

Review Article

Advances in Thyroid Hormones Function Relate to Animal Nutrition

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Received: April 06, 2016; Accepted: June 07, 2016;

Published: June 15, 2016

Abstract

This article provides an overview of the role and function of the thyroid hormones (T_3 , T_4), its modulation and regulation on animal nutrition, metabolism, production, and growth performance of domestic animals. Thyroid hormones play an important role in understanding the efficiency of production through strategic feeding management (nutrition) such as iodine and selenium supplementation leading to the modulation of balance and improved metabolism of energy, protein and lipid; correlation of animal's physiological status in meat and milk production; breeding programmes; genetics; and, environmental status. Several studies have proven the significant benefits of thyroid hormone regulation with great potential in determining the nutritional needs of individual animals. Reviews on the advanced works of numerous studies were presented to look over the competencies and requirements for a leading applied research innovation in animal nutrition, feed science and production.

Keywords: Thyroid gland; Thyroid hormones; Triiodothyronine (T_3); Thyroxine (T_4); Animal nutrition; Metabolism; Iodine; Selenium

Abbreviations

TH: Thyroid Hormones; T_3 : Triiodothyronine; T_4 : Thyroxine; ATP: Adenosine-Tri-Phosphate; TSH: Thyroid Stimulating Hormone; TSHR: Thyroid Stimulating Hormone Receptor; HRC: Hormone-Receptor Complex; DNA: Deoxyribonucleic Acid; THD: Thyroid Hormone Deficiency; AIDs: Autoimmune Diseases; GSH-Px: Glutathione Peroxidase; ALT: Alanine Transaminase; AST: Aspartate Amino Transferase; ALP: Alkaline Phosphatase; IGF-1: Insulin-like Growth Factor-1; GRH: Growth Releasing Hormone; IL: Interleukin; TNF α : Tumor Necrosis Factor- α ; DPI: Digestible Protein Intake; PFEI: Protein-Free Energy Intake; DMI: Dry Matter Intake; Hb: Hemoglobin; RBC: Red Blood Cell; PCV: Packed Cell Volume; MCV: Mean Cell Volume; WBC: White Blood Cells; BNeut: Band Neutrophils; SNeut: Segmented Neutrophils; Lymph: Lymphocytes; Mono: Monocytes; Eosin: Eosinophils; Baso: Basophils; BW: Body Weight; BCS: Body Condition Score; NEFA: Non-Esterified Fatty Acid; AMPK: AMP-activated Protein Kinase; CPT: Carnitine Palmitoyl-Transferase; Tg: Thyroglobulin; DIT: Diiodotyrosine; MIT: Monoiodotyrosine; ECF: Extra Cellular Fluid; TPO: Thyroid Peroxidase; LDL: Low-Density Lipoprotein; LPA: Apolipoprotein

Introduction

Thyroid hormones are endogenous substances secreted from the thyroid gland. The thyroid gland synthesizes Triiodothyronine (T_3) and Thyroxine (T_4) that influences most and every cells of the body's organ which helps regulate growth and the rate of most chemical reactions (metabolism). The fundamental role of TH in the whole body refers to the stimulation of its metabolic activity by increasing the circulating hormones particularly T_3 and T_4 plasma concentrations in order to sustain and improve animal nutrition and production [1]. The involvement of TH in the metabolic response of animals includes its regulations on certain disease-related problems, in addition to stimulation of ovarian functions particularly in

postpartum dairy cows. Interestingly, TH can also be a measure or criterion for breeding selection in the future [2]. Alterations of plasma thyroid hormone levels are an indirect measure changes in the activity of thyroid gland and circulating thyroid hormones [3]. Furthermore, it plays a significant role in most of the body's biological processes other than growth and development includes carbohydrate metabolism, oxygen consumption, and synthesis of protein [4].

Huszenicza et al. [2] have stated that T_3 and T_4 are known thermo regulators in organisms of animals, involved in energy and proteins metabolism homeostasis and, in nutritional and environmental metabolic activities of animals. T_3 and T_4 were thought to have an effect in the milk glands development and in the control of milk production. Likewise, TH concentration was found out to be dependent on several factors such as genetic, environmental and nutritional status of animals as reported by Todini [3] cited by Novoselec et al. [5].

Essential function and role of thyroid hormones

Thyroid follicle is responsible for the TH synthesis and storage.

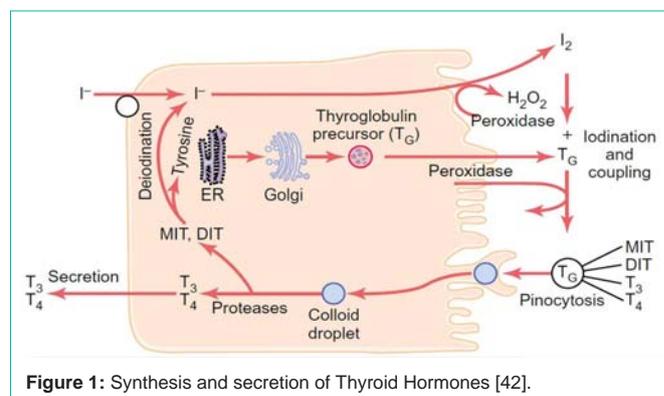


Figure 1: Synthesis and secretion of Thyroid Hormones [42].

