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Effects of iron oxide nanoparticles on MDA-MB-231 breast cancer cell line

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Abstract

Because of their small size, unique physics, and chemical properties, metal nanoparticles can easily cross obstacles and reach their target cells, which makes them an ideal choice for therapeutic purposes in various cancers. In this study, the effects of iron oxide nanoparticles on MDA-MB-231 breast cancer cell line were examined, and biomarkers related to oxidative stress were evaluated. Fe2O3 nanoparticles were suspended in a cell culture medium and diluted to appropriate concentrations (0, 10, 30, 60, and 120 µg/ml) for 24 and 48 h. GSH, superoxide dismutase, catalase, and ROS generation were evaluated. The results showed that iron oxide nanoparticles induced intracellular ROS generation in a dose- and time-dependent manner. The results further showed that iron oxide nanoparticles increased ROS and activated oxidative stress in cells.

INTRODUCTION

Today, the use of metal nanoparticles is one of the most important issues in various medical fields (1). Because of their small size and unique physics and chemical properties, metal nanoparticles can easily cross obstacles and reach their target cells, so they are an ideal choice for therapeutic purposes in various cancers (2). Numerous studies have investigated the side effects of using nanoparticles; however, there are still many unanswered questions about the toxic properties of these substances on biological systems (3). A recent study found that metal nanoparticles increased the production of oxidative stress in cells by increasing the production of reactive oxygen species (ROS) and reducing the activity of the intracellular glutathione system (4). Oxidative stress plays an important role in cellular processes such as cellular signaling, cell proliferation, and genotoxic responses (5). Superoxide dismutase, catalase, and GSH reductase are known natural antioxidants that neutralize excessive ROS and prevent it from damaging the cellular structure (6).

The most common cancers in females worldwide are breast and cervical cancers. An estimated 1 in 8 women in the United States will develop one of these diseases (7). The incidence of breast cancer in developing countries is 23% in young adults (15-49 years) compared with 10% in developed countries (8). In menopausal females (>50 years), the incidence rate is 28% in developing countries compared with 39% in developed countries (9). Iron oxide nanoparticles are of particular interest for in vivo applications, including magnetic resonance imaging for medical diagnosis, hyperthermia in cancer therapy, tissue repair, drug delivery, and cellular therapy (10). In the current study, the effects of iron oxide nanoparticles on a MDA-MB-231 breast cancer cell line were examined, and the biomarkers related to oxidative stress, including GSH, superoxide dismutase, catalase, and ROS generation, were evaluated.

MATERIALS AND METHODS

Human breast cancer cells (MDA-MB-231) were procured from the Pasteur Institute of Iran. They were preserved and subcultured in the laboratory and used to determine cytotoxicity against iron oxide nanoparticles. Iron oxide (Fe2O3) nanoparticles were suspended in the cell culture medium and diluted to appropriate concentrations (0, 10, 30, 60, and 120 µg/ml) for 24 and 48 h. Cells not exposed to iron oxide nanoparticles served as the control in each experiment. GSH levels were quantified by using Ellman's reagent (DTNB). The reaction was monitored at 412 nm, and the amount of GSH was expressed in terms of nanomoles of GSH per milligram of protein. Superoxide Dismutase was assayed by NTB buffer, and the absorbance of the reaction mixture was measured at 450 nm. Catalase

activity was measured by its ability to split hydrogen peroxide (H2O2) within 1 min of incubation time. Catalase activity was expressed as micromoles of H2O2 decomposed per minute per milligram of protein. ROS generation was assessed in MDA-MB-231 cells using DCFH-DA dye as the fluorescence agent. Data was expressed as mean (±SE) and analyzed by one-way analysis of variance (ANOVA). A p-value <0.05 was considered statistically significant.

RESULTS

The ability of iron oxide nanoparticles to induce oxidative stress was assayed by measuring levels of GSH, ROS, superoxide dismutase, and catalase in a MDA-MB-231 breast cancer cell line. The results showed that iron oxide nanoparticles induced intracellular ROS generation in a dose- and time-dependent manner (Table 1).

Table1. Effect of treatment of different doses of iron oxide nanoparticles at different times on oxidative stress biomarkers of MDA-MB-231 breast cancer cell line

Stress oxidative biomarker	ROS (DCF-fluorescence)		GSH (nMcSH/mg)		SOD (Unit/ml)		Catalase (% of control)	
Treatment time	24h	48h	24h	48h	24h	48h	24h	48h
Control	100	102	14.5	14.6	2.1	2.2	98	99
10 conc	110	115	14	13.8	1.9	1.9	100	1.5
30 conc	125	150	13.5	13	1.8	1.5	97	88
60 conc	170	180	12	11	1.5	1.3	87	75
120 conc	200	230	9	5	1.4	1.0	68	60

DISCUSSION

Iron oxide nanoparticles are widely used in a variety of medical fields, from magnetic resonance imaging to drug design. Still, there are concerns about the toxic properties and effects their use can have on the environment (11). This study evaluated the effect of this substance on the oxidative stress of the MDA-MB-231 breast cancer cell line. The results showed that iron oxide nanoparticles can increase the oxidative stress activity of breast cancer cells by inducing the production of free radicals; thus, they are cytotoxic**.** Previous studies have shown that nanoparticles of various sizes and different chemical compositions attack mitochondria, which are redox-active organelles. Mitochondria are a prominent site of ROS formation in cells exposed to nanoparticles. Therefore, nanoparticles may change the production of ROS and affect antioxidant defenses to induce oxidative stress (12). By increasing the dose of iron oxide nanoparticles and increasing the treatment time, this study showed that ROS was increased and the values of GSH, SOD, and catalase were decreased significantly, indicating an increase in cell stress and a decrease in the cell antioxidant system. ROS typically include the superoxide radical (O2−), hydrogen peroxide (H2O2), and the hydroxyl radical (OH), which cause damage to cellular components including DNA damage and ultimately apoptotic cell death (13). Previous studies have shown that ROS are involved in damaging DNA, causing damage to both purine and pyrimidine bases as well as the DNA backbone. The current results showed that iron oxide nanoparticles increased ROS and activate oxidative stress in cells.

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