CARBON QUANTUM DOTS IN NANOBIOTECHNOLOGY

A literature revive submitted in partial fulfilment of the requirements for the degree of Master of Science in Chemistry

BY

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CERTIFICATE

I certify that the literature review titled: “**CARBON QUANTUM DOTS IN NANOBIOTECHNOLOGY**” has been successfully completed under the guidance of Dr. Diptesh Naik during the year 2021 - 2022 in the partial fulfilment of the requirements for the degree of Master of Science in Chemistry.

Dr. Diptesh Naik
(project guide)

Dr. Vidhyadatta Verenkar
(Dean of SCS, Goa University)

DECLARATION

I declare that the literature review titled “**CARBON QUANTUM DOTS IN NANOBIOTECHNOLOGY”** has been carried out by me in the Chemistry Department, school of Chemical Sciences, Goa University. The information derived from the literature has been duly acknowledged in the text and a list of references is provided.

ACKNOWLEDGEMENT

The literature review titled **"CARBON QUANTUM DOTS IN NANOBIOTECHNOLOGY"** has been successfully completed under the guidance of Dr. Diptesh Naik during the year 2021 - 2022 in the partial fulfilment of the requirements for the degree of Master of Science in Chemistry.

I had a good learning experience in learning the importance and future prospects of undertaking a literature survey which was possible due to the timely guidance of Dr. Diptesh Naik and our respected Dean Dr. Vidhyadatta Verenkar. I also thank the entire library faculty for helping me out for searching relevant books with respect to my topic.

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INDEX

CARBON QUANTUM DOTS IN NANOBIOTECHNOLOGY

INTRODUCTION

Carbon quantum dots have been considered as a greener and more secure in biology and medicine. Carbon is normally considered as a black material and display brilliant fluorescence however are not toxic or cause harm to surrounding and is not very expensive to generate. Carbon quantum dots because of their size much less than 10 nm, attracts research interest which gave them advantages such as favourable biocompatibility, photobleaching, chemical inertness, good water solubility, facile modification and excellent permeability of cell membrane[1]. The major reason Carbon quantum dots have huge concerns is because of their sturdy Fluorescence and comparatively better solubility, consequently they are referred to as fluorescent carbon. Recently, improvement has been proposed in the properties, preparation and applications of carbon quantum dots.

The Two types of synthetic approaches are top-down method and bottom-up method have been used for the synthesis of Carbon Quantum Dots. In top-down process, the macromolecule is dispersed or destroyed into small-sized carbon quantum dots through physical or chemical methods. The bottom-up method refers to the polymerization and carbonization of a series of small molecules into carbon quantum dots by chemical reaction. The top-down method includes the arc discharge technique, laser ablation technique, and acidic oxidation method[2]. The bottom-up method includes the electrochemical technique, hydrothermal, microwave, pyrolysis and the template techniques.

The biological properties of Carbon quantum dots, which includes biocompatibility and low toxicity, cause them proficient for applications in biosensing, bioimaging and nanomedicine. Newly developed materials, promises wide application in the field of energy as photocatalyst, LEDs, rechargeable batteries, super capacitors due to their optical properties, low cost, large surface area, electronic conductivity and low toxicity. Also have applications in electrocatalysis such as oxygen reduction reaction, oxygen and hydrogen evolution reaction, etc.

ABSTRACT

Carbon quantum dots are the new members of the family of carbon of size less than 10 nm. It attracts much attention of researchers because of their distinctive characteristics like low cost, facile synthesis methods, excellent photoluminescence, easy surface modification, good water solubility and low toxicity. Because of their distinct properties they are used in photocatalytic reactions, in vitro and vivo bioimaging, drug or gene delivery and biological sensing. Mostly two types of techniques are possible in the literature for the synthesis of carbon quantum dots: top down method and bottom up method. Top down defined as breaking down a massive carbon structure into nanoscale particle. Bottom up defined as synthesis of carbon dots from smaller carbon units. In this, we have summarised the properties, synthesis, characterisation and applications based on the available literature.

LITERATURE REVIEW

In recent years, nanosize carbon quantum dots (CQDs) have received increasing attention due to their properties such as small size, fluorescence emission, chemical stability, water solubility, easy synthesis, and the possibility of functionalization. CQDs are fluorescent 0D carbon nanostructures with sizes below 10 nm. The fluorescence in CQDs originates from two sources, the fluorescence emission from bandgap transitions of conjugated p-domains and fluorescence from surface defects. The CQDs can emit fluorescence in the near-infrared (NIR) spectral region which makes them appropriate for biomedical applications. The fluorescence in these structures can be tuned with respect to the excitation wavelength. The CQDs have found applications in different areas such as biomedicine, photocatalysis, photosensors, solar energy conversion, light emitting diodes (LEDs), etc. The biomedical applications of CQDs include bioimaging, drug delivery, gene delivery, and cancer therapy. The fluorescent CQDs have low toxicity and other exceptional physicochemical properties in comparison to heavy metals semiconductor quantum dots (QDs) which make them superior candidates for biomedical applications. In this review, the synthesis routes and optical properties of the CQDs are clarified and recent advances in CQDs biomedical applications in bioimaging (in vivo and in vitro), applications in energy, application in electrocatalyst and drug/gene delivery are discussed.

