Madhuri Sharon, et. al. International Journal of Engineering Research and Applications
www.ijera.com
ISSN: 2248-9622, Vol. 14, Issue 12, December 2024, pp 97-118

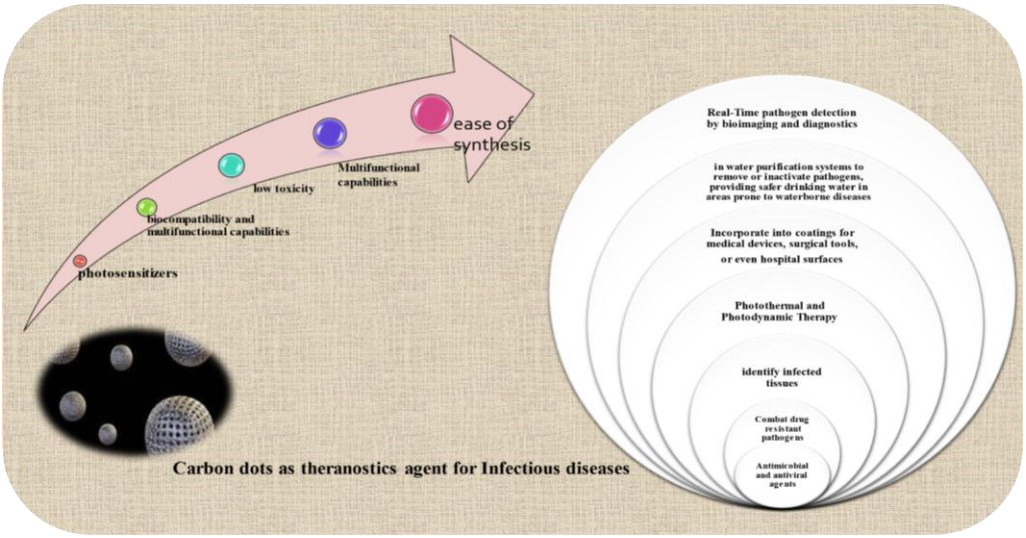
RESEARCH ARTICLE OPEN ACCESS

CARBON-DOTs: A Breakthrough Weapon in the Fight Against Infectious Diseases - A Review

Madhuri Sharon and Anuradha Pandey-Dubey
Sharon Institute of Nanotechnology, Parishkar College of Global Excellence (Autonomous), Jaipur, 302020, Rajasthan, India

Abstract
Fluorescent Carbon-dots, having unique optical properties has shown promise to be a nanomaterial for theranostics of infectious-disease. Here we include graphene quantum-dots, graphene nano-ribbons of less than 10 nm also as they exhibit unique photoluminescence property like carbon-dots, which enable the construction of fluorescent probes; and their electrocatalytic activity, which makes them potentially useful in construction of electrochemical materials. Carbon-dots are easily tunable through surface functionalization for desired properties to be used for disease diagnosis, drug delivery and to some extent in evolving vaccines. A brief introduction to its morphology, property, and synthesis is touched-upon. Carbon-dots are explored as Smart-Sensors. Early nano-diagnostic methods involved use of heavy-metal quantum-dots, Nano-shell, Gold, Iron oxide, Nanotube, Perfluorocarbons and Dendrimers. Some of them have been found to be toxic to living system. Hence, in last two decades with the advancement in biocompatible, biodegradable, water soluble and chemically inert Carbon-dots have attracted attention for theranostic of IDs, such as for imaging and detection pathogenic bacteria. There has been success in use of Carbon-dots for Multiphoton Imaging especially brain, for diagnostic applications in IDs, for virus theranostic as antimicrobial and microbe imaging agent. Carbon-dots are used for infectious agents like Prions, Virus, Pathogenic-Bacteria, Pathogenic-Fungi, Parasitic-Protozoa, and Parasitic-Helminths that causes ID. Infectious-diseases could be *Acute* which develops quickly, *Chronic*, which develops more slowly and *Latent* that may persist for longer period. Elderly, immunosuppressed and patients with chronic disease are more susceptible to IDs. Considering these facts use of carbon-dots has been developed for theranostic of infectious-diseases.
Keywords: Bacteria, Carbon-dots, Fungi, Helminths, Protozoa, Virus,

Date of Submission: 13-12-2024 Date of acceptance: 28-12-2024



Graphical abstract representing CARBON-DOTs: A Breakthrough Weapon in the Fight Against Infectious Diseases

I. INTRODUCTION

Infectious diseases (ID) have shaped human history in profound ways. In the last century, we have

witnessed remarkable breakthroughs in our fight against them. Some of the medical innovations that have made a significant impact are:

Vaccine has been a game-changer. Ever since Edward Jenner administered the first modern vaccine against smallpox in the late 1700s, vaccines have played a crucial role in eliminating ID. Childhood vaccinations against whooping cough, tetanus, diphtheria, and the BCG vaccine against tuberculosis all date back to the 1920s. Polio vaccinations followed in the 1950s, and annual flu shots that many of us benefit from even today. And control of Covid-19 pandemic in this century through vaccine.

Antibiotics have also revolutionized the fight against bacterial infections by targeting specific pathogens. From penicillin to modern antibiotics, have saved countless lives. However, their overuse and the emergence of antibiotic-resistant strains remain challenging.

Innovative Medicines (novel drugs) are also helping in combatting ID. Antiviral medications, transformed HIV from a death sentence into a manageable chronic infection.

Diagnostic, and Preventive Therapies for IDs and it is bolstered by technological advancements. Sophisticated diagnostic tools, rapid testing kits, and telemedicine have all played critical roles.

Despite these advances, challenges remain, mostly for IDs like malaria, HIV/AIDS, tuberculosis. There are continued multi-directional efforts to eradicate them. Additionally, after the Covid-19 pandemic, the concept of "Disease X"—an unknown pathogen that could cause the next pandemic—underscores the need for ongoing research and preparedness.

In a search to fight against IDs, Carbon-dots have emerged as fascinating nanomaterials. In this article we are going to concentrate on What Are Carbon-dotss? How they are synthesized? And based on their properties how they are used for diagnostic as well as therapeutic purpose of eradicating IDs.

CARBON-DOTS AND ITS PROPERTIES

Carbon-dots are emerging as a promising tool in the fight against IDs due to their unique optical, chemical, and biological properties. They are making an impact, because of their significant antimicrobial activity against a wide range of pathogens, including bacteria, fungi, and viruses; being safer due to low toxicity, biocompatibility, and biodegradable property. So far as their theranostic application is concerned Carbon-dots can be activated by light to generate heat (photothermal) or ROS (photodynamic), can serve as nanocarriers for delivering antimicrobial drugs, enhancing their efficacy.

Carbon-dots and Carbon Quantum Dots (CQD)

Carbon-dots and CQDs are the same thing**,** they are tiny nanoparticles <10 nm composed of carbon atoms. The term Quantum takes us to a domain of Physics where a material follows wave theory concept that introduces us to very small particles. quantum dots (QD) confines the motion of conduction band electrons, valence band holes, or excitons (bound pairs of conduction band electrons and valence band holes) in all three spatial directions. In a nut-shell QDs are semiconductor crystals having their excitons or electron and holes confined in all three dimensions of space. Hence, QDs have electronic properties that are intermediate between bulk semiconductors and those of discrete molecules. Carbon-dots was discovered accidently as a by-product during purification of SWCNTs **[1].** Carbon-dots possess sp2/sp3 disordered carbon or hybridized graphitic core functionalized with polar carboxyl or hydroxyl groups on the surface. They are often derived from carbon-rich sources like organic compounds, graphene, or carbon nanotubes. Graphene based or graphene derived Graphene Oxide (GrO) or Graphene Nano-Ribbons (GNR) also exhibit Carbon-dots like properties i.e. excellent fluorescence, high photostability against photobleaching and blinking, broad excitation spectra, narrow and tunable emission spectra, good biocompatibility and their small size and low toxicity making them superior to QD.

Properties of Carbon-dots

Carbon-dots has ability to act as photosensitizers. When exposed to light, they generate reactive oxygen species (ROS). These ROS play a crucial role in photodynamic therapy (PDT), for treating various diseases**.** Carbon-dots can exhibit PL emission in the near-infrared (NIR) spectral region under NIR light excitation. It should be noted that NIR PL emission of Carbon-dots excited by NIR excitation is particularly significant and useful for *in vivo* bionanotechnological studies because of the transparency of body tissues in the NIR ''*water window''*. Interestingly, the PL from Carbon-dots can be quenched efficiently by either electron acceptor or electron donor molecules in solution, indicating that photoexcited Carbon-dots s are excellent electron donors and electron acceptors. Mechanistically, the fluorescence emissions in Carbon-dots s are attributed to radiative recombination of the carbon particle surface-trapped electrons and holes, where the large surface (relative to the particle volume) and diverse surface energy trapping sites in the small carbon nanoparticles are stabilized by the surface passivation agents. Unlike the semi-conductor QDs containing heavy metals

such as cadmium, carbon is generally not considered as a toxic element. Carbon-dots characteristically show apparent optical absorption in the UV region, with a tail extending to the visible range. Majority of the Carbon-dots, such as those prepared by laser-passivation, electrochemical oxidation, microwave /ultrasonic, or supported method, have an absorption band around 220–320 nm[2]. However, the absorbance of C-dots was found to increase to longer wavelength after surface passivation with different chemical moieties. This characteristic absorption of Carbon-dots might be associated to the presence of surface emissive traps or due to quantum-confinement effect.

