CODEN: WJAPAC Impact Factor: 3.87 ISSN: 3049-3013

World Journal of Advance Pharmaceutical Sciences

Volume 1, Issue 1. Page: 39-44 Review Article www.wjaps.com

QUANTUM DOTS AN NOVEL APPROACH FOR CANCER THERAPY

Dr. Fatehalrahman F. Magbool[1]*, Tibian Gaffer M.[2], Magda Ali Y.[2], Zainab Mohammed Salih E.[2], Saga H. Alderdiri[2], Ayat Hassaballah[2], Esraa Alamein[2], Nasrh Abdalrhman[2], Randa Najim Eldeen[2], Safa Yaghob[2] and Mona Adil[2]

[1]Assisstant Professor of Pharmaceutics, Red Sea University - Sudan.
[2]College of Pharmacy, Al Neelain University - Sudan.

How to cite this Article Dr. Fatehalrahman F. Magbool, Tibian Gaffer M., Magda Ali Y., Zainab Mohammed Salih E., Saga H. Alderdiri, Ayat Hassaballah, Esraa Alamein, Nasrh Abdalrhman, Randa Najim Eldeen, Safa Yaghob, Mona Adil (2024). QUANTUM DOTS AN NOVEL APPROACH FOR CANCER THERAPY. World Journal of Advance Pharmaceutical Sciences, 1(1), 39-44.

Article Info

Article Received: 21 October 2024,

Article Revised: 11 November 2024,

Article Accepted: 01 December 2024.

DOI: https://doi.org/10.5281/zenodo.16928054

***Corresponding author:**

***Dr. Fatehalrahman F. Magbool**

Assisstant Professor of Pharmaceutics, Red Sea University - Sudan.

ABSTRACT

Nanotechnology has revolutionized the pharmaceutical and medical industries with its transformative potential, paving the way to early diagnosis and drug delivery. Quantum dots (QDs), also known as nanoscale semiconductor crystals, are nanoparticles with unique optical and electronic properties such as bright and intensive fluorescence. Nanocarriers materials containing QDs should contain the following characteristics: no drug interactions, more drug-loading capacity, low biocompatibility and toxicity. There is an increasing interest in the development of nano-theranostics platforms for simultaneous sensing, imaging and therapy. QDs have great potential for such applications, with notable results already published in the fields of sensors, drug delivery and biomedical imaging. This review focuses on the recent advances of quantum dots (QDs) and their applications in drug delivery, as well as the integration of GQDs in cancer treatment.

KEYWORDS: Quantum dot, Nanotechnology, Theranostic, Drug delivery, Delivery-release mode, Cancer Treatment.

INTRODUCTION

Nanotechnology has revolutionized the pharmaceutical and medical industries with its transformative potential, paving the way to early diagnosis and drug delivery.[1,2] At the forefront of this nanotechnological revolution are quantum dots (QDs), nanoscale zero-dimensional crystals[3] known for their various optical, spectral, magnetic, and electrochemical properties.[4] Among the various nanomaterials, QDs have shown substantial attention as an indispensable tool in cancer drug delivery and bioimaging.[5] Drug nanocarriers primarily consist of nanotransporters, lipid-based carriers, and other types, polymer nanostructures or nanocontainers, microemulsions or nanosized emulsions, nanomicelles, dendrimeric structures, inorganic nanotransporters like silica nanobeads, nanotubes, and QDs. Ultimately, QD nanocarriers for pharmaceuticals have the potential to boost effectiveness, minimise side effects, and enhance the therapeutic index of medications.[6] Furthermore, drug nanocarriers can enhance the absorption of small-molecule drugs efficiently. Simultaneously, studies on macromolecular drug delivery have shown promising potential as well. QD labelling advances research into nano-drugs at the cellular level, including in living animals. Surface modifications with targeted ligands are widely employed to improve medication delivery efficiency.