OBJECTIVES

- Despite many research on Carbon Dots synthesis and its modifications, the real mechanism of Carbon Dots formation is not understood fully till date. Furthermore, simple and controllable surface modifications are still crucial problems, which may help for designing Carbon Dots with very good photoluminescence property and other applications with high efficiency.
- Although CDs based chemical and biosensing technology is well applicable in real life samples, but studies on several other toxic metal ions, like $As3+$, $Po3+$, $Cd2+$, $Mn2+$, etc. are still missing. So further research with metal ions should be done to understand the potential of Carbon Dots as a sensing agent.
- More efforts are needed to apply the Carbon Dots in the field of in vivo imaging, drug and gene delivery systems as well as cancer therapies to widen the area of its applications. Furthermore, dual drug-gene delivery systems are not fully explored to date.
- Although the types of carbon quantum dots tend to be diversified at present, compared with semiconductor quantum dots, the fluorescent quantum yield of each carbon quantum dots is still low and the explanation of its luminescent or fluorescent mechanism still needs in-depth study
- The complexity of the food matrix limits the specificity and sensitivity of the carbon quantum dots-based detection strategies to a certain extent; most of the established methods are aimed at a single target and there are few studies on the simultaneous detection of multiple targets in one sample.
- The study on the large-scale preparation and surface functionalization of carbon quantum dots and the constant exploration on the combination of carbon quantum dots with immunoassays, instrumental analysis, electrochemical sensing and other technologies are another direction of the research on carbon quantum dots. This is conducive to expand the application of related analysis strategies in foods.
- Finally, the use of carbon dots in the area of energy storage is needed to be explored. Therefore, researchers should concentrate on those above said

issues and Carbon Dots will gain significant interest in the future undoubtedly after proper addressing such problems.

CARBON QUANTUM DOTS STRUCTURE

Carbon quantum dots have high water-solubility, high luminescence, and biocompatibility, because of several carboxyl groups and their distinct structure[3]. Principally all nanoscale carbon materials are referred to as carbon dots, and minimum one of its dimension is below 10 nm. However in this class of nanostructured materials, carbon quantum dots have their three dimensions in less than 10 nm in size. They need a sp^2/ sp^3 structure with fluorescence emission as their inherent feature[4].

The carbon quantum dots surface are encircled by changed or various connected chemical groups. Example oxygen containing groups, nitrogen based amino groups, polymer chain etc,. They show completely different chemical structures and fluorescent properties because of their synthesis methods. Now, graphene quantum dots, a class of carbon quantum dots possess a very few or single graphene layers, whereas carbon nanodots are spherical/ round. However, carbon quantum dots are always distinguishable in their structure[5]

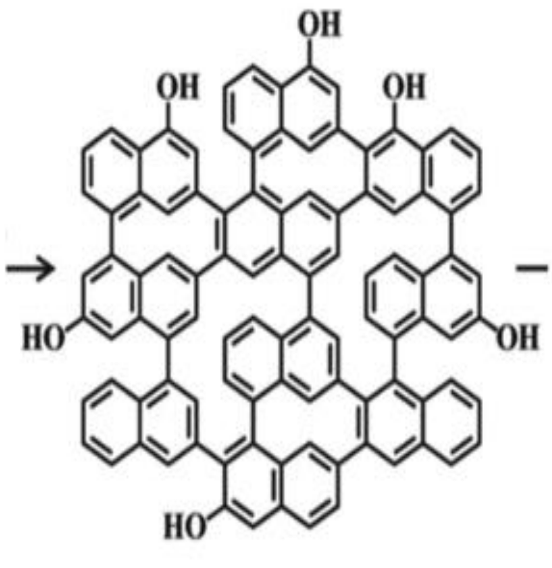


Fig 1 general chemical structure of carbon quantum dot

CARBON QUANTUM DOTS AND THEIR UNIQUE FEATURES

Carbon quantum dots are identified as newly discovered materials having unique properties. The carbon quantum dot surface includes numerous functional groups which include oxygen containing groups, polymer chain, amino groups, etc[6]. They have enormous impact on photoluminescence properties[7]. They have received excellent importance due to their enormous tunable optical properties, simplicity, low cost and much less toxic.

Carbon quantum dots exhibit short wavelength for photon harvesting caused by π–π* transition of C=C bonds and n-π* transition of the groups. Optical absorption become visible in ultraviolet region expanded to the visible region. The absorbance may be changed through different types of functionalization and surface passivating strategies. Lin et al. discovered synthesis of carbon quantum dots from poly (vinyl alcohol) and phenylenediamine. It expressed two bonds at 247 and 355 nm, displaying π–π* transition of C=C bonds and n-π* transition of C-N, C=N respectively[3,4].

Mostly carbon quantum dots are most successfully evaluated in surface passivation because of their ability for enhancing brightness due to quantum yield and much longer wavelength. Preparation of monochromatic fluorescent carbon dots and fluorescence mechanism is a vital research area for applicability of carbon dots.

PROPERTIES OF CARBON QUANTUM DOTS

ABSORBANCE

Carbon dots exhibits broad optical absorption maxima in the ultraviolet (UV) region (250 - 350 nm) together with weak absorption tail in the visible region of UV-Visible spectra. The absorption peaks appear at around ~240 nm are due to π-π∗ electronic transition of C=C bonds, and peaks at around ~340 nm are owed to n-π∗ transition from C=O bonds present as functionalities[8]. Surface engineering can modify corresponding absorption spectra of carbon dots that can alter their emission spectra also. Doping of heteroatom can also regulate absorption spectra for doped carbon dots by altering percentage of heteroatom because of their alteration in the π-π∗ energy level. Surface defects ingrained in carbon dots are considered to be responsible for broad spectral features in their absorption spectra[1,9]. Moreover, carbonyl and amino functionalities promote red shifts of band maxima in UV-Vis spectra due to the variations in HOMO - LUMO energy levels of CDs because of fictionalizations.

PHOTOLUMINESCENCE

Photoluminescence is one of the most fascinating features of Carbon Quantum Dots, both from the view of practical application and the fundamental research[10]. In general, one unique feature of the Photoluminescence for Carbon Quantum Dots is the distinct dependence of the emission wavelength and intensity. The reason for this unique phenomenon may be the optical selection of nanoparticles with different size or Carbon Quantum Dots with different emissive traps on the surface. The variation of particle size and Photoluminescence emission can be reflected from the broad and excitation-dependent Photoluminescence emission spectrum[11].Zhang et al. studied the emission behaviour of Carbon Quantum Dots under an irradiation at 470 nm wavelength with various concentrations. It was seen that the Photoluminescence strength of the Carbon Quantum Dots solution first increased and then it decreased as the concentration increased.

