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Investigation of the Cytotoxic Effect of Thorium on MRC-5 Cells

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Abstract

Thorium is a naturally occurring radioactive metal belonging to the actinide group. It is found at low levels in water, soil, rocks, plants and animals. Thorium is used as a nuclear fuel in nuclear technology, and its compounds are used in industry, chemistry, mining, ceramic production and high-quality lens production. It also occurs naturally in different sources, including phosphate fertilizers used in agriculture. Its increasing role in the nuclear and defense industries poses a risk to human health as a result of occupational and accidental exposure. Thorium enters the body mainly through inhalation of contaminated dust. Studies conducted on workers have found that inhaling thorium dust will cause an increased the risk of developing lung diseases such as lung cancer. This study aimed to determine the cytotoxic effect of thorium on normal human lung fibroblast cells (MRC-5) exposed to thorium in vitro. For this purpose, MRC-5 cells were cultured in a 96-well plate (1x105 cells/well; 200 µl) containing 150 µM thorium (the stock solution was 1000 µg/ml in 5% HNO3). Cell viability (cytotoxicity status) was evaluated by 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, yellow tetrazole (MTT) analysis method after 48 h of incubation. As a result of the MTT test, cell viability was determined as %99.52 in cells treated with 150 µM thorium. Accordingly, it was concluded that 150 µM thorium is not cytotoxic on MRC-5 cells. However, in later studies, it was decided to examine the cytotoxic effect of thorium at higher doses.

Keywords: Thorium; Cytotoxicity; MRC-5

Introduction

Thorium is a naturally occurring radioactive metal belonging to the actinide group. It is found at low levels in water, soil, rocks, plants, and animals. However, thorium is several times more abundant than uranium in the earth's crust and is a longer-lived element than uranium [1,2]. Thorium has thirteen radioactive isotopes, from Th223 to Th235. The Th232 isotope with a half-life of 14 billion years is the only naturally occurring isotope of thorium [3-8]. In addition to its use as a nuclear fuel, naturally occurring thorium has many uses in both industrial and medical fields [1,2]. Thorium metal, when in powder form, burns easily and turns into thorium oxide [4,5,9]. Wicks consisting of thorium oxide, 1% cerium oxide, and other components shine dramatically when heated in a gas flame and are used in portable gas lamps. Thorium oxide is also used in aerospace research, the manufacture of crucibles and ceramic parts, and scientific instruments. Because the energy required to remove electrons is low and the electron emission is high, thorium metal is used in tungsten lamp filament coating, electronic devices and televisions. Very pure thorium is used in small quantities in special optical glasses. Also in the industry, it is used as a catalyst for oxidizing sulfur dioxide to sulfur trioxide, carbon monoxide to water gas, and ammonium to nitric acid. In addition, thorium is a component of many organic reagents [3,6,10].

Thorium is one of the most dangerous heavy metals due to its environmental effects and industrial applications [11,12]. Radioactive pollution caused by rays such as alpha, beta, and gamma emitted by the disintegration of the atomic nuclei of radioactive minerals such as thorium and uranium causes serious damage to both living things and natural systems. As a result of radioactive pollution, the gene structure of living things deteriorates, the immune system weakens, cancer spreads, and deaths occur [13].

Exposure to thorium in industry and mining has led to an increased incidence of lung cancer, pancreatic cancer, colorectal cancers, chronic respiratory diseases, liver damage and other serious diseases. Studies have shown that inhaling thorium dust by thorium workers can lead to an increased chance of developing lung disease and lung or pancreatic cancer even years later. Genetic changes in body cells have also been found to occur in workers exposed to thorium dust. In these people, many types of cancer also appeared years later. Because thorium is radioactive and can be stored in bone for a long time, bone cancer is also a potential concern for people exposed to thorium. Studies have shown that exposure to thorium can also cause lung damage. Because the vast majority of thorium mining is done by open-pit methods, the radiological problems, especially the breathing hazards, are relatively minor compared to underground uranium mining. Respiratory hazards mainly arise from dust generated during the physical separation of the mineral components of placers [14-17]. Following inhalation, the accumulation and uptake of actinides along the inhalation route depends on their size (1 in 20 mm) and their chemical form (soluble/insoluble). Depending on these two factors, the rate of passage of actinide particles from the trachea to the bronchioles (1-10 days)and then from the alveolar regions to the blood (up to 100 days) changes. Therefore, the containing actinides can persist in lung tissue for up to several months and be located on alveolar epithelial cells, ultimately leading to inflammation and tissue damage [18].

Especially in occupational exposure; since inhalation is the main entry route and the lung is the first tissue area to be encountered, the effects of thorium on lung cells should be known. This study aimed to investigate the cytotoxic effect of thorium in normal human lung fibroblast cells (MRC-5) exposed to thorium in vitro.

Materials and Methods

Cell Culture

The human lung fibroblasts cell line (MRC-5) was obtained from the American Type Culture Collection (ATCC) and maintained as exponentially growing monolayers by culturing according to the supplier's instructions.

Determination of Cell Viability-MTT assay

MRC-5 was cultured in 96-well plates (1x105 cells/well; 200 µl) with increasing concentration of 150 µM of Th (the stock solution was 1000 µg/ml in 5% HNO_3). The test compounds were then incubated for 48 h. To estimate cell viability, MTT (3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide) (Sigma Aldrich, UK) reduction assay was performed as described before [19]. Following 48 h of incubation, the supernatant was discarded, the mixture of MTT and medium (1:9) was added, and the plates were incubated for 3 h at 37°C. The supernatant was removed and 200 µL of DMSO was added to dissolve the formazan crystals. Optical density was measured at wavelength 570 nm with a microplate reader (Varioscan, Thermo Fisher Scientific, US). 5% HNO_3 was used as a solvent control for Th. All tests were performed in triplicate.

Results

In this study, 150 µM thorium could be applied with 0.2% nitric acid in the cell medium in MTT analysis. For this purpose, 8 µl of the main stock was taken and a total of 200 µl of medium was applied to the cells. This gave us an intracellular concentration of 150 µM. It was determined that the cells treated with 150 µM thorium did not die and the cell viability was 99.52%.

Discussion and Conclusion

As a result of increasing and developing research in the field of energy, it is a fact that thorium production will increase considerably shortly, as small, new and portable fourth-generation thorium reactors are started to be handled up-to-date, escape from nuclear weapons/bombs, and countries rich in thorium reserves such as India and Norway define thorium as an alternative nuclear fuel [5,6,20]. Radionuclear pollution that may arise as a result of the development of the nuclear industry is of vital importance. The increasing role of 232 in the nuclear and defense industries poses a risk to occupational and accidental human health [21].

Similar to our study Das SK [22], examined the cytotoxic effects of thorium nitrate and thorium dioxide on normal human lung epithelial cells (WI26) using the MTT test. At lower Th-nitrate concentrations (1,5 and 10 µg/ml), the percent change in proliferation was found to be only ~15% at 48 h compared with Th-nitrate (IC50~25 µg/ml), it was determined that Th-dioxide suppressed cell proliferation by more than 50% even at a concentration of 5 µg/ml.

As a result, it was concluded that 150 µM thorium is not cytotoxic for MRC-5 cells. However, in later studies, it was decided to examine the cytotoxic effect of thorium at higher doses.

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