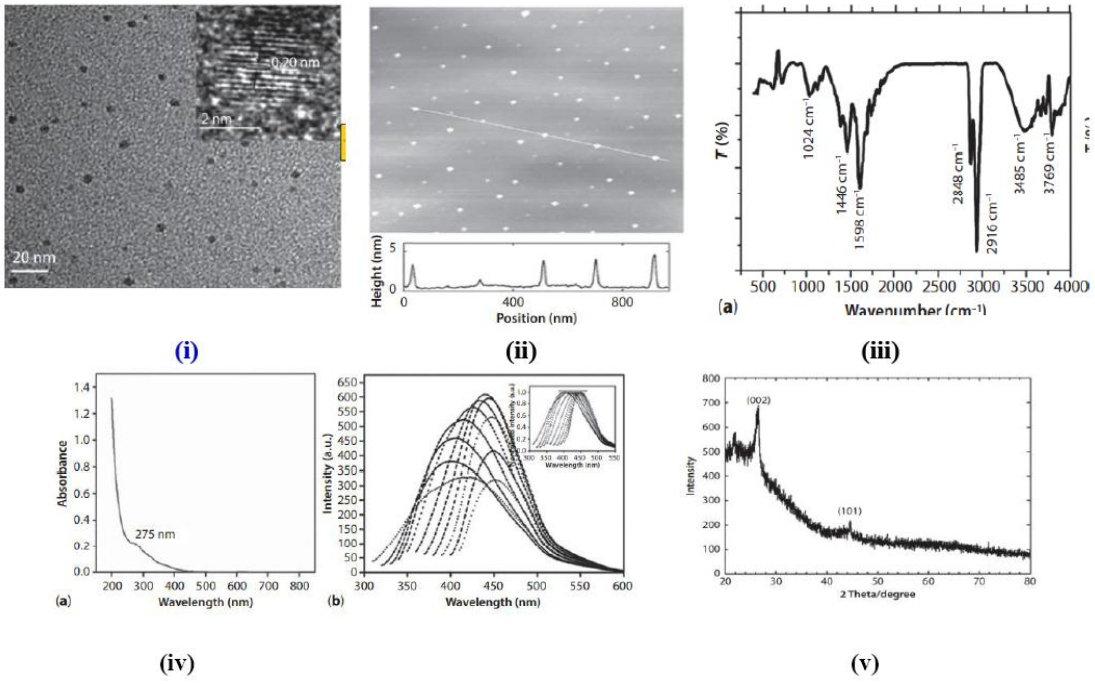
Synthesis of Carbon-dots

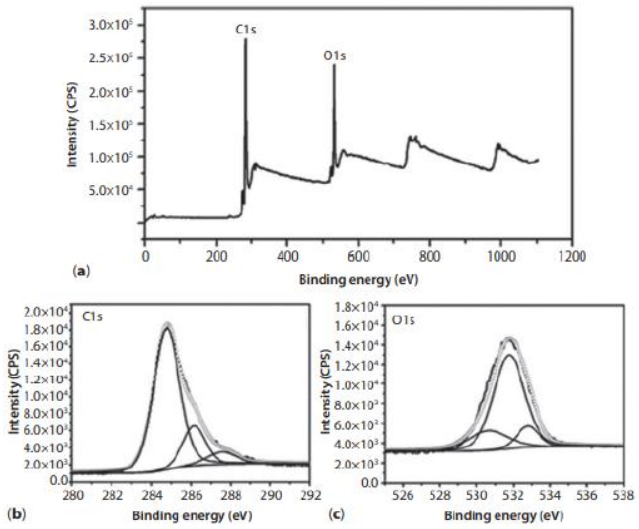
Carbon-dots are synthesized by both *Top-Down* approach, where graphite is used as precursor, via physical or chemical methods; and *Bottom-Up* approach, using carbon rich non-graphitic precursors. Some of the common methods[3] used for synthesis of Carbon-dots are: Electrochemical[4]; Combustion and Thermal Oxidation[5]; Hydrothermal Oxidation[6]; Solvothermal; Laser Ablation of Graphite[7]; Pulsed Laser Irradiation of Carbon Source[8]; Arc-Discharge[1]; Plasma Treatment[9] ; Opening of Fullerene-Cage[10] ; Ultrasonication[11]; Microwave-Assisted[12]; Solution-phase chemical methods by oxidative condensation of aryl groups[2]**;** Supported Synthetic Procedure[13]; and Biogenic methods[14, 15]**.**

Characterization of Carbon-dots

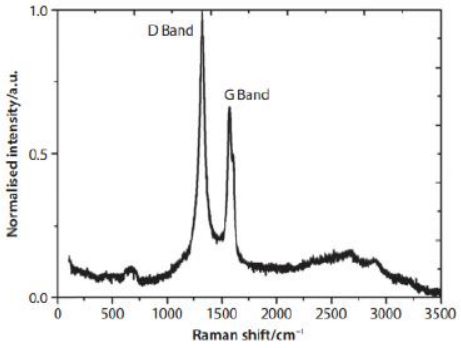
Characterization plays a very important part because it helps in better understanding of the structure and properties of Carbon-dots and accordingly allows to design particular types of Carbon-dots for various specific applications. Possible characterization techniques which are being used for identifying and measuring Carbon-dots are: Microscopy by SEM, TEM, and STM (Scanning Tunnelling); Spectroscopic methods using UV-Vis Spectroscopy for Band Gap Determination; Fluorescence Spectrometry; Fourier Transform Infrared (FTIR) Spectroscopy; X-Ray Diffraction (XRD) Analysis; X-Ray Photoelectron Spectroscopy (XPS); Dynamic Light Scattering/Photon Correlation Spectroscopy (DLS/PCS); Dual Polarization Interferometry (DPI); Raman Spectroscopy; Nuclear Magnetic Resonance (NMR) Spectroscopy (Figure 1).

Due to its unique morphology and strong fluorescence properties Carbon-dots are used for *Bioimaging*. They serve as contrast agents for imaging techniques like fluorescence imaging and magnetic resonance imaging (**MRI**) simultaneously. Carbon-dots can encapsulate drugs and serve as carriers for *targeted drug delivery.* Some studies have explored Carbon-dot's antibacterial properties, as antioxidants, and scavenging free radicals. Novel Carbon-dots have been designed for *gene delivery and multi-modal imaging* (combining MRI and fluorescence imaging) by inheriting properties from their precursor polymers[16].





(vi)



(vii)

Figure -1: Carbon-dots characteristics as exhibited by different analytical tools (i) TEM image of Carbon-dots Inset shows HRTEM image of a single dot. (*Reproduced with permission from Guan et al 2014*)[17] (ii) AFM image of Carbon-dots (iii) FTIR Spectra of a Biogenic Carbon-dots (iv) (a) UV-Vis absorption spectra of Carbon-dots and (b) Emission spectra when excited from 300–400 nm. Inset is normalized emission spectra (*Reproduced with permission from Roshni & Ottur 2017*)[18]. (v) A typical XRD graph of Carbon-dots (vi) (a) XPS, (b) C1s and (c) O1s spectra of as-prepared Carbon-dots (*Reproduced with permission from Chen et al 2016*)[19] (vii) Raman spectra of Carbon-dots displaying its defective nature based on D-band and G-band intensities. (*Reproduced with permission from Mewada et al 2014)*[20].

INFECTIOUS-DISEASES AND INFECTING AGENTS

Man has encountered existence of several IDs since ancient to contemporary period. Some of them have been devastating such as Smallpox, Malaria, Poliomyelitis, Plague, Influenza, AIDS and now the Covid-19 which is prevailing world over and has killed more than 2 crore people. IDs are caused by an infectious agent such as Prions, Virus, Pathogenic-Bacteria, Pathogenic-Fungi, Parasitic-Protozoa, and Parasitic-Helminths. They are capable of passing on from one host to others. Virulence of an infecting agent is their ability to cause rapid and severe disease in a host. Thes infectious agents produce poisonous chemicals such as toxins and enzymes; which destroys the cells and tissues causing disease. They either directly invade the host cells and destroys them or they trigger response from the host's immune system that leads to the signs and symptoms of disease.

CARBON-DOTS S TO FIGHT AGAINST DISEASES CAUSED BY PRION

Prions

'*Prion*' is a misfolded infectious proteins. of 30 – 50 kD size. These abnormal forms of a host protein, called prion protein (PrP), is normally found in neurons. Prion's site of propagation is intracellular. Prions are the heredity pathogen devoid of nucleic acid. Chesebro et al[21] and Harris[22] made a pivotal discovery that cells in the brain constitutively expressed the prion protein, prion acts as a template to change the conformation of recruited benign forms of the agent into the disease state which has a substantially different conformation from that of its precursor.

Diseases Caused by Prions

Prions infect sheep or goat's nervous system causing *Scrapie* a fatal [23] transmissible **Bovine Spongiform Encephalopathy (BSE)**, also known as mad cow disease in cattle[24].

In human it causes a fatal neurodegenerative disease called **Creutzfeldt-Jakob disease (CJD)**; it is associated with human cannibalism. It is probably transmitted to humans from BSE-infected cattle. Its common symptoms in animals are nervousness, aggression, excessive self-rubbing, and motor dysfunctions leading to immobility and death[25]. In human the symptoms are cerebellar ataxia, oculomotor disturbances, peripheral nerve pain, pyramidal syndrome, dementia associated with CJD[26]. Diseases occur when the PrP undergoes a conformational change that confers resistance to

proteases. which promotes conversion of the normal protease-sensitive PrP to the abnormal form, causing neuronal damage and spongiform pathologic changes; vacuolation, neuronal loss and Astrocytosis[27]. The protease-resistant PrP may be spontaneous or inherited mutations in PrP. Prions is transmissible spongiform encephalopathies (TSEs), diseases can be hereditary, infectious, or sporadic [28].

Carbon-dots as Theranostic Agent for Diseases Caused by Prions

Carbon-dots have been explored as potential theranostic agents for biomedical applications of diseases caused by prions. CJD is challenging to treat due to their unique nature. Styrylquinoline G8: One notable example is the Styrylquinoline G8, which was deliberately designed as a theranostic agent for prion diseases showed promising anti-prion activity in cell models without neurotoxicity. Researchers continue to explore novel materials, including Carbon-dots, to improve diagnosis, treatment, and monitoring of prion-related conditions. Since Carbon-dots mostly interact with the monomeric or oligomeric species of the proteins and not the aggregated ones. Studies have shown that GQDs can effectively inhibit the aggregation of Aβ peptides[29].

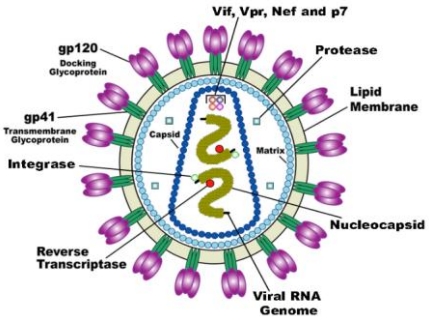
CARBON-DOTS TO FIGHT AGAINST DISEASES CAUSED BY VIRUS

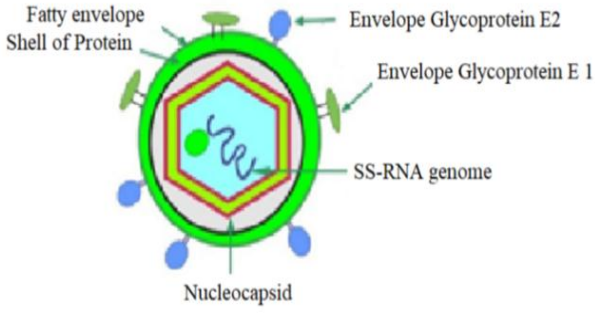
Virus

Viruses are 20 - 300 nm obligate intracellular parasite. Unlike other parasites, they are not alive, they depend on the host cell's metabolic machinery for their survival and replication. A typical virus consists of a *Nucleic Acid Genome* (DNA or RNA but not both), which is surrounded by a protein coat called a *Capsid* (Figure 2) that is sometimes encased in a lipid membrane. Capsid enables virus to enter a host cell. *Retroviruses* contains only RNA. Viruses are highly specific to the cells they infect and destroys the host cell by either by lytic cycle or lysogenic cycle. AIDS is the most infamous retrovirus. *Capsid* virus has icosahedral or helical shape of capsid.

