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Review Article

OVERVIEW ON CARBONDOTS

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ABSTRACT

As a prospective material for biosensing, drug administration, and bioimaging, carbon dots (C-dots) have grown in popularity due to their outstanding visual characteristics, great biocompatibility, and low cytotoxicity. As a result, there has been a lot of curiosity about the development, characteristics, and potential applications of CDOTs. Based on variations in precursors and methods of preparation, CDOTs were divided into two classes. The procedure for the formation of CDots was outlined, and their luminescence process was investigated. Also presented were CDOTs' uses in biosensing, medication administration, and bioimaging. For their continued development, CDOTs' challenges and challenges were reviewed.

Keywords: Biosensing, Carbon dots, Biocompatibility and Low cytotoxicity

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INTRODUCTION

Recently, a novel class of zero-dimensional fluorescent carbon nanostructures called carbon dots (C-dots; CDs) was discovered. In 2004, Xu *et al.* made the discovery of C-dots while utilising gel electrophoresis to purify single-walled carbon nanotubes (SWCNTs). Researchers' interest in this brand-new class of luminous carbon nanomaterial grew rapidly [1]. Carbon dots, often known as C dots, are a brand-new type of fluorescent carbon material that is smaller than 10 mm. Due to its makeup and biocompatibility, C dots are emerging as a possible substitute for metal-based quantum dots [2]. Due to their high fluorescence qualities, strong biocompatibility, and low toxicity, C dots were investigated as biosensors, drug carriers for gene transfer, and bio-imaging probes [3].

During the purification of carbon nanotubes, Xu *et al.* discovered a luminous fraction that was later shown to be carbon nanomaterial by atomic force microscopy characterisation [4]. Later, in 2006, Sun *et al.* laser-ablated the carbon target while using argon as a carrier gas and water vapour to produce 5 nm carbon nanoparticles (CNPs) [5].

CNPs were produced in 2007 utilising a simple combustion technique. Later, CDs with other topologies and morphologies, such as carbon quantum dots (CQDs), graphene quantum dots (GQDs), carbon nanodots (CNDs), polymer dots (PDs), and carbonised polymer dots, appeared (CPDs) [6, 7] Due to their unique and noteworthy properties, such as excellent electron conductivity, photobleaching and photoblinking properties, high photoluminescent quantum yield, fluorescence property, resistance to photo-decomposition, alterable excitation and emission attributes, increased electro-catalytic activity, good solubility in aqueous media, excellent biocompatibility, and long-term chemical stability, CDs have attracted a lot of attention from researchers (48-51) [8-10].

Here, we primarily cover the categorization of CDs, their ideal characteristics, general synthesis methods, and key characterization procedures. More significantly, we inform the audience on current CD usage patterns in healthcare applications (viz., their substantial and prominent role in the areas of electrochemical and optical biosensing, bioimaging, drug delivery, as well as in photodynamic therapy and photothermal therapy).

According to Liu *et al.* summary's CDs are currently among the most popular research and development issues in energy materials. Nonetheless, more research into the subject is required to enable new experimental methods to the functional processes of CDs [11].

Advantages

- Excellent yield, high purity, manageable size, excellent repeatability, and reasonable cost
- By altering experimental conditions, a straightforward experimental apparatus may generate particles with various sizes and adjustable morphologies.
- Expensive machinery and large-scale c-dot production
- Simplicity
- Rapid and constant volumetric heating
- Quick synthesis reaction [12, 13]
- Minimal cost, with easy control over important factors, including thereaction vessel's temperature, time, and pressure. The created c-dots are likewise non-toxic and have a high quantum efficiency.
- The process is simple to operate, solvent-free, inexpensive, and capable of producing c-dots on a large scale [14, 15]. It also has a quick reaction time and easy particle size control.

C-Dots's structure and morphology [16, 17]

In general, C-Dots are made up primarily of carbon skeletons, with smaller amounts of two other basic elements like oxygen and hydrogen. They typically have amorphous, spherical geometries and are composed of carbon atoms that have undergone both sp2 and sp3 hybridization and are less than 10 nm. As compared to graphene quantum dots (GQDs), which are made solely of sp2 hybridised carbon arranged in a two-dimensional honeycomb lattice, C-Dots are different. While making C-Dots, several species of carbon-based materials are formed using various precursors and synthesis techniques. Polar groups like carboxyl and carbonyl groups allow for extensive surface modification of C-Dots.