Quantum dots (QDs) are nanoparticles that are restricted in three dimensions to spherical shape, typically with a diameter of 2-8 nm, Because of the it small size, quantum dots display unique optical and electrical properties, QDs are characterized by compozition-dependent band gap energy.[7] The band gap energy is dependent on a size of nanoparticle QDs are semiconductor nanocrystals with unique optical

properties, such as high photochemical stability, broad excitation wavelength, narrow emission bandwidth and long fluorescent lifetime, and they have been widely used in many areas of life sciences. Different types of QDs can be excited with the same light wavelength, and their narrow emission bands can be detected simultaneously for multiple assays. The fluorescence bands of QDs are dependent on their composition, size and shell thickness (figure 1).[7,8] If the particle size is smaller than the bulk materials' Bohr radius, it causes the energy levels to pose atom-like properties and become discrete compared to the continuum energy levels observed in bulk materials; in other words, these unique properties result from the confinement of the states of charge carriers by the physical reduction in the size of the nanoparticles.[8]

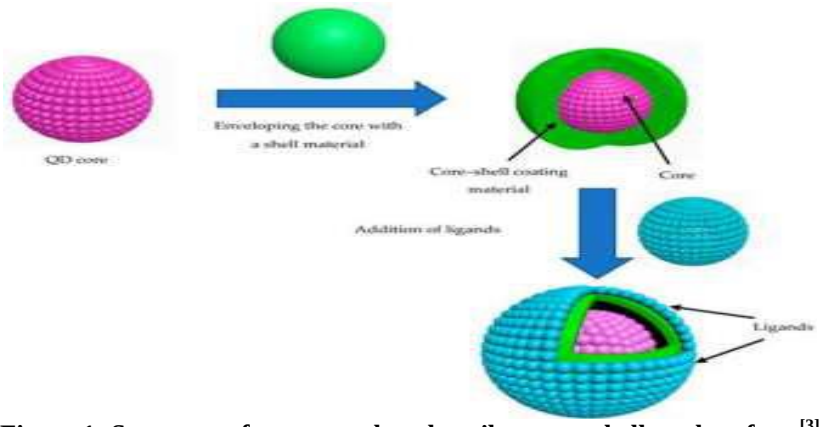

Figure 1: Structure of quantum dots describes core, shell, and surface.[3]

Properties and characteristics of quantum dots

Quantum dots possess many aspects, including size-modifiable light emission, enhanced signal luminosity, resilience against light-induced fading, and concurrent multi-phosphorescence emissions, due to their highly reactive surface[9], they must be used under ambient circumstances after being stabilised and passivated, due to their ability to emit multiple fluorescent signals, this material can be integrated into a traceable drug delivery system, enhancing the pharmacokinetic and pharmacodynamic effects of medications and when creating a biological substance which functions as an enhancement to pharmaceutical administration applications, quantum nanodots can serve as a template for a carrier that fits in dimensions and aspects. The properties of QDs are shown in Figure 2.

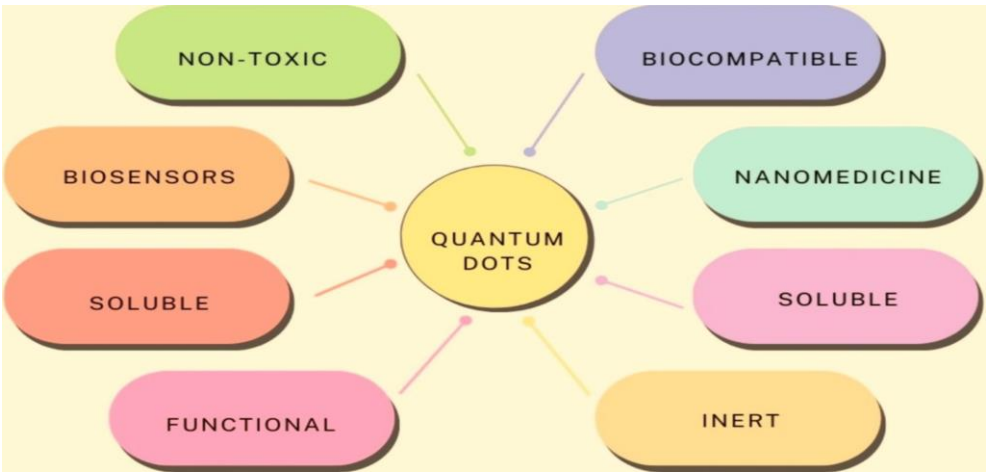

Figure 2: Properties and characteristics of quantum dots.

