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ROS-mediated apoptotic cell death in prostate cancer LNCaP cells induced by biosurfactant stabilized CdS quantum dots

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ABSTRACT

Cadmium sulfide (CdS) quantum dots (QDs) have raised great attention because of their superior optical properties and wide utilization in biological and biomedical studies. However, little is known about the cell death mechanisms of CdS QDs in human cancer cells. This study was designed to investigate the possible mechanisms of apoptosis induced by biosurfactant stabilized CdS QDs (denoted as "bsCdS QDs") in human prostate cancer LNCaP cells. It was also noteworthy that apoptosis correlated with reactive oxygen species (ROS) production, mitochondrial damage, oxidative stress and chromatin condensation in a dose- and time-dependent manner. Results also showed involvement of caspases, Bcl-2 family proteins, heat shock protein 70, and a cell-cycle checkpoint protein p53 in apoptosis induction by bsCdS QDs in LNCaP cells. Moreover, pro-apoptotic protein Bax was upregulated and the anti-apoptotic proteins, survivin and NF-κB were downregulated in bsCdS QDs exposed cells. Protection of N-acetyl cysteine (NAC) against ROS clearly suggested the implication of ROS in hyper-activation of apoptosis and cell death. It is encouraging to conclude that biologically stabilized CdS QDs bear the potential of its applications in biomedicine, such as tumor therapy specifically by inducing caspase-dependent apoptotic cell death of human prostate cancer LNCaP cells.

1. Introduction

A range of nanoparticles (NPs) kill human cancerous cells have been reported recently [1–4] of which metal-based NPs have been well studied and reported to kill the various type of cancerous cells. Although, these NPs can generate reactive oxygen species (ROS) [1] in the biological system. In comparison to NPs, quantum dots (QDs) have superior size-dependent ROS production capability and could be another type of attractive nanomaterials [2,5,6]. QDs are nanoscale crystalline clusters synthesized from semiconducting materials [7]. ROS are generated in all aerobic organisms and are indispensable for signal transduction pathways that regulate cell growth and redox status [8]. However, excess production of these ROS can initiate lethal chain reactions that involve oxidation of various biomolecules and damage cellular integrity and survival [9–11]. If they can be selectively over produced into tumor cells, ROS may exert remarkable antitumor potential due to their reaction with vital cellular targets [12]. This strategy of cancer treatment by generation of ROS selectively in tumor cells has been termed "oxidation therapy". In oxidation therapy, the principle is to generate excess ROS selectively in tumor cells causing maximum tumor killing without affecting the normal tissues [3].

To date, many approaches have been tested for the preparation of surface protected and stabilized QDs, since the surface protection and stabilization of QDs is one of the key problems to applications [2]. Surface protection and stabilization of QDs is difficult due to the high surface area to volume ratio and high surface energy. For this, surfactants, polymers, micelles, and ligands are widely used as surface protectors and stabilizers in order to obtain modified QDs [7,13–15]. Many of these commonly used chemically synthesized surface protection and stabilization agents have not been proven biocompatible and are probably toxic. In past years, numerous studies are specifically designed for assessing the cytotoxicity of QDs, but due to the lack of standardized QD synthesis protocols, solubilization ligands, dose, coatings, and cell systems, it is hard to obtain a straight answer. Nevertheless, from this diversity, an

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