ABSTRACT

The major aim and focus of this work is to develop an interaction between nanoparticle toxicity, oxidative stress and dosage. Various biochemical variables, expression levels and histological aspects have been studied so as to gain insight into the mechanistic process of nanoparticle toxicity. Nanoparticles largely used in our day-to-day life have been selected (TiO$_2$, ZnO, Al$_2$O$_3$, Ag and Au) and a therapeutic strategy has been used, so as to recover altered variables and toxic manifestations.

Nanoparticles interact with cellular components generate ROS, that lead to cellular toxicity if the magnitude of ROS production overwhelms the antioxidant defense status of the cell. Accumulation of TiO$_2$, ZnO, Al$_2$O$_3$ nanoparticles in brain disturbs the normal metabolism of neurotransmitters, ultimately leading to brain damage. These NPS affected the gene expression profile of antioxidant enzymes.

The study explained the mechanisms involved in nanotoxicity, when exposed to various metal oxide nanoparticles. Furthermore, oxidative stress activates a specific signaling pathway which together with the depletion of antioxidant defenses leads to release of pro-inflammatory cytokines. All NPs (Al$_2$O$_3$, TiO$_2$, ZnO) led to significant oxidative injury, although severity or degree of toxicity varies for each NP and also dosage used.

Silver nanoparticle was found to be more toxic at higher dose compared to lower dose. Metallothionein induction along with oxidative stress was established as the major mechanism for silver and gold nanoparticle toxicity. Elicitation of neurotoxicity following exposure to Ag NPs was also observed, even at lowest dosage of 20 µm.

Overall, my work specifically suggests and establishes that NP exposure causes oxidative injury, responsible for various systemic manifestations, which could be efficiently recovered through supplementation of antioxidants.

Administration of natural antioxidants was found to be a valuable therapeutic strategy. Alpha lipoic acid depicted partial recovery, whereas quercetin helped in marginal recovery on exposure to Al$_2$O$_3$ NPs.