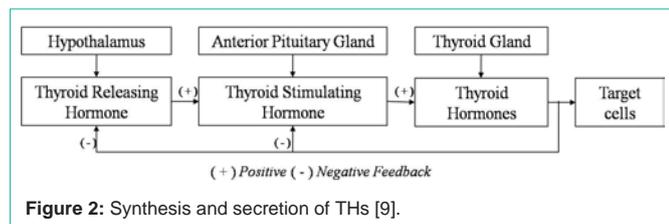


Figure 2: Synthesis and secretion of THs [9].

The thyroid follicular cell synthesizes Tg across the apical membrane into the follicular lumen forming a colloid that serves as a storage form of iodine. Colloid also serves as a substrate in the formation of TH. The action of the thyroid is controlled by TSH which stimulates resorption of colloid (Figure 1). Interestingly, fault in TH synthesis may lead to increased colloid storage and goiter [6].

The major function of the thyroid organ is to secrete TH, which helps the body utilize energy, keep warm and maintain the vital organ (brain, heart, muscles, and other organs) to work efficiently [7,8].

TH has profound physiological effects involving the body processes such as development, growth and metabolism. One vital role of thyroid hormones in mammals plays in the fetal and neonatal brain development. Growth-retardation is seen both in humans and animals if thyroid hormones are deficient, thereby neglecting its growth-promoting effect linked together with growth hormone. In addition, TH increases basal metabolic activity rate such as an increase in body heat production and or heat increment as a result from increased oxygen consumption and rates of ATP hydrolysis. T₃ and T₄ also act on lipid metabolism by increasing fatty acid concentration in the plasma as soon as TH levels increases. It was believed that TH improves tissue oxidation of fatty acids. Furthermore, T₃ and T₄ encourage the enrichment of insulin-dependent entry of glucose into cells and increased production of new and free glucose. It was also reported that T₃ and T₄ increases heart rate, cardiac contraction and vasodilatation, improving blood flow to several body organs as depicted in Figure 2. Changes in the mental state are also dependent on the increased or decreased levels of T₃ and T₄ including the reproductive behavior and responses of individuals [9].

Thyroid gland and its hormones are essentially vital on keeping the productive and efficient performance of domestic animals in particular the traditionally free-range and grazing small ruminants whose main physiological activities depends on feed intake (growth), milk production, reproduction, and hair growth (fiber). The increase and decrease of the TH concentrations in the plasma are an indirect measure of the thyroid gland activity. The circulating TH was the known markers of the metabolic and nutritional efficiency of individual animals, allowing them adapt their metabolic stability to various effects of the environment and to the alterations of their nutritional requirements. Endogenous factors such as breed, age, gender, physiological conditions and environmental factors such as climate, season, which greatly affect the role of nutrition, were able to influence the thyroid hormone levels in blood that is believed to help improve animal health, welfare and production [3].

The changes of T₃ and T₄ hormones in the blood serum of 14 female and 9 male white goats were studied for a year in different physiological periods such as breeding, gestation, postpartum-sucking and milking. It was reported that the T₃ and T₄ hormone levels

between sexes has no significant differences in different physiological periods; whereas, the changes in between sexes has significant difference (p<0.05). It was concluded that the TH concentrations in various physiological conditions were influenced by the alterations in environmental temperature [10].

The TH regulates the energy balance and protein metabolism, thermoregulation [11], growth, production, and leptin expression (“adipokine”, peptide hormone produced by white adipose tissue which stimulate appetite having high effect in food intake) as reported by Chilliard et al. (2005); Erhardt et al. (2003); Huszenicza et al. [2]; Legardi et al. (1997); and, Stephens et al. (1995) cited by Antunović et al. [12]. Barb (1999); Delavaud et al. (2002); Flier et al. (2000); Foster and Nagatani (1999); Houseknecht et al. (1998); Houseknecht and Portocarrero (1998); Ingvarsten and Boisclair (2001); and, Keisler et al. (1999) proposed that a drop in leptin levels gives feedback to the hypothalamus to increase hunger and appetite, to decrease energy output, and to alter neuro-endocrine function; consequently, includes suppression of growth and reproduction, as well as stress axis (thyroid axis) stimulation [2].

Todini et al. [13] have proposed in their study on TH in milk and blood of lactating donkeys affected by stage of lactation and dietary supplementation with trace elements that TH were thought to have an anti-proliferative effect and that could be helpful in the control and prevention of human immune-related diseases, as well as in the prevention of atherosclerosis.