Infectious Diseases Caused by Virus

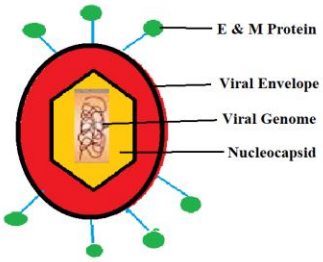
The ID caused by virus include: (i) **AIDS** caused by *HIV (Human Immunodeficiency Virus)/AIDS (acquired immunodeficiency syndrome)*; (ii) **Hepatitis C** caused by C Virus (HCV); (iii) **Dengue** caused by one of four closely related dengue virus that infects human by the female *Aedes aegypti* (mosquito) bite; (iv) **Polio or Poliomyelitis** is caused by a positive strand virus, also known as sense strand RNA virus (ssRNA); (v) **Meningitis** could be caused by virus or bacteria by infecting spinal cord fluids and the fluid that surrounds the brain. (vi) **Herpes** is caused by a DNA virus, Herpes Simplex Virus (HSV that infects epithelium & produces latent infections of neurons [HSV-1, HSV-2 & VZV]. – β-Group, are Cytomegalovirus that infects lymphocytes & can be latent in a variety of cell types [CMV, HHV-6.HHV-7]. – γ-Group are Lymphoproliferative virus that causes latency in lymphoid cells e.g. EBV and KSHV/HHV-8; (vii) **Influenza (Flu**) is caused by a RNA virus A & B and (viii) **Corona**

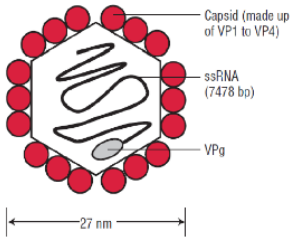




Schematic structure of HIV — Schematic structure of Hepatitis Virus

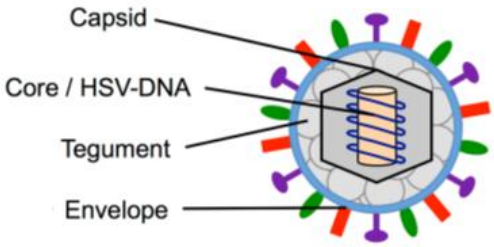
Source: Edzeamey & Ako.2018; Article no. IJR2H.43171.
Fig procured from US National Institute of Health 2005[33]

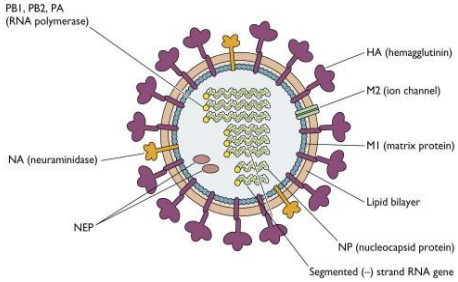




Schematic structure of Dengue Virus

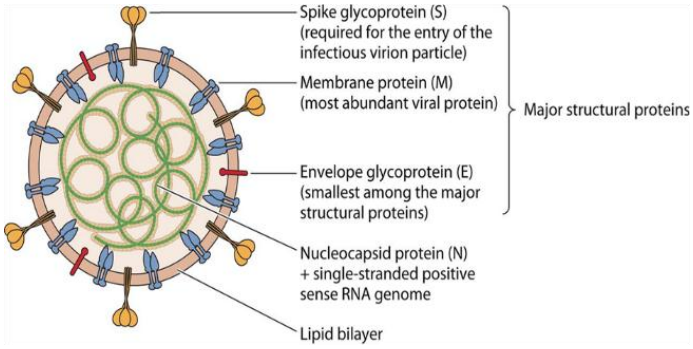
Schematic structure of Polio Virus





Schematic structure of Herpes Virus
(Source: Heilingloh, et al 2017 [34]

Schematic structure of Influenza Virus
(Source: Vincent Racaniello, 2009)[35]



Schematic structure of Covid-19 Virus *(Source: Kuldeep Dhama, et al 2020.)[36]*

Figure 2: Schematic diagram of structure of different IDs causing viruses

Virus causing Covid-19. Coronaviruses are composed of unsegmented, enveloped single-stranded, positive-sense RNA genome of around 30 kb, enclosed by a 5′-cap and 3′-poly(A) tail 30. The genome of SARS-CoV-2 is 29,891 bp long, with a G+C content of 38% 31. These viruses are encircled with an envelope containing helical viral nucleocapsid. It has a diverging spherical outline with some degree of pleomorphism, virion has diameters ranging from 60 to 140 nm. It has distinct spikes of 9 to 12 nm that gives the virus a solar corona like appearance. The CoV genome is arranged linearly as 5′-leader-UTR-replicase-structural genes (S-E-M-N)-3′ UTR-poly(A)32. Accessory genes, such as 3a/b, 4a/b, and the hemagglutinin-esterase gene (HE), are also seen intermingled with the structural genes30. The major structural spike proteins are Glycoprotein (S), that is required for the entry of the infectious virion particles; Membrane protein (M); Envelope Glucoprotein and apart from these three major proteins there is Nucleocapsid protein and also a lipid bilayer. (Figure 2).

CARBON-DOTS as Theranostic Agent for Diseases Caused by Virus

Viral diseases cannot be treated with antibiotics. Protection against most viral diseases are prevention, mostly by the vaccines, provided they are used before infection begins. High heterogeneity of viruses is a major challenge in development of

effective antiviral agents; whereas high mutation rate e.g. of coronavirus negatively affect virus detection process or the efficiency of drugs and vaccines.

There are two types of viral infections (i) Acute (Transient) Infections and (ii) Latent Infections, where virus present in the body are in resting state and do not multiply, hence, no noticeable symptom, till they become active. Presently clinical diagnostic technology for IDs is enzyme-linked immunosorbent assay (ELISA), chemiluminescent immunoassay (CLIA), polymerase chain reaction (PCR) and culture for microbial isolation and identification techniques[33,34]. However, these techniques, need to improvise some aspects e.g. better specificity, reduced high technical demands and expensive equipment, resulting in a heavy burden to large-scale medical examinations in developing countries. For example clinical detection of SARS-CoV-2, by traditional detection techniques are cumbersome, time-consuming [real-time fluorescence quantitative PCR (qRT-PCR)] and have low accuracy in the detection of window period (serological antibody detection). These diagnostic methods usually detect the biomarkers that are free in plasma or serum, which is less sensitive compared to the detection of living cells or pathogens. Hence there is a demand of high-throughput, ultra-sensitive and cost-effective novel diagnostics.

Carbon-dots have emerged as promising theranostic agents for diseases caused by viruses.. The **Antiviral** effects of Carbon-dots against various viruses, such as influenza, human papillomavirus (HPV), and coronavirus have been reported. They can inhibit viral entry, replication, and infection by interacting with viral proteins or binding to the viral envelope. Moreover, as mentioned earlier also Carbon-dots due to their small size, biocompatibility, and easy surface functionalization, can be used to deliver antiviral drugs effectively to infected cells, enhancing the therapeutic effect.

Diagnostic of Virus Using CARBON-DOTS

Carbon-dots has been found suitable as they exhibit strong fluorescence, which allows for the visualization and tracking of viral infections in cells and tissues. This feature can be used for imaging viral-infected areas and monitoring the progression of the disease. Carbon-dots can be functionalized to detect viral components, such as viral RNA or proteins, making them useful in biosensors for rapid viral diagnosis. Carbon-dots being highly photostable, are ideal for long-term imaging applications. Highly-sensitive biosensors for detection of very low virus concentration and real-time protections using the nanorobots as theranostic for viral diseases are being researched. Multivalent Carbon-dots are capable of interaction with multivalent viruses for viral detection and prevention of further infections.

Carbon-dots have been employed in ***Molecular Diagnostics*** of viral diseases, particularly as fluorescent labels, or barcodes due to their excellent optical properties, biocompatibility, and ease of functionalization. Carbon-dots are used in the molecular diagnostics of viral infections as fluorescent probes to detect viral nucleic acids or proteins. Their strong fluorescence, photostability, and tunable emission wavelengths make them excellent labels for various molecular assays. Carbon-dots be functionalized to bind specifically to viral nucleic acids (DNA or RNA). When they bind to their target, they emit fluorescence, enabling the detection and quantification of viral genetic material. This is particularly useful in detecting viruses like SARS-CoV-2, Influenza, and HIV. Advantages of using Carbon-dots in molecular diagnostics is that it provides high sensitivity due to their strong fluorescence, making them capable of detecting even low concentrations of viral material. Carbon-dots being less toxic than other fluorescent nanoparticles, are suitable for clinical applications. And the surface of Carbon-dots can be easily modified to enhance specificity for particular viral targets.

Carbon-dots can be conjugated with primers or probes used in ***PCR amplification***, acting as fluorescent reporters. As the viral RNA is amplified, the increase in fluorescence can be monitored, allowing for real-time detection.

Carbon-dots ***as Barcodes in Lateral Flow Assays (LFAs)*** can serve as fluorescent barcodes for detecting viral antigens or antibodies. This approach is widely used for point-of-care testing because it is rapid, cost-effective, and easy to use.

For ***Antigen/Antibody Detection*** Carbon-dots can be conjugated with antibodies that specifically recognize viral proteins (antigens). When a sample containing the target virus is introduced, the Carbon-dots bind to the antigen, resulting in a visible fluorescent signal on the test strip. By tuning the fluorescence emission of Carbon-dots to different wavelengths, it is possible to ***simultaneously detect multiple viral markers*** in a single assay, allowing for the identification of co-infections or differentiation between different viruses[35].

Carbon-dots incorporated ***Biosensors*** are used for the detection of viral infections. Their fluorescence properties enhance the sensitivity and specificity of these sensors. (i) To make ***Electrochemical Biosensors*** Carbon-dots can be combined with other nanomaterials to detect viral RNA or proteins[36]**.** For example, Carbon-dots functionalized with probes can recognize viral RNA, and when hybridization occurs, it results in a detectable fluorescence or electrochemical signal. (ii)

Fluorescent Biosensors using Carbon-dots act as signal transducers. Upon binding to a viral target, such as a specific viral protein or nucleic acid, the Carbon-dots emit a fluorescence signal, enabling rapid detection[37].

Here are some examples of viral diagnostics using CARBON-DOTS s for

(a) **SARS-CoV-2:** Carbon-dots have been used as fluorescent probes in RT-PCR and lateral flow assays for the rapid detection of SARS-CoV-2 RNA, enabling early diagnosis of COVID-19.

(b) **HIV and Influenza:** using Carbon-dots in biosensors to detect HIV and Influenza virus markers.

(c) **SARS-CoV-2** (**COVID-1:** detection is proposed using ultra-low-field NMR relaxometry[38]. For this a conjugate of the Carbon-dots with the SARS-CoV-2; so that the magnetic relaxation switches (MRSw) can specifically recognize SARS-CoV-2. It is done in vial completely sealed reducing the exposure of people to the virus and without any pretreatment. This one-step method is evaluated with ultra-low-field nuclear magnetic resonance (ULF NMR). Kotta et al[39] has discussed the use of Carbon-dots-based fluorescent biomarkers to help isolate DNA fragments and minimize the detection problems since they can act as signal enrichment tools. A possibility of using Carbon-dots as tools to improve the specificity and sensitivity of the COVID-19 detection immunoassays is proposed[40] . According to them Carbon-dots is to amplify the antigen-antibody binding signal. These labels can be used either as a direct signal or be involved in additional steps to produce a proper signal. Similarly, Kotta et al.[39] has suggested various possibilities for the detection of COVID-19 such as detecting viral RNA through an ultra-sensitive biosensor using carbon dots and gold nanoparticles and use of carboxylic CQDs for nucleic acid detection.

