Effect of maize (Zea mays) on thyroid status under conditions of varying iodine intake in rats

Amar K Chandra, Dishari Ghosh* and Smritiran Tripathy

Endocrinology and Reproductive Physiology Laboratory, Department of Physiology, University College of Science and Technology, University of Calcutta, 93, Acharya Prafulla Chandra Road, Kolkata 700009, India

* Present address: Defence Institute of Physiology and Allied Sciences, DRDO, Lucknow Road, Timarpur, Delhi 110 054, India

SUMMARY

Maize (Zea mays) is the third most planted food crop and one of the major energy sources among the people of the semiarid tropics. Presence of cyanogenic glucosides, which are antithyroidal substances, in maize is well established. However, the effect of chronic consumption of maize on thyroid status under varying levels of iodine nutrition remains unexplored. In this study, goitrogenic content and in vitro thyroid peroxidase (TPO) inhibiting activity of maize of Indian origin, along with its in vivo anti-thyroid potential without and with extra iodine supplementation, has been evaluated. Edible part of maize contains thiocyanate (20 ± 2 mg/kg), cyanogenic glucosides (10.12 ± 1.2 mg/kg) and glucosinolates (2.5 ± 0.2 mg/kg). In vitro inhibition of TPO activity was found in fresh maize extract but the presence of extra iodide in the incubation media showed reduction in such inhibition to a certain extent. Inhibition constant (IC$_{50}$) and PTU equivalence of fresh maize were 66.25 ± 1.42 µg and 1.36, respectively. Significant increase in urinary excretion of thiocyanate and iodine was observed in the rats fed maize for 45 days and 90 days, respectively, associated with increased thyroid weight, decreased TPO activity and serum total circulating T$_4$ and T$_3$ levels as compared to their respective controls. A relative state of morphological as well as biochemical hypothyroidism developed gradually in chronic maize fed rats. Adequate iodine supplementation in maize fed groups of rats improved the thyroid status to a certain extent but failed to prevent the antithyroidal activity of the plant food.

Key words: Maize, goitrogens, iodine, thyroid hormones, thyroid peroxidase

Introduction

The cyanogenic plant maize (Zea mays) is the third most planted food crop in most of the world including India and its subcontinents. Cyanogenic glucosides (thiocyanate precursors) have been found in several staple foods like cassava, bamboo shoot, sweet potatoes including maize (Gaitan, 1988; Chandra et al., 2004b). The cyanogenic glucoside present in maize is 2-O-β-D-glucopyranosyl-4-hydroxy-7-methoxy-1, 4-benzoxazin-3-one (Mirjam et al., 2001). Regular consumption of cyanogenic foods containing cyanogenic glucosides, glucosinolates and thiocyanate affect thyroid physiology and may develop endemic goitre in long run, especially in iodine deficient environment (Delange et al., 1982). Dietary supplies of iodine and cyanogenic plant food (thiocyanate precursors) are determined by measuring the excretory pattern of iodine and thiocyanate, respectively (Querido et al., 1974; Dunn et al., 1993).

Though maize is one of the most important food crops of the semiarid tropics and it constitutes the main source of food energy for many poor people, literature on its goitrogenic/antithyroid potential under varying states of iodine nutrition is not available. Since experimental studies on maize of Indian origin, especially with reference to aetiopathogenesis of thyroid disorders, are lacking the present study was undertaken to evaluate the thyroid status after chronic consumption of fresh maize under conditions of varying iodide intake in the rat.

Materials and Methods

Collection of maize

Fresh maize was collected from the local markets for the measurement of goitrogenic constituents, assay of in vitro TPO activity and also for feeding the experimental animals.