ELECTROLUMINESCENCE

The semiconductor nanocrystals are well known to display electroluminescence, there should be no surprise that Carbon Quantum Dots have inspired various interests for Electro chemical Luminescence studies which can be used in electrochemical fields[12] .Zhang et al. (2013) reported a Carbon Quantum Dots- based light- emitting diodes (LED) device, in which the emission colour can be controlled by the driving current. Colour - switchable ECL from the same Carbon Quantum Dots ranging from blue to white was seen under different working voltages. In order to understand the luminescence mechanism of Carbon Quantum Dots, the researchers proposed two models based on the band gap emission of the conjugated p domain and the edge effect caused by another surface defect[13]. The Photoluminescence characteristics of the fluorescence emission of Carbon Quantum Dots from the conjugated p domain are derived from the quantum confinement effect of p-conjugated electrons in the sp^2 atomic framework and can be adjusted by their edge configuration, size, and shape. Fluorescence emission of Carbon Quantum Dots with the surface defects results from sp^2 and sp^3 hybridized carbon and other surface defects of Carbon Quantum Dots, and even fluorescence intensity and peak position are related to this defect[14].

CHEMILUMINESCENCE

The Properties of Chemiluminescence of Carbon Quantum Dots were discovered when the Carbon Quantum Dots coexisted with some oxidants, such as potassium permanganate (KMnO4) and cerium (IV)[15]. The electron paramagnetic resonance announce that oxidants, such as $KMnO_4$ and cerium (IV), can inject holes into the Carbon Quantum Dots. This process increases the population of the holes in the Carbon Quantum Dots and increases the electron-hole annihilation, resulting in energy release in the form of Chemiluminescence emission. Moreover, the Chemiluminescence intensity was depends on the concentration of the Carbon Quantum Dots in a certain range. It was found that increasing the temperature had a positive effect on the Chemiluminescence because of the thermal equilibrium of electron distribution in the Carbon Quantum Dots. It is interesting to know that the Chemiluminescence properties can be designed by changing their surface groups[16].

CARBON QUANTUM DOT SYNTHESIS

A huge quantity of techniques have been developed. Mostly they are grouped into two groups that is top-down and bottom- up process. In top-down process, the macromolecule is dispersed or destroyed into small-sized carbon quantum dots through physical or chemical methods. The bottom-up method refers to the polymerization and carbonization of a series of small molecules into carbon quantum dots by chemical reaction.

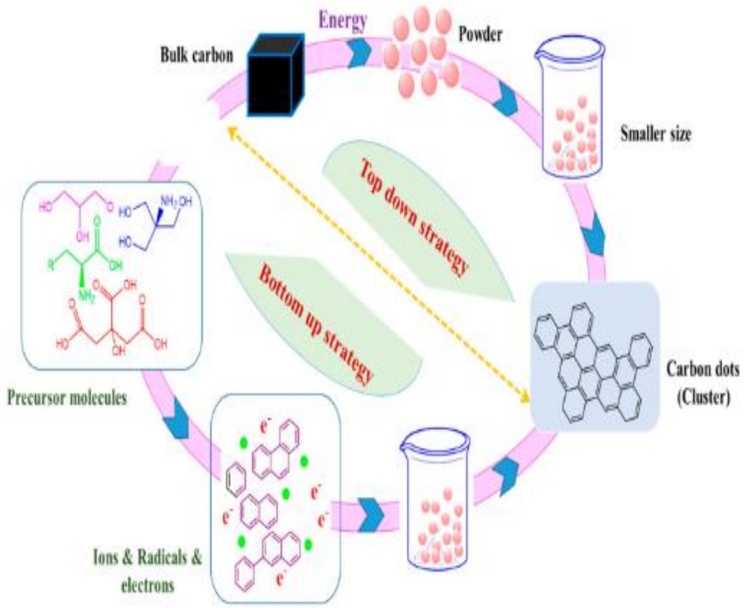
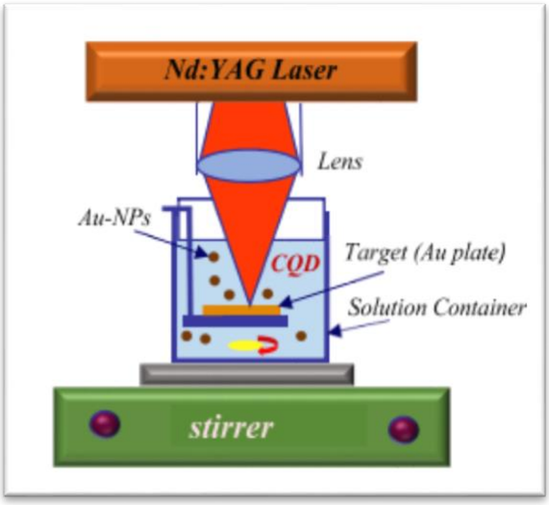


Figure 2. Generation of carbon dots by well-known Top-down and bottom-up approaches.

1. LASER ABLATION METHOD

Laser ablation is a method used for the synthesis of carbon quantum dots. Yu et al. prepared carbon dots via laser irradiation technique using toluene as the carbon source. By using laser furnace they controlled the size of carbon quantum dots[17]. Nguyen et al. reported the synthesis of carbon quantum dots from graphite powders via femtosecond laser ablation. They noticed that the size of carbon quantum dots and photoluminescence properties easily can be controlled by changes in the parameters including irradiation time, spot size, and laser influence. By increasing the radiation time smaller size carbon dots can be synthesized[18].



