

A Review On Biological Applications And Synthesis Of Carbon And Quantum Dots.

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Abstract

Carbon nanodots are a type of carbon nanoparticle that is increasingly being researched because of their astounding properties such as extraordinary luminescence, simplicity of amalgamation and surface functionalization, and biocompatibility. Nanoparticles possess fascinating properties and applications, and there has been increasing critical consideration of their use. These nanomaterials are promising for clinical and biomedical sciences, especially in bioimaging, diagnosis, bioanalytical assays and biosensors. Here we review green methods for the fabrication of quantum dots, and biomedical and biotechnological applications.

Introduction

The study of nanotechnology has resulted in the introduction of various types of nanomaterials, which possess diversified properties that can lead to the production of intriguing properties. Carbon nanodots, also called carbon dots (hereafter denoted as C dots), are a class of carbon nanoparticles that function within a nanosystem. They have recently gained significant attention due to their feasible and varied synthesis methods, unique optoelectronic properties, and strong luminescent behavior.

Nanotechnology is one of the most emerging fields of science in the last decade. With the emergence of modern technologies and a better understanding of nano-science, this advancement has proved to be a boon, increasing its application in medical, clinical, biomedical and pharmaceutical science, and more specifically in the field of disease diagnosis, imaging, drug delivery and therapeutics [1-2]. Carbonaceous and carbon-based nanomaterials have been attracting a significant research interest because of their exclusive characteristics, including good biocompatibility, non-toxicity, high mechanical/thermal properties, and relative ease of functionalization [3-11].

Carbon nanodots are a novel class of nanomaterials smaller than 10 nm in size that possess intriguing changes in their physicochemical properties such as optical capabilities and solubility. Carbon dots are the latest forms of quantum dots, which are a luminescent carbon nanomaterial with zero dimensions. The surface characteristics can be effectively altered and morphed so that they can become appropriately utilized. These dots exhibit very intriguing characteristics that include fluorescence, a lack of biological toxicity, resistance towards photobleaching, and homogenous dispersibility [12-16].

In addition to food, potable water, healthcare and communication, meeting the requirements of energy technologically – while keeping the environment reasonably safe – is an important challenge to be met. In

this regard, advancements in chemical catalysts are helping to improve the efficiency and ease of conversion of natural resources to useful energy materials. Thus, the primary challenge comes in the form of twin requirements: energy resources and energy utilizing devices – where one is a source of energy and the other one is a sink. Both need to be optimized based on advanced scientific developments. In this regard, recent developments in nanoscale science and technology hold promise that may go the beyond laboratory level. That the nanoscale materials exhibit dimension dependent special properties is particularly encouraging with regard to their application potential in the fields of healthcare, energy and the environment. Although research on energy resources especially renewable resources is of paramount importance, works on energy efficient devices portend to offer superior options through lowering of energy requirements. In addition, requirement of environmental friendliness provides new opportunities for the advancement of the field. In the context of developing novel and cost-effective devices, utilization of semiconductor quantum dots (QDs), perovskites, organic dyes, and metal or covalent organic frameworks is noteworthy [17-23].

Carbon dots are traditionally defined as a class of core–shell composites comprising a carbon core and surface passivation with various functional groups, including hydroxyl, carboxyl, and amine, etc., which renders them hydrophilic and facilitate various surface functionalization and passivation. Surface passivation is usually attained by the production of a thin insulating layer of oligomeric polyethylene glycol on an acid-treated carbon dot surface; high fluorescence intensities and high quantum yield of carbon dots can be achieved with an effective surface passivation [24].

Nanoparticles also trigger some irritation reactions and even stimulate many chemical releases which can alter the condition [25]. To predict the drug release pattern of a nanoparticle system is also difficult as when they enter the body, they get surrounded by phagocytic cells. Another problem with them is to extract them from the body after they have performed their function. Despite the fact that nanomedicine has been widely studied for overcoming challenges of tumour targeted delivery and adaptive resistance to therapy, it is due to the advantages that nanocarriers provide like multifunctionality that enables THE accommodation of drugs, affinity ligands, as well as imaging moieties all within a single nanoparticle carrier which can be exploited as A targeted and traceable delivery system [26].

