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Carbon Dots as Antimicrobial and Antiviral Nanomaterials and Drug Delivery Applications

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ABSTRACT

The methodologies for synthesizing Carbon Dots (CDs) in general are easy Carbon Dots are easy to produce, methodologies are simple, and can be made from polymers, carbon-based materials, biomass, and other carbon precursors. In general, CDs are carbon-based nanomaterial with a small size of 10 nm or below. Among its features are low toxicity, biocompatibility, and great chemical stability with photoelectric properties. CDs have targeted shipping applications that can be monitored with fluorescent properties. Recently, CDs have gained interest in biomedical applications due to their excellent antibacterial and antiviral activities and their use as drug delivery Nano carriers.

Introduction

Carbon Dots

CDs a novel class of carbon nanomaterials discovered in 2004 have gained considerable attention due to certain specific characteristics: excellent photoluminescence, high quantum yield (QY), low toxicity, biocompatibility, small size, chemical stability, and inexpensive and easy synthesis [1,2]. The size of CDs is less than 10 nm, made of carbon, an element abundant and generally nontoxic. CDs are particularly attractive in many applications such as bioimaging, biosensing, and nanocarriers for drug delivery [3] (Figure 1). CDs are mainly classified according to their different formation mechanism, surface functional groups, and properties: carbon quantum dots (CQDs), graphene quantum dots (GQDs), carbon nanodots (CNDs), and carbonized polymer dots (CPDs). In addition, associations can be built among them by changing the carbonization degree and graphene layer (4).

Structure and Properties

Carbon dots have been characterized to analyze their physic properties and to understand the mechanisms associated with their properties. Common techniques are transmission electron microscopy (TEM) to obtain morphology, size, and agglomeration by demonstrating that they are very small of approximately <10 nm and quasi-spherical form, Fourier-transform infrared spectroscopy (FTIR) to identify specific functional groups, X-ray diffraction for the evaluation of the crystalline nature of CDs. It is also known that CDs are usually the product of the carbonization of organic precursors, mainly consisting of sp^2 /sp^3 -hybrid carbon or sp^2 -domains embedded in amorphous carbon [5,6]. They also have several functional groups on their surface such as carbonyl, carboxylic and hydroxyl groups, which provide a rich part in oxygen and favor it to be soluble in water, in this way it can be useful in

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a wide variety of applications [7]. Carbon dots offer the flexibility to be able to manipulate both their structure and their properties depending on what type of carbon and organic molecules are made [8]. CDs have great properties such as

1) Optical absorption depending on the method of synthesis,
2) Excitation-dependent photoluminescence. The fact that the emission color of the CDs can be adjusted according to the excitation wavelength makes it very attractive for various applications.
3) Photo induced electron transfer,
4) Electrochemoluminescence,
5) Proton adsorption and
6) Low toxicity [3,9].

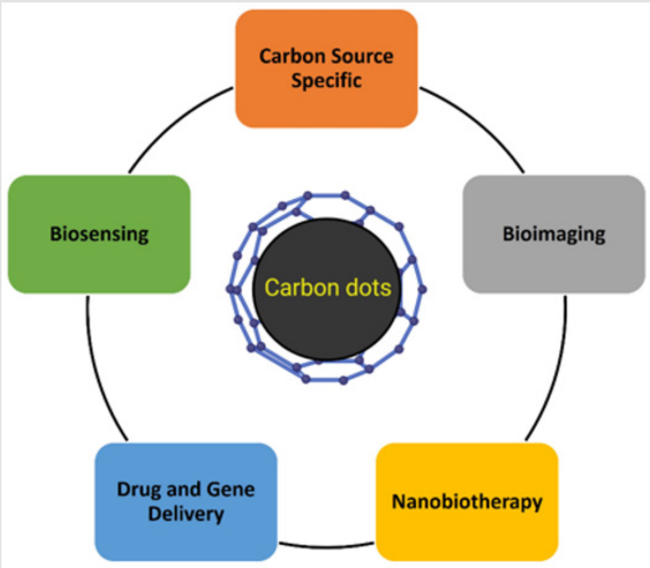

Figure 1: Biomedical applications of Carbon Dots.