Classification of carbon dots

- GQD (Graphene quantum dot)
- CQD (Carbon quantum dot)
- CND (Carbon nano dot)
- CPD (Carbonized polymer dot)

The inherent state luminescence and quantum confinement effect of CDs are imparted by a significant number of chemical groups in the CQDs, which are nanospheres with crystalline structures. The GDQs

are extremely small pieces of anisotropic graphene that are composed of mono or multiple layers of graphene sheets with graphene networks. Because GQDs have a variety of chemical functionalities on their edge or inside their interlayer defect, they exhibit quantum confinement and edge effects. Although the crystalline or polymeric structures are not visible, the CNDs have a high degree of carbonization with edge effects. Additionally, CNDs do not adequately exhibit the quantum confinement effect. In their ideal form, CPDs are cross-linked nano-hybrids of carbon and aggregated polymers, with a central carbonised core surrounded by either polymeric chains or functional groups [18, 19].

Properties of carbon dots

Electrochemical properties of CDs

1. CDs have superior charge transferability, improved electroconductivity, a bigger effective surface area, lower toxicity, and are comparably more cost-efficient than other carbon-based nanomaterials.

2. There are many functional groups on the surface of CDs, including hydroxyl, carboxyl, amine, etc. These functional groups can provide a lot of sites for surface modification as well as for improved electrocatalytic activity by accelerating intermolecular electroconductivity.

3. Because of the intramolecular charge transferability, CDs may have their electrical properties greatly enhanced by doping them with heteroatoms like nitrogen, phosphorous, sulphur, boron, etc.

4. In electrochemical processes, including the oxygen evolution reaction (OER), hydrogen evolution reaction (HER), oxygen reduction reaction (ORR), and alcohol oxidation reaction (AOR), CDs can significantly improve electrocatalysis [20, 21].

Hetro atom doping

Due to the augmentation of the inherent activity of functional surface sites, distortion of their electronic configuration, adjustment of local densities, and acceleration of adsorption and desorption events, heteroatom-doped CDs exhibit outstanding electrochemical performance [22].

Optical properties of carbon dots

Fluorescent CDs have been extensively employed in a wide range of healthcare applications, particularly in the areas of biosensing, bioimaging, and therapeutic development, because to the astounding optical properties they offer. Studying and comprehending CDs' optical characteristics is crucial if you want to build different CDs for a variety of bio-applications [23].

Fluorescence properties

Fluorescence that is down-converted

A thorough investigation of CDs' luminous process is still pending. The energy gap of CDs gets less as they get bigger. As a result, it is possible to control the fluorescence property of CDs by changing their quantum confinement effect. The surface oxidation that oxygen-containing groups experience at the borders of CDs is what causes the surface flaws that cause fluorescence [24].

Emission characteristics

Controlling the excitation wavelength of CDs can produce different fluorescence emissions, which is accomplished by adjusting a number of physiochemical parameters during CD synthesis [25].

Chemical resistance and photo-bleaching characteristics

Long-lasting, intense fluorescence may be produced by CDs. Typically speaking, CDs exhibit great photobleaching impedance because they are robust to a wide ph range (3–12) [26].

Phosphorescence

Due to its extended lifespan, the room temperature phosphorescence (RTP) feature of CDs is crucial. Although phosphorescence quenching is frequently seen in water due to solvent-assisted relaxation and the presence of dissolved oxygen, the creation of RTP in aqueous media is comparatively difficult [27].

Electro chemiluminescence

During electrical activation, CDs may release photons in the visible spectrum, which is crucial to understanding their electrochemiluminescence (ECL) features. A stable ECL is produced as a result of the increased electron transport caused by the substantial quantity of sp2 carbon in CDs [28].

Synthesis of carbon-dots

The two main methods for synthesizing C-dots are as follows:

- Top-down
- Bottom-up

These techniques seek to produce C-dots with the benefits of being straightforward, affordable, and available from a wide range of precursors [fig. 1]. After the synthesis step, large carbon particles, side products, unreacted precursors, and unreacted precursors are often present in addition to C-dots. Consequently, to get rid of unwanted products and any leftover big carbon particles, centrifugation/washing cycles must be performed numerous times. High-purity C-dots may be made from the supernatant by dialysis [29, 30].

