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I am submitting herewith a thesis written by Wilfred A. Lyke entitled "The Effect of Soybean and Cottonseed Meals on Metabolism of Iodine and Thyroxine in Calves." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Animal Science.

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THE EFFECT OF SOYBEAN AND COTTONSEED MEALS ON METABOLISM OF IODINE AND THYROXINE IN CALVES

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Wilfred A. Lyke

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ABSTRACT

Earlier work has indicated dietary iodine requirements of cattle may be increased by some of the protein supplements commonly used in cattle rations. This was investigated further in three experiments in which dairy-beef crossbred calves were fed different amounts of soybean or cottonseed meal.

In the first experiment five calves initially weighing 144 kg were fed hay and noniodized salt, alone or supplemented daily with 2.7 kg each of soybean (SBM) or cottonseed (CSM) meal. All calves were fed grass-clover mixed hay without protein supplements for 4 weeks (Period 1). During the next 11 weeks (Period 2), in addition to hay, SBM was fed to three calves and CSM to two calves. During the next 10 weeks, (Period 3) when no supplemental protein was fed, 8 mg potassium iodide was given each calf every other day in weeks 7 and 8 (Period 3a) and discontinued in weeks 9 and 10. Protein supplements fed during Period 2 were then reversed for 11 weeks (Period 4). Thyroid function, as measured by plasma protein-bound iodine (PBI), plasma thyroxine (T_4) and thyroid secretion rate (TSR) in the last 2 weeks of each period, was markedly reduced in Periods 2 and 4 as compared to Periods 1 and 3. Results were similar whether SBM or CSM was fed. Fecal excretions of ^{125}I (given orally as NaI) and ^{131}I (from intravenous thyroxine) were not changed by supplemental protein but urinary loss was moderately decreased suggesting an effort to conserve iodine.

Nine calves with an initial average weight of 136 kg were assigned to three replicates of a Latin square design in the second experiment. This experiment differed from experiment 1 in that rations were kept isonitrogenous by comparison of SBM and CSM with a low residue isolated soy protein and protein sources were fed at lower levels more comparable to practical rations. No treatment differences in PBI, T_4, or TSR were detected, indicating either that SBM and CSM at these levels had no measurable effect or isolated soy protein was equally as effective.

In the third experiment, nine 200-300 kg calves were divided into three groups fed forage alone or supplemented with SBM or CSM. These rations were continued for at least 5 weeks before calves were sacrificed. Digestive tracts were divided into rumen, omasum, abomasum, six equal lengths of small intestine, cecum, and two equal lengths of large intestine. Assays of butanol extracts of digesta indicated twice as much T_4 in small intestinal contents of calves fed either SBM of CSM than in those fed forage only.

These three experiments considered together indicated SBM and CSM fed at high levels may reduce absorption of thyroxine from the digestive tract and reduce the thyroid function measurements PBI, T_4 and TSR. However, these natural feed ingredients did not have sufficient iodine binding capacity to substantially increase iodine loss as measured by radioactive iodine.

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CHAPTER I

INTRODUCTION

Cows in an experiment designed to evaluate corn silage as the only forage gave birth to goitrous calves until fed iodized salt (Hemken et al., 1965, 1971). The ration consisted of corn silage and a concentrate mixture of corn, barley, soybean meal, 1% dicalcium phosphate and 1% non-iodized salt. Previous studies with monogastric animals had showed that soybean products could be goitrogenic (Van Middlesworth, 1957) so it was suggested that soybean meal interfered with iodine metabolism in the cows. Since supplemental iodine had an overriding action, the effect of soybean meal on the iodine requirement became of interest.

Both soybean and cottonseed meal interfered with utilization of thyroxine in rats (Dryden et al., 1960; Sharpless et al., 1939). Since soybean and cottonseed meals are important sources of supplemental protein in cattle rations, the present investigation was undertaken to study further the effect of these feeds on metabolism of iodine in calves.