Properties of quantum dots as nanocarriers

Nanocarrier materials containing QDs should contain the following characteristics: no drug interactions, more drug-loading capacity, low biocompatibility and toxicity, mechanical strength, long residence time *in vivo*, and improved stability and circulation time.[9] When used as nanocarrier particles on the nanometer scale, QDs exhibit various effects, including quantum confinement, size, and dielectric effects. The diagram of QDs as polymeric nanocarriers is illustrated in Figure 3. These unique properties have significant implications for their biological and life sciences applications. Currently, various types of QD nanocarriers are being explored for cancer therapy, including lipid nanoparticles, nano-sized hydrogels, chitin-derived polymers, folate, and carbon nanostructures, each offering distinct advantages and potential for targeted therapeutic administration and diagnostics.[10]

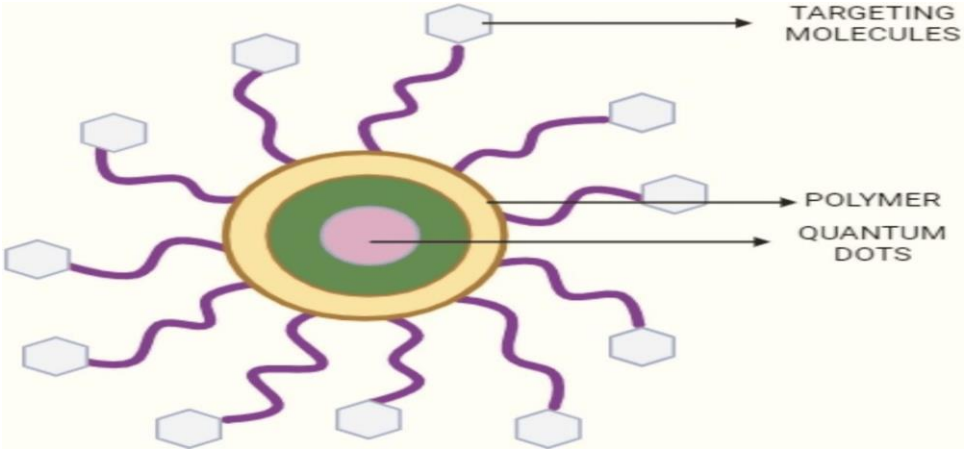

Figure 3: Quantum dots as a polymeric nanocarrier.

Applications of QDs[11]

1. Functionalizing specific ligands on QD surface.
2. Used as nano-carrier for drug delivery.
3. Used as a multimodel probe to monitor.
4. Used for identifying and differentiating biological molecules.
5. diagnosis.
6. cancer therapy:

Drug delivery

The development of diagnostic and treatment capabilities into one nanoparticle-based agent has been the focus of several groups.[9-11] QDs are good candidates as theranostic platforms, as they can act as the main nano-carrier or be part of a more complex architecture as the fluorescent labels. Paclitaxel (PTX), a widely acknowledged drug choice for the treatment of various human cancers, along with QDs were co-loaded in nano-structured lipid carriers in order to have theranostic approach in cancer therapy the results from Olerile et al 25 showed an encapsulation efficacy of ~80% and drug loading of 4.68% with a tumor growth inhibition rate of 77.85% In other study, hybrid silica nanocapsules that were loaded with core–shell and the anticancer drug PTX have been proposed by Zhao et al as theranostic platforms for chemotherapy and fluorescence imaging. The setup involved hydrophobic inner cores that contain the PTX molecules and the QDs and a hydrophilic silica outer shell with amino groups on the surface as anchors for the targeting molecules. Results showed that solubility of PTX was enhanced 630 times while the drug could be sustained released in 12 h.[9]

The Growing Role of QDs in Cellular Biology

Within the multi-encompassing descriptor of 'cellular biology', there are three primary subdivisions that can be used to characterize the function and potential applications of QDs in this area: (1) passive fluorophores, (2) active sensors, and (3) as potent theranostic research tools, As passive fluorophores, QDs are mainly used to label cells or specific subcellular structures such as organelles for imaging and tracking applications. Here the primary property that is exploited is that of fluorescence where the intrinsically broad absorption allows for one, or multiple differentially emissive QDs, to be excited with a single excitation wavelength. This can be either in a direct excitation modality (e.g., UV lamp) or when using a multiphoton laser source.[11]