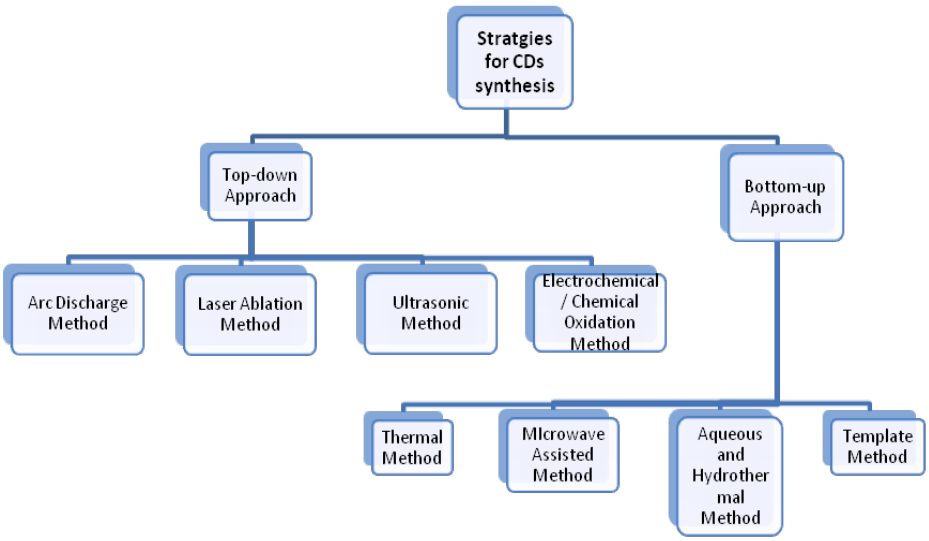

Fig. 1: Strategies for carbon-dots synthesis

Top-down approach

Carbon on a macroscale for the manufacturing of CDs, aceous materials such activated carbon, CNTs, and graphite are widely used through top-down techniques like arc discharge, laser ablation, ultrasonic treatment, and electrochemical procedures. Yet, these procedures are often carried out in environments with high potential, acidity, and energy [31].

Arc discharge method

While CDs produced by arc discharge treatment could have low QYs, the arc discharge approach can be used to prepare CDs from raw CNTs. Additionally, according to Arora and Sharma, the arc discharge method can be used to reorient the C-atoms that are created when bulky C-precursors disintegrate in order to achieve high energy within the reaction assembly during the synthesis of CDs. In general, the arc discharge process uses a lot of composite segments, and it can be challenging to purify these segments [32].

Laser ablation/irradiation method

In comparison to conventional chemical synthesis methods, laser ablation/irradiation is a single-step process that has advantages. The key benefits are the reduced byproduct production and the utilisation of fewer chemical precursors. At extremely high temperatures and pressures of the solid-liquid interface, the laser's light can induce the solid target to produce plasma through thermal evaporation. The plasma grows adiabatically, interacts with the environment, condenses, and causes clusters to form quickly. The nanoparticles are then launched into the liquid, where they interact with the surface of the liquid to create nanomaterials [33].

Electrochemical oxidation/exfoliation method

A potent method for the production of CDs is the electrochemical oxidation/exfoliation method, which utilises various bulk carbon sources as the precursors. Alcohol could be converted into CQDs by electrochemical carbonization in an alkaline environment. These CQDs were shown to grow in size and graphitization level with applied voltage, negating the requirement for labor-intensive passivation and purifying processes. These CQDs were reported to have a quantum yield of up to 15.9% [34, 35].

Ultrasonic-assisted methods

With the advantages of moderate preparation conditions and increased product yield, ultrasonic treatment can optimise the preparation of CDs. Graphite quantum dots (GQDs) of various shapes, sizes, and defect levels were also produced by exfoliating several graphite predecessors. Anthracite was used as a plentiful and affordable precursor in a straightforward one-step ultrasonic cutting procedure for the creation of blue luminous graphene quantum dots (C-GQDs), which are obtained from coal. The graphite rod was electrochemically stripped to form the CQDs, which were then mixed with ammonium hydroxide and subjected to a 3-hour ultrasonic treatment at 80 °C to produce N-CDs [36].

Bottom-UP approach

Samples with clearly specified molecular weight, size, shape, and characteristics can be targeted with C-dots in particular. In addition to offering more control, bottom-up approaches are frequently inexpensive and effective for mass-producing fluorescent C-dots, which are necessary for the practical use of these innovative C-dots. There are numerous methods for carrying out the dehydration and carbonization processes, including enhanced hydrothermal microwave-hydrothermal plasma hydrothermal methods, hydrothermal, microwave, and combustion methods, pyrolysis in concentrated acid, carbonization in a microreactor, and many others [37, 38].