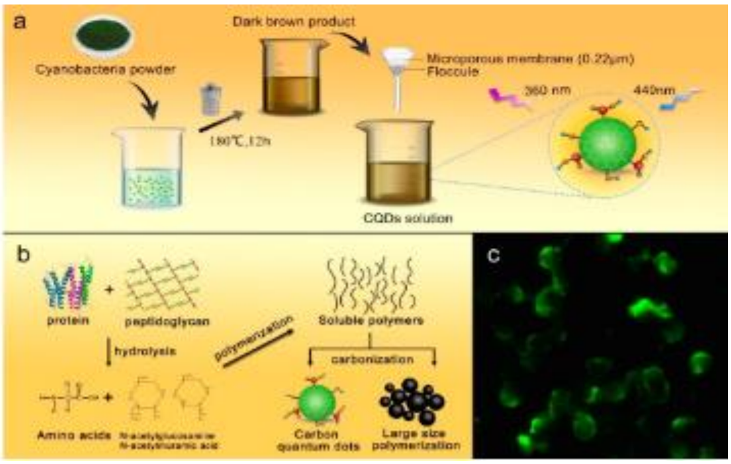
For the preparation of Au-NPs in carbon quantum dot solution, which involved the use of Q-switch Nd:YAG laser at 1064 nm wavelength. The laser beam in the 800 ml and 40 Hz repetition rate frequency was ablated. The ablation time was 4, 8, 12 and 16 minutes. The prepared samples were characterized in the solution form using UV-visible spectroscopy and FTIR. The shape was investigated using transmission electron microscopy[19].

2. ACIDIC OXIDATION

To exfoliate and decompose bulk carbon into nanoparticles and simultaneous introduction of hydrophilic groups, e.g., hydroxyl group or carboxyl group on the surface to obtain carbon quantum dots this method has been used[20], which can improve the water solubility and fluorescence characteristics. Firstly, carbon nanoparticles was oxidized by a mixture solution of HNO_3, H_2SO_4, and $NaClO_3$ from Chinese ink. Then the oxidized carbon quantum dots were hydrothermally reacted with dimethylformamide, sodium hydrosulfide, and sodium selenide as nitrogen source, sulfur source and selenium source, separately. The obtained N-CQDs, S- CQDs, and Se-CQDs exhibited tunable photoluminescence performance, higher quantum yield, and longer fluorescence lifetime than the pure carbon quantum dots[21]. The active heteroatoms on the surface of carbon quantum dots adjusts the electronic structure of the carbon quantum dots and therefore would enable good electrocatalytic activity when used as electrocatalysts[22].

3. HYDROTHERMAL/SOLVOTHERMAL TREATMENT

The hydrothermal/solvothermal reaction is a chemical reaction between the precursors in a solvent environment inside a closed system of high boiling point and under high pressure condition. Hydrothermal carbonization or solvent carbonization is an environmentally friendly, inexpensive, and non-toxic way to produce new carbon-based nanomaterials[23]. A high precision pre-formulation solution is reacted in a hydrothermal reactor[2]. HTC-made carbon quantum dots have been produced by many precursors including, glucose, chitosan, banana juice, citric acid, diammonium hydrogen citrate and proteins. By mixing different amounts of carbohydrates within octadecylamine and octadecene for 30 minutes at temperatures between 70 and 300˚C hydrophobic carbon quantum dots were prepared[24]. Whereas the hydrophilic ones were formed in a wide range of pH by heating a carbohydrate solution.



4. ELECTROCHEMISTRY METHOD

The electrochemical method is a simple and a convenient preparation technique, it can be carried out under normal temperature and pressure conditions[25,26]. In 2015, Hou et al. prepared a blue-emission carbon quantum dot with a particle size of 2.4 nm by electrochemical carbonization of sodium citrate and urea in deionized water, which can be utilized as a highly sensitive detector in waste water for Hg^{2+}. In electrochemical studies, cyclic voltammetry technique (CV), BAS 100 W electrochemical analyzer was utilized. In all experiments, glassy carbon electrodes as working electrodes were used. The platinum wire electrode as an auxiliary electrode and Ag/AgCl electrode as a counter electrode were also used. Little quantity of aluminum oxide (Al2O3) dust was transferred on a polishing cloth particularly made for this electrode and it was soaked with distilled water. The electrode surface in a circular way was polished[27]. After the pre-treatment, the polished electrode was washed with deionized water and then dried and placed in to the glass cell. The platinum wire auxiliary electrode and the Ag/AgCl reference electrode from the experiment cell were removed, washed with distilled water, dried with drying paper, and placed in the experiment cell. All the measurements were achieved at room temperature. 0.1 M phosphate buffer solution at pH 7.4 was used as a supporting electrolyte. The amount of sample in the electrochemical cell was arranged by completing the final volume buffer solution to 10 mL to contain 1 mL of this colloid carbon dot solution[28]

5. THERMAL DECOMPOSITION

In thermal decomposition, a substance or compound decomposes chemically by the heat action. This types of reactions are normally endothermic. The decomposition reactions may be either irreversible (decomposition of starch, proteins) or reversible (decomposition of ammonium chloride, limestone). This method has different advantages, like less time consuming, easy to operate, low cost, and large scale production[29]. Wang et al. synthesized luminescent carbon dots by the thermal decomposition using citric acid as the carbon source and organosilane, N-(amino ethyl)-γ-aminopropyl methyl dimethoxy silane as the passivation agent. They heated the mixture at 240°C for 1 min, and its diameter was ~ 0.9 nm[30]. Afterwards Wang et al. synthesized carbon dots from citric acid using this method. On a hot plate, they heated citric acid at 200°C for 30 min; neutralized with sodium hydroxide, and then it was dialyzed for purification. The size of carbon dots was within the range of 0.7 to 1 nm size [31]. These shows excitation, dependent as well as independent photoluminescent properties, with different quantum yield having different synthesis conditions. Wan et al. used the thermal decomposition of 1-butyl 3-methyl imidazolium bromide and l-cysteine for the synthesis of carbon dots at 240°C.

