Carbon Dots -A Turn-On Probe for Neurological Disorder

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Abstracts: The creation of novel methods is essential for the early diagnosis and treatment of neurological illnesses (NDs). The blood-brain barrier (BBB), which can prevent substances from accessing the central nervous system, is the most difficult obstacle to overcome in the development of neural medication delivery systems (CNS). For several biological applications, carbon dots (CDs) have emerged as highly outstanding and promising agents, including the treatment of brain tumours, ND, and bioimaging research. Because of their great qualities, they have a lot of potential for a range of scientific disciplines due to their biocompatibility, tiny size, tunable optical properties, photostability, and straightforward fabrication processes. This article's goal is to provide a summary of current CD research and to make recommendations for future work on creating neural drug delivery systems that can penetrate the BBB and reach the central nervous system. The two main subjects of this review are CD toxicity and unique optical properties. For a variety of neurological illnesses, a unique CD-based drug delivery system is designed in detail. This study also explores the possible applications of CDs for neurodegenerative disease therapies and imaging of brain tumours. The final section provides a summary of present CD sensing applications and projected future developments.

Keywords: Neurological Illnesses, Neuro Drug Delivery Systems, Carbon Dot, Biosensing, Bioimaging, Brain Tumour, Blood-Brain Barrier.

1.INTRODUCTION

Over the past 15 years, carbon dots have emerged as a new member of the Nanomaterials family and a rising star [1]. Carbon dots are a fascinating subtype of nano carbons that are less than 10 nanometers in size. Single-walled carbon nanotubes were initially produced and studied by preparative electrophoresis (SWCNTs) in 2004[2,3]. Carbon dots are a well-liked member of the nano carbon family because to its reliability, abundance, and affordability [4]. The full fluorescent carbogenic substance is referred to as "carbon dot" in this sentence. Terminology allows us to distinguish between two different kinds of materials: the first is few-layer graphene dots, which may be produced from precursors based on graphene and have a size range of up to 100 nm, and the second is graphite dots in three dimensions that are roughly spherical and can range in size from 5 to 10 nm. Dark-colored carbon has a low solubility in water and a low fluorescence. On the other hand, carbon dots are readily soluble and exhibit strong fluorescence [11]. Carbon dots, also referred to as glowing carbons, are a form of carbon. Carbon dots feature a graphite core with an exterior shell made of covalently bound oxygen and nitrogen atoms and an inner shell made of a carboxylic acid [12–15]. Carbon dots have excellent water solubility because of the numerous carboxylic acid moieties on their surfaces. They can also be functionalized exhibit qualities such as high photobleaching resistance, chemical inertness, low toxicity, and improved biocompatibility and bio stability [16,17]. Due to their tunable surface functionalities, well-defined, isotropic shapes, ultrafine dimensions, straightforward, quick, and affordable synthetic route, and a variety of applications, carbon dots, Other nanocarbons may be replaced with good results by materials including fullerenes, carbon nanotubes, quantum dots, and nanodiamonds. Carbon-based Quantum dots can successfully replace the harmful metal-based Quantum dots now in use [18–21]. Each nanomaterial is made up of a quickly moving band of incredibly bright material [22–25]. Each of the components that can be extracted from carbonaceous material has size-dependent fluorescence properties. Candle soot produces carbon atoms with SP2 hybridization but no saturated SP3 carbon atom, nuclear magnetic resonance (NMR) of carbon dots reveals that they are a conjugated system [26–30]. They are employed in a number of processes, including as catalysis, bioimaging, biosensing, drug administration, as light-emitting diodes, fluorescent printing ink, and for the detection of diseases and physical flaws through photoluminescence. Due to their exceptional optical and physicochemical properties, carbon dots are an excellent agent for cancer therapy and

imaging studies. Using carbon dots as a probe, substances such as amoxicillin, ascorbic acid, dopamine, and glucose have all been examined [31,32]. Parkinson's, Alzheimer's, Amyotrophic lateral sclerosis, and prion diseases are just a few examples of the neurological illnesses that can be brought on by damage to neurons in the spinal cord and brain [33–35]. There are few methods for identifying and treating a range of neurological conditions, as well as avoiding brain damage and impairment. When introducing medications or imaging agents into the brain is the trickiest barrier to get through [36,37]. The biological applications, such as drug delivery and cross-brain barrier crossing, carbon dots may be used as a new biocompatible agent [38–43]. One of the uses of carbon dots that are now being investigated, along with focusing on other diseases and brain tumours, is improving carbon dot penetration to deliver the right dose of medication to brain cancer target areas [44,45]. We will give a brief description of the creation of carbon dots in this post, along with some of its distinguishing characteristics. The various uses of carbon dots in neuro drug delivery systems have been compiled. We've also listed all of the challenges and potential future uses for carbon dots. In this paper, we examine the special attributes and production processes of carbon dots, which have the potential to develop into a useful nanomaterial in the near future.