Among the nanoparticle systems, the most widely discussed ones are buckyballs, fullerenes, carbon tubes, liposomes, nano-shells, dendrimers *etc.* [27-28] and among them, Quantum dots (QDs) have gained popularity in recent times. Apart from being a carrier for drug delivery, QDs can also act as a model platform as a diagnostic agent. QDs are complemented with features like small size, versatile surface chemistry and exceptional optical properties.

Synthetic strategies for C dots

In recent years, there have been large numbers of reports describing how to synthesize a wide assortment of C dots through both conventional chemical methods and green ecofriendly methods. Every one of these strategies attempts to improve the synthesis of C dots through techniques such as reducing the number of steps in the overall process and adopting biological reagents or products, which make the synthesis ecofriendly and cost-effective, with optimization of the reaction environment for controlling the size and properties of the end product. There have been reports describing the successful use of naturally abundant materials for the preparation of C dots that exhibit excellent emission properties [29]. The major preparation routes of C dots can be broadly classified by considering the nature of the processes, which include chemical methods and biological (eco-friendly/green) methods (Fig. 1).

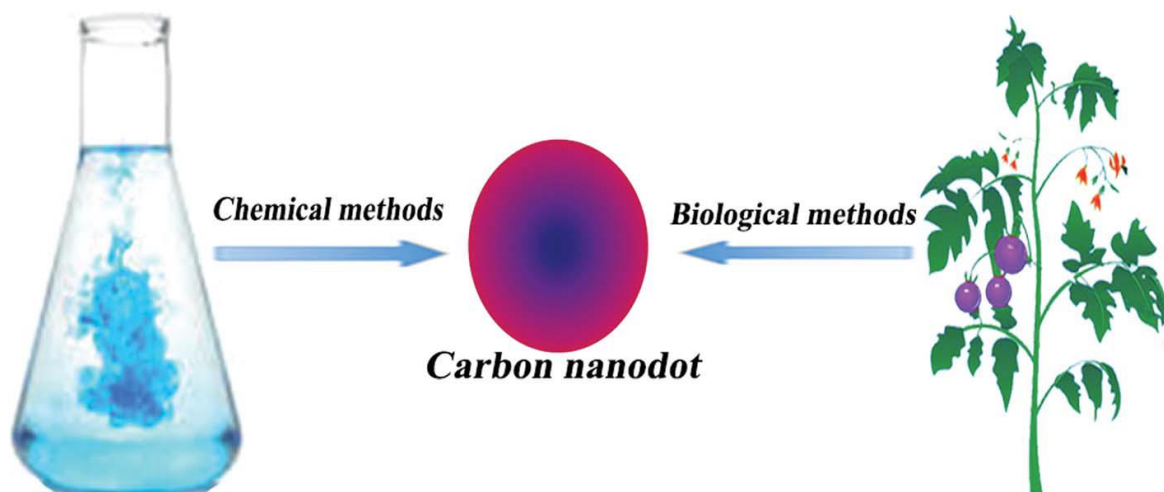


Fig.1. Different methods used to prepare C dots

Chemical methods

The prominent techniques that have been reported for the synthesis of C dots are described with clear emphasis on the conventional top-down or bottom-up approaches utilizing chemical preparation methods. These methods are further classified as described below.

1. Electrochemical method
2. Hydrothermal method
3. Microwave- and ultrasonic-assisted chemical synthesis.
4. Direct carbonization method.