Bioconjugation

The attachment of biological molecules to NPs, i.e., bioconjugation, Regardless of whether the biological is a small drug or peptide or a large supramacromolecular protein complex, the bioconjugation technique utilized should ideally provide for control over: (1) the ratio of biological per QD(valence); (2) the orientation of the biological on the QD; (3) the separation distance between QD and biological; (4) affinity of their interaction; moreover, (5) the orientation should be homogeneous for all biologicals; and (6) the chemistry used should be applicable with all manner of QDs and biologicals.

Cellular Delivery of QDS

Facilitated QD delivery typically relies on the association or decoration of the QD surface with a polymer of biological (e.g., peptide, protein) to drive initial interactions of the QD with plasma membrane and ultimately its internalization by endocytosis again.

Active techniques involve the direct, physical manipulation of the cell (e.g., microinjection) to introduce the QD to the cellular environment.

Passive QD Delivery

The primary advantage of passive QD delivery is its simplicity; the QDs are merely incubated with cultured cells and the physicochemical nature of the QD surface functionalization drives cellular internalization. Several studies have examined the utility of this approach for QD delivery with a focus toward the resulting impact on cellular homeostasis.[11]

Active QD Delivery

The active delivery of QDs to cells involves the direct manipulation of the cell to translocate the QD across the plasma membrane barrier with the goal of targeting the

cytosol or other subcellular structures. A boron nitride nanoneedle/electrode (50 nm diameter) coated with a thin layer of gold was decorated with streptavidin-coated QDs by their conjugation to a self-assembled monolayer (SAM) on the needle surface. Once in position, application of an electrical potential to the needle/electrode caused desorption of the SAM and the release of discrete amounts of monodisperse QDs that could be tracked within the nucleus the use of the hypotonic environment was critical to provide unidirectional flow of QDs present in the surrounding medium into the cell while eliminating the loss of intracellular contents.[11,12]

GQDs in Cancer Therapy

The integration of cancer diagnosis and treatment has been always a concern for the biomedical researchers. Although considerable progress has been made in targeting drug delivery systems to deliver anticancer drugs to specific sites of interest, new nanomaterials are often developed and explored for better drug delivery efficiency.[13,14] Generally, there are enhanced permeability and retention (EPR)-pH delivery-release mode, ligand-pH delivery-release mode, EPR-Photo-thermal Delivery-Release Mode, and Core/Shell-Photo-thermal/magnetic thermal delivery-release mode. In addition, other delivery-release modes are generally used to treat non-tumor diseases.[11,13] Quantum dot technology has significantly influenced cancer therapy, offering a promising approach to diagnosis and treatment.[15] The unique properties of QDs, such as their tunable size, stable photoluminescence, and large surface-to-volume ratio, enable them to be a desirable platform for a range of uses. in cancer management. Sentinel lymph node (SLN) mapping is a critical stage in cancer surgery, as it identifies the main lymph nodes responsible for receiving metastases from the primary tumour. Predictive staging and the direction of surgical procedures depend on this technique. Through the process of mapping the SLN, surgeons are able to precisely remove the initial set of nodes that are most likely to contain metastases, guaranteeing complete removal of the tumour and reducing the likelihood of recurrence. The SLN is typically identified using a blend of approaches, including radiographic lymph mapping, indigo colourant, and an intraoperative radiation detector.[14,15] Empirical evidence suggests that this methodology can augment the precision of lymph node staging, mitigate the necessity for supplementary lymph node dissections, and ameliorate overall patient outcomes. Earlier sentinel lymph node mapping techniques employed the use of radiotracers, such as technetium-99m (tc-99m), albumin colloids, and lymphazurin, for localization. However, these methods were limited by the potential for cellular damage, radiation dose, and the failure to visualise lymphatic tracers effectively. The precise identification and removal of SLN, which is essential for cancer surgery, was hampered by these restrictions. Quantum dots have been developed to improve the detection and resection of SLNs in cancer surgery. These nanoparticles offer enhanced light penetration through thick tissue, allowing for more accurate and minimally invasive SLN localisation. This improved penetration enables surgeons to minimise the size of surgical incisions, reducing patient morbidity and improving overall outcomes. Quantum dot application in SLN mapping has the potential to facilitate the complete removal of the primary tumour in a single surgical procedure. By providing enhanced visualisation and precise localisation of the sentinel lymph nodes, QDs enable surgeons to accurately identify and resect the lymph nodes most likely to harbour metastatic disease. Figure 4 shows how drugs are delivered to cancer cells via QDs mediated by receptors. Tumour-associated marker expression levels can be measured before and after cancer surgery using bioconjugated QD nanocrystals. This approach allows for the assessment of residual neoplastic cells that may remain following the primary surgical intervention. By utilising the unique optical properties and targeting capabilities of QDs, surgeons and clinicians can gain valuable insights into the tumour microenvironment and the presence of any residual disease.[16]

