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Carbon Dots: A Novel Nanotechnology Approaches Against HIV

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ABSTRACT

Despite significant progress in Antiretroviral Therapy (ART), the Human Immunodeficiency Virus (HIV) continues to represent a major global public health challenge. Persistent obstacles, including the emergence of drug-resistant viral strains, systemic toxicity, and the inability to achieve complete viral eradication, underscore the necessity for innovative therapeutic strategies. In this context, carbon dots (CDs), a novel class of carbon-based nanomaterial's, have recently attracted considerable attention as potential candidates in antiviral Nano medicine. This review critically examines the multifaceted role of CDs as both direct antiviral agents and Nano carriers for HIV therapeutics. A comprehensive analysis of current research indicates that CDs can induce reactive oxygen species (ROS)-mediated viral inactivation and inhibit key stages of the HIV life cycle, including viral entry, reverse transcription, and genome replication. Furthermore, CDs have demonstrated the capacity to enhance the stability, targeted delivery, and bioavailability of conventional antiretroviral drugs. However, despite these promising in vitro findings, extensive in vivo investigations and clinical trials remain limited. Collectively, these insights highlight CDs as an innovative and adaptable Nano technological platform with substantial potential to augment existing ART regimens and facilitate the development of next-generation HIV treatment paradigms

Keywords: Human Immunodeficiency Virus (HIV), Carbon Dots (CDs), Antiretroviral Therapy (ART), Reactive Oxygen Species (ROS), Acquired Immuno Deficiency Disease (AIDS), World Health Organization (WHO).

INTRODUCTION

OVERVIEW OF HIV AS A GLOBAL HEALTH CHALLENGE

The human immunodeficiency virus (HIV), identified as the etiological agent of acquired immunodeficiency syndrome (AIDS), has been recognized for over four decades, with the first clinical case reported in 1981. According to the World Health Organization (WHO), approximately 38.4 million individuals worldwide are currently living with HIV or AIDS. Since the onset of the epidemic, an estimated 40.1 million people have died from HIV/AIDS-related illnesses [1]. More recent estimates from UNAIDS and WHO indicate that, by the end of 2024, around 40.8 million people [37.0–45.6 million] were living with HIV globally, reaffirming that the virus continues to pose a major global public health concern despite considerable advancements in prevention, care, and treatment . The WHO African Region remains the most severely affected, accounting for over two-thirds of the global population living with HIV [2].Emerging evidence suggests an association between nutritional status, age, and the occurrence of locomotors disorders among HIV-infected individuals, particularly those aged over 45 years with a body mass index (BMI) ≥ 25 kg/m², who are encouraged to limit physical activity. These individuals appear to have a lower prevalence of locomotors impairments. African societies, in particular, face complex social and healthcare challenges in supporting older adults living with HIV, as many of them experience varying degrees of physical dependency [3]. Overall, HIV continues to represent an unparalleled global health crisis; although unknown four decades ago, the virus has already resulted in approximately 25 million deaths worldwide [4]. HIV progressively weakens the human immune system by targeting crucial cells, leading to immune exhaustion and AIDS; after

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decades of research, the relationship between HIV-induced immune activation and AIDS progression remains only partially understood, but generalized immune activation is recognized as a key factor driving disease progression [5].Global efforts inspired by research like Greenberg et al. (2015) are continually striving to minimize new HIV infections, bolster access to HIV care, and improve coordination at multiple levels of government for funding HIV/AIDS-related research, prevention, and care. These policies reflect a multifaceted approach combining prevention strategies, broad access to antiretroviral therapy, and structural changes to the health system [6].

