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Review Article

Quantum Dots: Method of Preparation and Biological Application

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ABSTRACT

Quantum dots are inorganic semiconductor crystal of nanometer size which having distinctive conductive property depend on its size & shape. After administration of quantum dots parentally they identify target and bound them. Also quantum dots having light emitting property depend on size & shape. Quantum dots are prepared by chemical synthesis method include both organic & water phase synthesis & also by top-bottom approach. Tumor cell targeting & detection of pathogen & toxin are the main application of quantum dots & also in targeting drug delivery system. This review provides the overview of method of preparation of quantum dots & its biological application.

Keywords: Quantum dot, targeting drug delivery, biological application

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Introduction:

Quantum dots established in 1980 by Alexie Ekimov in glass matrix & Louis E Brus in colloidal solution^[2], with the first biological imagine application reported in 1998.^[7]

Quantum dots are inorganic semi-conductor crystal of nanometer dimension with distinctive conductive property by its size and shape. The crystal having size range 1-10 nm. The quantum dots are made from group 2-6 & 3-5 like as Cd, Hg, Pb, Se, Zn & Ag etc.^[4] Smaller the crystal means larger the band gap. Crystal size inversely proportional to band gap.

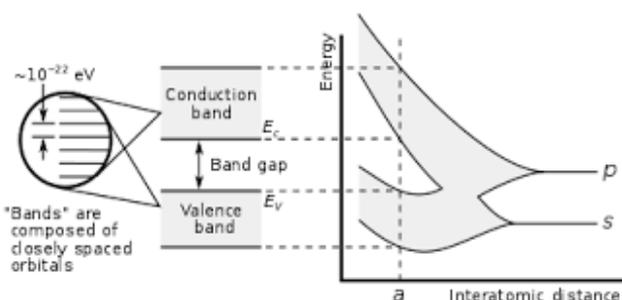


Figure 1 : Energy Diagram Of Quantum Dot.

Greater the difference in highest valence band and lowest conduction band becomes so more energy is needed to excite the dots. [2] generally crystalline solid called nano structure

& when size less than 100 nm. Fabricate them into two dimension called as quantum wells. Again fabricate them into one dimension called as quantum wire & zero dimensional are called as quantum dots.

Quantum dots consist semiconductor core which is made up of Cd, Se. the semiconductor core is coated by shell (ZnS). The ZnS coat for improve optical property of core material. The shells are encapsulated in organic cap (tri-n-octyl phosphine oxide) or with inorganic material having larger band gap for enhancing solubility in aqueous buffer solution.

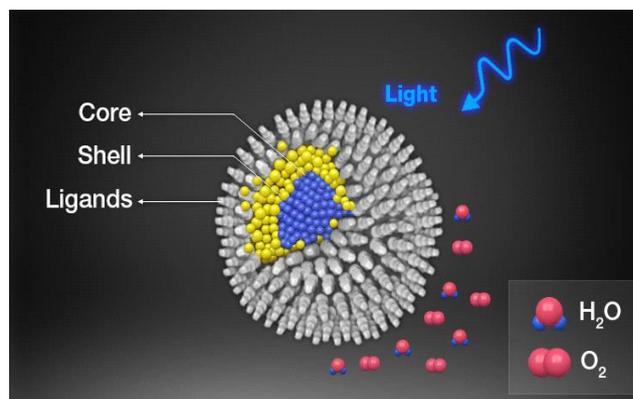


Figure 2: Structure Of Quantum Dot

When crystal is smaller color shifts from red to blue in light emitting. When the larger crystal they shifts towards red and having greater the spectrum.[2] the zero dimensional quantum dots have sharper density than other quantum dots and having superior transport and optical property.[2]

Mode of action of quantum dot:

After the administration of colloidal solution of quantum dot parent rally (i.v, s.c) they identify target and bound them. Once bound to target the quantum dot emit light depend on size. they can fluorescence in variety of color and detect by different technique.

