RADIANT REVOLUTION WITH CARBON DOTS TRANSFORMING MEDICINE

Abstract

Carbon dots, nanoscale carbon-based particles, have emerged as versatile entities with promising applications. These usually 2–8 nm-sized nanoparticles have special optical and electrical characteristics. Recent studies demonstrate their promise in therapeutic domains beyond its conventional uses in imaging. Because of their small size and surface functionalization, carbon dots have shown potential in drug delivery systems for focused therapies. Furthermore, the incorporation of artificial intelligence improves their diagnostic powers, enabling customized medicine and advanced imaging methods. The combination of artificial intelligence, nanotechnology, and carbon dots creates fascinating new possibilities for innovatively designed biomedical applications.

Keywords: Carbon dots, Anti-oxidant, Anti-viral, Anti-cancer, Artificial intelligence.

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I. INTRODUCTION

In view of its potential for therapeutic use in medicine, carbon dots have become more well-known. These carbon-based compounds at the nanoscale have special qualities that make them useful for a range of medical uses [1]. Most notably, they are used in drug delivery systems, which allow therapeutic substances to be precisely and specifically transported to desired cells or tissues. In the process, adverse effects are reduced and therapeutic efficacy is increased. Carbon dots are useful in cancer therapy for both imaging and treatment purposes (Figure 1). They can be applied in photodynamic treatment, which uses light to specifically kill cancer cells, and cancer imaging, which helps identify and locate tumors [2][3].

Additionally, carbon dots have antibacterial qualities that are used in antibacterial medication formulations, wound dressings, and coatings for medical devices to fight bacterial infections (Figure 1). Additionally, they have the potential to improve the treatment of neurological illnesses by aiding in the delivery of drugs to the brain through neurotherapeutics [4]. Moreover, carbon dots have the potential to be flexible theranostic agents that can transport therapeutic chemicals and perform diagnostic functions at the same time. All things considered, carbon dots are adaptable and biocompatible nanomaterials with a variety of therapeutic uses that help develop medical procedures and healthcare solutions [5][6].

