SUMMARY

Chapter I

The chapter deals with the material and various methods employed in the present investigation.

Chapter II

Although toxicological effects of fluoride have been studied using different animal models, very little efforts have been directed at understanding the median lethal dose (LD_{50}) of fluoride. By calculating the LD_{50}, information is obtained on the types of toxic effects the chemical produces, on the onset of toxicity, the duration of toxicity, etc. However, it has been documented that the median effective dose vary widely even in closely related species. Hence as a prelude to comprehend the toxicological effects of fluoride to growing chick, it was thought desirable to find out the LD_{50} of fluoride for female postnatal chicks, using the probit method of Finney (1971). The 24 h LD_{50} value obtained from dose-response curve was found to be 77.62 mg F^-/kg b.w.

Chapter III

In acute fluoride toxicity one of the most striking changes in humans is the alterations found in gastrointestinal mucosa. Damage to digestive system at the growing stage of an organism will in turn affect the progress of development. This is especially true in the case of poultry, where at the early period of postnatal development, intense growth of the organs of supply (intestine, pancreas, liver, etc.) is a characteristic feature. This is to meet the augmented requirement of the organs of demand at the later period of development.

The aim of the present study was to assess the extent of damage caused by fluoride to the development of digestive system and in turn the growth of the bird. Chronic fluoride poisoning had reduced the weight and curtailed the allometric growth of small intestine, pancreas and liver. Fluoride induced alterations in the cellular proliferative and synthetic activities might be

the possible reasons for such a change in development of digestive organs.

Chapter IV

Cytotoxic effects of fluoride on cell proliferation and DNA synthesis has been well established in cell and tissue cultures. However, such an action of fluoride is poorly understood in animal system. In the present study an attempt was made to analyse the effect of chronic fluoride poisoning on the nucleic acid and protein profiles in the postnatal developing chicks. Fluoride inhibited both DNA and RNA content in the tissues of growing chicks. However, the DNA/RNA ratio remained unaltered, but RNA/protein ratio exhibited an apperent hike, points to defective translatory process.

Chapter V

A haematological study of the red blood cell characteristics in growing chicks of domestic fowl subjected to subacute dose of fluoride was examined at various intervals (1, 5, 10, 20 and 30 days). The characteristics included Fe (iron), Hb (haemoglobin), PCV (Packed Cell Volume), RBC (Red Blood Corpuscular) Count, MCH (Mean Corpuscular Haemoglobin), MCV (Mean Corpuscular Volume) and MCHC (Mean Corpuscular Haemoglobin Concentration). The investigation showed that all the parameters studied tend to decline by day 20 of fluoride administration as compared to control birds. A further reduction in blood cell characteristics was registered at 30 d of treatment. The possible reasons for anaemia and erythropenia were discussed.

Chapter VI

In the present chapter, the role of sodium flouride on energy yielding metabolism in growing chicks is assessed. Hyperglycaemia together with depletion in tissue glycogen are the major changes noticed in the metabolic front. In the light of the results presented in chpter VII, it could be reasoned that hyperglycaemia could be an effect due to parasympathetic neuropathy in

the fluoride treated chicks. Cholinergic dysfunction usually leads to down regulation of glycogenetic hormones like insulin which is known to activate enzymes such as glycogen synthetase. This fact is suppoerted by the observation that, the activity of glycogen synthetase showed a parallel decrease in the tissues of fluoride treated chicks. Cholinergic dysfunction and resultant insulin deficiency set in due to fluoride administration could be expected to enhance the stimulation of glycogenolysis by glucagon and catecholamines. This fact is strengthened by the present findings that glycogenolytic hormones while inactivating glycogen synthetase caused the activation of glycogen phosphorylase. In the present study it was also observed that there are appreciable changes in the liver lipid metabolism. The accumulation of lipids and lowered SDH activity observed in the experimental birds points to a possible reduction in oxidative metabolism. The enhanced SDH activity observed in the present study also indicates a possible shift in the energy metabolism towards anaerobic pathways.

Chapter VII

Derangement in glucose uptake mechanism due to fluoride intoxication is evident from the fact that chronic fluoride poisoning leads to hyperglycaemia (Chapter VI). In the present context, an attempt was made to study the influence of fluoride on glucose transport and uptake mechanism in the liver and gastrocnemius muscle of postnatal chicks. In the case of birds, insulin dependent flow coupled and acetylcholine induced sugar transport mechanism are the two major glucose transport mechanisms. Reduction in the AChE activity observed in the fluoride treated birds indicates lowered ACh secretion from nerve endings.

Another component of the transport activity is the membrane bound enzyme, Na^+-K^+ ATPase. In the present study a decrease in Na^+-K^+ ATPase activity has been noticed in the tissues of experimental birds. Elevated cAMP concentration is known to inhibit Na^+-K^+ ATPase activity. Hence, it is possible that fluoride might have exerted its inhibitory effect on Na^+-K^+

ATPase through elevated cAMP level.

Currently examined hydrolases *viz.*, acid and alkaline phosphatases are not only lysosomal, but are known to be distributed in the soluble fraction of the cytoplasm as well. Such localization endows these enzyme with broad spectral functioning of not only lytic nature, but also in other metabolic reactions. There was a decrease in the phosphatase activity which may be construed to contribute towards histopathological events.