Method of preparation of quantum dots:

A. Chemical synthesis of quantum dots based on organic phase approach & water phase approach:

1. Organic phase method:

a. **Colloidal synthesis:** it is cheap & less toxic method. It consists of precursor organic surfactant & solvent. Reaction medium heated at 300 c with vigorously stirring the precursor are injected by syringe which transform chemically into monomer at super saturation level. The nano-crystal growth starts with nucleation process. The colorless solution transfer to color solution like yellow, orange, red called as quantum dots. In this system surfactant are added to avoid the aggregation and make water soluble quantum dots.

b. **Lithography:** Growing quantum dots in semiconductor hetero structure which refer as one semiconductor sandwich between two other semiconductors. If sandwich layer size less than 10 nm called as quantum wells. The create narrow strip of quantum well called as quantum wire. Rotate the quantum wire in 90° repeat the same procedure on above strip to get the quantum dot.

c. **Epitaxy:** epitaxy is the self-assembled dot. Egg, Germanium deposited on silicon.

This method applied when very thin semiconductor film is buckle.

2. water phase method:

a. **cap exchange :** hydrophobic layer of of organic solvent replace with bifunctional molecule having soft acidic group like thiol and hydrophilic group like carboxylic or amino group for make quantum dot surface with bulk water moluclue.

b. **Native surface modification:** the silica shell adding to nano particle using silica precursor during polycondensation the quantum dots are rendered water soluble by several method like water soluble ligand, silanization, encapsultaion with co-polymer micelles or with amphiphilic polymer .all these method solubilize the CdSe quantum dot.

B. Synthesis of quantum dot by two mechanism:

a. **Top-down synthesis process:** in this process, quantum dot size upto 30 nm formed by bulk semiconductor material with the help of electron beam lithography, laser beam reactive ion or wet chemical techniques.

1. **Electron beam lithography:**source of electron beam are hot lanthanum hexaboride for the lower resolution system. The lower resolution systems depend on minimum width electron beam source & development process. The higher resolution instrument uses

electron emission source such as heated W/ZrO₂for lower energy spread and increased brightness. electron beam lithography offers high degree of flexibility in quantum dot. Quantum dot size is inversally proportional to band gap. Fluroscent study of quantum dot indicate when emission frequency increases size of quantum dot decreases then occur red to blue shift in electromagnetic spectra.

2. **Focused ion beam technique:** Focused ion technique use in semiconductor manufacturing process . these technique is similar like SEM .focused ion beam use fine beam of ion. Size shape are depend ion beam size . Ion source for FIB are gallium ion .Energy of ion source is upto 1-50 keV. That are focused by electrostatic lense.

Spectral Characteristics of Quantum Dots

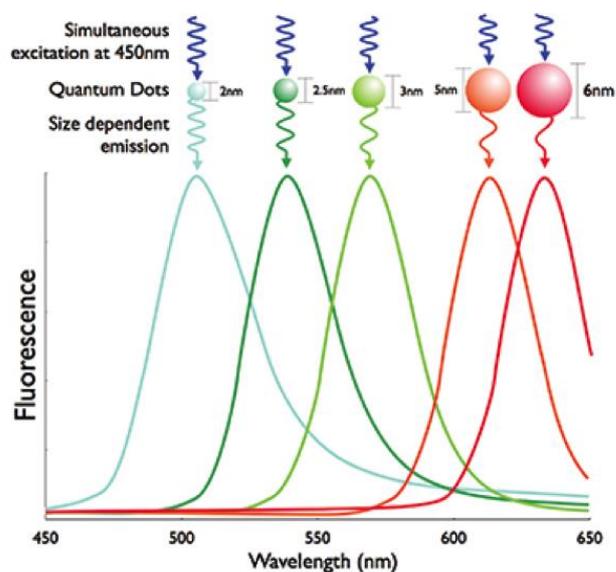


Figure 3: Spectral characteristics of quantum dots

b. **Bottom-up synthesis:** also in this approach of synthesis two methods are involve

a) Wet chemical method & b) vapor phase method

a) **Wet chemical method:** this method deals with reaction in solution phase. In this method formation of precipitation from single or mixture of solution with control on temperature of medium for preparation of particular size and shape. Wet chemical method involve different process like sol-gel process, microemulsion, hot solution decomposition etc.

1. **Sol-gel process:** This process involve hydrolysis and condensation then formation of gel. generally formation of solution by nanoparticle disperse in solvent system with addition of metal precursor(i.e. alkoxide and metal chloride) in acidic or basic medium for hydrolyse the medium and formation of sol by condensation .