Hydro/solvothermal methods

The most popular "bottom-up" methods for the synthesis of CDs are hydro and solvo-thermal techniques. To create CDs, the organic precursor solution is thermally processed at 150–200 °C in an oven while being sealed inside of a reactor. A typical method for the synthesis of CQDs involves solvo thermal carbonization, followed by organic solvent extraction. The extraction and concentration steps are carried out after the carbon compound is heated with an organic solvent with a high boiling point [39, 40].

Microwave-assisted method

The microwave-assisted process has high CD yields and is easy, affordable, quick, clean, and adaptable. Polar molecules' dipolar moments can interact with a solvent's alternative electric and magnetic fields during the synthesis process to cause molecular heating. This method enables good control of experimental parameters, safety, and reproducibility. Moreover, microwave processing is essential for quickly raising the product yield and lowering the size [41-43].

Template method

- Calcination of the desired CDs in a suitable template or mesoporous silicon spheres is the first stage in the template method's two-phase process for creating CDs.
- Etching procedure for removing supports [44, 45]

Other approaches

In addition to the methods mentioned above, other noteworthy approaches that can be utilised to prepare CDs include thermal pyrolysis, self-assembly, anchor/support-based methods, the metal-organic framework template-based approach, and so on [46].

Mechanism of carbon dots

In general, CDs are incorporated into inorganic substances through chemical adsorption to produce functional inorganic materials based on CDs, which can be accomplished in the following ways:

1) CDs are put together using different synthetic inorganic nanoparticles

2) Creation of CD/inorganic composite materials in a single pot.

Based on these functionalization techniques, CDs can be utilised to generate materials for a variety of applications (including SCs, batteries, and electrocatalysis) by combining them with metals, metal oxides/sulfides, carbon compounds, and polymers [47].

Characterization of C-DOTS

Characterization techniques for CDs

Various types of CDs made using various synthetic methods are currently being studied for their morphology (i.e., size, shape, and structure), topography, elemental composition, crystallographic information, size distribution, and granular orientation using a wide range of characterization techniques. Microscopy, spectrometry, spectroscopy, and diffraction techniques are the main components of these approaches.

Microscopy-based CD characterization

Atomic force microscopy (AFM), transmission electron microscopy (TEM), and scanning electron microscopy are used to characterise CDs (SEM).

Analysis of TEM and HRTEM

In-depth research on C-Dot characterization has recently been published in order to better comprehend their special characteristics. The average size of the C-Dots, which is less than 10 nm, can be utilised to determine their size and form via TEM examination.

Characterization of CDs by spectroscopy

Various spectroscopic techniques such as ultraviolet-visible (UV-Vis), photoluminescence (PL), infrared (IR), Raman spectroscopy (RS), energy dispersive X-ray (EDX), nuclear magnetic resonance (NMR), dynamic light scattering (DLS), and X-ray photoelectron spectroscopy have also been used for the characterization of CDs [48].

XPS and FTIR analysis

The surface characteristics of the C-Dots are investigated using X-ray photoelectron spectroscopy (XPS) and Fourier-transform infrared

spectroscopy (FTIR). While XPS identifies the components, FTIR spectrum catches the functional groups in C-Dots. The hydrophilic groups (-OH,-COOH, and-NH2) found in C-Dots indicate that they are easily dispersed in water [49].

Raman and XRD analysis

Raman spectroscopy is frequently employed to identify materials and analyse the spectrum properties of molecular structures. The structural features of the C-Dots can be further examined using X-ray powder diffraction (XRD) [50].

Characterization of CDs by mass spectrometry

An outstanding method for characterising CDs is mass spectroscopy, which allows for the clarification of the chemical structures of required Nano-sized CDs. His approach uses methods like matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and electrospray ionisation quadrupole time-off light tandem mass spectrometry (ESIQ-TOF-MS/MS) (MALDI-TOF MS).

Photoluminescence and ultraviolet-visible spectroscopy

The optical properties of CDs can be studied using PL and UV-Vis spectroscopies, which are frequently used techniques. These two spectroscopies can also be specifically used to determine the QY of CD. Typically, the UV-Vis portion of the electromagnetic spectrum is where all types of CDs exhibit their activity. Additionally, ex-dependent emission can be seen in the fluorescence of CDs. The most used method for determining the photoluminescent lifetime of CDs is PL spectroscopy. It provides examples of PL spectra at various wavelengths, UV-Vis absorption spectra, and time-resolved PL spectra of sulfur-doped carbon dots (S-CDs) [51].

