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Biomedical Applications of Carbon Nanodots: Antibacterial, Antibiofilm and Antiviral Properties

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ABSTRACT

Carbon nanodots (CNDs), a new class of zero-dimensional carbon-based nanomaterials typically of size less than 10 nm in diameter, have emerged as highly versatile nanoplatforms for biomedical applications. The unique physicochemical features of CNDs - including rare and extreme hydrophilicity, tunable biocompatibility, proper balance of amorphous and crystalline structure (hybrid hetero structure), extensive oxygen surface functionality and ease of surface functionalization, characteristic light absorption and emission (photoluminescence, PL), have driven extensive global research into their therapeutic and diagnostic potential. Among the most significant areas of investigation are their antimicrobial properties, particularly antibacterial, antibiofilm, antifungal and the antiviral activities. The rise of multidrug-resistant (MDR) microorganisms and persistent viral infections has intensified the search for alternative strategies to overcome the conventional antimicrobial resistance mechanisms. CNDs, due to their nanoscale interactions with microbial membranes and biomolecules as well as due to their peculiar PL property, represent model candidates for such application. They are the promising carriers of the free radical generators like the Zn-doped CuO and kill the MDR bacteria almost instantaneously. CNDs facilitate easy mobility of such free radical including (reactive oxygen species, ROS) generators to the remote and inaccessible places in the cell compartment. This review critically examines the latest research trends in the biomedical applications of CNDs, with particular emphasis on their mechanisms of antibacterial, antibiofilm, and antiviral action, and their synthesis-dependent functional behavior. New insight is provided on future prospects for clinical translation.

Keywords: Carbon Nanodots; CNDs; Antimicrobial Nanomaterials; Antibiofilm Activity; Antiviral Activity; Nanobiotechnology; Nanomedicine

INTRODUCTION

Nanobiotechnology has revolutionized biomedical science by enabling the development of biocompatible materials with properties that can be precisely engineered at the nanoscale. Among various nanomaterials investigated, carbon-based nanomaterials have received significant attention due to their chemical stability, tunable surface chemistry, and relatively low toxicity compared to metal-based counterparts. These carbonaceous quantum dots, or carbon nanodots (CNDs), have several advantages over traditional semiconductor-based quantum dots. They possess outstanding photoluminescence (PL), fluorescence, biocompatibility, biosensing, bioimaging, photostability, feedstock sustainability, extensive surface functionalization, bio-conjugation, colloidal stability, eco-friendly synthesis (from organic matter such as glucose, cellulose [Indra Neel Pulidindi, Tharikka S, Deepak Nallaswamy Veeraiyan, Highly fluorescent, ultra-small nitrogen doped carbon nanodots from cellulose, Indian patent application, 2026]. carboxy methyl cellulose. [Indra Neel Pulidindi, John T D Caleb, Jeevanathi J, Deepak Nallaswamy Veeraiyan, Carboxy metyl cellulose is a sustainable feedstock for the multifunctional nitrogen doped carbon nanodots, Indian patent application, 2026]. coffee, tea, and various other biomass), low toxicity, and cost-effectiveness [1, 2]. CNDs represent a relatively recent addition to the family of nano allotropes of carbon materials and are characterized by their quasi-spherical morphology, ultra-small size, abundant surface functional groups, and intrinsic fluorescence. Representative CNDs from glucose urea reaction were shown in the TEM image in Fig. 1. Their characteristic light absorption features were shown in Fig. 2.

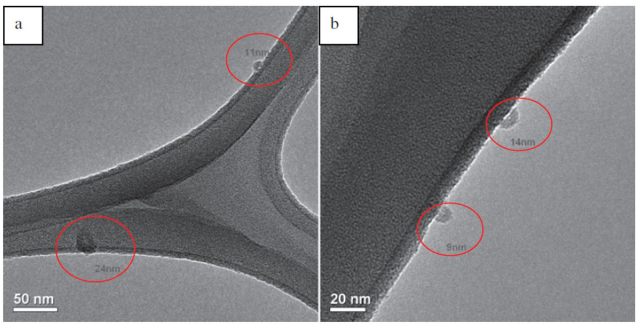

Figure 1: TEM images of the caarbon nanodots (CNDs) from the hydrothermal reaction of carbonization of glucose in alkaline (urea) environment (a) fresh CNDs and (b) CNDs of 3 months age [2].

