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Graphene Quantum Dots and their applications in regenerative medicine: A mini-review

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Abstract

Graphene quantum dots (GQDs) is a new class of fluorescent carbon materials that attracted increasing interest because of their special potentials for biomedical applications, their unique and tunable photoluminescence properties, high photostability, exceptional physicochemical properties, small size, and biocompatibility. This review purpose to update the latest results of The recently developed green synthetic methods of GQDs. In This article recent advanced applications of GQDs in vitro, particularly in regenerative medicine, Antibacterial activity, and Biocompatibility of GQDs, are included.

Keywords: Graphene quantum dots, green synthesis, Stem cell, Antibacterial, Biomedical

1.Introduction

Graphene quantum dot (GQD) is an important member of the graphene family have recently attracted special research attention owing to their unique spin3 and electronic. [1] GQDs are hexagonally symmetrical crystals 0D graphene material, characterized by an atomically thin graphitic plane (typically 1 or 2 layers, <2 nm thick) with lateral dimensions typically <10 nm And the particle size is about 2 to 20 nm.[2, 3] Besides, below and above the atomic plane have π-π bonds that give graphene particular electrical conductivity and thermal, compared with conventional semiconductor quantum dots, making GQDs possess their favorable attributes without incurring the burden of intrinsic toxicity. [4, 5] So far GQDs are synthesized in two ways, top-down and bottom-up. Top-down approaches involve cutting certain graphitic precursors including graphene oxide [6], chemically reduced graphene oxide [7], graphite [8], carbon nanotube [9, 10], carbon black [11, 12], carbon fiber [13], fullerenes etc[14]., into small graphene segment with sidelong size in the nano scale (<100 nm). In The top-down method used organic molecules to assemble dots. Although, GQDs from these methods different in chemical composition, shape and size, major part of them have photoluminescence (PL) which put GQD into the list of highly effective candidates for biology relevant applications (e. g. ,nanomedicine, bio-imaging and bio-sensing). [1] Owing to its phenomenal mechanical properties [15], surface grafting, excellent biocompatibility , stable fluorescence property, electrical conductivity [16, 17], good solubility, transparency, and non-toxicity. [16] GQDs has obtained quick growth as advanced tools for multipurpose in several fields of knowledge including solar cells [18, 19], photodetectors [20, 21], light-emitting diodes [22], photo-/electro-catalytic [23-25], composites, photonics, electronics, and energy.[26] Meantime, GQDs-based nanomaterials have already shown a hopeful future in biomedical fields [27, 28], particularly for, drug delivery [29], diagnostics [30, 31], in vitro and in vivo bioimaging [32, 33], near-infrared (NIR) light induced photothermal therapy.[34-36] Recent studies on GQD report that are more hydrophobic and less toxic with respect to graphene and endowed of stable strong fluorescence. [1] inherent fluorescence and existence of more active groups on the GQD surface let their multimodal conjugation, making them perfect nano carriers[37] for the concurrent tracking and treatment of cancer cells.[38] GQD has received a lot of attention in the field of biomedicine because GQDs enter the cytoplasm not only of human cell lines but also of primary human blood cells. [39] various studies have reported the utility of GQDs for labeling several types of cells including stem cells. GQDs are composed of frequently oxygen and carbon; therefore, unlike inorganic QDs such as CdSe, CdTe, and CdS, GQDs are generally biocompatible. In addition, they are biodegradable, because they can be degraded by granulocytes or macrophages. [40] In this article, the

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applications of GQDs in regenerative medicine, Antibacterial activity of GQD nano-particles and Biocompatibility of GQDs will be reviewed.