Applications OF C-DOTS

Analytical applications of C-dots (diagnostic)

C-dots offer a wide range of biomedical applications because of their distinct optical characteristics, substantial surface area, and adaptable surface functionalization capabilities. Although there are still some biosafety issues regarding the use of C-dots, research on *in vitro* cytotoxicity have shown that C-dots have low toxicity and good biocompatibility and that no acute toxicity or morphological alterations have been observed thus far [52].

Imaging

Due to their unique advantages, including their multicolor emission profile, small sizes, low cytotoxicity, good biocompatibility, and excellent photostability-as opposed to the majority of currently used fluorescence tracking dyes—C-dots tend to be superior to current organic dyes and semiconductor QDs. By a dehydration reaction in the solid state, the C-dots were heated in the presence of mannose and folic acid to produce mannose-and folic acid-functionalized C-dots, respectively [53, 54].

Sensing

Because of their distinctive characteristics, such as excitation-dependent emission, higher photostability, low cytotoxicity, and aqueous solubility, C-dots have been used by researchers as bio and chemical sensing materials. A change in their fluorescence properties, which can happen by a variety of mechanisms, including resonance energy transfer, the inner filter effect, and photo-induced electron and charge transfer, is the typical way that this sensing is carried out. Hydrogen peroxide (H2O2), glucose, vitamin B12, L-cysteine, and galactose are just a few of the biological substances and intracellular ions that can be detected with C-dots [55-57].

Metal ion detection

C-dots can be employed for direct chemical sensing of metal ions in addition to biological metal ions. These interactions with the surface functional groups of the C-dot result in the development of novel electron-hole rearrangements, which alters the C-dots' ability to fluoresce. This review paper will mostly focus on C-dots used for mercury sensing, while it can be used to detect other types of metal ions as well. Analysis of tap, lake, and saltwater samples with minimal matrix effects proved the practicality [58].

Other recent diagnostics

C-dots have recently been demonstrated to be helpful for quantifying misused medicines. The quantification of 4-cholorethcathinon has been done using C-dots made from L-arginine using a hydrothermal method. A straightforward one-step dry heating procedure was used to create the C-dots with nitrogen and chloride residues from spermidine trihydrochloride [59, 60].

Biomedical applications of C-dots (therapeutic)

Drug delivery and gene transfer

Moreover, C-dots were employed in the fields of gene transfer and medication administration. As an excellent method for developing cell screening and disease diagnostics, folic acid-modified C-dots by amide condensation reaction were used for the recognition of cancer cells. C-dots with PEI modifications were another common alteration. After transfection for three hours, C-dots DNA composites were able to penetrate the cell. Despite being excited at several wavelengths during the transport process, C-dots nonetheless retained their multicolor fluorescence characteristics [61, 62].

***In vitro* imaging**

It is possible to learn a great deal about the distribution, cytotoxicity, and imaging properties of probes in cells by using *in vitro* imaging. Many cell transfection imaging methods, including Hela, human neural stem cells, 4T1 NIH-3T3, A549, and HepG-, were successfully carried out using C-dots. Endocytosis was the primary mechanism by which C-dots entered cells, where they were primarily found in the cytoplasm. We created a biomolecule that mimics C-dots by subjecting dopamine-mimicking molecules to a neutralising heat treatment. Nuclear localization and imaging could be accomplished using C-dots to "fool" nuclear membranes [63, 64].

***In vivo* imaging**

Because of their clearly defined developmental stages and optical imaging propensity, zebrafish are frequently employed in fundamental medical science to study the progression of diseases, developmental mechanisms, and pattern creation. PEG-modified C-dots have a slower metabolism than unmodified ones. Following intravenous administration, C-dot fluorescence was seen at the stomach, where it accumulated after one hour. At 4 h after injection, the fluorescence signal dropped and gathered at the kidney, showing that C-dots were eliminated from animals through the urine. C-dots that emit blue light were also utilised for *in vivo* imaging, and it was discovered that they may enter the brain [65].

CONCLUSION

This review discusses several CD types, production techniques, and uses as electrode materials in SC and Li-/Na-/K-ion batteries, as well as electrocatalysts for water electrolysis cells, metal-air batteries, and fuel cells using HER, OER, and ORR. The findings of this study demonstrate that CDs are among the most effective Nanomaterials, with remarkable characteristics such as a large specific surface area, adjustable Nanoscale size, quick electron transfer ability, quantum size effect, abundance of surface functional groups, and various defects, which confirm their great potential in electrochemical energy applications.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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