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Review

Review of in vitro toxicological research of quantum dot and potentially involved mechanisms

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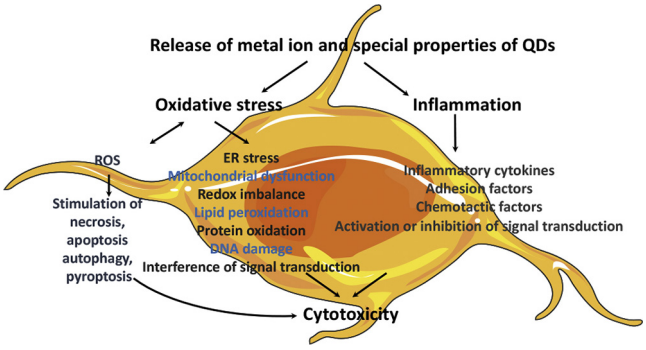
HIGHLIGHTS

- Oxidative stress, ROS, inflammation, release of metal ion and DNA damage have implications in cytotoxicity of QDs.
- QDs not only imperil innate immune system, but jeopardize adaptive immune system.
- Disturbance of organelles, including ER stress, mitochondrial dysfunction, is involved in the adverse effect of QDs.
- Chirality seems to be a newly proposed influence factor that determines the destiny of cells in response to QDs.

GRAPHICAL ABSTRACT



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ABSTRACT

Quantum dots (QDs) are one of emerging engineering nanomaterials (NMs) with advantageous properties which can act as candidates for clinical imaging and diagnosis. Nevertheless, toxicological studies have proved that QDs for better or worse pose threats to diverse systems which are attributed to the release of metal ion and specific characteristics of nanoparticles (NPs), hampering the wide use of QDs to biomedical area. It has been postulated that mechanisms of toxicity evoked by QDs have implications in oxidative stress, reactive oxygen species (ROS), inflammation and release of metal ion. Meanwhile, DNA damage and disturbance of subcellular structures would occur during QDs treatment. This review is intended to conclude the cytotoxicity of QDs in multiple systems, as well as the potential mechanisms on the basis of recent literatures. Finally, toxicity-related factors are clarified, among which chirality seems to be a newly proposed influence factor that determines the destiny of cells in response to QDs. However, details of interaction between QDs and cells have not been well elucidated. Given that molecular mechanisms of QDs-induced toxicity are still not clearly elucidated, further research should be required for this meaningful topic.

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Contents

1. Introduction

Quantum dot (QD), a semiconductor nanomaterial, usually consists of chemical elements from III-V or II-VI groups whose size always falls in the range from 1 nm to 10 nm. Due to a series of distinct effects regarding size effect, quantum confinement effect, macroscopic quantum tunneling effect and specific surface effect, QDs differ from bulk counterparts with the micrometer scale, which may act as possible diagnostic and therapeutic tools for the application in biomedical field, including fluorescent probes for basic labeling and clinical diagnosis (Yang et al., 2016). Compared with conventional dyes, QDs have the superiority in fluorescence and optical stability because of high fluorescence intensity, long duration, overt specificity and relatively low rate of quenching. The model of QDs has unique photophysical and electrical properties with the broad absorption and narrow emission spectra (Zhao et al., 2018). Moreover, the emission wavelength of QDs can be easily controlled by different sizes of the core. Fig. 1 demonstrated the typical structure of QDs with core/shell-conjugate and exhibited the photoluminescence image of QDs. Besides diagnosis of neuroscience disorders, QDs can be also involved in tumor tracing, microbial detection and drugs-targeted therapy (Matea et al., 2017; Pohanka, 2017). A complex of antibody-QDs fluorophore can be applied to distinguishing normal cells from cancer cells for the specific recognition of cancer cells since green fluorescence emission only exist in antibody-QDs labeled cancer cells while normal cells do not emit fluorescence (Matea et al., 2017). QDs-conjugated peptides have the specificity of identifying tumor surface antigens, which are specifically enriched in the corresponding tumor sites after an intravenous injection in mice that suffered from malignant tumor (Wu et al., 2013b). Through this targeted technique, QDs can be used to guide medicines to specific foci for targeted drug-therapy in the light of the recognition of peptides with receptors.

Although the wide attention to potential function of QDs have been paid, safety evaluation is indispensable for its safe application. Owing to the special nano-dimensional effects, QDs are quite different from those bulk counterparts. It has been authenticated that QDs have obvious toxicity through plenty of in vitro studies, which can be attributed to the special physiochemical properties like toxic chemical components (e.g. cadmium, mercury and arsenic) and quantum size effect (Kuznetsova et al., 2017; Peynshaert et al., 2017). In order to acquire information as comprehensive as possible to facilitate secure application of QDs to medical area, in vitro and in vivo experimental studies are particularly important when human epidemiological researches are absent to date. A decade ago, researchers started to focus on safety evaluation of QDs and found it really poisonous through a host of experiments

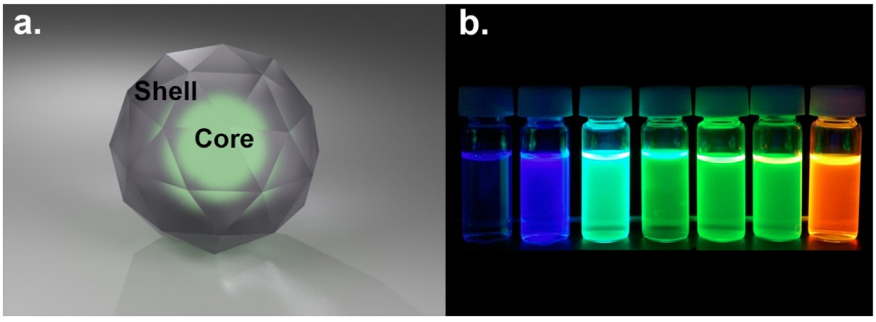

Fig. 1. The basic structure and fluorescence image of QDs. (a.) A typical QD is composed of core and shells. It also can be designed with addition of variable outer layer, like peptides, antibodies, oligonucleotides and so on for satisfying biocompatibility. (b.) Fluorescence image of QDs. In general, the fluorescence of QDs is dependent on the size. The larger QDs of the same material exhibit a smaller energy band-gap and thus a photoluminescence emission in the red, whereas smaller QDs fluoresce in the blue.