3. Graphene Quantum Dots

Nowadays, quantum dots (QDs) are being extensively used in various fields of biomedical research including bio-sensing, bio-imaging and disease diagnosis.[41, 42] QDs are normally contain heavy materials and owing to their physiochemical properties, mechanical strength and nanometer-scale dimensions. [43] Although QDs exhibit a broad spectrum of desirable characteristics which suit them for biomedical purposes, they also can potentially accumulate within the lungs (Figure 11). They can also induce apoptosis via oxidative stress that indicate their toxicity to biological tissues. Furthermore, the semi-conductive materials used in their structure such as Cadmium, Tellurium, Selenium and Cadmium are non-degradable. Conventional, heavy-metals based QDs also cause oxidative stress which can induce apoptosis and lead to toxicity in the body. Due to cytotoxicology issues the use of QDs-based materials is not yet approved for clinical applications. However, QDs were used in medical devices for imaging long before graphene-based quantum dots grew in popularity. [44] Conversion of graphene to nano-scale graphene quantum dots (GQDs) has to some extent overcome the limitations of conventional QDs. They have similar benefits as conventional QDs while heavy metals are absent in their structure. GQDs are commonly engaged with drug-delivery, bio-sensing agents, and tissue engineering applications.[45] Known as a novel type of zero-dimensional luminescent nanomaterials, GQDs are small graphene fragments to cause excitation confinement in 3-20 nm particles and quantum-size effect. [46] Not only GQDs exhibit extraordinary optoelectronic properties, but also they have been successful in fulfilling biocompatibility and cost-effective preparation method goals, which makes them a potential alternative to replace the well-known metal-based QDs. [23] Besides, the π-π bonds the atomic plane structure of graphene gives incomparable thermal and electrical conductivity, compared with conventional semiconductor quantum dots, making GQDs possess their favorable attributes without incurring the burden of intrinsic toxicity. [4, 5, 47]

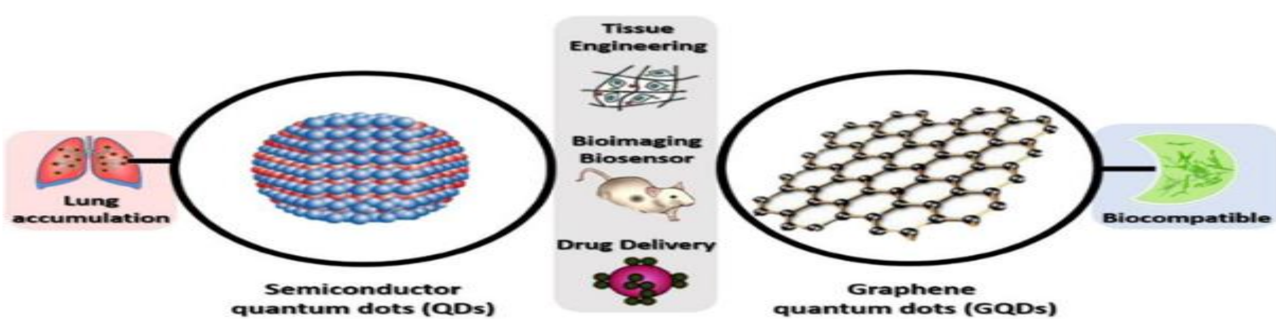

Figure 1. Schematic illustration of various applications of graphene quantum dots as compared to quantum dots **[48]**

3.1. Applications of GQDs in regenerative medicine

Lately, GQDs have been tested for regenerative medicine and stem-cell based tissue engineering applications. Efforts have been made via implementation of various techniques to differentiate stem cells into a variety of cells.[25] GQDs can be used to encourage specific differentiation of stem cells under certain circumstances. Qiu *et al*, [49] explored the important role of GQDs in osteogenic differentiation. Precisely, GQDs were found to stimulate early activation of ontogenesis. Given that GQDs can promote calcium abundance, these particles are considered to be invaluable in the regenerative-medicine field due to their differentiation potency, excellent mechanical properties, and low toxicity [48]. In a study by Yang *et al, [50]* stem cells from human exfoliated deciduous teeth (SHEDs) were evaluated in regard to osteogenic differentiation potential when treated with GO and GOQD particles. Conforming to previous observations, they perceived that both materials promoted differentiation of SHEDs after 7 days *in vitro* at a 1µg/ml concentration, however, GOQDs appeared to be a more efficient stimulator for ALP activity, calcium nodule formation and protein expression (Figure 12). Furthermore, homogenous distribution of GOQDs through cell cytoplasm was confirmed due to excellent photo-luminescent activity of QDs. In tissue engineering, GQDs can also act as reinforcing agents that improve mechanical properties of scaffolds in which orthopedic implants can be inserted. Interestingly, GQDs can be produced through green synthetic methods which have great advantages compared to chemical methods. The difficulty in removing by-products of chemical synthetic methods has limited the use of chemical cutting in large scale preparation of GQDs. Zhu *et al,* [4] have proposed a universal green method for rapid production of GQDs with a high quantum yield (0.7-0.8) in which UV irradiation facilitates free radical polymerization of oxygen containing aromatic compound. The by-products of this method is only water and Carbon dioxide.

