ABSTRACT

Background: Nanotechnology has emerged as a new science that provides promising technology breakthroughs and innovative applications due to the unique properties of nanoparticles. The field has progressed immensely from the time of its inception and has become a flourishing industry today. Nanotechnology utilizing engineered nanomaterials, specifically Titanium dioxide and Zinc oxide nanoparticles have found applications in every day life and a rapid rise in nano enhanced consumer and health care products has been observed. The unusual physicochemical properties of nanoparticles that lead to advances of nanotechnology also lead to unique biological effects, and therefore interactions between nanoparticles and biological systems needs to be studied to understand the adverse human health side effects. Since the properties of nanoparticles enable to them to travel easily through organisms, and result in biological interactions, there is a possibility that nanoparticles interfere with DNA causing deleterious effects. Genetic damage plays a key role in initiation and progression of carcinogenesis and in reproductive and developmental abnormalities, hence assessment of genotoxicity is important. The physicochemical properties of nanoparticles play a critical role in determining their toxic effects, therefore characterization in exposure media and evaluation of their bioavailability in nano form needs to be done.

Aim: The present study was done to investigate the *in vitro* genotoxicity of Titanium dioxide and Zinc oxide nanoparticles using short term cultured human peripheral blood lymphocytes through cytogenetic endpoints, Chromosomal aberration assay and Comet assay. To achieve this aim and elucidate the possible mechanism behind genotoxicity, stability and dispersion studies were carried out by characterization of physicochemical properties, particokinetic analysis followed by DNA binding studies and NP induced genotoxicity. This study emphasizes on the importance of physicochemical parameters for dispersion of NPs besides DNA damage induced at specific concentrations of NPs using *in vitro* lymphocyte cultures.

Methods: Characterization of nanoparticles was done using X-Ray diffraction and UV-Visible spectroscopy while physicochemical assessment and particokinetic analysis was done using data obtained from Borosil Mansingh Survismeter. Bioavailability and dispersion studies were performed using Dynamic Light Scattering and Zeta potential analysis. To assess the binding of DNA to nanoparticles, DNA binding studies were done using Electronic Absorption Spectroscopy and Fluorescence emission spectroscopy. These studies helped decipher the extent and strength of DNA binding, which corroborated with understanding genotoxicity of nanoparticles. Assessment of genotoxicity potential at low dose nanoparticle exposure for 24 hours was done by performing *in vitro* short-term human peripheral blood lymphocyte culture to detect clastogenic effects of NPs and DNA damage detection was studied by performing Comet assay in cultured cells.

Results & Conclusion: The results of physicochemical and particokinetic studies revealed better dispersion of Titanium dioxide and Zinc oxide nanoparticles in media than water. Moreover, Dynamic Light scattering and Zeta potential suggested nanoparticles were not agglomerated and were available in 'nano' form in culture media. Good binding affinity of nanoparticles to DNA indicated direct mode of genotoxicity supporting the genotoxicity results that indicated Titanium dioxide and Zinc oxide nanoparticles are genotoxic when exposed to low dose exposure for 24 hours.