6. CARBONIZATION SYNTHESIS

The precursor molecule for carbonisation is of low cost, very fast and simple one step method to fabricate carbon quantum dots. Carbonization is a chemical process I n which solid residues with higher content of carbon are formed from organic materials by prolonged pyrolysis in an inert atmosphere. Wei et al[32]. Synthesized N doped carbon dots using ultrafast carbonisation within 2 minutes using glucose as a source of carbon and ethylenediamine as source of nitrogen. Their size was from 1 - 7 nm having quantum yield of 48%. Wang et al. produced blue luminescent thermally reduced carbon dots having 4.8 to 9 nm size using citric acid carbonization. By using thermogravimetric analyser, it resulted in 5 times increment of quantum yield when compared with non - reduced carbon dots. Dolai et al. synthesized carbon dots having aerogel matrix using 6-O-(O-O-dilauroyl-tartaryl) - d-glucose as the carbon source. The diameter observed as approx. 2.4nm.

7. ARC DISCHARGE

Arc discharge is a technique to reorganize the carbon atoms decomposed from the bulk carbon precursors in the anodic electrode by the gas plasma generated in a sealed reactor. The temperature of the reactor can go upto 4,000 Kunder electric current in order to produce a very high energy plasma[33]. Xu et al. formed three types of carbon nanoparticles having different molecular mass and fluorescence property accidently during the preparation of single walled carbon nanotubes by this method[17]. They emitted blue - green, yellow and orange fluorescence at 365 nm range. Further he said that the surface of carbon quantum dots was attached with hydrophilic carbonyl group. The carbon dots formed have good water solubility. They also possess a large particle size. It decrease the specific surface area of carbon dots[34], which can limit the reaction sites during the electrocatalytic process.

8. TEMPLATE METHOD

This method includes two stages. Developing carbon dots by calcination in the mesoporous Si templates and etching to erase supports and create carbon dots of nanosized. Zong et al. obtained a technique for use of mesoporous spheres of Si as hard templates. They were saturated with a solution of citric acid and complex salts. These were calcinated and expelled[35]. It concluded interesting luminescence properties by the photostability of carbon dots with mono dispersed material.

Yang et al. found a method to develop morphological photoluminescence carbon dots using hard template method. Soft template - copolymer pluronic P123 was used and mesoporous silica as hard template, other organic molecule as diamine benzene, 1, 3, 5-trimethylbenzene as source of carbon. After removal of template, passivation and carbonization the carbon dots obtained had tunable sizes, composition[36]. Crystalline degree had in addition up conversion, high stability property and effective. The formation of aggregate was eliminated completely through soft - hard template method. And it formed carbon dots with a narrow distribution size due to size confinement[37].

Lai et al. generated carbon dots of mesoporous silica, it served as a nanoreactor to control the size distribution. Firstly he formed mesoporous silica nanoparticles, they were blended with PEG-NH_2 and glycerol. It was then heated to 30 minutes at 230°C and finally extraction of crude was obtained through centrifugation to form carbon dots. Also capping PEG onto the surface of $mSi0_2$[38]. The carbon dots formed have additional improvement in quantum yield, biocompatibility and colloidal stability. In the synthetic process, it was expected that the corrosive acid or base to etch the template as the formation of mesoporous silica was difficult. This method was expensive and time consuming. Also hard to etch completely because of high temperature pyrolysis. And process of separation and purification was difficult[39]. The quantum yield was very less.

METHOD	PROCEDURE	ADVANTAGES	DISADVANTAGES
Arc discharge method (top-down)[18]	Two graphite rods are used as anode and cathode electrodes in an open vessel, respectively, with a voltage produced in between the two.	This technique produces MWCNTs, where in theory may be broken down to form carbon quantum dots.	Nanotube soot show impurities. The sheets in the soot have a greater oxidative stability than the nanotubes.
Microwave pyrolysis (bottom-up)[40,41]	Combining a carbon containing source and a saccharide in water to give a transparent solution in an inert environment, then heated in a microwave oven.	A steady synthesis route, excellent commercialization, easy and environmentally friendly technique.	The highest quantum yield reported is 34%, lower than those of other methods noted with in the table.
Laser ablation (top-down)[42]	Toluene is used because the carbon source through laser irradiation technique. The size of carbon quantum dots is controlled by laser furnace.	The size/ photoluminescence properties of the carbon quantum dots can be easily managed by changing the parameters which include irradiation time.	This is not a greener method, a low yield of carbon quantum dots is generated from 4–10%. Low quantum yield, poor control over sizes, modification is needed. The closely doped heteroatoms can have an effect on the PL properties because of the electronegativity of N, S, and Se losses.

Acidic oxidation (top-down)[42]	Carbon nanoparticles are oxidised from mixing solution of HNO_3, H_2SO_4 and $NaClO_3$, then hydrothermally reacted with DMF, NaHS and NaHSe.	The generated carbon quantum dots show tuneable PL performance, excess quantum yield and longer fluorescence lifetime than others.	The closely doped heteroatoms have an effect on the PL properties because the electronegativity of N, S, and Se.
Hydrothermal /solvothermal (bottom-up)[43]	Small organic molecules/ polymers are dissolved in water/ organic solvent then transferred to a Teflon coated stainless- steel autoclave at excessive temperature to shape CQDs.	Quantum yield of the carbon quantum dots can attain 80%, facile synthetic process, green method, many carbon sources can be used.	Low quantum yield. Loss through the reactor wall can occur; gas is a side product. Poor control over size.
Plasma induced pyrolysis (bottom-up)[44]	A negative electrode and a platinum disc are connected to a negative power supply to ignite and sustain the plasma. The CQDs are generated from here	The amphiphilicity of the CQDs make them dispersible in water/most organic solvents. This method can be used to produce CQDs from a wide range of carbon sources	Losses to the reactor walls in the form of tar as well as gas leakage to the atmosphere as this uses higher temperatures than conventional pyrolysis

Combustion/thermal routes (bottom-up)	Combustion of a carbon source followed by functionalization with carboxyl groups through conjugation of acetic acid moieties under a high temperature	The obtained CQDs possess a uniform particle size and rich carboxyl groups on the surface. Facile, ease of scale-up production	Small polycyclic aromatic hydrocarbons (PAHs) are generated in soot formation; an environmental hazard
Template method (bottom-up)[38]		Carbon dots have biocompatibility and colloidal stability	Time-consuming and expensive method, have limited quantum yield

CHARACTERIZATION OF CARBON QUANTUM DOTS

To provide information about the synthetic properties of carbon dots, some of the techniques are used to characterise carbon dots, for example, nuclear magnetic resonance (NMR), X-ray diffraction (XRD), transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR) and ultraviolet (UV) spectroscopy.