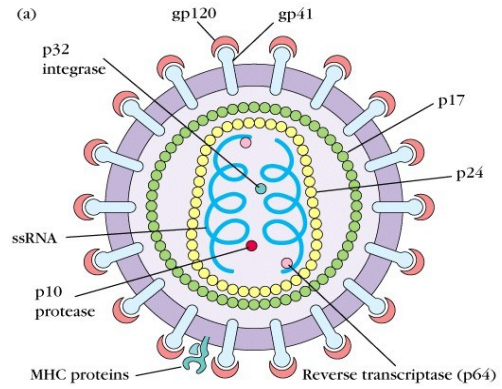

Figure 1: Structure of HIV

CURRENT STATUS OF ANTIRETROVIRAL THERAPY (ART) AS THE STANDARD OF CARE

The development, optimization, and global accessibility of highly active antiretroviral therapy (ART) have played a pivotal role in controlling the HIV pandemic. Advances in HIV management and the treatment of opportunistic infections have transformed the infection from a fatal disease into a manageable chronic condition, allowing individuals living with HIV to achieve prolonged and healthy lives [7]. Early initiation of ART provides substantial clinical advantages, including improved immune recovery and markedly reduced viral transmission, offering benefits at both individual and community levels [8]. Although implementing updated treatment guidelines requires the mobilization of additional resources, adherence to these protocols ensures that the most effective therapeutic strategies are available to combat and ultimately end the HIV epidemic. By 1996, research had demonstrated that combining multiple antiretroviral drugs was far more effective than monotherapy, leading to the establishment and widespread adoption of combination antiretroviral therapy (cART) as the standard of care [9]. ART involves the daily administration of several antiretroviral agents that suppress viral replication, preserve immune function, and significantly reduce the risk of HIV-related illnesses and transmission [10]. With the extension of life expectancy among individuals on long-term therapy, optimizing the safety, tolerability, and adherence of cART regimens has become increasingly crucial, as patients are likely to remain on treatment for decades. Despite these remarkable therapeutic advancements, complete eradication of HIV remains unattainable with current cART strategies due to the persistence of a stable latent reservoir of HIV-infected resting memory $CD4^+$ T cells, which form early during acute infection. These latently infected cells contain integrated, replication-competent proviruses that remain transcriptionally silent, thereby evading immune clearance and the effects of antiretroviral drugs [10]. Discontinuation of cART leads to rapid reactivation of these reservoirs and viral rebound within weeks. Thus, although cART effectively suppresses plasma viremia to undetectable levels and halts disease progression, it does not eliminate the latent viral pool [11]. Nevertheless, cART continues to markedly reduce HIV-associated morbidity and mortality, enhancing both survival and quality of life. Moreover, sustained viral suppression through cART effectively prevents sexual transmission of HIV by maintaining viral loads at non-transmissible levels. Early initiation of cART during the acute phase of infection has been shown to restrict the size and genetic diversity of the latent reservoir, thereby improving long-term immune reconstitution and viral control. Currently, continuous lifelong therapy remains essential to maintain viral suppression and prevent rebound viremia [12].

LIMITATIONS OF ART (DRUG RESISTANCE, TOXICITY, INCOMPLETE VIRAL CLEARANCE)

Antiretroviral therapy (ART) comprises a group of pharmacological agents designed to manage acquired immunodeficiency syndrome (AIDS), which arises from infection with the human immunodeficiency

virus (HIV). The therapeutic regimen typically involves the concurrent administration of multiple antiretroviral drugs (ARVs) that act at different stages of the HIV replication cycle. This combinational approach has proven to be highly effective in suppressing viral replication and reducing the risk of HIV transmission. In addition to its medical efficacy, ART provides substantial social and economic benefits, including enhanced quality of life, decreased stigma and discrimination, and improved workforce productivity and societal participation. Over the past decades, remarkable scientific progress has been achieved in the design and optimization of ART regimens. Historically, ART was initiated only after a significant decline in $CD4^+$ T-cell counts an indicator of immune system deterioration. However, current treatment guidelines advocate for the immediate initiation of ART following diagnosis, irrespective of $CD4^+$ levels, to improve long-term outcomes and limit viral spread. According to the World Health Organization (WHO), standard ART regimens should consist of at least two or three active agents drawn from distinct drug classes to ensure potent viral suppression and minimize resistance development. Expanded access to ART has further enabled the use of more effective, tolerable, and less toxic formulations, contributing to improved treatment adherence and patient outcomes. Despite these advancements, the extensive global use of ART has been accompanied by the emergence of HIV strains resistant to certain therapeutic agents, leading to virologic failure. Virologic failure is characterized by the inability of ART to suppress plasma viral load below 200 copies/mL and may result from a combination of factors, including viral resistance, drug toxicity, pharmacokinetic interactions, poor adherence, or comorbid health conditions. When virologic failure occurs, it can lead to elevated viral loads, increased risk of HIV-related complications and transmission, and the selection of multidrug-resistant viral variants. Understanding the molecular mechanisms and contributing factors underlying drug resistance particularly in the context of evolving ART strategies is critical for the development of next-generation antiretroviral agents. Accordingly, this review seeks to examine current ART regimens, elucidate their mechanisms of action, and explore the molecular basis of HIV drug resistance, while highlighting emerging therapeutic candidates for future antiretroviral drug development [13].

