SUMMARY AND
CONCLUSION
In the present study, the work has been attempted to investigate endocrinological, biochemical, antidefense and histological effects of fluoride in the form of sodium fluoride in liver, kidney, thyroid and adrenal of adult male Wistar rats (Rattus norvegicus). Ameliorative role of certain antioxidants viz. melatonin and amla on sodium fluoride induced toxicity were also investigated and compared with withdrawal studies.

Male Wistar rats were used as an animal model in the present work. These animals were fed with NaF low dose (5mg/kg) and high dose (10 mg/kg) for 60 days. On 61st day animals were sacrificed and then vital as well as endocrine organs were used for analyzing various biochemical parameters, oxidative stress indices and histopathological changes in different groups. Melatonin and Amla were co-supplemented with high dose of NaF for same duration and their mitigating efficiency with respect to their tissue profiles were also evaluated in this study.

Significant diminutions in the body and organ weights were declined in the NaF intoxicated rats. This decline could be accredited due to low intake of food due to NaF exposure. It also caused oxidative stress by generating reactive oxygen species (ROS) and augmented free radical toxicity in all tissues as observed by alteration in antioxidant enzymes like- superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR) and glutathione-s-transferase (GST) activities. This was accompanied by amplified lipid peroxidation (LPO) levels, while the levels of non-enzymatic antioxidant glutathione (GSH), total –SH and ascorbic acid (AA) were altered. The treatment also caused a significant diminution in the protein levels of all the tissues. This could be due to an inhibition of its synthesis and increased protein oxidation due to an increased oxidative stress.
Activity of various enzymes related to energy and general metabolism namely adenosine triphosphatase (ATPase), succinate dehydrogenase (SDH), acid phosphatase (ACPase) and alkaline phosphatase (ALpase) were declined in all the tissues of NaF intoxicated rats indicating amendment in the functions of these organs. Inhibition of enzymes activity involved in TCA cycle including ATPase and the abridged activities of ACPase and ALPase in the vital and endocrine organs of NaF treated rats were confirmed by histopathological observation. Estimation of glycogen recorded an increment along with depletion in phosphorylase activity. In addition carbohydrate metabolism, other functional parameters like creatinine observed a significant increase, where as a decrease in cholesterol in liver was observed after NaF treatment. Thyroid hormonal levels were also altered by NaF intoxication. In conclusion, it affected the balance of defence system, hormonal and other biochemical profiles of these organs.

Fluoride retention was further confirmed in all these tissues which correlated with the various altered indices after NaF exposure. Histomorphological studies also revealed supportive evidence with the biochemical indices explaining organ toxicity of NaF.

Supplementation of melatonin and amla to NaF treated groups; considerable amelioration was noticed with respect to tissue biochemical indices, defencing system and structure of these organs. Thus, these antioxidants effectively mitigated NaF induced toxicity by scavenging the free radicals, thereby reducing oxidative stress in our study. The protective effects of melatonin are due to it and its metabolites and their antioxidant action through trapping of free radicals, and activating antioxidant enzymes where as amla has numerous components including ascorbate that have defensive actions as cited in earlier. Upon withdrawal of the treatment for 30 and 60
days no recovery was observed comparable to control and supplemented groups in our study.

CONCLUSION

Our study revealed that NaF led to organ toxicity in rats affecting biochemical, histological as well as hormonal status. Melatonin and Amla proved to be very potent antioxidants against NaF exerted organ toxicity. Protective effect of melatonin and amla is attributed to their antioxidant properties. These compounds thus can be further studied to develop a possible antioxidant supplementation against NaF exposed population. Hence, the results of this work have a significant impact on the mitigation of NaF elicited toxicity.

FUTURE LINE OF WORK

- To investigate effect of NaF in combination with other toxicants.
- To study toxic effect of NaF on endocrine and immune systems of animals exposed to sodium fluoride.
- To study various pathways of cell death in cells exposed to NaF.
- Molecular mechanism needs to be evaluated in cells undergone oxidative stress.
- To study the molecular mechanism of herbal products on toxicant induced toxicity in alone or combination to understand their protection comparatively.
- To investigate efficacy of other antioxidants of herbal origin on NaF induced toxicity in population exposed to it.