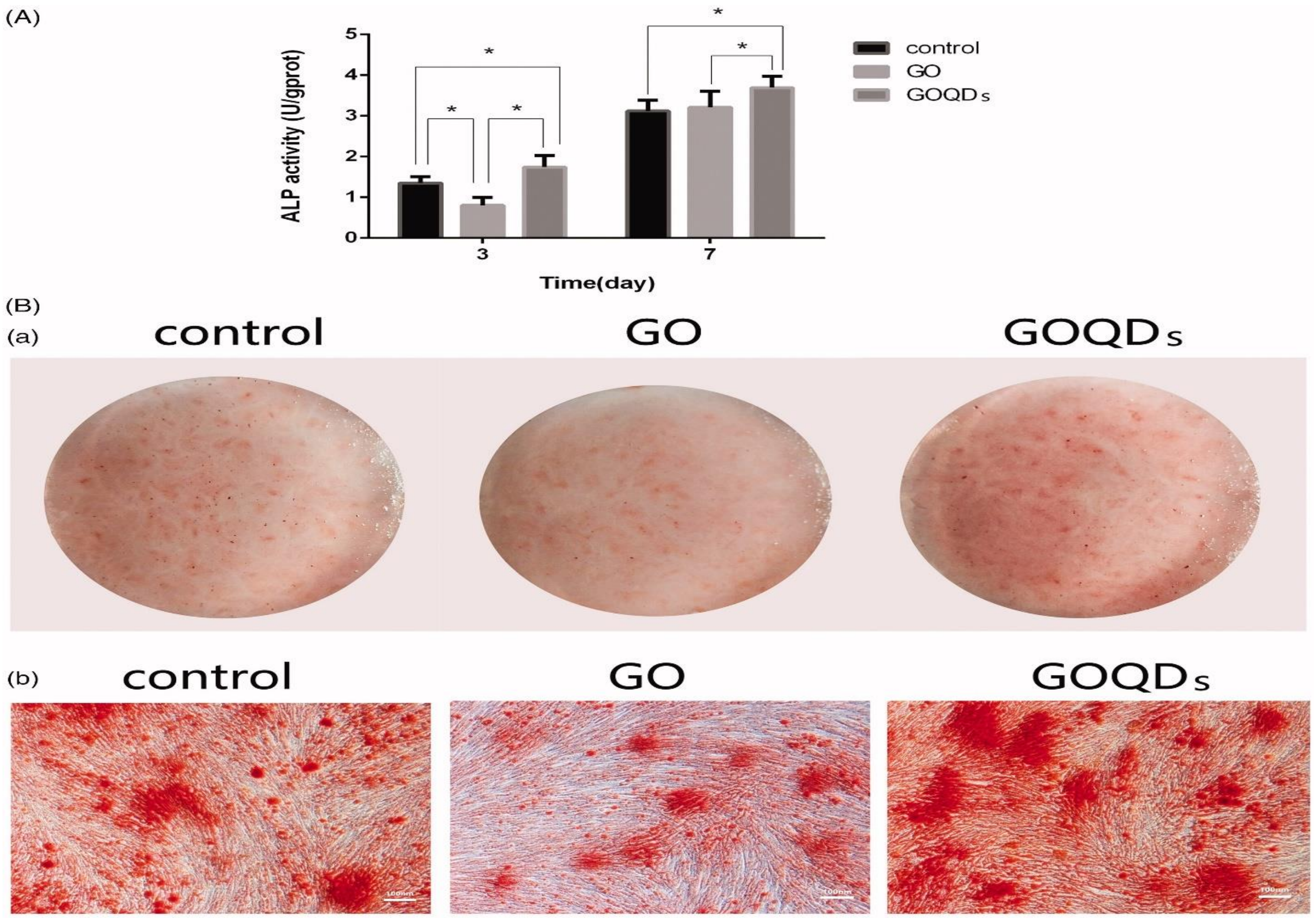

Figure 2. SHEDs were cultured in osteogenic induction medium containing GO or GOQDs. (A) Osteogenic differentiation was detected by ALP activity assay kit after 3 and 7 days. (B) Osteogenic differentiation was detected by Alizarin red S staining for 14 days. (a) Optical images (b) Microscopic images. [50]