Electrochemical method

The influence of applied potential on the size of C dots has been investigated, along with the preparation. There are many reports depicting the synthesis of C dots using the electrochemical process, such as Bao, et al., [30] who reported the electrochemical tuning of C dots, including their fluorescent behavior. Deng, et al. [31] successfully developed C dots directly from low-molecular weight alcohols. This process involved the transition of alcohols into carbon particles in a basic medium through electrochemical carbonization.

Carbon dots derived from green precursors (green c-dots)

Initially, synthesis of c-dots was limited to use of carbonaceous materials, which resulted in c-dots with low quantum yield (QY) and limited solubility. Further developments resulted in surface passivated c-dots with better solubility and QY; however, the trend for green synthetic approaches led to ever-increasing attention on green synthesis of c-dots. 'Green' c-dots can be defined as carbon quantum dots synthesized using 'green precursors' as the source of carbon; the term 'green precursors' refers to substances which are either naturally occurring or are derivatives of renewable natural products or processes. Various green carbon precursors have been investigated in attempts to achieve a simple, cost-effective, environmentally friendly method with exciting properties. These are

1. Pioneer work (use of coffee grounds for synthesis of green c-dots) [32-33]
2. Fruits, fruit juices and fruit peels as carbon sources [34-35]
3. Beverages as carbon source [36]
4. Animals and animal derivatives as carbon source [37]
5. Flour and bakery products as carbon sources [38-39]
6. Human derivatives as carbon source [40-41]
7. Vegetables and spices as carbon sources [42-44]
8. Waste material as a source of carbon [45-46]
9. Plant leaves and derivatives as a source of carbon [47]

Fruits, fruit juices and fruit peel as carbon sources

Fruit and fruit derivatives encompass an essential and significant portion of green sources used for c-dot synthesis. Following from use of grass, fruit sources such as pomelo peel were used as precursors for hydrothermal treatment at 200 °C, with the resultant c-dots having an average diameter of 2–4 nm with QY of 6.9%, higher than values for c-dots from grass and coffee ground sources.⁴³ Further improvement in QY to 26% was achieved by Sahu et al.⁴⁴ using orange juice as a carbon source. The authors isolated highly fluorescent small c-dots and less fluorescent big coarse particles simply by controlling the centrifugation speed (Fig. 2). The synthesis was performed at relatively low temperature, i.e. 120 °C, and the average particle diameter obtained was 1.5–4.5 nm.