1.1 SYNTHETIC APPROACHES

CD production typically involves top-down or bottom-up techniques [20–26]. Techniques include arc discharge, laser ablation, chemical or electrochemical oxidation, and other procedures for converting carbon precursors into nanoscale compounds [27–30]. However, using a variety of energy sources, including ultrasound, hydrothermal methods, microwave radiation, and ultrasonication, the bottom-up strategy enables the creation of carbon dots from sources of small-molecule carbon [12]. Crude medications are exposed to carbon dot dialysis against water to remove them. In two areas, quantum yield (QY) and surface energy, top-down methods perform better than bottom-up ones. While bottom-up methods are less expensive, top-down methods are more expensive [14]. More environmentally responsible methods of producing carbon dots include using natural materials like chitosan, bovine serum albumin, egg white, or any other natural material like onion, carrots, or black grapes. Carbon dots can be produced frequently by using these simple, environmentally friendly methods. enormous scale[16–18]. High oxygen concentrations of up to 40% and SP2 characteristics can be found in carbon dots with carboxyl, carbonyl, and epoxy groups. Different synthesis processes and precursors are responsible for determining the physical-chemical characteristics of carbon dots, such as their oxygen and nitrogen content, quantum yield (QY), crystallinity, size, colloidal stability, and compatibility with other chemicals. A top-down method will produce carbon dots with a 28 percent quantum yield and will produce carbon dots between 2 and 25 nm in size, in contrast to a bottom-up method, which does not need a surface passivation agent.

1.1.1 Optical Properties

Due to their outstanding photoluminescence characteristics, carbon dots are excellent candidates for bioimaging of various cells and animals. Less than 10 nanometers in diameter, carbon dots are the tiniest of particles [15]. Due to the conjugated system (-C=C-) and heteroatoms, carbon dots exhibit to * and n to * electron transitions. Due to this electrical change, carbon dots may absorb UV light with a wavelength between 270 and 320 nm. Due to their surface flaws and diverse chemical make-up, carbon dots exhibit exceptional optical features. When the size of the carbon dots is regulated or doping agents are added to the carbon dots, a sizable amount of blue fluorescence is produced [33,45].

Carbon dots could be employed as a photo catalyst because of their well-established reputation as trustworthy electron donors. Functional groups, such as epoxy, hydroxy, nitrogen, and phosphorus-containing compounds, carbon dots have been seen to emanate red-shifted emission. Due to their excellent properties and extreme small size, carbon dots are used for a variety of purposes, including medication delivery, bioimaging, and cancer treatment. Additionally, they have the ability to find and study traces of biomolecules [8,9,25].

In a bottom-up process, tryptophan, green precursors, and aspartic acid are converted into an average size of 2.8 nm for carbon dots, which emit mostly blue-shifted emission. When carbon materials are carbonised, bigger blue and green fluorescent carbon dots and red emission are produced [28,45].

If top down synthesis is performed, carbon dots will exhibit luminescence in the yellow-red region. According to multiple research projects, the emission wavelength is controlled by a mixture of H2SO4 and HNO3 during the oxidation of various graphite structures. Carbon dot particles with the highest negative charges emit in the orange range while those with the lowest negative charges emit in the blue range, according to ion exchange chromatography [9].

Because of their attractive light-emitting feature, carbon dots can prevent organic dyes and polymer dots from being photobleached. Red-light emitting carbon dots are typically employed in bioimaging applications. Since carbon dots emit red and near-infrared light, they can pierce tissue more deeply. The thrilling activity in biological windows is related to deep tissue penetration, which is essential for bio imaging applications. Carbon dots that emit a yellow or red shift frequently have a bigger size than those that emit blue light. The photoluminescence characteristics of carbon dots may be calculated using DFT, with an particle sizing expansion and aromatic ring conjugation leading to a decrease in the pi to pi star transition band gap [33]. The band gap can be narrowed by the presence of carboxylic or amino groups, which can affect photoluminescence emission and cause excited, wavelength-dependent emission.