INTRODUCTION OF CARBON DOTS (CDS) AS A NOVEL NANOTECHNOLOGY PLATFORM.

Carbon-based nanomaterial's represent a diverse and multifunctional class of materials encompassing a wide range of structural forms, including three-dimensional graphite, two-dimensional graphene and graphene oxide, one-dimensional carbon nanotubes (CNTs), Nano fibers, fullerenes, and nanodiamonds. The exceptional properties of these materials arise from carbon's unique ability to adopt various hybridization states (sp, sp^2, and sp^3) and form distinct nanostructures typically ranging from 1 to 100 nm. This versatility results in novel physical, chemical, electrical, optical, and mechanical behaviors that differ significantly from those of bulk carbon materials. Among these, carbon dots (CDs) a class of zero-dimensional carbon-based nanomaterial's have emerged as a promising and nontoxic alternative to traditional semiconductor quantum dots (QDs), such as cadmium selenide (CdSe) and lead sulfide (PbS), which often raise toxicity and environmental safety concerns. CDs have garnered significant scientific interest due to their distinctive optical characteristics, tunable surface functionalities, high biocompatibility, cost-effective synthesis, and environmentally benign production methods. Typically measuring less than 10 nm in diameter, these fluorescent nanoparticles exhibit unique features such as excitation-dependent emission, adjustable photoluminescence, and remarkable photo stability. Owing to these attributes, CDs have become a focal point of interdisciplinary research across chemistry, materials science, engineering, and biomedicine [14].

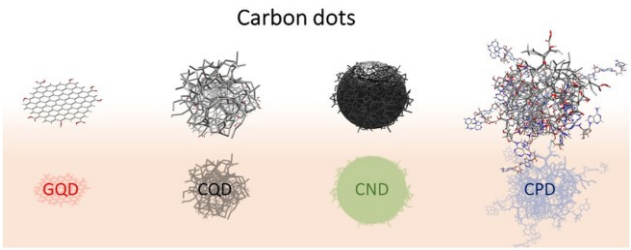

Figure 2: Structures of C-dots: GQD, CQD, Carbon Nano Dots And Carbon Polymer Dots (CPD) [15].

The behavior of the C-dots, which exhibit a great degree of structural variety, is often caused by a mix of surface and core properties, with defects also being a significant factor. Specifically, when a graphitic crystalline core emerges and in graphene- like dots, a quantum response can be assumed. The surface always contains some functional groups that are significant impact on the optical and electronic reaction, making it difficult to determine the quantum origin of the characteristics and quantum response [16].

GLOBAL IMPACT OF HIV AND LIMITATIONS OF CURRENT ART

Epidemiological and clinical consequences of HIV worldwide

Since the first reported cases in the early 1980s, the global HIV epidemic has undergone significant transformations. The number of new HIV infections peaked at approximately 3.7 million in 1997, followed by a notable decline in both new infections and AIDS-related mortality during the 2000s. By 2012, an estimated 9.7 million individuals in low- and middle-income countries were receiving antiretroviral therapy (ART). The widespread implementation of ART substantially improved survival rates, leading to an all-time high of approximately 35.3 million people living with HIV (PLHIV) in 2012 [17]. The HIV/AIDS epidemic has had devastating social and economic consequences, profoundly affecting individuals, families, and entire communities. Millions of children have been orphaned, and the disease has disrupted traditional community structures, undermining economic stability and social cohesion. According to estimates from the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO), by the end of 1999, approximately 34.3 million people were living with HIV/AIDS globally, with around 15,000 new infections occurring daily. Notably, 95% of all individuals living with HIV reside in developing nations, underscoring the disproportionate burden borne by low-resource settings [18]. The global pattern of the HIV/AIDS pandemic varies across regions. In certain parts of the world, HIV has rapidly expanded into the general population, while in others; it remains concentrated among key populations at higher risk, such as people who inject drugs (PWID), men who have sex with men (MSM), and sex workers and their clients. Women account for approximately 47% of global HIV infections, and the overall adult prevalence rate is estimated at 1.07% of the population [19]

