Carbon Quantum Dots in Healthcare: A Promising Solution for Sustainable Healthcare and Biomedical Practices

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Abstract. The pursuit of sustainable development refers to meet the present needs while safeguarding the resources for future generations ensuring the well-being of human societies. Nanoscience is contributing significantly to the field of public healthcare by delivering a number of cutting-edge technological applications and products related to healthcare. Carbon quantum dots (CQDs), carbon-based nanomaterials, are gaining recognition for their potential health benefits worldwide. The current study aims to review the applications of CQDs in the biomedical field based on existing literature. The methodology used is the collection of the literature studies from authoritative sources such as Google Scholar, PubMed, and ResearchGate, with keywords 'Carbon quantum dots in healthcare, biosensing, bioimaging, gene therapy, treatment, and theranostics'. The retrieved literature was comprehensively analyzed to construct the detailed review which suggests that CQDs have demonstrated remarkable potential across various domains, from disease treatment to biosensing, gene delivery, drug delivery, and bioimaging thus helping to achieve the 3rd goal of sustainable development. In addition to CQDs synthesized by chemical processes, natural CQDs developed by green chemistry from natural sources are gaining accreditation due to their evidenced potential health benefits. This article has reviewed the versatile applications of Carbon Quantum Dots (CQDs) in the biomedical field and discussed the possible contributions to achieve sustainable healthcare for the first time, suggesting CQDs as a potential target for future research and development. However, there are some limitations of CQDs including complex surface modification, toxicity, limited clinical translation which requires more attention in order to improve their healthcare applicability.

Keywords: Carbon Quantum Dots (CQDs), Healthcare, Nanoscience, Public health, Sustainable development goal (SDG 3), Theranostics, Wellbeing

1 Introduction

Synthetic chemistry and nanotechnology are playing an important role in today's health and medicinal field. As a key growth sector and continuously evolving field, sustainable practices are a must to be employed in global health care. A sustainable healthcare system can be defined as a system fulfilling the medical needs of the current generation by providing high-quality care and exerting minimal damage to the environment [1-3]. Drugs with significant toxicity, high costs, limited availability, improper diagnostic techniques, emerging infectious diseases, microbial drug resistance, treatment of fatal diseases, and biomedical waste are some of the factors that significantly block the way to achieve Sustainable Development Goal 3 (SDG 3) i.e. healthcare and wellbeing. Development of new tools, technologies, and therapeutic candidates with minimal side effects are warranted as possible alternatives to deal with challenges of healthcare sustainability [1-5].

The cutting-edge research and technological advancements in the field of nanotechnology, commonly known as nanomedicine, have shown a remarkable potential to address the healthcare sector challenges along with the promises of cost reduction and affordability in an eco-friendly manner [6]. Nanomaterials play a prominent role in the treatment of diseases, target drug delivery, electrochemical sensing, gene delivery, biomarker detection, food analysis-related sensing, and biosensing [7]. Quantum dots, polymeric nanoparticles, dendrimers, liposomes, metallic nanoparticles, carbon nanotubes, and micelles are just a few examples of different nanomaterials that have been extensively studied for their therapeutic potential against complex diseases [8]. Currently, there are many FDA-approved therapeutic nanoparticles, which were created by combining chemotherapeutic drugs with polymeric nanoparticles [9]. Nanoscience has recently grown and expanded tremendously and has become extremely influential in all disciplines of modern study, promising improvements in public health and causing notable changes in living and well-being. Nanotechnology is known as the medicine of the future [10]. A better understanding and the use of nanoparticles pave the path for the future development of innovative materials that may enhance health and quality of life. In the future, it is projected that the demanding scope will increase due to the betterment of health using a distinctive combination of nanomaterials and sustainability [11].

Carbon quantum dots (CQDs) hold a paramount significance in the realm of biomedical research, with their versatile applications spanning bioimaging, biosensing, drug delivery, gene delivery, and a host of therapeutic possibilities [7]. This narrative review paper compiles insights from various studies to elucidate the multifaceted role of CQDs in these domains. In bioimaging, CQDs serve as exceptional contrast agents, enabling precise and non-invasive visualization of biological structures. Their exceptional photoluminescent properties make them invaluable in biosensing, facilitating the detection of specific biomolecules and environmental contaminants with high sensitivity. CQDs' potential in drug delivery is a game-changer, allowing targeted and controlled release of therapeutic agents to enhance treatment efficacy while minimizing side effects. Moreover, their capacity for gene delivery holds promise in gene therapy, a cutting-edge field with transformative potential for genetic diseases [7-8,10].