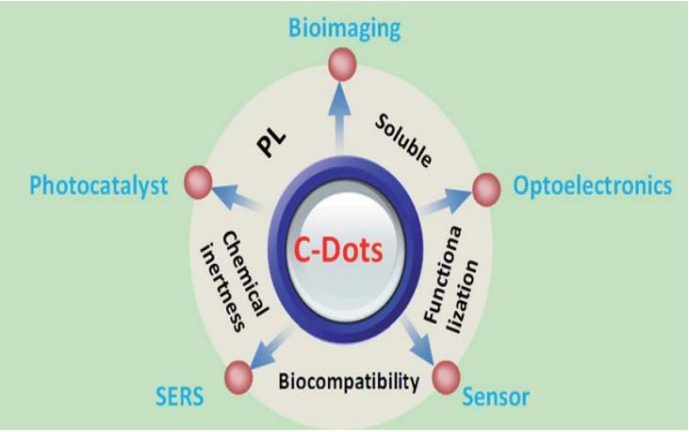

Figure 1. Different applications of carbon dot

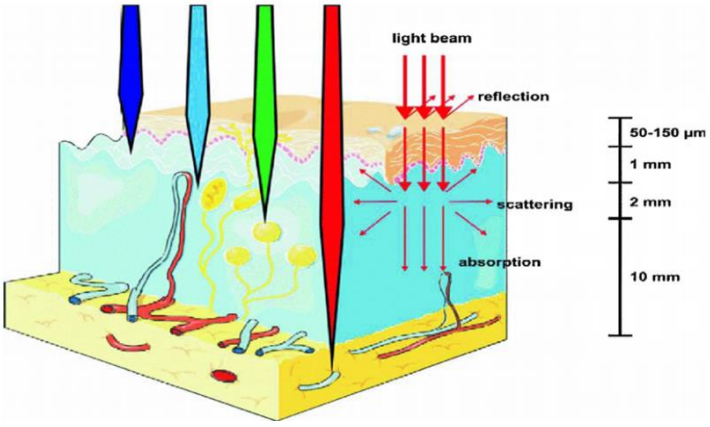

Figure 2. Different optical properties of carbon dot

1.2 Carbon Dots in Brain Tumor Imaging

Gliomas, which are malignant brain tumours, are divided into four categories by the World Health Organisation: astrocytotic, endometrial, oligodendroglial, and mixed gliomas. Since these gliomas can be lethal. Gliomas cannot be effectively treated. Utilizing drug delivery methods based on nanomaterials to treat brain tumours such gliomas has garnered a lot of interest [48]. High quantum yield and low interference, carbon dots, one of these nanoscale materials, can be used to imaging brain tumors [49,50]. It is crucial to create a carbon dot production technique that is simple to use, efficient, and environmentally friendly because carbon dots can traverse the blood-brain barrier. Carbon dots made from milk can be utilised to image the U87 cell line from a human glioma tumour using a hydrothermal process. According to numerous research, carbon dots are absorbed by U87 cell lines and provide amazing fluorescence for imaging cancer cells. By oxidising tyres with nitric acid, carbon dots can also be made, and because they meet in the near infrared range, they can be employed as IR imaging agents to look at various cells.

Carbon dots coated with Gd+3 polymer might be a promising option for glioma-specific MR fluorescence imaging. Dual model imaging systems (DETA) can be created using polymer-coated carbon dots and Gd+3 diethylenetriaminepentaacetic acid[52]. GD+3 polymer loaded carbon dots can be a good option for successfully penetrating BBB and reaching the brain for tumour imaging with good resolution (time and dose dependent) because of its enormous dispersity, uniform size, improved quantum yield, increased MRI contrast ability, and efficient uptake by tumours. To solve the issue of carbon dot accumulation in tumour cells, GD+3 laden carbon dots can have a hydrophilic polymer coating applied to their surfaces for effective uptake by human derived U87 cells, it may cause a 300 microgram per ml within two hours suppression of fluorescence resolution around the tumour tissues[53,14]. A polymer with GD+3 loaded carbon dots has been demonstrated to be able to penetrate leaky microvascular walls and successfully reach the target tumour in in vivo experiments Particle size significantly affects tumour cell imaging because larger GD+3 loaded carbon nanoparticles result in a darker image in the center and a brighter image close to the glioma's border[54,55]. Figures 3a, 3b, and 3c illustrate how carbon dots are functionalized with the DTPA derivative GD+3 ion and how they can penetrate brain glioma tumours and breach the blood-brain barrier. By adding nitrogen to carbon dots to create nanoparticles, the solvo-thermal approach has been demonstrated to be an effective synthetic method for manufacturing polymer coated nitrogen doped carbon dots with a size of 5–15 nm.