In addition, Konwar *et al*, [51] reported that chitosan-carbon dots nanocomposite hydrogel films extracted from "tea" offer remarkable biomedical applications. Considering the origin of these carbon dots (tea), they are presented to be biocompatible and physically strong. Through conjugation with tea carbon dots, the commonly-used chitosan hydrogel displayed improved physicomechanical properties. This effect can be used for a wide range of applications. Regarding high mechanical properties, GQDs demonstrated that they have a lot of potential to reinforce soft materials in tissue engineering. Green synthesized GQDs is proved to be non-toxic in *in vivo* studies. Lee *et al,* [52] claimed in their study that in spite of interferences with DNA function due to oxidative stress, green GQDs seem to be safe when used *in vivo*. Although GQDs are the most prominent product among graphene family materials, there are still controversial ideas regarding their application in the fields of biomedicine and human experiments.[53] However, GQDs' potential in replacing conventional methods of labeling, drug delivery systems, scaffolds and coatings in evident.

3.2. Antibacterial activity of GQD nano-particles

Graphene quantum dots (GQDs), generates ROS when photo-excited (470 nm, 1 W) inducing oxidative stress. Methicillin-resistant Staphylococcus aureus (MRSA) and E. coli were found to be inhibited by cell membrane damage. In the same study, mouse spleen cells were found to be less sensitive indicating a selective antibacterial photodynamic action of GQDs. [54] In another study, S. aureus, including its antibiotic-tolerant persisters were found to be killed by C60-GQDs. The Surface-Gaussian-curvature match between GQD and the target bacterium plays a critical role in the association of the GQD with bacterial cell surface considered to be the initial step for cell envelope disruption. [55, 56] The anti-bacterial activity of a CQD and hematite incorporated Ti surface was examined by Moradlou et al [57]; they observed sustainable antibacterial activity against *S. mutans* and *E. coli* and proposed that CQD in combination with other nanomaterials (α-Fe_2O_3) could present potential bactericidal activity against gram negative and gram positive dental pathogens.

3.3. Biocompatibility of GQDs

The toxicity of nanomaterials is one of the major challenges facing their applications in biotechnology.[58] Studies on the cytotoxicity of graphene-based materials have stated briefly that GQDs with a less than 50-nm side edge caused no obvious

toxicity. [59] Since single-dosing experiment had no obvious accumulation and mostly presented low toxicity of nanomaterials, multiple-dosing which simulated clinical drug administration was applied to the study of in vivo toxicity to further investigate the biosafety of GQDs.[60, 61] Nurunnabi et al. performed
in vitro cytotoxicity studies on carboxylated GQDs and observed no toxicity. [62] Peng et al. have found that nanosized graphene oxides did not lead to serious acute cytotoxicity to HeLa cells at a concentration of 40 lg /mL. [63] Li et al. observed no distinct cell death by incubating graphene oxide nanoparticles with gastric cancer cells and skin cells at a dose up to 100 lg mL21 to a series of cells. [64] A study by Li et al on dental pulp stem cells showed that not only could GQDs increase the proliferation of DPSC in a time-dependent manner, however inhibition to cell proliferation occurred at high concentrations (500 µg/ml). Further investigations in their study showed that GQDs did not interfere with the metabolic activity of the cells. [65]

Ethical issue

Authors are aware of and comply with, best practices in publication ethics, specifically about authorship (avoidance of guest authorship), dual submission, manipulation of figures, competing interests, and compliance with policies on research ethics. Authors adhere to publication requirements that submitted work is original and has not been published elsewhere in any language.

Conclusion

In this review, GQDs have been comprehensively introduced. GQDs are potentially abundantly available and at the same time, they have several proven benefits over CDs. GQDs are used in several applications, such as photodetectors, nanomedicine, bio-imaging, bio-sensing and, drug delivery. In addition, due to the unique properties of carbon quantum dots in the field of stem-cell based tissue engineering, such as encourage specific differentiation of stem cells under certain circumstances has been specifically studied. Due to its antibacterial properties and low toxicity, GQDs are recommended as an excellent option for biomedical studies.

Competing interests

The authors declare that no conflict of interest would prejudice the impartiality of this scientific work.

Authors contribution

All authors of this study have a complete contribution for data collection, data analyses, and manuscript writing.

