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Title of PhD Thesis : **Application of Metal and Metal oxide Nanoparticles Capped with Antioxidative Molecules to Balance the Oxidative Stress in Cellls**

ABSTRACT

The study led to synthesis, functionalization and characterization of ZnO nanoparticles capped with amines (Isopropylamine, Diethylamine & Triethylamine), glutathione (GSH) and curcumin. ZnO-NPs were synthesized via non aqueous sol-gel method using zinc acetate dihydrate and various amines as surfactant. FESEM showed 10-50 nm spherical ZnO-NPs while UV-Visible spectroscopy showed the tailoring of surface of ZnO-NPs. FTIR spectroscopy described the functional groups due to bio-functionalization. XRD reflected the crystallinity of ZnO-NPs while XPS described the elemental composition of ZnO-NPs. Zeta potential of amine and GSH functionalized ZnO-NPs was positive while curcumin functionalization led to negative zeta potential. Contact angle technique showed the wettability and hydrophobicity of nanoparticles. Growth kinetics and cellular viability study on Gram positive (*S. aureus*) and Gram negative (*E.coli*) bacteria along with human embryonic kidney cell line, HEK-293, using these bio-functionalized ZnO-NPs showed effective management of oxidative stress even in the induced condition. The hydroxyl radical scavenging activity of the synthesized nanoparticles was also performed which confirmed its anti-oxidative effect and control of ROS in biological systems. The effect of artificial oxidative stress in *E. coli* was higher than that of *S. aureus* due to thinner cell wall of *E. coli* which was getting damaged, affecting cellular viability and survivability. It was observed that MIC of both bacterial strains had decreased in case of treatment with $H_2O_2$when compared to that of without it by 30-70 %. However, the reduction in MIC was comparatively higher for GSH functionalized ZnO-NPs suggesting its better bio-compatibility and better oxidative management than curcumin and amine modified ZnO-NPs. Thus, with comparison to the

three groups of ZnO-NPs, GSH functionalized ZnO-NPs followed by amine modified ZnO-NPs and curcumin functionalized ZnO-NPs showed bio-compatibility and oxidative stress management in that order. Also, it was observed that DEA modified ZnO-NPs and their functionalization products like GSH and curcumin were more effective than IPA and TEA modification and their functionalization products under induced oxidative. In case of HEK-293 cell lines, oxidative stress by hydrogen peroxide was management as observed by growth kinetics, increased IC50 values, cellular morphology and biological assays by the application of ZnO-NPs. Amine modified ZnO-NPs shows reduction in IC-50 value under induced oxidative stress of H_2O_2 by 17.8 %, 8.8% and 12.1% in IPA, DEA and TEA respectively as compared to without H_2O_2 in cell culture. GSH functionalized over IPA, DEA and TEA modified ZnO-NPs similarly shows reduction by 2.8%, 7% and 2.4 % respectively while curcumin functionalized over IPA, DEA and TEA modified ZnO-NPs similarly had shown reduction by 2.8%, 7% and 2.4 % respectively. Thus, GSH functionalization of ZnO-NPs serves to be managing the oxidative stress better than amines and curcumin functionalized ZnO-NPs in HEK-293 cells. Diethylamine modified ZnO-NPs with subsequent functionalization by GSH and curcumin proved to be managing the oxidative stress better than isopropyl and triethylamine modified ZnO-NPs. These functionalized ZnO-NPs also helped in improving the bio-compatibility of ZnO-NPs. DNA damage by functionalized ZnO-NPs were found to be limited proving them of their better compatibility with cellular apparatus. They are internalized preferably by HEK-293 cells by endocytosis forming ionophores and to some extent by direct diffusion across membrane. These bio-functionalized ZnO-NPs neutralize both extracellular as well as intracellular ROS to manage oxidative stress. It is proposed that they invoke the antioxidant enzyme and the antioxidant genes apart from directly neutralizing the ROS inside the cell.

GSH functionalized ZnO-NPs were also used for feasibility study of organophosphate pesticide, chlorpyrifos, by amperometric method. The sensing capacity of ZnO-NPs modified with GSH was enhanced and used in fabricating chlorpyrifos pesticide sensor. It is found that bare ZnO NPs are insensitive to pesticides while GSH coated ZnO NPs exhibit monotonous increase of sensitivity as a function of OP concentration over the wide range (10 ppb to 1000 ppb) with sensitivity of 2.1 $\mu A/ppm/cm^2$, detection limit of 3 ppb and regression coefficient of 0.92. Electrochemical measurement indicated that sensors can be used for few times due to the known inhibitory nature of OP and AChE reaction.