma cells (HepG2) was determined to be 0.35 mg/mL. Viability percentage across various cell lines, including human cervical cancer (HeLa), human lung cancer (A549), human breast cancer (MDA-MB-231), and HepG2 cells, exceeded 60% at concentrations up to 12.5 wt% for ginger juice NCDs, indicating their super selectivity and enhanced inhibition efficiency. Consequently, naturally fabricated NCDs demonstrated significant anticancer potential in both in vitro and in vivo studies.

An in-depth in vivo toxicology assessment, both qualitative and quantitative, necessitates an understanding of biodistribution. Distribution studies help to (a) evaluate how well different types of carbon dots target specific areas for diagnosis, (b) clarify how they interact with tissues in a non-specific way, (c) assess how they spread and are cleared from the body to check for toxicity, and (d) examine how carbon dots interact with biological systems through blood and serum tests.[6] A review of the biodistribution of CDs utilizing the radiolabeling method was conducted. Following intravenous administration, the CDs exhibited significant accumulation in the kidney and the reticuloendothelial system, with excretion occurring via fecal and renal pathways. Furthermore, the CDs demonstrated safety at a dosage of 20 mg/kg when administered to animals over a duration of 3 months, as assessed through histological examination, complete blood panel, and time-course blood chemical analysis. Huang et al. conducted a thorough investigation of the in vivo cell imaging and histological toxicity of sugarcane molasses-derived NCDs. A study demonstrated that the primary distribution of sugarcane molasses NCDs was predominantly in the cytoplasm and cell membrane, as measured by confocal laser scanning microscopy in MCF-7 cells. Histological toxicity analysis evaluated the safety of these NCDs concerning the major organs, including the heart, lung, spleen, and kidney. observable damages, including pulmonary fibrosis, inflammatory responses, morphological damage, and necrosis, were detected in these NCDs when compared to the control. Distribution studies are critical parameters that confirm the preferential targeting of CDs/NCDs to the intended site for drug delivery and toxicity evaluation.

4.2. Applications in drug delivery

Recently, non-covalent drug delivery systems have attracted significant attention from researchers owing to their superior applications in drug delivery. Fluorescent characteristics of NCDs facilitate real-time tracking and sensing capabilities for drug delivery support. They serve as safe and biocompatible contrast agents that effectively facilitate the release of water-insoluble drugs. Distinctive applications of NCDs in drug delivery include photo-activated antimicrobial agents, antioxidants, and neurodegenerative agents.

NCDs serve as sensing and tracing probes in drug delivery systems. s exhibit a fluorescence mechanism akin to that of CDs, resulting in comparable real-time tracking and sensing capabilities that enhance drug delivery. characteristics of real-time tracking that elucidate the in vitro and in vivo interactions of nanocarriers with target cells include the visualization of drug translocation through microtubules, diffusion of membrane-bound receptors, receptor-mediated signal transduction, endocytic uptake, monitoring the exchange of CDs/NCDs between cells, and visualization of viral behavior within target cells. sensing properties of CDs/NCDs elucidate cell binding, uptake, and intracellular The sensing properties of CDs and NCDs clarify the processes of NCDs derived from Tulsi (Ocimum sanctum) through hydrothermal synthesis, demonstrating effective uptake of the NCDs in human breast cancer cells (MDA-MB 468), as evidenced by intense fluorescence imaging. images acquired from the fluorescence microscope demonstrated that the NCDs were distributed across the cell membrane, cell nucleus, and cytoplasmic region. The N-doped NCDs derived from cocoon silk, synthesized via the hydrothermal method, effectively functioned as sensors for MCF-7 at a depth of 60−120 nm. (**Figure 3**)

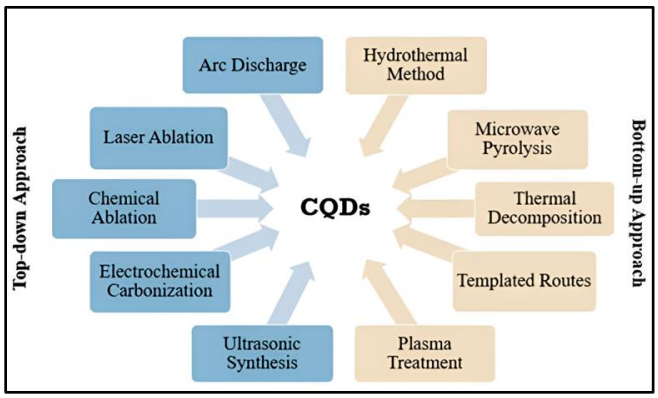

Figure 3: illustrates the applications of carbon quantum dots

The cellular luminescence demonstrated a red shift upon the entry of arginine CDs into the cells. observed red luminescence varied according to the specific cell lines utilized, including embryonic fibroblast cells (NIH 3T3), human embryonic kidney cells (HEK 293), cervical cancer cells (HeLa), and MCF-7 cells, thereby facilitating cell

