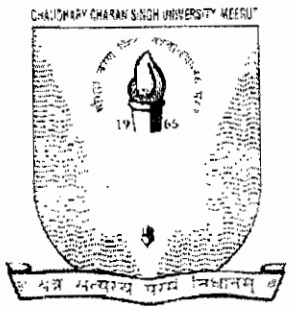
# PROTECTIVE EFFECTS OF ZINC OXIDE NANOPARTICLES ON DIMETHYLNITROSAMINE INDUCED HEPATOCARCINOGENICITY IN WISTAR RATS




**ABSTRACT OF THESIS**
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# Abstract

Biochemical mechanisms of hepatotoxicity of DMN, studied so far postulate that it is metabolized by CYP4502E1 in the liver. The resulting product hydroxymethylnitrosamine is unstable and decomposes to formaldehyde and methanol as end products. These electrophilic molecules react with cellular nucleophiles including DNA and initiate the process of tumor formation. Concurrent pathological manifestations include fibrosis, impaired liver function, oxidative stress and inflammatory responses.

Considering the unique properties of ZnONPs, a study on its effects on liver function of DMN treated rats was performed.

In present experiments, post treatment of ZnONPs to DMN treated rats also improved liver function. Serum bilirubin values also declined in DMN + ZnONPs treated rats. ZnONPs can facilitate improvement in liver function by diminishing liver cell necrosis, oxidative stress and other associated mechanisms. However, induction of zinc metallothionein by ZnONPs may also contribute in improving liver function through its antioxidative properties.

**In nut shell, present investigations demonstrated that ZnONPs presented as the strong inducer of zinc-metallothionein. Concentration of Zn-MT *in situ* was further increased in the liver of DMN+ ZnONPs treated rats. Thus it was concluded that zinc-metallothionein played a critical role in restoring hepatic structure and function disturbed by DMN. Future studies using ZnONPs as therapeutic platform against other hepatotoxins will strengthen our hypothesis. It is expected to be a big step in chemoprevention of liver cancer. Potent MT inducing character of ZnONPs contributed significantly to its therapeutic behavior against DMN induced hepatotoxicity in rats.**

*1. NPs that escape presystematic accumulation can accumulate in liver, leading to profound interactions with hepatic cells and other non parenchymal cells.*

*2. In hepatocytes, their effects are – increased ROS, oxidative stress reduced detoxication efficiency, plasma membrane disruption, cell content leakage and cell death.*

*3. However, ZnONPs have shown surprising effectiveness agoinst experimental hepatocarcinogenesis (HCC) in rat.*

*4. Properties of ZnONPs that were exploited during present study were antioxidative and pharmacological potential towards liver pathology such as amelioration of fotty liver, antifibrotic, antiapoptotic, antinecrotic as well as anticancer effects.*

*5. Biochemical investigations showed that ZnONPs could influence ROS formation, glutathione cycle, antioxidant enzymes, inflammatory cytokines and DNA damage in hepatocytes.*

*6. It is envisioned that similar therapeutic regimes on liver diseases can be exploited considering unique properties of NPs.*

*7. Modulation of HCC will depend on core properties of NP, dosage, redox potential, presence or absence of other NPs or toxic compounds, degree of aggregation and effectiveness of cellular enzymes.*

*8. We should understand that real life situations involving liver and metallic NPs s very complex. Surprising results "exceptions to the rule" ore very likely to be observed.*

*9. It is the first study that confirms protective effects of ZnONPs against HCC induced by DMN.*

*10. As more research on interaction between NPs and liver diseases is performed, more cases of their efficacy on toxicity are anticipated.*