Research on Carbon Quantum Dots (CQDs) has made significant strides, particularly in the context of green synthesis and biomedical applications. However, notable research gaps exist in these areas. In the domain of green synthesis, there is a need for more comprehensive studies exploring novel, sustainable methods of CQD production. While natural CQDs synthesized through green chemistry show promise, there is a dearth of standardized protocols and a limited understanding of their full potential [7]. Furthermore, in the realm of biomedical applications, the challenge lies in optimizing CQDs for specific therapeutic and diagnostic purposes. Tailoring CQDs to target particular diseases, improving their drug delivery efficiency, and enhancing their biocompatibility requires further investigation. Bridging these research gaps in green synthesis and biomedical applications of CQDs is pivotal for harnessing the full potential of these nanomaterials in sustainable healthcare and biomedicine [6-11]. The current article aims to summarize the biomedical applications of Carbon Quantum Dots (CQDs) on the basis of existing literature and their implication for sustainable development, and thus lays the foundation for future research and underscores CQDs' vital role in advancing the frontiers of biomedical science including diagnostics and treatment therapy.

2 Carbon quantum dots

Carbon quantum dots (CQDs) are recently discovered carbon nanomaterials that have accumulated apt interest as potential competitors to the traditional semiconductor quantum dots. These CQDs have promising applications in biosensing, bioimaging, drug delivery, electrochemical sensing, gene delivery, biomarker detection, food analysis-related sensing, treatments of diseases as well as in various drug formulations (**Fig. 1**). High tunable fluorescence along with low toxicity, high stability, resistance to photobleaching and more cellular compatibility are some of the properties due to which CQDs are more preferred over conventional semiconductor-based quantum dots (SQDs) [12]. From a structural point of view, CQDs possess unique particulate structures in the nanometer size range (<10nm), where carbon atoms are generally arranged in graphene-like hexagonal structures. These nanoparticles can be synthesized via multiple strategies including hydrothermal treatment, chemical oxidation, pyrolysis of carbon precursors and microwave aided synthesis. CQDs can be further modified by multiple carbonizations and polymerizations to control their chemical attributes, surface functionalization, passivation, fluorescence tuning, and other physical and biological properties. Carbon nanotubes, fullerenes, graphene sheets, and nano-diamonds are some other advanced carbon-based nanomaterials over which CQDs are superior due to their distinct shapes with superfine dimensions, modifiable functional groups over the surface with cheap and rapid synthetic preparations [12].