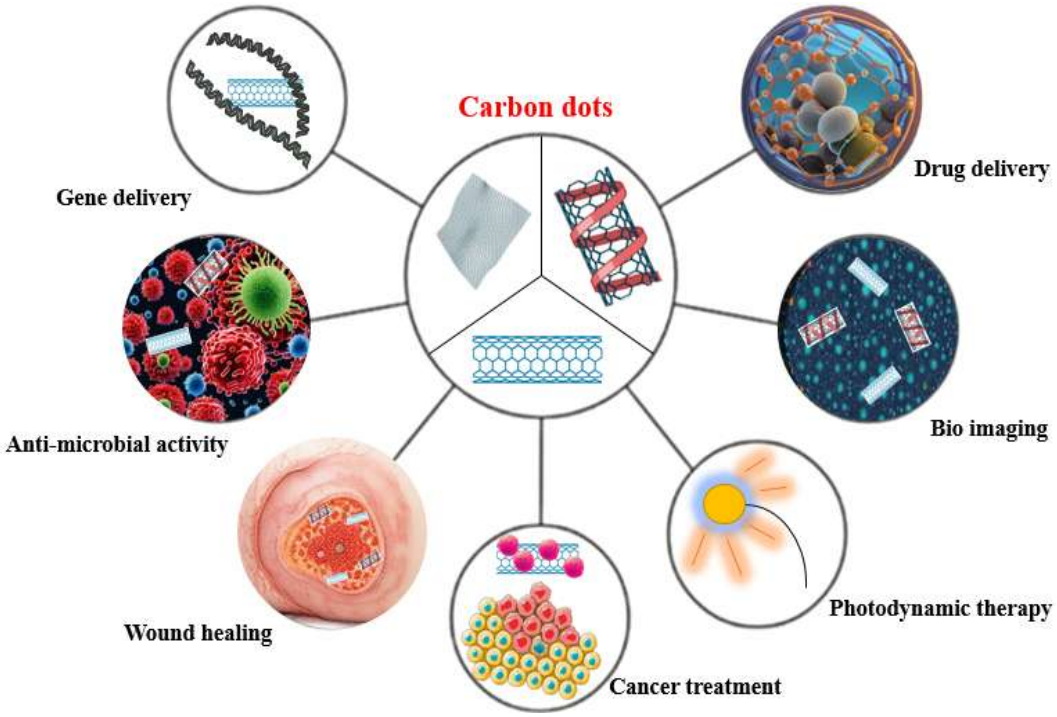

Figure 1: Represents the various application of carbon dots

II. DIFFERENT METHODS OF CARBON DOTS SYNTHESIS

- Hydrothermal/Solvothermal Synthesis
- Microwave-Assisted Synthesis

- Pyrolysis (Figure 2)
- Electrochemical Synthesis
- Laser Ablation
- Ultrasonication-Assisted Synthesis
- Photochemical Synthesis
- Template-Assisted Synthesis

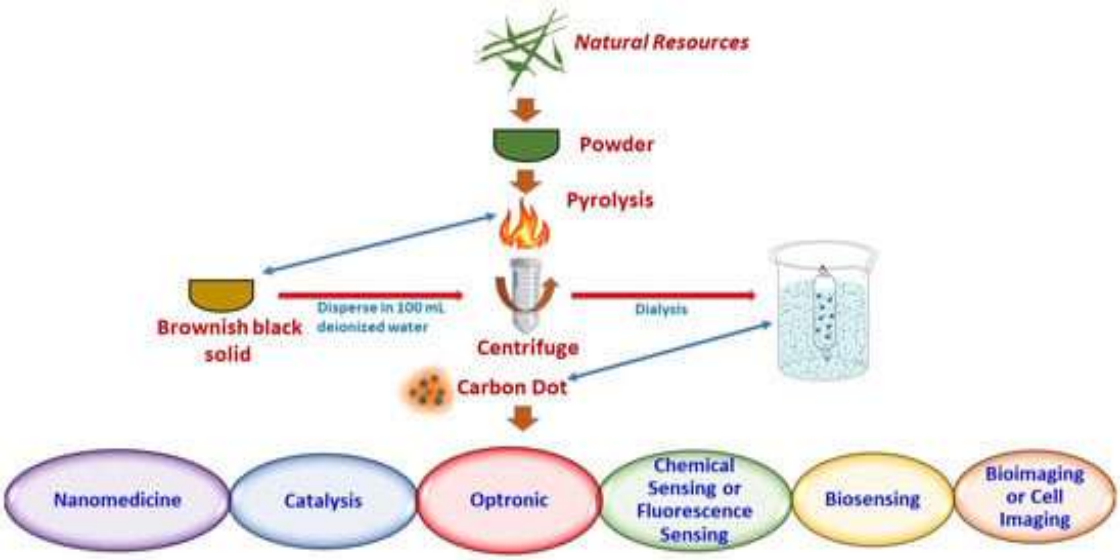

Figure 2: Synthesis of carbon dots from natural sources for a range of uses. **Figure 2** is reproduced from Ref.[7]

III. CARBON DOTS COMBINED WITH OTHER ANTIMICROBIAL AGENTS

1. **Antibacterial activity of Carbon Dots:** Over time, oxidizing chemicals such as hydrogen peroxide (H2O2) and sodium hypochlorite (NaOCl) have been widely used as effective disinfectants against a variety of pathogens. These oxidizing chemicals have antibacterial properties, but some strains of bacteria have shown resistance to them, requiring higher dosages that could be harmful to human tissues and other biological systems. A potential solution to this problem is to combine benign photo-activated carbon dots (CDots) with certain antimicrobial compounds in order to maximize antibacterial activity while utilizing the least amount of each component. This strategy seeks to prevent the spread of microbial resistance and lessen the possible harm that antimicrobial compounds could cause to the environment and public health (see Table 1 for specifics). Dong et al. investigated this strategy by combining acetic acid, H2O2, Na2CO3, and EDA-CDots with different antibacterial substances. Their research aimed to ascertain whether this combination may produce enhanced or synergistic antibacterial actions against cells of bacteria. The outcomes showed that Gram-positive B. subtilis and Gram-negative E. coli cells were successfully inhibited from growing when CDots and H2O2 were applied together. More specifically, the treatment with 10 g/mL CDots and 8.82 mM H2O2 led to a 2.46 log reduction in the number of viable cells for E. coli cells, which is considerably more than the sum of the viable cell reductions obtained from treatments with each of the parts of CD's for 0.14 log as well as H_2O_2 for 1.57 log. This synergistic action most likely worked by stimulating the breakdown of H2O2 resulting in additional

