International Journal of Pharmaceutics 466 (2014) 382–389

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Pharmaceutical nanotechnology

Synthesis and characterization of quantum dots designed for biomedical use

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ARTICLE INFO

Article history:
Received 6 January 2014
Received in revised form 17 March 2014
Accepted 18 March 2014
Available online 20 March 2014

Keywords:
Nanoparticles
Quantum dots
Cytotoxicity
Biocompatibility

ABSTRACT

Semiconductor quantum dots (QDs) have become promising nanoparticles for a wide variety of biomedical applications. However, the major drawback of QDs is their potential toxicity. Here, we determined possible cytotoxic effects of a set of QDs by systematic photophysical evaluation *in vitro* as well as *in vivo*. QDs were synthesized by the hydrothermal aqueous route with sizes in the range of 2.0–3.5 nm. Cytotoxic effects of QDs were studied in the human pancreatic carcinoid cell line BON. Cadmium telluride QDs with or without zinc sulfide shell and coated with 3-mercaptopropionic acid (MPA) were highly cytotoxic even at nanomolar concentrations. Capping with L-glutathione (GSH) or thioglycolic acid (TGA) reduced the cytotoxicity of cadmium telluride QDs and cadmium selenide QDs. Determination of the toxicity of QDs revealed IC_{50} values in the micromolar range. *In vivo* studies showed good tolerability of CdSe QDs with ZnS shell and GSH capping. We could demonstrate that QDs with ZnS shell and GSH capping exhibit low toxicity and good tolerability in cell models and living organisms. These QDs appear to be promising candidates for biomedical applications such as drug delivery for enhanced chemotherapy or targeted delivery of light sensitive substances for photodynamic therapy.

1. Introduction

Nanoparticles, previously associated only with physics or chemistry are gaining increasing interest in biomedical research. Among the many of newly synthesized nanoparticles of the last decades, semiconductor quantum dots (QDs) turned out to belong to the most promising ones in the field. The size of QDs can vary from 1 to 6 nm and absorption and luminescence properties can be precisely adjusted from the UV to the far infrared region by changing the QDs size and composition. Even more importantly, the surface coating of QDs can be functionalized to make them both water soluble and biocompatible. Last but not least, because of the ability to functionalize them, ODs have become interesting candidates for a variety of biomedical applications, such as photodynamic therapy, where they are under extensive investigation as carriers for targeted delivery of photosensitizers (Iga et al., 2007; Jamieson et al., 2007; Medintz et al., 2008; Ku et al., 2011; Medintz et al., 2005; Paszko et al., 2011).

Despite the exceptional properties of QDs, serious concerns about their potential long-term toxicity have limited their use in biomedical applications so far. Several critical studies have reported that the release of heavy metals (*e.g.,* Cd) from the core of QDs (*e.g.,* CdTe, CdSe or CdS) can be a reason for their toxicity (Chen et al., 2012; Su et al., 2010). Kirchner and co-workers have reported that any type of nanoparticle might reduce cell viability when applied at micromolar concentrations (Kirchner et al., 2005). Wang and colleagues have shown that even in nanomolar concentrations, QDs can exert toxic effects on microorganisms, leading to DNA damage and protein degradation (Wang et al., 2011). Nevertheless, a number of publications suggested that stabilization of the QD core with an inorganic shell such as ZnS and the type of capping agent on the surface of the QDs can reduce or entirely suppress their toxicity (Tiwari et al., 2011; Zhang et al., 2006; Jaiswal et al., 2003). Although the ZnS shell turned out as the most effective core protection, there is no certainty which capping (*e.g.,* mercaptoacetic acid (MAA), tri-*n*-octylphosphine oxide

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http://dx.doi.org/10.1016/j.ijpharm.2014.03.037
0378-5173/