imaging. various cell lines exhibited distinct fluorescence characteristics, as measured by a microplate reader and fluorescence intensities (red, green, blue), which were statistically analyzed using one-way ANOVA. Nitrogen-doped NCDs synthesized from date kernels via a hydrothermal method incorporating Fe3+ ions exhibited exceptional sensing capabilities for trace levels of zoledronic acid in biological samples. This was achieved through label-free, selective, and sensitive fluorescence signaling, alongside demonstrating significant cellular uptake efficiency. NCDs exhibit remarkable water solubility, photo and ionic stability, and a quantum yield of 12.5%. However, their fluorescence intensity was significantly quenched due to interactions between the functional groups of NCDs and ferric ions, resulting in a fluorescence sensor switch-off mode. Upon the addition of zoledronic acid, the interaction of its phosphate group with the functional groups of NCDs facilitated the removal of ferric ions, thus activating the fluorescence sensor switch-on mode. The synthesized NCDs-Fe3+ demonstrated efficacy as sensors for zoledronic acid, exhibiting a linear range of 0.1 mM to 10.0 mM, a precision of 2.70%, and a detection limit of 0.4 mM. Additionally, they showed low cytotoxicity and effective cellular uptake, as assessed in the human osteosarcoma (MG-63) cell line using the MTT assay. Furthermore, the efficient fluorescent mechanism of CDs/NCDs accounts for their presence in endosomal and lysosomal vesicles, as well as the trafficking pathway of drug-loaded CDs/NCDs, which can be observed using transmission electron microscopy (TEM) and confocal microscopy. The fluorescence property assists in assessing drug loading efficiency and monitoring drug release.

Delivery of antimicrobial agents, abundance, economic viability, and light-emitting properties of NCDs are attracting significant interest from researchers. These NCDs can be synthesized with relative ease and modified with various antimicrobial agents, addressing the growing issue of antibiotic resistance in bacterial pathogens. This contrasts with other nanostructures, which often exhibit limited light responsiveness, higher costs, and toxicity concerns. transmission of these infections can be managed through various methods, including photodynamic inactivation. Substances possessing photosensitizer properties emit visible light in the presence of molecular oxygen, resulting in the generation of microbial reactive oxygen species (ROS). Reactive oxygen species (ROS) interact non-specifically with viral or cellular components, resulting in significant damage and the inactivation of a broad spectrum of microbes, including parasites, fungi, viruses, and bacteria. Consequently, microbes that demonstrate antibiotic resistance are ultimately inactivated in a manner akin to their drug-susceptible counterparts, resulting in nonspecific damage to reactive oxygen species (ROS). This suggests that resistance to non-communicable diseases (NCDs) is improbable.

Delivery of antiviral drugs, as antiviral agents, represents a promising option for the treatment of contagious viral infections, particularly in addressing the pandemic challenges posed by certain viruses, especially coronaviruses. -s were effectively studied for their antiviral properties against porcine epidemic diarrhea virus (PEDV), which serves as a model for coronaviruses. form, cationic CDs were synthesized using a hydrothermal method and evaluated for their inhibitory effects on viral replication through the induction of proinflammatory cytokines and interferon-stimulating genes (ISGs). Virology tests indicated that treatment with Cur-NCDs may modify the surface protein structure of the virus, facilitating the inhibition of viral entry, decreasing the synthesis of negative-strand RNA, suppressing the accumulation of reactive oxygen species (ROS), and inhibiting viral budding [86]. Antiviral efficacy of Cur-NCDs against Enterovirus 71 (EV71) exhibited significant biocompatibility, reduced mortality rates, and provided substantial protection against lethal doses of EV71. The CUR-NCDs were synthesized in a single step by heating CUR at 180 °C and assessed for their antiviral potential. The study indicated that the inhibitory activity against EV1 infection in RD cells was negligible, with a half maximal effective concentration (EC50) exceeding 200 μg ml−1. In contrast, the half-maximal cytotoxic concentration (CC50) was below 13 μg ml−1, suggesting significant cytotoxicity towards RD cells. The EC50 for 0.2 μg ml^{-1} was greater than 1000-fold lower, while the CC50 for 452.2 μg ml^{-1} was greater than 34-fold higher. results indicate that the antiviral potential is significantly influenced by the synthesis of the bioactive compound, which is believed to undergo structural changes through dehydration, polymerization, and carbonization. This process leads to the formation of core-shell NCDs with a pyrolytic-curcumin-like polymer structure while retaining most of the polymeric moieties of curcumin that enhance antiviral properties.[7] The world currently faces a threat from the coronavirus, characterized by its biological diversity and rapid mutation potential. Consequently, there is an urgent need for therapeutic options for infections caused by highly pathogenic human coronaviruses. The viral infection cycle induces significant structural and biological alterations in the host cell, leading to cellular damage. The most effective strategy involves the interaction of the drug moiety with infected cells or viral replication to mitigate the viral infection and its spread.[8] These studies confirm the antiviral potential of NCDs, particularly CUR-NCDs, which can be effectively employed to mitigate the severity of this contagious and life-threatening disease.

