PREVALENCE AND PATHOLOGY OF HYPOTHYROIDISM IN CATTLE

By

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THESIS

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DECLARATION

I hereby declare that this thesis entitled **PREVALENCE AND PATHOLOGY OF HYPOTHYROIDISM IN CATTLE** is a bonafide record of research work done by me during the course of research and that the thesis has not previously formed the basis for the award to me of any degree, diploma, associateship, fellowship or other similar title of any other University or society.

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Certified that this thesis entitled PREVALENCE AND PATHOLOGY OF HYPOTHYROIDISM IN CATTLE is a record of research work done independantly by SRI J. N. RATNAKUMAR under my guidance and supervision and that it has not previously formed the basis for the award of any degree, fellowship or associateship to him.

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Dedicated to

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Introduction

1. INTRODUCTION

The important role of iodine deficiency in the causation of endemic goitre has been well established. One billion people was estimated to be exposed to the risk of goitre, because of deficiency of iodine and most of them dwell in the tropical regions of the third world. Because of its benign appearance, hypothyroidism ranks low in the heirarchy of acute and chronic diseases documented in the developing countries. Kelly and Snedden (1960) mapped out certain regions in India as endemic zones of goitre and this included coastal areas of Kerala. Various factors have been suggested to be responsible for the prevalence of iodine deficiency. Heavy rainfall can cause leaching of the surface soil and this leads to depletion of iodine in the soil. Besides this, the ubiquitous occurrence of environmental goitrogens, natural or artificial is an important factor that could lead to hypothyroidism. The intensive agricultural practices followed for increasing productivity necessitate extensive use of synthetic nitrogenous fertilizers and this in turn block the absorption and concentration of iodine by the plants. Therefore, in the food of human and animal population there is depletion of iodine and this could be a factor in inducing hypothyroidism. Although, the nature and magnitude of the effect of hypothyroidism has not been fully brought to light, Wilson (1975) summarised the effects of hypothyroidism as lowered milk production, infertility, lowered resistance to infection, increased susceptibility to ketosis, late abortion and retention of placenta. All these factors adversely affect the economical viability of the dairy industry.

There has not been any systematic study to assess the prevalence of hypothyroidism in livestock in the country, particularly in Kerala, except the limited survey study made by Mammen (1986) using serum PBI as marker. Therefore, with the objective of finding out the nature and prevalence of hypothyroidism, a survey ~~study~~ was undertaken employing thyroxine level in the serum as a marker.

Despite their ubiquitous occurrence, the many goitrogens identified in foods have generally been considered as subsidiary factors in the causation of hypothyroidism. However, the possible role of environmental goitrogens, in particular, cassava is now the subject of considerable speculation. The studies so far conducted indicated that cassava, which is extensively consumed as a staple food, can be a high risk factor for goitre in areas where iodine deficiency prevails. Cassava is the world's seventh most important food crop, following the major cereals, potatoes and yams. A major advantage of cassava is that it can grow on poor soil with little rain and it is the principal source of carbohydrates for about 300 million people, most of them in the developing countries of the tropics.

In Kerala, cassava is cultivated in an area of 193800 hectares and production is 32,92,300 tonnes. It is one of the staple food of people in the state and it is also fed to the livestock. Investigations conducted by Poulose (1984) in human population in the districts of Kottayam and Idukki indicated that hypothyroidism was prevalent among the people in those districts. On probing into their dietetic habits, he found that most of the hypothyroid patients were cassava eaters and concluded that it could ~~can~~ be an aetiological factor in causing hypothyroidism.

Livestock are fed cassava as an important diet ingredient in many places of Kerala. There has not been any reports on the goitrogenic effect in the animal population. Against this background, ~~therefore,~~ an experimental study was designed to assess the goitrogenic effect of cassava using broiler rabbit as the experimental model.

Review of Literature

2. REVIEW OF LITERATURE

2.1 Biosynthesis of thyroid hormones

Thyroxine (T_4) and Triiodothyronine (T_3) hormones elaborated by the thyroid gland, were characterized by their content of the element iodine. The initial substrate which get iodinated was shown to be the thyroglobulin of the colloid. DeRobertis (1941) identified that the release of thyroxine and triiodothyronine was accomplished by a group of peptidases and proteases present in the thyroid gland. In the body, 25 to 35% of the total ingested iodine was concentrated in the thyroid gland, though all tissues contained iodine (Riggs, 1952). Robbins and Rall (1960) pointed out that each thyroglobulin molecule contained approximately 110 thyroxyl residues. If the average molecule was 0.5% iodine it held 26 iodine atoms per molecule. Edelhock (1960) discovered that the complete protein was a tetramer of molecular weight of about 6,60,000. He observed that the thyroxyl residues of the thyroglobulin were first iodinated to monoiodotyrosine (MIT) and diiodotyrosine (DIT) was then formed by a second iodination. The ratio of MIT/DIT remained relatively constant from the earliest minutes of hormonogenesis and this suggested that iodination was not a random process, but an orderly one. Bush (1969) reported that T_3 forms were in greater proportion in the total hormone. Tong (1971) indicated that mono and diiodo tyrosines were coupled for the synthesis of T_3 and T_4. Three major steps were described in the synthesis of thyroxine. These involved concentration of iodide from the blood by the gland, enzymatic oxidation of iodide to iodine and the final synthesis of thyroxine was initiated by combining iodine with the protein thyroglobulin.

2.2 Hypothalamo-Hypophyseal-Thyroid Axis

Adams (1946) pointed out that the activity of the thyroid gland was influenced by the thyroid stimulating hormone (TSH), a glycoprotein formed in the specific basophilic cells in the pituitary gland called the thyrotroph. Normal thyroid function depended on a physical connection of the pituitary to the hypothalamus but isolated anterior pituitary retained some function. Scow and Greer (1955) induced hypothyroidism in animals and in man by section of the pituitary stalk. The stimulus for TSH secretion was presumably transmitted from the hypothalamic centres to the anterior pituitary in the form of chemical mediators called thyrotropin releasing factor (TRF) by way of the hypophyseal portal venous system. The response of the hypothalamic centres was presumed to be initiated by a metabolic effect of the iodothyronines (Gloldberg et al. 1955). The effect of TRF on TSH discharge was completely blocked by large amounts of thyroxine. Thus the secretion of TSH was governed by two interacting forces - hypothalamic drive on the thyrotrope cell, mediated by TRF and feedback inhibition mechanism exerted by thyroxine directly on the pituitary. Vale *et al.* (1967) found out that in the absence of hypothalamic drive, the pituitary was easily inhibited by T_4. On the other hand, the hypothalamus was capable of breaking through normal inhibitory effects of T_4 under such conditions as cold exposure. Kaneko (1970) observed that due to the action of TSH, the gland was increased in size, the height of the follicular epithelial cells was increased and there was loss of colloid. TSH hormone stimulated the accumulation of iodine, its organification and release of thyroxine (Jubb and Kennedy, 1970). When the level of stable iodine intake was low, there was an increase in the number and size of the cells and in the uptake and release of iodine and these changes were attributed to the increased level of TSH in circulation. Iodine was reported to enhance the hydrolysis of thyroglobulin liberated from the gland (Jubb and Kennedy, 1970). Khurana and Madan (1985) evaluated the functioning of Hypothalamo-Hypophyseal-Thyroid axis in bovines under tropical hot dry conditions by measuring T_4 and T_3. They found that the T_4 and T_3 increased significantly after the administration of thyrotropin releasing hormone (TRH). Also they observed that it initiated a biphasic response of T_3 and T_4 in bovines and the magnitude response of T_4 to TRH was higher than that of T_3.

2.3 Role of Thyroid hormones in metabolism

The work of Kendall (1915) led to the isolation, characterization and finally synthesis of thyroxine (T_4) from the thyroid gland. Harington and Barger (1927) identified the chemical structure of thyroxine. The primary function of the thyroid hormone was considered as regulation of cellular oxidation and stimulation of oxygen consumption for normal growth and development (Barker, 1951). Gross and Pitt-Rivers (1952) identified the tri-iodothyronine (T_3) in the gland and in the plasma. The compound was proved to be physiologically more potent and more rapid in onset of action than Tetra-iodo-thyronine (T_4) with four iodine atoms. Moreover, they speculated that Tetra-iodo-thyronine (T_4) was the form in which thyroid hormone was secreted, while tri-iodo-thyronine (T_3) was the form which was active at the tissue level.

Barker and Schwartz (1953) observed that oxygen consumption was increased in the heart, liver, muscle, kidney and in the white blood cells removed after the administration of thyroxine. They also found that some tissues such as brain did not share in this response. The activities of hexokinase, cytochrome reductase, cytochrome oxidase and other respiratory enzymes were augmented. Necheles and Beutler (1959) observed that the pentose phosphate pathway for glucose oxidation was stimulated. The thyroid hormone regulated the rate of energy turn over in vital organs and thus helped in maintaining basal metabolic rate of the body. Berman (1960) indicated that the thyroid hormones had an influence on the development of hair and pigmentation in animals.

Bush (1969) pointed out that along with other hormones, thyroid hormones exerted a control over the growth and development of young animals, temperature regulation, intermediary metabolism and reproduction.

Jubb and Kennedy (1970) observed that thyroxine hormone had the maximum influence on the growth rate in the presence of growth hormone, and in the absence of thyroid hormone, the effect of growth hormone was significantly reduced. Thyroxine was essential for full translation of genetic message into the ribonucleic acid and ribosomal synthesis of protein (Barker, 1971). Also according to Barker (1971) many metabolic processes were accelerated such as protein break down, carbohydrate and lipid turnover and calcium metabolism. Besides, microsomal protein synthesis was stimulated by thyroid hormones without dependence on cell nucleus. There was also apparent increase in RNA synthesis. Nervous functions at all levels were influenced by the thyroid. Werner (1971) reported that the thyroxine when given to normal animals not only caused mitochondria to swell, but also produced an increase in both the number of mitochondria per cell and the number of cristae per mitochondrium. Only mitochondria from tissues which respond to T_4 with increased oxygen consumption were shown to swell *in vitro*. Anderson and Harness (1975) observed that for every unit increase in body weight, there was a 69 unit increase in the thyroid hormone secretion rate.

Kaciuba-uscilko *et al.* (1987) observed that muscle glycogen utilization and lactic acid accumulation during exercise were enhanced in thyroidectomised goats in spite of the lower work rate and shorter duration of exercise in comparison with euthyroid goats.

2.4 Hypothyroidism

Marine and Lenhert (1910) termed congenital hypothyroidism occurring in an endemic iodine deficient area as endemic (enzootic) congenital hypothyroidism and sporadic congenital hypothyroidism, when occurring elsewhere. Also they reported that deficient maternal hormone production resulted in defective foetal development. Hojer (1931) indicated that ruminant hypothyroidism occurs mainly in areas of endemic goitre. Hypothyroidism had an adverse effect in young growing animals as it caused interference with the overall development than in mature adults (Ferguson *et al.* 1956). Calderbank (1958) reported cases of infertility associated with iodine deficiency. A close association between the thyroid and gonadal function and the loss of libido in males and suboestrum in females were reported (Calderbank, 1963). Wallach (1965) pointed out that hypothyroidism was generally characterized by lowered body temperature, increased sensitivity to low environmental temperature and growth retardation. Jubb and Kennedy (1970) reported that in hypothyroid domestic animals, the gestation period was significantly prolonged. They also pointed out that in the adult domestic animals, it was in the dog that hypothyroidism appeared as a predominant disorder of thyroid function. Also myxoedema, alopecia and high mortality rate were noticed in new born goats. Underwood (1971) reported that iodine deficiency was associated with reproductive failure. Mason and Wilkinson (1973) classified hypothyroidism into the following categories.

1. Primary hypothyroidism due to lack of functioning of thyroid without its associated enlargement.
2. Secondary hypothyroidism due to pituitary insufficiency.
3. Hypothyroidism due to iodine deficiency.
4. Hypothyroidism due to ingestion of goitrogens.
5. Hypothyroidism due to dyshormonogenesis
6. Hypothyroidism due to autoimmune thyroiditis
7. Hypothyroidism due to neoplasia.

Also they pointed out that serum cholesterol determination was a valuable tool in the diagnosis of hypothyroidism, since cholesterol synthesis was inversely proportional to the thyroid function. Wilson (1975) summarised the effects of hypothyroidism in ruminants as follows :

1. Retention of placenta
2. Infertility
3. Lowered milk production
4. Lowered resistance to infection
5. Increased susceptibility to ketosis
6. Late abortion, still birth and weak offsprings

Sreekumaran (1976) and Reddy (1982) observed increased serum cholesterol and protein levels and decreased protein bound iodine in goats, in experimental hypothyroidism. Kaelin et al. (1986) observed clinical signs such as lethargy, obesity and alopecia in dogs with confirmed hypothyroidism. They also observed that plasma cholesterol concentration was high in hypothyroid dogs. Apart from anaemia they observed increased creatinine phosphokinase activity and spontaneous muscle activity in those dogs with confirmed hypothyroidism. Mammen et al. (1986) induced hypothyroidism experimentally in calves using thiourea. They reported that there was alopecia, hypercholesteraemia, increased plasma protein and significantly lower level of protein bound iodine (PBI). Nasseri et al. (1986) induced hypothyroidism in ewes by feeding thiourea. They reported decreased serum thyroxine level, abortion, foetal death, and placental retention in hypothyroid ewes. Nelson and Ihle (1987) evaluated a series of 100 blood samples from twenty dogs with confirmed hypothyroidism, and found a normal T_4 concentration in only one sample, whereas 51 samples had normal

T_3 concentration. They concluded that this may be due to a failing thyroid glands preferential secretion of T_3 rather than T_4. Gillen (1987) reported a case of confirmed hypothyroidism in a cat. He observed bilateral symmetrical alopecia, subnormal T_3 and T_4 values, hypercholestraemia, hypercalcaemia, elevated alanine aminotransferase (ALT) and alkaline phosphatase level. Larsson (1988) indicated that determination of free thyroxine and cholesterol was the best single sample screening test for hypothyroidism.

2.4.1 Hypothyroidism due to iodine deficiency

Southcott (1945) pointed out that the major cause for simple hypothyroidism was iodine deficiency in the environment. The factors influencing the iodine content of the soil were studied by Goldschmidt (1954). Scott et al. (1961) observed that the composition of the diet as a whole also influenced the iodine requirements. Calderbank (1963) suggested that although soil is the source of iodine for both water and crops, there may be little or no correlation between the iodine content of the soil and pasture growing on it. Soil in the neighbourhood of the area was not always richer in iodine than those in lands but was dependent upon the prevailing wind, the amount of precipitation and the nature and reaction of the soil. Means et al. (1963) pointed out that when the surface soil was eroded, as for example by glaciation, the iodine content of that soil was low and the water derived from these regions was low in iodine content. Scrimshaw (1964) suggested that the effect of heavy rainfall also had an influence in the iodine content of the soil. Some microelements influenced the availability of iodine (Blokhina, 1970). Wilson (1975) stated that high protein intake interfered with the utilization of iodine. Walton and Humphrey (1979) reported that the iodine deficiency in the soil in the highlands of Papua New Guinea was due to high annual rainfall leaching the iodine from the soil. Pandav and Kochupillai (1982) reported that level of iodine in the drinking water was extremely low in the endemic zone, no value being higher than 3 microgram/l and most values considerably below this figure. Ghergariu et al. (1987) reported that an outbreak of goitre in new born piglets, was controlled by intra-muscular injection of potassium iodide to sows 3 or 4 times during late pregnancy and a single dose to 3 day old piglets, thereby proving that the outbreak was due to iodine deficiency in the diet.

2.4.2 Hypothyroidism due to environmental goitrogens

Greer and Whalton (1961) pointed out that thiocyanate was about 25 times more potent than nitrate in inhibiting thyroid function. Calderbank (1963) described two main types of goitrogens.

1. A thiocyanate type which inhibited iodide transport.
2. A thiouracil type which inhibited the organification of iodide. This effect was reversed by administration of thyroxine.

Catt (1970) described goitrogens like the thiocyanate as anionic goitrogens and those like thiouracil as organic goitrogens. Despite their ubiquitous occurrence many goitrogens identified in foods have generally been considered as subsidiary factors in the causation of hypothyroidism. But recent studies in Zaire indicated that cassava, which is extensively consumed as a staple food in that country can be a high risk factor for goitre in areas, where iodine deficiency also prevails (Gilbert, 1984).

2.4.2.1 Natural goitrogens

Rabbits fed on cabbage became hypothyroid and developed large hyperplastic goitre (Chensey et al. 1928). Sharpless et al. (1939) demonstrated the goitrogenic action of soyabean flour meal in rats by producing enlarged thyroid by feeding soyabean flour. Brassica seed when fed to rats produced goitre in rats (Kennedy and Purves, 1941). They recorded a 300 times increase in the weight of the thyroid glands and observed hyperplasia of the thyroid glands histologically. Moreover they observed a rapid increase in the basophil cells of the pituitary, which was associated with hyalinisation and vacuolation to form "signet ring" cells. Griesbach et al. (1941) reported that there was simultaneous loss of acidophil cells also in the rats fed with brassica seed diet. Wilson (1941) demonstrated fluorosis as one of the factors responsible for goitre in Punjab. Sharpless and Metzger (1941) pointed out that arsenic at 0.02 level in the diet in rams cause decreased growth, decrease in iodine concentration of the thyroid gland and an increase in the weight of gland. Astwood et al. (1945) discovered that the seeds of Ochlearia and Conringia orientalis contained the goitrogenic substance called 5, 5-dimethyl-2-thiooxazolidone. Astwood et al. (1949) isolated L-5-Vinyl-2-thiooxazolidone (Goitrin) from rutabagas and turnips, which was goitrogenic.

Spisni and Gravaglia (1954) discovered a marked decrease in follicular epithelium in sheep and goats fed cauliflower leaves. Clements and Wishart (1956) demonstrated that milk obtained from cows fed on narrow-stemmed kale or choumoellier (Brassica oleracea moellerii) interfered with the uptake of I^{131} both in the human subjects as well as in the experimental animals. In sheep fed white clover, a decrease in total iodine content of thyroid and inhibition of the conversion of inorganic iodine to organically bound iodine was observed (Butler et al. 1957). A heavy diet of kale to pregnant ewes caused high incidence of goitre and hypothyroidism in born lambs (Sinclair and Andrews, 1958). Setchell et al. (1960) reported the goitrogenic action of perennial grass. By enzymic hydrolysis Greer and Whalton (1961) derived 5-phenyl 2-thiooxazolidone from the seeds of Barbarea vulgaris and from the seeds, leaves, stem and roots of Rosedea luteola, which was found to be having antithyroid activity. He also found that 3-phenyl and 4-phenyl-2-analogues of this compound were also having thyroid antagonistic property. Greer (1962) isolated an active agent called "goitrin" from the yellow turnip and from Brassica seeds. In its natural state, it was shown to exist as an inactive thioglycoside. The intestinal bacteria hydrolysed the thioglycoside to the active compound. A high incidence of goitre in new born lambs of ewes and sheep grazing on pasture dominated by white clover, was reported by George et al. (1966). Russel (1967) observed heavier than normal thyroid glands and severe hyperplasia of the lining epithelial cells of the follicles and complete absence of colloid in lambs which had grazed rape. Blood and Henderson (1968) reported simple goitre and hypothyroidism in ruminants when fed Brassica seeds of Brussels sprints. Akiba and Matsumato (1977) observed 2 - 5 times enlargement of the thyroids in chicks fed rape seed meal compared to the controls. Gilbert (1984) pointed out that whatever the attributes of cassava as a food crop, they are far outweighed by the chronic cyanide toxicity, it induced that lead to hypothyroidism.

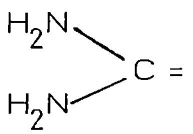
Purushotham et al. (1985) reported interfollicular fibrosis, squamous metaplasia of the follicular epithelium and rupture of follicles of the thyroid in sheep fed on castor bean meal (Ricinus communis).

Jham et al. (1987) suggested that pressed residue from cassava leaves could be incorporated into rabbit diets at levels of at least 10% without any loss in animal performance. Guercio et al. (1988)

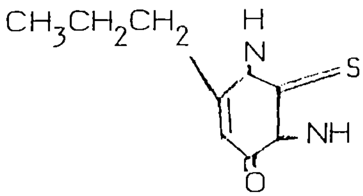
reported hyperplasia of thyroid of new born kids that died a few hours after being born to dams fed on cauliflower (Brassica oleracea) during pregnancy.

2.4.2.2 Chemical goitrogens

Chemicals like thiourea, propyl thiouracil and allied compounds have been used as goitrogens to induce hypothyroidism experimentally.



(Thiourea)



(Propyl thiouracil)

Treatment of hypertension with thiocyanate led to goitre and hypothyroidism in man (Barker et al. 1941). Rats treated with thiourea developed enlarged thyroids (Kennedy, 1942). He observed a three fold heavier thyroid glands, with follicles almost devoid of colloid. Also an increase in basophil cells and loss of acidophil cells were noticed in the pituitary. Baumann and Marine (1945) observed a decrease in the size of the adrenal gland among rats fed thiouracil. Jones et al. (1946) noted resorption of foetus in rats fed thiouracil which indicated that thyroid hormone was essential for utilization of oestrogen and progesterone. They observed hypertrophy of the thyroid, congestion of vessels, and depletion of colloid in rats treated with repeated doses of 1000 mg/kg body weight of thiourea. Zarrow and Money (1949) noticed involution of the adrenal cortex in rats treated with thiouracil. They stated that the involution of the adrenal cortex after thiouracil treatment was both morphological and physiological in nature. Sellers and Ferguson (1949) observed exopthalmus in rats treated with thiouracil.

Guinea pigs treated with propylthiouracil developed thyroid hyperplasia (D'Angelo et al. 1951). They observed increased vascularity and increase in the height of the acinar epithelial cells after 15 to 18 days of treatment. However, colloid resorption was an inconsistent feature. They also reported the microscopic changes in prolonged dosing with propyl thiouracil, as colloid resorption, high vascularity and cord like formation of follicular epithelial cells. Hall (1952) reported reduction in the serum cholesterol level in rats dosed with thiouracil. Swanson and Boatman (1953) noticed symptoms of hypothyroidism in two young and one old dairy bulls after treatment with thiouracil. They observed a two fold increase in the weight of the thyroid gland from that of the normal. Also, histologically the follicles were filled with colloid and lined by low cuboidal epithelial cells. Clausen (1954) stated that prolonged administration of thiouracil to rats resulted in macroscopical and microscopical changes simulating the late fibro-lymphoid stage of struma fibrosa. Durlach et al. (1954) observed an increase in the liver weight in guinea pigs treated with thiouracil. Harkness et al. (1954) recorded the effects of oral administration of thiouracil on the collagen content of thyroid of rats. They noticed increased weight and collagen content of the thyroid gland during the treatment.

Goldberg et al. (1957) observed enlarged thyroid glands with tall columnar cells, numerous mitotic figures, scanty colloid, papillary foldings and increased vascularity in rats treated with propyl thiouracil. They observed hyperplasia and hypertrophy of beta cells in the pituitary with a characteristic granularity and vacuolation of complete absence of granulated alpha cells. Lascelles and Setchell (1959) reported goitre and retardation of ossification centres in the offsprings of Merino sheep treated with methyl thiouracil at the dose rate of 0.5, 1.5 and 4.5 g daily, after conception. They also stated that there was reduction in the protein bound iodine (PBI) and increase in the cholesterol level. Follis (1959) produced colloid goitre in hamsters by thiouracil administration. McCarthy et al. (1959) reported adrenal atrophy among rats fed goitrogens, thiouracil and tapzole.