Carbon-dots as Theranostic Agents for Virus & Its Advantages

Antiviral activity - Carbon-dots has been found to exhibit promising antiviral activity against various types of viruses including SARS-CoV-2. Antiviral properties of Carbon-dots can be tuned by the selection of synthesis precursors, so that it could provide an opportunity to develop a flexible, broad range antiviral therapeutics. Surface of non-toxic, biocompatible Carbon-dots can be modified with various functional groups, enhancing targeting, therapeutic efficacy, along with imaging capabilities. Studies have shown that Carbon-dots functionalized with certain molecules (e.g., boronic acid, polyethylene glycol) have demonstrated antiviral activity against HIV, Herpes Simplex Virus (HSV), and SARS-CoV-2, making them promising candidates in the fight against viral infections. Here are some specific examples of Carbon-dots with suitable physicochemical characteristics that are being envisaged for site-specific therapeutic delivery, inactivation or destruction of the virus, functionalized Carbon-dots for modulating patient's immune response for attenuating the exaggerated inflammatory reactions (Table 1).

Table 1: Carbon-dots Derived from different precursors showing antiviral activity against different viruses.

Precursor for Carbon-dots	**Synthesis Method**	**Antiviral against**
PEG-diamine + ascorbic acid	Solid-phase thermal reaction	Pseudorabies virus (PRV) & Porcine Reproductive Respiratory Syndrome virus (PRRSV) [39, 41, 42]
Boronic acid-derived	Hydrothermal Ccarbonization	HIV & Herpes simplex virus type 1 (HSV-1)[43]
Carbon-dots with two different coatings, uncharged CARBON-DOTS s	passivated with 3-ethoxypropylamine (EPA) and positively charged CARBON-DOTS s passivated with 2,2′-(ethylenedioxy)bis(ethylamine) (EDA).	Noroviruses [44]
N & C co-doped **Carbon-dots** from citric acid, mixed with p-phenylenediamine and sodium tetraborate,	One-step hydrothermal method	Inhibitor of Human Corona Virus[45]
Curcumin	Pyrolysis	Suppress porcine epidemic diarrhea virus (PEDV).[46]

benzoxazine monomer (A Broad Spectrum anti-viral drug)-derived **Carbon-dots**	Hydrothermal procedure under alkaline conditions	Exhibited activity against *Flaviviruses* (Dengue Zika, & Japanese encephalitis) *Non-enveloped viruses* (Pporcine Parvovirus and Adenovirus-associated virus) in cell culture experiments.[47]
Gly- **Carbon-dots** prepared from an anti-viral glycyrrhizic acid (Wide-Spectrum Carbon-dots)	Hydrothermal synthesis under alkaline conditions	Exhibited activity against PRRSV, PRV and PEDV viruses.[48]
Carbon nano-powder modifed with EDA	Photo excited	photodynamic inactivation of microphage MS2 consisted of surface protein carbonylation and degradation of genomic RNA[49]
Pullulan-based **Carbon-dots** s and Carrageenan- based **Carbon-dots**	Facile, green, hydrothermal procedure	Against coronavirus MERS-CoV[50]
Allium sativum derived **Carbon-dots**		Is a potential theranostic agent to combat COVID-19; as it can modulate the activity of NFkB, MAPKinase, and scavenge ROS species; it can evade COVID-19 liaised inflammation and cytokine storm by activating Nrf2. And it might be capable of attenuating the progressive symptoms of COVID-19.[51]

CARBON-DOTS S TO FIGHT AGAINST DISEASES CAUSED BY PATHOGENIC BACTERIA

Pathogenic Bacteria

Pathogenic bacteria are called virulent bacteria. Routes of entry of infectious bacteria could be from
(a) Infected from mother to fetus or newborn child. i.e., placental transmission during birth (e.g., Gonococcus & Chlamydia)
(b) Person to person transmission via respiratory, fecal-oral, sexual, or transplacental routes.
(c) Animal-to-human transmission through direct contact or ingestion (zoonotic infections)
(d) Passive spread from insect or arthropod vectors to human for pathogen replication & development (e) Survival during extended periods in dust, food, or water;

Diseases caused by Pathogenic Bacteria

Suitable hosts for bacteria are (i) who do not possess defenses against infection via innate & adaptive immune systems. immunodeficiencies are due to Genetic immunodeficiencies (ii) Stalemate between host and bacteria may results in a state of bacterial latency. Subsequent diminution of host immunity can result in aggressive reactivation and disease such as EBV, TB etc. (iii) Infections in people with Antibody deficiencies; Complement proteins; Neutrophil function; and T-cell deficiencies. (iv) Infections in people with Acquired immunodeficiencies is due to HIV annihilation of T-helper cells.
Some very common disease-causing bacteria are mentioned in table 2.

Table 2: Infectious Diseases Causing Pathogenic Bacteria

BACTERIA	SOURCE	DISEASES
Bacillus megaterium rod-shaped, Gram +ve, Aerobic, Spore forming. Cell length 4 µm, and Cell diameter 1.5 µm	Soil, Sea-water, Sediments, Rice-paddy, Dried-food, Honey, Milk	Meningitis, [52,] Brain-abscess, [53,] Pleuritis[54]
Bacillus anthracis is rod-shaped, Gram +ve spore-forming,	In animals having contact with spore-contaminated soil. Humans contract	3-types of Anthrax Syndromes causing lesions by necrosis with neutrophil and macrophage exudates. (i) Cutaneous are Painless, pruritic papules that become edematous vesicles followed

	anthrax through exposure to contaminated animal products or Powdered spores (a biologic weapon).	by a black eschar. Inhalation rapidly leads to sepsis, shock, and death. (ii) GI grts infected when contracted by eating contaminated meat; causing severe, bloody diarrhea and often death. [55]
Bordetella pertussis is a gram-negative coccobacillus of 0.2 - 0.7 µm		Out of 9-species, 3 infect humans respiratory system causing Whooping-Cough (*B. pertussis*, *B. parapertussis* and *B. bronchiseptic*a) Infection causes Laryngotracheobronchitis with mucosal erosion & mucopurulent exudates associated with striking peripheral lymphocytosis. [56]
Campylobacter jejuni is curved/helical rod, non-spore forming, non-fermentative, gram negative, motile bacteria with single flagellum at one or both ends. When exposed to atmospheric oxygen, it is able to change into a coccal form.	Associated with poultry & animal feces.	Causes gastroenteritis, diarrhea & food poisoning. Reactive arthritis is associated with a genetic make-up, i.e., persons having the human leukocyte antigen B27 (HLA-B27) are most susceptible[57]
Chlamydia trachomatis is an obligate, aerobic, gram negative, coccoid or rod-shaped bacteria**.**	Spread through oral, vaginal or anal sex. It can not thrive outside the body	Is a cellular parasite of eukaryotic cells. Causes a sexually transmitted disease & infects columnar epithelium of cervix, urethra, & rectum[58]
Clostridium perfringens ***Clostridium septicum*** ***Clostridium botulinum*** ***Clostridium difficile*** are rod-shaped, gram-positive anaerobic,	Found in soil, water, intestinal tracts of humans &r animals. They produce spores in the soil. Dormant cells are highly resistant to heat, desiccation, toxic chemicals and detergents. ***C. botulinum*** grows in canned foods & releases neurotoxin	***C. perfringens*** causes food poisoning. ***C. septicum*** cause cellulitis, muscle necrosis in wounds (gas gangrene) & bowel infection in ischemic or neutropenic patients ***C. botulinum*** causes flaccid paralysis of respiratory and skeletal muscles ***C. difficile*** is a highly contagious bacterial infection of the colon[59]
Corynebacterium diphtheriae, a slender gram-positive rod with clubbed ends;	It is passed as an aerosol or through skin exudates. This disease is characterized by an oropharyngeal fibrinosuppurative exudate	Causes Diphtheria a life-threatening disease[60]
***Escherichia coli* 0157:H7** are gram-negative, facultative, either nonmotile or motile by peritrichous flagella, anaerobic. It may have a	Lives in human intestines. Comes from eating infected or undercooked ground beef, hamburger, from drinking raw milk or infected water	Causes bloody diarrhea[61]

fermentative and respiratory metabolism		
Klebsiella granulomatis ***Klebsiella pneumoniae*** are encapsulated coccus	Found in the environment and in humans and other animals: K. pneumoniae is found in human stool also in animal, plant, soil and water	***K. granulomatis*** causes granuloma inguinale, or donovanosis, sexually transmitted. [62,] ***K. pneumoniae*** Causes Pneumonia, Bloodstream infections, Meningitis, and Urinary tract infections [63]
Mycobacterium are aerobic, bacillary, either straight or slightly curved rods, between 0.2 and 0.6 µm wide and between 1.0 and 10 µm long with a thick outer cell membrane. They possess capsule, most of them do not form endospore, are nonmotile and characteristically acid-fast. It has 2 infectious species ***M. tuberculosis & M. bacterium or M. leprae***	When someone with active TB in their lungs coughs, sneezes, speaks, or sings, they release TB germs into the air. People nearby can breathe in these germs and become infected. M. leprae, spreads through close, long-term contact with an infected person, usually through nasal droplets and secretions	***M. tuberculosis*** affects almost any part of the body but is mainly an infection of the lungs causing Pulmonary TB[64] ***M. bacterium or M. leprae*** Causes Leprosy a slowly progressive infection affecting skin & peripheral nerves with resultant deformities[65]
Nisseria meningitidis & N. gonorrhoeae are 2 pathogenic species. They are aerobic, gram-negative diplococci that looks like a coffee bean		***N. meningitidis*** cause infection in the blood or lungs, it is also a major cause of meningitis in both children and adults. [66] ***N. gonorrhoeae*** causes bacterial meningitis, particularly in children below 2years. In adult it is sexually transmitted [67]
Nocardia asteroides ***Nocardia brasiliensis*** are actinomycetes, aerobic, gram-positive bacteria growing in branched chains; they also stain with modified acid-fast Fite- Faraco stain.	Found in soil immunocompromised	***N. asteroides*** causes opportunistic infections in immunocompromised hosts known a Nocardiosis an indolent respiratory infections which affects lungs, brain and skin in people with weak immune system. ***N. brasiliensis*** infects the skin. It elicits suppurative responses, surrounded by granulation tissue and fibrosis. [68]
Pseudomonas aeruginosa, and ***P. pneumonia*** opportunistic aerobic, gram-negative bacillus.	Normally inhabit soil, water, and vegetation and can be isolated from the skin, throat, and stool of healthy persons.	***P. aeruginosa***, frequently seen in patients with cystic fibrosis, burns, or neutropenia. It also causes corneal keratitis in contact wearers and external otitis (swimmer's ear) in normal hosts. ***P. pneumonia*** cause extensive tissue necrosis by vascular invasion with subsequent thrombosis. Skin infections give rise to well-demarcated necrotic and hemorrhagic skin lesions, ecthyma gangrenosum. [69]
Salmonella typhi ***S. para-typhoid*** ***S. Enterocolitis*** are gram-negative, enteric, motile with peritrichous flagella, non- sporing, non-capsulated aerobic, facultative anaerobe,	***Salmonella*** infection sources are raw or undercooked meat, poultry, and eggs or egg products or by drinking unpasteurized milk.	Salmonella causes three I clinical diseases[70]: ***S. typhi and S. para-typhi*** Causes Enteric fever i.e., typhoid ***S. para-typhi*** A, B, and C aalso causes pneumonia, osteomyelitis, pulmonary abscess, endocarditis and meningitis. ***S. Enterocolitis*** causes food poisoning or gastroenteritis

