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In vivo distribution, pharmacokinetics, and toxicity of aqueous synthesized cadmium-containing quantum dots

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ABSTRACT

Fluorescent II–IV Quantum dots (QDs) have demonstrated to be highly promising biological probes for various biological and biomedical applications due to their many attractive merits, such as robust photostabilty, strong photoluminescence, and size-tunable fluorescence. Along with wide ranging bioapplications, concerns about their biosafety have attracted increasingly intensive attentions. In comparison to full investigation of *in vitro* toxicity, there has been only scanty information regarding *in vivo* toxicity of the QDs. Particularly, while *in vivo* toxicity of organic synthesized QDs (orQDs) have been investigated recently, there exist no comprehensive studies concerning *in vivo* behavior of aqueous synthesized QDs (aqQDs) up to present. Herein, we investigate short- and long-term *in vivo* biodistribution, pharmacokinetics, and toxicity of the aqQDs. Particularly, the aqQDs are initially accumulated in liver after short-time (0.5–4 h) post-injection, and then are increasingly absorbed by kidney during long-time (15–80 days) blood circulation. Moreover, obviously size-dependent biodistribution is observed: aqQDs with larger sizes are more quickly accumulated in the spleen. Furthermore, histological and biochemical analysis, and body weight measurement demonstrate that there is no overt toxicity of aqQDs in mice even at long-time exposure time. Our studies provide invaluable information for the design and development of aqQDs for biological and biomedical applications.

1. Introduction

To date, while a variety of functional nanomaterials (e.g., carbon nanotubes, silicon nanowires, gold/silver nanoparticle, quantum dots et al.) have been well developed due to their unique electric/optical/mechanical properties, sufficient and objective assessment of nanomaterials-relative biosafety is necessary for their wide ranging bioapplications [1–6]. Among them, fluorescent II–IV Quantum dots (QDs) are recognized as novel high-performance biological probes and at the forefront of nano-biotechnology research, since they possess many attractive optical properties, including high photoluminescent quantum yield (PLQY), broad absorption coupled with narrow emission, and strong photostability [1,7,8]. To meet requirement of practical biological and biomedical applications, a large amount of studies on biosafety assessment of the QDs have been carried out [9–21]. Particularly, previous studies have suggested that cytotoxicity of QDs is ascribed to release of toxic metals [9,10] and production of reactive oxygen species [11,12], which could be largely alleviated by surface modification (e.g., epitaxial growth of ZnS shell) [10,16–18].

Such in vitro achievements are useful for biosafety assessment of the QDs; notwithstanding, comprehensive studies concerning *in vivo* toxicity are superior, since the results will assist in pinpointing the potential target organ and cells involved [13]. However, in comparison to sufficient investigations on the QDs cytotoxicity, there has been relatively scanty information regarding *in vivo* behavior of the QDs. Merely a few relevant studies have been reported up to present. Typically, Chan's group presented the first quantitative report on the *in vivo* biodistribution of QDs in 2006 [22]. In their latest study, they further