2. Micro emulsion process:

Micro-emulsion process is also carried out at room temperature like sol-gel process. This method having problem related to practical yield, impurity and defect. In this process, reverse micelle process is good one for synthesis of quantum dot. Micelle acts as nano-reactor. Growth of quantum dot is depending on ratio of water and surfactant.

3. Hot solution decomposition process :

In this method degassing and drying of solvent at 300°C are the important step moisture free mixture of Cd-precursor and solvent like tri-N-octyl phosphine selenide is prepared and injected into flask for homogenous nucleation process. Size and shape of quantum dots is also depend on purity of solvent, temprature ,precursor and solvent. This method have sufficient thermal energy and provide mono-disperse quantum dot.

B) Vapour phase method:

Growth of quantum dot is process like atom-by-atom. Vapour phase method include molecular beam epitaxy, physical vapour deposition & chemical vapour deposition.

1. Molecular beam epitaxy: this technique is used for growing quantum dot 3-5 semiconductor and 2-6 semiconductor crystal. Solid molecular beam epitaxy element like gallium and arsenic are heated in separate effusion cell until sublime. Then gases element are condense and the react to form gallium arsenide quantum dot. This method use for self-assembled quantum dot.

2. Physical vapour deposition: in this technique solid material vaporize to form liquid and covert to low pressure gas. Mostly this technique used in industry for sputtering, surface of sputtering target are bombard with gaseous ion under high voltage acceleration. Eg. Physical vapour deposition quantum dot Nb₂O₅, CdSe/CdTe quantum dot.

3. Chemical vapor deposition: in this technique molecule convert to gaseous phase after chemical reaction known as precursor into solid film deposit on substarte at high temperature. in that different type of technique are involved like phase epitaxy used for deosit single crystal film, metal organic chemical vapour deposition used when precursor or metal organic specimen, plasma enhance chemical vapor deposition used when plasma used in reaction.

Similarly other technique are involved like atmospheric pressure chemical vapor deposition , photo-chemical vapor deposition , laser chemical vapor deposition.(1)

Application:

- I. **Quantum dot act as carrier:** The hydrophobic drug incorporated between inorganic core and amphiphilic polymer coating layer. Polymer coating is act as diagnostic tool .small size quantum dot eliminated by renal filltration where as large particle by reticuloendothelial system. So size of quantum dot with polymer coating is 5-50 nm for activity. Hydrophilic SiRNA, antibody (targeting agent.) antisense oligonucleotide , peptide and aptamer immobilize into amphiphilic polymer they can identify ,bind ,treat disease and also emit detectable signal.
- II. **Quantum dot detect the death cell:**Quantum dot combine with gadolinium as MRI agent that can spot apoptosis using MRI and fluorescence imaging ,
- III. **Tumor cell marker:** By active and passive targeting we can locate the tumor cell.

Active targeting: QD conjugated with active binding site so they attach to tumor cell. Recently

immunofluorescent probe with antibody to detect the tumor cell.

Passive targeting: QD not having tumor specific targeting site.

- IV. **Immunoassay:** Using glass chip like sandwich assay approach .Antibody bound to glass chip to capture antigen Eg. ZnS coated CdSe QD to detwctantibody .
- V. **Gene technology:** QD conjugated with oligonucleotide sequence to bind with DNA or mRNA.
- VI. **QD for detection of pathogen and toxin:** Pathogen like cryptosporidium parvum and giardia lamblia , E-coli , salmonella typhi can detect by immunofluorescent method . Also they produce good signal to noise ratio. But ELISA test is better than this technique.
- VII. **Detection of viral infection:** QD are bind to virus coat and infected cell. QD detect and diagnose the respiratory syncytial virus (RSV) is an important for control the infection and develop the antiviral drug. Antibody conjugated QD can detect the particle of RSV within hour. RSV affects the lungs cell.
- VIII. **Neuroscience:** In the neuroscience QD are used to visualize, measure and track the individual molecule using fluorescence microscopy. the fluorescence microscopy able to imagine and locate individual molecule within minute . for the functioning the QD properly should having size between 15-20 nm. Antibody conjugated QD use to identify the infusion of glycine receptor in culture of spinal cord.
- IX. **QD are stable and sensitive:** QD improve the sensitivity of surgical lymphatic re-sectioning.
- X. Quantum dots targeted to assigned organelle in living cell.

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