Barriers in lifelong ART including drug resistance, side effects, and limited eradication

In the absence of antiretroviral therapy (ART), approximately 35 million individuals worldwide are living with the human immunodeficiency virus (HIV), with an estimated 19 million unaware of their infection status—placing them at risk of reduced life expectancy and higher morbidity (UNAIDS, 2014). To address this ongoing challenge, the International AIDS Society (IAS) introduced the "90–90–90" targets at its 2014 conference in Melbourne. These ambitious global objectives aim to ensure that 90% of all people living with HIV are aware of their status, 90% of those diagnosed initiate ART, and 90% of those receiving therapy achieve viral suppression. Achieving these targets has the potential to dramatically reduce HIV-associated morbidity and mortality on a global scale (Sterne et al., 2005) [20].

FUNDAMENTALS OF CARBON DOTS (CDS)

Definition: Carbon dots (CDs) are quasi-zero-dimensional (0D) carbon-based nanomaterial's characterized by their intrinsic fluorescence and surfaces enriched with functional groups. Typically measuring less than 10 nm in size, CDs consist of a carbon core with mixed sp^2/sp^3 hybridization and surface or edge functional groups, such as –OH, –COOH, and $–NH_2$, which play a crucial role in determining their optical and chemical properties [21].

Classification: Generally, CDs are divided into four main categories we have discussed above on (figure no.2) based on their structure and production mechanism:

Carbon Quantum Dots (CQDs): CQDs are nanostructures with crystalline carbon cores that exhibit fluorescence dependent on their size, a phenomenon attributed to quantum confinement effects.

Graphene Quantum Dots (GQDs): GQDs are derived from graphene sheets and possess layered structures with prominent edge effects and sp^2-hybridized domains, which contribute to their unique optical and electronic properties.

Carbon Nano dots (CNDs): They have good surface functionalization but are frequently amorphous and lack long-range crystallinity.

Carbonized Polymer Dots (CPDs): Usually created by polymerizing and carbonizing organic precursors, CPDs have both polymer and carbonized domains [22].

Carbon dots (CDs) possess several distinctive properties that make them highly attractive for a wide range of applications.

Table 1: Physicochemical features of carbon dots [23]

Feature	Description
Ultra small Size	Due to their typically small size of less than 10 nm, carbon dots (CDs) exhibit a high surface-area-to-volume ratio along with pronounced quantum effects.
Fluorescence & Photoluminescence	Display great resistance to photo bleaching, up-conversion, and excitation-dependent fluorescence perfect for imaging and sensing.
Tunable Surface Chemistry	The surfaces of carbon dots (CDs) are abundant in functional groups, such as –OH, –COOH, and $–NH_2$, which can be chemically modified to tune their solubility and optical emission characteristics.
High Biocompatibility & Low Toxicity	When compared to heavy-metal quantum dots, CDs often exhibit less cytotoxicity, making them suitable for use in biomedicine.
Excellent Stability	CDs are stable over wide pH and ionic ranges, photo stable, and chemically inert

SYNTHESIS APPROACHES (TOP-DOWN AND BOTTOM-UP METHODS)

There are multiple methods available for the synthesis of carbon quantum dots (CQDs), but researchers typically prioritize approaches that provide high yield, purity, and efficiency. The synthesis strategies for CQDs are generally classified into two main categories: top-down and bottom-up methods.

Top-Down Method: The top-down approach involves fragmenting bulk carbon materials into Nano scale structures. In this method, carbon quantum dots (CQDs) are produced from carbon-rich precursors such as graphite, nanodiamonds, carbon soot, and carbon nanotubes. Techniques commonly employed include acid oxidation, arc discharge, laser ablation, and ultra-sonication.

