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Quantum Dots: Need to Explore Potential for Delivery of Drugs and Biomolecules

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Editorial

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Editorial

Quantum dots (QDs) are the semiconductor nanoparticles having the range of 2 nm to 10 nm [1]. One of the properties of semiconductor metals of the group IV to group VI of periodic table, to show fluorescence is established in the biomedical research for quantitative fluorescence imaging and detection [2]. QDs based bio-imaging is widely used. Comparing with other nanoparticles, a distinct property of QDs is excitation of multiple color fluorescence based on particle size. QDs emit the same wavelength of light which is used as excitation wavelength. Therefore with single excitation light source, multiple QDs with different spectra can be observed. The term quantum dot was coined by Mark Reed.

The physics of a semiconductor metal is found to be helpful in the biomedical research. However, likewise, bio imaging properties, it is the need to explore the potential of quantum dots to deliver active pharmaceutical ingredients at the site. QDs can be explored for their potential to target the delivery as well as possibility to track the delivery inside the body. This can be utilized to understand bio-distribution of pharmaceutical active ingredients after administration into the body. In addition to its earlier role, it would be possible to target the drugs and to estimate them quantitatively at the site of action. Thus dual role of quantum dots would be appreciable.

Synthesis of QDs

Commonly used methods for preparation of QDs are colloidal synthesis, lithographic technique, fabrication, viral assembly, electrochemical assembly etc [3]. Besides, the methods reported for synthesis of QDs, green synthesis is also possible. Mariselvam R, et al. [4] reported green synthesis of copper QDs by using root extracts of plant Rubia *cardifolia* having a particle size 22.68 nm. The copper QDs were tested for antibacterial properties. Vidhya K, et al. [5] reported green synthesis of glucose capped ZnO: Fe QDs and used to test antibacterial properties. Vidhya K, et al. [6] similarly, also reported green synthesis of manganese doped, sucrose capped ZnO multifunctional QDs for anticancer activity having the particle size of 12 nm.

Structural Properties and Delivery Potential

Few years back, some of the researchers have carried out the synthesis of quantum dots from its source metal and characterized their particulate properties. The most important property found so far the changing color fluorescence with the particle size. It has been found that the QDs show blue color for the size range of up to 5-10 nm. This size generally increases to 20 nm after polymer application.

The quantum dots below the size of 5 nm are usually filtered and cleared by kidneys. However, relatively larger particles reach to the target site after passing through reticuloendothelial system. Hence the role of optimum particle size is important to evaluate and trace out delivery potential. Other supportive physical properties of quantum dots include narrow size distribution, good flowability, more resistant to degradation than other optical imaging probes. Quantum dots have greater photo stability due to their inorganic nature than other dyes [3] and long fluorescent lifetime after excitation [7]. The

inorganic core; consist of either of semiconductor metal mentioned above serves as imaging contrast agent, above which hydrophobic drug molecules are encapsulated by amphiphilic polymer. The hydrophilic drugs are immobilized on the other side of amphiphilic polymer which is hydrophilic in nature. The hydrophilic drugs and biomolecules are bounded by covalent or non-covalent bonds. This is depicted in Figure 1. Water soluble quantum dots can be designed with amphiphilic polymer, amphiphilic polymer conjugated with poly (ethylene glycol) or encapsulation with block co-polymer micelles [8]. Quantum dots are administered as a colloidal solution through intravenous route, they reach to target and due to their fluorescence, they can be detected.

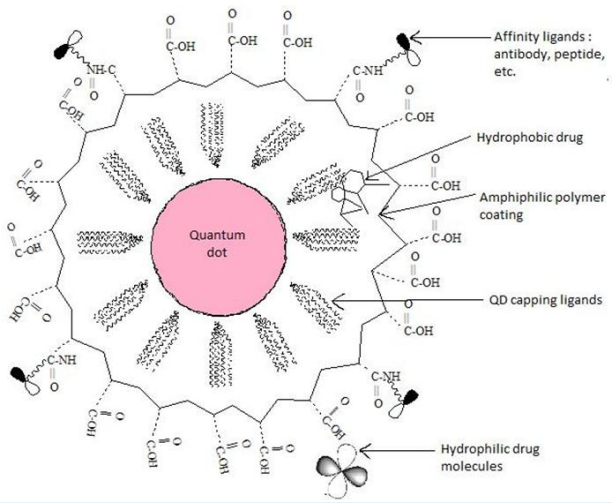

Figure 1: Typical structure of QD showing attachment of ligands, hydrophilic and hydrophobic molecules.