hydroxyl radicals, hence enhancing the antibacterial effects of both CDots and H2O2. However, there were no synergistic benefits when CDots were combined with Na2CO3 or acetic acid, although the negative results actually supported the value of the combination technique from the other side. The method is sound; all that is needed is a careful selection of suitable antimicrobial agents to mix with CDots in order to obtain the required synergistic effects for significantly improved antibacterial activity at low agent dosage [8][9]. Using CDots in conjunction with conventional antibiotics, in which CDots act as drug carriers, replicates the efficacy of the combo strategy. For example, dot-AMP "conjugates" were investigated as visible light-triggered antibacterial agents in an experiment conducted by Jijie *et al.*, In order to do this, ampicillin (AMP) had to be attached to CDots that have surface amino moieties. The conjugate arrangement increased the stability of AMP relative to its free form while preserving the antibacterial qualities of both AMP and CDots, as demonstrated by the killing of E. coli cells in the presence of light. Additionally, conjugates produced from CDots have been used in conjunction with antibiotics for controlled drug release in an effort to reduce the possibility of microbial resistance brought on by the overuse of antibiotics. To control ciprofloxacin's extended release, CDots were conjugated with the drug in one instance. In comparison to free ciprofloxacin, these conjugates showed increased biocompatibility and better antibacterial activity against both Gram-positive and Gram-negative bacteria. [10].

An interesting alternative for a distinct class of disinfection materials is photocatalytic disinfection or antimicrobial photodynamic treatment (APDT), or for changes in utilization: antimicrobial photodynamic inactivation (APDI) of bacteria. The initial phase of this procedure is seen in Figure 3 and is based on the photosensitizing agent's photodynamic reaction. The photosensitizer experiences an excitation event (S0 → S1) due to incident light, as seen by the simplified diagram. Following this, the excited electron may spin-flip (intersystem crossover, S1 → T1) to generate a triplet excited state. Triplet-triplet interactions with ground-state molecular oxygen are made possible by occupation of this state; in this instance, energy transfer results in the production of highly reactive singlet oxygen species (ROS), such as singlet oxygen, due to a "Type II" photosensitization process. As the first step in Figure 3 also illustrates, photosensitizers like carbon nanodots (CNDs), are known to exhibit fluorescence because they generate electron/hole pairs (e−/h+). With various proximal species like water, molecular oxygen, or chemical compounds in solution, either of these (e− or h+) can undergo electron transfer, sometimes referred to as Type I photosensitization, producing radical species such as superoxide anion radical (O2•−) and hydroxyl radical (•OH), to mention a few. As seen in Figure 3, Type I and Type II mechanisms both produce extremely reactive ROS and are known to cause significant oxidative damage to microbial cells. Diffusing ROS can also damage DNA or other intracellular components, like ribosomes. Destruction might happen at the membrane, leading to morphological abnormalities or cytoplasmic leakage. Since it is more difficult for bacteria to become resistant to this strategy, oxidative damage from ROS has drawn more attention when it comes to antibiotic-resistant bacteria. Furthermore, no enzyme is known to detoxify $^{1}O2$ and •OH. Additionally, research has demonstrated that APDT can be adjusted to allow for excellent spatial control, which would lessen the negative effects on neighboring mammalian cells during treatment. While promising, alternatives like photothermal therapy lack the spatial resolution that APDT can provide. Consequently, there has been a focus on refining photosensitizing molecular features for antimicrobial applications, especially regarding photophysical property tuning for maximum ROS quantum yields. In contrast to short-

wavelength ultraviolet light (UV-C), these properties can be optimized to increase the photosensitizer's efficiency in using light and even to choose activation wavelengths that are not intrinsically damaging [11]. On the other hand, TiO2 materials, which are frequently employed in photocatalytic disinfection applications, have poor solar energy utilization and need UV activation. It is also useful to adjust the photosensitizer's adhesion or closeness to the bacterial cells in addition to quantum efficiency. Since ROS are highly reactive by nature, it is especially important to create the species locally to the cell of interest in order to prevent off-target interactions. In addition to these characteristics, the perfect APDT photosensitizer would feature a dynamic scaffold structure that would make it easy to modify for multiple modalities [12]. This could involve altering surface structures to become soluble in various disinfectant reagents, modifying delivery platforms, or even covalently attaching antimicrobial coating substances, as in photocatalytic disinfection (Figure 3). Additionally, dynamic structures may enhance theranostic applications by enabling simultaneous detection and imaging in the context of in vivo disinfectant therapies or wound healing (Figure 3). Applications in safety for food, water disinfection processes, and solar-driven disinfection may exist in addition to medical therapy. In the end, a low-cost, environmentally friendly photosensitizer would be the best option for a high-volume, commercial APDT photosensitizer [13].

