SUMMARY AND CONCLUSION
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Adequate iodide intake is necessary for normal thyroid hormone synthesis since thyroid hormones are the only substances in the body that have iodine in their structure. The major sources of dietary iodine are iodized salt, iodated bread and dairy products. Individuals may also be exposed to iodide in medications, disinfectants and radiographic contrast agents. Concern that excess iodine intake may cause thyroid dysfunction has renewed interest in the role of iodine in the thyroid metabolism.

In the present study excess amount of iodine was fed to animals to observe the effects on the metabolic and developmental disorders. In the first experiment it was observed that when animals were fed the low iodine diet and excess iodine diet (5 times more than that present in the normal iodine diet) the results obtained suggested that the group fed excess amount of iodine had increased food intake throughout the entire study when
compared to the rest of the two groups whereas the body weights did not show any significant differences. The weight of the thyroid glands increased significantly in the group fed low iodine diet whereas no difference was observed in group fed high and normal iodine diets. This suggests that on feeding low iodine diet for a prolonged period of time i.e. 47 weeks, the thyroid showed enlargement indicating the presence of goiter. The serum thyroid hormone levels decreased in both the groups fed low and high iodine diets when compared to the group fed normal iodine diet. These observations indicate that low, high/excess iodine in the diet altered the thyroid hormones in the pattern as found in the hypothyroidism.

During the experimental period of 47 weeks the animals were bred twice to obtain progeny and to see the relative effects on reproduction. It was observed that only 50% of the female rats from all the groups conceived and delivered, during the first breeding, whereas in the second breeding only the group fed excess iodine delivered. The mortality was also maximum in the group fed excess iodine. As conception had taken place both the times in the group fed excess iodine it can be stated that the initial stage of reproduction was not affected. In the group fed the low iodine diet conception was affected as majority of the females did not conceive which may be due to the dietary iodine deficiency but it
is difficult to explain the failure of conception in the group fed normal iodine. Maximum number of pups were born in the group fed high iodine diets and the mortality was also high. Though mortality was present in the other two groups also. The relation between high iodine intakes and reproduction is not yet very well studied hence no definite statements can be made but observations during the experiments revealed that the milk secretion of the lactating dams may have been affected in the group fed excess iodine and hence the mortality of the pups could have occurred.

The remaining pups were fed their respective diets. After six weeks of age 5 animals from each groups were sacrificed. The results obtained suggest that though the animals were fed a similar diet as that fed to their parents, the thyroid gland enlargement was not present in both the groups fed low and excess iodine in the diet. Similarly thyroid hormones levels T\textsubscript{3} and T\textsubscript{4} also showed an increasing trend in both the groups when compared to control. This increased trend of thyroid hormones along with no increase in the weight of the thyroid gland indicate that hypothyroidism was not present after the feeding of 6 weeks. The possible reasons for the above obtained results may be firstly due to the fact that the animals were fed for a short period of time, secondly that when the adult animals were bred, the experimental feeding duration was only seven weeks and therefore the effect of
the experimental diet on the adult animals may not have occurred and hence the progeny may not shown any adverse effect and thirdly that the progeny sacrificed after six weeks were selected on body weight basis from each group. Hence due to these differences the progeny did not show any similar results to that seen in the adult, 47-week old animals.

The remaining progeny from the group fed low iodine and normal iodine diets were fed for a prolonged period of time i.e. nineteen weeks after which they were sacrificed. The results obtained suggest that on feeding the low iodine diet for a prolonged period induced alterations in the thyroid hormone levels along with thyroid gland enlargement as found in iodine deficiency hypothyroidism. Therefore to deplete the iodine stores of the body it required a longer duration of feeding the low iodine diets.

In an other experiment, animals were again fed low iodine diet, normal iodine diet with sodium perchlorate (goitrogen or inhibitory substance) through drinking water and high iodine diet (5 times more than that present in the normal diet). Similar observations were made after eleven weeks of feeding as seen in the earlier experiment. When sodium perchlorate was administered the effect on the thyroid gland and hormones was more profound. The increase in the weight of the gland and the reduction in the
levels of thyroid hormones was much more than that seen in the group fed the low iodine diet. The group fed excess iodine in the diet also showed similar results to those seen in the first experiment. The serum $T_3$ and $T_4$ levels had decreased when compared to the control group but no thyroid gland enlargement was present. This suggests and confirms the fact that high/excess dietary iodine induced hypothyroidism in the animals as observed in iodine deficiency-hypothyroidism. Hence the inhibition of the synthesis of thyroid hormone resulting from excess iodine often referred to as the Wolff-Chaikoff effect was observed in the rats fed high iodine in the diet. The peripheral metabolism had not yet been affected as the protein and cholesterol levels in the blood did not alter and were found to be within the normal range.