bacillus of 2-4 X 0.6 µm size		
Serratia marcescens is a Gram-negative, facultatively anaerobic, rod-shaped, typically 1–5 µm in length, do not produce spores, motile, red pigments producing bacteria	It is found in water, soil, plants, and animals. Frequently found in showers, toilet bowls, and around wetted tiles as a pinkish to red biofilm	This opportunistic pathogen causes urinary tract infections, pneumonia, endocarditis, soft tissue infection, septicemia, Meningitis, ventriculitis and cysts. Other species *S. plymuthica,* *S. liquefaciens,* *S. rubidaea, and* *S. odoriferae* have been shown to cause infection such as osteomyelitis and endocarditis. [71]
Shigella dysentriae is Gram negative bacilli, they are aerobics and facultative anaerobics This enterobacteria is mostly non-motile, non-sporing, its size varies from 2-4um x 0.4 -0.6 µm	Source is fecal–oral spread from an infected individual.	This species causes dysentery/shigellosis, which is an acute diarrheal disease characterized by passage of pus, blood or mucous through the stool. Infection occurs because of the ingestion of contaminated food or water. [72]
Staphylococcus aureus ***S faecalis***, are Gram-Positive pyogenic cocci that grow in clusters and are distinctive for local destructiveness	Humans are the primary reservoir for Staphylococcus	They cause a variety of skin infections (boils, carbuncles, impetigo), osteomyelitis, pneumonia, endocarditis, food poisoning & toxic shock syndrome. infect patients with catheters/prosthetic heart valves and Staphylococcus saprophyticus causes UTI. [73]
Streptococcus purogenes **S. pneumonia** **S. agalactiae** **S. mutans** Gram-Positive Cocci that grow in pairs or chains	found in many natural sources, including humans and animals:	**Streptococcus purogenes** cause partial or green hemolysis that causes pharyngitis, scarlet fever, erysipelas, impetigo, rheumatic fever, toxic shock syndrome, necrotizing fascititis and glomerulonephritis; **S. agalactiae** colonizes the female genital tract and causes chorioamnionitis in pregnancy; neonatal sepsis and meningitis **S**. **pneumonia**e, cause of adult community-acquired pneumonia and meningitis. **S. mutans** is the major cause of dental caries[74]
Treponema palidium helically coiled microbe, 6–15 µm long and 0.1–0.2 µm wide. Have a cytoplasmic and an outer membrane. *T. palidium* has 3 pathogenic sub-species	Humans are the only source of treponemal infection; there are no known nonhuman reservoirs	T. *p. pallidum*, *T. p. endemicum*, and *T. p. pertenue* cause Spirochetes-Syphilis, Bejel, Pinta & Yaws are chronic, tropical, nonvenereal spirochetal infections spread by body contact[75]
Vibrio cholera are aerobics facultative anaerobes, a gram-negative, rod-shaped bacteria with a small bend in the middle and has a long tail-like flagella	Sources are contaminated food or water	*Vibrio cholera* cause Cholera
Yersinia pestis is a gram-negative, facultative intracellular bacterium with three	It is transmitted from rodents to humans by aerosols or fleabites.	***Y. pestis*** causes plague ***Y. enterocolitica*** and ***Y. seudotuberculosis*** cause fecal oral transmitted ileitis & mesenteric lymphadenitis

clinically important species.		Yersinia proliferate in lymphoid tissues and causes massive lymph node enlargement (buboes), pneumonia, and sepsis, with massive bacterial proliferation, tissue necrosis, and neutrophilic infiltrates[75]

Carbon-dots as Theranostic Agent for Diseases caused by Pathogenic Bacteria

Carbon-dots hold significant potential as a breakthrough weapon against IDs, especially with their versatile antimicrobial properties, diagnostic capabilities, and drug delivery potential. However, more research is required to fully understand their mechanisms, optimize their applications, and ensure safety in clinical settings.

Carbon-dots have demonstrated significant antimicrobial activity against a wide range of pathogens, including bacteria, fungi, and viruses. Their small size (less than 10 nm) allows them to interact with microbial membranes, leading to cell disruption. Moreover, CARBON-DOTS s can be engineered to produce reactive oxygen species (ROS), which damage microbial cells, making them effective in killing pathogens. Their excellent fluorescence properties of CARBON-DOTS s make them suitable for bioimaging and diagnostics[76, 77, 78].

Carbon-dots has been tried for Photothermal and Photodynamic Therapy, as it can be activated by light to generate heat (photothermal) or ROS (photodynamic), which can kill pathogens selectively without harming the surrounding healthy tissues. This makes them excellent candidates for treating localized infections, including wound infections and biofilms, which are often resistant to antibiotics[79,80].

Efforts has also been on for using Carbon-dots as Drug Delivery Systems. Carbon-dots can serve as nanocarriers for delivering antimicrobial drugs, enhancing their efficacy. Due to their biocompatibility, high surface area, and ability to penetrate cells, Carbon-dots can improve drug solubility, stability, and targeted delivery to infected sites. This targeted approach helps reduce the required dosage of drugs and minimizes side effects[81]. However, there are challenges related to scalability. Producing Carbon-dots on a large scale while maintaining uniform properties can be challenging. There is a need for standard protocols in terms of synthesis, characterization, and testing of Carbon-dots to ensure consistent results. Long-term Safety: will be other consideration. While Carbon-dots are considered biocompatible, their long-term effects need further investigation before widespread use in humans.

CARBON-DOTS S TO FIGHT AGAINST DISEASES CAUSED BY PATHOGENIC FUNGI

Diseases caused by Pathogenic Fungi

Diseases caused due to fungal infection are known as Mycosis. Fungus invades the body and can affect the skin, hair, nails, mucous membranes, lungs, or other parts of the body. Fungal diseases are categorized into six groups they are (1) Superficial, (2) Cutaneous, (3) Subcutaneous, (4) Systemic and (5) Opportunistic and (6) Invasive Mycoses (Table 3).

Table 3: Different Types of Mycoses Caused by different Fungal Species

Types of Mycoses	Disease Causing Fungi
SUPERFICIAL MYCOSIS	***Piedraia hortae*** it infects scalp and are known as Black piedra. ***Trichosporon beigelii*** infects beard & mustache causing White piedra. ***Malassezia furfur***, it infects trunk, neck, face, arms and the disease is called Tinea versicolor.
CUTANEOUS MYCOSIS	***Trichophyton mentagrophytis, Trychophyton verrucossum*** and ***Trychophyton rubrum*** they infect beard hair and the disease is called Tinea barbae. ***Trichophyton sp., Microsporum canis*** infect Scalp hair causing a disease known as Tinea captis. ***Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum canis*** infect smooth or bare parts of skin causing Tinea corporis an etching infection ***Trichophyton rubrum , T. mentagrophytes , Epidermophyton floccosum*** infects groin, buttocks causing Tinea cruris or jock itch. ***Trichophyton rubrum, T. mentagrophytes, Epidermophyttum floccosum*** infects feet causing Tinea pedis or athlete's foot (***Trichophyton rubrum. Trichophyton mentagophytes, Epidermophytum floccosum***. Infects nails causing Tinea unguium (oncomycosis).

SUB-CUTANAEOUS MYCOSIS	***Phialophora verrucosa*** it infects legs and feet causing Chromoblastomycosis. ***Sporothrix schenckii*****,** causes chronic skin infection that can also affect the lungs causing Sporotrichosi
SYSTEMIC MYCOSIS	***Coccidiodes immitis*** it infects lungs and other parts of body. Causing Coccidioidomycosis**.** ***Cryptococcus neoformis*** infects lungs, skin, bones ,viscera, central nervous system, causing Cryptococcosis **.** ***Histoplasma capsulatum*** infects within phagocytosis causing a disease called Histoplasmosis
OPPORTUNISTIC MYCOSIS are caused by fungi having low inherent virulence, are non-pathogenic in mmuno-competent host, e	***Aspergillus fumigatus, Aspergillus flavus*****,** affects respiratory system and causing Aspergillosis ***Candida albicans*** infects skin or mucous membrane causing Candidiasis ***Pneumocystis jivoroveci*** infects lungs and sometime brain also causing Pneumocystis pneumonia ***Encephalitozooon*** also infects lungs and sometimes brain causing another disease called Microsporidiosis**.**
INVASIVE MYCOSIS	**Candida *(yeast)*** CAUSES Invasive Candidiasis which is a serious infection that can affect the blood, heart, brain, eyes, bones, and other parts of the body.

Carbon-dots as Theranostic Agent for Diseases Caused by Fungi

A number of antifungal drugs are exploited for the treatment of fungal infections, but most of the pathogenic fungi, especially yeasts, develop resistance towards antifungal drugs. Adverse effects of topical and systemic antifungal drugs due to dose related problems sometimes limit their use. Nanoparticles like Carbon-dots offer a lower risk of systemic side effects for the treatment of fungal infections especially due to nanoparticle-based formulations for targeted drug delivery, increased skin permeability and controlled release. They also offer advantage by increasing the bioavailability of active components with prolonged effect at the site of infection fungi.

CARBON-DOTS S TO FIGHT AGAINST DISEASES CAUSED BYPARASITIC PROTOZOA

Parasitic Protozoa

Parasitic protozoa are single-celled organisms that invade and live in the cells and tissues of other organisms, causing disease. Some of the common Protozoa (Fig.6) that cause disease in human are presented in Table 4.

Table 4 Parasitic Protozoa that invades human causing IDs.