Thyroid hormones mode and mechanism of action

The action of growth-promoting hormones has not been fully understood on its indirect influence throughout the changes in the balance of endogenous hormones. It was thought that increasing the concentrations of growth hormone were known to stimulate amino acid transport across the cell membrane [14]. One major TH secreted is T₄ which is converted in the liver to T₃ by the removal of an iodine atom (Figure 3). The amount of T₄ being secreted is controlled by TSH made in the pituitary gland. Inadequate level of T₄ forces the pituitary to produces more TSH and send feedback to the thyroid gland to synthesize more T₄. Adequate level of T₄ in the blood stream stops the

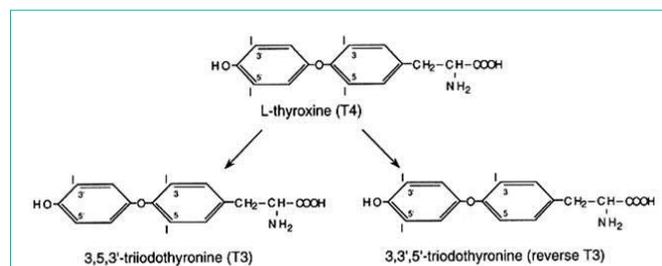


Figure 3: Structural formula of T₄ and its precursor compounds [6].

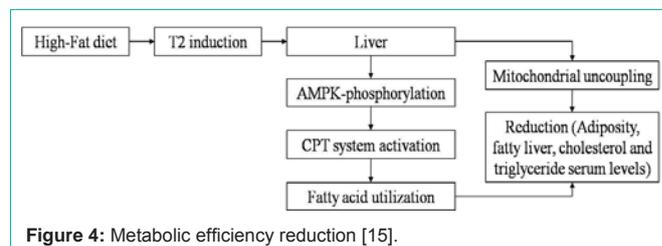


Figure 4: Metabolic efficiency reduction [15].

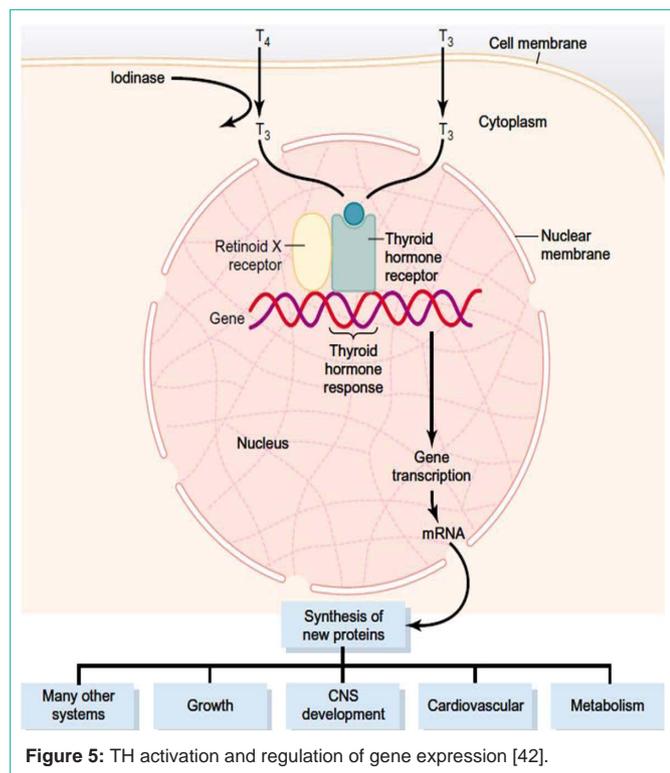


Figure 5: TH activation and regulation of gene expression [42].

pituitary to produce TSH [7]. T_3 and T_4 acts to stimulate metabolism while reducing metabolic (Figure 4) efficiency at the same time [15]. They enter the cell via membrane-transporter proteins that involve ATP hydrolysis and then bind to its receptor once inside the nucleus. The HRC interacts with DNA series leading to the modulation of gene expression by means of motivation and or inhibition of gene transcription [9].

TH (T_3 , T_4) regulates gene expression (Figure 5) mediated via THR which are a DNA-binding transcription factor that serves as a molecular switch to ligand. The THR activates transcription of gene through promoter context and ligand-binding responses where it interacts with a core-pressor complex that holds activity of histone deacetylase inhibiting gene transcription in the absence of ligand. Consequently, it triggers a conformational change in the THR resulting in the replacement of the core-pressor complex by a co-activator complex having histone acetyltransferase activity that leads to the activation of transcription upon remodeling of the chromatin structure [16].

Synthesis of cholesterol is being regulated by TH along with cholesterol receptors, and the degradation rate of cholesterol [17]. THR ideally attaches to T_3 leading to the metabolism of T_4 synthesize by the thyroid gland resulting in the production and degradation of receptor-active T_3 [18] T_3 regulates cholesterol and lipoprotein metabolism (Figure 6) by binding to THR α and β . THR β is the prime isoform found in the liver; while, THR α mediates T_3 effects on heart rate. A drug that targets THR β improves plasma lipid concentrations while sparing the heart [19].

