*Available online www.jocpr.com*

**Journal of Chemical and Pharmaceutical Research, 2015, 7(4):810-814**

**Review Article**

**ISSN : 0975-7384**
**CODEN(USA) : JCPRC5**

# Quantum dots: A potential candidate as a biomedical material

**Shefali Arora*[1], Mamta Latwal[1], Shaiely Singhal[1], Shilpi Agarwal[1], K. Mohan Reddy[1] and Deepak Kumar[2]**

[1]*Department of Chemistry, College of Engineering Studies (CoES), University of Petroleum and Energy Studies (UPES), Dehradun, Uttarakhand, India*
[2]*Department of Pharmaceutical Chemistry, Dolphin (PG) Institute of Biomedical and Natural Sciences, Dehradun, Uttarakhand, India*

---

**ABSTRACT**

*Quantum dots (QDs) have generated tremendous interest due to their unique optical properties that enable effective their direct applications in optoelectronics and biomedical fields. Recent assays developed so far comprising of quantum dots have paid attention on the fact these nano materials pose good fluorescence properties, in fluorescence the biosensor's capability of quenching the photoluminescence intensity meditated by the quantum dots is monitored as a quantity of analyte gets introduced in the biosensor solution media, resulting into a photon signal. The produced photoluminescence intensity is proportional to the substrate concentration added. As far as dyes are concerned quantum dots (QD) are proposed as novel alternative to replace costly dyes. Additionally, it has advantageous properties like solar spectrum matching, multiple electron hole generation ability and tailor made which make them suitable candidate as a sensitizer/co-sensitizer in DSSC. Despite the interesting properties hosted by these QDs, the potential leakage of metal ions by chemical dissolution under biological conditions may generate oxidative stress in living cells. Accordingly, the passivation of the surface of the QDs, in order to make them biologically inert without affecting their optical properties, becomes indispensable. In continuation of this, we tried to review the types and various biological applications of quantum dots.*

**Keywords:** Quantum dots, Biosensing, DSSC, optical device and fluorescence, biological applications.

---

## INTRODUCTION

Quantum dots (QDs) belong to a new class of fluorescent agent for biochemical, medicinal or other purposes. Semiconductor nanocrystals (NCs), also called quantum dots (QDs), range between 2 to 10 nm, or 10 to 50 atoms, in diameter. These dimensions lead to unique characteristics which are situated in between the molecular and solid state regime. Behavior of quantum dots can be described as oxidation and reduction of the core of QDs. The QDs confine electrons, holes, or electron-hole pairs. This confinement leads to discrete energy levels, which can be controlled by changing the size and shape of the QDs. As the particle diameter is reduced, the energy gap is blue–shifted due to the so-called "quantum confinement effect," which may be modeled as a particle in a three-dimensional spherical box. Therefore, the band gap energy ($E_{gap}$) of these materials is tunable over a wide spectral range. Because of their valuable physicochemical properties, QDs are most appealing candidates to play the role of active components in new generations of photochemical molecular devices. Nano-material especially quantum dots continue to pose interesting physical, electronic and chemical properties because of their small size, size tune able band gaps and the feasibility to surface modify them with a variety of capping agents for desired property or application [1-2] which makes them enormously popular for a variety of applications such as in: optical devices [3], biolabelling [4], biosensing [5] and recently these small semiconductors nanomaterials have been used for improvement of properties in existing light emitting diode devices; to improve features such as brightness and fluorescence [6]. Recent assays developed so far comprising of quantum dots have paid attention on the fact these

nano materials pose good fluorescence properties [7], in fluorescence the biosensor's capability of quenching the photoluminescence intensity meditated by the quantum dots is monitored as a quantity of analyte gets introduced in the biosensor solution media, resulting into a photon signal. The produced photoluminescence intensity is proportional to the substrate concentration added.

