Carbon Dots: An Overview Of Biomass Sources And The Importance In Biomedical Applications

Zeba Nazrin Z, Department of Biotechnology, Nehru Arts and Science College,
zebazakkirz@gmail.com

ABSTRACT

Carbon dots (C-dots) have gained increasing attention for their versatile properties, including nanoscale dimensions, photoluminescence, and surface functional groups, rendering them invaluable across various systems. Among these, biomass-derived carbon dots have emerged as a promising avenue due to their abundant availability and capacity to transform into high-value compounds with significant applications. Through a meticulous analysis of recent literature, we explore the different biomass sources for carbon dot synthesis and the potential biomedical utilities of carbon dots from diverse sources.

INTRODUCTION

Carbon quantum dots (CQDs) were first identified in 2004 through the examination of the residual substances produced during the electrophoretic purification of carbon nanotubes [1]. Since this discovery, interest in CQDs and the various techniques for their synthesis has steadily increased. CQDs can be synthesized using a bottom-up approach involving the assembly of carbon-containing molecules such as carbohydrates, amino acids, acids, and components sourced from biological materials, with plants being a commonly utilized source [2]. Synthesis methods encompass hydrothermal/solvothermal treatment, high-temperature pyrolysis, microwave irradiation, and electrochemical oxidation, among others [2]. Following synthesis, the resulting product undergoes additional processing steps such as centrifugation, filtration, or dialysis to isolate the larger particles.

CQDs are typically characterized using various analytical techniques, including elemental analysis (CHONS), X-ray photoelectron spectroscopy (XPS), photoluminescence spectroscopy, and UV-vis spectroscopy. To approximate the structure of CQDs, a combination of Fourier-transform infrared spectroscopy, X-ray spectroscopy, and high-resolution transmission electron microscopy is commonly employed [3]. Notably, CQDs are categorized as zero-dimensional nanomaterials, meaning all their dimensions fall within the nanoscale (below 100 nm) [4]. This unique dimensional property confers special characteristics distinct from bulk materials. One key attribute is the quantum confinement effect on electrons, elucidated by the "particle in a box" model from quantum mechanics, particularly applicable to semiconductors [5].

Carbon dots (C-dots) have emerged as a versatile class of nanomaterials with promising applications in diverse fields. One particularly intriguing aspect is their derivation from biomass sources, such as agricultural waste, fruit peels, and other organic materials. This approach not only offers a sustainable and environmentally friendly method for nanomaterial synthesis but also taps into an abundant and renewable resource. Biomass-derived carbon dots have gained significant attention for their potential to be transformed into high-value compounds with numerous applications, including in biomedicine.

In addition to biomass-derived carbon dots, researchers have explored the synthesis of carbon dots from various other sources, including graphene, carbon nanotubes, and organic molecules. These alternative sources offer distinct advantages in terms of scalability, tunability, and functionalization, expanding the repertoire of carbon-dot materials available for biomedical applications. The biomedical field has witnessed a surge of interest in utilizing the unique properties of carbon dots from diverse sources for applications ranging from bioimaging and biosensing to drug delivery and therapeutics.

BIOMASS-DERIVED CARBON DOTS

Focusing on green chemistry principles, particularly prioritizing waste reduction and reliance on renewable resources, the utilization of biomass emerges as the preferred approach in these processes [6]. Residual biomass, including agricultural and household waste from industrial food processing, stands out as a major contributor to land pollution, exerting significant ecological pressures [7]. Consequently, numerous investigations highlight the potential of plant-based biomass as a precursor for CQDs, owing to its abundant availability and high carbon content.

The fruit extract of Chionanthus retusus (*C. retusus*) was used for the synthesis of nitrogen-doped carbon dots using a simple hydrothermal-carbonization method, yielding a quantum yield of 9%. Their ability to detect metal ions and their impact on cell viability and bioimaging applications were investigated. N-CDs show promise as dual-purpose probes, capable of detecting cellular metal ion pools (Fe^{3+}) and early signs of yeast infections in biological samples [8]. Carbon quantum dots (CQDs) with both down- and up-conversion photoluminescence (PL) properties were synthesized via a one-step, eco-friendly process involving low-temperature carbonization of cabbage as the carbon source, achieving a quantum yield of 16.5%. The purified CQDs exhibited minimal cytotoxicity at higher concentrations (500 μg ml^{-1}) in cell viability tests against HaCaT cells, a non-tumorigenic human keratinocyte cell line. Under confocal microscopy, CQD-treated cells displayed distinct blue, green, and red colors during in vitro imaging. The environmentally friendly synthesis, high biocompatibility, excellent optical properties, low cytotoxicity, and effective cellular imaging capabilities of cabbage derived CQDs indicate their promising potential in various biomedical applications [9].