Ketoprofen and Dexketoprofen coated Zno quantum dots of size smaller than 10 nm were prepared for transdermal delivery. The permeability coefficients were estimated by using rat skin. It was observed that the permeability coefficient of Ketoprofen coated Zno quantum dots and Dexketoprofen coated Zno quantum dots were considerably higher than their aqueous solutions respectively [9]. Chakravarthy KV, et al. [10] have reported the ability of nanoconjugates of CdSe/CdS/ZnS quantum dots and doxorubicin to target alveolar macrophages. In the confocal study it was observed that alveolar macrophages cell nucleus and induction of apoptosis. Doxorubicin was showing its activity after coupling with nanoparticles. Ultimately the results demonstrated targeted macrophage selective therapy for the treatment of pulmonary disease. Godbole N, et al. [11] reported quantum dots as carrier for delivery of 5-flurouracil. Eudragit EPO coated ZnO quantum dots having mean particle size of 201.92 nm and zeta potential of +1.85 mv could be synthesized successfully by colloidal synthesis method.

Now the scientists are concentrating on the delivery of functional genes for therapeutic use by quantum dots. Gene delivery systems are mainly viral and nonviral based. However, non-viral is efficient and safe vector for gene delivery. Surface modifications of QDs hold promising approach for traceable gene delivery. For intracellular delivery and real-time imaging of siRNA into cancer cells with significantly reduced cytotoxicity has been reported with Cd-Se QD-amphipol technology, QD-peptide conjugates and 2-vinyl pyridine functionalized silicon quantum dots were designed for SiRNA transfection and therapeutic imaging [12,13]. Cysteamine capped, water soluble CdTe QD vectors, conjugated with plasmid DNA through electrostatic interaction, have been reported. QD-DNA complexes are capable for controllable release of DNA and gene expression in HEK293 cells in the visible mode [14].

Chitosan encapsulated ZnO quantum dots are smart nanocarriers for drug delivery. Chitosan is a natural polymer with *N*-acetyl glucosamine and D-glucosamine, with one amino group and two hydroxyl groups, is promising as to encapsulate quantum dots. Chitosan enables many properties suitable for encapsulation and delivery system. To note, water solubility, chelation with metal ions, easy ligand attachment, biocompatibility, ease of processing, strong electrostatic interaction with negatively charged biomolecules and quantum dots are few of them [15]. ZnO-chitosan-folate system has been used as a nanocarrier for delivery of doxorubicin, an antineoplastic agent used in tumor treatments, through physical and chemical interactions. The release of doxorubicin from ZnO-QD-chitosan-folate carrier is due to presence of folic acid that weakens the electrostatic interaction between doxorubicin and ZnO QDs [16]. Muhammad F, et al. [17] have evaluated ZnO QDs as a platform for targeted and pH responsive intracellular delivery of doxorubicin. Doxorubicin release to the cytosol is favored due to the weakened interaction between Zn^{2+} and doxorubicin in acidic conditions of dissolution. ZnO QDs have shown strong activity against some of Gram- positive and Gram-negative bacteria and biocompatibility with colloidal semiconductor luminescent inorganic materials [18].

Comparing the properties of other nanoparticles used for drug delivery, QDs possess additional property to target the receptors and to help to establish the concentration at the site by bio-imaging.

Water soluble QDs

To obtain biologically active and compatible QDs, newly synthesized QDs are functionalized by applying secondary coat that ensures core durability, water solubility. Water soluble QDs are compact and usually coated with monolayer of any hydrophilic surfactant. This hydrophilic surfactant prevents aggregation and promotes dispersion in aqueous medium. Different surfactants with different terminal groups allow different conjugation of biomolecules. The choice of end group includes primary amines, carboxylic acid and diols. Libin Tang, et al. [19] reported glucose derived water soluble crystalline quantum dots with average diameter of 1.65 nm by microwave assisted method. Yan Li, et al. [20] reported QDs stable at pH 2- 13, water soluble capped by poly (ethylene glycol) modified dithiocarbamate. The poly ethylene segment makes QDs water soluble. Apart from the delivery aspect of water stable quantum dots, its analytical use is admirable. Casa M, et al. [21] have synthesized water stable ZnO quantum dots by simple method by using green solvent at low temperature for detection of aniline compounds in water.

Oil soluble QDs

Oil soluble quantum dots have been prepared by Zeng R, et al. [22] Au: ZnCdS and Au: Zn CdS/ZnS core/shell QDs were prepared with tunable emission color. Au^{+} is used as primary dopant and trivalent cation is used as In^{3+} as co-dopant. This strategy may be useful to control optical properties.

Future Perspectives

QDs may produce immunogenic reactions [23]. They may be ineffective as a result of antibody binding. On the other hand, the metal such as cadmium produce liver toxicity due to it's unlike renal filtration. Cadmium telluride (Cd-Te) QDs are toxic. They are used as fluorescent probes for biological imaging and to track drug targeting. However, researchers were using gelatin in the process of its preparation to minimize toxicity [24]. Therefore, selection of source metal should be optimum. In this regard, Zno quantum dots are gaining much more attention. Thus, minimizing the toxicity would be one of the marked targets in future. None the less, the large numbers of clinical trials are needed to be carried out to improve efficiency and safety of quantum dots. One more critical factor which we must consider that determines the cytotoxicity of QDs is possibility of the leakage of a metal from the core due to photolysis or oxidation [25]. Like drug delivery, use of QDs in drug and chemical analytical field looks emerging in future.

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