**A: SMART PROPERTIES OF QUANTUM DOTS**

During the past few decades, the work on semiconductor nanocrystals has immensely improved due to their remarkable optical, electrical and catalytic properties. The surface chemistry behavior of luminescent quantum dots is of immense interest as it has strengthened the development of multiple probes based on linked recognition molecules, such as peptides, nucleic acids or small-molecule ligands. These highly luminescent semiconductor nanocrystals have found extensive applications in different fields, ranging from optoelectronic to bio-imaging. Their surface is also suitable for modification via incorporation of required functionality, and good biocompatibility [8-10], and they are also highly efficient multi-photon absorbers that can be potentially useful for three dimensional multi-photon microscopy and imaging [11]-a rapidly developing area for both biological and medical applications. These features make QDs one of the most promising nanomaterials for biological staining, detection of bio-macromolecules, and immunohistochemistry [12, 13]. The most popular types of QDs include CdTe, CdSe, ZnSe, and ZnS; however, metals, such as In, Ga, and many others also can be used [14, 15]. Despite the interesting properties hosted by these QDs, the potential leakage of metal ions by chemical dissolution under biological conditions may generate oxidative stress in living cells. Accordingly, the passivation of the surface of the QDs, in order to make them biologically inert without affecting their optical properties, becomes indispensable. In continuation of this, we tried to review the types and various biological applications of quantum dots.

The properties responsible for fluorophore behavior are the width of excitation spectrum, width of emission spectrum, photostability and the decay time. QDs have broad absorption spectra than conventional dyes which have narrow spectra. Due to this, different coloured QDs can be excited simultaneously using a single wavelength [16, 17]. QDs also have narrow emission spectra which allow them to emit light at a variety of precise wavelengths from UV to IR. These properties of QDs makes them well suited to multiplexed imaging, in which multiple colours & intensities are combined to encode genes, proteins and small molecules [17, 18]. Photostability is a critical feature in most fluorescence applications, and is an area in which QDs have singular advantage. Unlike organic fluorophores which bleach after only a few minutes on exposure to light, QDs are extremely stable and can undergo repeated cycles of excitation and fluorescence for hours with a high level of brightness and photobleaching threshold [17, 19]. QDs have been shown to be more photostable than a number of organic dyes [20, 21], including Alexa488, reported to be the most stable organic dye [22]. Dihydrolipoic acid (DHLA)-capped cadmium selenide-zinc sulfide (CdSe-ZnS) QDs showed no loss in intensity after 14 h, and were nearly 100 times as stable as, and also 20 times as bright as, rhodamine 6G [21]. QDs also have a long fluorescent lifetime after excitation, which may be taken advantage of in time-gated imaging. The fast fluorescence emission of organic dyes upon excitation (<5 ns) coincides closely with short-lived autofluorescence background from many naturally occurring species, reducing the signal-to-noise ratio. Conversely, QDs emit light with a decay time in the order of a few tens of nanoseconds (30–100 ns) at room temperature, which is slower than the autofluorescence background decay, but fast enough to maintain a high photon turnover rate [23, 24]. In time-gated analysis, photons hitting in the first few nanoseconds are disregarded to decrease background noise and increase sensitivity. The usefulness of this has been shown in producing images of 3T3 mouse fibroblasts with a high signal-to-background ratio [25], and in following erbB1 and erbB3 receptors.

Bare QDs have proven impractical for two reasons. Firstly, the crystalline structure of nanoparticles lends itself to imperfections and secondly, they are highly reactive due to large surface area : volume ratio [26]. Therefore the capping of QDs is done. ZnS capping have shown to increase the stability and performance of QDs [27].

Cytotoxicity of QDs has been observed in a large number of *in vitro* studies, affecting the cell growth and viability. It has been demonstrated that the degree of QDs toxicity is closely connected with different parameters such as cell number, cell growth, apoptosis, cellular morphology or metabolic activity change of targeted tissue [28]. Metals such as Cd and Se are very toxic and their toxicity is well documented by several researchers. These heavy metals can cross the blood-brain barrier, can accumulate in adipose tissue with biological excretion half-lives greater than ten years, are primarily toxic to the liver and kidneys, and are considered possible teratogens and probable carcinogens [29, 30]. In addition to this, the unique QD nanoscale structure presents a complex set of physiochemical characteristics that further compounds any simple studies or conclusions in this area. The crystalline core of QDs can be made from different combinations of binary semiconductors such as CdSe, CdTe, CdS, etc. The cores are commonly encapsulated with a secondary semiconductor material and are then functionalized with a variety of surface coating ligands including small thiolated molecules or larger amphiphilic polymers for aqueous compatibility [31].