Correspondence to be addressed to: Dr. Dishari Ghosh, E-mail: Dishari_l@yahoo.co.in
Animals

Wistar rats weighing 80 ± 5 g were allocated to control and experimental groups of ten each. Animals were caged in well-ventilated stainless steel cages and maintained in the laboratory on standardized normal diet (20% protein), which consisted of 70% wheat, 20% Bengal gram, 5% fish meal powder, 4% dry yeast powder, 0.75% refined til oil and 0.25% shark liver oil, and water ad libitum (Chandra et al., 2004b).

Feeding study

Control rats were fed normal laboratory diet. Experimental rats were fed normal laboratory diet replacing one-third of the diet with fresh maize. In potassium iodide (KI) supplemented group, rats were fed normal laboratory diet with extra iodide at 12-14 μg/rat/day (Gaitan and Merino, 1976). In maize-fed and potassium iodide (KI) supplemented group, rats were fed both maize (1/3 portion of diet) and extra iodide at 12-14 Ig/rat/day. The animals were maintained with above-mentioned regimen for 45 and 90 days, respectively. Based on change in body weight, the first set of rats treated for 45 days were considered as growing rats while the second set of rats treated for 90 days were considered as mature rats (Chandra et al., 2004b).

Feed consumption, corrected for feed wasted, and body weight were measured every seven days. During the last week of the treatment animals in each group were kept in metabolic cages for 24 hr to collect the urine over xylene for the analysis of iodine and thiocyanate. At the end of the experimental period the body weights of the animals were recorded and the animals were sacrificed at the end of the 45th and 90th days of the experiment following the prescribed ethical procedures. Just before sacrifice, the portal blood samples were collected from each rat under ether anesthesia and the serum was separated.

Measurement of dietary goitrogens in maize

Cyanogenic glucoside: It was measured following the method of Lambert et al. (1975). The test material was hydrolyzed by the enzyme glucosidase (β-glucosidase) and the hydrocyanic acid thus liberated was trapped in sodium hydroxide. Cyanide content of trapped hydrocyanic acid was then determined quantitatively.

Glucosinolates/thioglucosides: The enzyme thioglucosidase reacts with thioglucosides, producing thiocyanate. Following this principle total thioglucosides was measured according to Gmelin and Virtanen (1960). The thiocyanate thus produced was determined adopting the method of Aldridge (1945), as modified by Michajlovskij and Langer (1958).

Thiocyanate: The plant food was extracted with clean sand and water and refluxed subsequently. The extract containing thiocyanate was then allowed to react with benzidine hydrochloride and the intensity of color thus formed was measured photometrically following the method of Aldridge (1945), as modified by Michajlovskij and Langer (1958).

In vitro inhibitory effect of maize on thyroid peroxidase activity - To evaluate in vitro anti-TPO activity of maize, human thyroid tissue was collected from ENT Department, S.S.K.M. Hospital, Kolkata. Edible part of each fresh plant was homogenized in assay buffer (5 mg plant tissue in 5ml, pH 7.2, 100mM phosphate buffer) and then centrifuged at 700 xg for 10 min. After centrifugation, 50μl of aliquot of the supernatant was taken separately in 1ml cuvettes containing acetate buffer (pH 5.2, 50mM), potassium iodide (1.7 mM) and microsomal fraction of thyroid tissue. Freshly prepared hydrogen peroxide (0.3 mM) was added last to start the reaction to assay the TPO activity (∆OD/min/mg protein) under the influence of the respective extracts, following the procedure of Gaitan et al. (1989), modified by Chandra et al. (2004a).

Anti-TPO activity of the plant extract in the above-mentioned condition was also studied in presence of excess potassium iodide. For this purpose, in the cuvettes maintaining the same concentration of assay buffer, the extract and H2O2, the concentration of potassium iodide was increased and it was found highest after adding 20μl of KI (3.4mM) and ∆OD/min/mg protein was recorded.