Causes of impairment of thyroid function and its hormones

Impairment of thyroid function is usually caused by iodine,

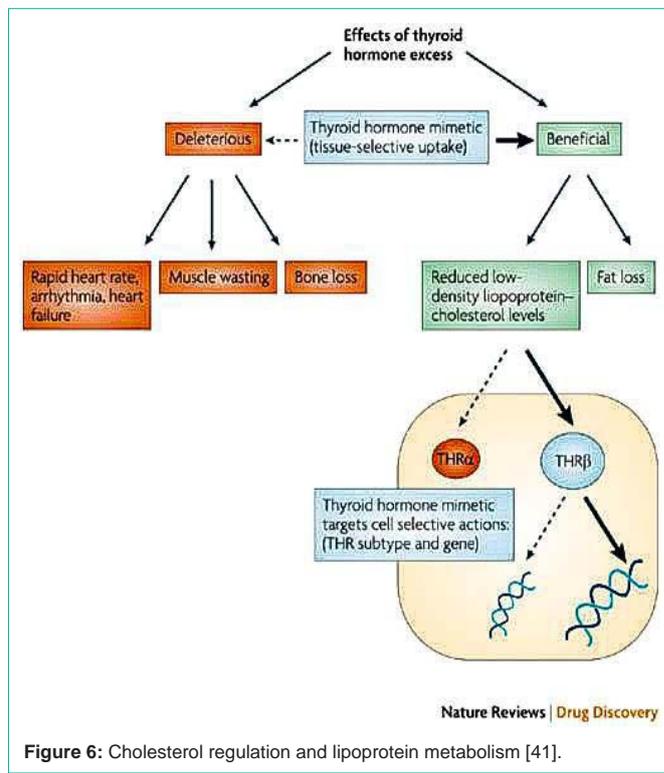


Figure 6: Cholesterol regulation and lipoprotein metabolism [41].

iron, selenium, and zinc deficiencies which affect the stability of TH production and metabolism (Figure 7). Iron deficiency anemia is one of the effects of iron insufficiency that impair the synthesis of TH by means of heme-dependent thyroid peroxidase process reduction. Selenium supplementation sustains the competent production and metabolism of thyroid hormone. Selenium deficit are oftentimes the fate and consequence of a long term medication for parenteral nutrition, phenylketonuria, cystic fibrosis, imbalanced nutrition, aged people, and ill patients [20]. Deficiency of selenium impairs TH metabolism by reducing the activity of the iodothyronine deiodinases to switch T_4 in its active metabolic form T_3 [21]. In reference to this, concurrent selenium deficiency was thought to be the chief

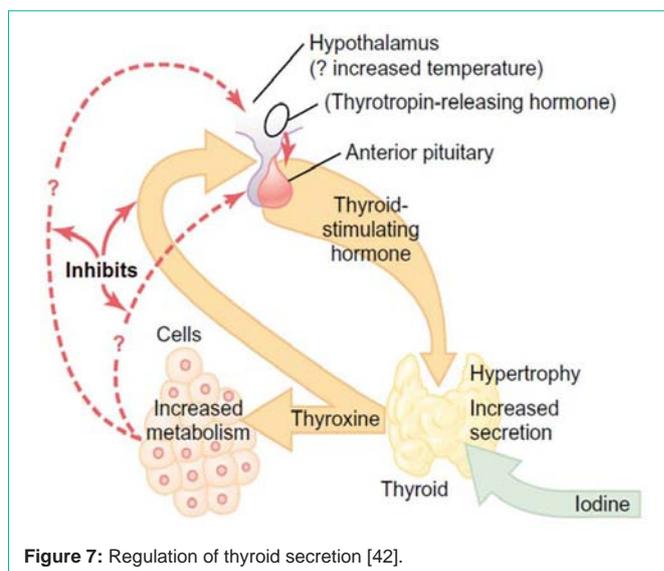
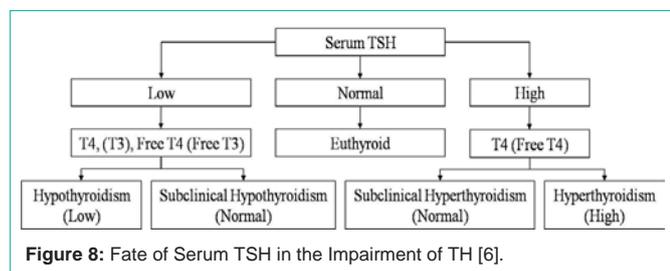


Figure 7: Regulation of thyroid secretion [42].



determinant of iodine deficiency status [22,23]. Some fates of an impaired TH metabolism were decreased growth rate and cold stress resistant selenium-deficient animal [22].

Plasma TH concentration in cattle can possibly be altered and or can be corrected by means of nutrition and metabolism management related factors, such as selenium and or iodine supplementation, GRH and somatotropin administration, addition of fatty acid and or fat/starch improved diet, provision of certain feed additives, and certain alkaloids (ergots) from endophyte fungi (*Neotyphodium coenophialum*) [24], (Bernal et al., 1999; Blum et al., 2000; Browning et al., 1998, 2000; Bunting et al., 1996; Gennano-Soffietti et al., 1988; Hurley et al., 1981; Kahl et al., 1995; Romo et al., 1997; Thrift et al., 1999a, b; and, Wichtel et al., 1996) as cited by Huszenicza et al. [2].