**B: Biological Applications**

Semiconductor nanocrystal quantum dots (QDs), owing to their unique opto-electronic properties determined by quantum confinement effects, have been the subject of extensive investigations in different areas of science and technology in the past two decades. Apart from executing a large number of biological applications, there have been dramatic improvements in understanding surface chemistry, biocompatibility, and targeting specificity by the use of QDs. Inorganic nanostructures that interface with biological systems have recently attracted widespread interest in biology and medicine. Nanoparticles are thought to have potential as novel intravascular probes for both diagnostic (e.g., imaging) and therapeutic purposes (e.g., drug delivery). Critical issues for successful nanoparticle delivery include the ability to target specific tissues and cell types and escape from the biological particulate filter known as the reticuloendothelial system.

The use of luminescent colloidal quantum dots in biological investigations has increased dramatically over the past several years due to their unique size-dependent optical properties and recent advances in biofunctionalization. Quantum dots (QDs) light-emitting particles on the nanometer scale are emerging as a new class of fluorescent agent for in vivo imaging [32]. QDs often consist of cadmium(II) ions and/or ions of other metal such as selenium, tellurium or zinc [33] and can be used for fluorescent labelling of biomolecules [34, 35]. In addition, these particles can be modified by a recognition molecule such as an antibody and then, QD–antibody complex can be used for identification and visualisation of necrotic lesions or tumour cells [36]. Wang et al. [37] showed that the QDs could be bound by proteins in an organism very easily. However, toxicity of QDs must be considered. Their toxicity is predominantly caused by their disintegration to well-soluble inorganic ions, mostly cadmium(II) [38]. Many studies have shown the great potential of using quantum dots as new probes in vitro and in vivo involving their usage in immunolabeling, cell tracking, in situ hybridization, FRET, in vivo imaging, and other related technologies.

Recent advances in nanomaterials have produced a new class of fluorescent labels by conjugating semiconductor quantum dots with biorecognition molecules. These nanometer-sized conjugates are water-soluble and biocompatible, and provide important advantages over organic dyes and lanthanide probes [39]. In particular, the emission wavelength of quantum-dot nanocrystals can be continuously tuned by changing the particle size, and a single light source can be used for simultaneous excitation of all different-sized dots. High-quality dots are also highly stable against photobleaching and have narrow, symmetric emission spectra. These novel optical properties render quantum dots ideal fluorophores for ultrasensitive, multicolor, and multiplexing applications in molecular biotechnology and bioengineering. Amelia et al. [40] have reported the comparison of photophysical properties of two series of CdSe quantum dots (QDs) differing in their particle size. They synthesized CdSe QDs according to frequently used protocols of the same synthetic procedure. For each sample the photophysical properties and the potentials for the first reduction and oxidation processes in organic solution were determined. The band gap obtained from electrochemical experiments is compared with that determined from the absorption and luminescence spectra. While the optical band gap decreases upon increasing the nanocrystal diameter, as expected on the basis of quantum confinement, the redox potentials and the electrochemical band gap are not monotonously related to the QD size. For both series, the smallest and largest QDs are both easier to oxidize and reduce than mid-sized QDs. In fact, the latter samples exhibit very broad voltammetric profiles, which suggested that the heterogeneous electron-transfer processes from/to the electrode are kinetically hindered. Conversely, the electrochemical band gap for the smallest and largest particles of each series is somewhat smaller than the optical band gap. These results indicate that, while the optical band gap depends on the actual electron–hole recombination within the nanocrystal, and therefore follows the size dependence expected from the particle-in-a-box model, the electrochemical processes of these QDs are strongly affected by other factors, such as the presence of surface defects. The investigations suggest that the influence of these defects on the potential values is more important for the smallest and largest QDs of each series, as confirmed by the respective luminescence bands and quantum yields. An interpretation for the size-dependent evolution of the surface defects in these nanocrystals is proposed based on the mechanism of their formation and growth.