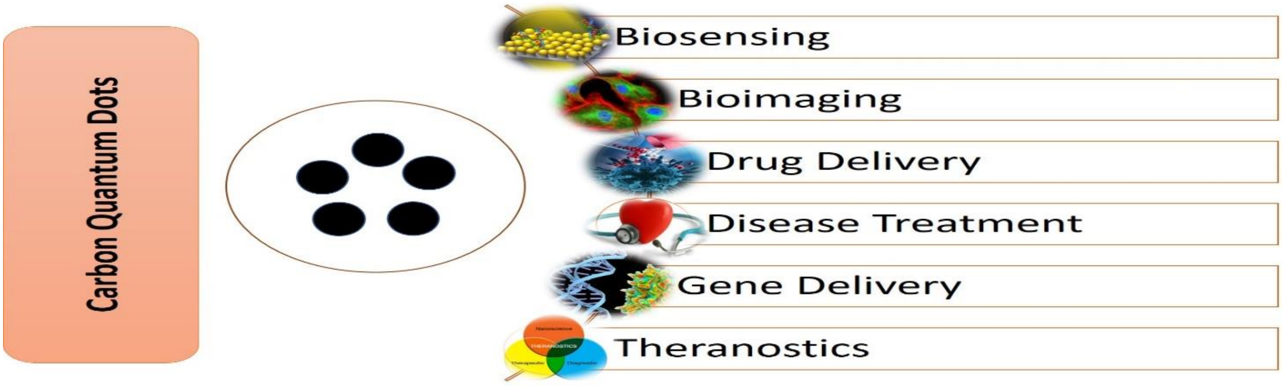

Fig. 1 Biomedical Applications of Carbon quantum dots

3 Biomedical Applications of CQDs

3.1 CQDs and Bioimaging:

Bioimaging is an evolving tool of biomedicine that is associated with the development of various imaging techniques to facilitate the visualization of internal organs and characterization of cellular and molecular processes inside living organisms without posing significant disturbance to the internal system [13]. Nanomaterials like CQDs can be conjugated with proteins, peptides, antibodies, or other small molecules to track the cancer cells to detect some biomarkers, or for drug delivery. Iron oxides used for MRI is one of the important examples where CQDs have been used in clinical setting. CQDs have been reported to be safe for bioimaging in various *in vitro* and *in vivo* setups. Semiconductor quantum dots (SQDs) such as Cadmium, Selenium containing QDs which are the older alternatives for bioimaging are associated with a few limitations like considerably large size, cellular accumulation, toxicity due to synthesis with heavy metals as well as blinking (fluctuating fluorophore emission which limits the application at single particle level). CQDs, however, are considerably superior nanomaterials for cellular and bioimaging due to their better biocompatibility, low toxicity as well and no-blinking properties [14,15].

Graphene quantum dots (GQDs), a type of CQDs, were first time reported to be used in cancer cell imaging by [16], where these QDs exhibited stable fluorescence emission. Various CDs synthesized from natural precursors were further reported to be tested for cellular imaging properties in different cell lines of breast cancer (T47D, MCF-7) as well as cervical cancer (HeLa) [17,18,19]. The investigated CQDs-graphene QDs, Boron doped GQDs, and linseed derived CQDs exhibited negligible toxicity, considerable solubility in water, photo-bleaching resistance, and superior biocompatibility. The property of having a small size (less than 10nm) enables CQDs to probe small biological entities [20]. In an attempt to develop CQDs with strong luminescence, Cao *et al.* used poly (propionyl ethylenimine-*co*-ethylenimine) for surface passivation and two-photon excitations to synthesize water-soluble CQDs with small size (~5nm). These CQDs were able to tag the cell membrane and cytoplasm but were unable to reach the nucleus when incubated with MCF-7 cells as suggested by observation under fluorescence microscope. Tagging of these CQDs with an HIV-1 derived translocation protein TAT (Trans-Activator of Transcription) may enable the probing of the nucleus by overcoming the hurdles associated with the cell membrane and by enhancing the labeling efficiency within the cells [21].

CQDs are beneficial in regenerative therapy where stem cells are used to form different tissue-specific cells after differentiation, and CQDs have been successfully demonstrated to efficiently label different kinds of stem cells like pancreas progenitors, cardiac progenitors as well as neurosphere cells. This stable, long-term term, and non-toxic CQD-facilitated imaging of stem cells in regenerative medicine helps to understand the stem cell contribution, migration, and development into regenerative tissue [22-24]. Graphene Quantum Dots were also used to label human neural stem cells (hNSCs) without affecting the self-renewal capacity as well as the expression of specific hNSC markers [25]. GQDs synthesized using Rhodamine derivative were also reported to be useful in cancer stem cell imaging [26].

CQDs have also been explored for their utility in *in vivo* bioimaging. Hydrothermally generated CQDs of 2-5nm size and passivated with urea were applied for optical imaging in L929 fibroblasts as well as in mice [27]. These CQDs exhibited low cytotoxicity and remarkable performance as bioimaging tools. Various studies demonstrated the synthesis of CQDs for *in vivo* imaging and suggested that longer wavelength-based excitation is preferred due to the deeper penetration required for specimen imaging [28,29,30]. CQDs synthesized by Li *et al*. (2017) when injected intravenously exhibited tumor-selective fluorescence with comparatively very low or no fluorescence signals in normal tissues. Tumor-specific fluorescence was due to folate-based specific targeting of tumor area by tested IR70/ folic acid functionalized GQDs [31].

CQDs are also being considered as a promising candidate for per-acoustic imaging with deeper tissue penetration and high resolution. Radiotracers **^{125}I-F56 Peptide** and ^{68}Ga-DOTA-PA1targeting VEGFR1 and Somatostatin receptor 2 respectively were synthesized and shown to be promising diagnostic agents in PET scanning of gastric tumors as well as lung cancers [32,33].