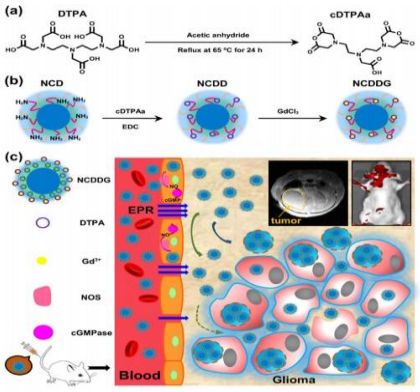

Figure 3. (a) the creation of DTPA derivatives using acetic anhydride. (b). Adopted from [48]

1.3 Carbon Dots and Its Cytotoxicity

Studies of the cytotoxicity of various nanosize materials have recently been conducted in vitro and in vivo. [56]. According to in vivo toxicity investigations of these materials, the cytotoxicity of nanoscale carbon nanomaterials varies on concentrations, surface charge, and time. Zebrafish, phytoplankton, and zooplankton have all been used in in vitro experiments to determine CD toxicity [6,57]. Since there was no evidence of toxicity or harm to the aforementioned species, these results showed that the functionalized CDs and GQDs were biocompatible with a

variety of cell lines [9,58]. Furthermore, these nanoparticles have served as the basic building blocks for the development of useful nanomaterials. GQDs are created when a single sheet is joined to CDs that range in diameter from 2 to 10 nm. GQDs are CD subsets and share many of their electrical and optical properties. Furthermore, CDs are now more promising than metal-based quantum dots (QDs) for applications such as medication delivery, photocatalysis [17–20] due to a multitude of characteristics, including their hydrophobic nature and their capacity to penetrate cells. Since CDs don't contain any heavy metals, unlike typical QDs, they can be used as biocompatible materials for a variety of biological studies[60,61]. On the other hand, the PEI-pristine-CDs accelerated cell proliferation while slowing the cell cycle, which resulted in oxidative stress. These findings demonstrated how CD surface chemistry affects cell cycles and survival. Similar to fluorescent CDs, fluorescent CDs demonstrated their non-toxicity by not affecting the growth and development of zebrafish [62]. The potential for brain-influencing metal-laced CDs was also studied. There are numerous claims that the CDs were only slightly dangerous. For instance, endogenous CDs, which are created during the digestion of food, have been proven to negatively affect a number of bodily organs and systems [63,64]. Cell viability dramatically decreases as a result of these endogenous CDs containing carbon, nitrogen, and oxygen, which leads to autophagic cell death.

1.4 Carbon Dots in Biosensing

Numerous scientific fields, including bioimaging, sensing, and biomedicine have shown a considerable degree of interest in CDs due to their complex surface chemistry, adjustable emission capabilities, and ultra-small size[8]. Additionally, AA(Ascorbic acid) affects dopamine and glutamate neurotransmission in the nervous system[65]. Because they can be utilised to pinpoint the pathological states of numerous neurological illnesses, it is crucial to develop fresh techniques for measuring AA levels[66,67]. The potential for one-step pyrolysis to yield Tris-based CDs with a QY of 7.3% was investigated. CoOOH nanoflakes and CDs work together to create a situation that resembles a redox system. When tris-derived CDs-CoOOH is exposed to AA, the alcohol's enediol group forms a redox connection with hexagonal CoOOH nanoflakes [68]. When AA was added, the CDs' fluorescence emission dropped. Functionalized CDs can be used to measure the antioxidant activity of AA since oxidants and antioxidants interact. When Fe3+ ions are added to the surface of CDs, it appears that redox reactions take place [69]. The coordinated covalent link that forms between the ion and the chemical allows Fe3+ to be functionalized on the surface of CDs. An oxidation-reduction reaction turns Fe3+functionalized CDs into Fe2+ when they are exposed to AA[70,71].

Due to the Fe3+ ion's increased chelating capacity, which makes up for the Fe2+ ion's decreased chelating capacity with CDs, fluorescence emission increases [70,72].

But understanding the dynamic and intricate processes of the CNS has proven to be difficult. CDs have recently shown to be helpful in the research of the intricate connections in the CNS[73].

The creation of a CD-linked antibody immunosorbent test with a detection limit of 25 pg/mL serves as evidence for this. Cholinesterase inhibitors, which restrict acetylcholinesterase (AChE) activity and hence delay acetylcholine breakdown, may be used to treat Alzheimer's disease [74]. Alzheimer's disease symptoms can be effectively managed with tacrine, a cholinesterase inhibitor [75]. As a result, tacrine significantly reduced AChE activity while restoring the fluorescence of N-GQDs, AChE, and ATC. The relationship between tacrine concentration and GQD fluorescence restoration is favourable, with higher tacrine concentrations resulting in more GQD fluorescence restoration [76].

These results support the characteristic fluorescent probe used in the MIP@C-dots composite and open the door to a cutting-edge method for assessing AChE activity [77]. It is straightforward to use an analytics system that, by scanning for AChE activity, can recognise Alzheimer's disease promptly.