A very interesting application of QDs is the assaying of cell mortality which is widely accepted to correlate strongly with metastatic potential [41]. For measuring this, there is one method in which phagokinetic tracks are measured which are left when cell pass over a layer of markers and ingest them. Previously, gold nanoparticles were used but due to some practical difficulties they did not give good response. Now, QDs have been investigated as an alternative, and with substrate incorporating QDs, phagokinetic tracks created by human mammary epithelial cells and non-tumour cells have been observed [42].

One of the broadest uses of fluorescent probes in biology is the labeling of cellular structures. Naturally, the earliest demonstrated uses of QDs in biology were to label cells with a new class of bright and stable fluorophores. Multicolor labeling of cells is a powerful technique for visualizing many of these structures simultaneously, such as cytoskeletal proteins or organelles, and to elucidate intracellular processes. Although cell labeling with organic dyes

has been commonplace for decades, using multiple labels simultaneously remains a cumbersome procedure due to the narrow absorption profiles of most dyes. Effective multicolor labeling requires an assortment of filters to properly excite and collect fluorescence from specific dye molecules. Moreover, if laser excitation is used, multiple sources are typically required to excite all of the dyes labeling the cell which can be expensive and requires a complex microscopy arrangement specific to the experiment. The continuous excitation of dyes inevitably results in significant photobleaching that quenches the luminescence over short time scales (seconds to minutes). This severely limits the practical observation time for a sample, even with the addition of various anti-bleaching chemical agents [43].

Gao et al. [44] have reported the development of multifunctional nanoparticle probes based on semiconductor quantum dots for cancer targeting and imaging in living animals. Their work involved encapsulation of luminescent QDs with a copolymer and then linking this amphiphilic polymer to tumor-targeting ligands and drug-delivery functionalities. Their work reflects that sensitive and multicolor fluorescence imaging of cancer cells can be obtained under *in vivo* conditions which could be very helpful for ultrasensitive and multiplexed imaging of molecular targets.

de Farias et al. [45] have reported a new methodology for the determination of red blood cell antigen expression by a simple labeling procedure employing luminescent semiconductor quantum dots. They obtained highly luminescent and stable core shell cadmium sulfide/cadmium hydroxide colloidal particles with a predominant size of 9 nm. The core-shell quantum dots were functionalized with glutaraldehyde and conjugated to a monoclonal anti-A antibody to target antigen-A in red blood cell membranes. Erythrocyte samples of blood groups A+, A2+, and O+ were used for this purpose. Confocal microscopy images showed that after 30 min of conjugation time, type A+ and A2+ erythrocytes presented a bright emission, whereas the O+ group cells showed no emission. Fluorescence intensity maps showed different antigen expressions for the distinct erythrocyte types. These results strongly suggested that this simple labeling procedure may be employed as an efficient tool to investigate quantitatively the distribution and expression of antigens in red blood cell membranes.

Stsiapura et al. [46] have developed a methodology for incorporating solubilized CdSe/ZnS core/shell nanocrystals (NCs) into functionalized carboxylated polystyrene latexes 0.3-1 microm in diameter via a swelling procedure. They used them for the production of homogeneous, highly fluorescent polymeric beads (HFPBs), which were found to be comparable in brightness to standard polymeric microspheres doped with organic fluorophores and more photostable than the latter by more than 50 times. The three-dimensional (3D) confocal analysis of individual 1-microm HFPB demonstrated that the beads were doped with the NCs almost homogeneously. HFPBs 0.3 microm in diameter were conjugated with anti-mouse polyvalent immunoglobulins and used for immunofluorescent detection of p-glycoprotein, a mediator of the multidrug resistance phenotype, overexpressed in the membrane of MCF7r breast adenocarcinoma cells. The photostability of NCs-tagged HFPBs offers obvious advantages for the reconstruction of 3D confocal fluorescence images of antigen distribution, and their exceptionally high brightness combined with photostability permits the detection of a single antigen molecule using a standard epifluorescence microscope.