NMR

An NMR is typically used for structural information of carbon quantum dots. Hybrid types of carbon atoms within the crystalline network and the binding mode among the carbon atoms is decided by NMR. Tian et al[45] used natural gas burning sediment as a carbon supply and carried out the refluxing with nitric acid, which resulted in the development of carbon dots. Aromatic (sp^2)

carbons display resonance in the region extending from 90- 180 ppm and aliphatic (sp^3) carbons in the region extending from 8- 80 ppm, structural determination of carbon dots is determined with the help of NMR measurements by distinguishing sp^3 carbons from sp^2. In the absence of aliphatic carbons, indicated by a carbon 13 (13C) NMR range, which depicted the absence of a single peak below 120 ppm[45]. Within the region extending from 120- 150 ppm, a chain of peaks appeared and maximum of those peaks emerged from aromatic carbons. 13C NMR spectroscopic estimations affirmed that the carbon dots had evolved from sp^2 carbons[44].

XRD

XRD is used in the characterization of carbon quantum dots and to attain information of phase purity, particle size, and crystal structure. In addition, it determines the crystalline phases of carbon quantum dots. Liu et al. through the use of hexaperihexabenzocoronene as the precursor used for the synthesis of carbon quantum dots. Carbon dots of size ~60 nm in breadth and 2- 3 nm thickness have been produced, at high temperature after pyrolysis, reduction treatment, surface functionalization and oxidative peeling. They possessed a fluorescence quality yield of 3.8 %. Mao et al.[46] developed photoluminescent carbon dots with glycerol through a one stage pyrolysis of poly (acrylic acid). The XRD validated an extensive peak close to $2\theta=24°$, forming white fluorescent carbon dots graphite structure[47,48] Bourlinos et al. synthesized carbon dots through calcination of ammonium citrate salt at 300 °C; the relating XRD confirmed two reflections that were superimposed, which showed the presence of tremendous carbon alkyl groups that were surface modified.

FTIR

FTIR used to determine the functional groups present on the surface of carbon dots. FTIR spectra were seen in transmission mode within the range of 4000-400 cm^{-1} using a spectrometer Perkin-Elmer Spectrum 100. The dry samples in caesium iodide cells had been analysed[49]. In the spectra, peaks at 1244, 1637 and 1603 cm^{-1} for stretching frequency of C-O, C=C and C=O are seen. Broad band for OH and NH from 2800-3600 cm^{-1} and 2950 and 1122 cm^{-1} for CH and NH bonds group, respectively[10].

TEM

TEM have been used to get the structures of compounds since it possesses a higher resolution of 0.1 - 0.2 nm. It has a large advantage in pharmaceuticals, material science, development departments and other researches. The morphology of the particle are studied, in order to understand about their shape, size and dispersion. In order to determine thin structures high resolution TEM used.

Their crystalline nature of carbon dots can be categorised into two types of lattice fringes that is interlayer spacing and in-plane lattice spacing, respectively[50]. Interlayer spacing mainly focussed around 0.34 nm, whereas in-plane around 0.24 nm. In the oxidation of graphite to synthesize carbon dots, their lattice spacing was less than 0.3 nm, showing that their large portion of carbon dots are separated graphenes.

UV SPECTROSCOPY

In the carbonation of citrus acid to produce photoluminescent carbon dots at around 200^{o} C. the carbon dot are nanosheets of thickness 0.5 - 2 nm and ~15 nm in width, demonstrate UV absorption at 362 nm range. The nanoparticles are consistent in size, this showed by their narrow peak width. Tang et al. did pyrolysis of glucose solution with the help of microwave to prepare carbon dots. The diameter obtained was 1.65 nm with fluorescence quantum yield of 7 -10 %[44]. Two UV absorption peaks at 228, 282 nm showed by the aqueous solution. Intensity of both the peaks was increased by increasing the microwave heating time. But their position remained unaltered.

APPLICATIONS OF CARBON QUANTUM DOTS

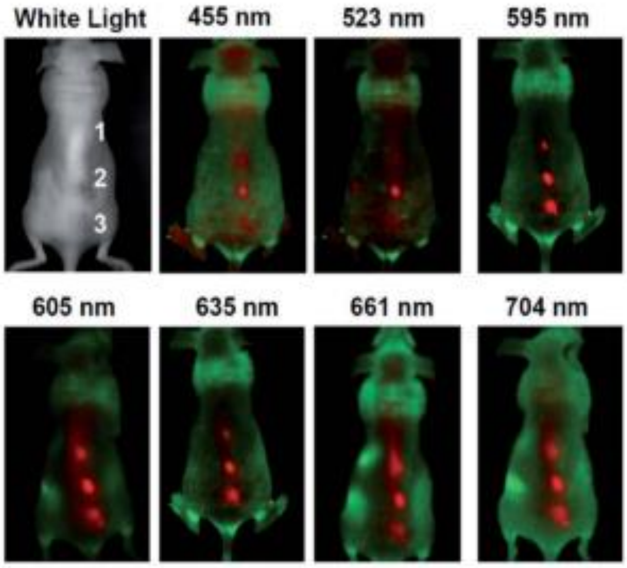
1. BIOMEDICAL APPLICATIONS

Most promising and repeatedly reported application of carbon dots is in biomedicine. Vivo methods indicate that carbon dots rapidly excreted by kidney or hepatobiliary system. Since no symptoms are seen in heart, lungs, liver, brain, spleen, kidney, testicles and bladder in rats by haematological analysis therefore carbon dots are safer for biomedical applications. Biomedical applications includes:

BIO-IMAGING

Carbon quantum dots performs important function in biomedical applications. Bio-imaging is described as the process in which images of living organisms are produced with the help of techniques such as magnetic resonance imaging, X-rays and ultrasound. Also to determine 2-D structural information. Due of their properties like biocompatibility, low toxicity, and strong photoluminescence, they are advantageous in the visualization of biologic structures both in vivo and in vitro[21]. Carbon quantum dots are nontoxic, since it is a passivating agent and is particularly responsible for the cytotoxicity. Surface passivating agents having low toxicity can be utilized in vivo imaging at higher concentrations. When mice were injected with doses of carbon quantum dots and NaCl control, all physiologic signs were at the same levels. Therefore at numerous levels, they suggest non-toxicity at periods beyond the once that are used for in vivo imaging studies[51].

It was shown that the carbon quantum dots used as a fluorescence contrast agent in mice. An aqueous solution of PEGylated carbon quantum dots was injected into mice at numerous excitation wavelengths and fluorescence images were obtained[14]. A noticeable contrast was observed for imaging in both green and red emissions. Another property is multimodal bioimaging, which can be described as the combination of optical imaging and MRI modalities. MRI demonstrates high spatial resolution and the potential to obtain anatomic and physiologic records. On the other hand, rapid screening was determined by optical imaging[44].



BIOSENSORS

Carbon dots are used as biosensor carriers for flexibility in surface modification, high water solubility, nontoxic, excellent biocompatibility, high photostability and good cell permeability.

It can be used for visual sensing of glucose, phosphate, iron, pH, cellular copper and nucleic acid. Carbon dots used as an effective fluorescent sensing stage for detection of nucleic acid with single base mismatch[29]. The concept was based on adsorption of fluorescent marked single stranded DNA probe by carbon dots. Which is followed by substantial fluorescence quenching. Followed by hybridisation with its target to produce double standard DNA. This resulted in desorption of the hybridised double stranded DNA from the carbon dot structure[52].

NANOMEDICINE

Being carriers, carbon dots display therapeutic performances such as anticancer activity, antibacterial activity, antioxidant and antiviral activity. Usually drug molecules (e.g., gentamicin sulfate, metronidazole, glycyrrhizic acid) as precursors, the prepared CPDs include similar or superior therapeutic performances. When compared with drug molecules, these drug- CPDs have higher water solubility and biocompatibility additionally more potent fluorescence and may be used as green bioimaging probes for theranostics activity[53]. If compared with metronidazole, Met-CPDs has higher water solubility and excellent biocompatibility because of the formation of new functional groups like carbonyl, hydroxyl, and amino groups. Biological experimental data demonstrated the Met-CPDs, confirmed excellent selective antibacterial activity against obligate anaerobes due to presence of nitro group, a pharmacophore, in accordance with the principle mode of action of metronidazole. However, further studies are needed to clearly identify the exact molecular mechanism of the drug CPDs in the antibacterial, anticancer, antiviral activities[54].

DRUG/GENE DELIVERY

Aside from anticancer phototherapies, carbon dots can combine imaging tools with genes or drugs to form imaging guided nanohybrids for improving the delivery efficiency or offering benefits in the therapeutic strategy[55]. Drug delivery is the safe and efficient treatment, which carries the medicine to a specific location in the body and releasing it in a sustained manner. Thus, the controlled drug release and robust selectivity in drug delivery systems are crucial for increasing local therapeutic effects and reducing side effects of non-infectious and/or non-cancerous tissue. Carbon dots have advantages to visualize drug accumulation and activities at pathological sites with their fluorescent properties, which are vital for estimating therapeutic efficacies of medicines[56].

Through tracking the green emission from folic acid-modified CPDs (FA-CPDs) combined with chloroquine, Fan et al. realized the real-time imaging/monitoring of tumor therapy. To improve tumor specific imaging and drug delivery performance, Zhou and co-workers designed deep red emissive carbon quantum dots with multiple paired α- carboxyl and amino groups, which will target tumors including glioma due to their multivalent interactions with large neutral amino acid transporter. Thus, loaded with topotecan hydrochloride, the carbon quantum dots could be used for fluorescence/PA imaging and the treatment of brain cancer, showing potential clinical applications in imaging and drug delivery diseases of the central nervous system[57].

Effective vectors in gene therapy can deliver genetic materials into cells, and possess high gene transfection efficiency. Viral vectors with the natural ability to invade and deliver their genetic material have served as effective gene carriers. However, severe safety risks based upon their immunogenicity and their oncogenic potential have kept them far from safe for clinical use. Carbon dots possess abundant functional groups, low toxicity and excellent biocompatibility[58]. The small size of carbon dots contributes to adequate cellular uptake of vectors, enhancing gene transfection efficiency.

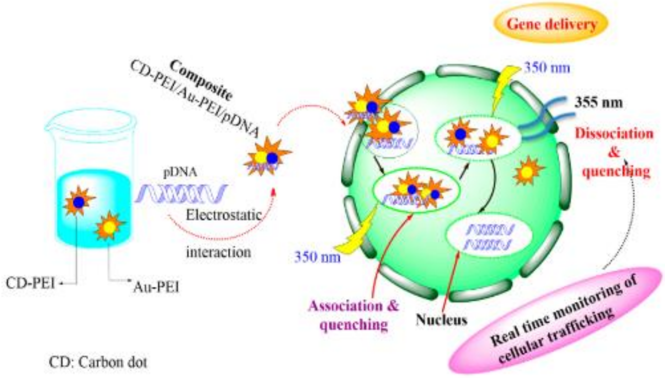


Figure 11. Schematic chart of gene delivery of CQDs.