References

1. Wang, S., I.S. Cole, and Q. Li, *The toxicity of graphene quantum dots.* RSC Advances, 2016. **6**(92): p. 89867-89878.
2. Mousavi, S.M., et al., *Modification of phenol novolac epoxy resin and unsaturated polyester using sasobit and silica nanoparticles.* Polymers from Renewable Resources, 2017. **8**(3): p. 117-132.
3. Chen, F., et al., *Graphene quantum dots in biomedical applications: recent advances and future challenges.* Frontiers in Laboratory Medicine, 2017. **1**(4): p. 192-199.
4. Zhu, J., et al., *Green, rapid, and universal preparation approach of graphene quantum dots under ultraviolet irradiation.* ACS applied materials & interfaces, 2017. **9**(16): p. 14470-14477.
5. Zhang, N., et al., *Quantum-dots-based photoelectrochemical bioanalysis highlighted with recent examples.* Biosensors and Bioelectronics, 2017. **94**: p. 207-218.
6. Li, L.L., et al., *A facile microwave avenue to electrochemiluminescent two-color graphene quantum dots.* Advanced Functional Materials, 2012. **22**(14): p. 2971-2979.
7. Pan, D., et al., *Hydrothermal route for cutting graphene sheets into blue-luminescent graphene quantum dots.* Advanced materials, 2010. **22**(6): p. 734-738.
8. Sohal, N., B. Maity, and S. Basu, *Recent advances in heteroatom-doped graphene quantum dots for sensing applications.* RSC Advances, 2021. **11**(41): p. 25586-25615.
9. Minati, L., et al., *Luminescent graphene quantum dots from oxidized multi-walled carbon nanotubes.* Materials Chemistry and Physics, 2012. **137**(1): p. 12-16.
10. Dong, Y., et al., *Etching single-wall carbon nanotubes into green and yellow single-layer graphene quantum dots.* Carbon, 2013. **64**: p. 245-251.
11. Wang, S., et al., *The dual roles of functional groups in the photoluminescence of graphene quantum dots.* Nanoscale, 2016. **8**(14): p. 7449-7458.
12. Dong, Y., et al., *One-step and high yield simultaneous preparation of single-and multi-layer graphene quantum dots from CX-72 carbon black.* Journal of Materials Chemistry, 2012. **22**(18): p. 8764-8766.

13. Peng, J., et al., *Graphene quantum dots derived from carbon fibers.* Nano letters, 2012. **12**(2): p. 844-849.
14. Amani, A.M., et al., *Electric field induced alignment of carbon nanotubes: methodology and outcomes*, in *Carbon nanotubes-recent progress*. 2017, IntechOpen.
15. Huang, X., et al., *Graphene-based composites.* Chemical Society Reviews, 2012. **41**(2): p. 666-686.
16. Wang, C., et al., *Electrochemical properties of graphene paper electrodes used in lithium batteries.* Chemistry of Materials, 2009. **21**(13): p. 2604-2606.
17. Becerril, H.A., et al., *Evaluation of solution-processed reduced graphene oxide films as transparent conductors.* ACS nano, 2008. **2**(3): p. 463-470.
18. Li, Y., et al., *An electrochemical avenue to green-luminescent graphene quantum dots as potential electron-acceptors for photovoltaics.* Advanced materials, 2011. **23**(6): p. 776-780.
19. Tsai, M.-L., et al., *Efficiency enhancement of silicon heterojunction solar cells via photon management using graphene quantum dot as downconverters.* Nano letters, 2016. **16**(1): p. 309-313.
20. Yu, T., et al., *Graphene coupled with silicon quantum dots for high-performance bulk-silicon-based Schottky-junction photodetectors.* Advanced Materials, 2016. **28**(24): p. 4912-4919.
21. Zhang, Q., et al., *Solution-processed graphene quantum dot deep-UV photodetectors.* ACS nano, 2015. **9**(2): p. 1561-1570.
22. Song, S.H., et al., *Graphene: Highly Efficient Light-Emitting Diode of Graphene Quantum Dots Fabricated from Graphite Intercalation Compounds (Advanced Optical Materials 11/2014).* Advanced Optical Materials, 2014. **2**(11): p. 1009-1009.
23. Arvand, M. and S. Hemmati, *Analytical methodology for the electro-catalytic determination of estradiol and progesterone based on graphene quantum dots and poly (sulfosalicylic acid) co-modified electrode.* Talanta, 2017. **174**: p. 243-255.
24. Hashemi, S.A., et al., *Superior X-ray radiation shielding effectiveness of biocompatible polyaniline reinforced with hybrid graphene oxide-iron tungsten nitride flakes.* Polymers, 2020. **12**(6): p. 1407.
25. Mousavi, S.M., et al., *Development of hydrophobic reduced graphene oxide as a new efficient approach for photochemotherapy.* RSC Advances, 2020. **10**(22): p. 12851-12863.
26. Hashemi, S.A., et al., *Integrated polyaniline with graphene oxide-iron tungsten nitride nanoflakes as ultrasensitive electrochemical sensor for precise detection of 4-nitrophenol within aquatic media.* Journal of Electroanalytical Chemistry, 2020. **873**: p. 114406.
27. Mousavi, S.M., et al., *Development of graphene based nanocomposites towards medical and biological applications.* Artificial cells, nanomedicine, and biotechnology, 2020. **48**(1): p. 1189-1205.
28. Mousavi, S.M., et al., *Development of clay nanoparticles toward bio and medical applications*. 2018: IntechOpen.
29. Iannazzo, D., et al., *Graphene quantum dots for cancer targeted drug delivery.* International journal of pharmaceutics, 2017. **518**(1-2): p. 185-192.
30. Huang, H., et al., *Fluorescence turn-on sensing of ascorbic acid and alkaline phosphatase activity based on graphene quantum dots.* Sensors and Actuators B: Chemical, 2016. **235**: p. 356-361.
31. Zhao, J., et al., *Graphene quantum dots as effective probes for label-free fluorescence detection of dopamine.* Sensors and Actuators B: Chemical, 2016. **223**: p. 246-251.
32. Kuo, W.-S., et al., *Graphene quantum dots with nitrogen-doped content dependence for highly efficient dual-modality photodynamic antimicrobial therapy and bioimaging.* Biomaterials, 2017. **120**: p. 185-194.