Different Top Down Approaches For CQDs Synthesis:

Acidic Oxidation: Acidic oxidation is a top-down technique in which complex carbon materials are broken down into carbon quantum dots (CQDs) through the action of strong acids and oxidizing agents. Common oxidants include chlorine dioxide (ClO_2), hydrogen peroxide (H_2O_2), hydroxyl radicals (•OH), and ozone (O_3), while acids such as nitric acid (HNO_3), sulfuric acid (H_2SO_4), sodium chlorate ($NaClO_3$), and toluene are frequently employed in the process. This process breaks both saturated and unsaturated organic compounds, introduces hydrophilic –OH and –COOH groups on CQD surfaces, and enhances water solubility and fluorescence properties. The technique is fast, cost-effective, and low-maintenance. Zhang et al. (2017) synthesized yellow-emitting CQDs from fullerene carbon soot (FCS) using a 1:1 HNO_3–H_2SO_4 mixture under sonication (80–120 °C, 12–36 h), followed by neutralization and purification. Similarly, Yang et al. (2014) produced CQDs from Chinese ink via oxidation with HNO_3, H_2SO_4, and $NaClO_3$, followed by hydrothermal doping with DMF/NaHS/NaHSe (240 °C, 12 h) to obtain N-, S-, and Se-doped CQDs exhibiting high quantum yield and prolonged fluorescence lifetime.

Arc-Discharge Method: Iijima (1991) invented arc discharge, a top-down method that effectively produces high-quality carbon quantum dots (CQDs) by electrically breaking down carbon compounds. Carbon precursors are vaporized in this technique by creating an arc between graphite electrodes in an inert gas chamber, which raises the temperature. On the cathode, the resultant carbon vapors condense to create nanostructures. Plasma and steady current are essential for high-quality products. Single-walled carbon nanotubes and CQDs with unique fluorescence properties have been created using this technique, which produces nanoparticles (~20 nm).

Laser-Ablation Method: Carbon quantum dots (CQDs) are created by laser ablation, a thermal method that uses strong laser irradiation to extract atoms from solid carbon precursors. This method allows bulk carbon to be broken down into nanoparticles with adjustable photoluminescence (PL). Hu et al. (2008) achieved in situ surface passivation through solvent interactions by laser-irradiating carbon powder in organic solvents to make fluorescent CQDs. Li et al. (2010) used Nd:YAG laser irradiation in basic solvents (ethanol, acetone, and H2O) to create stable, visible-emitting CQDs. While Donate et al. (2018) created highly fluorescent CQDs (~3 nm) for bio imaging with 15% greater efficiency and strong excitation-dependent emission, Liu et al. (2015) produced Si–C nanoparticles using laser-induced pyrolysis of silica. A quick, easy, and additive-free method for producing high-quality, photos table CQDs is laser ablation.

Ultra Sonication Method: High-frequency sound waves (>20 kHz) are used in the ultra-sonication (sono-chemical) method to scatter and activate carbon precursors, preventing aggregation and facilitating uniform CQD production. Haitao Li et al. (2010) used a one-step acid/alkali-assisted ultrasonic technique to create water-soluble, luminous carbon nanoparticles from glucose. Due to surface hydroxyl functionalization, the resultant CNPs showed outstanding up-conversion capabilities and strong, tunable photoluminescence throughout the visible–NIR range. For the synthesis of CQD, ultra sonication provides a straightforward, effective, and environmentally friendly method.

Bottom-Up Methods: The bottom-up approach involves the synthesis of carbon quantum dots (CQDs) from small molecular precursors through chemical reactions. This strategy builds CQDs from the molecular level rather than breaking down larger carbon structures. Common techniques in bottom-up synthesis include hydrothermal treatment, combustion, electrochemical methods, and microwave-assisted synthesis.

Hydrothermal Method: In the hydrothermal method, organic precursors are subjected to carbonization under elevated temperatures and pressures, typically ranging from 120 to 280 °C, within a sealed Teflon-lined autoclave. This process promotes the formation of CQDs with controlled size and surface properties. Water promotes CQD nucleation and surface functionalization by serving as a solvent and reaction media. Green precursors such as tulsi leaf extract and lemon extract have produced spherical CQDs (3-5 nm) with surface –OH, –COOH, and $–NH_2$ groups that show blue to blue-green fluorescence with quantum yields of 3–21%. Particle shape and optical characteristics can be effectively controlled with this straightforward, scalable, and environmentally friendly method.

Combustion Method: By thermally breaking down carbon precursors, combustion synthesis is a quick, inexpensive, and high-temperature (>2000 K) method of creating carbon quantum dots (CQDs). Depending on the reactant phase, it can happen by solid-state or solution combustion. By burning organic solvents (ethanol, n-butanol, candle soot, and benzene), Zhang et al. (2018) created CQDs, which were 2-4 nm particles with comparable photoluminescence and UV–vis absorption characteristics. The existence of methyl, carbonyl, and C=C groups was verified by FTIR. The process is easy to use, scalable, and appropriate for producing CQD on a big scale.