CHAPTER II

LITERATURE REVIEW

Goiter has been recognized since ancient times. In the third century B. C. the legendary Chinese emperor Shennung mentioned sea weed as a remedy for goiter in his treatise on herbs and roots (Langer, 1960). It was also reported that ancient Greeks used burnt sponges as a treatment for goiter. Iodine was first discovered in the ash of seaweed by the French physician Bernard Courtois in 1811 and a short time later the Swiss physician Francois Goindet recognized the medical properties of iodine as an antigoitrogen (Gross, 1962).

The first suggestion that iodine deficiency might be the cause of goiter did not appear until about 1830 (Underwood, 1962). The German chemist Baumann then showed that iodine was a normal constituent of body tissue, especially in the thyroid gland (Underwood, 1962). Soon after this Oswald (1899) identified thyroglobulin and in 1919 Kendall is reported to have isolated thyroxine. In 1927 Harrington published the structure of thyroxine and a method for its synthesis.

Despite the early discovery that iodine would prevent goiter, there were about 200 million goiterous people as late as 1960 (Kelley and Snedden, 1960). Iodine deficiency has been stated to be the most widespread of mineral deficiencies in grazing livestock (Allman and Hamilton, 1948).

A mature animal's body is estimated to contain 0.00004% iodine (Maynard and Loosli, 1969). If this minute amount is not maintained, disaster can result. It is known that 0.002 to 0.004 mg iodine per kilogram of body weight per day will prevent goiter (Maynard and Loosli, 1962). A year or more on low iodine diet may be required before deficiency symptoms are noticed (Hemken, 1971; Swanson, 1972). Usually the first obvious sign is enlarged thyroid glands in the new-born even though the dam may appear normal (Hemken et al., 1971). Deficiency during pregnancy may result in birth of hairless, weak or dead young but moderate goiter may be present in young animals with normal hair (Aschbacher, 1968; Hemken et al., 1971).

Obvious goiter has not been reported in adult cattle. Other signs of long term insufficient iodine included decreased milk yield, irregular breeding intervals, low conception rate, and retained placentas (Hemken, 1970). Iodine concentrations below 20 µg/liter are typical in milk from cows in iodine deficient areas (Alderman and Stranks, 1967).

Absorption of Iodine

Most of the iodine ingested by cattle is in inorganic form. Iodine levels in drinking water usually reflect iodine content of soil and rocks in the water's source. Dietary iodine is reduced to iodide prior to absorption (Cohn, 1932). This iodine is rapidly and almost completely absorbed by cattle (Barua et al., 1964). The forestomach is a major site of absorption with between 70 and 90% absorbed from the rumen, reticulum and omasum. In the abomasum, iodide secretion is about 18 times the rate

of absorption (Miller et al., 1975). Net absorption subsequently occurs from the small and large intestines, including the cecum, at a rate similar to that of dry matter.

Iodine Recycling

In the calf, Miller (1966) found secretion of ^{131}I into the abomasum exceeded ^{36}Cl by 15 times; Howel and Van Middleworth (1956) reported clearance rates of iodide in gastric juice of dogs were 50 times greater than chloride. Concentration of iodide by the abomasum was reduced by the goitrogen thiocyanate (Moss et al., 1968) but not by dietary iodine levels high enough to block uptake of iodine by the thyroid (Miller et al., 1975). Specific iodide transport by the gastric stomach occurs at the site of the mucous neck cells of the glandular area. Another site is the parietal cells of the glandular area which seem to be non-specific halide concentrators, secreting chloride and bromide as well as iodide (Gross, 1962).

Another site of entry of iodine into the digestive tract is the salvia. Chloride secretion is directly related to the rate of saliva secretion (Freinkel and Ingbar, 1953) whereas iodide concentration is inversely related to saliva volume. Moss et al., (1968) found concentration of iodine into saliva to be much lower in calves than in man and dogs and suggested this may reflect the large volume of saliva produced by ruminants. Values for apparent absorption of iodide from the rumen would be influenced by entry of iodide in saliva.

