7. SUMMARY AND CONCLUSION

The present study was intended to test the hypothesis that Fe$_3$O$_4$ NPs could cause learning and memory impairments, since these NPs have been shown to induce neurotoxicity mediated by oxidative damage. Brain seems to be more vulnerable to oxidative stress due to its rich content of fatty acids. Oxidative stress has been confirmed as a primary candidate in any pathological condition. Furthermore, a close link has also been demonstrated between oxidative damage and learning and memory impairments long back. The key fact of this present investigation was to evaluate the safety measurement of Fe$_3$O$_4$ NPs, as its usage in biomedical applications has been growing in recent years.

This current investigation of impacts of Fe$_3$O$_4$ NPs was carried out both in vitro and in vivo models. Human neuroblastoma (IMR-32) cells were used as in vitro model. Total decrease in all the antioxidant enzymes suggests that antioxidant defense system was impaired after the exposure of cells to Fe$_3$O$_4$ NPs. Decreased cell viability, increased cell death and DNA damage was observed in a dose dependent manner. Oxidative stress to the cellular constituents through Fenton/Haber-Weiss reaction mediated by the iron internalized inside the cell could be explained as possible reasons for all the consequences. In addition, an alteration in the cellular morphology was also observed.

The increased iron content in the sub-brain regions of NPs administered mice confirms that the Fe$_3$O$_4$ NPs accumulated in CNS which lead to disturbed brain iron homeostasis. The suppressed antioxidant defense system indicates that the Fe$_3$O$_4$ NPs exposure resulted in a steep ROS generation leading to severe oxidative stress and damage to brain cells. The neuronal DNA damage and tissue aberration in the cerebral cortex, hippocampus and cerebellum evident the oxidative damage to CNS. This study demonstrates that exposure to Fe$_3$O$_4$ NPs results in DNA damage, oxidative stress and histological aberrations in mice brain which in turn affects learning and memory processes. Furthermore, this finding indicates that iron accumulation in brain disturbs the cholinergic system which impairs the motor coordination, motor activity and learning and memory.
Summary and Conclusion

Considering the great progress of iron NPs application study, comprehending the behavior of the materials in living system will have implications not only for safety consideration but also for their valid applications in biomedical and disease treatment in the future. Since human exposure to ferrofluids is predicted to increase in nanomedicine-based therapeutics, these findings warrant the need to devise adequate testing strategies in order to ensure that a given ferrofluid has not incorporated changes in its valence shell that might influence its cellular interaction and the ensuing downstream toxicity. Alternatively, it may be necessary to design iron NPs that are highly stable chemically and oxidation resistant without compromising on cellular damage. Thus, these results suggest that, though Fe$_2$O$_3$ NPs have added advantages over other metal ion NPs in biomedical applications, its safety has to be considered before considering for the clinical diagnosis and therapies.