33. Reina, G., et al., *Promises, facts and challenges for graphene in biomedical applications.* Chemical Society Reviews, 2017. **46**(15): p. 4400-4416.
34. Mazraedoost, S. and G. Behbudi, *Nano materials-based devices by photodynamic therapy for treating cancer applications.* Advances in Applied NanoBio-Technologies, 2021. **2**(3): p. 9-21.
35. Yang, Y., et al., *Increasing cancer therapy efficiency through targeting and localized light activation.* ACS applied materials & interfaces, 2017. **9**(28): p. 23400-23408.
36. Khodadadei, F., S. Safarian, and N. Ghanbari, *Methotrexate-loaded nitrogen-doped graphene quantum dots nanocarriers as an efficient anticancer drug delivery system.* Materials Science and Engineering: C, 2017. **79**: p. 280-285.
37. Mousavi, S.M., et al., *Gold nanostars-diagnosis, bioimaging and biomedical applications.* Drug metabolism reviews, 2020. **52**(2): p. 299-318.
38. Gholami, A., et al., *3D nanostructures for tissue engineering, cancer therapy, and gene delivery.* Journal of Nanomaterials, 2020. **2020**.
39. Fasbender, S., et al., *The low toxicity of graphene quantum dots is reflected by marginal gene expression changes of primary human hematopoietic stem cells.* Scientific reports, 2019. **9**(1): p. 1-13.
40. Kim, J., et al., *Multiphoton luminescent graphene quantum dots for in vivo tracking of human adipose-derived stem cells.* Nanoscale, 2016. **8**(16): p. 8512-8519.
41. Ghahramani, Y. and N. Javanmardi, *Graphene Oxide Quantum Dots and their applications via stem cells: A mini-review.* Advances in Applied NanoBio-Technologies, 2021. **2**(3): p. 54-56.
42. Chen, N., et al., *The cytotoxicity of cadmium-based quantum dots.* Biomaterials, 2012. **33**(5): p. 1238-1244.
43. Gvozdyuk, A.A., et al. *Synthesis of high luminescent carbon nanoparticles*. in *Saratov Fall Meeting 2016: Optical Technologies in Biophysics and Medicine XVIII*. 2017. International Society for Optics and Photonics.
44. Kairdolf, B.A., et al., *Semiconductor quantum dots for bioimaging and biodiagnostic applications.* Annual review of analytical chemistry, 2013. **6**: p. 143-162.
45. Bahrani, S., et al., *Zinc-based metal–organic frameworks as nontoxic and biodegradable platforms for biomedical applications: review study.* Drug metabolism reviews, 2019. **51**(3): p. 356-377.
46. Benítez-Martínez, S. and M. Valcárcel, *Graphene quantum dots in analytical science.* TrAC Trends in Analytical Chemistry, 2015. **72**: p. 93-113.
47. Zhao, H., et al., *Graphene-based nanomaterials for drug and/or gene delivery, bioimaging, and tissue engineering.* Drug Discovery Today, 2017. **22**(9): p. 1302-1317.
48. Lee, J.S., et al., *Recent advances in quantum dots for biomedical applications.* Journal of Pharmaceutical Investigation, 2018. **48**(2): p. 209-214.
49. Qiu, J., et al., *Effects of graphene quantum dots on the self-renewal and differentiation of mesenchymal stem cells.* Advanced healthcare materials, 2016. **5**(6): p. 702-710.
50. Yang, X., et al., *Effects of graphene oxide and graphene oxide quantum dots on the osteogenic differentiation of stem cells from human exfoliated deciduous teeth.* Artificial cells, nanomedicine, and biotechnology, 2019. **47**(1): p. 822-832.
51. Konwar, A., et al., *Green chitosan–carbon dots nanocomposite hydrogel film with superior properties.* Carbohydrate polymers, 2015. **115**: p. 238-245.
52. De Menezes, F.D., et al., *Graphene quantum dots unraveling: Green synthesis, characterization, radiolabeling with 99mTc, in vivo behavior and mutagenicity.* Materials Science and Engineering: C, 2019. **102**: p. 405-414.
53. Avval, Z.M., et al., *Introduction of magnetic and supermagnetic nanoparticles in new approach of targeting drug delivery and*