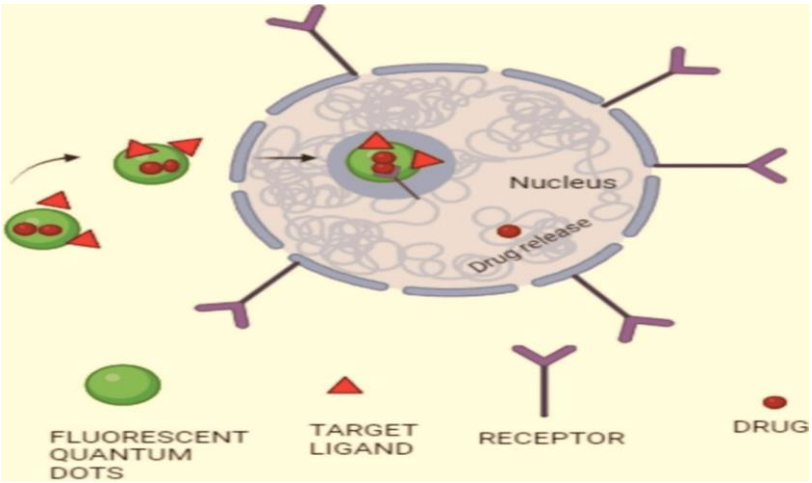

Figure 4: Drug delivery through quantum dots by receptor-mediated in cancer cells.

Sources and Rationale Behind NCDs

Natural products have always gained the interest of researchers because of their limitless source and eco-friendly nature. NCDs are CDs which are synthesized from natural raw materials, which are economical non-toxic, mostly renewable and easy to synthesize. There are numerous other naturally occurring raw materials which have been employed for the preparation of NCDs such as carrot roots, egg yolk oil, chitosan, sucrose, raw cashew gum, lotus root, konjac flour, curcumin, mangosteen peel, N-acetyl-L-cysteine. In addition, researchers are also focusing on recycling biomass wastes because of the alarming effects of the environment. These recycled sources are low cost, eco-friendly, sustainable and help reduce the environmental burdens of the society. synthesis method and modifications of NNCDs Basically two main approaches are adopted for the synthesis of NCDs which are broadly categorized into 'Bottom – up' and 'Top – down' method. The 'Bottom-up' method utilizes small organic molecules through partial dehydration and dehydrogenation accompanied by microwave, thermal pyrolysis, hydrothermal or solvothermal decomposition whereas the 'Top-down' method proceeds via the breakdown of relatively large particles into smaller molecules or nanoparticles via laser ablation, arc discharge, ultrasonic or chemical oxidation. In the Bottom-up approach, the hydrothermal method is the most popular which proceeds by directly heating aqueous solutions containing the intended natural source. This single method is capable of covering four crucial stages which are dehydration, polymerization, passivation and carbonization. This method is widely accepted because it can be easily controlled, simple, economic, energy-efficient and results in non-toxic NCDs.[15] However, the requirement of high temperature, lengthy process time, low quantum yield and necessarily require high temperature furnace, which is not practically available in laboratories are some major drawbacks. Another method is Microwave-assisted synthesis which involves electromagnetic radiation for transforming the precursors into desired NCDs. This method is highly efficient, selective, high yield, short reaction times, easy, rapid, energy-saving, controlled temperature, controlled size, low impurity, improved safety, better reproducibility, and cost-effective. However, this method lack in in-depth penetration. In the 'Top-down' approach, the ultrasonic method is most popular which involves high intensity wavelength to produce NCDs via chemical modifications. The credit to this method is consumption of low external energy and ameliorated precursor reactivity. However, these modifications results in low yield. After synthesis, the prepared uneven sized NCDs are subjected to filtration, centrifugation and/or dialysis to remove the larger particles and to obtain the desired particle size.[16,17]