3.2 CQDs and Biosensing

Biosensors aid early disease diagnosis which improves the chances of successful treatments. These biosensors measure the organic/ inorganic and bio-molecules in living systems and have applications in various fields like biomedicine, food safety, agriculture or industrial monitoring [34]. The detector part of biosensors is majorly based on bio-receptors (like enzymatic, nucleic acid, biomimetic, cellular based and immunosensors). CQDs as biosensors has been devised for monitoring of various metabolites like nucleic acids, glucose, phosphate ions, potassium ions, iron and cellular pH [12]. These biosensors exhibit various kinds of interactions like π-π conjugation, electrostatic interactions or electron transfers, which facilitates turn on-off status of quantum dots. Additionally, CDs and CQDs offer wonderful electrical conductivity, enhanced dispersibility and large surface area which enable the stable interaction with target biomolecule, thus acting as excellent fluorescent biosensing probes. For example, Rhodamine-functionalized graphene quantum dots (RBD-GDQs) were used as iron detecting biosensors in cancer stem cell membranes [26]. CDQs can also be used for detection of other metal ions and free radicals like peroxynitrite [35, 24]. Reactive oxygen species (ROS), also known as free radicals serve as important biomarkers for DNA damage, inflammation, infections, arthritis, neurodegeneration or cancers and to sense the drug efficacy. Bhattacharya *et al*. developed an ascorbic acid containing hydrogel based CQDs for ROS sensing and used for evaluation of the chemotherapeutic drug efficacy by measuring the ROS levels after drug administration [36].

In another study, Lu *et al*. demonstrated the synthesis of CQDs using one-pot pyrolysis method for detection of β-glucuronidase inhibition. β-glucuronidase is used as a biomarker in cancers and its inhibition is associated with controlled proliferation of cancer cells. Reduced β-glucuronidase activity leads to changed fluorescence intensity of CQDs [37]. There are other reports of CQDs usage for detection of Glutathione (GSH) levels and intracellular pH changes in cancer cells (cancer cells exhibit comparatively acidic pH) [38, 39]. Raveendran and Kizhakayil designed mint based Green CQDs, which can sense folic acid levels. Folic acid deficiency is associate with several disease conditions like neural tube defects, mental retardation and stroke, so tracing this analyte is crucial in biomedical setup [40]. Additionally, CQDs can facilitate the residual antibiotic sensing in milk, milk products or other environmental targets

Due to high stability and good electrical conductivity, CQDs have also been used to develop electrochemical sensors for detection of molecules like cholesterol, nucleic acids, oval-albumin, glucose, ascorbic acid, L-cysteine etc. Polymeric CQDs further exhibited high sensitivity and specificity for hemoglobin detection [41].

3.3 CQDs and Efficient Drug delivery

Major cancer therapeutics include chemotherapy, radiotherapy or surgical resection all of which are associated with multiple side effects. Chemotherapy is associated with non-specific killing of tumor as well as normal cells due to lack of precision and thus results in drug toxicity as well as multiple drug resistance. Controlled drug delivery to a specific site may deal with these limitations of otherwise effective chemotherapeutic drugs. CQDs have been proposed as efficient drug carriers containing bioimaging systems and specific drug delivery with low cytotoxicity as compared to conventional chemotherapeutics [18]. CQDs containing surface amino acids, which enables cross linking with tumor therapeutic as well as diagnostic candidates. CQDs prepared from citric acids using microwave pyrolysis and Schiff's base linkage delivered the theragnostic molecules in tumor microenvironment in a controllable manner [41].

Targeted drug delivery in nucleus and mitochondria has also been exhibited by CQDs prepared by hydrothermal method [42]. Additionally, these carbon dots have also been utilized to differentiate the normal and apoptotic cells of A549 cell line, and to deliver the anticancer drug to the targeted areas of MCF-7. These CQDs showed less toxicity when used to deliver anticancer drug to normal HepG-2 cells [43,44].

Not only in cancer studies, drug delivery science is looking for development of such systems, which will improve the retention, absorption and elimination related parameters of the drugs, otherwise facing low efficacy due to poor delivery at target or fast elimination by metabolic system. Khan *et al*. designed CQDs for controlled delivery of drug named Dopamine Hydrochloride (DH) (Hydrochloride salt of a neuromodulatory molecule-Dopamine) to target the neuro-related ailments [45]. CQD-DH conjugates were shown to efficiently deliver the drug for extended periods without exerting any toxicity both in *in vitro* and *in vivo* model systems. CQDs designed for performing multiple functions like delivery of signaling molecules/ magnetic/ MRI agents along with drugs or dual drug delivery have also been reported. A pH-sensitive CQD for dual delivery of doxorubicin and heparin was reported by Zhang *et al*., which showed more specific drug release to the cancer cells. Doxorubicin is an anticancer drug that otherwise is associated with various side effects due to non-specific delivery, whereas, heparin is used to suppress high blood coagulation and venous embolism in cancer patients [46].

