Mutation of p53 as a tumor suppressor gene in lung fibroblast cells exposed to nano-alumina and zinc oxide nanoparticles

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Abstract

An increase in the broad usage of metal oxide nanoparticles in biological applications may have novel interactions with biological systems and result in emerging health problems. In this study, the effect of aluminum oxide (Al2O3, 35-45 nm) and zinc oxide (ZnO, 30 nm) nanoparticles (NPs) on the mutation of codon 248 of the p53 gene, a key gene in the tumor cell suppression, was conducted in the cellular growth medium. After 72 hours of exposure to the mentioned NPs (5, 10, 25, 50 μg/ml), lung fibroblast MRC-5 cells were evaluated through MTT assay for cytotoxicity and subsequent PCR and sequencing analysis for in vitro genotoxicity assessment. After zinc oxide nanoparticle (ZnO-NPs) treatment, cells underwent substantial cytotoxicity, and these toxicities were significant at doses of 25 and 50 μg/mL. Regarding aluminum oxide nanoparticles (nano-alumina, Al2O3-NPs), a concentration of 50 μg/mL affected the viability of MRC-5 cells. There was no significant difference in other treated groups compared to the control. Interestingly, the mutation in the 248 codons of the P53 gene was observed following 72 hours incubation of MRC-5 cells with 5 μg/mL of Al2O3-NPs. This mutation occurred in the form of the CGG to CCG, transforming the arginine codon into proline generators. The mutation in codon 248 p53 (replacement cytosine instead of guanine) will result in non-functional P53 protein production. Hence, following the modulation of p53 in lung cells, the possibility of cancer emerging will be increased. Moreover, determining the nanoparticles' accurate cytotoxic concentration is of great importance to reduce deleterious effects on the body's normal cells.

Key words: Aluminum oxide, Mutation, p53, Lung fibroblast MRC-5 cells, Zinc oxide

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