Water-soluble carbon nanodots co-doped with nitrogen, sulfur, and phosphorus were synthesized from culinary waste onion peel powder (OPP) through a brief microwave treatment. These onion-derived carbon nanodots (OCND) consist of amorphous nanodots with hydrophilic groups, displaying vibrant and stable fluorescence upon excitation at 450 nm and emission at 520 nm, along with exhibiting free radical scavenging properties. OCND demonstrates excellent stability across various pH levels and under UV exposure [10]. Furthermore, lemon and onion were utilized for the first time in the synthesis of carbon dots (CDs), showcasing satisfactory optical properties and boasting a high quantum yield of 23.6%. A fluorescent resonance energy transfer between CDs and riboflavin was achieved, enabling the development of a successful method for quantifying riboflavin in supplements [11].

Nitrogen-doped carbon quantum dots (N-CQDs) were successfully produced through a one-step hydrothermal method using rice residue and glycine as carbon and nitrogen sources. These N-CQDs, which have a high quantum yield of 23.48%, have been notably employed as probes for detecting Fe^{3+} ions and tetracycline (TC) antibiotics, demonstrating exceptional performance. By exploiting the linear correlation between fluorescence intensity and Fe^{3+} concentration, the N-CQDs serve as a straightforward and efficient sensor for ultrasensitive Fe^{3+} detection across a broad range [12]. Utilizing hydrochar derived from food waste processed via hydrothermal carbonization (HTC), multicolor carbon dots (C-dots) were synthesized, exhibiting unique selectivity for detecting Fe^{3+} ions as fluorescence probes. This breakthrough not only highlights the potential for obtaining high-value products from food waste but also paves the way for innovative advancements in carbonaceous materials, promoting the utilization of "green resources" [13]. Furthermore, carbon quantum dots (CQDs) derived from spent coffee grounds (SCG) as biomass demonstrate visible-light-driven antimicrobial activity following microwave treatment. Integration of CQDs synthesized from SCG with organic acid (malic acid) facilitates practical application in washing fresh produce, such as apple surfaces [14].

BIOMEDICAL APPLICATIONS OF CARBON DOTS

Carbon dots (CDs), characterized by their exceptional properties such as high quantum yield (QY), low toxicity, photostability, and resistance to photobleaching and degradation, offer considerable promise in biological applications [15].

BIOIMAGING

Bhamore et al. utilized Manilkara zapota fruits to synthesize carbon dots (CDs) emitting multiple colors. These biocompatible and non-toxic CDs, ranging from 1.9 to 4.5 nm in size, hold great promise for bioimaging applications [16]. While achieving CDs with specific functionalities for diagnosis and therapy remains challenging, their potential in bioimaging, where selective labeling is not required, is noteworthy. To enhance CD selectivity, Zhu et al. developed ruthenium-doped CDs (Ru-CDs) using a one-pot hydrothermal method [17]. These hydrophilic Ru-CDs, exhibiting red emission with a quantum yield of 20.79%, were biocompatible and evaluated for applications in bioimaging, cancer therapy, and light-induced DNA cleavage. In a separate study, Gudimella et al. synthesized CDs from citrus peels, resulting in biocompatible CDs with low toxicity and notable radical scavenging properties [18]. These CDs, when conjugated with folic acid, can serve as biological labels for cell imaging. Additionally, Jiang et al. produced CDs using neutral red and levofloxacin as precursors through microwave-assisted synthesis [19]. Neutral red contributed to the formation of the carbon core and emission centers, while levofloxacin, with its nitrogen-containing group, attached to the CD surface via an amide bond, enabling binding to RNA. With a high quantum yield of 22.83% and selectivity for RNA, these CDs hold promise for monitoring RNA dynamics in cells and phase separation procedures.