Lazo-wasen (1960) stated that in thiouracil fed rats, there was thyroid and pituitary hypertrophy with concomittent reduction in the Adrenocortico-trophic hormone (ACTH) level.

Mayberry and Astwood (1961) attributed the mode of action of thiourea and related compounds to inhibition of the formation of iodothyronine and their coupling to form iodothyronine. Danowski (1962) reported that thiourea and related compounds also diminished the inorganic iodide content of the thyroid and had a slight inhibitory effect on iodide pump.

In methimazole treated birds, hypercholesteraemia and hyperproteinaemia were observed (Nangia et al. 1975). Retarded growth in methimazole treated birds were recorded (Nangia and Gulati, 1976). Sreekumaran (1976) induced hypothyroidism in kids using thiourea. He observed hypertrophy of the follicular epithelium in the thyroid, hypertrophy and hyperplasia of the basophil cells in the pituitary and depletion of fat and petechiae in the adrenals. Prasad and Singh (1979) reported decreased plasma protein bound iodine in methimazole treated hypothyroid birds. They counteracted the effects of methimazole by the administration of thyroxine. Burstein et al. (1979) recorded a significant drop in the level of growth hormone in hypothyroidism induced by propyl-thiouracil with consequent loss of weight in rats. Davidson et al. (1979) demonstrated that in rats thiourea inhibited in vivo protein bound iodine formation. Reddy et al. (1982) induced hypothyroidism experimentally with thiourea in goats. They observed stunting of growth and apparent reduction in body weight of the goats. There was significant decrease in the protein bound iodine, and increase in the total serum protein and cholesterol level in all the animals dosed with thiourea. The values reached the normal level on discontinuation of treatment with thiourea. Reduction in quantity and quality of semen was observed in hypothyroid goats. Mammen et al. (1986) experimentally induced hypothyroidism in calves with thiourea. The calves became progressively anaemic and registered high serum cholesterol and plasma protein levels, but significantly low PBI level as compared to the control calves. There was significant increase in the relative weight of the thyroid, adrenal and pituitary gland but reduction in the relative weight of testes. Todd (1986) reported that in rats fed a diet containing 90 ppm methimazole, the weight of the thyroids increased with the duration of exposure; by six months the weight of the thyroid was ten times the weight of the thyroids from the control rats. After six months exposure to the antithyroid compound, there was diffuse hyperplasia, protrusion of follicular tissue through the gland capsule and into vascular spaces and the development of follicular nodules. Arnya et al. (1986) induced hypothyroidism in White Pekin ducks by administering methimazole. The thyroid glands showed signs of hypertrophy and hyperplasia of follicular epithelium. On administering L-thyroxine, the ~~normal~~ glands recovered to the normal state. Nasseri et al. (1986) studied the foetal pathology in experimental hypothyroidism in sheep employing thiourea. Serum thyroxine level decreased significantly and during the feeding of thiourea, abortion, foetal death, and placental retention occurred in hypothyroid ewes. Aborted foetuses and lambs from affected ewes showed poor body growth, alopecia, congenital goitre and degeneration of ovaries/testes.

Georgiev et al. (1987) reported that when sheep were fed on forage containing 0.6% potassium nitrate (dry matter) for 15 weeks, there was decrease in serum T_4, serum T_3, carotene and vitamin A. The blood sugar and methaemoglobin level were increased.

2.4.3 Hypothyroidism - the genetic factor

Falconer (1966) reported a condition termed dyshormonogenesis, in which the thyroid failed to produce normal quantities of thyroid hormone because of an inborn defect in the synthesis in Merino sheep. This led to increased production of thyroid releasing hormone (TRH) and resulted in thyroid hyperplasia. He recorded low hormonal iodine and high serum protein bound iodine concentration in the goitrous sheep than the controls. The concentration of the thyroid stimulating hormone was also significantly high in goitrous sheep. In their study on congenital goitre, Rac et al. (1968) observed enlargement of the thyroid glands in Merino sheep 25 times more than that of the control. They recorded a significant increase in the cholesterol level in the affected sheep. Mayo and Mulhearn (1969) suggested that in Merino sheep, the condition was due to the formation of abnormal iodoproteins, probably controlled by an autosomal recessive gene showing high penetrance and variable expressivity. Studies conducted by Poulose et al. (1984) also indicated the involvement of a genetic factor in the causation of goitre and hypothyroidism in man, apart from iodine deficiency and cassava factor in Kerala. Ricketts et al. (1987) reported hereditary goitre in Afrikander cattle caused by mutation, unmasking the alternative splicing of thyroglobulin transcripts. The hereditary goitre of Afrikander cattle was described as an autosomal recessive disease; homozygotes were shown to produce an abnormal thyroglobulin (Tg) and their thyroid contained normal sized 8.4-kilobase (Kb) Tg mRNA together with a miss-spliced 7.3 Kb mRNA which had lost exon 9. In their studies, the cDNA segment corresponding to the abnormal exon 8-exon 10 junction and the relevant genomic DNA region were cloned and sequenced. The mutation responsible for the disease was found to be a cytosine-to-thymine transition creating a stop codon at position 697 in exon 9.

2.5 Thyroidectomy

2.5.1 Surgical thyroidectomy

Marston and Pierce (1932) observed reduction in the growth rate and metabolic rate in thyroidectomised sheep. Silberg and Silberg (1940) reported a delay in endochondral ossification in thyroidectomised immature guinea pigs. Contopoulos et al. (1958) stated that after thyroidectomy in rats, there was atrophy of the pituitary gland and the plasma contained only decreased amounts of thyroid stimulating hormone, interstitial cell stimulating hormone and growth hormone. Yatwin et al. (1964) recorded a decrease in protein deoxyribonucleic acid ratio in thyroidectomised rats. Belonje (1967) reported an increase in plasma globulin and sedimentation of red blood cells in thyro-parathyroidectomised Merino rams. Symonds (1969, 1970) stated that in thyroidectomised goats, there was reduction in phosphorus excretion into long bones and endogenous excretion of phosphorus resulted in hypophosphataemia. McIntosh et al. (1979) observed somatic changes like delayed caseous development in the limbs and increase in the pituitary weight after foetal thyroidectomy. The thyroidectomised lambs failed to survive for more than few hours after birth. Li et al. (1986) studied the effects of thyrotropin releasing hormone on the serum concentration of T_4 and T_3 in thyroidectomized dogs. They observed that mean serum T_4 concentration decreased considerably within one day of thyroidectomy. Clinical signs of hypothyroidism including lethargy, dry coat, and diffuse alopecia were present a month later. Zdelar et al. (1986) performed total thyroidectomy in six simmental beef cattle, while six remains as controls. Thyroidectomised cattle showed clinical signs of hypothyroidism and low T_4 and T_3 values.

Kaciuba-Uscilko et al. (1987) studied the work performance, thermo-regulation and muscle metabolism in thyroidectomized goats (*Capra hircus*). They found that after thyroidectomy, the work efficiency of goats exercising on tread mill at an ambient temperature of 30°C greatly diminished. The close relationship between the exercise-induced increase in core temperature and the magnitude of evaporative heat loss characteristic for intact animals was nearly completely abolished after thyroidectomy. They also observed that muscle glycogen utilization and lactic acid accumulation during exercise were enhanced in thyroidectomized animals in spite of the lower work rate and shorter duration of exercise in comparison with euthyroid goats. Lowe et al. (1987) studied the reproductive patterns in cyclic and pregnant thyroidectomized mares. They reported that the thyroidectomized mares were lethargic and the rear limbs showed oedema, and coarse hair coats. The mares displayed a tranquil estrus behaviour when exposed to a stallion and were only mildly antagonistic when not in estrus. The serum LH peak level during the estrus for the control and thyroidectomized mares was 60 mg/ml, with no difference between the two groups. But peak progesterone level on day 7 after ovulation was lower in thyroidectomized mares. Pregnancy was achieved in both groups of mares by the use of semen from a thyroidectomized stallion. Thyroxine was detectable in one pregnant thyroidectomized mare out of three, during the last 2/3 of pregnancy.

2.5.2 Radiothyroidectomy

Goldberg and Chaikoff (1951) induced an early state of hypothyroidism in rats by injecting various doses of I^{131}. They observed in the pituitary, hypertrophy and hyperplasia of the basophil cells accompanied by degranulation of the acidophils. Lewis (1956) observed a drop in protein bound iodine from 6.7 to 0.8 /ug % in a Jersey bull after subcutaneous injection of carrier free I^{131}. Bustad et al. (1957) produced thyroid adenoma, fibroma and fibrosarcoma in sheep following daily administration of I^{131} at different dose levels. Marks et al. (1957) also reported interfollicular fibrosis, oedema and arterial damage on administration of radio iodine. Potter et al. (1960) induced papillary and follicular carcinoma in rats by single injection of I^{131}. On administration of radio iodine to goats, damage of the thyroid gland and reduction in the rate of radioactive iodine uptake by the thyroid and its release into the blood plasma were observed (Ayoub, 1968). Cons et al. (1975) recorded high plasma thyroid stimulating hormone level in radio thyroidectomized rats.

2.6 Pathological conditions associated with the thyroid gland

Bush (1969) classified thyroid diseases capable of producing clinical signs as goitre, hypothyroidism, hyperthyroidism, thyroiditis and thyroid neoplasia.

2.6.1 Goitre

Cohrs (1966) defined the term goitre as a non-inflammatory, non-neoplastic enlargement of the thyroid gland. He made a morphological classification of goitre.

1. Atoxic goitre which included most sporadic forms

2. Goitre with functional change which may be athyroid or hypothyroid goitre and hyperthyroid goitre.

Kaneko (1970) classified goitre into two types

1. Non-toxic goitre, which produced normal amount of hormone (simple goitre) or less than normal amount of hormone (hypothyroid).

2. Toxic goitre which was characterized by the excessive production of hormone (Hyperthyroid).

Smith et al. (1972) classified goitre on the morphological basis into four patterns.

1. Colloid goitre
2. Hyperplastic goitre
3. Nodular goitre
4. Exopthalmic goitre

2.6.1.1 Endemic goitre

The geographical distribution of this condition has been well studied. The terms endemic and sporadic atoxic goitre were often used, in view of the occurrence of the disease. The main aetiological factor for endemic goitre was considered to be an absolute or relative deficiency of iodine. McCarrison (1913) attributed goitre in the

Himalayas to water pollution. Stott et al. (1930-31) pointed out the association between high goitre rates and dolomitic lime in India. They concluded that drinking of hard water containing excessive amount of calcium was of aetiological importance in Himalayan endemic zones.

Levine et al. (1933) stated that the element iodine and inorganic iodine themselves in large doses have goitrogenic properties. Wilson (1941) suggested that excessive intake of flourine might be a causative factor of endemic goitre in Punjab. Murray et al. (1948) reported that there was a relationship between the distribution of goitre and calcium concentration of drinking water in England. Stanbury et al. (1954) indicated that there was an inverse correlation between the quantity of iodine excreted in the urine of patients in an endemic area and the radioactive iodine uptake and concluded that lack of iodine in the diet was the most probable cause. Kelly and Snedden (1960) suggested that the mountain slopes of Himalayas, Alps, Pyrenees and Andes were the worlds's most notorious foci for endemic goitre. Ramalingaswamy et al. (1961) stated that in the Indian sub-continent, the northern frontier extending from Kashmir in the north, Bengal and Assam in the east formed the extensive Himalayan goitre belt. Scrimshaw (1964) reported that cold climate influenced the prevalence of endemic goitre in regions of border line iodine supply as a result of incrased demands for thyroid hormone. Suzuki et al. (1965) reported endemic goitre in Japan due to excessive iodine intake. Koutras (1971) defined an endemic goitre area as one in which more than 10% of the population showed clinical signs of thyroid enlargement.

Kochupillai et al. (1976) conducted an epidemiological study of the nodular lesion of the thyroid in a population living in an area of high background radiation in coastal Kerala, and compared the results with those obtained from a comparable population without any high background radiation. They could not observe any high incidence of nodular lesions or neoplasms in the area without any high background radiation. Mass outbreaks of goitre in breeding rams in an endemic goitre area were recorded by Halik and Zavadsky (1978). The goitre regressed after the administration of iodine. Endemic goitre due to iodine deficiency affected an estimated 40 million people in India (Pandav and Kochupillai, 1982). In areas where goitre prevalence was high, endemic cretinism, deaf-mutism and feeble mindedness were present in about 4% of the population. Pandav and Kochupillai (1982) suggested that iodization of salt was an effective prophylactic measure against goitre. Gilbert (1984) suggested that consumption of cassava can be a key factor in the aetiology of endemic goitre in areas, where there is a deficiency of iodine in the people's diet. Poulose et al. (1984) reported prevalence of goitre in the Kottayam and Idukky districts of Kerala in human population. Kochupillai et al. (1984) recorded significant lower levels of T_4 in the newborns from the Gonda district, an endemic area with environmental iodine deficiency, when compared to newborns from non-endemic zones. Ghergariu et al. (1987) reported an outbreak of simple non-toxic goitre in newborn piglets on a farm with 2000 Bazna pigs, which caused a mortality of 25 - 30%. The outbreak was controlled by intramuscular injection of potassium iodide to sows three or four times during late pregnancy and a single dose to three day old piglets.

2.6.1.2 Colloid goitre

Follis (1959) suggested that colloid goitre was an involutionary phase of hyperplastic goitre. Typically the goitre was asymptomatic. Means et al. (1963) stated that the gland was usually symmetrically enlarged and was soft or spongy to feel. The gland was unable to return to its normal size, when the demand for thyroxine was met or increased in size due to accumulation of colloid in quantities commensurate with the increase in thyroid epithelium. Follicles were packed with colloid and there was greater variation in their size and sometimes they coalesced to form cysts. Jubb and Kennedy (1970) observed follicles with deeply staining colloid. Wilson (1975) stated that the follicular epithelium remained taller than normal and increased vascularity persisted.

2.6.1.3 Parenchymatous goitre

Jubb and Kennedy (1970) reported that the morphological indication of increased stimulation of the thyroid gland by the thyroid stimulating hormone was hyperplasia of the thyroid epithelium. The vascularity of the gland and the total volume of the gland were greatly increased in this condition. The follicular lumina were smaller and many disappeared and the colloid was reduced in amount with variable staining affinity or was completely absent. Wilson (1975) pointed out that an early and characteristic sign of stimulation was the appearance of vacuoles around the periphery of the colloid, or peripheral scalooping.

2.6.1.4 Nodular goitre

Smith et al. (1972) reported that nodular goitre was frequent in older animals. They described well defined nodules in one or both thyroid lobes. These nodules were clearly demarcated from the rest of the thyroid tissue and the histological appearance of the nodular goitre usually varied from nodule to nodule. Many follicles were greatly distended with colloid, while others were small and devoid of colloid. In the simplest form, the epithelial cells were inactive and colloid was deeply stained. Retrogressive changes were reported to be common in nodular goitre (Smith et al. 1972).

2.7 Thyroid and female reproduction

Chu and You (1944) reported that the feeding of small doses of desiccated thyroid to thyroidectomized rabbits prevented the hypertrophy of ovarian follicles, while large doses had inhibitory action. Similar treatment in normal rabbits had no effect on the ovary and large doses caused incomplete inhibition of ovarian activity. Spielman et al. (1946) stated that in thyroidectomized females, there was a failure to show external signs of estrus although physical examination revealed these females to be cycling with ovulation occurring regularly. Krohn (1947) observed that daily subcutaneous injection of propyl thiouracil disturbed the estrus rhythm of adult albino mice, causing lengthening, irregularity or complete disappearance of cycles. Krohn and White (1950) found longer and variable oestrus cycles in hypothyroid rats. Conception was normal with small litter size and high foetal resorption.

Soliman and Reineke (1952) reported that thiouracil fed mice exhibited continuous oestrus while slightly hyperthyroid mice showed regular oestrus cycles. They observed that the thiouracil fed groups had ovaries packed with follicles but not corpora lutea. Brownstand and Flowler (1959) stated that the ovulation rate tended to be lower among sows maintained on 0.15% thiouracil. Moberg (1959) reported retention of placenta in bovines associated with sub-optimal iodine intake.

Kovalskii et al. (1970) treated anoestrum associated with iodine deficiency in dairy cows by supplementing potassium iodide. They induced oestrum with normal ovulation and fertilization within an average period of 148 days, by treatment with 1.75 mg of potassium iodide per kg. Barakat et al. (1971) observed no variation in the total thyroid iodine content in normal female buffaloes and in buffaloes with cystic ovary, inactive ovary, hydrosalphinx, mucometra, metritis, perimetritis with salpingitis and cophoritis. Srinivas (1979) recorded very low concentration of PBI among buffaloes with cystic ovarian degeneration. The mean value was 1.68 ± 0.04 μg %. The highest concentration of serum PBI was seen in animals with uterine infection. Louvet et al. (1979) reported that hypofunction of the thyroid gland evidenced by low T_4 and T_3 levels caused anovulation and sterility. Vadodaria et al. (1980) observed that in ovulatory phase, the thyroid gland follicles were less active compared to the luteal follicles. Mammen et al. (1986) in their survey studies recorded significantly lower levels of PBI in cows with non-infectious infertility.

Sharawy et al. (1987) reported that levels of T_4 and T_3 were significantly higher in normally cycling buffaloes in the follicular phase than during the luteal phase. Also they observed significantly lower levels of T_3 and T_4 in buffaloes with inactive ovaries.

2.8 Thyroid and male reproduction

McKenzie and Berliner (1937) reported that summer sterility in the ram was influenced by the thyroid. Turner and Cupps (1940) recorded lower levels of anterior pituitary gonadotropin content in thyroidectomized male rats. Reineke et al. (1941) observed a reduction in the gonadotropic potency of the pituitary following thyroidectomy among male goats. Peterson et al. (1941) stated that, in bull calves, following thyroidectomy, there was normal development of gonads, but at the usual age of sexual maturity, they lacked libido. Schuttze and Davis (1946) observed a decrease in the conception rate, sperm motility and greater resistance of spermatozoa in bulls fed iodinated casein. Kumaran and Turner (1949) induced mild hypothyriodism in birds by feeding 0.6% thiouracil and observed a progressive depression of the secretion of the interstitial cell stimulating hormone (ICSH) without having any effect on follicular stimulating hormone unlike mild hyperthyroidism. Maqsood (1952) suggested that the thyroid gland had a pivotal role in the maintenance of male fertility. In his study on the effect of of thyroxine supplementation, he recorded precocious sexual development, increased sex libido and improvement in semen picture.

Hignett (1952) observed a decline in libido and deterioration of semen quality in iodine deficient bulls. Jovanovic et al. (1953) reported decreased libido and high percentage of sterility in males associated with enzootic goitre. Lenon and Mixner (1958) observed better reproductive performance in Holstein cattle associated with high PBI values. Brooks and Ross (1962) observed that exogenous administration of L-thyroxine in feed at 0.2, 0.3 and 0.4 μg % level failed to have any significant effect on the adverse influence of high ambient temperature on the semen quality of rams. Mahtiev (1966) recorded an improvement in fertility and semen picture following iodine supplementation in infertile rams maintained in iodine deficient areas. Prasad and Singh (1971) recorded the effects of propylthiouracil and thyroxine on the testes of chicks. A four fold increase in the weight of the testes was observed when compared with normal chicks at eight weeks of age. Testes of propylthiouracil treated birds showed tightly arranged coils of seminiferous tubules as compared with the loose arrangement of such tubules in normal birds. Sharma and Singh (1975) observed more coiled seminiferous tubules lined with two or more layered germinal epithelium in hypothyroid birds as against single layer of epithelium in the control groups.

Sreekumaran (1976) observed that the seminiferous tubules contained only few primary and secondary spermatocytes in experimentally induced hypothyroid state in male kids. There was complete absence of spermatozoa and germinal layer in some tubules. Peczely et al. (1979) reported that although thyroidectomy or treatment with thyroxine did not affect the basal testosterone concentration, there was a marked inhibition of the growth of the testes. Reddy (1982) observed a significant decrease in the relative weight of the testes in all the goats dosed with thiourea. There was also a decrease in the relative weight of epididymis, and accessary sexual glands. There was complete absence of spermatogenesis, on histological observation. Mammen et al. (1986) recorded reduction in the relative weight of the testes in male calves dosed with thiourea. Microscopic picture of the testes showed slight obliteration of the seminiferous tubules with no evidence of mitotic activity in the spermatogonial cells.

2.9 Prevalence of goitre and hypothyroidism in sheep and goats

McIntosh (1943) observed that in hypothyroidism, the newborn lambs were weak and the wool growth was poor. Southcott (1945) recorded congenital goitre in lambs. Baumann (1948) described goitre in newborn kids. Andrews et al. (1949) noticed hyperplasia of the thyroid epithelium and depletion of colloid in the thyroid gland of newborn lambs from the dams which were fed a diet free of iodized salt. Investigation on the prevalence of goitre in domestic animals revealed that its prevalence in animals and humans was parallel. The number of animals affected with goitre was large. Lall (1952) reported congenital goitre in three kids with enlarged thyroid. The thyroid glands, histologically showed hyperplasia of the lining cells of the follicles. Jovanovic (1955) reported that the diffuse colloid type goitre was the commonest in sheep and goats. The parenchymatous goitre was observed only in goats. Dutt and Kehar (1959) studied 1000 thyroid glands collected from sheep and goats from Bareilly slaughter house. They found that the incidence of goitre was common in goats (10%), particularly in female goats. They could not record a single case of goitre in sheep. Setchell et al. (1960) reported neonatal mortality associated with thyroid enlargement in lambs. Growth (1962) reported hypothyroidism in sheep. He observed adverse effect on wool growth and increased incidence of alopecia, and still born lambs and kids. Dutt and Vasudeva (1963) reported a case of hypothyroidism in a ram. There was loss of weight, irregular appetite and intermittent diorrhoea. On autopsy, the thyroid glands were found to be cystic and slightly enlarged. Histologically the follicles were found to be atrophic and lined with low cuboidal epithelium. Roy et al. (1964) conducted a comparative study of the thyroid glands of 25 human and 50 goats collected from a severely endemic area in the Himalayan belt. The thyroid glands of goats were large, pale and hyperplastic with intense lobular hyperplasia. In human thyroids, grossly visible, well circumscribed greyish white multiple nodules were noticed. Wallach (1965) observed low basal metabolic rate, retardation of growth rate and increased sensitivity to low environmental temperature in feeder lambs with hypothyroidism. George et al. (1966) conducted histopathological study of the thyroid glands of dead lambs in order to assess the prevalence of goitre. They observed parenchymatous and transitional parenchymatous goitre. Rajkumar (1970) reported goitre in kids in a Government farm in Uttar Pradesh. Taking gross enlargement of the thyroid gland as the criterion for the diagnosis of goitre in village flock, he recorded an incidence of 0.54% in local goats, 7.02% in Barbari x Local, and 16.67% in Alpine x Local goats.

Sreekumaran (1976) described the clinicopathological features of experimental hypothyroidism in kids. Histologically the thyroid gland showed formation of colloid depleted microfollicles. Reddy (1982) also studied the clinico-pathological features of experimental hypothyroidism in goats with particular reference to the reproductive organs. There was complete absence of spermatogenesis and degenerative changes in the tubules, which were found to be reversible. In the case of females the ovaries were smooth and inactive.