## CONCLUSION

In this study of the review, most applications of the QDs in analytical purposes make use of their fluorescent properties like physico-chemical properties. Although QDs show excellent electrochemical properties when properly functionalized, their use in electrochemical systems for analytic purposes are at the onset. ZnO semiconductors electrodepostions on the surface of a glossy carbon electrodes for determination of various acids such as uric acid, ascorbic acid. The main work reflects that sensitive and multicolor fluorescence imaging of cancer cells can be obtained under *in vivo* conditions which could be very helpful for ultrasensitive and multiplexed imaging of molecular targets.

**Acknowledgment**
All the authors are acknowledging the UPES, Dehradun, Uttarakhand, India for their continuous support and financing the work and R&D of UPES, Dehradun, India for the facilities and support.

## REFERENCES

[1] P Kumara; K Singh. *Journal of Optoelectronic and Biomedical Materials Wurtzite*, **2009,** 1, 59 - 69.
[2] KP Singh; WK Kang; R Hee-Woo. *Electrochemistry Communications*, **2009,** 11, 1247–1250.
[3] L Yang; J Yang; X Liu; Y Zhang; Y Wang; H Fan; D Wang; J Lang. *Journal of Alloys and Compounds*, **2008,** 463, 92–95.
[4] MA Walling; JA Novak. *Journal of Molecular Science*, **2009,** 10, 441-491.