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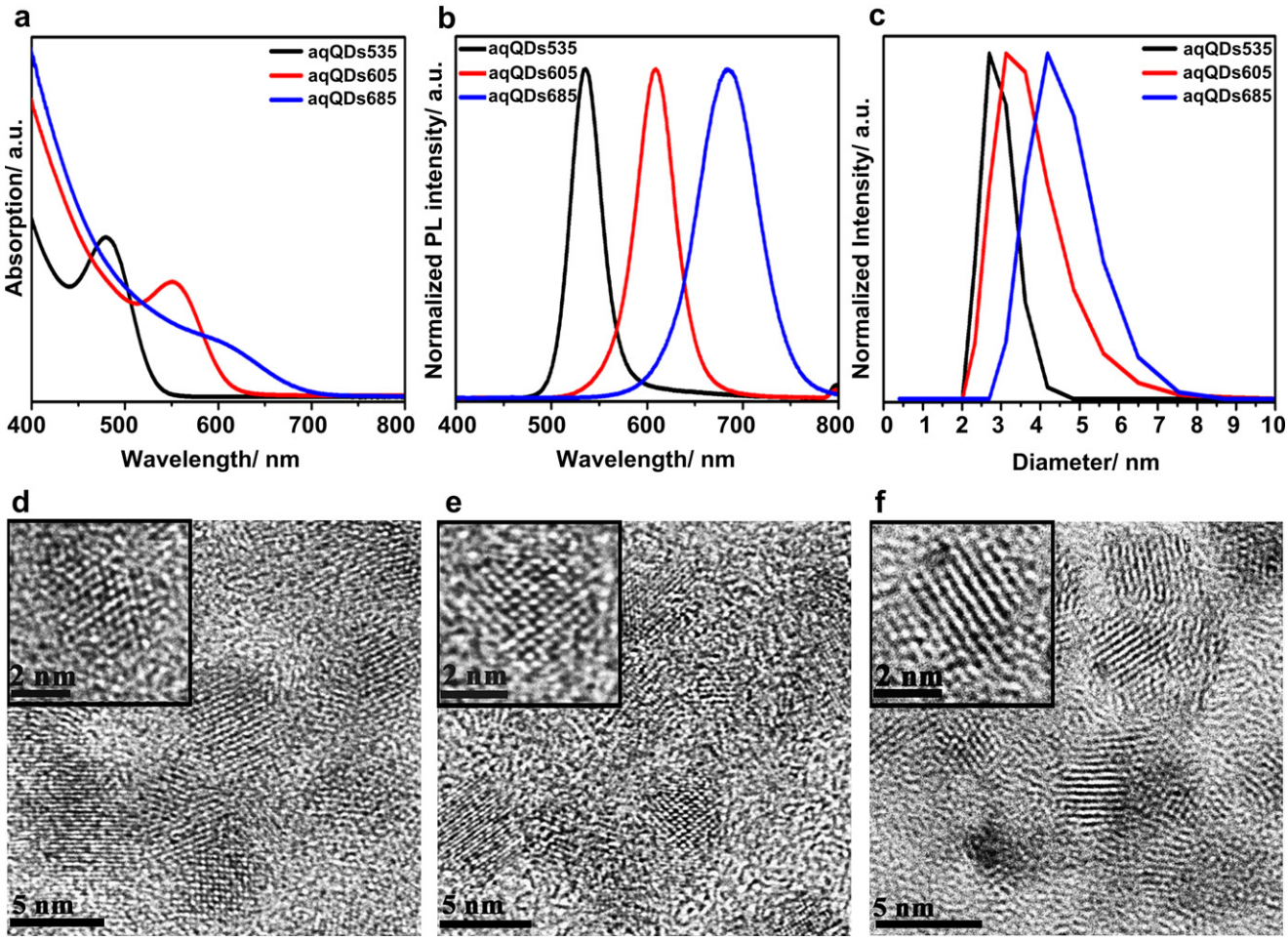

Fig. 1. Absorption (a) and photoluminescence (b) spectra of three-sized aqQDs used in our study, whose maximum luminescent wavelength is 535 nm (aqQDs535), 605 nm (aqQDs605), and 685 nm (aqQDs685), respectively. (c) displays representative dynamic-light-scattering histogram of the three-sized aqQDs. Their corresponding TEM images are shown in (d)–(f).

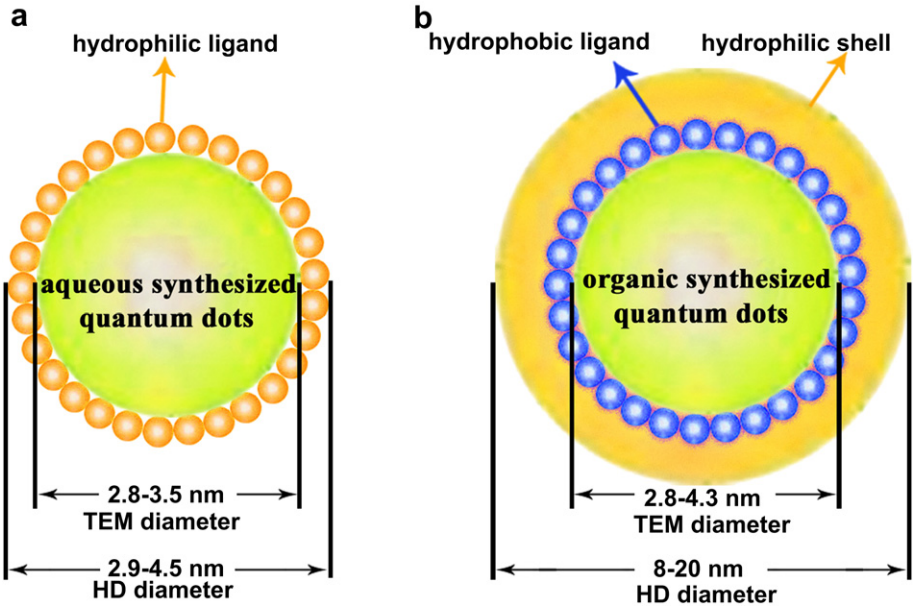

Fig. 2. Schematic structures of the aqueous synthesized quantum dots (aqQDs) and organic synthesized quantum dots (orQDs). Hydrophilic ligand indicates thiol- and carboxyl-modified short chain organic molecules with hydrophilic property (e.g., 3-Mercaptopropionic acid and thioglycolic acid). Hydrophobic ligand indicates long hydrophobic chain organic molecules often used in synthesis of orQDs, such as trioctylphosphine oxide and trioctylphosphine. Hydrophilic shell includes silica shell or polymer shell, which is generally used for improve hydrophibility of the orQDs.