Electrochemical Method: A straightforward, low-temperature, low-pressure method for creating carbon quantum dots (CQDs) is electrochemical synthesis. At platinum electrodes, carbon precursors like sodium citrate, urea, glycine, or o-phenylenediamine undergo electro oxidation, carbonization, and passivation to produce fluorescent CQDs (2–3 nm) containing carboxyl, hydroxyl, and amino functional groups. The

resultant CQDs have great salt stability, excitation-dependent photoluminescence, and uses in fingerprint identification, bio imaging, and sensing (such as hemoglobin, Fe3+, and ascorbic acid).

Microwave-Assisted Synthesis: A quick and effective way to create tiny carbon nanoparticles is using microwave irradiation. Dipolar polarization and ionic conduction allow for consistent internal heating, which shortens reaction times and increases yield and reproducibility. A widely used technique for synthesizing carbon quantum dots (CQDs) involves the direct transformation of microwave radiation (0.3–300 GHz) into thermal energy, which effectively breaks chemical bonds in the carbon-containing precursors [24].

ANTIVIRAL MECHANISMS OF CARBON DOTS AGAINST HIV

Blocking Viral Entry (gp120–CD4 interaction)

Carbon dots (C-dots) have been investigated for their potential antiviral activity against human immunodeficiency virus type 1 (HIV-1). HIV-1 is an enveloped RNA virus of the Retroviridae family, featuring surface glycoproteins such as gp120 and gp41, along with two lipid layers. The gp120 glycoprotein, with a molecular weight of approximately 120 kDa, is essential for binding to specific cell surface receptors. Consequently, designing nanoparticles that specifically target gp120 offers a promising strategy for inhibiting viral replication. The antiviral efficacy of C-dots is enhanced when their surfaces are functionalized with targeted ligands; for example, boronic acids, which contain hydroxyl groups, facilitate binding to the virus. A practical implementation of this approach involves modifying C-dots with citric acid and 2-amino phenylboronic acid (APBA), both containing amino groups. These modified C-dots were synthesized via pyrolysis at 240 °C. Their antiviral activity was evaluated using human acute T lymphoblastic leukemia (MOLT-4/MT-4) and human cervical cancer (HeLa) cell lines. The APBA-functionalized C-dots effectively interacted with gp120, thereby inhibiting HIV-1 replication [25].

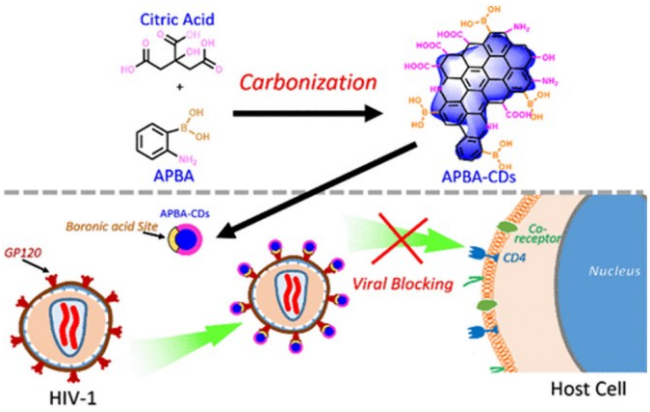

Figure 3: Mechanism of Carbon Dot Against HIV

Therapeutic Advantages of Carbon Dots

Infectious diseases continue to be a leading cause of illness and death worldwide, particularly affecting populations in low- and middle-income countries. The application of carbon-based nanomaterial's, such as carbon dots (CDs) and cyclodextrins, for antiviral therapy represents a rapidly emerging and promising area of research. Carbon dots (CDs) and graphene quantum dots (GQDs) have been explored for their ability to combat viral infections through multiple mechanisms. These nanoscale materials function as versatile antiviral agents with significant potential for therapeutic applications [26].