Protozoa	Source	Causing IDs
Entamoeba histolytica	Contaminated drinking water with feces containing cysts; contaminated food, by fecally contaminated hands of food handlers.	**Amoebiasis, Amoebic dysentery**[82]
Giardia intestinalis	Dormant microbial cysts in contaminated water, food, or by the faecal-oral route	**Giardiasis** (diarrhea, abdominal cramps, vomiting, fever) [83]
Leishmania	Transmitted by female Phlebotomine sandflies bites. Wild and domestic dogs and small rodents are common hosts	**Leishmaniasis** (weight loss, low blood count, fever, dark skin pigmentation, renal failure, skin ulcers) **Muco-cutaneous leishmaniasis (MCL**) affects the mucosal tissue of mouth, nose and throat and can lead to the partial or total disintegration of these tissues[84]
Naegleria fowleri known as "brain-eating amoeba".	Found in warm fresh water (lakes, rivers, hot springs), in inadequately chlorinated swimming pool water	**Primary Amebic Meningoencephalitis (PAM)** a fatal infection destroying brain tissues and causing death within about 5 to 12 days. [85]

	or heated and contaminated tap water and soil.	
Plasmodium spp	Mosquitoes (Anopheles) are vector for Plasmodium	**Malaria** caused by **4** species *P. falciparum, P. vivax, P. ovale,* and *P. malariae*. High fever, joint pain, vomiting, weakness, renal failure, confusion, seizures. **Cerebral Malaria** is caused by *P. falciparum*, results in tissue death in the brain. [86]
Trypanosoma brucei		**Trypanomiasis.** orAfrican sleeping disease in humans Symptoms are fever, headaches, joint pains, and itching. severe swelling of lymph nodes & disruption of the sleep cycle [87]

Carbon-dots as Theranostic Agent for Diseases Caused by Parasitic Protozoa

Theranostic agents are materials that combine therapeutic and diagnostic capabilities, offering potential for simultaneous disease treatment and monitoring. Carbon-dots with functionalized with antiparasitic drugs have been explored as theranostic agents for treating parasitic protozoa-caused diseases. Kumar et al [88] have unravelled the potential Carbon dots as well as gallium doped CARBON-DOTS s (Ga@ Carbon-dots) of 4 and 7 nm and dispersed in a commercial ointment. Both exhibited higher activity against Leishmania. The interesting part was that it needed a minimal concentration of 30 µg/ml for Carbon-dots /Ga@ Carbon-dots, compared with a commercial counterpart. They suggested that ointments could be considered as a new class of emerging drugs to combat Leishmaniasis. Torkashvand et al [89] have tried to antimalarial nano-drug delivery system based on graphene quantum dot on *Plasmodium falciparum* for its toxicological evaluation. They incorporated artesunate (Art), mefloquine (Mef) alone, chitosan (chi), and in combination (Art-Mef) form in the graphene quantum dot (GQD)-based nanocomposites; and observed the release of drugs continued during 98 %, 96 % and 90 % (36 h) for GQD-Art/Chi, GQD-Mef/Chi and GQD-Art-Mef/Chi, respectively. Hence they concluded that the prepared nanodrugs had a suitable effect on the cultured P. falciparum in this study.

Carbon-dots can be used to monitor the progress of the therapy by providing a visual readout of treatment effectiveness, helping to detect any remaining parasitic load. Some research has demonstrated the use of carbon dots for imaging malaria-infected red blood cells, as well as their potential for enhancing the effects of traditional antimalarial drugs.

Since Carbon-dots is biocompatible and non-toxic to the host it is also being tried especially for in vivo applications. Making Carbon-dots **w**ithout affecting healthy cells to improve therapeutic outcomes. While still an emerging field, the use of carbon dots as theranostic agents against protozoan diseases shows promising potential and is the subject of ongoing research.

CARBON-DOTS S TO FIGHT AGAINST DISEASES CAUSED BY PARASITIC HELMINTHS

Parasitic Helminths

Helminths are parasitic worms, which infect intestine and feed on a living host causing poor nutrient absorption, resulting in weakness and disease in the host. It enters in human body is through Ingestion; Arthropod bite and Penetration of intact skin or mucous membranes. Helminths exists in three life-cycle stages: eggs, larvae, and adults. Adult worms infect definitive hosts, whereas larval stages may be free-living or parasitize in intermediate or paratenic hosts (vertebrate vectors). There are three groups of helminths - Nematodes, Trematodes and Cestodes (Table 5).

Table 5: **Diseases caused by Parasitic Helminths**

Parasitic Helminths	**Source**	**Diseases caused by Parasitic Helminths**
NEMATODES or Roundworms	found in soil contaminated with young roundworm larvae,	***Stongiloides***, causing **GI** track upset, rash, bronchospasm, diarrhea, eosinophilia.[91] ***Trichinosis*** caused by *Trichinella spiralis.* Infection occurs by ingestion of uncooked pork having larvae, from stomach larvae

	Contaminated water, Fruits & Vegetables and Dogs, Pigs, primates, and insects	moves to small intestine and there in penetrates through the mucosa. There adult male and female round worm emerges and produce larva, which penetrate intestine and circulate in blood stream. Larvae enter skeletal muscle cells and encyst, causing muscle pain, fever, , edema, eosinophilia, elevated creatinine phosphokinase. It induces neurological and myocardial symptoms. [92] ***Filaria*** caused by (i) Lymph dwelling roundworm (*Wuchereria bancroftii*) through mosquito bite, here adult stays in peripheral lymphatics, produces larvae and larvae is circulated in blood, it causes elephantitis. (ii) Skin dwelling roundworm caused by biting black flies that is the vector for *Onchoceros volvulus*. Adult forms skin nodules and migrate through dermis. It causes degradation and allergic responses in the skin.
TREMATODES Flukes or Flatworms.	Freshwater snails where is produces eggs. To cause infection Larva migrate to lungs	***Schjitosomiosis*** caused by Schistosoma spp (blood flukes) Cercarial dermatitis, for Intestinal schistosomiasis involves granulomas leading to polyp formation, protein loss, malabsorption and strictures**.** ***Hepatosplenic schistosomiasis*** causes portal hypertension leading to ascites, varices, splenomegaly, normal hepatic function). ***Urinary schistosomiasis*** i.e., chronic infection and obstruction. Also, in some cases cardiopulmonary and CNS involvement is seen.
CESTODES or Tapeworm.	Humans acquire infection either by ingestion of eggs from feces (to acquire tissue cysts) or by ingestion of tissue cysts in undercooked meat (to acquire a tapeworm).	There are Definitive Hosts that harbor adult worms, and Intermediate Hosts harbor tissue cysts containing worm heads. Three diseases are caused by tapeworms Cysticerosis, Taeniasis and Echinococcosis (Hydatid disease or Hydatid Cyst) ***Cysticercosis*** is caused by a Tapeworm called *Echinococcus*, when cysts enter in brain it causes seizures. ***Taeniasis*** from uncooked pork ***Echinococcosis*** is caused from ingestion of eggs in Pasteur infecting liver or lung with massive cysts.\ The larval stage of the tapeworm *Echinococcus granulosus* is the causative agent of hydatid disease in humans.

Carbon-dots as Theranostic Agent for Diseases caused by Parasitic Helminths

Carbon-dots -therapeutic efforts have been directed to combat all the three types of parasitic Helminth. Though, not much of therapeutic treatment at the moment is in practice, however, they show a great promise for the future. No vaccine is currently available for filariases caused by nematodes.

These Carbon-dots are used in the context of helminthic diseases for Diagnosis in bioimaging applications by modifying their surface to target specific parasitic helminths, allowing them to be used for imaging the parasites in infected tissues. Functionalized Carbon-dots can be used in biosensors to detect helminth-related biomarkers in biological samples like blood, urine, or stool, potentially aiding in the early diagnosis of parasitic infections. For therapeutic applications like direct drug delivery to the site of infection Carbon-dots can deliver drugs directly to the site of infection, enhancing therapeutic efficiency and reducing side effects. And Carbon-dots can even generate reactive oxygen species (ROS) or heat when exposed to specific wavelengths of light, enabling photodynamic or photothermal therapy against helminths. This approach can directly damage the parasites or disrupt their life cycle. Carbon-dots can combine diagnostic and therapeutic functions in a single platform. For instance, they can be used to detect parasitic helminths through imaging, while simultaneously delivering a therapeutic payload or applying photothermal/photodynamic effects.

However, there are challenges and considerations such as although Carbon-dots show great potential, their application in parasitic helminth diseases is still in the early stages of research. Issues such as large-scale synthesis, precise targeting, and understanding long-term toxicity need further exploration. More research is needed to optimize Carbon-dots functionalization and therapeutic efficacy specifically against parasitic helminths compared to other disease applications. While there

is promising evidence suggesting Carbon-dots could be valuable theranostic agents for helminthic diseases, further investigation is necessary to realize their full potential in clinical settings.

II. CONCLUSION AND FUTURE PERSPECTIVE

Carbon-dots have emerged as promising nanomaterials in the fight against IDs due to their unique properties, including biocompatibility, low toxicity, ease of synthesis, and multifunctional capabilities. Carbon-dots offer a versatile platform for developing novel antimicrobial and antiviral strategies, potentially revolutionizing the way IDs are managed in the future.[93]

Some future perspectives for using Carbon-dots to combat IDs could be using them as antimicrobial agents by engineering them to exhibit direct antimicrobial properties by generating reactive oxygen species (ROS) or through photothermal effects that disrupt bacterial cell membranes.[94] Their ability to combat drug-resistant pathogens holds significant promise. Carbon-dots can be combined with traditional antibiotics to enhance their efficacy, potentially reversing antibiotic resistance, or reducing the required dosage, thus minimizing side effects[95]. Carbon-dots can also be used to inhibit Virus entry and replication, because Carbon-dots can interact with viral proteins or cell surface receptors to inhibit viral entry into host cells.[96] They can also interfere with the replication process of viruses, offering a potential strategy for treating viral infections. Functionalizing Carbon-dots with specific molecules or ligands can enable them to target a range of viruses, including influenza, HIV, and SARS-CoV-2, making them versatile Broad-Spectrum antiviral agents. Carbon-dots can be functionalized to carry antimicrobial or antiviral drugs directly to the site of infection. This targeted approach can increase drug concentration at the infection site, improving therapeutic efficacy while reducing systemic toxicity. It can be designed to release their cargo in response to specific stimuli (e.g., pH, light, or temperature), allowing for precise control over drug release and enhanced treatment effectiveness. Another approach can be to use Carbon-dots to stimulate or modulate the immune system's response to infectious agents. This approach could improve vaccine efficacy or be used as an adjuvant to enhance the body's natural defense mechanisms. In combination with immunotherapeutic agents, Carbon-dots may enhance the targeting of infectious agents or infected cells, potentially improving outcomes in diseases like chronic viral infections. Real-Time pathogen detection by bioimaging and diagnostics, due to their fluorescent properties, can be used as diagnostic tools for detecting pathogens at very low concentrations. They can be functionalized with specific targeting agents (e.g., antibodies) for rapid and accurate detection. Combining diagnostic and therapeutic functions into a single platform, Carbon-dots can be used to identify infected tissues and simultaneously deliver therapeutic agents, providing a dual approach to combating infections. Photothermal and Photodynamic Therapy will be another potential approach to combat IDs. Carbon-dots can absorb near-infrared light and convert it into heat, which can be used to kill pathogens or infected cells. This method is especially useful for treating localized infections. Carbon-dots can generate ROS under light irradiation, leading to the inactivation of pathogens. This approach can be used to treat a wide range of bacterial, viral, and fungal infections. Carbon-dots have shown the ability to penetrate and disrupt biofilms, which are often resistant to conventional antibiotics. This makes them valuable for treating chronic and device-associated infections. Carbon-dots can be incorporated into coatings for medical devices, surgical tools, or even hospital surfaces to prevent microbial colonization and transmission of IDs. Carbon-dots can be used in water purification systems to remove or inactivate pathogens, providing safer drinking water in areas prone to waterborne diseases.

Challenges and future directions will involve understanding the mechanisms of how Carbon-dots interact with different pathogens and host cells; standardization and scaling-up while synthesizing Carbon-dots with consistent properties on a large scale remains a challenge. And finally comprehensive safety evaluations are required before Carbon-dots can be widely used in clinical settings.

REFERENCES

[1]. Xu X, Ray R, Gu Y, Ploehn HJ, Gearheart L, Raker K, Scirivens W, J.Am.Chem.Soc. 126, 12736, 2004.