Natural CQDs derived from different plant species like C*urcuma longa, Ocimum sanctum, Aloe vera, Azadirachta indica* etc. are gaining accreditation in drug delivery as compared to the synthetic conventional CQDs due to their properties like greater abundance, more biocompatible and environment friendly nature as well as solubility in aqueous fractions. The diverse functional groups over the surface of natural CQDs improve the optical properties, sensing and biosensing functions along with the drug delivery. These CQDs are being used to deliver drugs with the potential to treat cancers, neurodegenerative diseases as well as microbial infections (**Table 1**) [47].

Table 1. Discusses the different types of natural CQDs being used for drug delivery and disease treatment [48-67]

Name of CQDs	**Size**	**Applications**
Aloe vera	5nm	Anti-proliferative, Wound healing
Ascorbic acid	2nm	Promoting capillary elasticity, lowering blood cholesterol levels & boosting immunity.
Curcumin	5.4 –7.0nm	Anti-bacterial, Wound healing & Anti-tumor
Citric Acid, dicyandiamide	2.5 nm to 3.8 nm	Biosensing
Carrot juice	3.75nm	Cellular imaging
Orange Juice	1.5- 4.5nm	Biosensing
Hair	4.56nm	Bioimaging
Neem leaves	1.5- 2.5nm	Bioimaging, antioxidants & antimicrobial
Tulasi leaves	3-7nm	Antimicrobial
Wheat straw	5.7nm	Drug delivery, biosensors, bioimaging, and photocatalysis
Onion waste	1-7nm	Biocompatibility, good photostability, low cytotoxicity & high photocatalytic activity
Bamboo leaf cellulose	2 nm	Anti-cancer
Coconut husks	2nm	Targeted drug delivery & bioimaging
Rice residue	5-10nm	Soil contamination, Water & air pollution control
Coffee ground	1.6-4.4nm	Necro apoptosis
Prawn shell	---	Bio-imaging & antibacterial
Pasteurized milk	10 nm	Hypertension & renal problems
Chrysanthemum buds	3.45 nm	Photocatalytic activity
Saffron	1.5 – 3.0 nm	Local anaesthetic
Mulberry leaves	1-2 nm	Anticancer

3.4. CQDs and Disease Treatment

CQDs have also gained enormous attention in the therapeutics field as multiple reports emerged suggesting specifically designed carbon dots targeting various diseases in last decade **(Figure 2)**

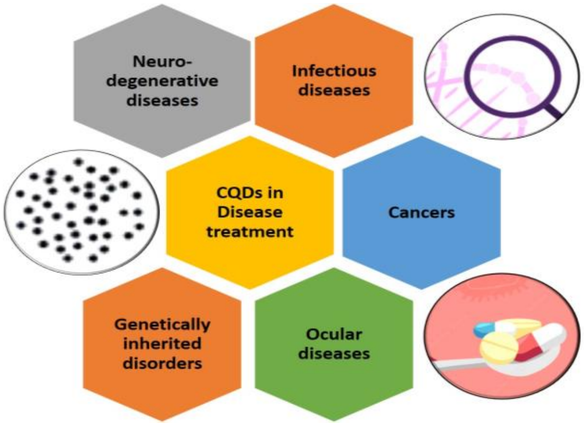

Fig. 2 Use of CQDs in the treatment of various diseases

Nanomaterials propose comparatively simple surface therapy for different infectious pathogens like viruses, bacteria, fungi, or parasites by photodynamic therapy. During photodynamic inactivation CQDs with photosensitization capacity generate ROS in microbes by utilizing molecular oxygen, thus inactivating those pathogens [68]. Polyamine-based CQDs were designed and demonstrated to exhibit antibacterial potential against multiple bacterial species including *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella enterica* (Enteritidis serovar) etc. These CQDs were also effective against a corneal disease bacterial keratitis induced by *S. aureus* in the rabbit model system [22]. Carbon dots synthesized from Aloe vera extract exhibited metal ion sensing as well as photosensitive bactericidal activity against S. aureus and E. coli [69]. CQDs with antiviral properties has also been designed which possess the capacity to enter the host cells and inhibit viral replication or act as carriers of antiviral agents. Curcumin based CQDs exhibited antiviral activity against different enteric coronaviruses [47,70].