2. ENERGY APPLICATIONS

Economic growth and industrial development caused fast consumption of energy shortage, fossil fuel, climatic condition and environment degradation. Due to this renewable, stable, efficient, eco-friendly and storage techniques are important[59]. Carbon dots are newly developed materials, which promise wide application in the field of energy as photocatalyst, LEDs, fuel cells, rechargeable batteries, super capacitors due to their optical properties, low cost, large surface area, electronic conductivity and low toxicity.

PHOTOCATALYST

Carbon quantum can absorb light and are used for different photocatalytic action. To generate H_2 fuel from water from carbon dot based photocatalyst are the current discussion. Sun et al. reported photodecomposition of Co_2 by the use of doped carbon dots with gold. Liu et al. received environment friendly and low cost CDs- C_3N_4 composite catalyst which formed H_2 by splitting of H_2O[52]. PEG_{1500N} functionalization carbon dots has capability to transform active components coated with gold of Co_2, greenhouse gas or acetic acids. Numerous poisonous chemicals can be better transformed to less toxic once through CD based photocatalyst. Lie et al. obtained oxidation of benzyl alcohol to benzaldehyde with very excessive conversion rate of 192% and 100% selectivity[9].

SOLAR CELLS

Carbon dots are studied extensively in solar cells. A small amount is added to a bulk heterojunction to improve the efficiency in different works their distinct optical properties, high electron mobility and abundant functional groups (amino, carbonyl, hydroxyl)[60].

The roles of carbon dots in solar cell are

- Separation of photogenerated e^- - hole pairs, carrier recombination suppressing
- To broaden light absorption range
- To improve environmental stability

SUPERCAPACITORS

They show fast charging and discharging rates, long life cycle and high power density. But inferior energy density limits their practical applications in storage of energy. Carbon dots mixed with other carbon material, metal oxide or polymer are reported for the improvement of electrochemical performance[61]. Kaner et al. converted N and O co - doped CPDs to open pore 3D graphene networks to form supercapacitors.

3. ELECTROCATALYSIS APPLICATIONS

Carbon materials have gained numerous interest in the field energy conservation and storage. The functional group (OH, COOH, NH_{2}) present on surface of carbon dots act as active coordination site with transition metal ions[62].Carbon quantum dots hybridised with other inorganic compounds like metal sulphides, metal phosphides, etc. can be used as important electrocatalysts for oxygen reduction reaction, oxygen evolution reaction, hydrogen evolution reaction, etc.

OXYGEN REDUCTION REACTION

Oxygen reduction reaction, as a main route for metal - air batteries and fuel cells attracted much importance in recent years. The rich functional groups in nitrogen and oxygen make them stable in water and other organic polar solvents. Jin et al[63]. obtained a novel based on carbon ORR catalysts by hybridising graphene quantum dots with graphene nanoribbons by in situ reaction. It exhibited excellent performance and high durability in alkaline conditions[64].

OXYGEN EVOLUTION REACTION

It was found that CoP/ CQDs exhibits better OER performances with an overpotential of about 400 mV in alkaline electroytes. Their enhanced activity due to the abundance of functional groups, good conductivity, rapid transfer of electrons and small size. Tang et al. concluded a CQD nanocomposite catalyst by coprecipitation process[65]. Followed by a solvothermal treatment. The obtained CQDs showed excellent OER electrochemical activity having low potential ~25 mV at 10 mA cm^{-2} and has better durability in 1M KOH[66].

ADDVANTAGES OF CARBON QUANTUM DOTS

- They are inexpensive: carbon quantum dots are not expensive and are abundant.

- Photostability: Composition and stability of carbon quantum dots leads to larger photostability when they are compared with traditional quantum dots and dyes.

- Wider excitation and narrower emission: they have a sharp emission peak and much wider excitation spectra than the organic dyes and other cadmium quantum dots[67].

- Biological properties: the biologic properties of carbon dots for example chemical stability, good biocompatibility and low toxicity secure their application in biosensors, bioimaging and drug delivery.

- Luminescent property: it has greater luminescent than other quantum dots.

- Aqueous stability: have high aqueous stability as compared to other quantum dots and organic dyes.

- Electronic properties: very good properties of carbon quantum dots as e^- donors and acceptors that cause the electrochemical luminescence and chemiluminescent, and contain broad potential in optronics, sensors and catalyst[68].

- Chemical inertness: the chemical stability of carbon dots is high when compared with others.

CONCLUSION

We have portrayed the progress in the field of carbon quantum dots, focussing on its structure, their properties, synthetic methods, characterization and their applications in different fields. Carbon quantum dots have core shell structure in which they are either sp^2 (crystalline) or sp^3 /sp^2 (amorphous). Carbon dots structure consisting of functional groups like oxygen, amino, polymer chains etc. The absorbance and photoluminescence properties of carbon quantum dots are both interesting and intriguing, as becoming an active and hot research topic[20].

The Two types of synthetic approaches are top-down method and bottom-up method have been used for the synthesis of Carbon Quantum Dots. The top-down method includes the arc discharge technique, laser ablation technique, and acidic oxidation method[2]. The bottom-up method includes the electrochemical technique, hydrothermal, microwave and the template techniques. Among the synthesis methods, the bottom down method is of low cost and eco-friendly and the top down method is expensive one. Many studies have shown the carbon dots versatility in biomedicine: (i) multimodal bioimaging for its flexibility in surface modification to combine other imaging agents for its high biocompatibility,

(ii) Biosensors for its multi stimulus responses,

(iii) Delivery carrier for its various combination with biomolecules or drugs via multi reaction and stimulus responses.

With the development of advanced technology and characterizations, we believe that controllable synthetic methods, large-scale production, and a better understanding on the structure performance relationship can be found, which will greatly extend the application scope of CDs-based materials. Unique features will bring the bright future of carbon quantum dots.

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