GLUCOSE SENSING

Diabetes mellitus, a prevalent metabolic disorder impacting individuals across age groups, particularly adults and the elderly, poses significant health challenges due to its potential for multi-organ damage. Continuous monitoring of blood glucose levels is imperative for effective disease management. Numerous studies have aimed to develop reliable methods for detecting glucose levels, with carbon dots emerging as promising candidates owing to their impressive fluorescent properties. In a study led by Yen-Linh Thi Ngo et al., a novel paper-based biosensor employing both colorimetric and fluorescent techniques was devised for glucose detection. The researchers synthesized metal oxide hybrid nitrogen-doped carbon dots, showcasing intrinsic peroxidase-like activity. This facilitated the oxidation of colorless TMB (3,30,5,50-tetramethylbenzidine) to blue-colored oxidized TMB (oxTMB) with an absorption peak at 652 nm in the presence of hydrogen peroxidase. Glucose detection relied on the fluorescent quenching of metal oxide hybrids with nitrogen-doped carbon dots and TMB, exploiting the inner filter effect induced by H_2O_2. Quantitative determination of glucose was achieved by monitoring fluorescence and absorbance intensities upon sample addition, with a reported detection limit of 0.85 mM through fluorescent detection. Moreover, the integration of a colorimetric readout on a paper-based device with smartphone platforms enabled on-site glucose analysis without the necessity of a spectrometer [20]. Su, Ke, et al. conducted a study where they synthesized nitrogen-doped carbon dots (N-CDs) using locust powder via a self-exothermic reaction. These N-CDs displayed peroxidase-like activity, catalyzing the oxidation of 3,3′,5,5′-tetramethylbenzidine (TMB) in the presence of H_2O_2 to form a blue oxidized product (TMBox) with a peak absorption at 654 nm. Optimization of reaction conditions showed N-CDs had strong affinity for both TMB and H_2O_2. They developed a smartphone-based colorimetric method for glucose (Glu) detection by recording 1/L values of TMBox solution through an iPhone application, achieving a detection limit of 1.09 μM. [21].

CHOLESTEROL SENSING

Recent concerns over cardiovascular diseases, which contribute significantly to global mortality rates, have spurred the development of novel diagnostic tools. One such advancement involves a fluorescence probe composed of carbon quantum dots (CDs) and gold nanoparticles (AuNPs) designed for efficient cholesterol sensing. The synthesis of the gold-carbon-dot nanohybrid (AuCD) utilized a simple hydrothermal method. The resulting immobilized cholesterol oxidase on AuCD exhibited notable fluorescence emission upon excitation at 360 nm. Förster resonance energy transfer (FRET) was observed between Ch-AuCD and graphene oxide, leading to a visible fluorescence intensity reduction. This reduction was reversed upon the addition of varying cholesterol concentrations, resulting in fluorescence intensity enhancement. This "on-off" mechanism enabled the efficient detection of cholesterol within the concentration range of 10–100 nM, with a lower detection limit of approximately 10 nM. Furthermore, the probe's selectivity for cholesterol was confirmed through analysis of various interfering analytes, including ascorbic acid, urea, glucose, galactose, and L-cysteine. This FRET-based "nano-switch" offers high selectivity and sensitivity for cholesterol sensing [22].

SENSING OF PATHOGENS

Food-derived carbon dots (C-dots) have been developed for the label-free detection of food pathogens using photoluminescence techniques. Kailasa et al. utilized sugarcane juice as a carbon source to produce C-dots, which were employed as fluorescence labels for E. coli and the yeast Saccharomyces cerevisiae. Cytotoxicity studies revealed that these nanoparticles were non-toxic up to 400 mg/mL, a concentration 10,000 times higher than their effective concentration for fluorescence labeling of both organisms [23]. In another study, Kailasa's group utilized apple juice as a carbon source to synthesize hydrophilic C-dots through a hydrothermal process at 150°C for 12 hours. These C-dots were applied for the detection of bacteria such as Mycobacterium tuberculosis and Pseudomonas aeruginosa, as well as the fungus Magnaporthe oryzae, via endocytosis. Distinct fluorescence images of these microbes were obtained under excitation at 405, 488, and 561 nm at a C-dots concentration of 10 μg/mL. Similar to the C-dots derived from sugarcane juice, these C-dots were not bactericidal but exhibited effective labeling at significantly lower concentrations [24].

CONCLUSION

In summary, this review highlights the increasing significance of biomass-derived carbon dots in biomedical research. Their abundant availability and transformative properties make them appealing for further exploration in research and development. Additionally, we discuss the potential applications of carbon dots synthesized from various sources in biomedicine. Our examination includes synthesis techniques used, distinctive attributes, and their utilization in diverse areas such as bioimaging, pathogen sensing, and toxicological studies. Carbon dots demonstrate considerable potential for advancing biomedical research and hold promise for enhancing research outcomes in the future.

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