Selective killing of cancer cells by iron oxide nanoparticles mediated through reactive oxygen species[#]

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Abstract

Iron oxide (Fe_3O_4) nanoparticles (NPs) are increasingly recognized for their utility in biomedical applications. This study was designed to investigate whether Fe_3O_4 NPs induced toxicity in a cell-specific manner and determine the possible mechanisms of toxicity caused by Fe_3O_4 NPs in cancer cells. Fe_3O_4 NPs (23nm) used in this study were synthesized by green method using α-D-glucose as a reducing agent. Cytotoxicity of Fe_3O_4 NPs was examined against two types of cancer cells (human hepatocellular carcinoma HepG2 and human lung adenocarcinoma A549) and two normal cells (human lung fibroblast IMR-90 and rat hepatocytes). Fe_3O_4 NPs exerted distinct effects on cell viability via killing of cancer cells while posing no toxicity on normal cells. Fe_3O_4 NPs were found to induce depletion of glutathione and induction of reactive oxygen species (ROS) in both types of cancer cells (HepG2 and A549). Further, co-exposure of ascorbic acid significantly attenuated the Fe_3O_4 NPs induced oxidative stress. The mRNA levels of tumor suppressor gene p53 and apoptotic genes (caspase-3 and caspase-9) were up-regulated in cancer cells due to Fe_3O_4 NPs exposure. Protein level of p53, along with the higher activity of caspase-3 and capase-9 enzymes, was also up-regulated by Fe_3O_4 NPs. Our data demonstrated that Fe_3O_4 NPs selectively induced apoptosis in cancer cells (HepG2 and A549) through up-regulation of p53 that might be mediated by ROS through which most of the anticancer drugs trigger apoptosis.

Keywords: Fe_3O_4 nanoparticles; anticancer activity; apoptosis; oxidative stress; p53