Assay of IC50 and 6-n-propyl-2-thiouracil (PTU) equivalence (Chandra et al. 2004a) - The activity of raw plant extract was also evaluated in terms of the concentration necessary to produce 50% inhibition (IC50) of thyroid peroxidase activity. The effect of raw plant extract was studied at different concentrations ranging from 10 μg to 150 μg original fresh plant to determine the concentration required to produce IC50 of thyroid peroxidase activity. The TPO activity under the influence of the plant at a particular concentration, as percentage of inhibition of the control value, was plotted against the concentration of the original plant extract, and the concentration at which 50% inhibition occurred (IC50) was...
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determined from the plot. The IC_{50} value of the plant given is mean ± SD of 6 observations. To compare the relative anti-TPO activity of the plant against a known antagonist, IC_{50} of 6-n-propyl-2-thiouracil (PTU obtained from Sigma Chemical Co.) was determined.

Analysis of urine

Estimation of iodine: It was measured by dry-ashing following the method of Karmarkar et al. (1986). In this method the iodine content in the urine sample was estimated by drying urine at 60°C, in presence of potassium carbonate, and the iodine present in the ash was measured by cerric-arsenite system.

Estimation of thiocyanate: It was measured following the method of Aldridge (1945) as modified by Michajlovskij and Langer (1958). Trichloroacetic acid was added to urine sample, mixed and centrifuged. Saturated bromine water was added to the supernatant and 4% arsenic trioxide (As,O_3) was then added to oxidise all bromine present in the sample. After that, benzidine hydrochloride and pyridine mixture were added and the color developed gradually. After 30 min, the optical density was measured at 525 nm.

Measurement of thyroid peroxidase activity

A 10% homogenate of thyroid tissue was prepared in phosphate buffer (pH 7.2, 100mM) and sucrose solution (500 mM) at 4°C. Homogenization was carried out in a Potter-Elvehjem glass homogenizer for 45-60 sec at 2000 rpm and about 15 strokes min^{-1}. The homogenate was centrifuged at 1000 xg for 10 min and the resultant supernatant was further centrifuged at 10,000 xg for 10 min at 4°C to obtain the mitochondrial fraction. The microsomal fraction containing most of the peroxidase activity was obtained by centrifuging the post-mitochondrial supernatant at 1,05,000 xg for one hour. After centrifugation, the precipitate was solubilized in phosphate buffer. Thyroid peroxidase activity was measured following I_1 formation from iodide using spectrophotometer (UV-1240 Shimadzu, Japan) at 353 nm by the method of Alexander (1962). For performing the kinetic assay, in a 1 ml cuvette, 0.9 ml of sodium acetate buffer (pH 5.2, 50 mM), 10 µl KI (1.7 mM) and 20 µl microsomal fraction of thyroid tissue containing 0.03-0.04 mg protein were added and the reaction was started by the addition of 20 µl freshly prepared H_2O_2 (0.3 mM) according to laboratory standardization. The thyroid tissue protein level was determined by the method of Lowry et al. (1951) using bovine serum albumin as standard. The results are expressed as ΔOD /min/mg protein.

Assay of total circulating thyroxine and triiodothyronine using ELISA Kit

Total serum thyroxine and triiodothyronine were measured using ELISA kit supplied by Lilac Chemicals, (USA).

Histological study of the thyroid gland

At the end of the experiments, the thyroid glands of rats were dissected out and fixed in formal buffer solution and then embedded in paraffin after usual processing. Sections were cut at 5-6 µm thickness, stained with hematoxylin and eosin, and observed in a microscope.

Statistical analysis

All data were statistically analyzed and presented as mean ± SD. Comparison among the groups was performed by ANOVA followed by multiple comparison t-test.

Results

Goitrogen content

Goitrogen content in fresh edible portion of maize was measured. Cyanogenic glucosides formed 10.12±1.2 mg/kg wet weight, glucosinolates 2.5±0.2 mg/kg wet weight and free thiocyanate 20±2 mg/kg wet weight.