cancer therapy application. Drug metabolism reviews, 2020. **52**(1): p. 157-184.

54. Ristic, B.Z., et al., *Photodynamic antibacterial effect of graphene quantum dots.* Biomaterials, 2014. **35**(15): p. 4428-4435.
55. Hui, L., et al., *Antibacterial property of graphene quantum dots (both source material and bacterial shape matter).* ACS applied materials & interfaces, 2016. **8**(1): p. 20-25.
56. Hashemi, S.A., et al., *Decorated graphene oxide flakes with integrated complex of 8-hydroxyquinoline/NiO toward accurate detection of glucose at physiological conditions.* Journal of Electroanalytical Chemistry, 2021. **893**: p. 115303.
57. Moradlou, O., Z. Rabiei, and N. Delavari, *Antibacterial effects of carbon quantum dots@hematite nanostructures deposited on titanium against Gram-positive and Gram-negative bacteria.* Journal of Photochemistry and Photobiology A: Chemistry, 2019. **379**: p. 144-149.
58. Sanaee, M.R., et al., *The influence of particle size and multi-walled carbon nanotube on physical properties of mineral trioxide aggregate.* Materials Research Express, 2019. **6**(6): p. 065413.
59. Wang, J., et al., *Synthesis, characterization and cells and tissues imaging of carbon quantum dots.* Optical Materials, 2017. **72**: p. 15-19.
60. Hashemi, S.A., et al., *Coupled graphene oxide with hybrid metallic nanoparticles as potential electrochemical biosensors for precise detection of ascorbic acid within blood.* Analytica chimica acta, 2020. **1107**: p. 183-192.
61. Chong, Y., et al., *The in vitro and in vivo toxicity of graphene quantum dots.* Biomaterials, 2014. **35**(19): p. 5041-5048.
62. Nurunnabi, M., et al., *In vivo biodistribution and toxicology of carboxylated graphene quantum dots.* ACS nano, 2013. **7**(8): p. 6858-6867.
63. Peng, C., et al., *Intracellular imaging with a graphene-based fluorescent probe.* Small, 2010. **6**(15): p. 1686-1692.
64. Li, J.L., et al., *Graphene oxide nanoparticles as a nonbleaching optical probe for two-photon luminescence imaging and cell therapy.* Angewandte Chemie International Edition, 2012. **51**(8): p. 1830-1834.
65. Li, X., et al., *Fluorescent labelling in living dental pulp stem cells by graphene oxide quantum dots.* Artificial cells, nanomedicine, and biotechnology, 2019. **47**(1): p. 115-122.