Mechanism Behind Optical Properties Useful for Drug Delivery of NCDs

are well suited for monitoring the drug release and real-time tracking of individual nanocarriers, because of the fact that CDs absorb light over a wide UV spectrum to emission wavelength of the particle and also emit light with high intensity in a narrow spectral range, which depends upon the core size of the dots. Besides, common organic fluorophores are too dim to detect with high sensitivity and get quenched rapidly under continuous illumination. This feature is compromised in CDs which possess high brightness, long term monitoring and can also be improved by surface functionalization and passivation of CDs. Moreover, the most biological molecules emit light in the blue-green spectral range and CDs shift emission toward red and near infrared region (NIR). Therefore, clear contrast could be easily achieved between CDs and the tissue displaying auto-fluorescence allowing excitation by the blue green light. CDs which emit light in the NIR region are useful for in vivo fluorescence imaging because of the absorption and scattering of visible light by biological tissues. The small dimension CDs with optical properties as well as extremely large Red (Stokes) shift prove promising model as nanocarrier for real-time intravital tracking and biodistribution study.[14,15]

CONCLUSION

It is clear that QDs have great potential for applications in areas such as drug delivery,. In order to see QDs realistically translated in clinical applications, several issues still need to be addressed, such as overall toxicity, body clearance, synthesis protocol scalability, environmental impact, manufacturing costs and so on. By combining QDs with other types of nanoparticles and/or biological active molecules, theranostic platforms are constantly being developed. GQDs have been proved to be able to not only delivery anticancer drugs in various DDRS modes, but also act as nanocarriers to transport gene, peptides, and other non-anticancer drugs. However, before their practical applications in biomedicine and clinical practice, many challenges need to be addressed. Despite of the large improvement in the biocompatibility of GQDs, systematic studies on their potential long-term toxicity and how GQDs affects the immune systems, reproductive systems, and nerve systems in different animal models are needed. GQDs synthesized with different ways exhibited tremendous variations in their physic-chemical properties. Conflicting claims with respect to the biological properties of GQDs have been reported, such as their inherent antibacterial ability. Therefore, a standard for characterization of GQDs is needed and would help to understand more clearly about the various GQDs researches. In addition, the size of GQD has great influence on its toxicity, surface functionalization and the ability to cross biological barriers. More systematic studies involving the size of GQDs are still needed in the future.

