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**REVIEW** 

# Surface Modifications Technology of Quantum Dots Based Biosensors and Their Medical Applications

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**Abstract:** Quantum dots (QDs) as a new type of nano-structured luminescent materials has been widely used in biology, materials science, and physical optics. QD-based biosensors can be used for the rapid and accurate detection of biological macromolecules or inorganic molecules both in vivo and in vitro. To enhance their fluorescence properties and lower their biological toxicity, the surface of QDs needs to be modified. Currently, the surface modification technologies mainly include multidentate ligand, sulphydryl group coupling, amphiphilic molecules, cavity-chain, and dendrimer technology. Meanwhile, various biosensors have been developed by adopting different modification techniques to locate and track a variety of disease-specific biological molecules. Although enormous literatures have reported the biological applications of QD-based biosensors, few systematic reviews of surface modification technologies on QDs have been published. This paper reviews the surface modification technologies of QDs in biosensors and their medical applications.

Key Words: Quantum dots; Surface modification; Mercaptopropione acid; Biosensor; Review

#### 1 Introduction

Quantum dots (QDs) is composed of a finite number of semiconductor materials (briefly IIB- VI B or IIIB-VB elements), and the typical QDs size is in the range of 10–50 nm. Because of the considerably existed defect centers and non-radiative transition paths on the quantum dot surface, the QDs surface atoms are active which trigger the low fluorescence productivity of QDs. Under this circumstance, QDs with high-efficiency, highstability and functionalizedare desired. As a new type of nanostructured luminescent materials, QDs is a research focus in recent years. Based on their unique luminescent and optical physical property, QDs can be used to construct novel quantum dots biological sensing systems.

The surface modification process is to connect a variety of organic and inorganic or biological materials to the surface of QDs through a series of physical or chemical reactions. Then the surface modified QDs can reduce or even eliminate the

surface defects and in turn enhance the QDs light sensitivity, water solubility and biocompatibility. At present, many methods have been proven effective in synthesizing QDs, which are mainly divided into two categories, metal organic synthesis and water phase synthesis method<sup>[1,2]</sup>. The luminous intensity of QDs from metal organic synthesis is high, but the biocompatibility is poor. Water-soluble quantum dots have advantages in biological compatibility, but their quantum efficiencies are low and the fluorescence emission intensities are weak. Trung et al<sup>[3]</sup> theorized that the luminous efficiency mainly depended on the surface luminous efficiency of the semiconductor or the number of particles inside the trap. The larger the number of trap is the more electronics are deactivated by the way of non-radiativation and therefore luminous efficiency significantly reduced. So the research hotspot today is aiming at the surface modification of QDs to improve their fluorescent stability, solution dispersion and biocompatibility. The QDs surface modification techniques mainly include polymer modification, thiol compounds

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modification, mercapto propionic acid compounds modification, and organic groups modification (Fig.1). The applications of each modification technique in biological sensors have both the advantages and the disadvantages. In this review, we mainly focus on the surface modification technologies of QDs and their applications in medicine.

#### 2 Surface modification technology

### 2.1 Multidentate ligand surface modification technology

The ligands around the center ion and the ligands atoms are directly bond to the center ion. Two or more ligands atoms simultaneously bonding to one center ion are called multidentate ligand (MDL). The principle of the MDL surface modification technology is coordinated complexation, and the

mechanism is to form complexes by connecting ligand's amino or carboxyl with the QDs center ion-CdSe/CdSfor achieving surface modification<sup>[4]</sup>.

Cucurbituril is a macrocyclic cavity and compound with two portals. It has the shape of a cucurbit with oxygen atoms of the carbonyl lying in the bottom. Cucurbituril is one of the most common MDL and cucurbituril modified QDs can be adopted to analyze the concentration of double pyridine salt in the solution. The detection principle is that cucurbituril can competitively bind to double pyridine salt binding sites simultaneously contrasting with QDs. When QDs combine to double pyridine salt, QDs is non-illuminant, revealing that double pyridine salt has fluorescence quench effect. When cucurbituril is added, double pyridine salt separated from QDs and combine to the gourd lacuna of cucurbituril, then QDs emit visible fluorescence (Fig.2)<sup>[5]</sup>.

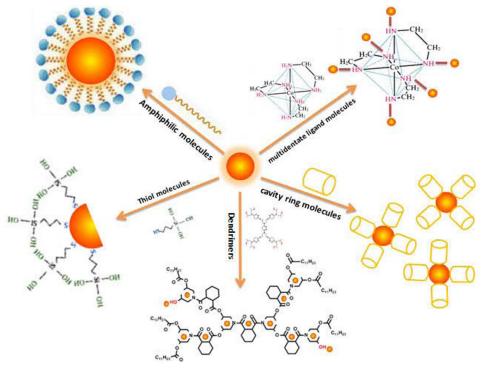
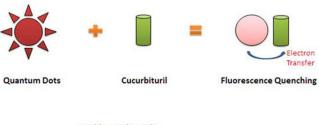


Fig.1 Schemes of different QDs surface modification technologies



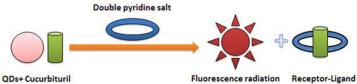


Fig. 2 Fluorescence quench triggered by the combination between bipyridinium quencher and macrocyclic receptor<sup>[5]</sup>

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