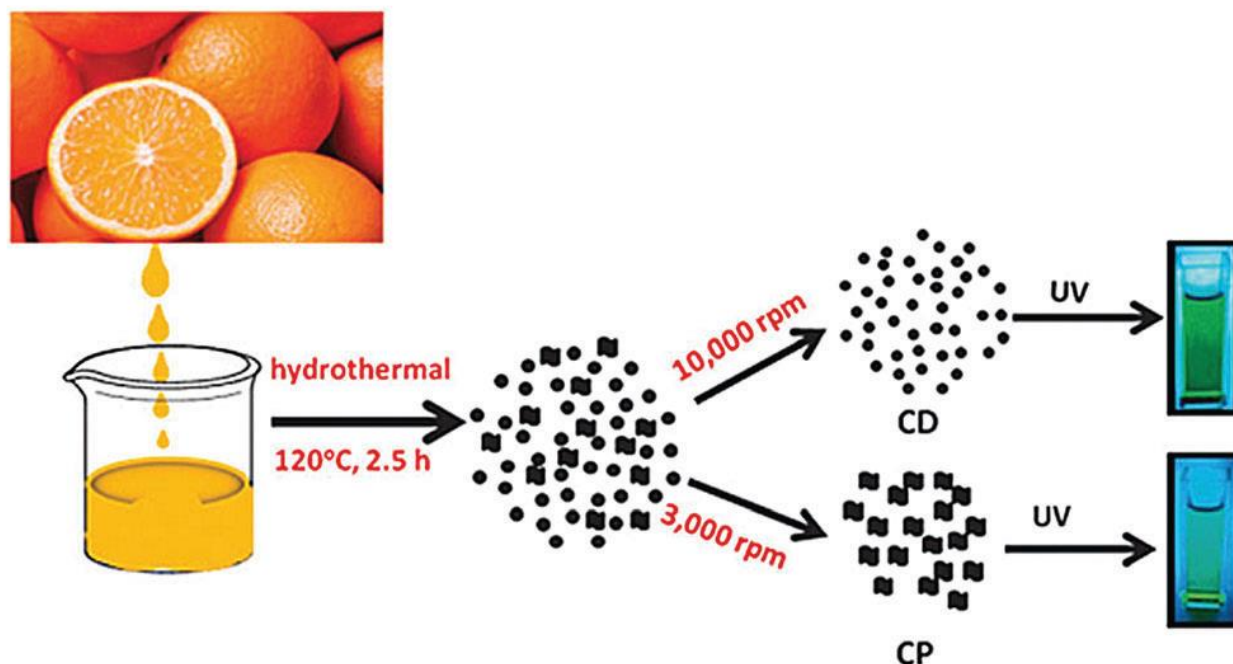


Fig. 2. Hydrothermal preparation of c-dots using orange juice.

Application of C dots

Nanoparticles are monomeric building blocks of nanotechnology and possess features such as strong bonds, delocalization of electrons with variation in size, and ability to make structural changes and affect physicochemical features ranging from melting points, electronic properties, magnetic properties, and surface charges. The following applications are

1. Bioimaging probes
2. Photodynamic therapy
3. Biological and chemical sensors
4. Photocatalysis

Photocatalysis

There has been significant research interest in photocatalysts over the past decade due to the scenario of environmental safety and sustainable energy. The applications of nanomaterials for efficient fabrication of photocatalysts made the journey fast and effective. It has been reported that C dots have been developed as useful photocatalysts for the degradation of organic dyes and also for the photo-splitting of water for hydrogen generation, as shown in Fig. 3.

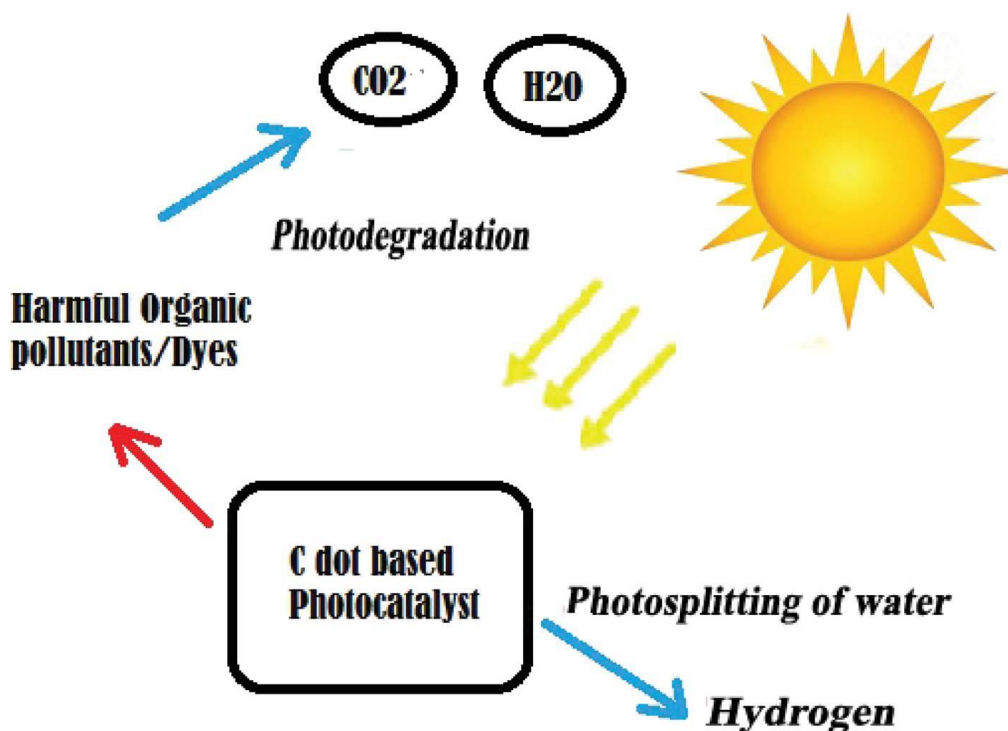


Fig.3. Principle of C dot-based photo catalysts

Properties of QDs that influences its biological application.