Age-related macular degeneration, diabetic retinopathy and bacterial keratitis are among the major causes of ocular diseases leading to loss of vision, and different treatment approaches are associated with a major limitation of drug delivery to ocular posterior segment [71]. Kumar *et al*. thoroughly reviewed the application of CQDs in ocular imaging and eye disease treatments and suggested that biocompatible and eco-friendly nanomaterials derived from synthetic or natural polymers could be helpful to solve the drug delivery as well as safety concerns [73]. Various reports on gene therapy for retinal dystrophy, anti-angiogenic properties of CQDs, CQD based eye drop formulation and many more prove them as potential therapeutic molecules for ocular disease treatment [71-73].

Neurodegenerative diseases (NDs) like Alzheimer's, Parkinson's, Amyloid sclerosis, Huntington's disease and other disorders of central nervous system pose a substantial and continuously increasing burden on healthcare worldwide [74]. NDs are characterized by misfolded proteins or prion like proteins which include amyloid beta, α-synuclein, tau, mutant huntingtin protein etc. Guerrero *et al.* synthesized the sodium citrate derived CQDs and showed the inhibition of amyloidogenic fibril formation as well as disaggregation of mature fibrils into their monomers using a model amyloidogenic protein named as hen egg white lysozyme [75]. The studied CQDs exhibited low cytotoxicity in *in vitro* studies using SH-SY5Y cell line. CQDs prepared by Koppel et al. mitigated the lipopolysaccharide induced amyloid-β and human islet amyloid polypeptide plaque formation in zebra fish [76]. These reports suggest CQDs as potential prophylactic and therapeutic candidates for neurodegenerative diseases. However, majority of drugs developed for treatment of brain disorders face the major issue of crossing blood brain barrier. To enable the drug delivery or diagnostic probes to be delivered at specific sites, the CQDs take the advantage of their small size, and CQDs of size smaller than human capillaries can cross the blood brain barrier. Wang *et al.* developed nitrogen doped nanodots of carbon for fluorescence imaging which entered in glioma cells in *in vitro* as well as showed good fluorescence imaging of glioma in *in vivo* conditions [77].

In addition to cancer cell imaging or tracking, some CQDs with therapeutic potential against cancer have also been reported which has been discussed more in detail under theranostics section [78].

3.5 CQDs and Gene therapy

Gene therapy, being a rapidly flourishing technique has emerged as a great therapeutic approach for treatment of incurable diseases. This approach attempts to treat the ailment or strengthen body's resistance to disease by introduction of a new gene or replacement of a faulty gene. This broad treatment modality may be used to treat various recessively inherited genetic disorders like cystic fibrosis, sickle cell anaemia, muscular dystrophy and haemophilia as well as diseases associated with acquired genetic changes such as viral infections, cancers etc [79]. Effectiveness of the approach depends on delivery of gene of interest to the nuclei of specific/ unhealthy cells with the help of vectors. Synthetic vectors offer a safer option as a vector as compared to viral based vectors being utilized for gene delivery, but synthetic vectors come with the limitation of low transfection efficiency in *in vivo* systems. CQDs synthesis with properties of low toxicity, lack of blinking, chemical stability and biocompatibility has been attempted for gene delivery, e.g. hyaluronic acid-based carbon dots developed by surface passivation with polyethylenimine exhibited the targeted cell imaging ability and showed the potential for effective transfection by releasing the DNA cargo into cytoplasm [80]. Cao *et al*. demonstrated the use of CQDs for delivery of pSOX9 plasmid in mouse embryonic fibroblasts. These CQDs with fluorescence property enabled intracellular tracking of nanoparticles and also induced chondrogenic differentiation in studied fibroblasts [81]. In another previous report, polyethylenimine based CQDs showed good biocompatibility and ability to act as labelling agent for gene delivery [82,83].

3.6 CQDs and Theranostics

In addition to above discussed applications, CQDs are being targeted in the field of theranostics which offers several benefits for both disease diagnosis and treatment. Theranostics are suggested to play an important role in personalized medicine, which is focussed on optimizing the effective treatment followed by minimal post-diagnosis delay [84,85]. The term theranostic has evolved to the term theragnostic as it better represents the combination of disease characterization (diagnosis) and treatment strategies, whereas theranostic is considered to provide more focus on disease characterization [86].