According to the information that is currently available, having the APO e4 allele increases one's risk of getting Alzheimer's. Using a dual sensing technique and the probe curcumin (Cur)-GQDs (Cur-GQDs), the APO e4 allele was found [78].

The efficiency of the bioconjugated ITO as a sensor for APO e4 DNA and the method's huge potential for APO e4 DNA detection were shown by the amperometric signal [79].

Selectivity, long storage stability, reproducibility, and repeatability were some of this platform's increased analytical capabilities. Damage brought on by oxidative stress, such as AD and PD, is the main cause of NDs [80]. A lower detection limit was achieved by functionalizing quinolinate phosphoribosyl transferase (QPRTase) on N-doped CQD surfaces for the detection of QA at trace levels (3.22-41 M) [81]. N-doped CQDs were produced by heating urea and citric acid in the microwave and then mobilising them using QRPTase. The new technology's success in finding QA in human serum and aqueous solution led to the development of a straightforward analytical technique for disease detection [83,84].

GABA concentrations in cerebral fluid were shown to be lower in meningitis patients (0.11- 0.15 nM) than in healthy individuals (167-249 nM). To identify CDs that are appropriate for detecting GABA fluorescence, CDs have been researched. This process of hydrothermally producing CDs from juice of maize was employed[85]. The researchers used the GABase enzyme to start an electron transfer route from the enzyme to decrease NADPH. Numerous biofluids, including serum and cerebrospinal fluid, were successfully identified with the help of the described approach.

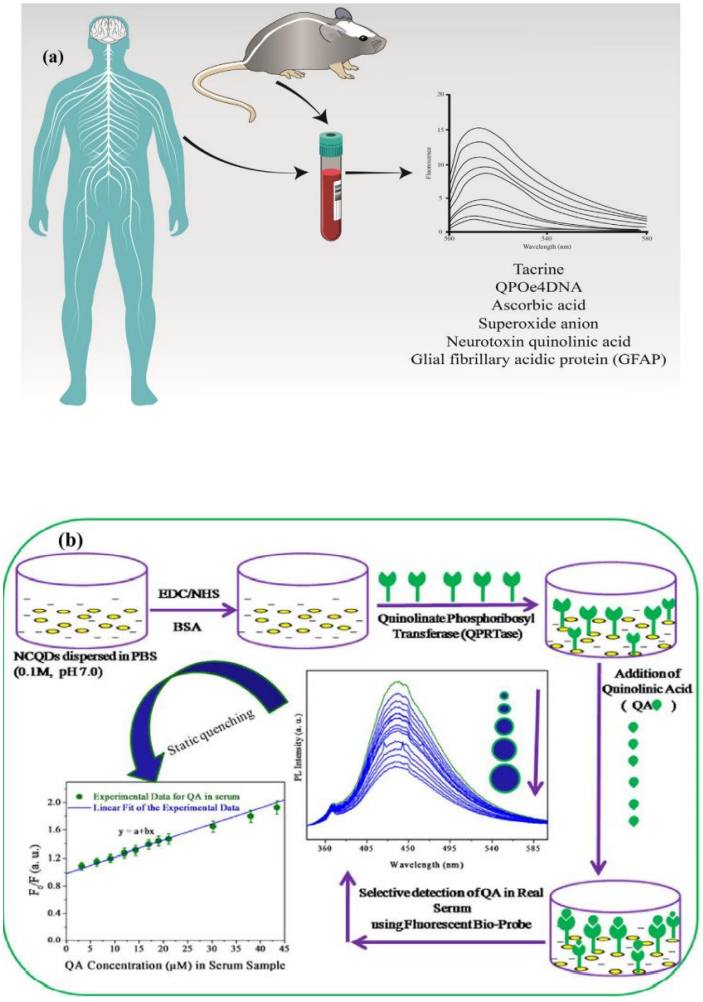

Figure 4. (A) CDs for the detection and assessment of several biomarkers in biofluids (B) Fluorescence spectrometric quality-assurance [81]

1.5 Carbon Dots and Its Theranostics Applications

Due to their improved signal-to-background ratio, photostability, and non-toxic makeup, hetero atom-doped CDs with organic ligands have become a new class of smart theranostic possibilities for cancer therapy.[87]. Based on the near-infrared (NIR) chemical absorption properties, imaging research was classified into two categories: NIR-I and NIR-II, with NIR-I being able to perform biomolecular or cell imaging[88,89]. Particularly NIR-II demonstrated remarkable good characteristics for in vivo imaging studies. In the NIR window-II, CDs have shown a great capacity for energy absorption, making it possible to conduct efficient in vivo and in vitro imaging tests[90]. The built-in GQDs showed a peak in their emission at 1000 nm, suggesting that they could be used as imaging probes in the near-infrared range. Additionally being researched as a potential therapy for brain tumours is N-BGQDs[91].