The edges of the meshes in the TEM grid made up of Copper coated with carbon were seen in the TEM images. In addition, the "dots" around 9-15 nm sticking to the edge of the meshes of the TEM grids were observed. The quasi spherical nanoparticles seen are the CNDs formed by the carbonization of glucose in the presence of urea in a hydrothermal reaction [2]. A colourless solution of glucose and urea before heat treatment is shown in Fig. 2A (a). This solution suddenly changes to dark yellow colour. The dark yellow colour after the hydrothermal reaction at 120 ^{0}C for 20 min. in this case is typical of the carbonization of carbon precursor glucose. Formation of carbon nanodots from the carbonization of glucose is evident from the characteristic absorption band with a λ_{max} at 275 nm (Fig. 2 B b). The broad and intense absorption band in the UV region is attributed to the aromatic π-π^* transition in the –C=C- chromophore generated in the hydrothermal reaction. Moreover, a shoulder is seen at 330 nm. Such a shape of UV band with a shoulder is typical of doping of the hexagonal ring of six carbon atoms in the aromatic carbon nanoparticle structure with the heteroatom namely nitrogen. Urea with inbuilt nitrogen, under the synthetic condition, facilitates the doping of carbon nanoparticle structure with the hetero atom nitrogen enhancing the absorption and emission property.

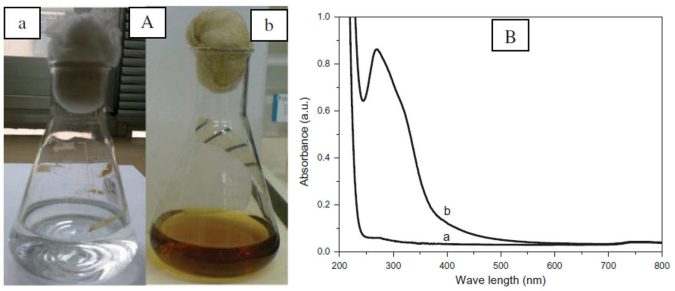

Figure 2A: Erlenmeyer flask with a solution of glucose and urea before (a) and after (b) hydrothrmal reaction; B. UV-Vis spectrum of the afore mentioned samples [2].

Originally discovered as fluorescent by-products during carbon nanotube purification processes, CNDs have since been synthesized through diverse top-down and bottom-up approaches using a wide range of precursors including organic molecules, biomass, polymers, and waste materials. Their surface typically contains oxygen- and nitrogen-containing surface functional groups such as hydroxyl, carboxyl, carbonyl, and amine moieties, which confer hydrophilicity and enable further chemical modification. The core of the CNDs is a unique combination of both amorphous and crystalline structure quite often with a d-spacing value of ~ 0.307 nm which is lower than that of classical graphite. These features make CNDs highly adaptable for biomedical applications including bioimaging. Water soluble carbon nanoparticles generated in situ in the glucose–urea solution, upon hydrothermal reaction, have been effectively exploited as a sensor for the determination of mM levels of glucose in the analyte [2], drug delivery, biosensing, and antimicrobial therapy and for the detection of the antibiotics [3]. Fine tuning of size of the carbon particles is possible by changing the reaction time and the synthesis temperature. One such fine example is provided in the specific case of the synthesis of carbon nanoparticles using glucose as the carbon precursor and ampicillin as the source of hetero atoms (both N and S). Such hetero atom doping in the carbon structure caused the nanoparticles of carbon (doped CNDs) to emit blue colour. When the reaction time is changed from just 40 min (Fig. 3 a) to 12 h (Fig. 3 b) the size of the CNDs is increased from 40 nm to 0.88 µm. The application of nanoparticles is different and the application of microparticles is different. In the present instance, the CNDs (Fig. 3a) were used as sensor for the antibiotic ampicillin. Moreover, the CNDs can be functionalized by specific antibacterial, antifungal materials like the Zn doped CuO [4] developed by Gedanken at al and enrich the CNDs with the ability to kill instantaneously multi drug resistant bacteria.