In vitro inhibitory effect of maize on thyroid peroxidase activity

TPO activity of control (10µl KI, 1.7 mM) rat was 1.62±0.054 ΔOD/min/mg protein. In vitro inhibitory effect of edible part of maize on thyroid peroxidase activity was determined after application of fresh maize extract with and without extra iodide in the incubation media. In vitro TPO activity was 0.562±0.02 ΔOD/min/mg protein in rat exposed to aqueous extract of fresh maize and it was just 65% as compared to control. After addition extra iodide in the incubation medium (20 µl KI, 3.4 mM) inhibitory effect was reduced to a certain extent, and TPO activity was 0.590±0.03 ΔOD/min/mg protein (69%) as compared to control.

Relative anti-TPO potential

The relative anti-TPO potential of the test material and PTU was determined by estimating the amount of plant food or PTU capable of producing 50% inhibition (IC_{50}) of TPO activity. IC_{50} and PTU equivalence of maize were 66.25±1.42 µg and 1.36, respectively.

Urinary thiocyanate, urinary iodine as well as thyroid weight, thyroid peroxidase activity and serum circulating levels of total T_4 and T_3 in control, maize-fed,
KI supplemented and maize-fed + KI supplemented groups of rats, treated for 45 days and 90 days, respectively, were measured and the results are presented in the table 1.

**Urinary thiocyanate concentration**

Rats fed maize for 45 days and 90 days showed significant increase in urinary thiocyanate concentration (£p<0.001 and £p<0.01, respectively) as compared to their respective controls. Of these two sets (45 days and 90 days) thiocyanate excretion was higher in the longer duration maize-fed group. Iodine supplementation increased the thiocyanate excretion in both the maize-fed groups treated for different durations, in comparison to maize-fed iodine non-supplemented groups.

**Urinary iodine concentration**

Urinary excretion of iodine was increased, but not significantly, in maize-fed groups of rats treated for 45 days and 90 days, respectively, when compared to their respective controls. Urinary excretion of iodine was higher in iodine-supplemented groups of rats.

**Thyroid weight**

Significant increase in thyroid weight was observed in both the maize-fed groups of rats treated for different durations in comparison to their respective control groups (£p<.001 and £p< 0.05). The gain in thyroid weight was more in the group fed maize for the longer duration. The apparent gain in thyroid weight was more in both the groups fed maize for different durations compared to the groups fed maize non iodine supplemented groups but the differences were not significant.

**Histological studies of thyroid**

In control rats thyroid follicles were lined by low cuboidal epithelial cells filled with colloid and all the follicles were almost equal and regular in size. There was an increase in the number of irregularly shaped small follicles

**Table 1-** Maize induced alteration on urinary thiocyanate, urinary iodine and thyroid weight thyroid functional status under varying iodide intake in rats for (A) 45 days and (B) 90 days