Multifunctional CDs are specifically needed enabling simultaneous imaging and focused delivery to tumour areas. This method has led to the development of multifunctional polymer-CDs containing an IL-6 fragment peptide (pCDPI) for successful BBB bridging and selective accumulation inside glioma tumour cells[92]. I6P8 conjugation was found to increase fluorescence intensity in the vicinity of glioma tumours, suggesting that it enhances the effect of targeting glioma tumours in vivo and permits long-term accumulation of CDs in glioma tumours with no change in fluorescence intensity [93].

Doxorubicin (DOX), which was released from the multipurpose polymer-CDs as a medicine delivery system, caused glioma cells to undergo dramatic apoptosis, demonstrating their great anti-tumor efficiency. While this is going on, IL-6 is thought to be an oncogenic agent that encourages tumour cell malignancy [94]. In order to prevent glioma cells from multiplying in response to IL-6, CDs were labelled with pCDPI and used as a carrier agent [95]. In cytotoxicity tests, the HCFCDs were discovered to be safe even at 1000 g/mL, proving their biocompatibility [96]. These results showed that the brightest imaging of glioma cells in vivo is possible with HCFCDs[97].

Additionally, a large amount of cell death is caused when HCFCDs are used as photothermal treatment candidates on cells that have been incubated with them.

It's important to note that current medicines aren't perfect for treating cancer. However, some tumour cells have been found to be resistant to apoptotic cell death, despite the fact that apoptotic induction has been shown to be helpful in the therapy of cancer. As a result, researchers have focused their attention on various biological routes for eliminating tumour cells. One promising method for treating cancer seems to be autophagy.

Autophagy is used by tumour cells to cause cell death, and certain medications have been developed with autophagy as a target. Therapy for cancer, especially for brain tumours, is interested in the use of CDs to modify autophagy. As a result, cancer cells' capacity for survival and reproduction was significantly diminished [98]. For the one-step hydrothermal synthesis of CDs, phytochemicals have been used as precursors [99]. Tr was applied on CDs to enable their entry into cancer cells, enabling tailored distribution. In the BBB, Tr receptors are highly prevalent. Recent research suggests that using CDs as potential agents can activate Tr receptors on brain tumour cells[100]. For example, carbon sources like gelatin and polyethylene glycol (PEG) were used to make blue emissive CDs. Fluorescence tests show that gelatin-based CDs have a lower QY than PEG-CDs.

The PEG-CDs are used to deliver methotrexate, a drug that lessens the effects of cancer treatment by preventing the formation of tumours [101].

These cytotoxic tests showed that brain tumour cell types were extremely sensitive to the two medications contained on Tr-functionalized CDs.

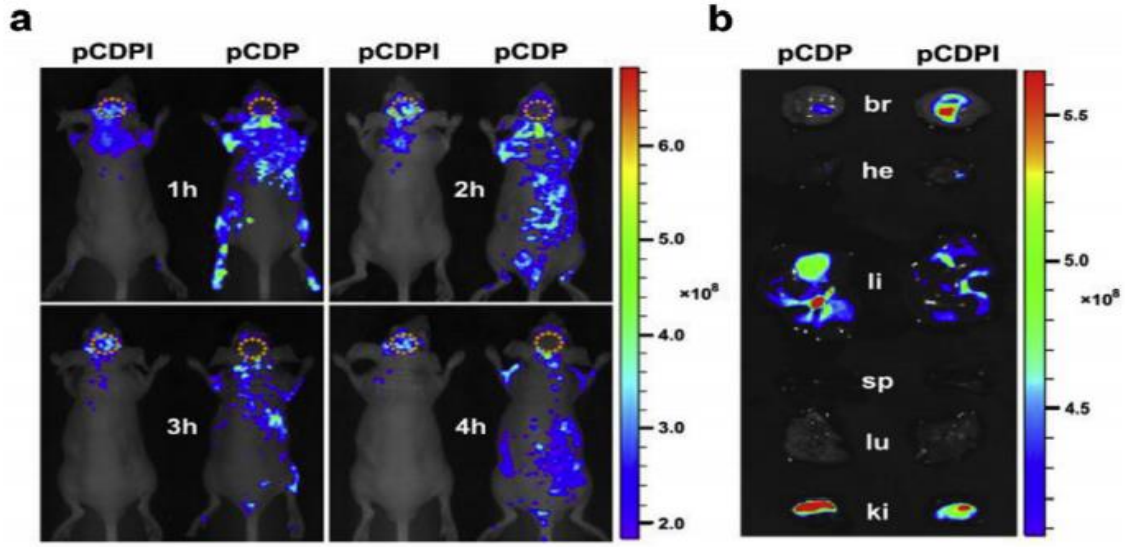

Figure 5. (a) In vivo investigations of pCDPI and pCDP at time intervals. (b) The ex-vivo examination of the retention of the major organs. [88]