2.10 Cassava as a goitrogen

Dorozynski (1978) reported that a steady diet of cassava in human beings, inhibited iodine uptake by the thyroid gland. He stated that when iodine supply was marginal, this can cause endemic goitre, cretinism and mental retardation. According to him cassava contained cyanogenic glucosides; when ingested, these glucosides were detoxified, yielding thiocyanate as a by-product and this inhibited iodide uptake by the thyroid gland. Thampan (1979) suggested that to avoid problems of toxicity to human beings, fresh well washed and properly cooked cassava tubers only should be used. He stated that however, these often contained substantial residual quantities of hydrocyanic acid, which may be sufficient to produce chronic toxic symptoms. He pointed out that cassava flour prepared from peeled tubers contained about 3 ppm of hydrocyanic acid. He reported that investigations on cassava toxicity conducted in various parts of the world showed that ecological conditions exerted a strong influence on the cyanogenic glucoside content of the tuberous roots. Nitrogen fertilization had been found to increase the hydrocyanic acid content but the supply of potash and phosphoric acid decreased it. Drought increased glucoside content whereas shading decreased the content in the roots, but increased it in the leaves.

Gilbert (1984), in their studies on goitre in Zaire, indicated that cassava, which is extensively consumed as a staple food in that country can be a high risk factor for goitre in areas, where iodine deficiency also prevailed.

Poulose et al. (1984) made survey studies on human population on the incidence of goitre in Kottayam and Idukki districts of Kerala. They conducted medical camps and collected details of dietetic habits, especially consumption of cassava, drinking water source, and relevant family history. They found that the incidence of goitre in the various areas and schools surveyed in these districts varied from 13% to 39% except in coastal areas, where the incidence was very low.They concluded that there may be a relationship between cassava consumption and goitre observed in those areas, since almost 75% of people examined were cassava eaters.

Prawirodigdo et al. (1985) fed cabbage to rabbits with various levels of cassava root. They fed cabbage leaves with four levels of cassava root supplementation (0g, 25g, 50g and 75g respectively). Measurements were made on feed intake, body weight gain and feed conversion ratio (FCR) for eight weeks.

Results indicated that feed consumption was not significantly affected by the feed schedule, but body weight gain and feed conversion ratio were significantly different. Body weight gain for the four treatments were 306, 314, 538 and 470 g/animal respectively, while the FCR values were 18.4, 17.6, 10.4 and 11.6 respectively.

Jham et al. (1987) evaluated pressed residue from cassava leaves as a substitute for commercial feed for rabbits. They concluded that pressed residue from cassava leaves could be incorporated into rabbit diets at levels of atleast 10% without any loss in animal performance.

Materials and Methods

3. MATERIALS AND METHODS

3.1 Assessment of the thyroid status of cattle in different districts of Kerala

The thyroid status of cows in the districts of Cannanore, Trichur, Ernakulam and Idukki was assessed at random using T_4 as a marker. Blood samples (5ml each) from the jugular vein were collected from those cows and serum separated. The serum thyroxine level of each sample was estimated by radio-immunoassay method (Abraham, 1977). The radioimmunoassay kit was obtained from the Bhabha Atomic Research Centre, Trombay, Bombay. Also blood samples of cows at the University Livestock Farm, Mannuthy and those cases presented at Kokkalai Veterinary Hospital and Mannuthy Veterinary Hospital were collected and the serum T_4 level was estimated.

3.2 Experimental studies

3.2.1 Experimental animals

Thirty-six (males and females) clinically healthy Grey Giant broiler rabbits (45 - 70 days old) were selected at random from the AICRP Station for rabbits at Mannuthy. The rabbits were reared in a hygienic environment and they were housed separately in specially devised cages.

3.2.2 Design of the experimental study

The thirty-six rabbits procured were divided at random into three groups of twelve each (Group T_1 T_2 and T_3). Group T_2 was given cassava flour procured from the local market at the rate of 25% in the diet daily for a period of six months, for testing the goitrogenicity of cassava. Group T_3 was given propyl thiouracil orally at the rate of 1mg/day/animal, for inducing hypothyroidism for a period of six months. The third group of twelve rabbits (T_1) were kept as controls for six months.

3.2.3 Experimental diets

Group I (T_1 - control group)

Bengal gram	-	25%
Wheat	-	35%
G.N.C	-	28.5%
Meat cum bone meal	-	10%
Mineral mixture	-	1%
Salt	-	0.5%

Group II (T_2 - Cassava group)

Cassava flour	-	25%
Bengal gram	-	28.5%
G.N.C	-	35%
Meat cum bone meal	-	10%
Mineral mixture	-	1%
Salt	-	0.5%

Group III (T_3 - Propyl thiouracil group)

The diet fed to the control group and propyl thiouracil at the rate of 1mg/day/animal (Sigma, USA) was administered orally.

3.2.4 Parameters studied

The rabbits were observed regularly and clinical symptoms shown, if any were recorded. From each group, four rabbits were sacrificed at intervals of two months and blood was collected. The following parameters were observed and recorded during the experiment.

1. Body weight and fur weight
2. Observation on behaviour and clinical symptoms
3. Hemogram
4. Serum chemistry
5. Gross pathology
6. Histopathological changes in tissues

3.2.5 Techniques

3.2.5.1 Body weight and fur weight

All the rabbits were weighed at the start of the experiment, and thereafter at fortnightly interval and on the day of the slaughter. The fur was removed after slaughter as per the standard method. described by Rougeot (1986) and the weight was recorded for each rabbit.

3.2.5.2 Clinical symptoms

The rabbits in the different groups were observed regularly for any clinical symptoms and behavioural changes, and the observations were recorded.

3.2.5.3 Hematological studies

For hematological studies, blood was collected from the jugular vein at the time of slaughter of the rabbits. Reagent grade Ethylene diamino tetra acetic acid (disodium salt EDTA) at the rate of 1mg/ml of blood was used as the anticoagulant. For blood sugar estimation sodium fluoride at the rate of 5mg/ml of blood was used as the anti-coagulant. For estimation of plasma proteins, serum cholesterol, T_4 and T_3, blood was collected without any anticoagulant and allowed to clot and then serum was separated by centrifugation.

For erythrocyte counts and differential leucocyte counts, technique of Schalm (1965) was followed. Haemoglobin was estimated by employing the modified method of Miale (1967). The cyanmethaemoglobin was prepared as detailed by Miale (1967), but the final readings were taken in Erma haemophotometer, instead of Spectronic 20.

3.2.5.4 Blood sugar

Estimation of blood sugar was done following the method of Folin and Wu (Oser, 1971).

3.2.5.5 Serum proteins

The Biuret assay method of Inchiosa (1964) was adopted for the estimation of protein in blood plasma.

3.2.5.6 Serum cholesterol

Serum cholesterol was estimated employing the method of Zak (1957).

3.2.5.7 Estimation of T_4 and T_3

Serum thyroxine (T_4) and Triiodothyronine (T_3) level were estimated by adopting the radioimmunoassay method (Abraham, 1977). The RIA kits were purchased from BARC, Trombay, Bombay.

3.2.5.8 Post-mortem examination

The rabbits were slaughtered by dislocation of the atlanto-axis joint and exsanguination. Detailed autopsy was performed after the slaughter of the rabbits. The thyroid glands were dissected out and weighed after removing the loose fat and fascia. Testes were separated from the epididymis and weighed.

3.2.5.9 Histopathology

Appropriate samples of tissues from liver, kidney, heart, spleen, testes, thyroid and adrenal were collected in 10% buffered neutral formalin for histopathological examination. Routine paraffin embedding technique (Armed Forces Institute of Pathology, 1968) was employed for processing the tissues. Paraffin sections were cut at 5 to 6 microns thickness and stained with hematoxylin and eosin method of Harris as described by Disbery and Rack (1970).

3.2.5.10 Statistical analysis

The experimental data were subjected to statistical analysis employing the completely Randomized Design as described by Snedecor and Cochran (1967).

Results

4. RESULTS

4.1 Survey of thyroid status of cattle with normal and impaired reproductive performance, using serum T_4 as marker

The thyroid status of two hundred and sixty-seven animals were assessed using serum T_4 as the marker. The sera were collected from Cannanore, Trichur, Ernakulam and Idukki districts, by attending cattle infertility camps, organised by Animal Husbandry Department. Also sera were collected from the University Livestock Farm, Mannuthy and also from Veterinary Hospitals, Kokkalai and Mannuthy. The number of serum samples collected and the serum T_4 level recorded is listed in Tables 1a, b, c and d.

Out of 267 cases, 47 were having infantile genitalia, 80 were repeat breeders, 115 were suffering from anoestrum and 22 cases were clinically healthy. The mean value obtained for the above conditions are detailed below. Infantile genitalia condition was associated with the lowest thyroxine level (Fig. 1).

	Conditions	T_4 level (μg/dl)
1.	Clinically healthy	4.8727 ± 0.1209
2.	Infantile genitalia	3.5617 ± 0.1089
3.	Anoestrum	3.6913 ± 0.1136
4.	Repeat breeder	3.9175 ± 0.1130

Table 1. a

The serum T_4 level of cows/heifers collected from Cannanore district

Sl. No.	Animal	History	T_4 level (μg/dl)
1	Heifer	Infantile genitalia	3.8
2	Heifer	Repeat breeder	3.2
3	Heifer	Repeat breeder	4.0
4	Cow	Anoestrum	2.4
5	Heifer	Repeat breeder	3.0
6	Heifer	Repeat breeder	2.8
7	Heifer	Repeat breeder	3.4
8	Heifer	Repeat breeder	3.8
9	Heifer	Repeat breeder	3.0
10	Heifer	Repeat breeder	4.2
11	Cow	Anoestrum	3.2
12	Cow	Anoestrum	3.8
13	Cow	Anoestrum	3.6
14	Heifer	Repeat breeder	4.0
15	Cow	Anoestrum	3.6
16	Heifer	Repeat breeder	4.2
17	Cow	Anoestrum	4.8
18	Cow	Anoestrum	3.2
19	Cow	Anoestrum	3.0
20	Cow	Anoestrum	4.2
21	Cow	Anoestrum	5.2
22	Cow	Anoestrum	3.4
23	Cow	Anoestrum	3.8
24	Cow	Anoestrum	4.6
25	Cow	Anoestrum	2.2

(Contd ....)

(Table 1. a contd ....)

1	2	3	4
26	Heifer	Repeat breeder	4.2
27	Heifer	Repeat breeder	4.6
28	Heifer	Repeat breeder	3.2
29	Cow	Anoestrum	3.0
30	Cow	Anoestrum	4.8
31	Cow	Anoestrum	3.2
32	Cow	Anoestrum	3.6
33	Cow	Repeat breeder	5.6
34	Heifer	Anoestrum	4.2
35	Heifer	Anoestrum	3.4
36	Heifer	Anoestrum	3.2
37	Heifer	Repeat breeder	4.2
38	Heifer	Anoestrum	4.0
39	Heifer	Normal (Clinically healthy)	5.0
40	Heifer	Normal (Clinically healthy)	5.4
41	Heifer	Normal (Clinically healthy)	4.8
42	Heifer	Normal (Clinically healthy)	6.2
43	Heifer	In heat	5.0
44	Cow	Repeat breeder	4.6
45	Heifer	Anoestrum	3.1
46	Cow	Anoestrum	1.5
47	Cow	Repeat breeder	2.2
48	Heifer	Anoestrum	4.8
49	Heifer	Anoestrum	4.8
50	Cow	Normal (Clinically healthy)	4.2
51	Cow	Anoestrum	0.6
52	Cow	Repeat breeder	1.4

(Contd ....)

(Table 1. a contd ....)

1	2	3	4
53	Heifer	Repeat breeder	4.4
54	Cow	Repeat breeder	5.4
55	Heifer	Repeat breeder	4.4
56	Cow	Anoestrum	4.2
57	Cow	Anoestrum	3.2
58	Heifer	Anoestrum	4.2
59	Cow	Repeat breeder	5.6
60	Cow	In heat	5.8
61	Cow	Normal	5.0
62	Heifer	Normal	4.8
63	Cow	Anoestrum	1.0
64	Cow	Anoestrum	2.6
65	Cow	Anoestrum	0.2
66	Cow	Anoestrum	4.4
		Mean T_4 in Cannanore district	3.7939 ± 0.1496

Table 1. b

The serum T_4 level of cows/heifers collected from Trichur district

Animal No.	Animal	History	T_4 level (μg/dl)
1	Cow	Anoestrum	2.8
2	Heifer	Anoestrum	1.8
3	Heifer	Anoestrum	1.8
4	Heifer	Infantile genitalia	3.4
5	Heifer	Infantile genitalia	3.4
6	Cow	Anoestrum	2.6
7	Cow	Repeat breeder	2.8
8	Cow	Anoestrum	4.4
9	Heifer	Anoestrum	4.6
10	Heifer	Anoestrum	2.4
11	Cow	Anoestrum	3.4
12	Cow	Repeat breeder	2.8
13	Cow	Repeat breeder	5.6
14	Heifer	Normal (Clinically healthy)	4.0
15	Cow	Normal (Clinically healthy)	4.6
16	Cow	Anoestrum	3.5
17	Cow	Anoestrum	3.5
18	Heifer	Infantile genitalia	2.8
19	Heifer	Infantile genitalia	3.2
20	Heifer	Infantile genitalia	3.8
21	Cow	Anoestrum	4.1
22	Cow	Repeat breeder	5.1
23	Cow	Repeat breeder	3.6
24	Cow	Anoestrum	3.1
25	Cow	Anoestrum	3.4

(Contd ....)

(Table 1. b contd ....)

1	2	3	4
26	Heifer	Infantile genitalia	3.2
27	Cow	Anoestrum	2.8
28	Cow	Repeat breeder	4.6
29	Cow	Repeat breeder	4.0
30	Cow	Repeat breeder	3.8
31	Cow	Repeated breeder	4.0
32	Heifer	Infantile genitalia	3.2
33	Heifer	Repeat breeder	3.6
34	Heifer	Infantile genitalia	3.8
35	Heifer	Infantile genitalia	3.8
36	Cow	Anoestrum	5.0
37	Heifer	Infantile genitalia	4.6
38	Cow	Anoestrum	5.0
39	Heifer	Infantile genitalia	4.2
40	Heifer	Infantile genitalia	4.6
41	Heifer	Infantile genitalia	3.8
42	Heifer	Infantile genitalia	3.6
43	Heifer	Infantile genitalia	4.0
44	Heifer	Infantile genitalia	4.4
45	Heifer	Infantile genitalia	3.8
46	Heifer	Infantile genitalia	4.2
47	Heifer	Infantile genitalia	4.2
48	Heifer	Normal (Clinically healthy)	4.4
49	Heifer	Normal	4.4
50	Heifer	Anoestrum	4.6
51	Heifer	Anoestrum	3.8
52	Heifer	Anoestrum	5.6

(Contd ....)

(Table 1. b contd ....)

1	2	3	4
53	Heifer	Anoestrum	4.0
54	Heifer	Anoestrum	3.8
55	Cow	Anoestrum	4.2
56	Cow	Anoestrum	6.0
57	Cow	Anoestrum	4.4
58	Cow	Anoestrum	4.0
59	Cow	Anoestrum	2.2
60	Cow	Anoestrum	4.8
61	Cow	Normal (Clinically healthy)	4.6
62	Cow	Repeat breeder	3.8
63	Cow	Repeat breeder	3.4
64	Cow	Repeat breeder	5.0
65	Cow	Repeat breeder	4.2
66	Cow	Repeat breeder	4.6
67	Cow	Repeat breeder	4.4
68	Cow	Repeat breeder	4.8
69	Cow	Repeat breeder	4.0
		Mean T_4 in Trichur district	3.8898 ± 0.1043

Table 1. c

The serum T_4 level of cows/heifers collected from Ernakulam district

Animal No.	Animal	History	T_4 level ($\mu g/dl$)
1	Cow	Repeat breeder	1.8
2	Cow	Repeat breeder	1.0
3	Cow	Normal (Clinically healthy)	4.6
4	Cow	Anoestrum	0.8
5	Cow	Anoestrum	6.8
6	Cow	Anoestrum	4.8
7	Cow	Anoestrum	4.2
8	Cow	Anoestrum	6.2
9	Heifer	Repeat breeder	4.8
10	Cow	Normal (Clinically healthy)	5.6
11	Cow	Anoestrum	5.4
12	Cow	Anoestrum	5.6
13	Cow	Anoestrum	4.0
14	Cow	Anoestrum	3.0
15	Cow	Anoestrum	4.6
16	Cow	Anoestrum	4.0
17	Cow	Anoestrum	3.2
18	Heifer	Repeat breeder	5.0
19	Heifer	Repeat breeder	3.8
20	Heifer	Repeat breeder	2.8
21	Heifer	Repeat breeder	4.8
22	Cow	Anoestrum	1.2
23	Cow	Normal (Clinically healthy)	4.6
24	Heifer	Normal (Clinically healthy)	5.0

(Contd ....)

(Table 1. c contd ....)

1	2	3	4
25	Cow	Repeat breeder	3.8
26	Cow	Repeat breeder	4.0
27	Cow	Anoestrum	5.0
28	Cow	Anoestrum	2.4
29	Cow	Anoestrum	3.0
30	Cow	Anoestrum	4.8
31	Cow	Anoestrum	5.0
32	Heifer	Normal (Clinically healthy)	5.0
33	Heifer	Infantile genitalia	3.6
34	Cow	Repeat breeder	4.0
35	Cow	Repeat breeder	4.8
36	Cow	Anoestrum	3.2
37	Heifer	Anoestrum	2.8
38	Heifer	Anoestrum	2.8
39	Heifer	Anoestrum	3.4
40	Heifer	Anoestrum	1.0
41	Heifer	Anoestrum	3.9
42	Heifer	Anoestrum	3.0
43	Heifer	Repeat breeder	3.8
44	Heifer	Anoestrum	3.0
45	Cow	Normal (Clinically healthy)	4.8
46	Cow	Normal (Clinically healthy)	4.6
47	Cow	Repeat breeder	4.8
48	Cow	Repeat breeder	4.8
49	Cow	Repeat breeder	3.8
50	Cow	Repeat breeder	3.6
51	Cow	Repeat breeder	4.2

(Contd ....)

(Table 1. c contd ....)

1	2	3	4
52	Cow	Repeat breeder	4.4
53	Cow	Repeat breeder	4.8
54	Cow	Repeat breeder	3.2
55	Cow	Repeat breeder	3.4
56	Cow	Repeat breeder	4.6
57	Cow	Repeat breeder	4.6
58	Cow	Repeat breeder	4.4
59	Cow	Normal (Clinically healthy)	5.2
60	Cow	Normal (Clinically healthy)	5.0
61	Cow	Normal (Clinically healthy)	4.8
62	Cow	Normal (Clinically healthy)	6.0
63	Heifer	Anoestrum	3.4
64	Cow	Repeat breeder	3.6
65	Heifer	Infantile genitalia	2.8
66	Cow	Repeat breeder	2.1
67	Heifer	Infantile genitalia	2.8
68	Heifer	Infantile genitalia	3.4
69	Cow	anoestrum	4.1
70	Cow	Anoestrum	3.6
		Mean T_4 Ernakulam district	3.9529 ± 0.1457

Table 1. d

The serum T_4 level of cows/heifers collected from Idukki district

Animal No.	Animal	History	T_4 level (μg/dl)
1	Cow	Anoestrum	3.8
2	Heifer	Infantile genitalia	4.6
3	Heifer	Anoestrum	4.2
4	Heifer	Infantile genitalia	3.8
5	Heifer	Anoestrum	3.0
6	Cow	Repeat breeder	3.8
7	Heifer	Anoestrum	4.8
8	Heifer	Repeat breeder	4.2
9	Heifer	Infantile genitalia	4.2
10	Heifer	Infantile genitalia	4.8
11	Heifer	Infantile genitalia	2.4
12	Heifer	Infantile genitalia	3.4
13	Heifer	Infantile genitalia	2.8
14	Heifer	Infantile genitalia	3.0
15	Heifer	Infantile genitalia	3.0
16	Heifer	Hypoplastic genitalia	5.2
17	Heifer	Luteal cyst	5.2
18	Cow	Infantile genitalia	2.2
19	Cow	Anoestrum	2.2
20	Cow	Repeat breeder	2.4
21	Cow	Anoestrum	4.4
22	Heifer	Repeat breeder	2.2

(Contd ....)

(Table 1. d contd ....)

1	2	3	4
23	Cow	Anoestrum	4.8
24	Cow	Anoestrum	5.0
25	Heifer	Infantile genitalia	3.2
26	Cow	Anoestrum	1.0
27	Cow	Anoestrum	3.4
28	Cow	Repeat breeder	2.2
29	Cow	Repeat breeder	2.6
30	Cow	Repeat breeder	3.4
31	Heifer	Repeat breeder	4.6
32	Cow	Anoestrum	4.0
33	Heifer	Anoestrum	4.8
34	Heifer	Infantile genitalia	4.2
35	Heifer	Infantile genitalia	4.2
36	Heifer	Infantile genitalia	3.8
37	Heifer	Infantile genitalia	2.4
38	Heifer	Infantile genitalia	4.6
39	Heifer	Infantile genitalia	4.0
40	Cow	Anoestrum	3.0
41	Heifer	Anoestrum	3.4
42	Heifer	Infantile genitalia	5.2
43	Heifer	Anoestrum	4.6
44	Heifer	Anoestrum	5.4
45	Heifer	Anoestrum	4.2
46	Heifer	Anoestrum	4.2
47	Heifer	Anoestrum	3.8
48	Heifer	Anoestrum	4.0
49	Heifer	Anoestrum	5.2

(Contd ....)

(Table 1. d contd ....)