Role In Improving Solubility, Stability And Cellular Uptake

Through surface functionalization and a high surface area-to-volume ratio, carbon dots (CDs) enhance solubility and stability. This allows for strong interactions with other molecules, which is especially helpful in applications like medication administration and photo catalysis Increasing Solubility Carbon dots (CDs) naturally possess various hydrophilic functional groups on their surfaces, including carboxyl (–COOH), hydroxyl (–OH), and amino (–NH_2) groups. These functional groups enhance the aqueous solubility and dispensability of CDs by forming strong interactions, primarily through hydrogen bonding, with surrounding water molecules [27]. Surface engineering: CDs' affinity for various solvents can be changed by adjusting their surface chemistry either during or after production. For instance, CDs can become soluble in organic solvents through functionalization with alkyl chains, and they

can become soluble in both polar and non-polar media when the right precursors are used [28].

Enhanced Stability and Chemical Inertness: Carbon dots (CDs) are highly stable, tolerating extreme pH levels and high salt concentrations, which protects associated compounds from environmental degradation.

Photo stability: CDs resist photo bleaching and maintain consistent fluorescence over extended periods, outperforming traditional organic dyes and metal-based quantum dots.

Aggregation Prevention: In Nano composites, CDs act as stabilizers, preventing aggregation of other nanoparticles (e.g., metal oxides) via steric hindrance or electrostatic repulsion from surface functional groups and polymer chains.

Antioxidant Activity: Certain CDs can scavenge reactive oxygen species (ROS), enhancing biological stability and reducing oxidative damage [29].

Facilitated Cellular Uptake: CDs' small size (<10 nm) allows efficient endocytosis, while surface charge and functionalization further improve cellular internalization [30]

Electrostatic Interactions: Positively charged CDs are drawn to negatively charged cell membranes, promoting uptake [31].

Targeted Delivery: CDs functionalized with ligands like folic acid, transferrin, or hyaluronic acid bind to overexpressed receptors on specific cells, enhancing selective uptake by target cells while minimizing impact on healthy cells [32].

POTENTIAL FOR TARGETED DELIVERY AND REDUCED SYSTEMIC TOXICITY

Targeted Delivery: Carbon quantum dots (CQDs) are highly effective carbon-based nanomaterial's for various biological applications due to their excellent biocompatibility. Their minimal cytotoxicity makes CQDs promising candidates for safe and efficient targeted drug delivery. Additionally, CQDs are well-suited as theranostic agents, combining therapeutic and diagnostic functionalities. For instance, a multifunctional theranostic system (CD-Oxa) was created by conjugating amine-functionalized C-dots with the anticancer drug oxidized oxaliplatin [Oxa (IV)-COOH]. This CD-Oxa system integrates the therapeutic effects of oxaliplatin with the intrinsic optical properties of carbon dots [33].

Reduced Systemic Toxicity: The lower systemic toxicity of carbon dots (CDs) in comparison to many conventional nanomaterial's has drawn attention. Excellent biocompatibility and few negative biological consequences are a result of their tiny size, high water solubility, and easily adjustable surface chemistry. According to studies, when given at reasonable levels, CDs cause very little organ damage in vivo, minor hemolysis, and modest cytotoxicity in vitro. Long-term toxicity is further decreased by their quick renal clearance and minimal buildup in important organs. The modification of CDs with biocompatible compounds (such folic acid or polyethylene glycol) can greatly reduce toxicity by decreasing nonspecific interactions and enhancing dispersion in biological mediums. This is another important aspesssscct of surface functionalization. Additionally, CDs frequently have inherent anti-inflammatory and antioxidant qualities that enable them to scavenge reactive oxygen species (ROS) and Lessen tissue damage brought on by oxidative stress, all of which reduce systemic toxicity. Because CDs are mostly inert and carbon-based, they are a safer option for biological applications than metal-based quantum dots, which can produce harmful ions [34].

CHALLENGES AND RESEARCH GAPS

LIMITED IN VIVO AND CLINICAL EVIDENCE

CHALLENGES: Although numerous research show that CDs operate well in vitro (toxicity tests, imaging, drug administration), there aren't many reliable in vivo investigations, and clinical translation is still mostly unrealized. The confidence in advancing CDs towards therapeutic or diagnostic application in humans is limited by the paucity of clinical studies and significant animal-model data [35].