Delivery of antibacterial agents using issues such as the rapid transmission of pathogens from contaminated surfaces to hosts and the development of antimicrobial resistance poses significant threats to humanity. Activation of microbial growth through photodynamic therapy presents a promising solution to this situation. employing a green synthesis approach is advantageous due to their abundance, lack of

need for chromatographic purification, cost-effectiveness, small size, biocompatibility, scalable photosensitizing properties, and multicolour emissive characteristics. nanoscale dimensions enhanced distribution within the cytoplasm, and their non-toxic characteristics demonstrated biocompatibility, thereby expanding their applications in imaging and antibacterial drug delivery.[9] The NCDs derived from oyster mushroom (Pleurotus species) have exhibited significant antibacterial activity against Klebsiella pneumoniae, Staphylococcus aureus, and Pseudomonas aeruginosa, as indicated by the MIC assay (MIC value – 30 μg/mL). NCDs demonstrated a dose-dependent inhibition of bacterial growth. antibacterial activity of NCDs synthesized from seaweeds using κ-carrageenan and lemon juice through hydrothermal methods, followed by quaternization with benzalkonium chloride to enhance fluorescence properties, showed promising results. NCDs effectively inhibited E. coli (gram-negative).[9] s, when combined with various agents to enhance fluorescence, have demonstrated potential as effective antibacterial agents.

Delivery of anticancer agents to vehicles designed for targeting diseased tissues through conjugation must exhibit specific characteristics, including abundance, high affinity, flexibility for chemical modification, and binding specificity to cell surface receptors. interactions between ligands and receptors, aptamer targeting, or antigen-antibody complexes facilitate the molecular identification of diseased cells at the affected site. conjugation ability, combined with a diverse submicron size range, positions CDs as a promising candidate for crossing physiological barriers and reaching various tissues, thereby enhancing intracellular internalization and cellular uptake. Consequently, CDs enhance the efficient delivery of the drug to specific sites through conjugation, ensuring the required dosage is achieved. situation is analogous for green CDs. Friendly fluorescent CDs synthesized from Daucus carota subsp. sativus (carrot) facilitate the delivery of mitomycin through hydrogen bonding, which dissociates in the acidic tumor extracellular microenvironment at pH 6.8, thereby releasing the drug. The formulation exhibited an ultra-small size and biocompatibility, enabling a high affinity for cancer cell membranes, which facilitates the internalization of mytocin CDs by Bacillus subtilis cells.

4.3. Neurodegenerative disease

The fundamental approach to treating various disorders with nanomaterials relies on the efficacy, cellular uptake, and transport of drugs to the target organ, cell, or tissue. Neurodegenerative diseases present challenges for drug delivery because of the blood-brain barrier, characterized by a tightly packed layer of endothelial cells.[11] A nontoxic vehicle, specifically CDs in the nanoscale range, synthesized using chitosan via carbonization, demonstrated consistent dopamine release as monitored through in vitro studies at varying pH levels, indicating effective drug delivery across the blood-brain barrier. cytotoxicity observed in IC-21 and SH-SY5Y cell lines indicated approximately 97% cell viability, demonstrating potential efficacy against neurodegenerative diseases. HR-TEM images and Raman spectra (D, G, and 2D bands) confirmed the synthesis of carbon dots (CDs). The particle size was determined to be 3 nm via dynamic light scattering (DLS) analysis. The photoluminescence (PL) properties showed that when excited at 510 nm, the carbon dots emitted light at a peak of 550 nm, proving they are effective for bioimaging in tracking drug delivery.