QDs are usually prepared using organic or aqueous solvents, which in the current form are unsuitable for biological purposes. Thus, surface modification is required to make the quantum dots suitable for biological applications. The application of quantum dots as biological tools depends on their physiochemical and photophysical properties (Fig. 4).

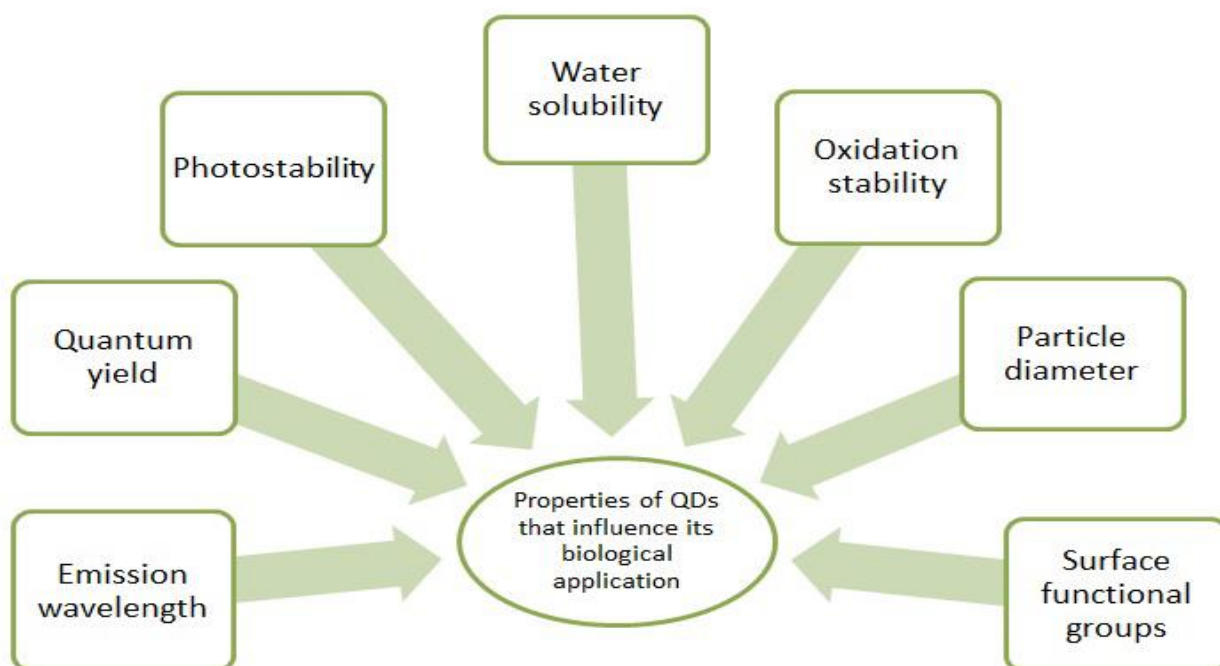


Fig. 4. Properties of QDs that influences its biological application.