There are various studies demonstrating the application of CQDs in cancer theranostics such as 'Large amino acid mimicking CQDs' (LAAM-CQDs) for multiple *in vitro* and *in vivo* cancers, 'Nitric oxide-releasing CQDs' (NO-CQDs) for lung and colon cancers, and biocompatible 'trichome tryptophan sorbitol CQDs' (TC-WS-CQDs) for hepatocellular carcinoma [87-89]. Li and group targeted the amino acid transporters, specifically LAT-1 (large neutral amino acid transporter-1) for taking leverage in tumor theranostics and synthesized LAAM-CQDs. There are four LATs (LAT-1,2,3 and 4) out of which LAT-1 is known to be specifically upregulated in the tumor cells. Loading of CQDs (targeting LAT-1) with chemotherapeutic drugs increase the accumulation of drugs in targeted tumor cells, resulting in the increased treatment efficacy. The designed LAAM-CQDs were shown to have a high degree of tumor specificity and interaction with multiple tumors including brain tumors. A large cell panel including cancerous cell lines (lung, kidney, colon, cervical, ovary etc.), cancer stem cell cultures derived from patients, and non-cancerous cells were examined for LAAM-CQDs interaction, which suggested the potential of these CQDs to penetrate cancer cells irrespective of their origin. However, these CQDs showed limited penetration in non-cancer cells. *In vivo* brain tumors in U87MG glioma-bearing mice were also examined at different intervals in this study upon intravenous injections of LAAM TC-CQDs and by using NIR fluorescence imaging [90]. It was observed that, when the fluorescence signals were mostly detected in the brain, 8–12 hours after injection when the accumulation of LAAM TC-CQDs in the brain was at peak [87].

NO-CQDs were prepared by hydrodynamic method of β-cyclodextrin modification with functional groups and further incubation in alkaline environment with NO gas which resulted in particles with a range (0.2–1.1 μmol/mg) of different adjustable NO payloads and different surface functionalization (primary amine, hydroxyl). These CQDs were tested against Pa14c, SW480 and A549 cell lines which are used to mimic pancreatic, kidney and lung cancers, respectively and exhibited significant growth inhibition. The anticancer property of NO-CQDs was dependent upon the surface functionalization group and the payload capacity with maximum activity shown by modified primary amine functionalization with payload of ~1.11 μmol/mg [88].

Further, TC-WS-CQDs were also synthesized upon hydrothermal break down of tryptophan and sorbitol in an environmentally safe manner. TC-WS-CQDs had a better targeting capacity into hepatocellular carcinoma cells than normal hepatocytes, which could enable early and effective tumor cell monitoring via fluorescence imaging. Tumor imaging and inhibition property TC-WS-CQDs were checked on Huh7 cell line as well as in a BALB/nu mice with induced hepatocellular carcinoma (HCC) and was found that i*n vitro* and *in vivo* HCC prevention were improved simultaneously by these green fluorescence-emitting TC-WS-CQDs without the need for medication delivery as these nanoparticles produce large amounts of free radicals in targeted tumor cells. Large amounts of free radicals induce autophagy via activation of p53-AMPK pathway rendering the anticancer potential to these CQDs [89].

Enzyme based CQDs with nanozyme synthesized from coffee exhibited the glutathione peroxidase like activities and promoted the apoptosis of cancer cells. These coffee derived CQDs also reduced the size of tumor in mice bearing HepG2 induced tumor by recruiting the immune cells thus activating the anti-tumor immune system [78]. In another study CQDs synthesized from ginger selectively suppressed the growth of hepatocellular carcinoma cells (HepG2) by activating the cancer cell apoptosis while exhibiting low cytotoxicity to breast cancer, lung cancer and ovarian cancer cells [43]. CQDs based photodynamic therapy against cancers is also reported as potential tool for treating tumors and non-invasive lesions with less side effects. Magnetofluorescent Fe_3O4 CQDs developed by Zhang *et al.* (named as SWCNTs-PEG-Fe3O4@CQDs) exhibited the multiple roles of photodynamic, photo dermal and chemotherapy [46].

CQDs have also been reported to have application in mitochondria based theranostics, which could have utility in cancer as well other diseases. These CQDs has various benefits including high specificity, easy surface functionalization, great photostability, cost effective and simple synthesis, excellent photostability, applicability for long term imaging and negligible cytotoxicity over the commercially available mitochondrial tracking molecules. A study by Hua *et al.* reported the synthesis of fluorescence CQDs which target mitochondria via endocytosis mediated via caveolae and temperature dependent transport rather than being captured by lysosomes or endosomes in the cell [90]. Additionally, CQDs have application in infectious disease theranotics. N-doped CQDs from single step production showed antibacterial action against MRSA and *Staphylococcus,* even breaking down their cell walls; however, these CQDs were ineffective against *E. Coli*. Their mode of action shows that Staphylococcus bacteria bind to positively charged N-doped CQDs at particular places and interact with negatively charged bacteria. When applied to MRSA-caused wound infections, these N-doped CQDs showed outcomes comparable to vancomycin [91].