Numerous studies highlight the effectiveness of quantum dots (QDs) as probes for cancer cells and as diagnostic tools, both in vitro and in vivo, thereby establishing a strong foundation for carbon dots (CDs) and non-conjugated dots (NCDs). A 0-day study on rhesus macaques, non-human primates, subjected to chloroform-dispersed phospholipid micelle QDs/CDs via intravenous injection, showed no acute toxicity with chronic exposure to QDs. Furthermore, after three months, elevated concentrations of CDs were detected in the spleen, liver, and kidneys, as analyzed through inductively coupled mass spectrometry. Nevertheless, a gradual degradation of quantum dots was noted, leading to the accumulation of heavy metals in various organs of the primates, which may potentially impact health and lifespan. Additionally, extensive research reports indicate the beneficial effects of CDs/NCDs. It is recommended that the therapeutic and diagnostic potential of these CDs/NCDs be prioritized, with an emphasis on conducting more clinical trials in a systematic and coordinated manner. Cited studies have been reported concerning the in vitro or in vivo clinical trials of NCDs. A recent study demonstrated the efficacy of NCDs in hemorrhage control, particularly with the aqueous extract of Pollen Typhae carbonisata (PTC). The NCDs were characterized using TEM, HR-TEM, FTIR, UV, and fluorescence spectroscopy, revealing a monodisperse, spherical morphology with a narrow size distribution ranging from 2 to 8 nm. Eight male Kunming mice were categorized into four groups based on their weight (mg/kg): high (8), medium (4), low (2), and control. Sprague-Dawley rats were utilized to analyze the antihemorrhagic coagulation effects. tests indicated that following treatment with PTC-CDs, mice showed a reduction in bleeding time (hemostasis effect), while rats demonstrated a decrease in activated partial thromboplastin time and an increase in fibrinogen and platelet count (coagulation effect). in vivo animal studies demonstrated that NCDs produced by PTC through pyrolysis are effective antihemorrhage agents, thereby expanding the potential of NCDs as drug delivery systems.[9] A separate study demonstrated the wound-healing properties of green chiliDs, synthesized via microwave irradiation, through in vitro and in vivo investigations using MSCs (mesenchymal stem cells derived from Wharton's jelly of the umbilical cord). cells were observed for 21 days to assess wound healing, and the ROS scavenging activity was analyzed using

the MTT assay. A study demonstrated that these non-communicable diseases (NCDs) positively influenced wound healing by promoting micro-vessel formation, modifying tissue granulation distribution, and downregulating the expression of reactive oxygen species (ROS) gene scavenging enzymes.[10] The actual entities of CDs/NCDs remain largely unidentified; thus, further research aimed at elucidating these entities is necessary to address the challenges associated with obtaining ethical approval, thereby facilitating the collection of additional in vivo data. Furthermore, quantum dots have commenced clinical trials for breast cancer, presenting new opportunities for non-communicable diseases. The efficient synthesis of NCDs using natural materials is garnering significant interest among researchers. These nanomaterials are abundant, cost-effective, and nontoxic, while also exhibiting light-emitting characteristics comparable to those of CDs, including narrow emission spectra and enhanced photostability. Additionally, their surface modification capabilities in both in vivo and in vitro settings enhance their applicability. The ability to emit light, especially in the infrared range, allows light to pass through tumors or sick tissues or cells, helping to see their structure. This ability helps with painless imaging and treatment methods, especially for delivering drugs, showing the need for more clinical trials, including larger studies with people.

4.4. Overview and future perspective

This feature article delineates current advancements in the domain of CQDs, emphasizing their synthetic methodologies, size regulation, modification techniques, photoluminescent features, luminescence mechanisms, and applications in biomedicine, energy conversion and storage, catalysis, and sensing challenges. Despite numerous approaches described for the synthesis of CQDs, achieving well-defined structures and accurate sizes remains challenging. It is essential to synthesize carbon quantum dots (CQDs) in an efficient and environmentally friendly manner, with tailored structure and dimensions for property investigations and specific applications. The investigated characteristics of CQDs and their rules are intriguing for a wide range of scientific applications, as evidenced by demonstrations.

The emergence of new qualities and the nuanced adjustment of these characteristics, including novel phosphorescence and contentious UCPL, pose challenges due to the obscure luminous mechanism involved. The amorphous to nearly crystalline internal structure, nonquantitative surface structure, and virtual size polydispersion may obstruct the elucidation of the luminescence mechanism. This issue will be addressed by precise synthesis, meticulous analysis, and astute assessment. Numerous studies have evidenced the versatility of carbon quantum dots (CQDs) in biomedicine: (i) multimodal bioimaging due to their adaptability in surface modification to integrate with other imaging agents, coupled with high biocompatibility; (ii) biosensors for their multifaceted stimulus responses; and (iii) delivery carriers for their diverse combinations with biomolecules or drugs through multiple reactions and stimulus responses.

These characteristics make CQDs a promising candidate for advancing therapeutic strategies and enhancing diagnostic techniques. As research progresses, the potential applications of CQDs in targeted therapy and personalized medicine are expected to expand significantly. This will stimulate research interest in the application of CQDs in optronics, encompassing photovoltaic conversion, photochemical transformation, and energy storage, due to the optical properties of CQDs, including electroluminescence, down- and up-conversion, along with their dual function as electron donors and acceptors, characterized by excellent conductivity and distribution.

5. Source of Funding

None.

6. Conflict of Interest

None.

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