[2]. Li Haitao, Xinyi Zhang, Douglas R. MacFarlane. Quantum Dots: Carbon Quantum Dots/Cu2O Heterostructures for Solar-Light-Driven Conversion of CO2 to Methanol. Advanced Energy Materials; 5(5), 2015, https://doi.org/10.1002/aenm.201570024

[3]. Sharon Madhuri, Ashmi Mewada, ADVANCES IN NANOMATERIALS & APPLICATIONS: Carbon Dots as Theranostic Agents. WILEY, USA, 2018.

[4]. Zhou J, Booker C, Li R, Zhou X, Sham T, Sun X, Ding Z, J.Am.Chem.Soc. 129(4), 744, 2007.

[5]. Liu H, Ye T, Mao C, Angew.Chem.Int.Ed. 46(34), 6473, 2007.

[6]. Hsu PC, Chang H-T, Chem.Commun. 48, 3984, 2012. http://dx.doi.org/ 10.1039/c2cc30188a
[7]. Sun YP, Zhou B, Lin Y, Wang W, Fernando KA, Pathak P, Meziani MJ, Harruff BA, Wang X, Wang H, Luo PJ, YangH, Kose ME, Chen B, Veca LM, Xie SY, J.Am.Chem.Soc. 128, 7756, 2006
[8]. Habiba K, Marakov VI, Avlos J, Guniel MJF, Weiner BR, Morell G, Carbon 64, 341–350, 2013
[9]. Jiang H, Chen F, Lagally MG, Denes FS, Langmuir 26, 1991–1995, 2010
[10]. Loh YH, Hartung O, Li H, Guo C, Sahalie JM, Manos PD, Urbach A, Heffner GC, Grskovic M, Vigneault F, Lensch MW, Park IH, Agarwal S, Church GM, Collins JJ, Irion S, Daley GQ, Cell Stem Cell 7(1), 15–19, 2010
[11]. Li HT, He XD, Liu Y, Huang H, Lian S, Lee ST, Kang Z, Carbon 49, 605–609, 2011.
[12]. Zhu W, Wang X, Li Y, Wang Z, Yang F, Yang X, Chem. Commun. 2009, 5118–5120, 2009.
[13]. Zong J, Zhu YH, Yang XL, Shen JH, Li C, Chem. Commun. 47, 764, 2011.
[14]. Mewada Ashmi, Sunil Pandey, Sachin Shinde, Neeraj Mishra, Goldie Oza, Mukeshchand Thakur, Maheshwar Sharon, Madhuri Sharon. Green synthesis of biocompatible carbon dots using aqueous extract of Trapa bispinosa peel; Materials Science and Engineering: C, 33 (2013) 2914–2917 Doi:10.1016/j.msec.2013.03.018
[15]. Thakur Mukeshchand, Sunil Pandey, Ashmi Mewada, Ritu Shah, Goldie Oza, and Madhuri Sharon. Understanding the stability of silver nanoparticles bio-fabricated using Acacia arabica (Babool gum) and its hostile effect on microorganisms. Spectrochimica-Acta Part-A: Molecular and Biomolecular Spectroscopy. 109 (2013) 344–347 http://dx.doi.org/10.1016/j.saa.2013.03.044,
[16]. Wan Jiafeng, Xiaoyuan Zhang, Kun Fu,/ Highly fluorescent carbon dots as novel theranostic agents for biomedical applications. Nano Scale 41 (1921)
[17]. Guan W, Gu W, Ye L, Guo C, Su S, Xu P, Xue M, Int.J.Nanomed. 9, 5071–5078, 2014
[18]. Roshni V, Ottur D, Curr. Science 112(2), 385–390, 2017.
[19]. Chen W, Hu C, Yang Y, Cui J, Liu Y, Materials 9, 184–191, 2016
[20]. Mewada A, Pandey S, Thakur M, Jadhav D, Sharon M, J.Mater.Chem. B2, 698, 2014
[21]. Chesebro B, R Race, K Wehrly, J Nishio, M Bloom, D Lechner, S Bergstrom, K Robbins, L Mayer, JM Keith, C Garon, A Haase. Identification of scrapie prion protein-specific mRNA in scrapie-infected and uninfected brain. Nature; 315, 331, 1985.
[22]. Harris A. Cellular Biology of Prion Diseases. Clin. Microbiol.Rev.;12, 429–444, 1999.
[23]. Srithayakumar V, GB Mitchell, BN White. BMC Vet.Res.; 12, 59, 2016
[24]. Liberski PP, JW Ironside, Chapter 23 - Prion Diseases A2 - Zigmond, Michael J, in:L.P. Rowland, J.T. Coyle (Eds.), Neurobiology of Brain Disorders, Academic Press, San Diego 2015, pp. 356–374.
[25]. Geschwind MD. Prion Diseases. Continuum (Minneapolis, Minn.); 21, 1612–1638, 2015.
[26]. Appleby BS, CG Lyketsos, Rapidly progressive dementias and the treatment of human prion diseases. Expert.Opin.Pharmacother.; 12, 1–12, 2011
[27]. Dearmond SJ. Discovering the Mechanisms of Neurodegeneration in Prion Diseases. Neurochem. Res.; 29, 1979–1998, 2004.
[28]. Jucker M, LC Walker. Self-propagation of pathogenic protein aggregates in neurodegenerative diseases. Nature; 501, 45, 2013.
[29]. Liu, Y.; Xu, L.P.; Dai, W.; Dong, H.; Wen, Y.; Zhang, X. Graphene quantum dots for the inhibition of β amyloid aggregation. Nanoscale, 2015, 7(45), 19060-19065.
[30]. Fehr AR, Perlman S. Coronaviruses. Coronaviruses: An Overview of Their Replication and Pathogenesis. Methods Mol Biol.; 1282, 1–23, 2015. doi:10.1007/978-1-4939-2438-7_1.
[31]. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, Yuen KY. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerg Microbes Infect.; 9, 221–236, 2020, doi:10.1080/22221751.2020.1719902.
[32]. Brian DA, Baric RS. Coronavirus genome structure and replication. Curr Topics Microbiol Immunol.; 287, 1–30, 2005. doi:10.1007/3-540-26765-4_1.
[33]. He, X.P., H. Tian, Photoluminescence architectures for disease diagnosis: from graphene to thin-layer transition metal dichalcogenides and oxides, Small, 12 (2016) 144–160, https://doi.org/10.1002/smll.201502516.
[34]. Gill A.A.S., Gill, S. Singh, N. Thapliyal, R. Karpoormath, Nanomaterial-based optical and electrochemical techniques for detection of methicillin-resistant Staphylococcus aureus: a

review, Microchim. Acta 186 (2019) 114, https://doi.org/10.1007/s00604-018-3186-7.

[35]. Li, P. Jing, L. Sun, Y. An, X. Shan, X. Lu, D. Zhou, D. Han, D. Shen, Y. Zhai,S. Qu, R. Zbo————————————————ril , A.L. Rogach, Near-infrared excitation/emission and multiphotoninduced fluorescence of carbon dots, Adv. Mater. 30 (2018) 1705913, https://doi.org/10.1002/adma.201705913.

[36]. Pandey RR., CC Chusuei, Carbon nanotubes, graphene, and carbon dots as electrochemical biosensing composites, Molecules 26(2021) 6674, https://doi.org/10.3390/molecules26216674

[37]. Ji C., Y. Zhou, R.M. Leblanc, Z. Peng, Recent developments of carbon dots in biosensing: a review, ACS Sens. 5(2020) 2724–2741, https://doi.org/10.1021/acssensors.0c01556.

[38]. Y. Li, P. Ma, Q. Tao, H-J. Krause, S. Yang, G. Ding, H. Dong, X. Xie, Magnetic graphene quantum dots facilitate closed-tube one-step detection of SARS-CoV-2 with ultra-low field NMR relaxometry, Sensors ActuatorsB Chem (2021), 129786, https://doi.org/10.1016/j.snb.2021.129786.

[39]. Kotta S., H.M. Aldawsari, S.M. Badr-Eldin, N.A. Alhakamy, S. Md, A.B. Nair, P. K. Deb, Exploring the potential of carbon dots to combat COVID-19, Front.Mol.Biosci. 7(2020), 616575, https://doi.org/10.3389/fmolb.2020.616575.

[40]. Santiago I., Trends and innovations in biosensors for COVID-19 mass testing, Chembiochem 21(2020) 2880–2889, https://doi.org/10.1002/cbic.202000250.

[41]. Innocenzi P, Stagi L (2020) Carbon-based antiviral nanomateri als: graphene, C-dots, and fullerenes. A perspective. Chem Sci 11:6606–6622. https://doi.org/10.1039/D0SC02658A

[42]. Du T, Liang J, Dong N et al (2016) Carbon dots as inhibitors of virus by activation of type I interferon response. Carbon N Y 110:278–285. https://doi.org/10.1016/j.carbon.2016.09.032

[43]. Barras A, Pagneux Q, Sane F et al (2016) High efciency of functional carbon nanodots as entry inhibitors of herpes simplex virus type 1. ACS Appl Mater Interfaces 8:9004–9013. https:// doi.org/10.1021/acsami.6b01681 102.

[44]. Dong X, Moyer MM, Yang F et al (2017) Carbon dots' antiviral functions against noroviruses. Sci Rep 7. https://doi.org/10.1038/ s41598-017-00675-x

[45]. Garg P, Sangam S, Kochhar D et al (2020) Exploring the role of triazole functionalized heteroatom co-doped carbon quantum dots against human coronaviruses. Nano Today 35:101001. https://doi.org/10.1016/j.nantod.2020.101001

[46]. Lin CJ, Chang L, Chu HW et al (2019) High amplification of the antiviral activity of curcumin through transformation into carbon quantum dots. Small 15. https://doi.org/10.1002/smll.201902641

[47]. Huang S, Gu J, Ye J.(2019) Benzoxazine monomer derived carbon dots as a broad-spectrum agent to block viral infectivity. J Colloid Interface Sci 542:198–206. https://doi.org/10.1016/j.jcis.2019.02.01

[48]. Tong T, Hu H, Zhou J et al (2020) Glycyrrhizic-acid-based carbon dots with high antiviral activity by multisite inhibition mechanisms. Small:16. https://doi.org/10.1002/smll.201906206

[49]. Dong X, Edmondson R, Yang F et al (2020) Carbon dots for effective photodynamic inactivation of virus. RSC Adv 10:33944–33954. https://doi.org/10.1039/D0RA05849A

[50]. Emam HE, Ahmed HB (2021) Antitumor/antiviral carbon quantum dots based on carrageenan and pullulan. Int J Biol Macromol 170:688–700. https://doi.org/10.1016/j.ijbiomac.2020.12.151

[51]. Kalkal Ashish, Prince Allawadhi, Rangadhar Pradhan, Amit Khurana, Kala Kumar Bharani, Gopinath Packirisamy. Allium sativum derived carbon dots as a potential theranostic agent to combat the COVID-19 crisis. Sensors International, 2,2021,100102, ISSN 2666-3511, https://doi.org/10.1016/j.sintl.2021.100102

[52]. Dib EG, Dib SA, Korkmaz DA, Mobarakai NK, Glaser JB. Nonhemolytic, Nonmotile Gram-Positive Rods Indicative of Bacillus anthracis. Emerg Infect Dis.; 9(8), 1013-1015, 2003. https://dx.doi.org/10.3201/eid0908.030205