So, CQDs hold a great potential in theranostics and their integration in clinical theranostic could advance the personalized medicine to great extent including cancer, mitochondrial and infectious disease [92,93,94]. Ongoing research on nanotheranostics aims to develop CQDs with high functionality, less toxicity, high specificity and effective clinical translation.

4. Sustainable development and CQDs

The goal of sustainable development is to fulfill the requirements of current generations without compromising the capacity to fulfill the requirements of future generations. Embracing and following sustainable practices protect and preserves the planet's vitality also safeguarding human health and ensuring a harmonious coexistence for current and future generations [95]. Understanding the intersection of sustainability and health is crucial for developing comprehensive solutions that protect both ecosystems and human societies from the multiple effects of climate change, urbanization, and unrestrained consumerism.

Infectious and non-infectious diseases contribute significantly to the disease burden worldwide impacting economy, social life, environment and health security. Due to increased disease burden there is a continuous rise in global healthcare costs as well less loss of productivity. On the social front, in addition to mortality diseases also result in imbalanced economic status of an individual, impacting mental health due to suffering and social discrimination as well as disrupted necessary education. Further, the disease burden deprives individuals from necessary healthcare due to overwhelmed health facility upon emergence of diseases. Environment and other sustainable practices also suffer due to disease burden as it could lead to resource and efforts reallocation from planned strategies towards urgent healthcare needs. Thus, the impaired health and disease burden serve as one of the major roadblocks of sustainability for any nation or worldwide. To address this healthcare challenge, advancements in disease diagnosis and treatment strategies are required to achieve the early and correct diagnosis and thus reducing the suffering period by early treatment. Nanomaterial based strategies have gained much attention of the researchers to develop different entities with applications in the field of biomedical sciences. CQDs has various applications such as utility in effective drug delivery, gene delivery, imaging, biosensing and as well as serve as therapeutic molecules for cancer and other diseases which helps in achievement of sustainable development goal 3 (SDG3). Additionally, these materials also contribute to targets of other SDGs such as to achieve environment remediation (applications in water and air purification), energy conservation and storage, environmental sensing, waste disposal and management etc. which are not discussed in the current article.

5 CQDs and associated challenges

Although CQDs opened a promising window of applications in the biomedical field and are superior to some other types of quantum dots, however, they are still associated with challenges being faced by quantum dot technology [96,97]. These challenges are associated with synthesis, fabrication, size, specificity, toxicity, quantum yield, and reproducibility which need to be addressed to ensure their sustainable use in biomedicine. Synthesis and fabrication of the CQDs is challenging to ensure consistent size, shape, functionalization, and particles without any surface defect, which are further critical for the reproducibility of the promised results. Surface functionalization and different fabrication practices also impact the quantum yield (fluorescence emission efficacy) and toxicity index. CQDs can convert. More research is required to explore different fabrication techniques to increase the quantum yield of CQDs by rendering them low or no toxicity. Further, CQDs have shown great potential in biosensing, but with change in size impacts the specificity and sensitivity of sensors significantly, which could be addressed by developing the strategies to deliver CQDs with uniform properties. Additionally, the field of CQDs as biotags for testing allergies, antibiotic sensitivity, etc. is also less explored.

6 Conclusion

Carbon quantum dots (CQDs) have garnered significant attention in biomedicine due to their biocompatible and eco-friendly design.
Potential applications of CQDs in biomedicine include:

- Bioimaging
- Biosensing
- Drug delivery
- Disease treatment
- Gene delivery
- Theranostics

CQDs can also be utilized in the detection of food toxins and the formulation of pharmaceutical drugs, further contributing to biosensing and disease treatment. These applications of CQDs have the potential to significantly contribute to the achievement of sustainable development goals. CQDs offer a promising avenue to shape a healthier and more environmentally friendly future for both humanity and the planet. The exploration of CQDs in these various applications has the potential to lead to groundbreaking advancements that transcend disciplinary boundaries.
These advancements are essential for the well-being of present and future generations. Despite the potential, there are research gaps such as optimization of specific surface functionalization, limited clinical translation, etc that need to be addressed to understand the full scope of CQD formulation and applications and optimize their performance in various biomedical and environmental contexts.

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