Biological application of QDS

1. QDs as Diagnostic Agents
2. QDs as a Drug Carrier System
3. QDs for the Detection of Cell Death
4. QDs in Immunoassay
5. QDs in Neuroscience
6. QDs in RNA Interference (iRNA)
7. QDs in Pharmacokinetic Studies
8. Effects of QDs on Toxicity Studies

QDs in Neuroscience

QDs can be used to visualize, measure and track molecular events using fluorescence microscopy. With the small size and optical resolution, they are able to reach and detect the anatomy of neuronal and glial interactions, synaptic cleft, astrocyte process and neurons. Antibody functionalized quantum dots are used to track the lateral diffusion of glycine receptors in cultures of primary spinal cord neurons. They were able to track the trajectory of individual glycine receptors for tens minutes at spatial resolutions of 5-10 nm, demonstrating that the diffusion dynamics varied depending on whether the receptors were synaptic, presynaptic, or extrasynaptic [48-50]. The brain function depends on the structure of negatively charged cell surface proteoglycans and sialoglycoconjugates in the brain. The invention compared three zwitterionic quantum dots (QDs) coatings differing only in their regions of positive or negative charge, as well as a positively charged (NH₂) polyethylene glycol (PEG) coat, for their ability to deliver the cell-membrane-penetrating chaperone lipopeptide JB577 (WG(Palmitoyl) VKIKKP9G2H6) to individual cells in neonatal rat hippocampal slices.

Conclusion

Carbon-based nanomaterials are of great interest to nanotechnologists due to their fascinating behavior and great potential for various optical, electronic, and in vitro and in vivo applications. This broad acceptance of carbon nanomaterials depends primarily on their comparatively feasible preparation methods and the proper tuning of their desired properties. This review addressed the three major applications of C nanodots: bioimaging, photocatalysis, and sensors.

References.

1. Priyadarshini E, Rawat K. Quantum Dots as Nanoreporters in Biomedicines: A View Point. *JSM NanotechnolNanomed* 2017, 5(2): 1053.
2. Jahangir MA, Imam SS, Kazmi I. Type 2 diabetes current and future medications: a short review. *Int J Pharm Pharmacol* 2017; 1: 101.
3. Iravani S (2011) Green synthesis of metal nanoparticles using plants. *Green Chem* 13:2638–2650. <https://doi.org/10.1039/C1GC15386B>.
4. Iravani S, Varma R (2019a) Plant-derived edible nanoparticles and miRNAs: emerging frontier for therapeutics and targeted drug delivery. *ACS Sustain Chem Eng* 7:8055–8069. <https://doi.org/10.1021/acssuschemeng.9b00954>.
5. Iravani S, Varma RS (2019b) Biofactories: engineered nanoparticles via genetically engineered organisms. *Green Chem* 21:4583–4603. <https://doi.org/10.1039/C9GC01759C>.
6. Mohammadinejad R, Karimi S, Iravani S, Varma RS (2016) Plant-derived nanostructures: types and applications. *Green Chem* 18:20–52. <https://doi.org/10.1039/C5GC01403D>.
7. Varma RS (2012) Greener approach to nanomaterials and their sustainable applications. *Curr Opin Chem Eng* 1:123–128. <https://doi.org/10.1016/j.coche.2011.12.002>.
8. Varma RS (2014a) Greener and sustainable chemistry. *Appl Sci* 4:493–497. <https://doi.org/10.3390/app4040493>.