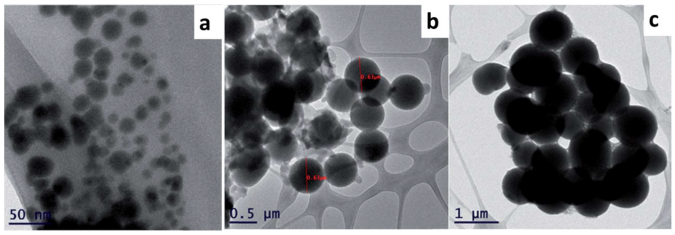

Figure 3: Carbon particles from the hydrothermal reaction of glucose and ampicillin at different temperatures (T, 120 and 150 °C) and for different reaction times (t, 40 min to 12 h): (a) Carbon nanodots (CNDs) of size < 40 nm (t, 40 min; T, 120 °C); (b) Carbon particles of size 0.63 µm (t, 4 h; T, 150 °C); (c) Carbon particles of size 0.88 µm (t, 12 h; T, 150 °C) [3].

The emergence of antimicrobial resistance has become a major global health concern, necessitating the development of alternative therapeutic strategies. Conventional antibiotics are increasingly ineffective against resistant bacterial strains and biofilm-associated infections. Similarly, viral outbreaks and emerging viral pathogens continue to challenge existing antiviral therapeutics. In this context, CNDs have attracted considerable interest as multifunctional antimicrobial agents capable of targeting bacteria, biofilms, and viruses through mechanisms distinctly different from traditional drugs.

MAIN CONTENT

Physicochemical Properties of Carbon Nanodots (CNDs) Relevant to Biomedical Applications

The biomedical performance of CNDs is closely linked to their physicochemical characteristics. Their nanoscale size enables

efficient cellular penetration and interaction with microbial membranes. Surface functional groups determine solubility, charge distribution, and interactions with biomolecules, while quantum confinement and surface state effects contribute to photoluminescence and photodynamic properties. One of the defining advantages of CNDs is their generally favorable biocompatibility profile. Compared to heavy metal-based quantum dots, CNDs exhibit reduced cytotoxicity and lower environmental impact. Their surface chemistry can be tailored through doping with heteroatoms such as nitrogen, sulfur, phosphorus, or boron, which modifies the electronic structure and enhances the antimicrobial activity. The ability of CNDs to generate reactive oxygen species ROS under light irradiation is particularly important for antimicrobial applications. Photoluminescent CNDs can act as photosensitizers, producing singlet oxygen and other reactive species capable of damaging microbial membranes, proteins, and nucleic acids. Even in the absence of external irradiation, certain surface-engineered CNDs exhibit intrinsic antimicrobial activity through membrane disruption and oxidative stress induction.

Antibacterial Properties of Carbon Nanodots

The antibacterial activity of CNDs has been widely investigated against both Gram-positive and Gram-negative bacteria. Numerous studies across different regions have demonstrated that CNDs can inhibit bacterial growth through multiple synergistic mechanisms. The antibacterial activity of CNDs is primarily mediated through interactions with bacterial cell membranes. Positively charged or functionalized CNDs can bind to negatively charged bacterial surfaces, leading to membrane destabilization and increased permeability. This interaction results in leakage of intracellular components and eventual cell death. Another key mechanism involves the generation of reactive oxygen species (ROS). CNDs, particularly those doped with nitrogen or other heteroatoms, can induce oxidative stress within bacterial cells. reactive oxygen species (ROS) damage lipids, proteins, and nucleic acids, disrupting essential metabolic processes. Under light irradiation, photodynamic activation enhances reactive oxygen species (ROS) production, leading to rapid bacterial inactivation.

CNDs have also been shown to interfere with intracellular processes such as DNA replication and protein synthesis. Their nanoscale dimensions allow them to penetrate bacterial cell walls and interact directly with intracellular targets. Some studies suggest that CNDs can bind to bacterial DNA, causing structural damage and inhibiting replication [5]. The antibacterial efficiency of CNDs depends significantly on their synthesis method and surface chemistry. Nitrogen-doped CNDs often exhibit enhanced antimicrobial activity due to increased electron density and improved reactive oxygen species (ROS) generation. Surface functionalization with cationic groups enhances electrostatic interactions with bacterial membranes, thereby improving antibacterial efficacy [6]. CNDs synthesized from natural biomass sources have also demonstrated significant antibacterial activity. These green-synthesized nanodots often contain diverse functional groups that contribute to membrane disruption and oxidative stress induction. One of the most promising aspects of CNDs is their effectiveness against multidrug-resistant (MDR) bacterial strains. Unlike conventional antibiotics that target specific biochemical pathways, CNDs exert physical and oxidative damage on bacterial cells. This multimodal mechanism reduces the likelihood of resistance development.