1	2	3	4
50	Cow	Repeat breeder	6.4
51	Cow	Repeat breeder	4.6
52	Heifer	Anoestrum	5.0
53	Cow	Anoestrum	4.2
54	Cow	Anoestrum	4.4
55	Heifer	Infantile genitalia	2.2
56	Heifer	Infantile genitalia	2.4
57	Cow	Repeat breeder	5.4
58	Heifer	Infantile genitalia	3.0
59	Cow	Anoestrum	4.0
60	Heifer	Infantile genitalia	3.2
61	Cow	Repeat breeder	4.4
62	Cow	Repeat breeder	4.2
63	Cow	Repeat breeder	2.8
64	Heifer	Infantile genitalia	2.4
65	Cow	Anoestrum	3.0
		Mean T_4 in Idukki district	3.7908 ± 0.1312

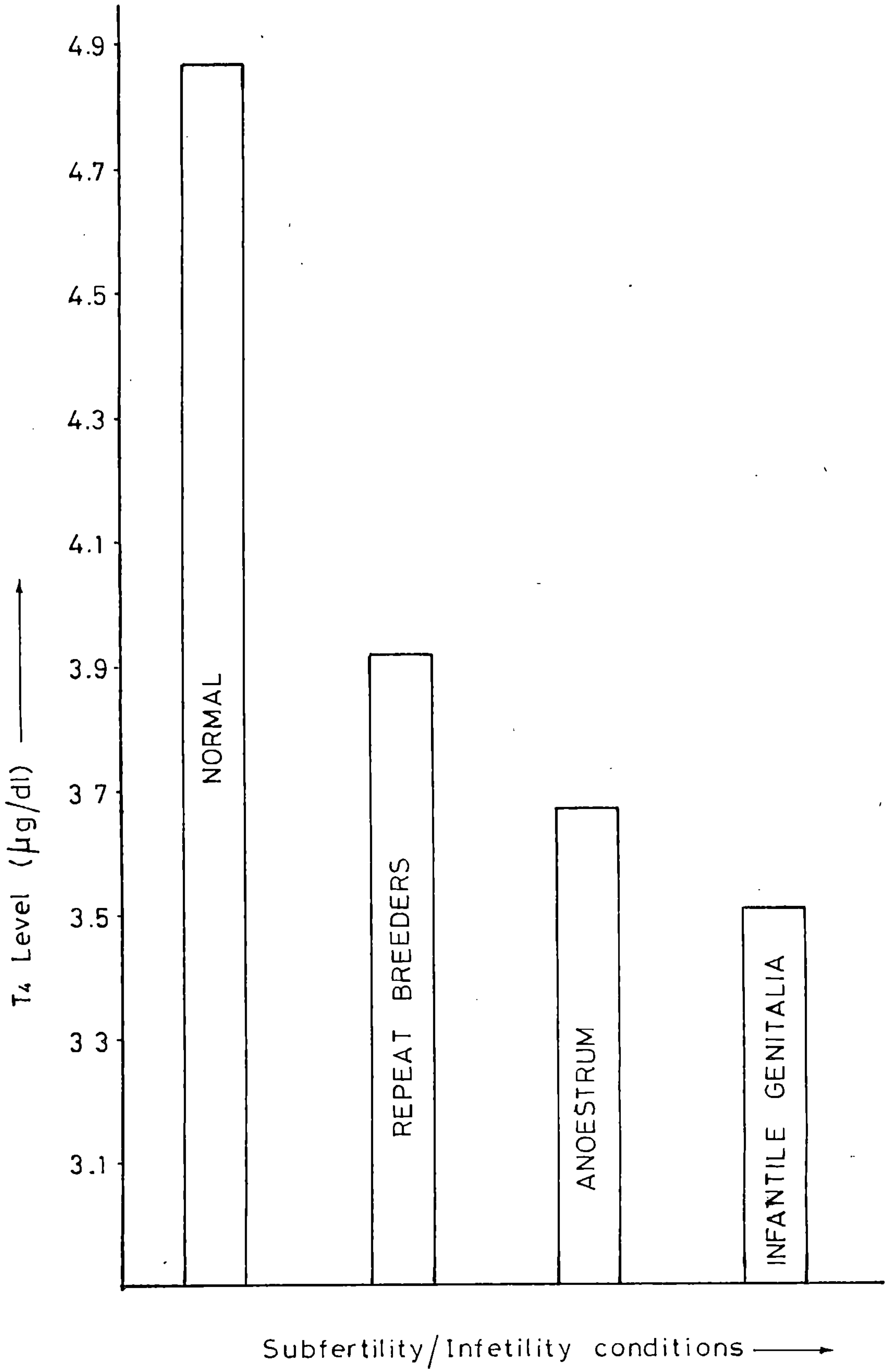


Fig-1. SERUM T_4 LEVEL IN SUBFERTILITY/INFERTILITY CONDITIONS

4.2 Experimental studies

4.2.1 Clinical symptoms

Rabbits fed cassava and the control group of rabbits did not manifest any symptoms of disease or change in behaviour till four months. But at the end of six months the cassava fed rabbits became obese although there was slight degree of variation in obesity between individual rabbits. They appeared to be apparently healthy, but were slightly dull and lethargic (Fig. 4).

The rabbits which were given propylthiouracil became dull and weak from the second fortnight onwards. Lethargy, dullness and disinclination to move were seen in the rabbits in this group by the fourth month. By the 5th month, bilateral alopecia on the ventral side of the belly, base of the ear and around the eyes developed (Fig. 5). There was slight to moderate watery discharge from the eyes, and considerable diminution of subcutaneous fat.

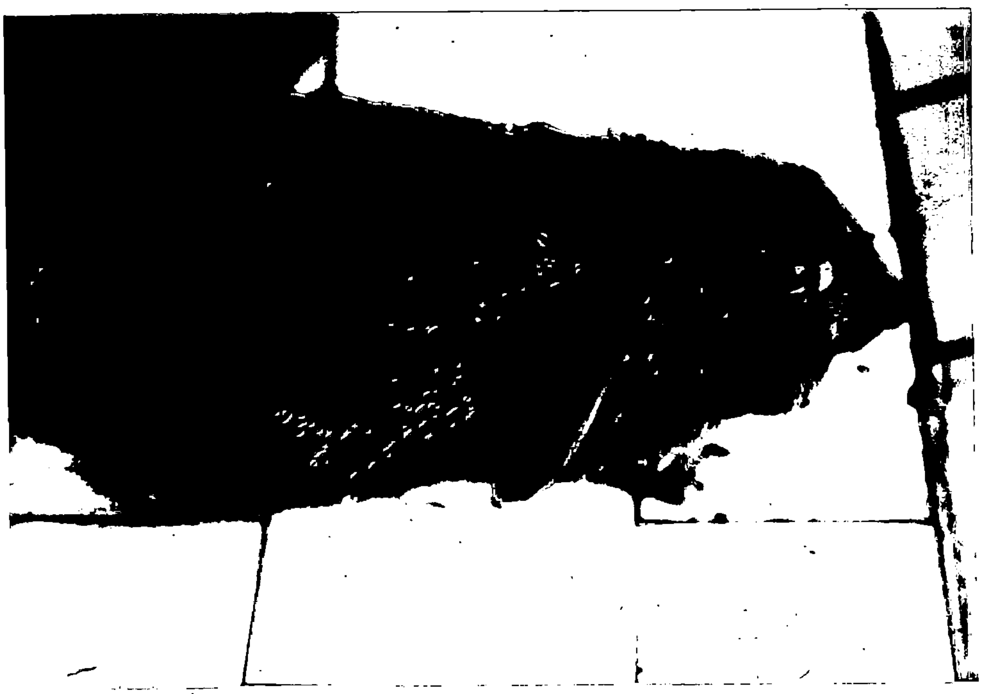
The rabbits in the control group remained healthy and consumed the feed given to them (Fig. 3). Feed consumption of the rabbits in the cassava group was slightly reduced by the end of six months. There was marked reduction in the feed consumption of rabbits, which were fed propylthiouracil from the second month onwards.

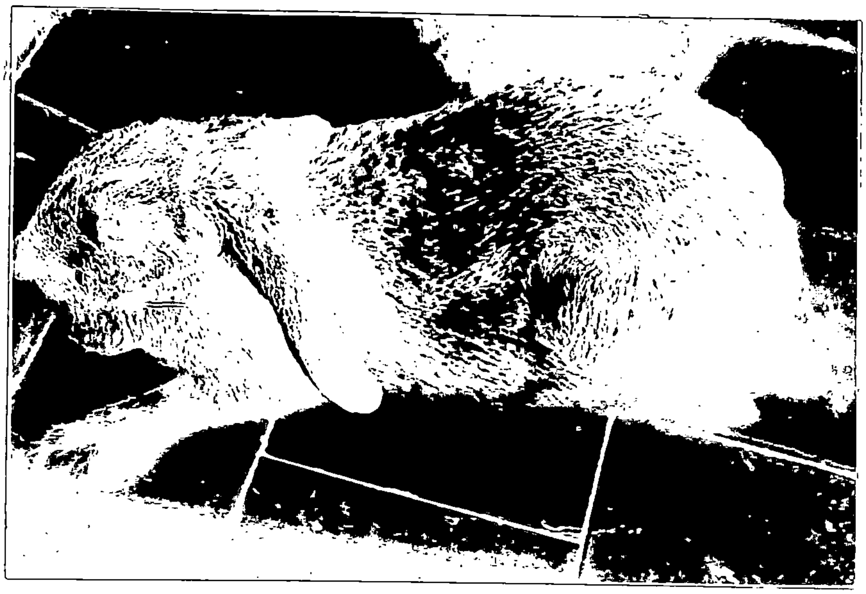
Fig. No. 3 Control rabbit - Healthy with smooth hair coat

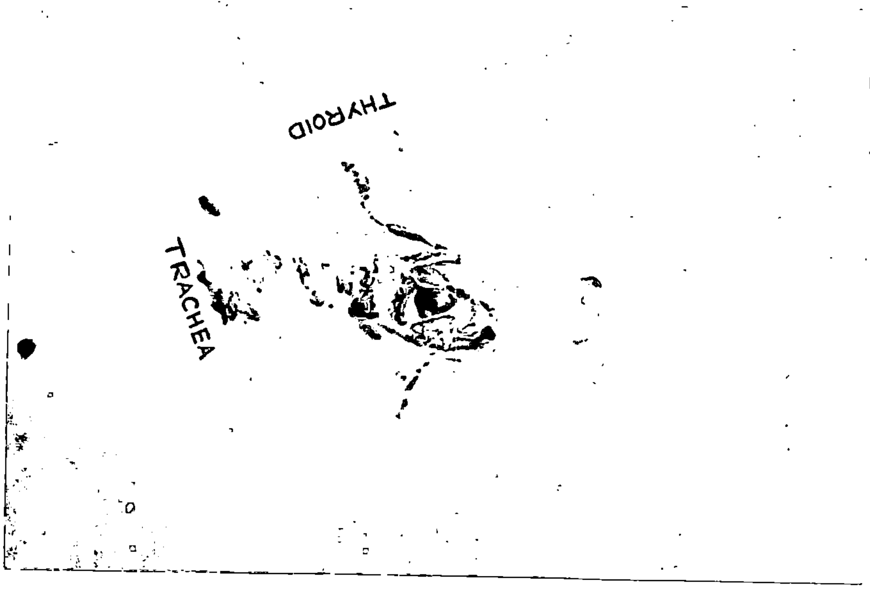
Fig. No. 4 Cassava fed rabbit - Rough hair coat

Fig. No. 5 Propylthiouracil fed rabbit - Alopecia of the belly region.

Fig. No. 14 Thyroid gland of rabbit fed propyl thiouracil - Enlarged thyroid gland surrounding the trachea.






THYROID
TRACHEA

4.2.2 Body weight

The data on the body weight of rabbits during the experimental period are shown in the table 2 and Fig. 2.

4.2.2.1 Body weight at two months

There was significant difference between T_1 and T_3, and T_2 and T_3 ($P<0.01$). But there was no significant difference between T_1 and T_2 ($P<0.01$). There was significant reduction in the body weight of rabbits fed propylthiouracil when compared to the control and cassava fed rabbits.

4.2.2.2 Body weight at four months

There was significant reduction in the body weight of rabbits in the T_3 group when compared to the rabbits in the group T_1 and T_2 ($P<0.01$). However, there was no significant difference in the weight of rabbit in the groups T_1 and T_2.

4.2.2.3 Body weight at six months

Body weight of rabbits in the T_2 group was significantly higher than T_3 and T_1 ($P<0.01$). The rabbits fed cassava were found to have more weight than rabbits in other two groups. Also there was a significant reduction in the body weight of rabbits in the T_3 group when compared to T_1 and T_2 groups ($P<0.01$).

4.2.3 Fur weight

The mean values of fur weight at two months, four months and six months are set out in table 3 and fig. 6.

4.2.3.1 Fur weight at two months

There was significant difference between T_1 and T_3, T_2 and T_3 and no significant difference between T_1 and T_2 group ($P<0.01$). The cassava fed rabbits showed no reduction in fur weight when compared to that of the control. The rabbits fed propylthiouracil showed a significant reduction in fur weight ($P<0.01$).

4.2.3.2 Fur weight at four months.

There was significant difference between T_1 and T_2 group and T_2 and T_3 group ($P<0.01$). Cassava fed rabbits had increase in fur weight, but there was no significant variation in fur weight between control rabbits and propylthiouracil fed rabbits.

4.2.3.3 Fur weight at six months

There was significant difference between T_1 and T_2, T_2 and T_3

and T_1 and T_3 ($P<0.01$). Both cassava fed rabbits and propyl thiouracil fed rabbits had low fur weight when compared to the control.

Although the effect was more significant in the rabbits fed propylthiouracil, the study on fur weight indicated that there was significant reduction in the fur weight of rabbits in hypothyroidism induced by cassava and propylthiouracil.

4.2.4 Serum thyroxine

The mean values of serum thyroxine recorded at two months, four months and six months are shown in table 4 and fig. 7.

4.2.4.1 Serum thyroxine level at two months

There was no significant difference in the thyroxine level between T_1, T_2 and T_3 group ($P<0.01$).

4.2.4.2 Serum thyroxine level at four months

There was no significant difference between T_1 and T_2 group. But there was significant difference between T_2 and T_3, T_1 and T_3 group ($P< 0.01$). This indicated that there was significant reduction in the thyroxine level of rabbits fed propyl thiouracil when compared to cassava fed and control rabbits.

4.2.4.3 Serum thyroxine level at six months

There was significant difference in the thyroxine level between T_1 and T_2 ($P < 0.05$). Between T_2 and T_3, T_1 and T_3 the difference was significant at ($P < 0.01$). This implied that there was marked reduction in the serum thyroxine level in the propyl thiouracil fed rabbits, when compared to the control and cassava fed rabbits. In the cassava fed rabbits there was significant reduction in the thyroxine level when compared to control rabbits ($P < 0.05$).

4.2.5 Serum T_3 (serum triiodothyronine)

The mean values of T_3 obtained at two months, four months and six months are presented in table 5 and fig. 8.

4.2.5.1 Serum T_3 level at two months

There was no significant difference between T_1, T_2 and T_3 groups ($P < 0.01$). This indicated that there was no significant variation in serum T_3 level between cassava fed, propylthiouracil dosed and control rabbits.

4.2.5.2 Serum T_3 level at four months

There was no significant difference between T_1 and T_2, T_2 and T_3.

But there was significant difference between T_1 and T_3 ($P<0.05$). This showed that there was significant reduction in the serum T_3 level in the propyl thiouracil fed rabbits, when compared to the control rabbits.

4.2.5.3 Serum T_3 level at six months

There was significant difference between T_1 and T_2, T_2 and T_3, T_1 and T_3. The reduction in serum T_3 level was marked in the propyl thiouracil fed rabbits when compared to the control rabbits. The investigation also indicated that T_3 level was significantly low in cassava fed rabbits, when compared to the control rabbits. ($P<0.01$)

4.2.6 Serum cholesterol

The mean values of serum cholesterol level at two months, four months, and six months are shown in table 6 and fig. 9.

4.2.6.1 Serum cholesterol level at two months

There was no significant difference in the serum cholesterol level between T_1 and T_2, T_2 and T_3 and T_1 and T_3.

4.2.6.2 Serum cholesterol level at four months

There was no significant difference between T_1 and T_2 group. But there was significant difference between T_2 and T_3 and T_1 and T_3 group ($P < 0.01$). This indicated that there was marked increase in the cholesterol level in the propylthiouracil fed rabbits when compared to the control and cassava fed rabbits. But the increase in the cholesterol level in the cassava fed rabbits was not significant when compared to control rabbits ($P<0.01$).

4.2.6.3 Serum cholesterol level at six months

There was significant difference in the serum cholesterol level between T_1 and T_2, T_2 and T_3, T_1 and T_3 groups ($P<0.05$). The increase in the cholesterol level in the propyl thiouracil fed rabbits was marked when compared to the control rabbits. Also cassava fed rabbits showed a significant increase in the cholesterol level when compared to the control rabbits ($P<0.05$).

4.2.7 Serum proteins

The mean values of serum proteins obtained are tabulated in table 7 and fig. 10.

4.2.7.1 Serum protein level at two months

There was no significant difference in the serum protein level between T_1 and T_2, T_2 and T_3 and T_1 and T_3 group ($P<0.01$).

4.2.7.2 Serum protein level at four months

There was no significant difference in the serum protein level between T_1 and T_2, T_2 and T_3 and T_1 and T_3 ($P<0.01$).

4.2.7.3 Serum protein level at six months

There was no significant difference in the serum protein level between T_1 and T_2, T_2 and T_3 and T_1 and T_3 ($P<0.01$).

4.2.8 Blood sugar

The mean values of blood sugar level of rabbits at two months, four months and six months are tabulated in table 8 and fig. 11.

4.2.8.1 Blood sugar level at two months

There was no significant difference between T_1 and T_2, T_2 and T_3 and T_1 and T_3.

4.2.8.2 Blood sugar level at four months

There was no significant difference between T_1 and T_2, T_2 and T_3 and T_1 and T_3.

4.2.8.3 Blood sugar level at six months

There was no significant difference between T_1 and T_2, T_2 and T_3. But between T_1 and T_3 groups, the difference was significant. This indicated that blood sugar level of propyl thiouracil treated rabbits was significantly low, when compared to the control rabbits. ($P < 0.01$)

4.2.9 Haemoglobin

The mean values of haemoglobin level of rabbits at two months, four months and six months are shown in table 9 and fig. 12.

4.2.9.1 Haemoglobin level at two months

There was no significant difference between the haemoglobin level of rabbits in T_1, T_2 and T_3 groups.

4.2.9.2 Haemoglobin level at four months

There was significant difference between T_1 and T_2, T_1 and T_3 and no significant difference between T_2 and T_3 ($P < 0.05$). There was reduction in the haemoglobin level of rabbits fed propyl thiouracil and cassava, when compared to the control rabbits.

4.2.9.3 Haemoglobin level at six months

There was significant difference between T_1 and T_2, T_2 and T_3 and T_1 and T_3 ($P<0.01$). This indicated that there was marked reduction in the haemoglobin level of propyl thiouracil fed rabbits and cassava fed rabbits, when compared to the control rabbits.

4.2.10 Total leucocyte count

The mean values of total leucocyte count of rabbits at two months, four months and six months are set out in table 10.

4.2.10.1 Total leucocyte count at two months

There was no significant difference in the leucocyte count among T_1, T_2 and T_3 groups ($P<0.05$).

4.2.10.2 Total leucocyte count at four months

There was no significant difference in the leucocyte count between T_1, T_2 and T_3 groups ($P<0.05$).

4.2.10.3 Total leucocyte count at six months

There was significant difference between T_1 and T_2 ($P<0.05$). The leucocyte count was found to be higher in cassava fed rabbits when compared to the control rabbits. However, it was within the normal range. But there was no significant difference between T_1 and T_3, T_2 and T_3 groups, although the mean value of leucocyte count in the propyl thiouracil fed rabbits was higher than that of the control rabbits.

4.2.11 Erythrocyte count

The mean values of erythrocyte count of rabbits obtained at two months, four months and six months are given in table 11.

4.2.11.1 Erythrocyte count at two months

There was no significant difference in the erythrocyte counts of rabbits of T_1, T_2 and T_3 groups ($P<0.05$).

4.2.11.2 Erythrocyte count at four months

There was no significant difference between the erythrocyte count of T_1 and T_2 group. But there was significant difference in the erythrocyte count of T_2 and T_3, T_1 and T_3 group. This indicated that rabbits fed propyl thiouracil showed a reduction in erythrocyte count, when compared to the control rabbits. But there was no significant change in the erythrocyte count of rabbits fed cassava when compared to the control rabbits ($P<0.01$).

4.2.11.3 Erythrocyte count at six months

There was no significant difference in the erythrocyte count of T_1 and T_2 group. But there was significant difference in the erythrocyte count of T_2 and T_3, T_1 and T_3 group. This indicated that rabbits fed propyl thiouracil showed a reduction in the erythrocyte count and there was no significant change in the erythrocyte count of rabbits fed cassava, when compared to the control rabbits ($P<0.01$).

4.2.12 Differential leucocyte count

The data on the differential leucocyte count at two months, four months and six months are shown in the table 12 a, 12 b, 12 c.

4.2.12.1 Differential leucocyte count of rabbits at two months

There was no significant variation between T_1, T_2 and T_3 groups.

4.2.12.2 Differential leucocyte count at four months

There was no significant variation between T_1, T_2 and T_3 groups.

4.2.12.3 Differential leucocyte count of rabbits at six months

There was no significant variation between T_1, T_2 and T_3 groups.

4.2.13 Relative weight of the thyroid gland

The data on the relative weight of the thyroid gland recorded at two months, four months and six months are set out in table 13 and Fig. 13.

4.2.13.1 Relative weight of the thyroid gland at two months

There was no significant variation between T_1 and T_2 group. But there was significant variation between T_1 and T_3, T_2 and T_3 group. The increase in the relative weight of the thyroid gland in the propyl thiouracil fed rabbits was significant when compared to the control and cassava fed rabbits ($P<0.01$).

4.2.13.2 Relative weight of the thyroid gland at four months

There was an increase in the relative weight of the thyroid gland in T_2 and T_3 group when compared to T_1 group. The increase in the relative weight of the thyroid gland was significant ($P<0.01$) in propyl thiouracil fed rabbits.

4.2.13.3 Relative weight of the thyroid gland at six months

The data collected indicated that at six months there was increase in the relative weight of the thyroid gland of rabbits of T_2 and T_3 group, when compared to T_1 group.

4.2.14 Relative weight of the adrenal gland

The data on the relative weight of adrenal gland recorded at two months, four months and six months are tabulated in table 15.

4.2.14.1 Relative weight of the adrenal gland at two months

There was significant difference between T_1 and T_2, T_2 and T_3, T_1 and T_2 ($P < 0.01$). The relative weight of the adrenal gland of T_2 group was significantly lesser than T_1 and T_3 group ($P < 0.01$).

4.2.14.2 Relative weight of the adrenal gland at four months

There was no significant difference between T_1 and T_2 group. But the relative weight of the adrenal gland of T_3 group was significantly increased when compared to T_1 and T_2 group.

4.2.14.3 Relative weight of the adrenal gland at six months

There was significant difference between T_1 and T_2, T_2 and T_3, T_1 and T_2 ($P < 0.01$). The relative weight of the adrenal gland in T_2 group was significantly lesser than T_1 and T_3.

4.2.15 Relative weight of the testes and ovaries

Data on the relative weight of testes and ovaries are set out in table 15. There was no significant change in the relative weight of testes and ovaries between the different groups during the entire period of observation for six months.

4.2.16 Erythrocyte sedimentation rate

The data on ESR of rabbits at two months, four months and six months are tabulated in table 16. There was no variation in the ESR in different groups at two months, four months and six months.

4.2.17 Gross pathology

Out of the twelve rabbits in group T_2, one rabbit (No. 4573) died on 3-4-1987, two weeks after the commencement of the experiment. Post-mortem examination was performed. The cause of death was diagnosed as coccidiosis. At two months of experiment, four rabbits from each group were sacrificed and autopsy was conducted. There was no gross lesions in any of the organs in the rabbits of group T_1 and T_2. However, in group T_3, there was slight to moderate enlargement of the thyroid gland and adrenal gland. There was depletion of fat in the eye socket. At the end of the four months in group T_2, there was slight enlargement of the thyroid gland. However, other organs did not show any changes. In group T_3, the enlargement of the thyroid gland was much more marked than in group T_2. There was severe depletion of fat, and gelatinisation of subcutaneous fat, paleness of visible mucous membrane and enlargement of the adrenal gland. In group T_1, there was no changes in any of the organs.

At the end of six months, in group T_2 and T_3 there was enlargement of the thyroid gland and they were oval to round and dark brown in colour. They encircled the trachea as a dark brown mass of tissue. However, it was much significant and pronounced in T_3 group (Fig. 14). The carcasses of T_3 group were severely dehydrated than T_2 group. The other organs did not show any gross changes.

4.2.18 Histopathology

4.12.18.1 Cassava fed rabbits

In the thyroid gland, no changes were observed in the initial two months of the experimental period. At the fourth month, there was dilatation of the follicles. They were filled with pale staining colloid and the lining epithelial cells were cuboidal to columnar type (Fig. 15). There was congestion of vessels. By the sixth month the changes were little more prominent (Fig. 16). There were both micro and macro follicles. These follicles were lined with cuboidal to columnar epithelial cells in certain areas. There was tendency to form two or more layers of epithelial cells in the follicles. Some of the follicles did not contain any colloid, while some other follicels contained very pale staining colloid with scallooping of the colloid at the periphery. No lesions were seen in other organs.