1.6 Crossing Blood-Brain Barrier Carbon Dots

The BBB is thought to serve as a significant barrier between the brain and the blood molecules in circulation. This neighbourhood gateway protects the brain from the effects of circulating viruses or cells [102]. It is now recognised that BBB integrity is essential for brain defence and homeostasis. Astrocytes, smooth muscle cells, pericytes, microglia, and endothelial cells make up this barrier [2, 3]. Strong connections prevent tight junction transcellular transmission, keeping the cells' distance from one another. As a result, it is challenging to transfer therapeutic and diagnostic agents over the BBB and into the brain. [103]. Polymers, inorganic nanoparticles, and CDs are just a few of the nanomaterials that have been investigated as possible pharmaceuticals [39].

Today, it is understood that BBB integrity plays a crucial role in brain defence and homeostasis. Astrocytes, smooth muscle cells, pericytes, microglia, and endothelial cells make up this barrier [2, 3]. Tight junction transcellular transmission is decreased because strong connections keep cells close to one another. Therefore, it is difficult to deliver therapeutic and diagnostic substances across the BBB [103]. Numerous nanomaterials have been researched as potential medicinal agents, including polymers, inorganic nanoparticles, and CDs[39]. The brain, spinal cord, and cerebral spinal fluid make up the zebrafish central nervous system (CNS). Tr-CDs were then functionalized with green fluorescent protein to designate the neurons and introduced into zebrafish to confirm this[107]. The green fluorescence of green fluorescent neuron cells in the zebrafish CNS showed that Tr-CDs were successfully transported into the CNS by crossing the BBB. In a different experiment, the L-type amino acid transporter 1 was used to successfully transport CDs generated from tryptophan through the BBB (LAT1). To dope nitrogen atoms onto CDs, the authors utilised urea and 1,2-ethylenediamine (EDA) as supplementary chemicals[108]. When the CDs-EDA was present, the zebrafish vasculature and central canal of the spinal cord fluoresced blue, demonstrating that it could cross the BBB to interact with the CNS and reinforcing the requirement for tryptophan in this process[109,110]. Due to their likeness to brain tissue and their modest size (b5.0 nm), the CDs were able to pass across the BBB. It's crucial to keep in mind that CDs can detect BBB degeneration, making it simpler to focus fresh treatments[111,112]. After an ischemic stroke, the blocked channel is opened using a variety of treatment methods.

The BBB's integrity is compromised after thrombolysis and reperfusion, which could result in intracranial haemorrhage. CDs are used to assess bleeding risk and measure BBB degeneration in order to target. The CDs may potentially be used to deliver thrombolytic medications.[113,114]

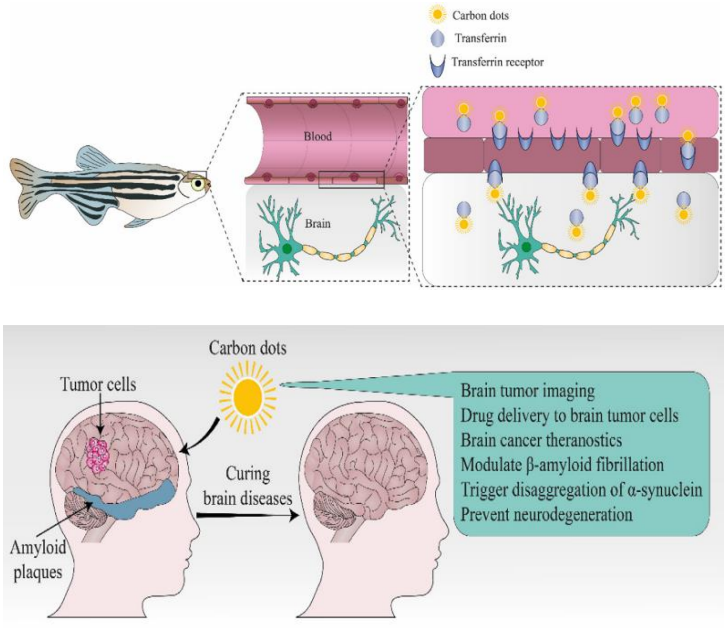

Figure 6. (a) The zebrafish central nervous system's capacity to respond to transferring CDs via the BBB. (b) A diagram showing how functionalized CDs are used to treat neurological illnesses.