9. Varma RS (2014b) Journey on greener pathways: from the use of alternate energy inputs and benign reaction media to sustainable applications of nano-catalysts in synthesis and environmental remediation. *Green Chem* 16:2027–2041. <https://doi.org/10.1039/C3GC42640H>.
10. Varma RS (2016) Greener and sustainable trends in synthesis of organics and nanomaterials. *ACS Sustain Chem Eng* 4:5866–5878. <https://doi.org/10.1021/acssuschemeng.6b01623>
11. Varma RS (2019) Biomass-derived renewable carbonaceous materials for sustainable chemical and environmental applications. *ACS Sustain Chem Eng* 7:6458–6470. <https://doi.org/10.1021/acssuschemeng.8b06550>.
12. Y. Zhou, D. Benetti, X. Tong, L. Jin, Z. M. Wang, D. Ma, H. Zhao and F. Rosei, *Nano Energy*, 2018, 44, 378–387.
13. J. Xu, Y. Miao, J. Zheng, H. Wang, Y. Yang and X. Liu, *Nanoscale*, 2018, 10, 11211–11221.
14. L. Hu, H. Li, C. Liu, Y. Song, M. Zhang, H. Huang, Y. Liu and Z. Kang, *Nanoscale*, 2018, 10, 2333–2340.
15. C. Liu, Y. Fu, Y. Xia, C. Zhu, L. Hu, K. Zhang, H. Wu, H. Huang, Y. Liu, T. Xie, J. Zhong and Z. Kang, *Nanoscale*, 2018, 10, 2454–2460.
16. B. B. Chen, M. L. Liu, C. M. Li and C. Z. Huang, *Adv. Colloid Interface Sci.*, 2019, 270, 165–190.
17. B. C. M. Martindale, G. A. M. Hutton, C. A. Caputo and E. Reisner, *J. Am. Chem. Soc.*, 2015, 137, 6018–6025.
18. C. Hu, Y. Lin, J. W. Connell, H. Cheng, Y. Gogotsi, M. Titirici and L. Dai, *Adv. Mater.*, 2019, 31, 1806128.
19. X. Zhang, P. K. Santra, L. Tian, M. B. Johansson, H. Rensmo and E. M. J. Johansson, *ACS Nano*, 2017, 11, 8478–8487.
20. T. Leijtens, T. Giovenzana, S. N. Habisreutinger, J. S. Tinkham, N. K. Noel, B. A. Kamino, G. Sadoughi, A. Sellinger and H. J. Snaith, *ACS Appl. Mater. Interfaces*, 2016, 8, 5981–5989.
21. N. Tetreault, E. Arsenaault, L. Heiniger, N. Soheilnia, J. Brillet, T. Moehl, S. Zakeeruddin, G. A. Ozin and M. Gratzel, *Nano Lett.*, 2011, 11, 4579–4584.
22. D. Wu, Z. Guo, X. Yin, Q. Pang, B. Tu, L. Zhang, Y. Wang and Q. Li, *Adv. Mater.*, 2014, 26, 3258–3262.
23. F. Xu, S. Yang, X. Chen, Q. Liu, H. Li, H. Wang, B. Wei and D. Jiang, *Chem. Sci.*, 2019, 10, 6001–6006.
24. Lim SY, Shen W, Gao Z (2015) Carbon quantum dots and their applications. *Chem Soc Rev* 44:362–381. <https://doi.org/10.1039/C4CS00269E>
25. Tuncer Degim I, Kadioglu D. Cheap, suitable, predictable and manageable nanoparticles for drug delivery: quantum dots. *Curr Drug Del.* 2013; 10(1): 32-8.
26. Probst CE, Zrazhevskiy P, Bagalkot V, Gao X. Quantum dots as a platform for nanoparticle drug delivery vehicle design. *Adv Drug Del Rev.* 2013; 65(5): 703- 18.
27. Ghaderi S, Ramesh B, Seifalian AM. Fluorescence nanoparticles “quantum dots” as drug delivery system and their toxicity: a review. *J of drug target.* 2011; 19(7): 475-86.
28. Malam Y, Loizidou M, Seifalian AM. Liposomes and nanoparticles: nanosized vehicles for drug delivery in cancer. *Trends PharmacolSci*, 2009; 30: 592-599.
29. J. Mathew, J. Joy and J. Philip, *J. Lumin.*, 2019, 208, 356–362.
30. L. Bao, Z. L. Zhang, Z. Q. Tian, L. Zhang, C. Liu, Y. Lin, B. Qi and D. W. Pang, *Adv. Mater.*, 2011, 23, 5801–5806.
31. J. Deng, Q. Lu, N. Mi, H. Li, M. Liu, M. Xu, L. Tan, Q. Xie, Y. Zhang and S. Yao, *Chemistry*, 2014, 20, 4993–4999.
32. S. Liu, J. Tian, L. Wang, Y. Zhang, X. Qin, Y. Luo, A. M. Asiri, A. O. Al-Youbi and X. Sun, *Adv. Mater.*, 2012, 24, 2037–2041.
33. P.-C. Hsu, Z.-Y. Shih, C.-H. Lee and H.-T. Chang, *Green Chem.*, 2012, 14, 917–920.
34. W. Lu, X. Qin, S. Liu, G. Chang, Y. Zhang, Y. Luo, A.M. Asiri, A. O. Al-Youbi and X. Sun, *Anal. Chem.*, 2012, 84, 5351–5357.
35. S. Sahu, B. Behera, T. K. Maiti and S. Mohapatra, *Chem. Commun.*, 2012, 48, 8835–8837.
36. C. Zhu, J. Zhai and S. Dong, *Chem. Commun.*, 2012, 48, 9367–9369.
37. J. Wang, C.-F. Wang and S. Chen, *Angew. Chem., Int. Ed.*, 2012, 51, 9297–9301.
38. M. P. Sk, A. Jaiswal, A. Paul, S. S. Ghosh and A. Chattopadhyay, *Sci. Rep.*, 2012, 2, srep00383.
39. X. Qin, W. Lu, A. M. Asiri, A. O. Al-Youbi and X. Sun, *Sens. Actuators, B*, 2013, 184, 156–162.
40. D. Sun, R. Ban, P.-H. Zhang, G.-H. Wu, J.-R. Zhang and J.-J. Zhu, *Carbon*, 2013, 64, 424–434.
41. S.-S. Liu, C.-F. Wang, C.-X. Li, J. Wang, L.-H. Mao and S. Chen, *J. Mater. Chem. C*, 2014, 2, 6477–6483.