4.12.18.2 Propylthiouracil fed rabbits

By the second month, the follicles were of varying size in the thyroid. Some of the follicles were very much enlarged while others were small in size. These follicles were filled with colloid. The colloid was pale pink staining and the follicles were lined with cuboidal to flattened epithelial cells (Fig. 17). There was peripheral scallooping of the colloid. By the fourth and sixth months there was progressive hypertrophy and hyperplasia of the lining epithelial cells. The lining epithelial cells were tall columnar (Fig. 18) and some of the follicles contained two or three layers of cells. The lumen of the follicles was small or medium sized. In some of the follicles the lining epithelial cells were seen thrown into small papillary folds into the lumen (Fig. 19). The vessels were engorged. Some of the follicles contained pale staining colloid while others did not contain any colloid (Fig. 20). The hypertrophic and hyperplastic changes were more pronounced by the sixth month. Some of the follicles showed more severe scallooping of the colloid. The micro follicles did not contain any colloid, but they were almost filled with hypertrophic tall columnar epithelial cells. These cells were having a basophilic cytoplasm and the prominent nucleus was located basally.

Histological picture of the testis of the control group of rabbits is projected in Fig. 21. In the propylthiouracil fed rabbits, there was no change in the testes at the second month, it was mild at the fourth month and the changes were more appreciable at the sixth month. (Fig. 22, 23) The testes showed degenerative changes. The spermatogonial cells were few and did not show active division and spermeogenesis. Some of the seminiferous tubules showed degeneration and desquamation of the spermatogonial cells. A few scattered degenerating cells were seen in the lumen of the seminiferous tubules. There was slight interstitial oedema. In the rabbits fed propyl thiouracil, there was mild degenerative changes in the ovarian follicles (Fig. 24). Primary follicles were few. They showed degeneration and desquamation of epithelial cells. There was slight interstitial oedema and stromal cells were seen arranged loosely.

The testes and ovary of rabbits fed cassava did not show any changes even at the sixth month.

There was no change in any of the other organs examined in the propyl thiouracil and cassava fed rabbits.

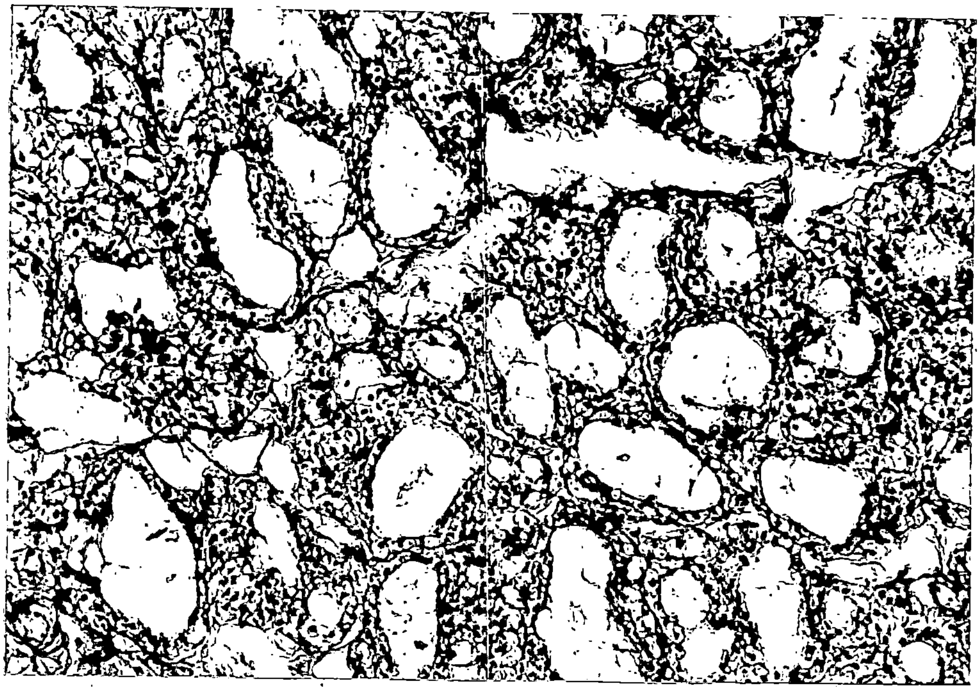
There was no histological changes in any of the organs of the control rabbits.

Fig. No. 15

Thyroid gland - cassava group rabbit - 4th month. Thyroid follicles lined by cuboidal to columnar epithelial cells and filled with vaccuolated colloid. H & E x 250.

Fig. No. 16

Thyroid gland - Cassava fed rabbit - 6th month. Follicles depleted of colloid and lined with prominent cuboidal to columnar cells H & E x 250.



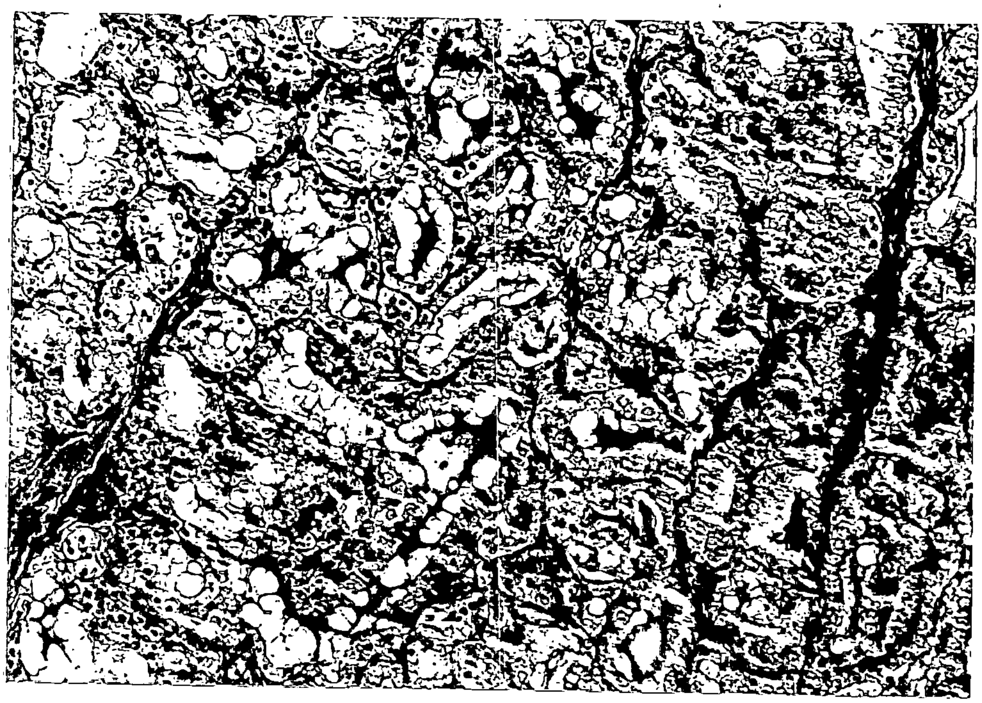


Fig. No. 17	Thyroid gland - propyl thiouracil fed rabbit - 2nd month. Dilated follicles filled with vaccuolated colloid and lined with cuboidal to columnar epithelial cells. H & E x 250.

Fig. No. 18	Thyroid gland - Propylthiouracil fed rabbit - 4th month. Dilated follicles filled with pale staining vaccoulated colloid. The follicles are lined with tall columnar epithelial cells. H & E x 250

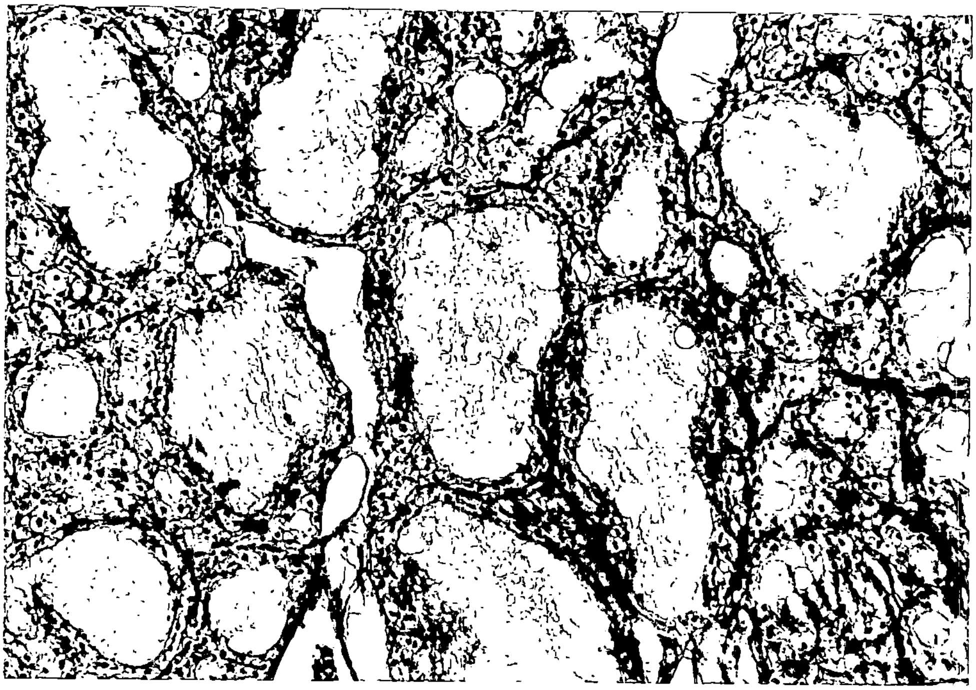
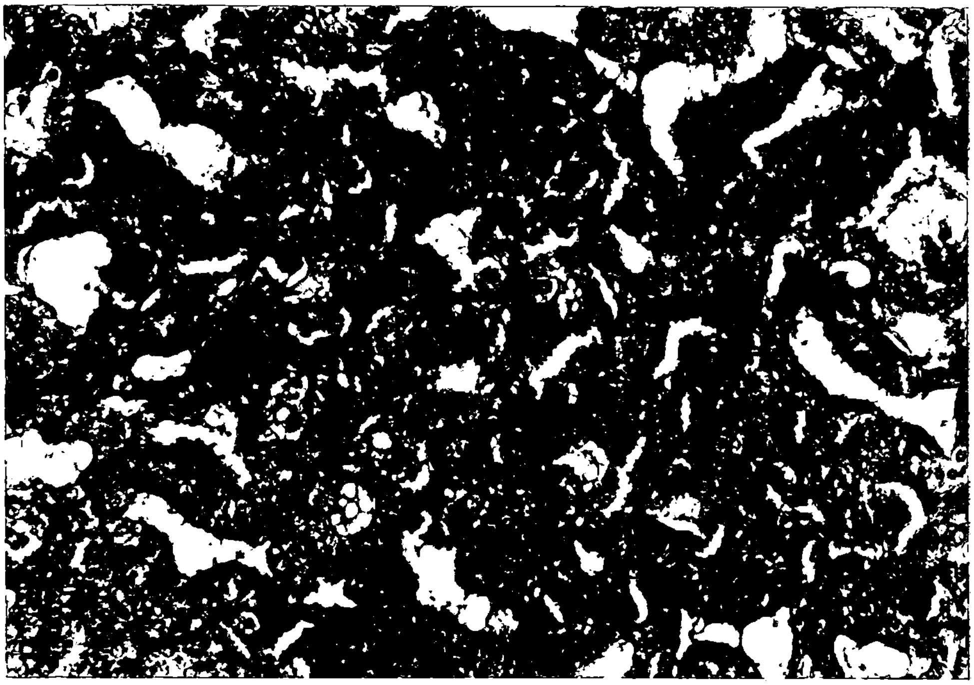


Fig. No. 19

Thyroid gland - propyl thiouracil fed rabbit - 6th month. Many micro follicles lined with very tall columnar cells. In some areas, more than one layer and thrown into small papillary folds. H & E x 250.

Fig. No. 20

Thyroid gland - propyl thiouracil fed rabbit - 6th month. Most of the follicles are small and devoid of colloid. The lining epithelial cells are tall columnar. H & E x 250.



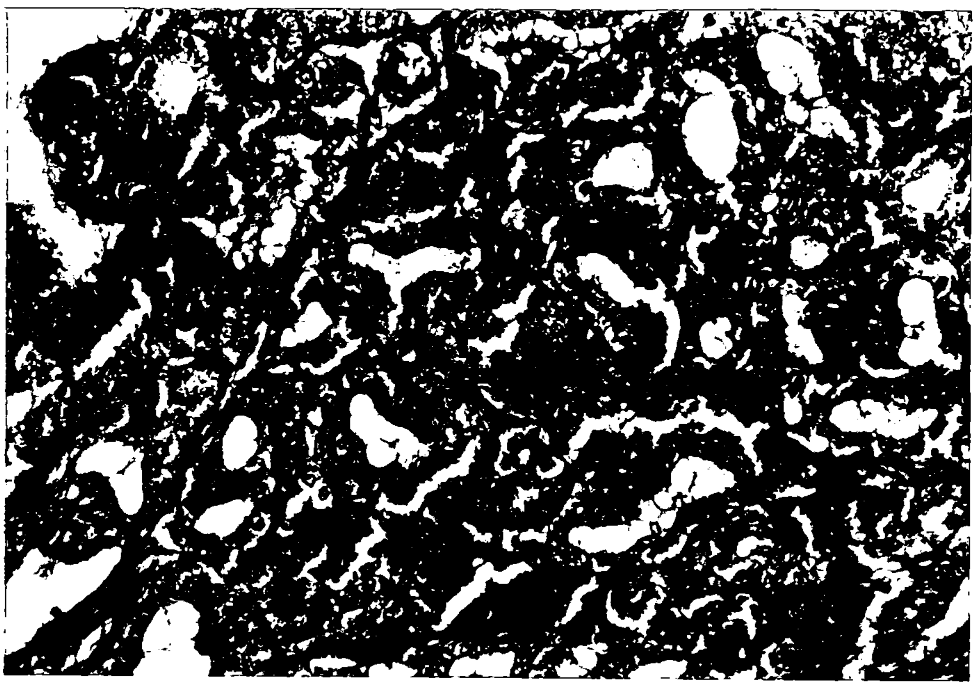


Fig. No. 21

Testis - control rabbit. Uniform sized seminiferous tubules. Active spermatogonial cells and sperms are also evident. H&EX250

Fig. No. 22

Testis - propyl thiouracil fed rabbit - 6th month. Varying sized seminiferous tubules. Degeneration of the epithelial cells. Desquamated cells are seen in the lumen. No active spermeogenesis and sperms. H & E x 250.

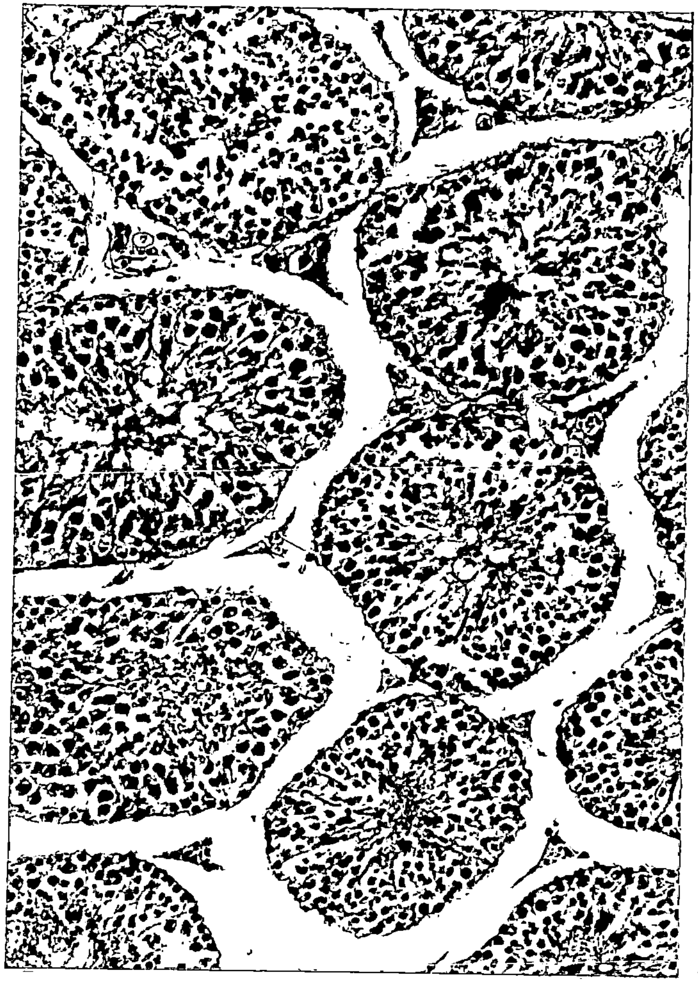



Fig. No. 23

Testis - propylthiouracil fed rabbit. Mild degenerative changes in the seminiferous tubules. H & E x 250.

Fig. No. 24

Ovary - propylthiouracil fed rabbit. Degeneration of the primary follicles in the cortex. H & E x 250.

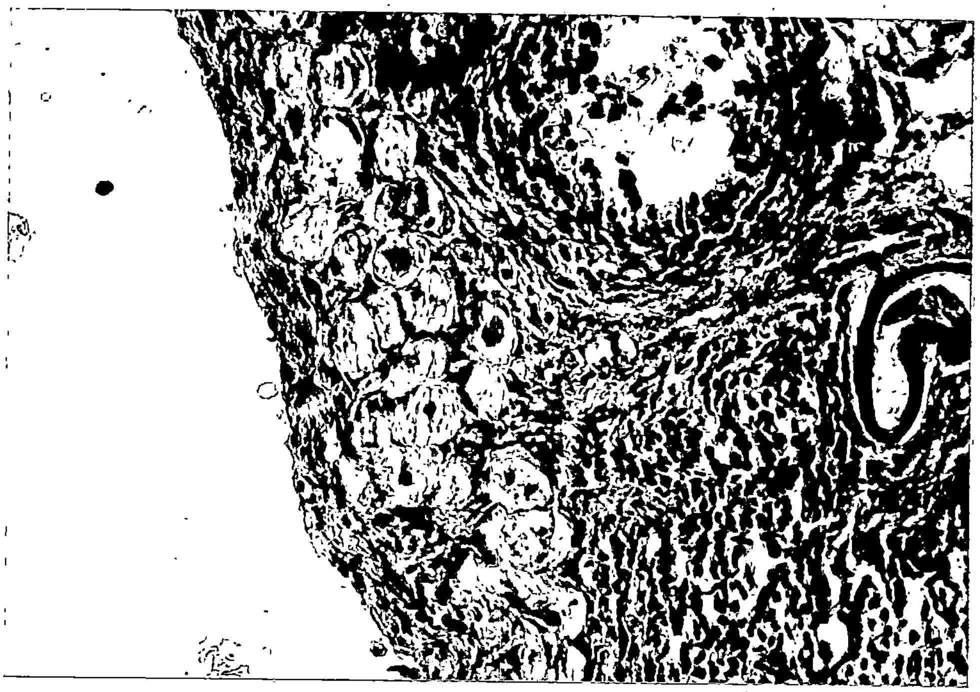


Table 2

Body Weight of Rabbits (g)

Period	Rabbit No. (T_1)	Body weight (T_1)	Rabbit No. (T_2)	Body weight (T_2)	Rabbit No. (T_3)	Body weight (T_3)
2nd month	4584 M	2100	4571 M	2200	5206 M	1750
	4587 F	2050	4579 M	2100	5207 M	1800
	4586 F	2200	4582 F	2350	5208 F	1850
	4576 F	2100	4585 M	2350	5209 M	1650
	Mean	2112.50	Mean	2250	Mean	1762.50
4th month	4587 F	2750	4572 M	2650	5214 M	2250
	4581 M	2500	4574 M	2450	5215 F	2150
	4569 F	2500	4577 M	2950	5216 M	2150
	4583 M	2450	4580 F	3000	5217 M	2050
	Mean	2550	Mean	2762.50	Mean	2150
6th month	4588 F	2500	4590 M	2950	5210 F	2200
	4589 M	2600	4578 F	2750	5211 M	2150
	4591 M	2800	4575 F	3100	5212 M	2150
	4592 M	2800	--	--	5213 M	2150
	Mean	2675	Mean	2933.33	Mean	2162.50

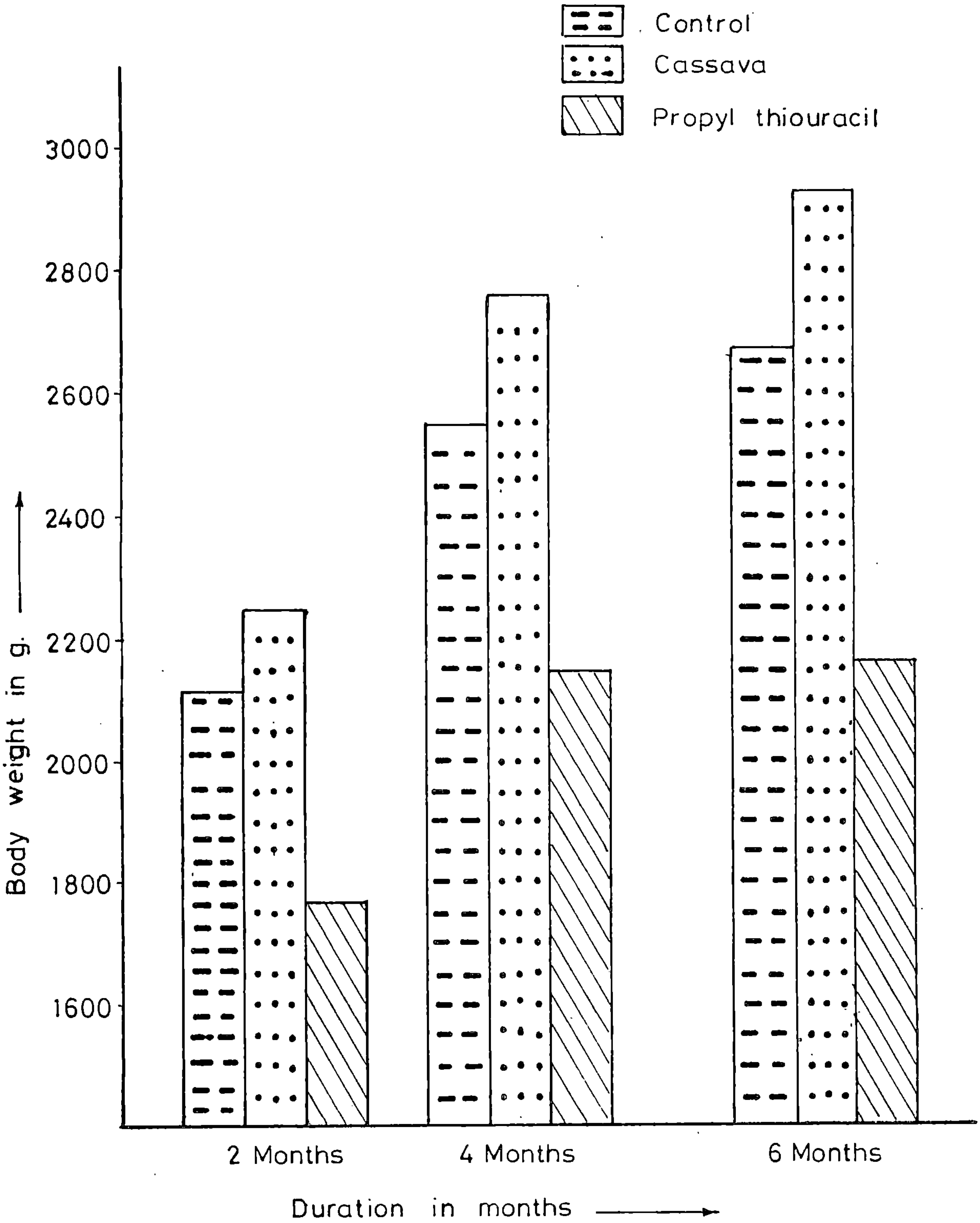


Fig - 2. BODY WEIGHT OF RABBITS

Table 3

Fur Weight of Rabbits (g)