Antibiofilm Properties of Carbon Nanodots (CNDs)

Biofilms represent a major challenge in clinical settings due to their resistance to antibiotics and host immune responses. These structured microbial communities are embedded within an extracellular polymeric matrix that protects bacteria from environmental stress. CNDs have shown considerable promise in preventing biofilm formation and disrupting established biofilms. CNDs can interfere with the initial stages of biofilm formation by preventing bacterial adhesion to surfaces. Their interaction with bacterial membranes alters cell surface properties, reducing the ability of bacteria to attach and aggregate. Surface-modified CNDs can also disrupt quorum sensing mechanisms that regulate biofilm formation [7].

In addition to preventing biofilm formation, CNDs can penetrate and disrupt mature biofilms. Their small size allows them to diffuse through the extracellular polymeric matrix and reach embedded bacterial cells. Once inside, they generate reactive oxygen species (ROS) and induce membrane damage, leading to bacterial death and biofilm destabilization.

Photodynamic activation further enhances antibiofilm activity. Light-activated CNDs produce higher levels of reactive oxygen species (ROS), enabling efficient eradication of biofilm-associated bacteria. This property is particularly valuable for treating chronic infections associated with medical devices and implants. CNDs have demonstrated synergistic effects when combined with conventional antibiotics. By disrupting biofilm structure and increasing membrane permeability, they enhance antibiotic penetration and efficacy.

Antiviral Properties of Carbon Nanodots (CNDs)

Recent global research has increasingly focused on the antiviral potential of CNDs. Viral infections continue to pose significant challenges due to rapid mutation rates and limited therapeutic options. CNDs offer a novel approach to antiviral therapy through multiple mechanisms of action. CNDs can inhibit viral infection by interacting with viral particles and host cells. One mechanism involves direct binding to viral surface proteins, preventing attachment and entry into host cells. Functionalized CNDs with specific surface charges or ligands can block receptor-mediated viral entry. Another mechanism is the inhibition of viral replication within host cells. CNDs can interfere with viral RNA or DNA synthesis, reducing viral proliferation. Some studies have demonstrated that CNDs can bind to viral nucleic acids, thereby inhibiting replication processes.

ROS generation also contributes to antiviral activity. Oxidative stress induced by CNDs can damage viral envelopes and genetic material. Photodynamic antiviral therapy using light-activated CNDs has shown promising results in inactivating enveloped viruses. Beyond direct antiviral activity,

CNDs may modulate host immune responses [8]. Some studies indicate that they can enhance antiviral immune signaling pathways and reduce inflammatory damage.

Future Perspectives and Challenges

Despite significant progress, several challenges must be addressed before CNDs can be widely adopted in clinical practice. Standardization of synthesis and characterization methods is necessary to ensure reproducibility and scalability. Understanding the relationship between structure and antimicrobial activity will facilitate rational design of more effective nanodots. Integration of CNDs into medical devices [9], coatings, and therapeutic formulations represents a promising direction. Their multifunctional properties enable simultaneous imaging and therapy, opening avenues for theranostic applications [10]. Continued interdisciplinary research combining material's science, microbiology, and clinical medicine will be crucial for translating laboratory findings into practical healthcare solutions.

Currently, there is an explosion of research on, CNDs and in particular on the biomedical applications of CNDs [11-29] including the latest patents [Indra Neel Pulidindi, Haritha SR, Deepak Nallaswamy Veeraiyan, Ultra-small, highly fluorescent, nitrogen and boron co-doped carbon nanodots (N, B-CNDs) for catalytic application. Indian patent, File number, 202641011120 (Ultra-Small), filed on 03/02/2026; Indra Neel Pulidindi, Haritha SR, Deepak Nallaswamy Veeraiyan, Nitrogen enriched highly fluorescent carbon nanodots (N-CNDs) as sensor in biorefinery. Indian patent, File number, 202641011119 (Nitrogen) filed on 03/02/2026]. We hope the research fraternity make good use of the opportunity and come up with epochal findings that would alleviate the suffering of mankind due to anthropogenic bacterial, fungal, and viral contaminations.

To conclude, the following Figure 4a describes the killing potential of the carbon nanodot – antibiotic composites via enhanced generation of reactive oxygen species in the presence of CNDs as shown in Figure 4b.