REFERENCES

1. Chatterjee, P.; Dhibar, S. Nanomaterial Marvels: Pioneering Applications and Cutting-Edge Advancements in Drug Delivery. Nano Med. Mater, **2023;** 3: 220. [CrossRef]
2. Chehelgerdi, M.; Chehelgerdi, M.; Allela, O.Q.B.; Pecho, R.D.C.; Jayasankar, N.; Rao, D.P.; Thamaraikani, T.; Vasanthan, M.; Viktor, P.; Lakshmaiya, N.; et al. Progressing Nanotechnology to Improve Targeted Cancer Treatment: Overcoming Hurdles in Its Clinical Implementation. Mol. Cancer, **2023;** 22: 169. [CrossRef] [PubMed]
3. Sathe, K.P.; Garud, N.S.; Bangar, V.B.; Gadakh, N.R. A Review on Quantum Dots (QDS). J. Adv. Sci. Res., **2022;** 13: 23–27. [CrossRef]
4. Ebeid El-Zeiny, M.; Okba, E.A. Quantum Dots: Their Unique Properties and Contemporary Applications. In Advances in Semiconductor Physics, Devices and Quantum Dots—Nanotechnology and Future Challenges; IntechOpen: London, UK, 2024; 1–26.
5. Khan, M.S.; Sheikh, A.; Abourehab, M.A.S.; Gupta, N.; Kesharwani, P. Understanding the Theranostic Potential of Quantum Dots in Cancer Management. Mater. Today Commun., **2023;** 36: 106424. [CrossRef]
6. Zahid MU, Ma L, Lim SJ, Smith AM. Single quantum dot tracking reveals the impact of nanoparticle surface on intracellular state. Nat Commun., 2018 May 8; 9(1): 1830. Doi: 10.1038/s41467-018-04185-w. PMID: 29739927; PMCID: PMC5940692.
7. Matea CT, Mocan T, Tabaran F, Pop T, Mosteanu O, Puia C, Iancu C, Mocan L. Quantum dots in imaging, drug delivery and sensor applications. Int J Nanomedicine, 2017 Jul 28; 12: 5421-5431. Doi: 10.2147/IJN.S138624. PMID: 28814860; PMCID: PMC5546783.
8. Jain S, Shukla K, Jain V, Saraf S, Saraf S. Nanoparticles: emerging carriers for delivery of bioactive agents. Pharma Times., 2007; 39(1): 30-5.
9. Zhao C, Song X, Liu Y, Fu Y, Ye L, Wang N, Wang F, Li L, Mohammadniaei M, Zhang M, Zhang Q, Liu J. Synthesis of graphene quantum dots and their applications in drug delivery. J Nanobiotechnology, 2020 Oct 2; 18(1): 142. Doi: 10.1186/s12951-020-00698-z. PMID: 33008457; PMCID: PMC7532648.
10. Jain NS, Somanna P, Patil AB: Application of quantum dots in drug delivery. Nanosci Nanotechnol – Asia, 2021; 12: e070921191305. 10.2174/2210681211666210211092823
11. Singh R, Lillard JW Jr. Nanoparticle-based targeted drug delivery. Exp Mol Pathol, 2009 Jun; 86(3): 215-23. Doi: 10.1016/j.yexmp.2008.12.004. Epub 2009 Jan 7. PMID: 19186176; PMCID: PMC3249419.
12. Ho YP, Leong KW. Quantum dot-based theranostics. Nanoscale, 2010 Jan; 2(1): 60-8. Doi: 10.1039/b9nr00178f. Epub 2009 Oct 6. PMID: 20648364; PMCID: PMC2965651.
13. Probst CE, Zrazhevskiy P, Bagalkot V, Gao X. Quantum dots as a platform for nanoparticle drug delivery vehicle design. Adv Drug Deliv Rev., 2013 May; 65(5): 703-18. Doi: 10.1016/j.addr.2012.09.036. Epub 2012 Sep 20. PMID: 23000745; PMCID: PMC3541463.
14. Qiu J, Zhang R, Li J, Sang Y, Tang W, Rivera Gil P, Liu H. Fluorescent graphene quantum dots as traceable, pH-sensitive drug delivery systems. Int J Nanomedicine, 2015 Oct 28; 10: 6709-24. Doi: 10.2147/IJN.S91864. PMID: 26604747; PMCID: PMC4630193.
15. Pardo J, Peng Z, Leblanc RM. Cancer Targeting and Drug Delivery Using Carbon-Based Quantum Dots and Nanotubes. Molecules, 2018 Feb 10; 23(2): 378. Doi: 10.3390/molecules23020378. PMID: 29439409; PMCID: PMC6017112.
16. Iannazzo D, Pistone A, Celesti C, Triolo C, Patané S, Giofré SV, Romeo R, Ziccarelli I, Mancuso R, Gabriele B, Visalli G, Facciolà A, Di Pietro A. A Smart Nanovector for Cancer Targeted Drug Delivery Based on Graphene Quantum Dots. Nanomaterials (Basel), 2019 Feb 18; 9(2): 282. Doi: 10.3390/nano9020282. PMID: 30781623; PMCID: PMC6409783.
17. Yong KT, Wang Y, Roy I, Rui H, Swihart MT, Law WC, Kwak SK, Ye L, Liu J, Mahajan SD, Reynolds JL. Preparation of quantum dot/drug nanoparticle formulations for traceable targeted delivery and therapy. Theranostics, 2012; 2(7): 681-94. Doi: 10.7150/thno.3692. Epub 2012 Jul 27. PMID: 22896770; PMCID: PMC3418929.