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urinary thiocyanate (m moles/L)</th>
<th>Urinary iodine (m moles/L)</th>
<th>Thyroid weight mg/100g body weight</th>
<th>ΔOD/min/mg protein</th>
<th>SerumT4 µg/dl</th>
<th>Serum T3 ng/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.17 ± 0.01</td>
<td>24.85 ± 0.85</td>
<td>7.19 ±0.18</td>
<td>4.02 ± 0.03</td>
<td>4.2 ± 0.11</td>
<td>126.34 ± 2.54</td>
</tr>
<tr>
<td>B</td>
<td>0.19 ± 0.05</td>
<td>32.51±1.4</td>
<td>8.47 ± 0.7</td>
<td>5.16 ± 0.52</td>
<td>4.52 ± 0.33</td>
<td>144.33±2.43</td>
</tr>
<tr>
<td>Maize fed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.73 ± 0.12 *)</td>
<td>30.64±0.29</td>
<td>8.72 ±0.18</td>
<td>3.04 ± 0.09 **</td>
<td>3.75 ± 0.08 **</td>
<td>118.34±1.2 *</td>
</tr>
<tr>
<td>B</td>
<td>0.95±0.11 **</td>
<td>38.43±0.81</td>
<td>10.81±0.58 **</td>
<td>1.81±0.18 **</td>
<td>3.57±0.07 *</td>
<td>125.78±1.2 *</td>
</tr>
<tr>
<td>KI supplemented</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.18 ± 0.02</td>
<td>178.01 ± 2.68</td>
<td>5.84 ± 0.21</td>
<td>7.56 ± 0.48</td>
<td>4.47±0.1</td>
<td>135.24±4.47</td>
</tr>
<tr>
<td>B</td>
<td>0.21 ± 0.09</td>
<td>187.77±1.51</td>
<td>7.7 ± 0.15</td>
<td>9.84 ± 1.64</td>
<td>4.76±0.31</td>
<td>151.87±2.54</td>
</tr>
<tr>
<td>Maize fed KI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.88 ± 0.04 *)</td>
<td>188.15±1.25</td>
<td>7.09±0.07</td>
<td>5.33±0.34</td>
<td>3.9±0.1</td>
<td>123.57±0.59</td>
</tr>
<tr>
<td>B</td>
<td>1.08 ± 0.16 *)</td>
<td>196.27±1.00</td>
<td>9.07±0.08</td>
<td>3.67±0.29</td>
<td>3.98±0.08</td>
<td>130.86±0.76 **</td>
</tr>
</tbody>
</table>

Values are mean ± SD of ten observations. Those bearing superscripts are significantly different by ANOVA followed by multiple comparison t test

*£p<0.001, ** £p<0.05 when compared with (A) 45 days control

*p<0.001, ** p<0.05 when compared with (B) 90 days control
Fig. 1. Photomicrographs of thyroid glands of the different groups (H&E, X20). A, control; B, control + KI treated; C, maize-fed; D, maize-fed and KI treated
filled with relatively less colloid, showing hypertrophied and hyperplastic follicular epithelial cells in the thyroid of maize-fed groups of rats. Variation in the number and size of follicular cells and colloid content were observed in KI-supplemented and non-supplemented maize-fed groups of rats. In addition, the colloid stained more intensely with eosin in maize-fed rats compared to control and KI-supplemented group of rats (Fig 1).

**Thyroid peroxidase activity**

In maize-fed rats the thyroid peroxidase activity decreased significantly compared to the corresponding controls (p<0.05 for 45 days and p<0.05 for 90 days). Between the two maize-fed groups i.e., one for 45 days and the other for 90 days, TPO inhibition was more in the group fed maize for 90 days than 45 days. Supplementation of iodine to both the maize-fed groups resulted in increase of the TPO activity in comparison to only maize-fed groups but failed to restore its activity to normal.

**Serum T4 and T3 levels**

Total circulating T4 and T3 levels were determined in rats fed maize for different durations and compared with their respective controls. Total serum T4 and T3 levels decreased significantly (p<0.05 and p<0.001) after feeding maize. Between the two maize-fed groups the reduction was more pronounced in the group treated for longer duration. Supplementation of iodine in both the maize-fed groups resulted in increase of the serum T4 and T3 levels to that of maize only fed groups but did not bring it back to the normal level.