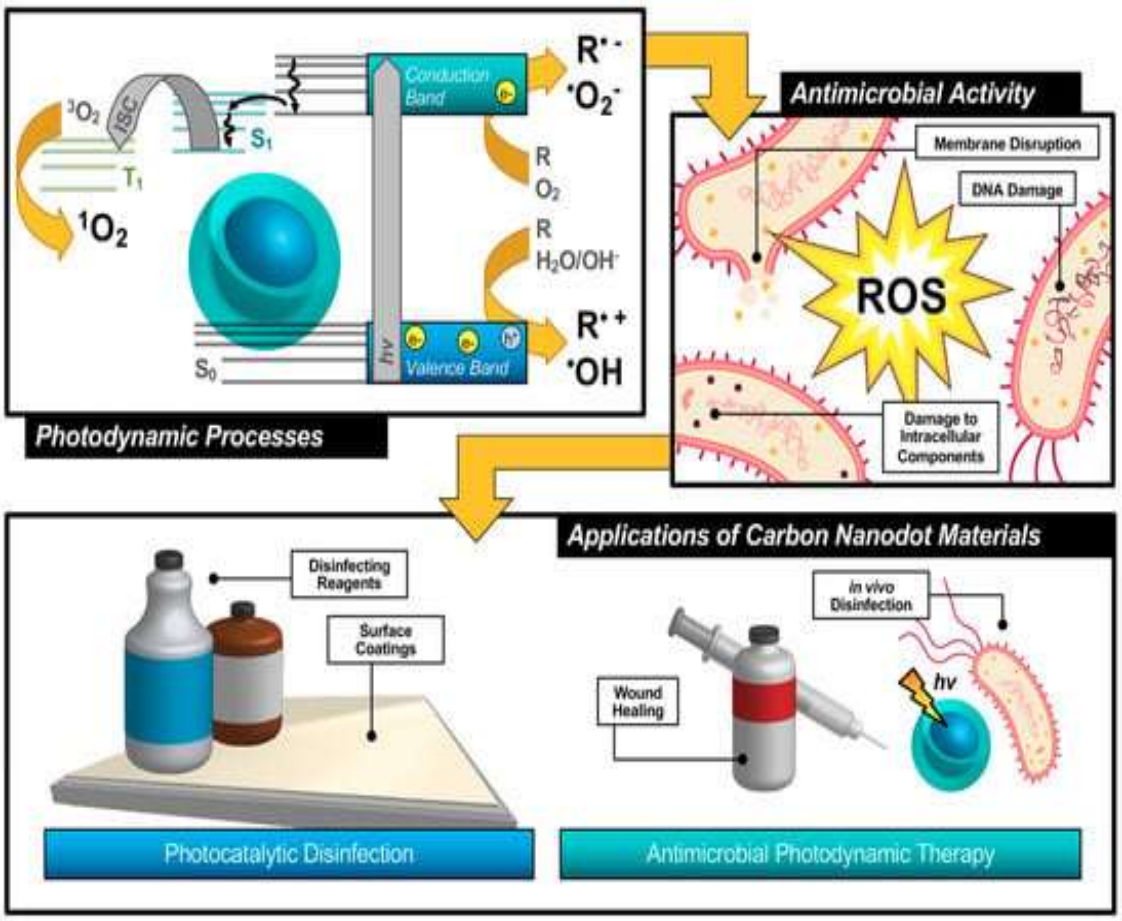

Figure 3: Diagrammatic representation of carbon nanodot-based photocatalytic disinfection and antimicrobial photodynamic treatment. **Figure 3.** is reproduced from Ref.[13]