[53]. Guo Fu-Ping, Hong-Wei Fan, Zheng-Yin Liu, Qi-Wei Yang, Yi-Jia Li, Tai-Sheng Li. Brain Abscess Caused by Bacillus megaterium in an Adult Patient. Chin Med J (Engl); 128(11), 1552–1554, 2015. doi: 10.4103/0366-6999.157697

[54]. Crisafulli Ernesto, Ilaria Aredano , Ilaria Valzano ,Francesco Andrani ,Alfredo Chetta. Pleuritis with pleural effusion due to a Bacillus megaterium infection. Respiratory case Reports; 7(1), e00381, 2019. doi: 10.1002/rcr2.381

[55]. Chambers J, Yarrarapu SNS, Mathai JK. Anthrax Infection. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL):

StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK535379/

[56]. Finger H, von Koenig CHW. Bordetella. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 31. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7813/

[57]. Fischer GH, Hashmi MF, Paterek E. Campylobacter Infection. [Updated 2024 Jan 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK537033/

[58]. Mohseni M, Sung S, Takov V. Chlamydia. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK537286

[59]. Yao PY, Annamaraju P. Clostridium perfringens Infection. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK559049/

[60]. Murphy JR. Corynebacterium Diphtheriae. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter-32. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7971/

[61]. Ameer MA, Wasey A, Salen P. Escherichia coli (e Coli 0157 H7) In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK507845/

[62]. Santiago-Wickey JN, Crosby B. Granuloma Inguinale. [Updated 2023 Mar 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK513306/

[63]. Ashurst JV, Dawson A. Klebsiella Pneumonia. [Updated 2023 Jul 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK519004/

[64]. Smith Issar. Mycobacterium tuberculosis Pathogenesis and Molecular Determinants of Virulence. Clin Microbiol Rev. 2003; 16(3): 463–496. doi: 10.1128/CMR.16.3.463-496.2003

[65]. Sugawara-Mikami Mariko, Kazunari Tanigawa, Akira Kawashima, Mitsuo Kiriya, Yasuhiro Nakamura, Yoko Fujiwara, and Koichi Suzuki. Pathogenicity and virulence of Mycobacterium leprae. Virulence. 2022; 13(1): 1985–2011. 2022. doi: 10.1080/21505594.2022.2141987

[66]. Rouphael Nadine G. and David SS. Neisseria meningitidis: Biology, Microbiology, and Epidemiology. Methods Mol Biol. Author manuscript; available in PMC 2015.Published in final edited form as: Methods Mol Biol. 2012; 799: 1–20. doi: 10.1007/978-1-61779-346-2_1. PMCID: PMC4349422NIHMSID: NIHMS665308PMID: 21993636

[67]. Springer C, Salen P. Gonorrhea. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK558903/

[68]. FOLB PI, R. JAFFE, G. ALTMANN. Nocardia asteroides and Nocardia brasiliensis Infections in Mice. INFECTION AND IMMUNITY, 13(5): 1490-1496. 1976

[69]. Wilson MG, Pandey S. Pseudomonas aeruginosa. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK557831/

[70]. Felipe Cabello, Carlos Hormaeche, Pasquale Mastroeni, Letterio Bonina (Ed) Biology of Salmonella 1993, NATO Science Series A: (NSSA, volume 245)

[71]. Khanna Ashish,Menka Khanna,and Aruna Aggarwal. Serratia Marcescens- A Rare Opportunistic Nosocomial Pathogen and Measures to Limit its Spread in Hospitalized Patients. J Clin Diagn Res. 2013; 7(2): 243–246. doi: 10.7860/JCARBON-DOTSR/2013/5010.2737

[72]. Hale TL, Keusch GT. Shigella. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter-22. https://www.ncbi.nlm.nih.gov/books/NBK8038/

[73]. Foster T. Staphylococcus. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter-12. https://www.ncbi.nlm.nih.gov/books/NBK8448/

[74]. Patterson MJ. Streptococcus. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter-13. https://www.ncbi.nlm.nih.gov/books/NBK7611/

[75]. Dong Xiuli, Weixiong Liang, Mohammed J Meziani, Ya-Ping Sun Liju Yan. Carbon Dots as Potent Antimicrobial Agents. Theranostics. 2020, 1;10(2):671–686. doi: 10.7150/thno.39863

[76]. Liang Jiarong, Wei Li, Jianying Chen, Jianying Chen. Xiaoman Huang, Yingliang Liu, Xuejie Zhang, Wei Shu, Bingfu Lei, Haoran Zhang. Antibacterial Activity and Synergetic Mechanism of Carbon Dots against Gram-Positive and -Negative Bacteria. ACS Appl. Bio Mater. 2021, 4(9):6937–6945

[77]. Hussen Narmin Hamaamin, Aso Hameed Hasan, Yar Muhammed FaqiKhedr, Andrey Bogoyavlenskiy, Ajmal R. Bhat, Joazaizulfazli Jamalis. Carbon Dot Based Carbon Nanoparticles as Potent Antimicrobial, Antiviral, and Anticancer Agents. ACS Omega 2024, 9(9):9849–9864

[78]. Naskar Atanu and Kwang-sun Kim. Friends against the Foe: Synergistic Photothermal and Photodynamic Therapy against Bacterial Infections. Pharmaceutics 2023, 15(4), 1116; https://doi.org/10.3390/pharmaceutics15041116

[79]. Jia Qingyan, Qing Song, Peng Li, Wei Huang. Review: Rejuvenated Photodynamic Therapy for Bacterial Infections. Advanced Healthcare Materials; 8(14), 2019, 1900608 https://doi.org/10.1002/adhm.201900608

[80]. Kaurav Hemlata, Dhriti Verma, Amit Bansal, Deepak N Kapoor, Sandeep Sheth. Progress in drug delivery and diagnostic applications of carbon dots: a systematic review. Front Chem. 2023;1:1227843. doi: 10.3389/fchem.2023.1227843

[81]. Chou A, Austin RL. Entamoeba histolytica Infection. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK557718/

[82]. Dunn N, Juergens AL. Giardiasis. [Updated 2024 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK513239/

[83]. Lezama-Dávila CM, Pan L, Isaac-Márquez AP, Cesar Terrazas, Steve Oghumu, Ricardo Isaac-Márquez, M Y Pech-Dzib, Joseph Barbi, Edward Calomeni, Narasimham Parinandi, A Douglas Kinghorn, Abhay R Satoskar. Pentalinon and rieuxii root extract is effective in the topical treatment of cutaneous leishmaniasis caused by Leishmania Mexicana. Phytother Res.; 28(6), 909-916, 2014. https://doi.org/10.1002/ptr.5079

[84]. Mohd Ammar Ihsan Ahmad Zamzuri Farah Nabila Abd Majid, Massitah Mihat Siti Salwa Ibrahim, Muhammad Ismail, Suriyati Abd Aziz, Zuraida Mohamed, Lokman Rejali, Hazlina Yahaya, Zulhizzam Abdullah, Mohd Rohaizat Hassan, Rahmat Dapari. Abd Majid Mohd Isa. Systematic Review of Brain-Eating Amoeba: A Decade Update. Int J Environ Res Public Health. 2023, 9;20(4):3021. doi: 10.3390/ijerph20043021

[85]. Laurent Rénia, Shanshan Wu Howland, Carla Claser, Anne Charlotte Gruner, Rossarin Suwanarusk, Teck Hui Teo, Bruce Russell, Lisa Ng. Cerebral malaria: Mysteries at the blood-brain barrier. Virulence. 2012;3(2):193–201. doi: 10.4161/viru.19013

[86]. Alicia Ponte-SucreAlicia Ponte-Sucre. An Overview of Trypanosoma brucei Infections: An Intense Host–Parasite Interaction. Frontiers in Microbiology, 7. 2017.

a. DOI: 10.3389/fmicb.2016.02126

[87]. Kumara Vijay Bhooshan, Avishay Dolitzky, Shulamit Michaeli, Aharon Gedanken. Antiparasitic ointment based on biocompatible carbon dot composite. ACS Appl. Nano Mater., 1(4):1-26, 2018, DOI: 10.1021/acsanm.8b00213

[88]. Torkashva Hossein, S. Ahmad Dehdast, Mehdi Nateghpour, Afsaneh Motevalli Haghi, Ghazaleh Chizari Fard, Taher Elmi, Mohammad Shabani, Fatemeh Tabatabaie. Antimalarial nano-drug delivery system based on graphene quantum dot on Plasmodium falciparum: Preparation, characterization, toxicological evaluation. Diamond & Related Materials 132 (2023) 109670

[89]. Keleş S, Alakbarli J, Akgül B, Baghirova M, Imamova N, Barati A, Shikhaliyeva I, Allahverdiyev A. Nanotechnology based drug delivery systems for malaria. Int J Pharm. 2024 Dec 5;666:124746. doi:10.1016/j.ijpharm.2024.124746.

[90]. Segarra-Newnham, M. "Manifestations, diagnosis, and treatment of Strongyloides stercoralis infection". Ann Pharmacother. 41(12):1992–2001.2007. doi:10.1345/aph.1K302.

[91]. Gamble HR (1999). "Trichinella". Encyclopedia of Food Microbiology. pp.

2181–2186. doi:10.1006/rwfm.1999.1595. ISBN 978-0-12-227070-3.

[92]. Mattia Ghirardello, Javier Ramos-Soriano, M Carmen Galan. Editor: Constantine D Stalikas. Carbon Dots as an Emergent Class of Antimicrobial Agents. Nanomaterials (Basel). 2021 Jul 22;11(8):1877. doi: 10.3390/nano11081877. Nanomaterials (Basel). 2021.11(8):1877. doi: 10.3390/nano11081877.

[93]. Lagos, K. J., García, D., Cuadrado, C. F., Mezzacappo, N. F., Inada, N., Bagnato, V., & Romero, M. P. (2023). Carbon dots: Types, preparation, and their boosted antibacterial activity by photoactivation. Current status and future perspectives. Wiley Interdisciplinary Reviews: Nanomedicine Nanobiotechnology, 15(4), e1887. https://doi.org/10.1002/wnan.1887

[94]. Walid Daoudi, Mohamed el Mahamdi, Omar Dagdag, W. B. Wan Nik, Adyl Oussaid, and Abdelmalik El Aatiaoui. Carbon Dots: Recent Developments and Future Perspectives. Chapter 4pp 81-10. 2024 ACS Symposium SeriesVol.1465. eISBN: 9780841296992. DOI: 10.1021/bk-2024-1465.ch004.

[95]. Yaung Kwee, Yiqun Zhou, Mochamad ZF, Madhuri Sharon and Alfinda NK. Review: Progress on Applying Carbon Dots for Inhibition of RNA Virus Infection. Nanotheranostics, 6(4): 436-450, 2022. doi: 10.7150/ntno.73918 (

[96]. Yaung Kwee, Alfinda NK, Madhuri Sharon, Mochamad ZF. A Review of Promising Selected Agents Combined with Carbon Dots for Biomedical Applications. Int. J.Nanosci. Nanotechnol., Vol. 18, No. 1, March 2022, pp. 11-44 11