Period	Rabbit No. (T_1)	Fur weight (T_1)	Rabbit No. (T_2)	Fur weight (T_2)	Rabbit No. (T_3)	Fur weight (T_3)
2nd month	4584 M	200	4571 M	250	5206 M	100
	4587 F	300	4579 M	200	5207 M	100
	4586 F	250	4582 F	300	5208 F	75
	4576 F	250	4585 M	250	5209 M	100
	Mean	250	Mean	250	Mean	93.75
4th month	4570 F	225	4572 M	350	5214 M	200
	4581 M	250	4574 M	300	5214 F	250
	4569 F	275	4577 M	300	5216 M	200
	4583 M	250	4580 F	400	5217 M	250
	Mean	250	Mean	337.50	Mean	225
6th month	4588 F	300	4590 M	250	5210 F	200
	4589 M	350	4578 F	300	5211 M	200
	4591 M	350	4575 F	250	5212 M	200
	4592 M	350	--	--	5213 M	200
	Mean	339.50	Mean	266.66	Mean	200

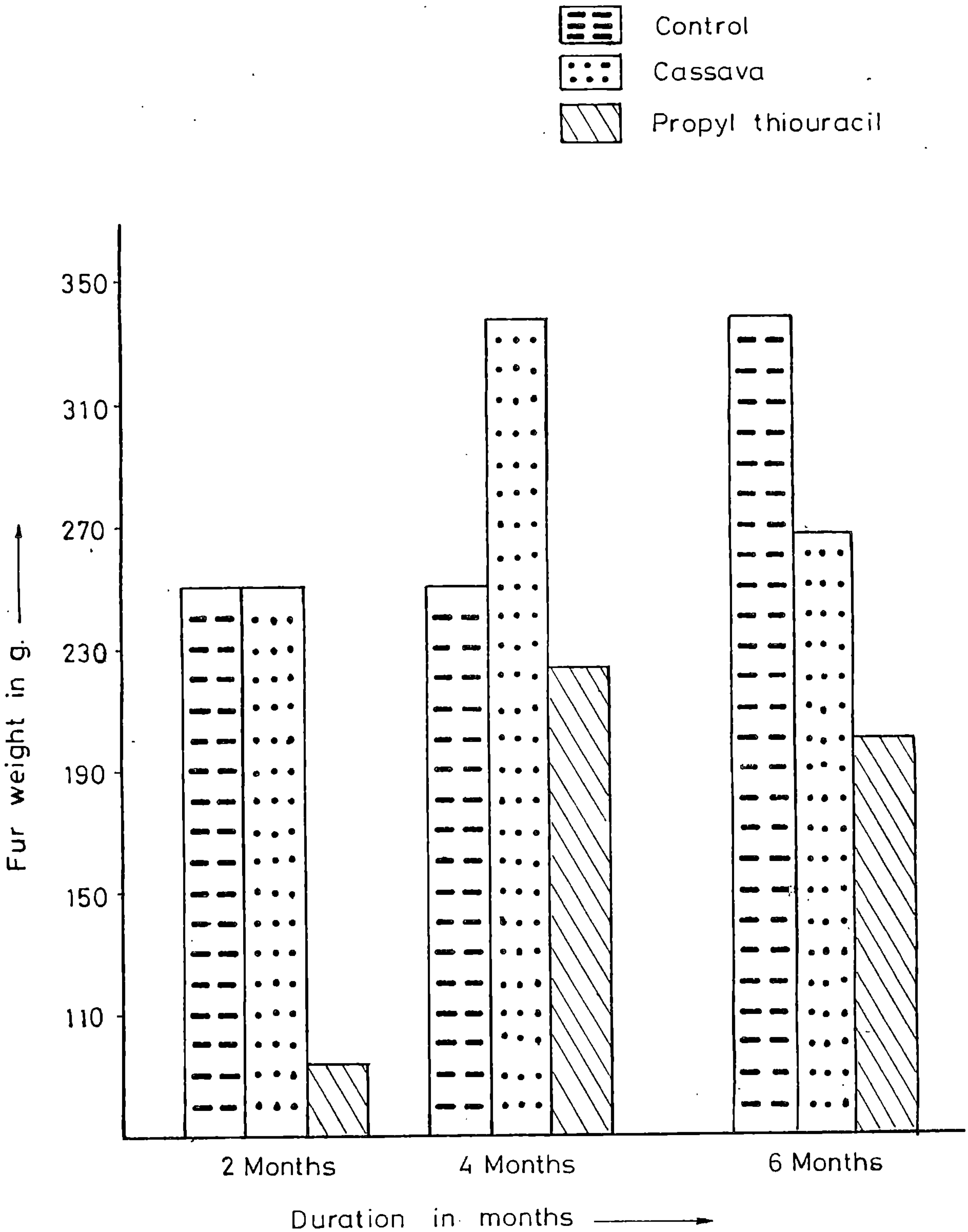


Fig - 6. WEIGHT OF FUR

Table 4

Serum Thyroxine Level of Rabbits (T_4 - µg/dl)

Period	Rabbit No.	Serum thyroxine	Rabbit No.	Serum thyroxine	Rabbit No.	Serum thyroxine
	(T_1)		(T_2)		(T_3)	
2nd month	4584 M	6.2	4571 M	4.6	5206 M	4.6
	4587 F	7.4	4571 M	7.2	5207 M	5.2
	4586 F	4.8	4582 F	5.4	5208 F	5.6
	4576 F	4.6	4585 M	7.2	5209 M	4.8
	Mean	5.75	Mean	6.10	Mean	5.05
4th month	4570 F	6.8	4572 M	3.8	5214 M	1.80
	4581 M	4.8	4574 M	6.4	5215 F	2.8
	4569 F	7.4	4577 M	4.8	5216 M	1.8
	4583 M	6.6	4580 F	4.6	5217 M	2.0
	Mean	6.40	Mean	4.90	Mean	2.10
6th month	4588 F	5.6	4590 M	4.2	5210 F	1.1
	4589 M	4.6	4578 F	4.0	5211 M	2.0
	4591 M	8.0	4575 F	4.6	5212 M	2.2
	4592 M	6.2	--	--	5213 M	1.2
	Mean	6.10	Mean	4.26	Mean	1.62

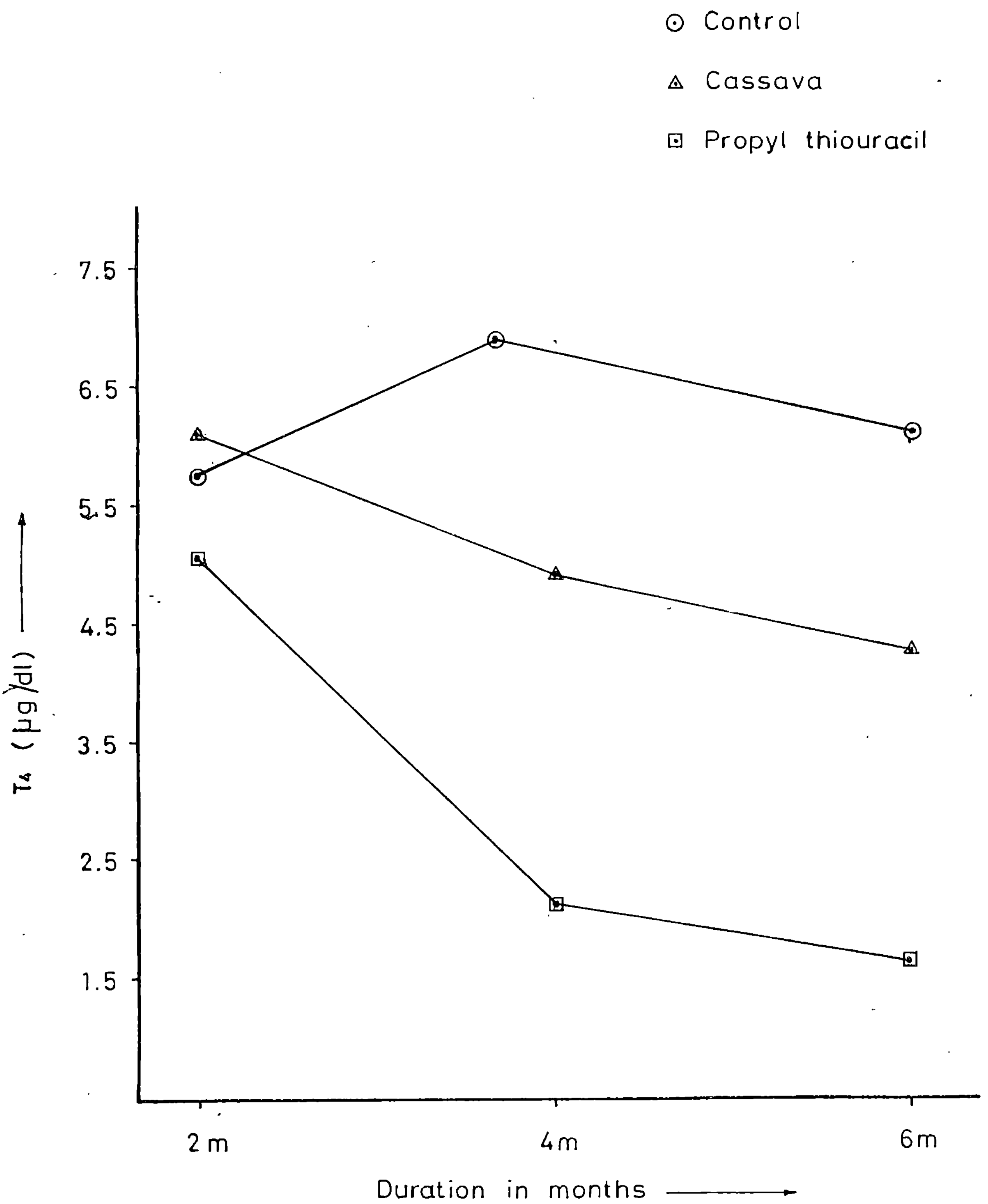


Fig- 7. SERUM THYROXINE LEVEL IN µg/dl

Table 5

Serum Triiodothyronine Level of Rabbits (T_3 - ng/dl)

Period	Rabbit No. (T_1)	Serum T_3 (T_1)	Rabbit No. (T_2)	Serum T_3 (T_2)	Rabbit No. (T_3)	Serum T_3 (T_3)
2nd month	4584 M	1.08	4571 M	0.90	5206 M	0.84
	4587 F	1.20	4579 M	1.46	5207 M	0.96
	4586 F	0.94	4582 F	1.20	5208 F	1.04
	4576 F	1.20	4585 M	1.64	5209 M	0.90
	Mean	1.105	Mean	1.300	Mean	0.935
4th month	4570 F	0.94	4572 M	0.98	5214 M	0.52
	4581 M	1.26	4574 M	1.20	5215 F	0.96
	4569 F	1.76	4577 M	1.14	5216 M	0.98
	4583 M	1.20	4580 F	1.12	5217 M	0.74
	Mean	1.29	Mean	1.11	Mean	0.80
6th month	4588 F	1.40	4590 M	0.66	5210 F	0.28
	4589 M	1.36	4578 F	0.94	5211 M	0.78
	4591 M	1.40	4575 F	1.04	5212 M	0.20
	4592 M	1.60	--	--	5213 M	0.40
	Mean	1.440	Mean	0.879	Mean	0.415

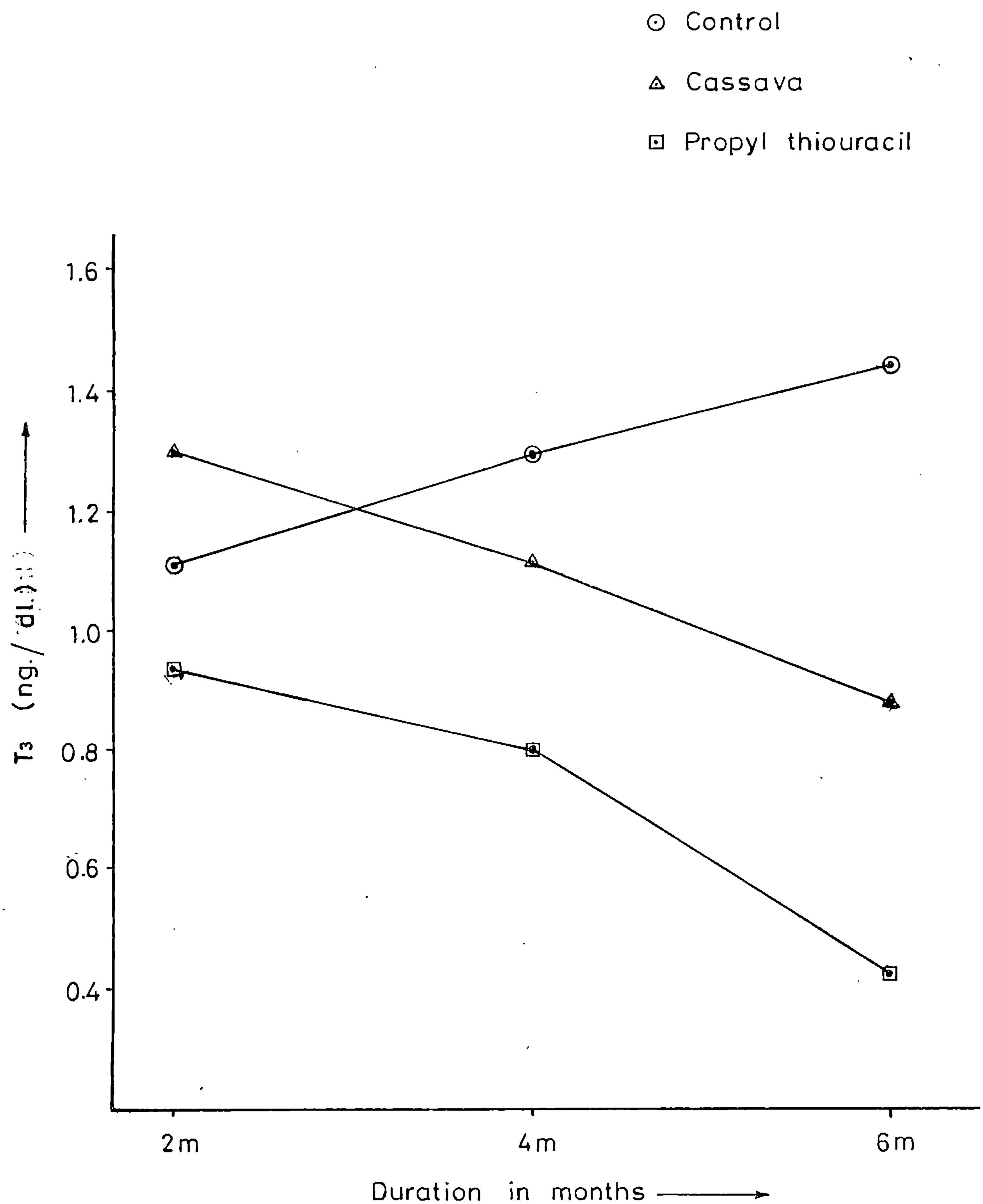


Fig-8. SERUM T_3 LEVEL

Table 6

Serum Cholesterol Level of Rabbits (mg/dl)

Period	Rabbit No. (T_1)	Serum cholesterol (T_1)	Rabbit No. (T_2)	Serum cholesterol (T_2)	Rabbit No. (T_3)	Serum cholesterol (T_3)
2nd month	4584 M	74	4571 M	64	5206 M	65
	4587 F	48	4579 M	60	5207 M	70
	4586 F	66	4582 F	72	5208 F	62
	4576 F	72	4585 M	55	5209 M	65
	Mean	65	Mean	62.75	Mean	65.50
4th month	4570 F	63	4572 M	63	5214 M	100
	4581 M	53	4574 M	70	5215 F	128
	4569 F	50	4577 M	66	5216 M	126
	4583 M	58	4580 F	60	5217 M	108
	Mean	56	Mean	64.75	Mean	115.50
6th month	4588 F	73	4590 M	82	5210 F	100
	4589 M	65	4578 F	86	5211 M	140
	4591 M	60	4575 F	84	5212 M	132
	4592 M	66	--	-	5213 M	136
	Mean	66	Mean	84	Mean	127

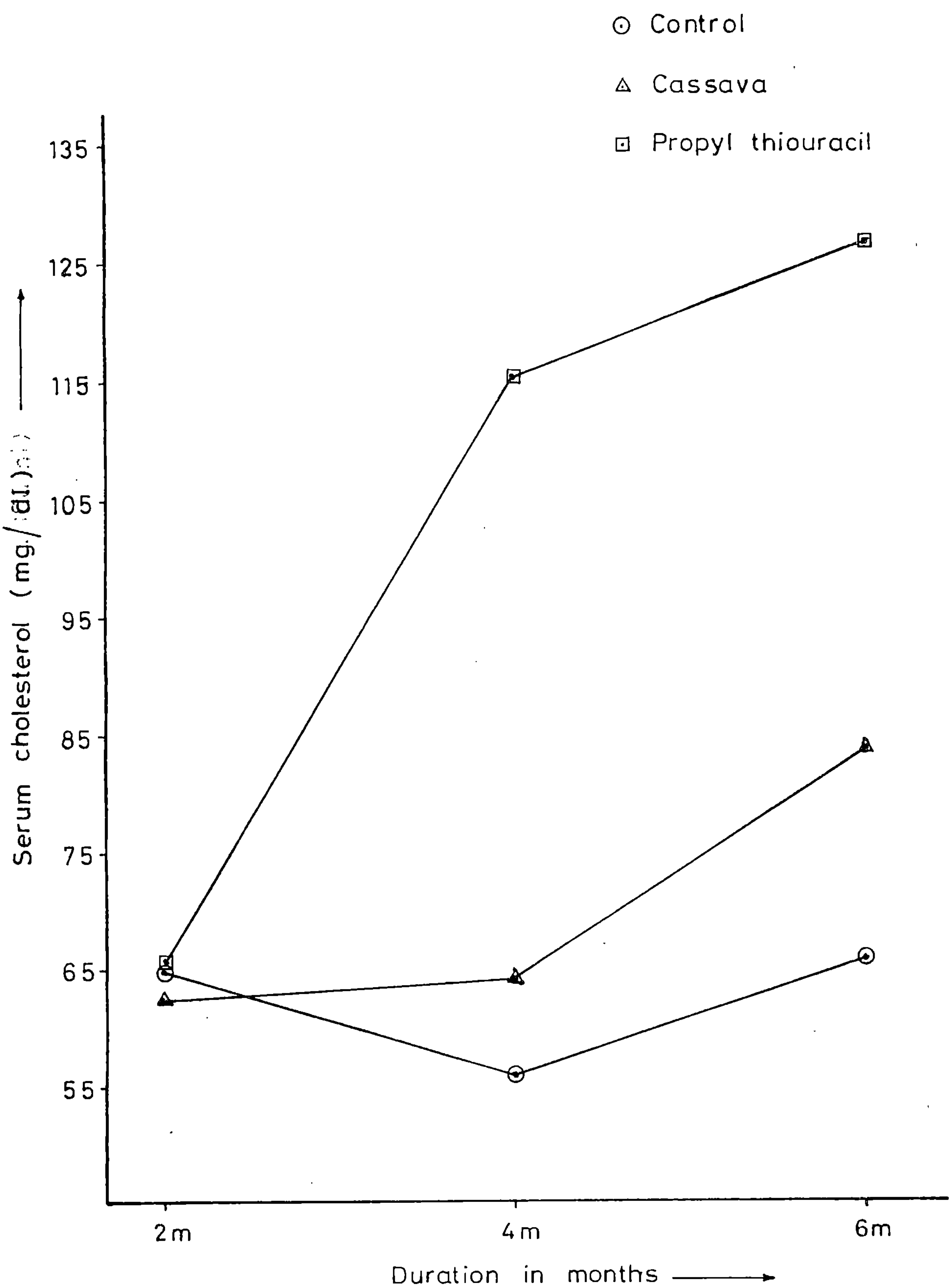


Fig-9. SERUM CHOLESTEROL

Table 7

Serum Proteins Level of Rabbits (g/dl)

Period	Rabbit No. (T_1)	Serum proteins (T_1)	Rabbit No. (T_2)	Serum proteins (T_2)	Rabbit No. (T_3)	Serum proteins (T_3)
	4584 M	8.4	4571 M	7.4	5206 M	7.8
	4587 F	8.8	4579 M	8.8	5207 M	8.2
2nd month	4586 F	7.8	4582 F	6.2	5208 F	8.4
	4576 F	9.2	4585 M	10	5209 M	9.0
	Mean	8.55	Mean	8.10	Mean	8.35
	4570 F	7.8	4572 M	7.4	5214 M	8.6
	4581 M	8.2	4574 M	8.8	5215 F	8.8
4th month	4569 F	8.0	4577 M	9.2	5216 M	9
	4583 M	8.8	4580 F	8	5217 M	8.6
	Mean	8.20	Mean	8.35	Mean	8.75
	4588 F	7.8	4590 M	8.6	5210 F	8.8
	4589 M	8.2	4578 F	7.4	5211 M	9.2
6th month	4591 M	7.6	4575 F	9.2	5212 M	9
	4592 M	8.8	--	-	5213 M	8.8
	Mean	8.10	Mean	8.40	Mean	8.95

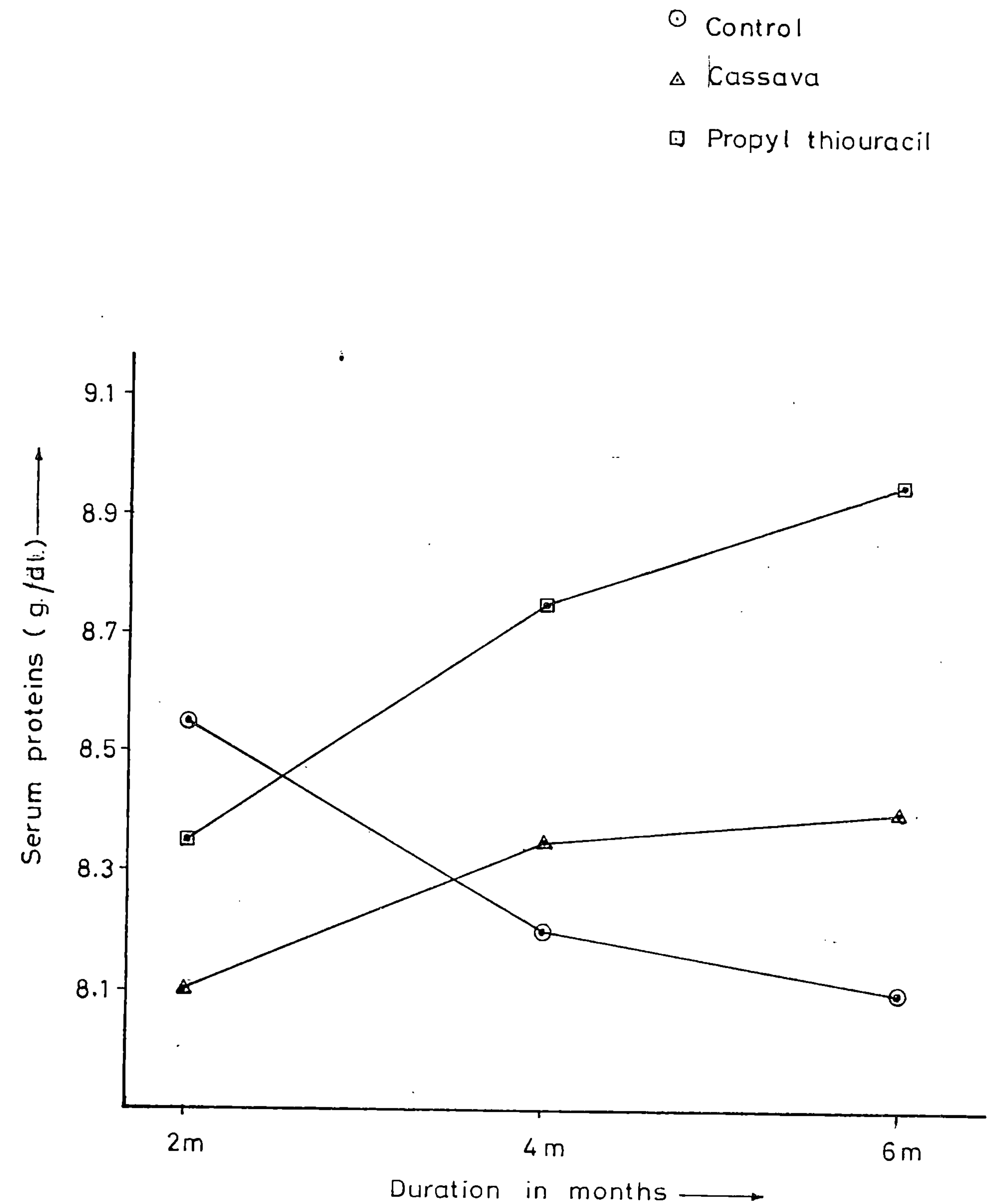


Fig-10. SERUM PROTEINS

Table 8

Blood Sugar Level of Rabbits (mg/dl)