Synthesis of Carbon Dots

According to the strategies, there are two types of synthesis “top-down” and “bottom-up” [10]. The top-down approaches include arc discharge, acidic exfoliation, laser ablation electrochemical oxidation, and microwave-assisted hydrothermal synthesis, where CDs formed from a larger carbon structure. This advantage is abundant raw materials, large-scale production, and simple operation [7]. The obtained CDs generally present graphite-like structures with weak fluorescence luminescence is a synthetic process and requires complex steps [11]. In the bottom-up synthesis, it has been used small molecules carbonized as precursors for example citric acid. This technique is efficient to produce fluorescent CDs. It has been produced under simple and mild conditions through microwave or hydrothermal reactions [12].

CDs Antimicrobial Activity

One of the biggest public health problems that fear is antibiotic resistance. This is due to the abuse of antibiotics, which has allowed new mechanisms of Resistance to be generated that is why new strategies are needed that are fast, easy to produce, affordable. These strategies include Carbon dots since it has been reported to have antimicrobial activity, due to its photosensitizer properties to produce oxidative stress by ROS and attack a wide range of microbes in the following ways: with physical or mechanical damage to the cell wall, disrupting the EPS matrix, causing biofilm splitting, inhibiting growth and even killing [13] Heteroatoms in carbon dots enhance the generation of ROS due to extra free electron incorporation in carbon dots. The functional characteristics of Carbon dots depend strictly on the precursors from which they are made, solvents that are used, as well as the functional groups of their surface. It has been shown that depending on the load of the carbon dot interacts or not with the bacteria. Something more interesting is that when preparing the CDs they can incorporate heteroatoms; they are called doped CDs, to make their activity more powerful [14]. Another strategy is to combine CDs with antimicrobial agents for example sodium hypochlorite (NaOCl), hydrogen peroxide (H_2O_2) to reach the maximum antimicrobial effect [15].

CDs Antiviral Activity

Viral diseases continue affecting millions of people around the world causing serious problems, many alternatives have been proposed to try to avoid them, and one of the strategies is CDs based on different carbon sources and synthesis methods, which can bind to viral proteins to stop multiplication or blocking the entry of the virus into the cell. The studies that exist are very recent but this activity has already been demonstrated with CDs from different methods and precursors, for example, curcumin carbon dots to prevent the entering and replication of coronavirus, benzocaine carbon dots to prevent the attachatchment of dengue, and zika virus, carbon dots to inhibit the binding of human norovirus, glyzhyrric acid carbon dots to inhibit the replication of herpes virus, boronic acid functionalized carbon dots to prevent entry step of human immunodeficiency virus 1, etc. The action of the CDs depends on the size, Surface, and load [16,17]. Lin et al., 2019 have suggested that C-dots can act at different levels of infection [18]. Actually, with the SARS-COV2 coronavirus pandemic in which there are no drugs to completely cure, CDs have been proposed as alternatives to stop the infection inside people's bodies or detect it [16]. In a study conducted by Lai-Di Xu et al 2021, they used a new lateral flow immunochromatography technology in which they used red emission-enhanced CDs based-silica spheres as signals to detect SARS-COV2. In addition, the incorporation of the desired functional groups with QDs could effectively interact with the virus input receptors and affect genomic replication [19].

There are already some analyses that suggest that the cationic surface charges of CQDs interact with the negative RNA chain of the virus-producing reactive oxygen species within SARS-COV2. Also incorporating some specific functional groups to these CQDs would interact with the virus receptors and thus inhibit replication. One of the areas of opportunity to attack the SARS-COV2 virus is to look for alternatives to make CDs more efficient, perhaps using natural compounds to make them such as curcumin [20]. In general, we are facing a new field of research because although it has been shown that CDs have antiviral activity, many of these are *in vitro* and *in vivo* there are few so it is necessary to do more to understand the mechanism of action and know the real potential of these.

Conclusion

CDs have emerged as a new type of Nano carrier, breaking down barriers of production methodologies using carbon abundant raw materials and have begun to take an important place as nanomaterials with great potential for applications in the field of biomedicine. The antimicrobial and antiviral properties of CDs give them a promising future as new nano-drugs against resistant and emerging pathogens.

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