ABSTRACT

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Metallic nanoparticles have extensive medical, consumer and industrial applications due to their unique characteristics. Exposure of these particles to humans and other biological systems has aroused global concerns regarding their fate in biological systems resulting in a demand for their toxicity assessment.

This project was designed to obtain key data on the cytotoxicity, mutagenicity and genotoxicity of iron oxide, aluminium oxide, copper, titanium oxide and silver nanoparticles both *in vitro* and *in vivo*. *In vitro* data was gathered by exposing bacterial cells and monkey kidney cell line (CHS-20) to iron oxide, aluminium oxide and copper nanoparticles. The cytotoxicity, mutagenicity, decrease in cell viability and genotoxicity were studied by using Ames test, *in vitro* cytotoxicity assay, trypan blue assay, micronucleus assay and comet assay.

In vivo acute oral (LD50) toxicity evaluation, serum biochemical analysis and histological examination were carried out for iron oxide, aluminium oxide and copper nanoparticles. *In vivo* cytotoxic and genotoxic potential of iron oxide, aluminium oxide, copper, titanium oxide and silver nanoparticles was observed in mice bone marrow cells using micronucleus assay and comet assay. *In vivo* mutagenicity of titanium dioxide and silver nanoparticles was observed using *Pig-a* assay. Inductively coupled plasma-mass spectrometry was used to determine the amount of titanium oxide nanoparticles that reached the bone marrow.

Results from *in vitro* studies showed decrease in cell viability, cytotoxicity, mutagenicity in dose dependent manner and genotoxicity at the highest tested dose for only copper nanoparticles. *In vivo* acute oral toxicity evaluation showed moderate toxicity of copper nanoparticles with oral LD50 value 325 mg/kg. *In vivo* toxicological assessment demonstrated that only copper and titanium oxide nanoparticles were cytotoxic (decrease in percentage of reticulocytes). Furthermore copper nanoparticles showed a significant increase in micronuclei and DNA damage at a highest tested dose.

The results from inductively coupled plasma-mass spectrometry suggested that the titanium oxide nanoparticles reached the bone marrow, the target tissue for the genotoxicity assays. Serum elevated level of liver enzymes was observed in mice treated with copper nanoparticles along with mild to moderate vacuolation in hepatocytes.

The finding of this thesis will advance the knowledge about the toxicological effects and safety of metallic nanoparticles in view of their tremendous applications in various fields of life.