1.7 Carbon Dots to Treat Neurodegenerative Diseases

The ability to distinguish between unhealthy high resolution and sensitivity tissues/cells and normal cells has been made possible in recent years by the introduction of a variety of NIR imaging probes for imaging varied cells. There is unmistakably a learning deficit and a decline in memory function in NDs [115]. As a result, there is significant amyloid-beta (A) accumulation and a rise in inflammatory cytokines. Therefore, concentrating on A and inflammation is a smart option if you want to prevent NDs. Inhibiting A accumulation while lowering pro-inflammatory cytokines, and tumour necrosis factor- (TNF-) have been shown to improve learning and memory function as well as dendritic spine in GQDs loaded with the neuroprotective peptide glycine-proline-glutamate[116,117]. It has been demonstrated that CDs are helpful in disaggregating hIAPP. According to the results of the trials, A may be a candidate for the aetiology of Alzheimer's disease[118,119]. When exposed to light, the bPEI-CDs were discovered to have a strong ability to adversely target A buildup and improved function. In CD cytotoxicity against A, the precursor in particular is crucial[119,120]. L-lysine is used as a precursor for the production of CDs because it has a larger inhibitory impact against A accumulation than D-lysine does. High membrane interaction in L-lysine-CDs leads to enhanced cytotoxicity. Synuclein (-syn) aggregates similarly to apolipoprotein (PD) in NDs, particularly Parkinson's disease [121].

This reduces the loss of -syn-mediated dopamine in neurons by reducing the abnormal transfer of -syn from neuron to neuron. High concentrations of Cu2+ ions can facilitate the aggregation of A, which causes oxidative damage to neurons and predisposes to a variety of NDs, most notably AD. It is thought that polymers with polyaromatic (phenylenediamine) functionalities found in N-doped CDs can couple with Cu-bound A complexes[122]. This conjugation inhibits the aggregation of A and the photooxygenation of A peptides. Along with A aggregation, the molecular routes of A synthesis can also be changed. BACE1 (-secretase 1) is a crucial enzyme in the synthesis of A from APP (amyloid precursor protein)[123,124]. The proposed CDs have shown a potent ability to prevent BACE1, which limits the production of A peptides and reduces A's fibrillation and toxicity. It has been found that using CDs as neurological agents can reduce the expression of A and APP, suggesting that CDs may be used as potential AD treatment options.

CONCLUSION

This study summarises recent developments in CDs for biomedical applications. The prospective applications of functionalized CDs in brain tumours, NDs, and theranostic therapy were carefully examined. Functionalized CDs were used as intelligent probes for the treatment of NDs, and CD-based systems efficiently crossed the BBB to enter the brain and circumvent BBB barriers.

As a result, CDs have a high degree of selectivity and effectiveness when targeting brain tumour cells for imaging and killing cancer cells for therapeutic purposes.

Additionally, due to their capacity to lower A aggregation, lower inflammatory cytokines and IAPP, lower ROS formation, and suppress synucleinopathy, CDs are helpful in the therapy of NDs. Particularly, CDs can be used as potential detectors for a range of neurochemically important substances.

Despite extensive study on the use of CDs in NDs diagnosis and the detection of CDs have the potential to be used in the clinical treatment of NDs, however this potential has not yet been thoroughly examined. Due to a number of issues, including expensive ligands for CD modification, insufficient mechanisms for CD-Research on CD-based medicine delivery to brain tumours via crossing BBB is still in progress, as is research on the impact of CDs on the CNS after crossing BBB. Therefore, more study is needed to demonstrate the validity and efficacy of using CDs to diagnose a variety of NDs. In order to speed up the process and increase the sensitivity of the device, CD surfaces were further functionalized with bioaffinity molecules as synthetic technologies advanced. These molecules allowed them to only interact with target DNA or biomarkers. To enhance CDs' optical and physicochemical characteristics, proteins or polymers were either added to them, or they were doped with metal ions or hetero atoms. Due to their improved water solubility and multicolor fluorescence, CDs are now feasible alternatives for bioimaging and in vivo imaging studies. With the development of synthetic methods, CD surfaces were further functionalized with bioaffinity molecules that allowed them to bind selectively with target DNA or biomarkers, speeding up the procedure and raising the instrument's sensitivity. CDs were either altered using proteins or polymers, or they were doped with metal ions or hetero atoms to enhance their optical and physicochemical capabilities.

Making CDs with up-conversion emission would therefore require a lot of care and potentially present fresh opportunities for biological applications. The development of CDs with reliable emission characteristics, which would make them acceptable for the thermal theranostics for cancer therapy and ND treatment, also requires further research.

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