42. B. Yin, J. Deng, X. Peng, Q. Long, J. Zhao, Q. Lu, Q. Chen, H. Li, H. Tang, Y. Zhang and S. Yao, *Analyst*, 2013, 138, 6551–6557.
43. C.-L. Li, C.-M. Ou, C.-C. Huang, W.-C. Wu, Y.-P. Chen, T.-E. Lin, L.-C. Ho, C.-W. Wang, C.-C. Shih, H.-C. Zhou, Y.-C. Lee, W.-F. Tzeng, T.-J. Chiou, S.-T. Chu, J. Cang and H.-T. Chang, *J. Mater. Chem. B*, 2014, 2, 4564–4571.
44. A.-M. Alam, B.-Y. Park, Z. K. Ghouri, M. Park and H.-Y. Kim, *Green Chem.*, 2015, 17, 3791–3797.
45. J. Wei, J. Shen, X. Zhang, S. Guo, J. Pan, X. Hou, H. Zhang, L. Wang and B. Feng, *RSC Adv.*, 2013, 3, 13119–13122.
46. J. Wei, X. Zhang, Y. Sheng, J. Shen, P. Huang, S. Guo, J. Pan, B. Liu and B. Feng, *New J. Chem.*, 2014, 38, 906–909.
47. Y. Liu, Y. Zhao and Y. Zhang, *Sens. Actuators, B*, 2014, 196, 647–652.
48. Baoquan S, XieW, Guangshun Y. Microminiaturized immunoassays using quantum dots as fluorescent label by laser confocal scanning fluorescence detection. *J of Immunol Meth.* 2001; 249: 85-89.
49. Dey NS, Rao MEB. Quantum Dot: novel carrier for drug delivery. *IJRPBS* 2011; 448-458.
50. Pathak S, Cao E, Davidson MC, *et al.* Quantum Dot Applications to Neuroscience: New Tools for Probing Neurons and Glia. *The J. of Neurosci* 2006; 26(7):1893-1895.