[5] PM Ndangili; OA Arotiba; PGL Baker; EI Iwuoha. *Journal of Electroanalytical Chemistry*, **2010,** 643, 77–81.
[6] B Suo; X Su; J Wu; D Chen; A Wang; Z Guo. *Materials Chemistry and Physics*, **2010**, 119, 237-242.
[7] WR Algar; AJ Tavares, UJ Krull. *Analytica Chimica Acta*, **2010,** 673, 1-25.
[8] FH Huang; GN Chen. *Spectroc. Acta A*, **2008,** 70, 318–323.
[9] P Juzenas; W Chen; YP Sun; MAN Coelho; R Generalov; N Generalova, LL Christensen. *Adv. Drug Deliv. Rev.*, **2008**, 60, 1600–1614.
[10] MG Lu; KT Al-Jamal; K Kostarelos; J Reineke. *ACS Nano.*, **2010,** 4, 6303–6317.
[11] T Jamieson; R Bakhshi; D Petrova; R Pocock; M Imani; AM Seifalian. *Biomaterials*, **2007** 28, 4717–4732
[12] S Jin; YX Hu; ZJ Gu; L Liu; HC Wu. *J. Nanomater*, **2011,** 2011, 1–13.
[13] SJ Rosenthal; JC Chang; O Kovtun; JR McBride; ID Tomlinson. *Chem. Biol.*, **2011,** 18, 10–24.
[14] M Green; P O'Brien. *Chem. Commun.*, **1998,** 22, 2459– 2460.
[15] M Ryvolova; J Chomoucka; L Janu; J Drbohlavova; V Adam; J Hubalek; R Kizek. R. *Electrophoresis.*, **2011,** 32, 1619–1622.
[16] WCW Chan; DJ Maxwell; XH Gao; RE Bailey; MY Han; SM Nie, *Curr Opin Biotechnol*, **2002**, 13, 40–46.
[17] MY Han; XH Gao; JZ Su; S Nie. *Nat Biotechnol*, **2001**, 19, 631–635.
[18] XH Gao; SM Nie. *J Phys Chem B*, **2003,** 107, 11575–11578.
[19] AP Alivisatos. *Science*, **1996**, 271, 933–937.
[20] XY Wu; HJ Liu; JQ Liu; KN Haley; JA Treadway; JP Larson. *Nat Biotechnol*, **2003**, 21, 41–46.
[21] WCW Chan; SM Nie. *Science*, **1998**, 281, 2016–2018.
[22] N Panchuk-Voloshina; RP Haugland; J Bishop-Stewart; MK Bhalgat, PJ Millard; F Mao. *J Histochem Cytochem*, **1999**, 47, 1179–1188.
[23] D Gerion; F Pinaud; SC Williams; WJ Parak; D Zanchet, D; S Weiss. *J Phys Chem B*, **2001,** 105, 8861–8871.
[24] F Pinaud; X Michalet; LA Bentolila; JM Tsay; S Doose; JJ Li. *Biomaterials*, **2006,** 27, 1679– 1687.
[25] M Dahan; T Laurence; F Pinaud; DS Chemla; AP Alivisatos; M Sauer. *Opt Lett*, **2001**, 26, 825–827.
[26] RM Raab; G Stephanopoulos. *Biotechnol Bioeng*, **2004,** 88, 121–132.
[27] L Manna; EC Scher; LS Li, AP Alivisatos. *J Am Chem Soc*, **2002**, 124, 7136–7145.
[28] P Calvo, P; C RemunanLopez; JL VilaJato; MJ Alonso. *J Appl Polym Sci*, **1997**, 63, 125–132.
[29] VL Colvin. *Nature Biotechnol.*, **2003,** 21, 1166–1170.
[30] PH Hoet; I Bruske-Hohlfeld; OV Salata. *J Nanobiotechnol.*, **2004**, 2, 2–12.
[31] IL Medintz; HT Uyeda; ER Goldman. *Nature Mater.*, **2005**, 4, 435–446.
[32] XH Gao; LL Yang; JA Petros; FF Marshal; JW Simons; SM Nie. *Curr Opin Biotechnol*, **2005**, 16, 63–72.
[33] X Michalet; FF Pinaud; LA Bentolila; JM Tsay; S Doose; JJ Li; G Sundaresan; AM Wu; SS Gambhir; S Weiss. *Science*, **2005,** 307, 538–544
[34] F Wang; WB Tan; Y Zhang; XP Fan; MQ Wang. *Nanotechnology*, **2006** 17, R1–R13.
[35] JK Jaiswal; ER Goldman; H Mattoussi; SM Simon. *Natural Methods*, **2004,** 1, 73–78.
[36] FQ Chen; D Gerion. *Nano Letters*, **2004**, 4, 1827–1832.
[37] QS Wang; PF Liu; XL Zhou; XL Zhang; TT Fang; P Liu; XM Min. *J Photochem Photobiol A Chem*, **2012**, 230, 23–30
[38] AM Derfus; WCW Chan; SN Bhatia. *Nano Letters*, **2004,** 4, 11–18.
[39] WCW Chan; DJ Maxwell; X Gao; RE Bailey; M Han; S Nie. *Current Opinion in Biotechnology*, **2002**, 13, 1.
[40] M Amelia; S Impellizzeri; S Monaco; I Yildiz; S Silvi, FM Raymo; A Credi. *Chem Phys Chem***, 2011**,12, 2280–2288.
[41] AW Partin; JS Schoeniger; JL Mohler; DS Coffey. *Proc Natl Acad Sci USA*, **1989**, 86, 1254–1258.
[42] WJ Parak; R Boudreau; M Le Gros; D Gerion; D Zanchet; CM Micheel. *Adv Mater*, **2002**, 14, 882–885.
[43] JR Lakowicz. Principles of Fluorescence Spectroscopy. *Kluwer Academic/Plenum Publishers*, **1999.**
[44] X Gao; Y Cui; RM Levenson; LWK Chung; S Nie. *Nature Biotechnology*, **2004**, 22, 969 – 976.
[45] PMA de Farias; BS Santos; FD de Menezes. *J Biomed Optics*, **2005**, 10, 044023 -044023-4.
[46] V Stsiapura; A Sukhanova; M Artemyev. *Anal Biochem.*, **2004,** 334, 257–265.

.