Associated nutrition and health disorders with thyroid hormones

Impaired synthesis and secretion of the TH leads to a decreased metabolic rate which is observed in conditions of hypothyroidism commonly seen in dogs; while, the other species such as cats, horses, and other large, domestic animals rarely develops this disorder. On the other hand, excessive synthesis and secretion of T₄ and T₃ leads to an increased metabolic rate resulting to a clinical hyperthyroidism [25] as shown in Figure 8.

Generally, hypothyroidism is well-documented condition of THD in particular due to iodine deficiency which is essential for T₃ and T₄. This is a usual problem in areas with iodine-deficient soils [26]. Primary thyroid disease (Table 1) is another inflammatory condition linked with hypothyroidism in the case of iodide deficiency which may result to an altered the thyroid metabolism [27] destroying the gland parts of the thyroid resulting to goiter. In case of over and or excess secretion of TH, hyperthyroidism is seen but less common than hypothyroidism. This condition is less common than hypothyroidism in most species. In humans, an AID known as Graves disease were observed in which auto-antibodies attach to and activates the TSHR, thus stimulating the synthesis of thyroid hormone [9].

Lohuis et al. (1988); Jánosi et al. (1998); and, Pang et al. (1989) have proposed that IL and TNFα were thought to drop

off the 5'-deiodinase activity (production of fully inactive, more potent, forms of 3,3',5'-triiodothyronine known also as reverse-triiodothyronine or rT₃) in peripheral tissues during starvation, as well as in an inflammatory-endotoxin mediated diseases known as euthyroid sick syndrome or low T₃ syndrome which is observed during a systemic non-thyroidal illness characterized by a decrease in plasma T₃ concentration, an increase in rT₃ level and, in a decrease of T₄ and TSH concentrations seen in domestic ruminants [2].

Applied researches and recent advances in thyroid hormones function

Dietary iodine and selenium supplementation: The effects of increased iodine supply on goat's selenium status of 7 kids from doe with high iodine supplementation (1st group: potassium iodide, 440–590 µg per head daily and day in comparison with 140–190 µg per head) and 7 kids from doe with hypiodaemia (2nd group: feeding ration only; no supplementation) were studied from 14 to 90 days of age to observe the concentration of selenium, activity of GSH-Px, TH concentration (T₃ & T₄) and the weight of the kids. The first group, at 105 days lower Se concentration (88.1±10.9 µg/l; P<0.01) and lower activity of GSH-Px (484±125.4 µkat/l; P<0.05) were monitored; whereas, the second group Se concentration has 131.8 ± 23.2 µg/l and GSH-Px has 713.3±153.3 µkat/l. It was found out that there were no significant differences in the T₃ or T₄ concentrations of both groups. It was concluded that the increased iodine supplementation may have an adverse effect on selenium metabolism in kids and that the decrease of T₃ and T₄ concentrations were associated with the discontinuation of milk feeding from the doe [28].

Modulation of TH and energy metabolism by supplementation of dietary selenium (47 µg/d or 595 nmol/d for 0-21 d; while, 297 µg/d or 177 nmol/d or 3.8 µmol/d for 99 d and onwards) in men for 120 d was studied in contrast to rats' regulation of TH. It was found out that plasma T3 decreased with high selenium group and increased with the low selenium group. The decreased in T3 were reverse in the reported study in rats, while it is consistent with other metabolic changes. At d 64, a gain in weight was observed with the high selenium group and weight loses in low selenium group on the other hand. It was concluded that the decreases in plasma T3 concentration suggests a subclinical hypothyroidism that was induced in the high selenium group resulting increased body weight; whereas, the increases in plasma T3 concentrations suggest a subclinical hyperthyroidism that was induced in the low selenium group resulting to body weight lose [29].

The effect of dietary selenium (selenite-20, 60, or 120 ppm; selenomethionine from selenized yeast-60 ppm) on plasma -TH concentration, -immunoglobulins (IgG and IgM) and colostrum on the productivity of beef cows and calves were determined. 60

Table 1: Pathophysiological conditions associated with thyroid uptake [6].

Increased	Nature	Decreased
Low iodine intake; Early pregnancy	Physiologic	High iodine intake; Exogenous thyroid administration
Grave's disease; Nodular goiter; Hashimoto's thyroiditis with hyperthyroidism (hashitoxicosis); Trophoblastic disease; and, TSH producing pituitary tumors	Hyperthyroidism	Subacute thyroiditis; Thyrotoxicosis factitia; Iodine-induced thyrotoxicosis; Silent/painless thyroiditis; Ectopic thyroid tissue; Struma ovarii; and, Metastatic functioning thyroid carcinoma
Hashimoto's thyroiditis	Euthyroid	Hashimoto's thyroiditis
	Hypothyroidism	Primary & Secondary

gestating cows were treated for 90 d prepartum. It was reported that treatments did not affect the cow's final body weights or birth weights and the calves weaning weights. Results showed a statistical significance ($P < 0.01$) affecting the T_3 plasma concentration and the ratio of plasma $T_3:T_4$ in cows. The plasma T_3 concentration observed in cows was 14% in the provision of salt with 20 ppm Se in contrast with 60 ppm selenomethionine. Plasma IgG was seen to be the lowest ($P < 0.01$) amongst treatments. Hence, it was concluded that salts with 60 and 120 ppm dietary Se enhanced measures in determining the nutritional needs for Se in cattle [24].