RESEARCH GAPS: There aren't many long-term animal studies that assess immunogenicity, accumulation, clearance, repeated dose, and chronic

exposure. Human safety, efficacy, and dosage are still unknown due to the lack of human/clinical datasets for CD-based medicines or diagnostics. Absence of standardized in vivo protocols that would enable regulatory assessment and cross-study comparison (dose scaling, administration route, bio distribution/time-course) [36].

PHARMACOKINETICS, BIO-DISTRIBUTION, AND LONG-TERM SAFETY CONCERNS

CHALLENGES: Knowing how a nanomaterial spreads throughout the body, how long it lasts, how it is metabolized or eliminated, and any potential long-term impacts is crucial for any nanomaterial used for biomedical use. These pharmacokinetic (PK), bio distribution (BD), and long-term safety aspects of CDs are not well researched [37].

RESEARCH GAPS: There are few studies that provide comprehensive PK/BD profiles (absorption, distribution, metabolism, and excretion) for various CD types. For instance, inulin-tethered B-doped amine-functionalized CDs exhibit restricted bio distribution data. It is yet unclear how CD physicochemical characteristics (size, surface charge, doping, and functional groups) relate to in vivo fate. Uncertainty surrounds long-term accumulation or retention (particularly in organs including the liver, spleen, and kidney), chronic toxicity, and immunological/inflammatory effects. Systematic research across CD variants is required to determine the clearance routes (renal, hepatic, and reticuloendothelial). The absence of standardized long-term safety data (genotoxicity, reproductive toxicity, immunotoxicity) is another regulatory problem. Reviews of food packaging and f-applications, for instance, show that the long-term exposure dangers of CDs are not well understood [38].

POSSIBLE RESISTANCE DEVELOPMENT AND REGULATORY HURDLES

CHALLENGES

The development of microbial resistance or unintentional biological adaptation may occur when CDs are employed for therapeutic or antimicrobial reasons, albeit this risk is currently speculative. In addition, the legislative environment around CDs is ill-defined, which restricts translation and commercialization [39].

RESEARCH GAPS

The long-term effects of repeated exposure on microbial populations have not been investigated, despite some reviews claiming little possibility of resistance for CDs (e.g., due to ROS generation rather than single-target drug). For instance, it's unclear if sub-lethal CD doses could result in tolerance or adaptability. It's unclear how CDs are classified under regulations: are they "nanomaterial's," "drugs," "medical devices," or "food additives" (in packaging)? Safety and regulatory pathways are complicated by this ambiguity. Reviews of the use of food packaging, for example, highlight regulatory ambiguities about CDs. CDs lack industrial, scale-up, reproducibility, and standardization; for approval, regulatory bodies need uniform production and characterization criteria. "Regulatory approval processes. Which are still limited for CDCQDs," according to one analysis [40].

FUTURE PERSPECTIVES IN HIV NANO MEDICINE

There are a lot of fascinating possibilities for using Nano medicine to treat HIV. It is common knowledge that many candidates will not make it to the clinic throughout the development of a novel treatment. Toxicity, insufficient effectiveness, and poor pharmacokinetics are frequently cited as causes of failure in Phase I and Phase II trials. Careful post-licensing optimization is frequently necessary, even when medications move into commercial uses. The development of ways to overcome the shortcomings of existing, upcoming, and even unsuccessful treatments is made possible by nanotechnology. Significantly, improving safety Achieving lower dosages or more efficient delivery specifically to diseased cells has been a crucial focus in the advancement of Nano medicine. However, despite increasing interest in this field, significant gaps remain in our understanding of the underlying mechanisms [41].

CONCLUSION

Although carbon dots are a well-known type of nanomaterial, research on their potential uses in antiviral therapy and viral illness diagnostics is still in its early stages. This review has summarized the core physicochemical properties of carbon dots (CDs) and highlighted the latest findings regarding their antiviral activity and their use as platforms for virus detection. With their exceptional physicochemical and biological characteristics, carbon dots (CDs) have become a promising and adaptable nanotechnology platform. They are positioned as cutting-edge instruments for biological applications, such as antiviral treatments, due to their adjustable size, biocompatibility, and potential for functionalization. CDs have great potential to address existing therapeutic issues with HIV, including medication resistance, targeted delivery, and side effect minimization. Further investigation into their clinical translation, safety profiles, and mechanistic interactions may lead to new CD-based approaches that could revolutionize HIV treatment.

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