Period	Rabbit No. (T_1)	Blood sugar (T_1)	Rabbit No. (T_2)	Blood sugar (T_2)	Rabbit No. (T_3)	Blood sugar (T_3)
2nd month	4584 M	105	4571 M	106	5206 M	94
	4587 F	116	4579 M	116	5207 M	105
	4586 F	90	4582 F	104	5208 F	85
	4576 F	85	4585 M	120	5209 M	100
	Mean	99	Mean	111.5	Mean	96
4th month	4570 F	90	4572 M	90	5214 M	76
	4581 M	115	4574 M	98	5215 F	88
	4569 F	102	4577 M	105	5216 M	95
	4583 M	85	4580 F	--	5217 M	90
	Mean	98	Mean	97.66	Mean	87.25
6th month	4588 F	130	4590 M	102	5210 F	88
	4589 M	88	4578 F	96	5211 M	90
	4591 M	126	4575 F	108	5212 M	75
	4592 M	130	--	-	5213 M	90
	Mean	118.5	Mean	102	Mean	85.75

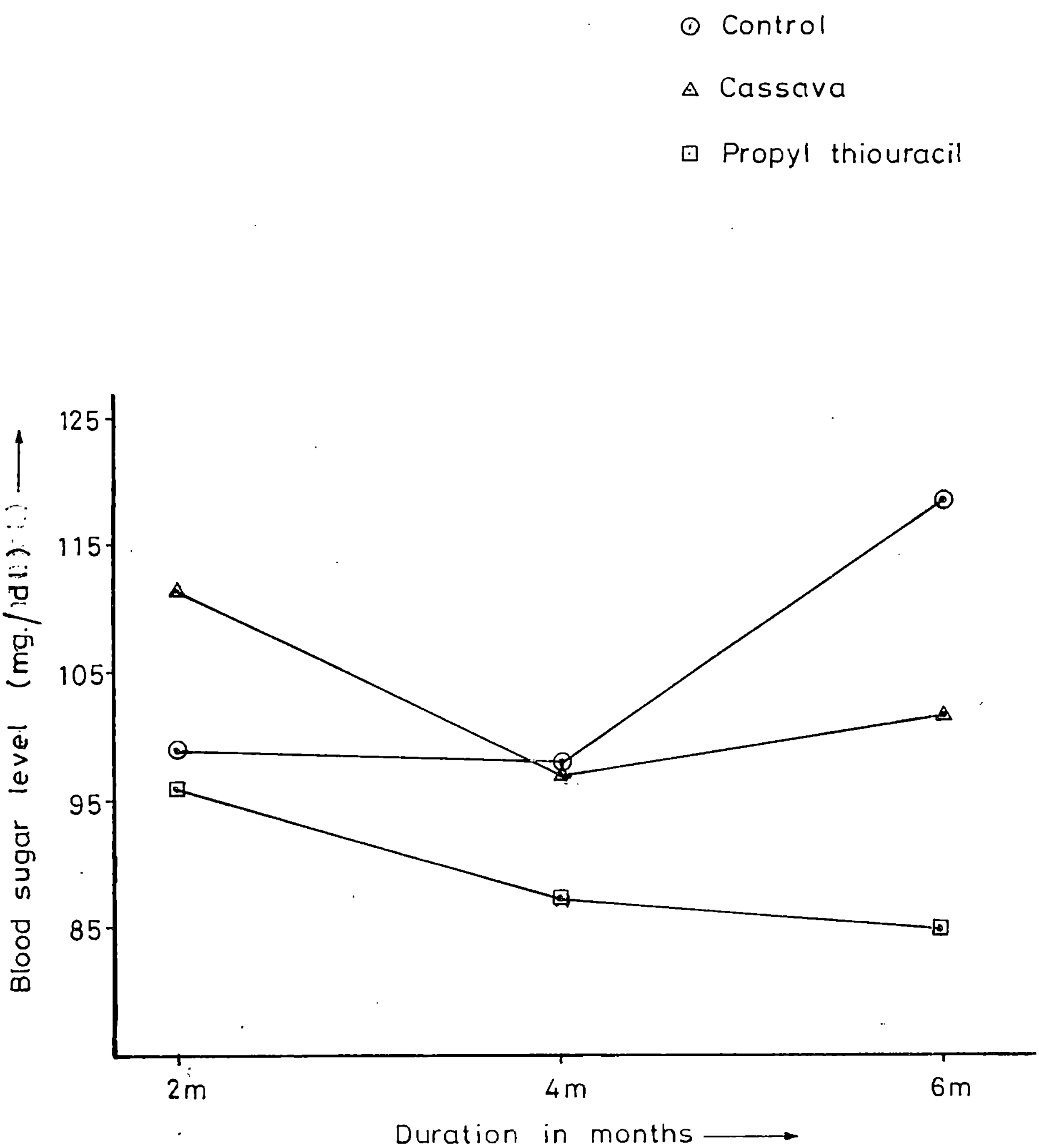


Fig-11. BLOOD SUGAR

Table 9

Haemoglobin Level of Rabbits (g/dl)

Period	Rabbit No. (T_1)	Hb (T_1)	Rabbit No. (T_2)	Hb (T_2)	Rabbit No. (T_3)	Hb (T_3)
2nd month	4584 M	10.4	4571 M	10.2	5206 M	10.2
	4587 F	8.6	4579 M	12.8	5207 M	10.8
	4586 F	10.8	4582 F	9.8	5208 F	10.6
	4576 F	9.6	4585 M	10.4	5209 M	10.4
	Mean	9.85	Mean	10.8	Mean	10.5
4th month	4570 F	10.8	4572 M	10.8	5214 M	9.8
	4581 M	14.6	4574 M	9	5215 F	9.2
	4569 F	12.8	4577 M	10.6	5216 M	8.4
	4583 M	12.2	4580 F	12	5217 M	9.6
	Mean	12.6	Mean	10.6	Mean	9.25
6th month	4588 F	12.2	4590 M	9.6	5210 F	8.4
	4589 M	11.6	4578 F	10.2	5211 M	8.8
	4591 M	11.8	4575 F	10	5212 M	8.4
	4592 M	12.0	--	-	5213 M	9.4
	Mean	11.90	Mean	9.93	Mean	8.75

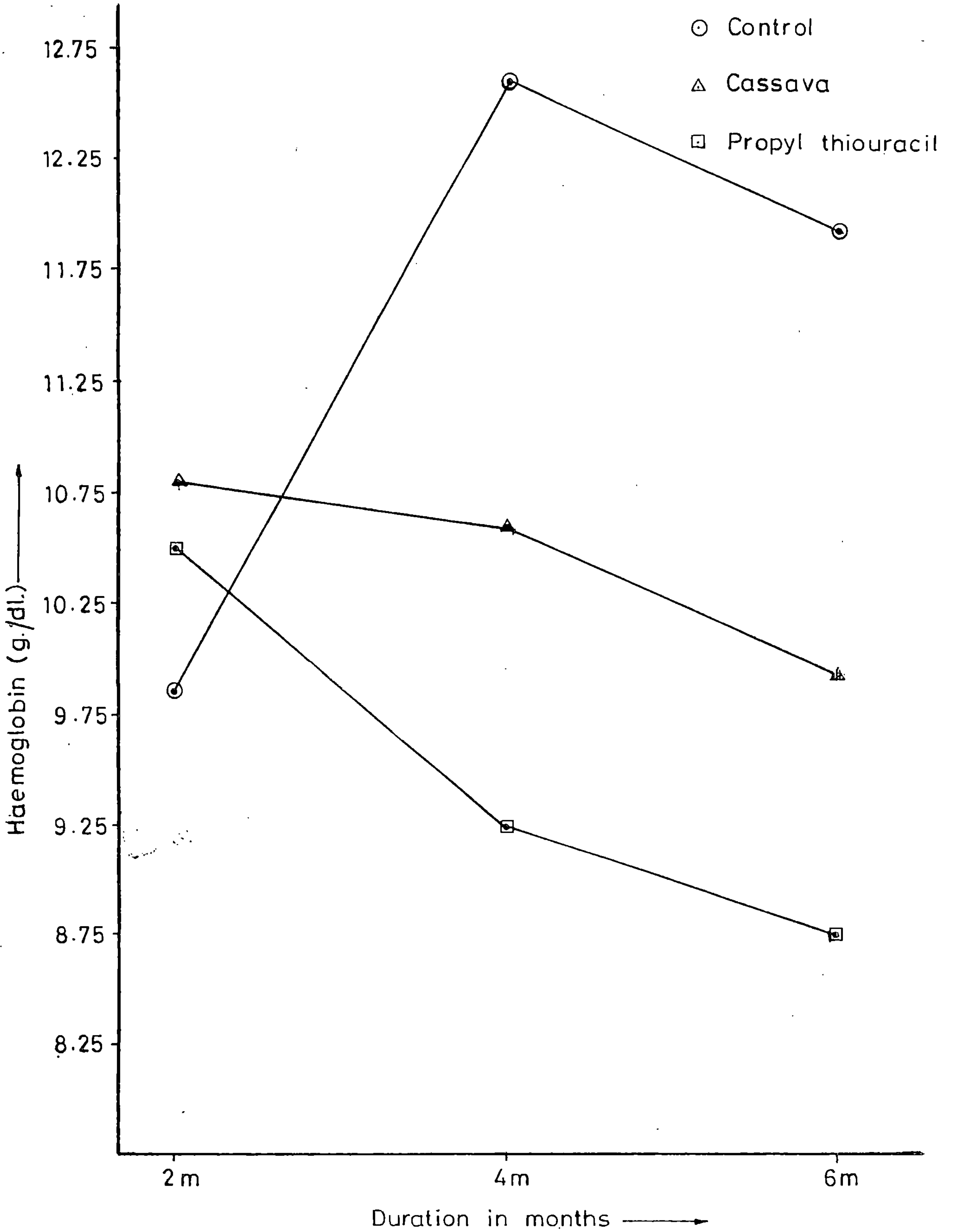


Fig-12 HAEMOGLOBIN

Table 10

Total Leucocyte Count of Rabbits (Thousands/cu.mm)

Period	Rabbit No. (T_1)	Total Leucocyte count (T_1)	Rabbit No. (T_2)	Total Leucocyte count (T_2)	Rabbit No. (T_3)	Total Leucocyte count (T_3)
2nd month	4584 M	8.60	4571 M	8.80	5206 M	8.60
	4587 F	7.85	4579 M	8.40	5207 M	9.35
	4586 F	8.00	4582 F	7.80	5208 F	8.20
	4576 F	6.20	4585 M	6.40	5209 M	7.80
	Mean	7.663	Mean	7.850	Mean	8.487
4th month	4570 F	9.76	4572 M	7.80	5214 M	9.80
	4581 M	9.86	4574 M	9.45	5215 F	10.30
	4569 F	8.25	4577 M	8.25	5216 M	9.80
	4583 M	8.24	4580 F	10.20	5217 M	10.60
	Mean	9.028	Mean	8.925	Mean	10.125
6th month	4588 F	9.60	4590 M	11.80	5210 F	10.25
	4589 M	8.00	4578 F	9.85	5211 M	9.95
	4591 M	8.40	4575 F	10.30	5212 M	9.60
	4592 M	9.20	--	-	5213 M	8.85
	Mean	8.800	Mean	10.650	Mean	9.663

Table 11

Erythrocyte Count of Rabbits (Millions/cu.mm)

Period	Rabbit No. (T1)	Erythrocyte count (T1)	Rabbit No. (T2)	Erythrocyte count (T2)	Rabbit No. (T3)	Erythrocyte count (T3)
2nd month	4584 M	4.8	4571 M	4.6	5206 M	4.2
	4587 F	4.6	4579 M	5.4	5207 M	4.6
	4586 F	5.2	4582 F	5.0	5208 F	4.2
	4576 F	4.0	4585 M	4.8	5209 M	3.8
	Mean	4.65	Mean	4.95	Mean	4.20
4th month	4570 F	4.6	4572 M	5.2	5214 M	4.0
	4581 M	5.4	4574 M	5.8	5214 F	3.8
	4569 F	5.2	4577 M	4.6	5216 M	3.6
	4583 M	5.8	4580 F	6.4	5217 M	3.8
	Mean	5.25	Mean	5.50	Mean	3.80
6th month	4588 F	5.2	4590 M	4.4	5210 F	3.60
	4589 M	4.6	4578 F	4.9	5211 M	3.20
	4591 M	4.8	4575 F	4.8	5212 M	2.80
	4592 M	5.2	--	-	5213 M	3.00
	Mean	4.95	Mean	4.70	Mean	3.15

Table 12 (a)

Differential Leucocyte Count of Rabbits at Two Months

Rabbit No.	Heterophils (%)	Lymphocytes (%)	Monocytes (%)	Basophils (%)	Eosinophils (%)
		Group (T_1)			
4584 M	14	78	1	3	4
4587 F	22	72	2	2	2
4586 F	19	69	3	5	4
4576 F	20	75	1	4	-
		Group (T_2)			
4571 M	17	78	2	2	1
4579 M	18	74	3	3	2
4582 F	21	74	2	3	-
4585 M	19	76	1	3	1
		Group (T_3)			
5206 M	11	86	-	2	1
5207 M	14	84	-	-	2
5208 F	19	78	2	1	-
5209 M	21	74	1	3	1

Table 12 (b)

Differential Leucocyte Count of Rabbits at Four Months

Rabbit No.	Heterophils (%)	Lymphocytes (%)	Monocytes (%)	Basophils (%)	Eosinophils (%)
		Group (T_1)			
4570 F	16	82	1	1	-
4581 M	18	75	2	3	1
4569 F	20	76	1	3	-
4583 M	22	74	2	2	-
		Group (T_2)			
4572 M	16	76	3	3	2
4574 M	25	74	1	-	-
4577 M	19	80	-	1	-
4580 F	13	81	4	2	-
		Group (T_3)			
5214 M	14	80	3	1	2
5215 F	18	74	4	3	1
5216 M	-	-	-	-	-
5217 M	12	81	2	2	3

Table 12 (c)

Differential Leucocyte Count of Rabbits at Six Months

Rabbit No.	Heterophils (%)	Lymphocytes (%)	Monocytes (%)	Basophils (%)	Eosinophils (%)
		Group (T_1)			
4588 F	12	86	-	2	-
4589 M	17	83	-	-	-
4591 M	14	80	2	1	1
4592 M	16	79	3	2	-
		Group (T_2)			
4590 M	26	71	2	1	-
4578 F	22	72	3	2	1
4575 F	18	81	-	-	1
-	-	-	-	-	-
		Group (T_3)			
5210 F	15	73	2	2	5
5211 M	18	78	1	2	1
5212 M	14	76	2	4	4
5213 M	13	82	2	-	3

Table 13

The Relative Weight of the Thyroid glands of Rabbits
(Percentage body weight)

Period	Rabbit No. (T_1)	Relative weight (T_1)	Rabbit No. (T_2)	Relative weight (T_2)	Rabbit No. (T_3)	Relative weight (T_3)
2nd month	4584 M	0.00320	4571 M	0.001360	5206 M	0.00385
	4587 F	0.00170	4579 M	0.001336	5207 M	0.00375
	4586 F	0.00136	4582 F	0.001480	5208 F	0.00310
	4576 F	0.00136	4585 M	0.002120	5209 M	0.00348
	Mean	0.001905	Mean	0.001580	Mean	0.003545
4th month	4570 F	0.00118	4572 M	0.002540	5214 M	0.01800
	4581 M	0.00044	4574 M	0.002510	5215 F	0.006510
	4569 F	0.00142	4577 M	0.001900	5216 M	0.02490
	4583 M	0.00040	4580 F	0.00210	5217 M	0.01050
	Mean	0.00086	Mean	0.00226	Mean	0.01490
6th month	4588 F	0.0014	4590 M	0.00140	5210 F	0.01100
	4589 M	0.00123	4578 F	0.00163	5211 M	0.00790
	4591 M	0.00121	4575 F	0.00153	5212 M	0.02130
	4592 M	0.00146	--	--	5213 M	0.01030
	Mean	0.00132	Mean	0.00152	Mean	0.0126

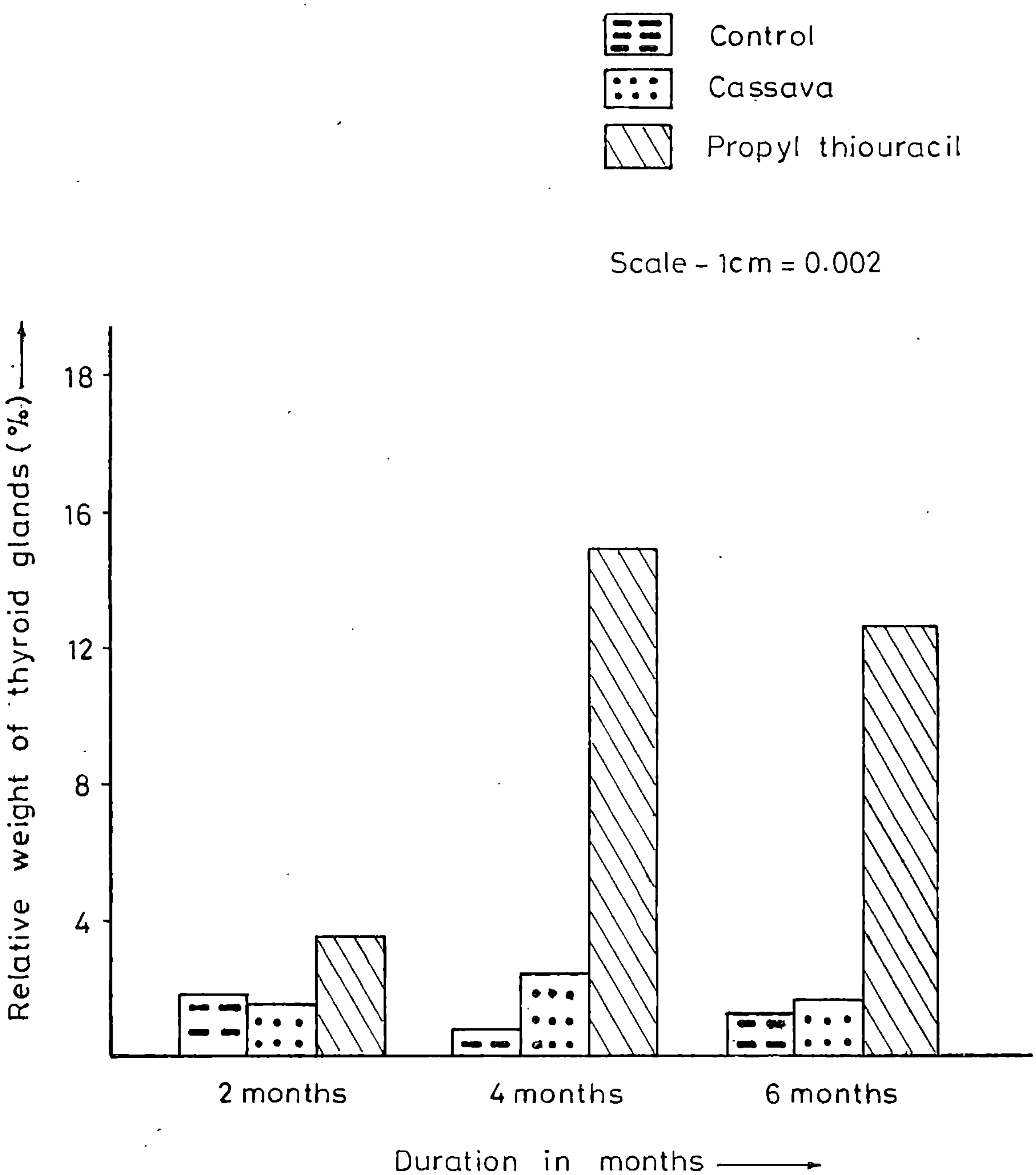


Fig-13. RELATIVE WEIGHT OF THYROID GLANDS

Table 14

The Relative weight of the Adrenal glands of Rabbits
(Percentage body weight)

Period	Rabbit No. (T_1)	Relative weight (T_1)	Rabbit No. (T_2)	Relative weight (T_2)	Rabbit No. (T_3)	Relative weight (T_3)
2nd month	4584 M	0.00714	4571 M	0.00340	5206 M	0.00900
	4587 F	0.00682	4579 M	0.00523	5207 M	0.00930
	4586 F	0.00590	4582 F	0.00510	5208 F	0.00810
	4576 F	0.00523	4585 M	0.00404	5209 M	0.01000
	Mean	0.00627	Mean	0.00444	Mean	0.00910
4th month	4570 F	0.00396	4572 M	0.00462	5214 M	0.00950
	4581 M	0.00584	4574 M	0.00714	5215 F	0.00670
	4569 F	0.00360	4577 M	0.00466	5216 M	0.00720
	4583 M	0.00663	4580 F	--	5217 M	0.00790
	Mean	0.00500	Mean	0.005473	Mean	0.007840
6th month	4588 F	0.00600	4590 M	0.00372	5210 F	0.00830
	4589 M	0.00576	4578 F	0.00418	5211 M	0.00860
	4591 M	0.00553	4575 F	0.00250	5212 M	0.00906
	4592 M	0.00678	--	--	5213 M	0.00825
	Mean	0.006017	Mean	0.003467	Mean	0.008552

Table 15

The Relative Weight of testes and ovaries of Rabbits
(Percentage body weight)

Period	Rabbit No.	Relative weight	Rabbit No.	Relative weight	Rabbit No.	Relative weight
	(T_1)		(T_2)		(T_3)	
2nd month	4584 M	0.0819	4571 M	0.0859	5206 M	0.0802
	4587 F	0.00365	4579 M	0.1071	5207 M	0.0811
	4586 F	0.00772	4582 F	0.00404	5208 F	0.00432
	4576 F	0.00452	4585 M	0.1338	5209 M	0.0882
4th month	4570 F	0.0040	5272 M	0.1116	5214 M	0.1266
	4581 M	0.1602	4574 M	0.1529	5215 F	0.0039
	4569 F	0.0060	4577 M	0.0068	5216 M	0.1386
	4583 M	0.1439	4580 F	0.0027	5217 M	0.1487
6th month	4588 F	0.0054	4590 M	0.1388	5210 F	0.0075
	4589 M	0.1444	4578 F	0.0069	5211 M	0.1430
	4591 M	0.1407	4575 F	0.0027	5212 M	0.1348
	4592 M	0.1316	--	--	5213 M	0.1418

Table 16

The Erythrocyte Sedimentation rate of Rabbits (mm/hr)

Period	Rabbit No. (T_1)	ESR (T_1)	Rabbit No. (T_2)	ESR (T_2)	Rabbit No. (T_3)	ESR (T_3)
2nd month	4584 M	1	4571 M	1	5206 M	2
	4587 F	1	4579 M	1	5207 M	1
	4586 F	1	4582 F	1	5208 F	1
	4576 F	1	4585 M	2	5209 M	1
4th month	4570 F	1	4572 M	1	5214 M	2
	4581 M	1	4574 M	1	5215 F	1
	4569 F	1	4577 M	1	5216 M	1
	4583 M	1	4580 F	1	5217 M	1
6th month	4588 F	1	4590 M	2	5210 F	1
	4589 M	1	4578 F	1	5211 M	1
	4591 M	1	4575 F	1	5212 M	1
	4592 M	1	--	-	5213 M	1

Discussion

5. DISCUSSION

The random survey studies conducted at Cannanore, Trichur, Ernakulam and Idukki districts for assessing the thyroid status of cattle using serum T_4 as a marker, confirmed that hypothyroidism is prevalent in cattle in these districts. The mean value of T_4 in clinically healthy cattle was found to be 4.8727 ± 0.1209 μg/dl. In condition like infantile genitalia, the mean T_4 value was 3.5617 ± 0.1089 μg/dl, and in anoestrum cases, the mean T_4 level was 3.6913 ± 0.1136 μg/dl. Repeat breeders showed a mean T_4 level of 3.9175 ± 0.1130 μg/dl.