The effects on blood hematology (Hb, RBC, PCV, MCV, WBC, BNeut, SNeut, Lymph, Mono, Eosin, and Baso), plasma TH and GSH-Px status in twenty four (7-8 mos old, 22 ± 1.17 kg live weight) Kacang crossbred male goats fed (100 d) inorganic iodine and selenium supplemented diets (0.6 mg/kg DMI) were studied. Plasma concentrations of selenium and iodine were reported to increased significantly ($P < 0.05$) amongst treatment; whereas, the combined dietary supplementation of both Selenium and Iodine significantly increased serum T_3 concentrations and GSH-Px activity of the Kacang goats [30].

A comparative study on the effects of combined iodine and selenium deficiency on T_3 & T_4 metabolism in rats in determining the severity of the hypothyroidism was conducted. It was reported that T_3 , T_4 , thyroidal total iodine, and hepatic T_4 were significantly lower, and plasma TSH and thyroid weight were significantly higher with iodine deficiency alone. Selenium deficiency repressed hepatic type I Iodothyronine Deiodinase (ID-I) activity regardless of the iodine status. Additionally, type II Deiodinase (ID-II) activity was significantly higher but significantly lower in combined deficiency [31].

TH levels and cortisol concentrations on offspring growth potential influenced by maternal supranutritional selenium (adequate - 9.5 mg/kg BW; high - 81.8 mg/kg BW) supplementation at breeding and maternal nutritional plane (60, 100, or 140 % req's; on day 50 of gestation) in ewes were examined. After 24 h, result showed a significant relationship ($P = 0.02$) between maternal Se supplementation and nutritional plane on cortisol concentrations. In conclusion, TH synthesis affects growth difference earlier in life causing a significant T_4 concentrations on offspring (sex) \times age (d) interaction ($P = 0.01$) and on maternal selenium supplementation \times nutritional plane \times age (d) interaction ($P = 0.04$) as cited by Vonnahme et al. [32].

In a study conducted, dietary selenium (Exp. 1- 0.0, 0.1, 0.3 and 0.5 mg Se/kg diet + purified diet; Exp. 2- 0.3 mg Se/kg diet, w/ or w/o iopanoic acid, 50-deiodinase inhibitor, 5 mg/kg diet; Exp. 3- 0.1 and 0.3 mg/kg) supplementation was reported to influence the growth of 56 broiler chickens (12 d old) via TH metabolism along with the skeletal muscle protein turnover. Results showed that the growth rate, feed conversion efficiency and the rate of skeletal muscle protein breakdown was enhanced and significantly increased plasma T_3 concentration, whereas as plasma T_4 concentration decreased in response to the effect of Se inhibited by the provision of iopanoic acid. An inverse response was observed to low dietary T_3 (0.1 mg/kg diet) supplementation which promotes growth; while, there is a growth depression for a high concentration of T_3 in response to selenium deficiency [33].

Protein and protein-free energy intakes: Two experiments were conducted to study the protein intake and PFEI effect on plasma concentrations of IGF-I, TH and its long-term nutritional regulation in pre-ruminant calves weighing 80-160 kg (Exp. 1) and 160-240 kg (Exp. 2). Exp. 1 were given with DPI and PFEI ranging between 0.90 & 2.72 g N·BW^{-0.75}·d⁻¹ and, 663 & 851 kJ·BW^{-0.75}·d⁻¹ correspondingly; whereas, Exp. 2 received DPI and PFEI ranging between 0.54 & 2.22 g N·BW^{-0.75}·d⁻¹ and, 564 & 752 kJ·BW^{-0.75}·d⁻¹ respectively. Experiments 1 & 2 were shown to have a direct relationship on the plasma IGF-I and T_4 concentrations with protein intake ($P < 0.01$), but observed to be unaffected by PFEI ($P > 0.10$). Interestingly, plasma T_3 concentrations has a direct relationship with PFEI level ($P < 0.01$) and with protein intake in both Exp. 1 ($P = 0.19$) and Exp. 2 ($P < 0.01$). Thus, the study found out that IGF-I was responsible in the response of protein deposition to increased protein intakes; whereas, T_3 was responsible in the response of protein deposition to increased PFEI. Hence, plasma T_4 concentration is only affected by protein intake [34].