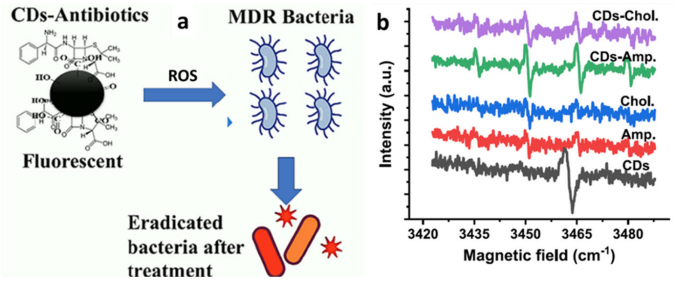

Figure 4 (a): Schematic representation of the ability of the carbon nanodot (CD)-antibiotic (chloramphenicol and ampicillin) composite on the multi-drug resistant (MDR) microorganism via enhancement in the generation of reactive oxygen species (ROS).

(b) Electron paramagnetic resonance (EPR) spectra of the reactive oxygen species generated by the antibiotics (chloramphenicol and ampicillin) as well as the carbon nanodot (CD) – antibiotic composites. [Adapted with permission from the American Chemical Society, 30]

The enhancement in the ability of the CND-antibiotic composites to eradicate microorganisms is through the enhancement in the production of the reactive oxygen species in the presence of CNDs as shown in Fig .4b. The four distinctly different peaks with a hyperfine splitting constant value of 14.9 G originally seen in the case of the antibiotics, namely, ampicillin (amp) and chloramphenicol (Chol) though of lower intensity were enhanced in signal intensity in the presence of the carbon nanodots. As such, in the prestine carbon nanodots (CDs) no such hyperfine splitting is seen. But an intense signal typical of free electron spin is observed. Though it is surmised that the origin of such paramagnetic centers in carbon materials, in general, with a g value of 2.00082 is due to the dangling bonds of carbon in the neighborhood of dangling H centers [31]. The truth is "yet" to be found using the systems like CNDs as molecular models.

Biocompatibility and Toxicological Considerations

The clinical translation of CNDs depends on their safety profile. Most studies indicate that CNDs exhibit low cytotoxicity and good biocompatibility, particularly when synthesized using biocompatible precursors. Surface modification plays a crucial role in determining toxicity. Properly functionalized CNDs show minimal adverse effects on mammalian cells while maintaining antimicrobial efficacy. However, long-term toxicity, biodistribution, and clearance mechanisms require further investigation. Standardization of synthesis methods, exploration of biocompatible feedstock and comprehensive in vivo studies are essential for ensuring safe biomedical applications. For improved understanding the readers are advised to consult the following literature [32-39]. In brief, the excellent biocompatibility and the negligible or non-toxicity of CNDs is evident from the reports described in Table 1.

S No	Feedstock and method of synthesis	Biocompatibility	Toxicity	Reference
1	Ginsenoside Rg1; Hydrothermal	Good biocompatibility	Low toxicity; CNDs promoted tumor apoptosis; therapeutic agent for human non-small cell lung cancer	32
2	Ginsenoside Rg1; Hydrothermal	High biocompatibility	Negligible toxicity; Nano medicine for human cervical cancer; excellent therapeutic effect	33

Table 1: Biocompatibility and toxicity of carbon nanodots.

CONCLUSION

Carbon nanodots (CNDs) represent a rapidly evolving class of nanomaterials with significant potential in biomedical applications owing to their hydrophilicity, biocompatibility and negligible or non-toxicity. Their antibacterial, antibiofilm, and antiviral properties stem from unique physicochemical characteristics and multifaceted mechanisms of action. By disrupting microbial membranes, generating reactive oxygen species (ROS), interfering with genetic material, and modulating host responses, CNDs offer a versatile platform for combating infectious diseases. The growing body of global research underscores their promise as next-generation antimicrobial agents capable of addressing challenges posed by multidrug-resistant bacteria, persistent biofilms, and emerging viral pathogens. Continued investigation into their mechanisms, safety, and clinical applicability will be essential for realizing their full potential in modern medicine in general and cancer therapy, in particular.

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AUTHOR'S CONTRIBUTION

AGR wrote the original review article. INP edited the manuscript. AG provided the guidance and insight.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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