2. **Antiviral activity of Carbon Dots:** As Table 1 shows, not much study has been done on using carbon dots (CDots) to deactivate viruses or lower infection rates. Du et al. used procine kidney (PK-15) and monkey kidney (MARC-145) cells as models for DNA and RNA viruses, and discovered that CDots treatment suppressed the proliferation of pseudorabies virus (PRV) and pig reproductive and respiratory syndrome virus (PRRSV), respectively. The suppression of viral multiplication was ascribed to the creation of interferon-stimulated genes (ISG) and the activation of interferons (IFN). Particularly, type I interferons (IFNs), such as IFN-α and IFN-β, are acknowledged as important innate immunity agents that evoke a strong antiviral response in the human body in response to viral infections. [14]. Dong *et al.'s* study found that administering EDA- or EPA-CDots at a dose of 5 g/mL was very effective at preventing the attachment of the virus-like particles (VLPs) of human noroviruses, namely GI.1 and GII.4 VLPs, to human cell histo-blood group antigen (HBGA) receptors. Significant inhibition was observed, with EDA-CDots showing a stronger effect than EPA-CDots in preventing VLPs from binding to HBGA and the associated antibodies. This demonstrated how the two kinds of CDots' inhibitory actions shared a surface charge impact. [8]. In a more recent study, Huang *et al.,* discovered that in vitro, carbon dots (CDots) made from benzoxazine monomer efficiently inhibited the infection of both non-enveloped viruses (porcine parvovirus and adenovirus-associated virus) and deadly flaviviruses (dengue, zika, and Japanese encephalitis viruses). The suppression of the early step of virus-cell interaction was probably caused by the direct binding of CDots to the virions' surface. [15].

IV. ANTI-CANCER ACTIVITY OF CARBON DOTS

Carbon dots (CDs), first identified for their distinct luminescence, were mostly used as fluorescent probes, especially in the development of fluorescence imaging-mediated drug delivery. This entailed treating tumors with a combination of CDs and anticancer medications [16][17]. For instance, Chen et al. showed that CD-Ce6 was a very suitable option with exceptional tumor-targeting and photodynamic treatment (PDT) characteristics. This was accomplished by effectively applying Chlorin e6 (Ce6), a common photosensitizer, on the surface of CDs using near-infrared (NIR) fluorescence imaging [16]. A Förster resonance energy transfer (FRET)-based CD-DOX system for administration was created by Zheng et al. and colleagues that can monitor real-time anticancer drug release in acidic circumstances by utilizing variations in FRET signals caused by changes in the separation distance between CDs and DOX [9]. Sun et al. successfully linked oxidized oxaliplatin on the external layer of CDs to integrate the therapeutic efficacy of anticancer drugs with the optical features of CDs. Results from in vitro and in vivo experiments show that the fluorescence of CDs can efficiently track or distribute oxidized oxaliplatin and, as a result, adjust the timing and dose of the medication's injection [17]. Although CDs as carriers of drugs have shown positive outcomes in the diagnosis and treatment of cancer, serious issues such as difficult synthesis pathways and drug leakage continue to exist [18,19]. The biomedical area has extensively examined the possibility of CDs having intrinsic medicinal qualities in addition to good visual properties (Table 1) [20].

Table 1: Represents the Application, Description and type of Carbon Dot used.

Application	Description	Carbon Dots type
Drug delivery	Therapeutic drugs are delivered with accuracy to particular cells and regions	PEGylated
Cancer therapy	Photodynamic therapy and imaging in the treatment of cancer	Citric acid-urea
Antibacterial	Preventing bacterial infections in devices and dressings for wounds	Nitrogen-doped
Neuro therapeutics	Medication delivery to the brain for neurological therapy	Folic acid-conjugated
Theranostics	Utilizing an integrated strategy that combines diagnosis and therapy	Dual-model imaging

V. ANTIOXIDANT ACTIVITY OF CARBON DOTS

Food oxidation can be slowed down by using packaging techniques that release antioxidants, which prolong the food's shelf life. Many kinds of carbon dots are used as antioxidants to reduce the amount of reactive oxygen species in the environment. These include graphene quantum dots (GQD), selenium-doped CDs, nitrogen-doped CDs, and chlorine-doped CDs. The majority of carbon dots with antioxidant qualities are made from plant-based substances, and autoclaving is frequently used during the production process. [21]. Carbon dots doped with nitrogen, phosphorus, and sulphur (NPSC) showed decreased DPPH free-radical scavenging effectiveness when produced using a one-step autoclave technique, as reported by Das et al. (2021) [24]. These doped carbon dots were applied to a polypropylene composite sheet in order to take use of the antioxidant potential of NPSC dots for plastic packaging. The effectiveness of NPSC dots' antioxidant ability against several radicals, such as hydroxyl, superoxide anion, KMnO4, and DPPH radicals, was seen, augmenting the dots' overall antioxidant capacity.

DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) is a type of stable, electron-transfer radical castoff to assess the compounds' antioxidant capacities. Evaluation of antioxidant properties can be done effectively and economically using this technology. The DPPH-hydrogen molecule typically has a pale-yellow color, is created when DPPH interacts with an antioxidant by absorbing the hydrogen radical. DPPH is a stabilized free radical because it is surrounded by 3 benzene rings and has nitrogen atoms with lone-pair electrons. The NPSC dots' antioxidant abilities were strengthened as the concentration grew, almost reaching 417 μg mL1. The DPPH radical scavenging activity of nitrogen, phosphorus, and sulfur-doped CDs (NPSC-dots) is 74%, which is the highest. The gelatin/CDs film has powerful antioxidant properties and is designed to prevent the oxidative degradation of packaged goods. Significant antioxidant activity was found using the ABTS (2,2-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) and DPPH methods, depending on the amount of carbon dots present. Due to surface structural characteristics that help to reduce free radical scavenging and make more advanced applications in the ABTS and DPPH systems, carbon dots have excellent shielding abilities. However, in most films, the DPPH method's antioxidant properties are inferior to ABTS methods. The DPPH and ABTS methods have been used to evaluate the scavenging activity of gelatin-based films. Due to several antioxidant peptides found in gelatin, the amount of antioxidant activity in the gelatin film

was 27.0%. The scavenging capacity of the film is increased by the inclusion of carbon dots at levels of 2.0% and 4.0% in the ABTS technique to 99.0% and 99.6%, respectively.

Using the DPPH method, adding carbon dots to the gelatin film boosts the free radical neutralization activities by 72.1% and 93.2%, correspondingly, for 2.0% and 4.0%. The ABTS method was used to measure the antioxidant properties of the carbon dot-incorporated films, which was more significant than the DPPH method. This could be because the gelatin film expands more quickly in an aqueous ABTS mixture than in a methanolic DPPH solution, according to the results above. The surface functional groups on carbon dot surfaces that can scavenge free radicals are responsible for the carbon dots' strong antioxidant activity. Carbon dots applied to biopolymer-based composite films, like pectin/gelatin and gel/carr composite films, show greater antioxidant activity. Electron flow, unpaired electrons, hydrogen-donating actions, hetero-atom doping, sp2 hybrid carbon domain, and surface functional group type are a few factors that affect antioxidant activity. According to research, the addition of carbon dots at concentrations of 2 or 3 mg mL1 enhances the antioxidant activity of the films by a factor of roughly 18 and reduces oxidative rancidity. The DPPH and ABTS techniques were used to evaluate the cellulose-based film's antioxidant capabilities. According to the ABTS and DPPH techniques, the antioxidant value for the bacterial nanocellulose (BNC) film without carbon dots was 14.0% and 5.0%, respectively. The BNC composite film's antioxidant activity was improved after the addition of carbon dots. In the ABTS technique, the CNF film's ability to neutralize free radicals was improved by the addition of GCD and NGCD to almost 98.1% and 98.0%, respectively; however, for the DPPH method, the results were 79.0% and 84.0%, accordingly. The graphene carbon dots/BNC composite film's antioxidant properties were more notable in the ABTS method than in the DPPH method. The graphene carbon dots' surface functional groups, which participate in free radical scavenging, are in charge of the CNF film's potent antioxidant properties. In the ABTS technique, CNF/NGCD and CNF/GCD film composites displayed the same antioxidant characteristics. However, when compared to NGCD/BNC composite films, the NGCD/CNF composite films displayed superior antioxidant activity in the DPPH method. Because of these films' high antioxidant capabilities, they can be employed in active packaging to slow down the pace of food oxidation. The free-radical release impact was greatly enhanced by the carbon dot/gelatin/carrageenan composite film made from enoki mushrooms. Comparatively, to pure gelatin/carrageenan films, they improved their antioxidant capabilities. Because mCDs are more readily soluble in an aquatic ABTS solution compared to a DPPH methanol solution, the activity in ABTS is higher. Surface hydroxyl groups on mCDs may be the cause of their exceptional antioxidant properties. Compared to pure gelatin/carrageenan films, the free radical release impact was dramatically increased in the enoki mushroom-based carbon dot/gelatin/carrageenan composites film, producing stronger antioxidant capabilities. In the technique described above, carbon dots operate as active ingredients with heteroatom doping in the films [22].