Physiological status of the animal: The effects of nutritional deprivation on the synthesis of IGF-I, somatotropin, insulin, and TH in swine were conducted. Findings on feed restriction influenced the increase of plasma GH levels, decreased of circulating IGF-I levels by 53% ($P < 0.05$) and plasma T_3 and insulin ($P < 0.05$); whereas, T_4 did not decrease and plasma glucose concentration remained unchanged. Refeeding after feed restriction was thought to be linked with a decrease in circulating GH ($P < 0.05$) levels and an increase in plasma insulin and T_3 ($P < 0.05$) together with plasma IGF-I ($P < 0.05$). In conclusion, nutritional/feed restriction in swine leads to the limitation of the anabolic effects of GH expression [35].

Influence of different levels of concentrate diet on T_3 and T_4 plasma concentrations in 20 does fed with hay ad libitum during the dry phase (D_1 -30 days; D_2 -3 days prior to the synchronized estrus), pregnancy/ gestation (P_1 -week 13; P_2 -week 17; P_3 -week 21) and lactation (L_1 -5 weeks; L_2 -13 weeks following parturition) were studied. The control group (C, $n = 10$) was fed with either 0.2 kg in periods D_1 , D_2 and P_1 or 0.4 kg maize grain per day individually in P_2 , P_3 , L_1 and L_2 . The high energy diet group (H, $n = 10$) was fed with either 0.4 kg in D_1 , D_2 and P_1 or 0.7 kg maize grain per day individually in P_2 , P_3 , L_1 and L_2 . As a result, T_3 plasma concentrations were seen to be significantly higher in P_1 period (0.96 ± 0.05 ng/ml) than in the dry period (0.72 ± 0.04 ng/ml) and in P_3 (0.70 ± 0.02 ng/ml); whereas, C group T_4 plasma concentration was observed in P_1 (65.6 ± 2.6 ng/ml) and L_1 (62.8 ± 5.2 ng/ml) to be significantly higher than P_3 (40.2 ± 3 ng/ml). It was concluded that during the last 2 months of pregnancy, a direct relationship was seen with concentrate diet and T_3 (0.92 ± 0.06 ng/ml) and T_4 (67.2 ± 6.6 ng/ml) plasma concentrations in contrast to the C (T_3 - 0.76 ± 0.04 and T_4 - 45.1 ± 3.2 ng/ml) group. The effect of energy intake on T_3 and T_4 secretion during late pregnancy could be influenced by a negative energy balance [36].

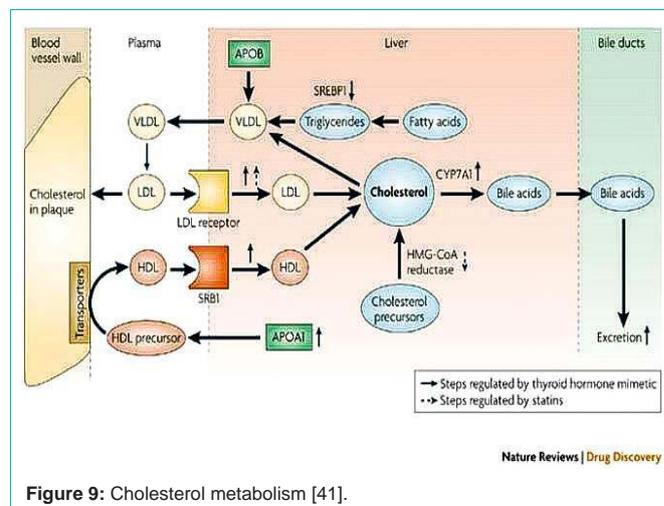
Alterations of TH plasma concentration influenced by age and reproductive status was tested in 10 gestating sheep (on 15th d prior lambing), 10 lactating sheep (on 20th d of lactation) and in 10 non-gestating sheep. Results suggested that TH plasma concentration in a 30 d old lambs had significantly higher ($P < 0.01$) concentration in contrast to other age brackets; while in a 100 d old lambs have shown to have a significantly higher concentration of T_4 in contrast to 1 and

3 year old sheep. The reproductive status of sheep have shown to have a significantly lower ($P < 0.01$) concentration of T_3 in the lactating sheep than of non-gestating and gestating sheep. In the study, results have shown to be influenced by insufficient energy supply in the mature and older sheep, on late gestation and sheep at the beginning of lactation [5].

A study in blood metabolic profiling, enzymes and hormones concentration determination in Egyptian Buffalo cows during different physiological periods were evaluated on 12 gestating cows (60 d prior parturition) and 12 lactating cows (on 10th d of lactation). Along the study, it was found out that there were drop in calcium, sodium, phosphorus and potassium concentration level during early stage of lactation; whereas, the plasma concentrations of glucose, urea, cholesterol, triglycerides and total protein were higher during gestation period together with the blood enzymes activities such as AST, ALT and ALP but insignificantly higher. In addition, the plasma IGF-1, thyroid hormones and leptin concentrations were higher in gestation period. Chelikani *et al.* (2004) and Karapehlihan *et al.* (2007) proposed that postpartum IGF-I is more reliable marker of circulating leptin TH such as T_3 and T_4 levels. Riis and Madsen (1985) projected that the decrease in plasma T_3 concentration was thought to reduce the rate of oxidation, breakdown and formation of protein and fats as cited by Ashmawy [37].