These observations indicated that hypothyroidism was one of the important reasons for non-infectious reproductive disorders in cattle. These findings, therefore, points out the need for evaluating the T_4 level in cattle to clarify and establish the aetiology of non-infectious reproductive disorders. Mammen (1936) in the survey studies conducted to evaluate the thyroid status of cattle in Kerala with non-infectious reproductive disorders, employing protein bound iodine as the marker indicated that hypothyroidism is prevalent in cattle with non-infectious reproductive disorders. The observation made by Louvet et al. (1979) that hypofunction of the thyroid gland evidenced by low T_3 and T_4 levels caused anovulation and sterility also supports the observation made in this investigation. In this context, it may be pointed out that Sharawy et al. (1987) have reported lower levels of T_3 and T_4 in buffaloes with inactive ovaries.

It is relevant to point out that Kerala is considered as an endemic area of iodine deficiency as per the reports of Kelly and Snedden (1960). Poulose et al. (1984), while investigating into the prevalence of goitre in human patients in and around Kottayam district demonstrated that water in these localities is deficient in iodine. However, in this investigation, the iodine content in water in these districts was not probed into. There is need to undertake an investigation to assess the prevalence and magnitude of iodine deficiency in water.

Goitrogens have been shown to have a significant role in inducing hypothyroidism in man (Dorozynski, 1978; Gilbert, 1984). Certain unconventional feeds like rubber seed cake, Leucaena, castor bean seed cake were shown to be goitrogenic in nature (DST Scheme report, 1988; Purushotham et al. 1985). This observation has relevance since in many places in Kerala, livestock are fed these dietary ingredients, which have proven goitrogenic effect.

In this context, it may also be pointed out that Government of India has declared India as an endemic zone of iodine deficiency, and has initiated supply of iodized salt for human consumption. Since man and animal shares the same environment, iodine deficiency and hypothyroidism is bound to happen in the animal population. The limited investigations undertaken in this study have also convincingly clarified that animals are also manifesting hypothyroidism.

As far as the livestock is concerned, the productivity is associated with thyroid function and subclinical hypothyroidism leads to lowered productivity and reproductive dysfunction. The studies undertaken in various species of animals like goat, cattle, duck and chicken (Sing et al. 1964; Sreekumaran, 1976; Reddy, 1982; Mammen, 1986, Arnya et al. 1986 and DST Scheme Report, 1988) have demonstrated this.

From the observations made in this study, there is justification to recommend iodide supplementation in cases of non-infectious reproductive disorders, reduced growth and productivity. It will be a wise line of approach to estimate the thyroxine level in non-infectious reproductive disorders and institute iodide therapy or thyroxine administration as a therapeutic schedule.

In order to evaluate the goitrogenic effect of cassava, which is being consumed by both human and animal population on a large scale, an experimental study was undertaken using broiler rabbit as the experimental model. Since the broiler rabbits are fast growing and rearing of broiler rabbits on a large scale has been taken up, the observations made, will have great relevance.

With the objective of comparing the cassava induced hypothyroidism, an experimental model of hypothyroidism was structured in rabbits employing propyl thiouracil as the goitrogen. The low level of serum T_4 and T_3 in propyl thiouracil fed rabbits along with other clinical symptoms indicated that the dose of propyl thiouracil employed, created a model of hypothyroidism in the rabbits.

The low T_4 and T_3 level in cassava fed rabbits gave evidence to the surmise that cassava flour was a mild goitrogen when fed at the rate of 25% in the ration for a period of six months. Jham et al. (1987) evaluated pressed residue from cassava leaves as a substitute for commercial feed for rabbits and found that pressed residue from cassava leaves could be incorporated into rabbit diets at levels of atleast 10% without any loss in animal performance.

The observations made on the goitrogenic effect of cassava has been controversial. In Zaire, it is a staple food of the population as in Kerala and cassava was considered as an important risk factor to develop hypothyroidism (Gilbert, 1984). Thampan (1979) stated that the E E C. countries import cassava almost exclusively for use in animal feeds, and no harmful results were observed with upto 40% of an animal ration consisting of cassava. The rate of utilisation of cassava products in animal feeds had been reported as 10 to 40% for swine, 20 to 25% for cattle and 10 to 20% for poultry (Thampan, 1979).

According to Thampan (1979) cassava contains hydrocyanic acid, the nature and quantity varies in different strains of cassava and the extent of hydrocyanic acid varies according to the soil and climatic conditions. The hydrocyanic acid gets converted to thiocyanates in the system, which in turn acts as the goitrogen. The thiocyanates acts as a goitrogen by inhibiting the iodide transport (Calderbank, 1963).

It is significant to point out that there was increase in productive performance indicated by increase in body weight in cassava fed rabbits by about the fourth month. This weight gain can be ascribed to low BMR and consequent transient anabolic effect in hypothyroidism. On the contrary there was reduction in body weight gain in rabbits fed propyl thiouracil, as it caused severe hypothyroidism. It is known that feeding goitrogens at low levels is of value in fattening pigs (Pearson et al. 1966). From the present investigation undertaken, it can be concluded that cassava flour can be incorporated in the ration of broiler rabbit diet upto a level of 25%, without any undesirable effect on weight gain and growth as broiler rabbits are to be reared and sacrificed at two months. It is also pertinent to point out that cassava is an economically cheap dietary ingredient and hence it contributes to the economic rearing of broiler rabbits. In this context, it may be pointed out that scanning of literature did not reveal any reference on the use of cassava flour as a feed ingredient in the ration for broiler rabbits.

The fur appear to be effected in hypothyroidism in rabbits. In the case of propyl thiouracil fed rabbits, there was a progressive reduction in fur weight from the second month onwards, whereas in in cassava fed rabbits, the reduction in fur weight was observed by the end of sixth month only. This is indicative of the mild goitrogenic action of cassava. In the propyl thiouracil group, the hair coat of the rabbits became rough progressively and bilateral hairless patches were extensive especially on the ventral side of the abdomen. But in cassava fed rabbits, the skin and hair changes appeared only by the end of six months and the changes were minimal when compared to propyl thiouracil fed rabbits. Changes in the skin and hair in hypothyroidism have been reported earlier by Sreekumaran (1976), Rijnberk et al. (1977), Reddy (1982) in goats and in calves by Mammen (1986), in cats by Gillen (1985) and in pigs by Bussian (1975). The epidermal layer of the skin was considered to be an important target organ for the action of thyroxine (Freedberg, 1971) and hence pathological changes in the skin can almost be considered as a pathagnomonic symptom in hypothyroidism.

It may be pointed out that the reduction in the fur weight and mild changes in the skin and hair in cassava fed rabbits appeared only by the end of six months. Since the rabbits will be sacrified at four months for fur and at this period of time cassava feeding at 25% will not cause any undesirable effect on fur, cassava flour can be fed advantageously to rabbits without inducing damage to the fur. However, in this context, it may be cautioned that feeding of cassava to rabbit at levels of 25% should not be resorted to long periods by the farmers in the case of rabbits which have to be maintained for long periods for fur. In rabbits, fur is of good value and the farmers should be cautious of feeding any ingredient which is damaging to fur.

In propyl thiouracil fed rabbits, there was progressive and marked reduction in the serum T_4 and T_3 level from the fourth month onwards, whereas in cassava fed rabbits subnormal level of T_4 and T_3 was observed only by the end of six months, indicating a mild hypothyroid state. This observation implied that cassava induced hypothyroidism was mild as it took six months to induce hypothyroidism of mild nature. At the same time, the observation confirmed the goitrogenicity of cassava. This observation is in agreement with the observation of Nasseri et al. (1987), that serum thyroxine decreased significantly in ewes in experimental hypothyroidism using thiourea as the goitrogen. Gillen (1987) reported confirmed hypothyroidism in a cat and this was associated with subnormal T_4 and T_3 levels, hypercholesteraemia and bilateral symmetrical alopecia.

Serum cholesterol level was found to be abnormally high in propyl thiouracil fed rabbits. The cholesterol level was slightly higher in cassava fed rabbits when compared to the control rabbits and lower when compared to propyl thiouracil fed rabbits. This goes to confirm the observation made by Mason and Wilkinson (1973) in dogs that cholesterol synthesis is inversely proportional to the thyroid function.

Increase in the serum cholesterol level has been reported in experimental hypothyroidism in sheep (Lascelles and Setchell, 1959; Belonje, 1967) in chicken (Nangia et al. 1975), in goats (Sreekumaran, 1976; Reddy, 1982), in calves (Mammen, 1986) and in cats (Gillen, 1987). The increase in the serum cholesterol level was considered to be an indication of a specific change in lipid metabolism in hypothyroidism in human myxoedema by Peters and Man (1950). Fletcher and Myant (1958) indicated that in hypothyroid rats, the hepatic synthesis and release of cholesterol from acetate was subnormal, but the peripheral breakdown and biliary excretion was lowered and this they attributed as the reason for hypercholesteraemia.

Blood sugar values of propyl thiouracil fed rabbits were significantly low by the end of six months. But there was no significant reduction in blood sugar values of cassava fed rabbits. This indicates the weak goitrogenic action of cassava, when compared to propyl thiouracil. The low blood sugar value in the propyl thiouracil fed rabbits must be due to the relatively low metabolic rate developed in hypothyroidism. In this connection, it should be noted that a significant reduction in the blood sugar level was observed only at the end of six months. It can, therefore, be concluded that blood sugar level was affected only when the hypothyroid state was prolonged and when the energy transactions were reduced due to hypothyroidism.

There was progressive reduction in the haemoglobin content of rabbits fed propyl thiouracil and cassava, from the fourth month onwards. There was reduction in the erythrocyte count of rabbits fed propyl thiouracil, but the erythrocyte count of rabbits fed cassava did not show any significant reduction. The anaemia observed can therefore be classified as microcytic hypochromic in propyl thiouracil fed rabbits and normocytic hypochromic in cassava fed rabbits. Here again, the observation is an implication of the weak goitrogenic nature of cassava when compared to propyl thiouracil. Sreekumaran (1976), Reddy (1982) and Mammen (1986) observed that deficiency of thyroxine would lead to anaemic state. The observation of anaemia is in consistence with their findings. Adamson and Finch (1966) demonstrated a decrease in erythropoietin production in hypothyroidism. Rivlin (1971) observed a reduction in intestinal absorption of vitamin B_{12} as a significant effect of hypothyroidism in man. These factors may play a role in causing anaemia in hypothyroidism.

There was progressive increase in the relative weight of the thyroid and appreciable enlargement from the second month onwards in rabbits fed propyl thiouracil. Rabbits fed cassava also registered an increase in the relative weight of thyroid, and enlargement from the 4th month onwards. This is yet another observation, which proves that cassava is a milder goitrogen compared to propyl thiouracil. Enlargement of the thyroid has been consistently reported in experimental hypothyroidism in different species of animals (Kennedy, 1942; Jones et al. 1946; Harkness et al. 1954; Goldberg et al. 1957; Lascelles and Setchell, 1959; Lazo-wazen, 1960; Sreekumaran, 1976; Reddy, 1982; and Mammen, 1986) and in spontaneous hypothyroidism in sheep and goats (Southcott, 1945; Lall, 1952; Dutt and Kehar, 1959).

The gross enlargement of the thyroid gland was microscopically characterized by hypertrophy and hyperplasia of the epithelial cells of the follicles and hypertrophy of lining epithelium, with depletion of colloid. While the changes appeared in the propyl thiouracil fed rabbits, at the end of second month itself, cassava fed rabbits showed prominent histological changes only by the end of six months. This again is an indication of the mild goitrogenic nature of cassava when compared to the propyl thiouracil. This observation is a reflection on the compensatory hyperplastic reaction of the thyroid gland mediated through the pituitary in response to the low thyroxine levels. Though the hyperplasia of the thyroid gland was a compensatory mechanism, functionally it was not found to be compensatory, since the T_4 and T_3 level in propyl thiouracil and cassava fed rabbits were lower when compared to the euthyroid control rabbits. By the end of the sixth month in the cassava fed rabbits and by the end of second month in propyl thiouracil fed rabbits, there was absence of colloid in certain follicles, accompanied by hyperplasia of the lining follicular cells.

Similar observations were reported by Sreekumaran (1976), Reddy (1982) in goats and Mammen (1986) in calves, in hypothyroidism induced by thiourea. Wilson (1975) pointed out that an early and characteristic sign of stimulation was the appearance of vacuoles around the periphery of the colloid or peripheral scalooping. Although there was stimulation by thyroid stimulating hormone (TSH) and consequent hyperplasia of the thyroid epithelium, there was no synthesis of thyroxine due to non-availability of iodine, in the presence of residual cyanides in cassava flour, and in the presence of propyl thiouracil. It was postulated that the residual cyanide in cassava, got converted to less toxic thiocyanate and this was attributed to the goitrogenic action of cassava. Thampan (1979) and Gilbert (1984) attributed the goitrogenic effect of cassava to the presence of hydrocyanic acid.

The testes of cassava fed rabbits did not show any histological changes. However, testes of rabbits fed propyl thiouracil showed mild changes at the fourth month, and more appreciable changes at the end of six months. The spermatogonial cells were few and did not show active division and spermeogenesis. Some of the seminiferous tubules showed degeneration and desquamation of the spermatogonial cells. There was slight interstitial oedema. These observations draw attention to the fact that cellular components of testes were affected in hypothyroid state. Similar changes were reported in experimental hypothyroidism induced by thiouracil in rams and rabbits (Maqsood, 1951) and thiourea induced hypothyroidism in goats (Reddy, 1982) and in calves (Mammen, 1986). In the ovaries of rabbits fed propyl thiouracil, there was mild degenerative changes from the fourth month onwards. According to Gorbman and Bern (1974), thyroxine has a priming effect on the action of hormones on cells and they indicated that in the absence of thyroxine, the gonadotropic hormone of the pituitary will not function effectively and this will lead to degenerative changes in the testicular tissue.

No changes were observed in the adrenal glands of both the cassava fed and propyl thiouracil fed rabbits, histologically.

The low T_4 and T_3 level, enlargement of the thyroid gland, hypercholesteraemia, anaemia and changes in the fur seen in cassava fed rabbits were all classical features of hypothyroidism and in the experimental model of hypothyroidism induced in rabbits fed propyl thiouracil, all these clinicopathological features were seen. This investigation, therefore, clarified that cassava flour is a weak goitrogen at levels of 25% in the diet of broiler rabbits, and can be advantageously fed to broiler rabbits, without causing undesirable effects.

Summary

6. SUMMARY

In order to guage the prevalence of hypothyroidism in cattle, a survey study was conducted in Cannanore, Trichur, Ernakulam and Idukki districts of Kerala state, by employing serum T_4 as the marker. The serum was collected by attending the infertility camps organised by the Animal Husbandry Department, and from the University Livestock Farm, Mannuthy; Veterinary Hospitals at Mannuthy and Kokkalai.

The survey study confirmed that hypothyroidism is prevalent in cattle in these districts. The mean value of T_4 in clinically healthy cattle was found to be 4.8727 ± 0.1209 µg/dl. In conditions like infantile genitalia the mean T_4 value was 3.5617 ± 0.1089 µg/dl and in anoestrum cases, the mean T_4 level was 3.6913 ± 0.1136 µg/dl. Repeat breeders showed a mean T_4 level of 3.9175 ± 0.1130 µg/dl. These observations indicated that hypothyroidism was one of the important aetiological factors for non-infectious reproductive disorders in cattle. These findings pointed out the need for evaluating the T_4 level in cattle with non-infectious reproductive disorders to rule out hypothyroidism before instituting a therapeutic schedule.

The goitrogenic effect of cassava flour was evaluated by taking broiler rabbit as the experimental model. Cassava flour was incorporated at 25% level in the diet of twelve broiler rabbits. Also a model of hypothyroidism was structured in another twelve broiler rabbits using propyl thiouracil as the goitrogen, for comparison. Another group of twelve rabbits were kept as controls. The duration of the experiment was six months.

Rabbits fed cassava did not manifest any symptoms of disease or change in behaviour till four months. But by the end of six months, the cassava fed rabbits became obese although there was slight degree of variation in obesity between individual rabbits. They appeared to be apparently healthy, but were slightly dull and lethargic. The rabbits which were fed propyl thiouracil became dull and weak from the second fortnight onwards. Lethargy, dullness and disinclination to move were seen in the rabbits of propyl thiouracil group by the fourth month. Bilateral alopecia on the ventral side of the belly, base of the ear and around the eyes developed in propyl thiouracil fed rabbits by the fifth month.

The cassava fed rabbits registered an increase in the body weight and reduction in fur weight by the end of six months. There was progressive reduction in body weight and fur weight in the propyl thiouracil fed rabbits.

The blood picture revealed a normocytic hypochromic anaemia in cassava fed rabbits, whereas in propyl thiouracil fed rabbits it was microcytic hypochromic anaemia.

The low T_4 and T_3 level in cassava fed rabbits gave evidence to the surmise that cassava flour when fed at the rate of 25% in the ration for a period of six months acted as a mild goitrogen. In propyl thiouracil fed rabbits, there was progressive and marked reduction in serum T_4 and T_3 level.

Serum cholesterol level was found to be abnormally high in propyl thiouracil fed rabbits. The cholesterol level was slightly higher in cassava fed rabbits when compared to the control rabbits and lower when compared to the propyl thiouracil fed rabbits.

Blood sugar values of propyl thiouracil fed rabbits were significantly low by the end of six months. But there was no significant reduction in blood sugar values of cassava fed rabbits.

There was progressive increase in the relative weight of the thyroid gland and appreciable enlargement from the second month onwards in rabbits fed propyl thiouracil. Rabbits fed cassava also showed an increase in the relative weight of the thyroid and enlargement when compared to the control rabbits from the 4th month onwards.

Hyperplasia and hypertrophy of the follicular epithelial cells of the thyroid, with depletion of colloid in follicles were demonstrated in the thyroid of cassava fed rabbits at the end of six months. Extensive hyperplasia and hypertrophy of the follicular epithelial cells, with marked depletion of colloid were observed in propyl thiouracil fed rabbits by the fourth month itself.

Histological sections of the testes and the ovaries revealed degenerative changes in propyl thiouracil fed rabbits, but there was no changes in the testes and the ovaries of cassava fed rabbits.

The low T_4 and T_3 level, enlargement of the thyroid gland, hypercholesteraemia, anaemia and changes in the fur seen in cassava fed rabbits were all classical features of hypothyroidism and in the experimental model of hypothyroidism induced in rabbits fed popyl thiouracil, all these clinicopathological features were seen. This investigation, therefore, clarified that cassava flour at 25% in the diet of broiler rabbits is a weak goitrogen.

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PREVALENCE AND PATHOLOGY OF HYPOTHYROIDISM IN CATTLE

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ABSTRACT OF A THESIS

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ABSTRACT

A random survey study conducted employing serum T_4 as a marker, in Cannanore, Trichur, Ernakulam and Idukki districts of Kerala indicated that hypothyroidism was one of the major aetiological factors responsible for non-infectious reproductive disorders in cattle. The mean value of T_4 observed in clinically healthy cattle was 4.8727 ± 0.1209 µg/dl. In conditions like infantile genitalia, the mean T_4 value was 3.5617 ± 0.1089 µg/dl and in anoestrum cases, the mean T_4 level was 3.6913 ± 0.1136 µg/dl. These observations emphasized the need to estimate the serum thyroxine level of cattle, in non-infectious reproductive disorders to exclude hypothyroidism as a causative factor.

The goitrogenic effect of cassava was assessed employing broiler rabbit as the experimental model. The experimental design included three groups of twelve rabbits each. One group (T_2) was fed cassava flour at the rate of 25% in the diet for six months. Another group (T_3) was administered propyl thiouracil at the rate of 1 mg/day/animal for a period of six months. A group (T_1) of twelve rabbits was kept as control.

Body weight of rabbits at fortnightly interval was recorded. Four rabbits in each group were sacrificed at the second, fourth and sixth month. At the time of slaughter, fur weight, serum T_3, T_4 levels,

serum cholesterol, blood sugar, haemoglobin, ESR, total leucocyte count, differential leucocyte count, erythrocyte count, were estimated. Also relative weight of the thyroid, adrenal, testes and ovaries were recorded. Detailed autopsy was performed after the slaughter of the rabbits. Appropriate samples of tissues from liver, kidney, spleen, testis, ovary, heart, thyroid and adrenal were collected for histopathological examination.

Rabbits fed cassava showed changes only after a period of four months. They registered an increase in the body weight and reduction in fur weight, by the end of six months. Normocytic hypochromic anaemia, hypercholesteraemia, low T_3, T_4, increase in the relative weight of the thyroid gland were also observed by the end of six months. Histologically the thyroid gland showed hyperplasia and hypertrophy of the follicular epithelial cells and depletion of colloid at the end of six months. Rabbits fed cassava did not show any changes in the testis and ovary. However, the changes in the rabbits fed cassava were minimal when compared to the propyl thiouracil fed rabbits.

In the propyl thiouracil fed rabbits, there was progressive reduction in body weight and fur weight from the second month onwards. Bilateral alopecia on the ventral side of the belly, base of the ear and around the eyes were observed in them. Microcytic hypochromic anaemia, hypercholesteraemia, low T_4, T_3 levels, and low blood sugar were very much significant in propyl thiouracil fed rabbits. The thyroid glands were very much enlarged and conspicuous. Histologically, the thyroid follicular epithelial cells exhibited predominant hyperplastic changes and varying degrees of degeneration along with significant depletion of colloid. Microscopic picture of the testes in propyl thiouracil fed rabbits showed degenerative changes, with no evidence of spermeogenesis. Also the ovaries showed degenerative changes in the propyl thiouracil fed rabbits.

From the study it was concluded that cassava flour, although, a mild goitrogen can be advantageously fed to broiler rabbits at the level of 25% in the ration without causing undesirable effects.