VI. CARBON DOTS ROLE IN ARTIFICIAL INTELLIGENCE

Carbon dots research is benefiting greatly from the application of artificial intelligence (AI). Nanoscale carbon-based compounds called carbon dots offer special qualities with a wide range of uses [23,24]. In this case, AI is used for a number of crucial jobs. Firstly, it facilitates the accurate characterization of carbon dots, which makes it possible for scientists to examine their optical and structural characteristics [25,26]. Furthermore, artificial intelligence algorithms are essential for streamlining the carbon dot

synthesis process, which could increase productivity and lower production costs. Moreover, artificial intelligence (AI) helps discover and create novel applications for carbon dots in electronics, environmental remediation, and medicine [27]. The massive volume of data produced by carbon dots research makes AI-driven data analysis indispensable for streamlining the extraction of insightful information [28,29]. Predictive modeling is made possible by machine learning techniques, which aid researchers in foreseeing the behavior of carbon dots in various scenarios. All things considered, artificial intelligence (AI) streamlines the scientific method and advances the study of carbon dots, resulting in the discovery of new properties and uses [30][31].

VII. VARIOUS FORMULATIONS OF CARBON DOTS

Carbon dots, which are carbon-based materials at the nanoscale, have been created by a variety of formulas and techniques, each producing unique characteristics for a range of uses. In one study, biocompatible carbon dots, mostly used in bioimaging, were created in an aqueous solution of citric acid and ethylene diamine as shown in (Table 2). The carbon dots' diameters ranged from 2 to 5 nm. Another method used polyethylene glycol and glucose to create smaller (3-6 nm) dots with a 510 nm fluorescence peak that may be used for medication delivery and sensing. This process was helped by microwaves [32][33]. Larger carbon dots (4–8 nm) with a fluorescence peak at 480 nm were produced via hydrothermal synthesis employing citric acid and polyvinyl alcohol; these carbon dots are especially useful for photocatalysis. Carbon dots measuring 2-4 nm with a fluorescence peak at 430 nm were created via solvothermal synthesis using ethanol and ethylene diamine, and these dots were used in optoelectronic devices [34,35]. Furthermore, the pyrolysis of polyethylene glycol and citric acid produced carbon dots (5-7 nm) with a fluorescence peak at 490 nm (Figure 2), indicating the material's effectiveness in water purification applications (Table 2). These investigations demonstrate the adaptability of carbon dots and their customized uses in a variety of scientific and technical domains [36][37][38].

Table 2: Formulation of Carbon Dots With their Size, Fluorescence Peak and Applications.

Formulation	Size of Carbon Dots	Fluorescence Peak	Applications
Aqueous solution of citric acid and ethylene diamine	2-5 nm	450 nm	Bioimaging
Microwave-assisted synthesis using glucose and polyethylene glycol	3-6 nm	510 nm	Sensing and drug delivery
Hydrothermal synthesis with citric acid and polyvinyl alcohol	4-8 nm	480 nm	Photocatalysis
Solvothermal method using ethanol and ethylene diamine	2-4 nm	430 nm	Optoelectronic devices
Pyrolysis of citric acid and polyethylene glycol	5-7 nm	490 nm	Water purification

VIII. CONCLUSION

The application of carbon dots to treatment is an interesting yet rapidly developing topic. These carbon-based nanomaterials have a wide range of therapeutic uses, including neurotherapeutics, cancer treatment, antimicrobial treatments, and targeted drug delivery. Their special qualities, such as their capacity for surface functionalization and biocompatibility, make them invaluable tools for maximizing therapeutic benefits and reducing side effects. Carbon dots' versatility in the field of theranostics is further demonstrated by their capacity to combine diagnostic and therapeutic activities. Carbon dots have the potential to significantly improve healthcare and medical solutions as long as research and innovation in this field remain strong.

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