The changes in pattern of prolactin hormone associated with milk-yield and composition associated with the physiological responses in ewes was evaluated in relation to thyroxin, glucose, cholesterol and total protein with growth performance of lambs using four genotypes namely, Ossimi (O), Saidi (S), Fl Chios-Ossimi (CO) and Fl Chios×Saidi (CS). Genotype CS & CO had a significant ($P < 0.01$) effect on prolactin hormone concentration, and Chios revealed a statistical significance ($P < 0.05$) on the average daily milk yield, total milk yield and lactation period length in contrast to the local breeds; hence, milk composition such as fat, total solids, solids non-fat and lactose were not-affected by genotype. Results showed that milk production was associated with prolactin hormone concentration ($r = 0.667$, $P < 0.05$). Plasma T_4 concentrations, glucose, cholesterol and total protein with growth performance were significantly ($P < 0.05$) higher in the Chios crossbred lambs [38].

A comparative study on the levels of hormones (prolactin, growth hormone, insulin and T_4) and metabolites (glucose, NEFA, β -hydroxybutyric acid and l-lactic acid) in the plasma of high ($n = 8$) and low ($n = 7$) yielding cattle at lactation were conducted to determine the endocrine control of energy metabolism (dietary energy partition between body weight and milk production). Results showed that there were no significant differences found between the groups in the diet digestibility. Furthermore, the milk protein content obtained from low-yielding cows was greater than the milk from high-yielding cattle. As a result, the growth hormone concentrations ($P < 0.001$), NEFA ($P < 0.01$) and β -hydroxybutyric acid ($P < 0.05$) were higher in the high-yielding than in the low-yielding group, whereas the insulin concentration ($P < 0.01$) and T_4 ($P < 0.05$) was higher in the low-yielding dry cattle. Prolactin concentration on the other hand was higher in both high- ($P < 0.01$) and low-yielding ($P < 0.001$) cattle; whereas, T_4 concentration in the low-yielding dry cows was higher ($P < 0.01$). Increased glucose concentration ($P < 0.01$) on a high-yielding dry cattle go along with a significant reductions in the growth



hormone concentrations ($P < 0.001$) and NEFA ($P < 0.001$) [39].

Effects of plasma T_3 , T_4 , and $T_3:T_4$ ratios of market-size broilers in response to Thermo-Neutral (TN) constant and Warm Cyclic (WC) temperatures particularly in diurnal variations were determined. An increase in plasma T_3 , T_4 , and $T_3:T_4$ was observed and peaked at 0 & 16 h, 8 & 16 h, and 0 & 12 h under TN condition, respectively; and, at 0 & 12 h, 0 & 8 h, and 4 & 12 h under WC temperatures. A constant decrease was also noted during heat exposure to WC conditions; consequently, plasma T_3 and T_4 daily mean decreased significantly ($P < 0.05$) during heat exposure and, no significant change in $T_3:T_4$. The study revealed that plasma T_3 provides a better heat stress indicator than T_4 in the evaluation of hormonal responses of market-size broilers during thermal variations [40].

Lipid metabolism: A study on selective THR modulation by GC-1 determined the reduction of serum lipids in euthyroid mice as an approach to enhance lipid metabolism in dyslipoproteinemia. Results showed that the THR β - and the liver uptake-selective agonist GC-1 affected the cholesterol (25% plasma concentration reduction) and triglyceride (75% plasma concentration reduction) metabolism. In addition, GC-1 plasma lipoprotein cholesterol concentration was reduced; increased the expression of the hepatic lipoprotein receptor; stimulated 7α -hydroxylase of cholesterol; and, increased bile acids fecal excretion [19] as depicted in Figure 9. The TH effect on lipid metabolism is biphasic in character. Lipid metabolism is in its anabolic state on low physiological concentrations; whereas, at higher concentrations the lipid metabolism is in its catabolic state [18]. Likewise, a succeeding research on TH function was found to have potential application against atherosclerosis, obesity and diabetes Type II by improving the heart rate, reducing serum lipids, body weight and metabolic rate (lipid, carbohydrate, protein and mineral) in mice, rats, monkeys and in humans. As a good result of the study, it specifically lowers total or LDL-cholesterol levels; Lowers LPA levels; Lowers triglyceride levels; Blunts atherosclerosis; reduces adipose tissue; as well as, Lowers blood glucose [41].

Conclusion and Perspectives

In general, modulation of TH particularly T_3 & T_4 have regulated the energy balance and protein metabolism, thermoregulation, growth, and production in order to sustain an efficient and improve

animal nutrition and performance of domestic animals involving the body processes such as development, growth and metabolism. Thus, these outcomes were well thought-out indicators of the metabolic and nutritional efficiency of individual animals which could also be a basis for increases in daily gains, improvements in feed conversion efficiency and improvement of carcass quality chiefly increased lean and/or fat ratio in consideration to a substantial reduction in the amount of energy required per unit weight of protein produced, and its economic implications.

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