Further experiments were planned to observe the effect of different increasing doses of iodine in the diet. Hence the animals were fed low iodine, no-mal iodine diet with and without perchlorate and high iodine diets for a period of eleven weeks. The different high iodine diets contained 5, 10, 15 and 20 times excess iodine than that present in the normal diet. The results obtained in the group fed low iodine and normal iodine with sodium perchlorate were similar to that present in the earlier experiments. The animals fed high/excess dietary iodine showed a similar picture to that seen in animals fed sodium perchlorate.
Hence it strongly indicates that high/excess dietary iodine has induced hypothyroidism in the animals as the dietary intake of iodine increased. The Wolff-Chaikoff effect was clearly observed as the iodine dose became progressively larger. Inhibition of inorganic binding of iodine began to occur and resulted into a decreased yield of organic iodine and an augmented formation of thyroid hormone. Since till now the experimental duration was restricted to a maximum of eleven weeks another experiment was carried out as a sequel to the previous one. The animals were fed sodium perchlorate and excess iodine in the diet i.e. 20 and 25 times more than the normal iodine containing diet. The animals were fed for a prolonged period of time during which they were bred. This experiment was carried out in two phases. In phase-I, four animals from each group were sacrificed after eighteen weeks of feeding and in phase-II the rest of the animals were sacrificed after 31 weeks of feeding. The remaining animals of phase-II were bred after phase-I to observe the effect on the reproductive cycle. The results obtained in phase-I were different from those seen in the earlier experiments. The group fed excess iodine (20 times) showed a failure to escape the Wolff-Chaikoff effect whereas animals fed 25 times excess iodine inhibited the Wolff-Chaikoff effect and hence depicted increased levels of serum $T_3$ and $T_4$. This indicates that excessive amounts of iodine fed to animals for a particular period of time did not induce
hypothyroidism, indicating increased levels of T₃ and T₄. Therefore the dose of iodine and the duration of ingestion was very crucial to observe the Wolff-Chaikoff effect.

In phase-II when the remaining animals were fed for a prolonged period of time the Wolff-Chaikoff effect was observed. This failure to escape the effect again suggests that the duration of feeding the high amounts of iodine is very important. In phase-II the serum T₃ and T₄ levels were found to be lowered when compared to the control. The groups fed sodium perchlorate in phase-I showed a classical picture of hypothyroidism with decreased levels of serum T₃ and T₄ levels and enlarged thyroid gland but in phase-II when the animals were fed for a longer duration the levels of reduction was not as severe as that seen in phase-I possibly suggesting that the animals may have adapted to the goitrogen present in the diet. The peripheral metabolism did not show any significant differences.

On breeding the animals fed normal iodine diet with sodium perchlorate, normal iodine diet and a high iodine diet to the animals, the pups obtained showed a similar thyroid status as that found in their respective parents. In groups fed perchlorate and high iodine in the diet, serum thyroid hormone levels decreased when compared to the control group. As the age of the
pups increased the levels decreased significantly indicating the presence of hypothyroidism.

Finally to confirm whether the animals adapted to the prolonged ingestion of sodium perchlorate (goitrogen), a group of animals were fed for twelve months. At the end of the experimental study the results indicated that on feeding perchlorate for such a prolonged period, hypothyroidism was induced with increased thyroid gland weight suggesting the presence of goiter and a severe lack of thyroxine. The reduction in the levels was much more than that present when the animals were fed for 31 weeks. Therefore the hypothesis that adaptation to perchlorate may be present was not justified as the serum thyroxine levels decreased significantly though triiodothyronine levels remained above normal.

Studies presented here indicate that deficiency of dietary iodine resulted in decreased synthesis of the iodine containing thyroid hormones T\textsubscript{3} and T\textsubscript{4} but required a longer duration of feeding low iodine diets. Similarly when any goitrogen was present in the diet the degree of iodine deficiency was much more significant and faster than on feeding low iodine diets. When large doses of iodine was given for short and long term periods it led to decreased levels of serum T\textsubscript{3} and T\textsubscript{4}, providing a basis for
iodine induced hypothyroidism but during the experimental feeding at a particular juncture i.e. after 18 weeks of feeding, giving a dose of 25 times more iodine in the diet showed increased serum $T_3$ and $T_4$ levels suggesting that iodine induced hypothyroidism was not present, suggesting the Wolff-Chaikoff effect which depends on the attainment of the critical level of iodine in the thyroid gland, depending on the duration of exposure to iodine.

The response to excess iodine is variable as seen from the present experiments. When these data are extrapolated to humans it can be stated that some individuals would tolerate large intakes without side effects whereas others may respond adversely. The amount of iodine required to cause adverse effects would be highly individual depending upon the dose and the duration of exposure to iodine. The interaction of iodine with the thyroid gland is complex but further studies are needed to understand the effect of iodine on the thyroid gland and to make rational public health decisions on dietary intakes.