**Discussion**

The major goitrogenic substances of cyanogenic origin viz., cyanogenic glucosides, glucosinolates and thiocyanate were found in different concentrations in the edible part of fresh maize. Goitrogenic/antithyroid potential of cyanogenic glucosides, glucosinolates and thiocyanate is well established (Gaitan, 1990). These goitrogenic substances act in conjunction with iodine deficiency in the development of endemic goitre and associated disorders (Lagasse et al., 1980). This emphasizes the need to investigate the importance of goitrogens in influencing thyroid function under varying states of iodine intake. Though maize is one of the major plant foods in the third world countries including India but its antithyroidal potential under varying intakes of iodide has not been evaluated. In India, consumption of cyanogenic plant, as evidenced by urinary thiocyanate level, is considered an etiological factor for the persistence of residual goitre in post-salt iodization phase (Chandra and Ray, 2001; Marwaha et al., 2003). To find the possible antithyroidal activity of maize, if any, its in vitro inhibitory effect on thyroid peroxidase activity using human thyroid tissue was studied with aqueous extract of fresh maize and found that the edible part of the fresh plant has potent inhibitory activity on this regulatory enzyme for thyroid hormone synthesis. There are evidences to reverse the goitrogenic/antithyroid potential of thiocyanate or thiocyanate-like compounds present in cyanogenic plants by supplementing extra iodine (Schone et al., 1990; Rao and Lakshmy, 1995). Therefore, in vitro anti-TPO potential of maize in the presence of extra iodide was also determined and it was found that extra iodide supplementation reduced the anti-TPO activity to a certain extent but failed to obviate it totally.

After ingestion, cyanogenic glucosides and glucosinolates of cyanogenic plant foods are converted to thiocyanates, isothiocyanate-like active goitrogenic substances, by widespread glucosidases, sulfur transferase and myrosinase enzymes present in the plant itself and the animal tissues (Montgomery, 1969; Van Etten and Wolff 1973). Urinary excretion of thiocyanate is considered as a marker to evaluate the dietary supplies of cyanogenic foods (Querido et al., 1974) because the thiocyanate thus formed in the body, after metabolism of cyanogenic constituents, determines its concentration in the blood followed by its appearance in the urine (Michajlovskij and Langer, 1958). Thus, the increased concentration of thiocyanate in the urine in maize-fed rats further indicates that these goitrogens are metabolized to thiocyanate. The concentration of thiocyanate in urine was more in the group fed maize for a longer duration. Supplementation of extra iodine in maize-fed rats further increased the thiocyanate excretion and this observation was consistent with the earlier observation by Dehlberg et al. (1984). Thiocyanate or thiocyanate-like compounds that arise from cyanogenic plants inhibit the uptake of iodide by the thyroid gland (Tewe et al., 1984), interfering with the iodide-concentrating mechanism of the gland (Bobek et al., 1992). Thiocyanate, when present in excess concentration, also stimulates the efflux of iodide from thyroid gland (Halmi 1961; Ermans and Bourdoux 1989) that results in increased excretion of iodine in urine (Malooof and Soodak, 1959). Earlier
workers also reported that presence of cyanogenic glucosides, glucosinolates, in the diet cause increased urinary excretion of iodine (Duhlberg et al., 1984; Schone et al., 2001). In the present study the urinary excretion of iodine in maize-fed groups of rats for different durations was increased markedly because of the conversion of these cyanogenic constituents to thiocyanate. The free thiocyanate of maize might have prevented the uptake of iodide by the thyroid gland and stimulated the efflux of iodide from thyroid, resulting in an increase in urinary iodine. Excretion of iodine through urine is considered as a marker of iodine nutritional status because 90% of body’s iodine is excreted in urine (Dunn et al., 1993). Thus, in spite of adequate iodide intake, thyroid gland fails to concentrate iodide for synthesis of thyroid hormone because of the interference of excess thiocyanate or thiocyanate-like compounds present in maize. This study further indicates that iodine-retaining capacity of the thyroid gland / body depends on the concentration of thiocyanate or consumption pattern of cyanogenic plant foods that are ultimately metabolized to thiocyanate.

The weight of the thyroid gland was increased in maize-fed rats, mediated through its goitrogenic constituents. Supplementation of extra iodine though prevented the gain in thyroid weight in the maize fed rats to an extent but was not capable to normalize it because of the effect of thiocyanate, when present in a low concentration, may be precipitated by iodine (Ermans and Bourdoux, 1989) but such an effect for excess thiocyanate that arises from cyanogenic glucosides and the intermediate derivatives of glucosinolates viz., isothiocyanate, goitrin, etc., is not generally antagonized by excess iodine (Schone et al., 1994; Lakshmy et al., 1995; Chandra et al., 2004).

Thyroid histology was also altered in both the treated groups of rats, and the changes were almost similar in nature but the variation was in severity. Thyroid follicles in treated rats were lined with high follicular epithelial cells containing less colloid, reduced in size, irregular in shaped and stained deeply with eosin. The number of follicles was more, indicating hypertrophy and hyperplasia of the follicular epithelium under the influence cyanogenic constituents of the plant. Deeply stained eosinophilic colloid in the follicles of the treated animals indicated that the entry of iodine into the follicles for synthesis of thyroid hormones was reduced markedly under the influence of goitrogenic constituents and their metabolites present in maize. The changes as noted in the thyroid gland histology in maize-fed rats were almost similar in nature to that of TSH-stimulated diffuse goiter, as suggested by Kanno et al. (1990). In the control group of rats, the thyroid follicles were almost regular in shape and normal in size, filled with relatively more homogeneous colloid and they were lined by flat cuboidal epithelial cells. The more eosinophilic colloid in the treated rats indicated an iodine deficient colloid as reported by Gaitan et al. (1993), and in the present study similar observation was made in the thyroid section of experimental animals. In KI-supplemented groups the deterioration in thyroid structure were more less than treated group but iodine supplementation could not bring back its normal structure.

Thiocyanate having the same molecular size as that of iodide inhibits the incorporation of iodide into thyroglobulin by competing with iodide at the thyroid peroxidase level (Ermans and Bourdoux, 1989). Besides, thiocyanate prevents the iodide oxidation by thyroid peroxidase, depending upon the binding of thiocyanate to the substrate site with lower affinities (Virion et al., 1980). In maize fed groups of rats TPO activity was markedly reduced because thiocyanate that arises from enzymatic degradation of thiocyanate precursors in maize had inhibited thyroid peroxidase activity probably by inhibiting the incorporation of iodide or iodide oxidation or both the mechanism. Like morphological alteration in thyroid, TPO activity was reduced in proportion with the duration of maize feeding inspite of the intake of adequate iodine.

Diet deprived of iodide but rich in thiocyanate lowers the circulating level of thyroxine and triiodothyronine in rats (Papas et al. 1979; Lakshmy et al., 1995). In both the maize fed groups the urinary concentration of thiocyanate was high while the circulating thyroid hormones were low indicating that thiocyanate and its precursors present in maize had reduced the circulating T4 and T3 levels. Decreased circulating hormone levels were associated with decreased thyroid hormone synthesis because of inhibition of TPO activity of thyroid gland in rats fed with fresh maize was observed in the present study. The regulatory role of TPO on thyroid hormone synthesis has been confirmed by earlier studies (Taurog 1970; Gaitan 1990; Virion et al., 1980). Inhibition of iodide uptake and thyroidal iodide efflux due to excess thiocyanate (Ermans and Bourdoux, 1989; Maloof and Soodak, 1959) might be other reasons for the decreased synthesis of
thyroid hormones in maize fed rats. Supplementation of iodide through diet had increased the thyroid hormone levels to an extent along with slight increase TPO activity but failed to bring back at normal level.

The overall results showed that chronic consumption of chronic consumption of maize gradually developed a relative state of biochemical as well as morphological hypothyroidism even in presence of adequate iodine in circulation. Besides the inhibition of iodide uptake and iodide efflux, the other etiological factor underlying this phenomenon is the in vivo inhibition of TPO activity in chronic maize fed animals. Prolonged feeding showed more deleterious effect on thyroid status even in presence of adequate iodine intake. Extra iodide supplementation had reduced the antithyroidal activity of maize to some extent but failed to mitigate the effect totally. In vivo TPO inhibitory activity under the influence of maize has further been confirmed by in vitro study using human thyroid tissue with and without extra iodide.

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