Circulating thyroid hormones are partially deiodinated and deaminated in body tissues, particularly in the liver (Von Euler and Heller, 1963). After the liver acts on these, the degraded byproduct of the thyroid is secreted into the bile, primarily as water-soluable conjugates (Williams and Bakke, 1963). In man about 56 mg of degraded thyroxin appears in the bile daily (Mynat, 1956). Not all of the organic iodine is reabsorbed from the remainder of the intestinal tract, which makes the iodine excreted in the feces organic and of bilary origin (Keatings and Albert, 1949). Organic iodine is present in minute quantities in meat, eggs and milk. With the exception of nursing offspring, organic iodine is not an important source of iodine. However, interest in feeding iodinated casein and other organic iodine compounds that might increase circulating thyroid hormone levels, thus increase milk production, has prompted considerable study of the absorption of organic iodine compounds by ruminants. While inorganic iodine is essentially 100% absorbed, oral doses of L-thyroxine are only about 12% absorbed by lactating dairy cows (Mixner and Lennon, 1960). Additional iodine should have become available for absorption when organic iodine compounds of a thyroid hormone nature were digested, hydrolyzed and deiiodinated. Iodinated amino acids appear to be well absorbed as such, although more slowly and less completely than iodide itself (Underwood, 1962). Swanson et al., (1965) used ^{125}I as the iodide and milk bound ^{131}I to compare the two forms of iodine in milk fed to 6 and 12 week old calves, and found much of the milk bound ^{131}I was absorbed as such from

the rumen and excreted into the urine about twice as efficiently as the ^{125}I from iodide. Iodide was efficiently absorbed from the rumen and about twice as much ^{125}I as ^{131}I was taken up by the thyroid gland but the chemical form of ^{131}I at this time was not known.

Iodine exists in the blood in both inorganic and organic forms. Wayne et al. (1964) indicated that an inorganic value below 0.08 mg/100 is a deficiency state. Organic iodine of the blood is present mainly as thyroxine bound to plasma proteins. When iodine enters the blood as iodine, it becomes part of the iodide pool. Iodide in the saliva and gastric juices is also generally considered as part of the iodide pool, since it is secreted from the plasma and is constantly reabsorbed and recycled. Gross (1962) refers to this recycling as a "salivary gastro-luteric cycle." From this "iodide pool," the iodide is available for secretion, excretion and concentration. The latter occurs whenever tissue levels are higher than plasma iodide levels. In the case of the iodide in the thyroid gland, salivary gland, abomasum, skin and ovaries, iodide is available for reabsorption into the plasma, thus they are part of the "iodide pool." However, hair, sweat, urine, feces and milk once removed from the body contribute to an irreversible iodide drain.

Iodine is taken up by the thyroid gland and concentrated at least 25 times (White et al., 1968). This concentration in the thyroid occurs against a concentration gradient by an active transport mechanism, the "thyroid iodide trap." As to how exactly this concentration comes about is not yet known, but Vilkki, (1960) isolated a lecithin - like fraction

from thyroid glands that had a tremendous affirmity for iodide absorption. Once iodide enters the thyroid it is rapidly converted into thyroglobulin, a protein which, when acted upon by enzymes yields thyroid hormones as thyroxin (T_4) and 3, 5, 3, triiodothyronine (T_3).

The uptake of iodide and release of thyroid hormone are under the control of thyroid stimulating hormone (TSH) which is secreted by the anterior lobe of the pitituary. If the thyroid hormone level that is circulating is low, it causes an increase in the release of TSH which increases iodine uptake of the thyroid. Since the thyroid is an endocrine gland and its hormones are secreted directly into the blood stream, they are transported in the plasma, bound to one of three carrier proteins, thyroxine binding globulin, pre albumin or albumin. The hormone protein complex in which we are interested is called protein bound iodine (PBI). PBI varies from animal to animal and diet to diet as well as with many other factors. The thyroid hormones account for close to 90% of the organic iodine circulating in the plasma and the remaining iodide comes from absorption of inorganic iodide. Nunez and Jacquemin, (1961) list the following reactions involved in the metabolism of thyroid hormones: 1) Deiodination, 2) Conjugation of the phenolic and hydroxyl groups, 3) Oxidative deamination of the side chain, and 4) Rupture of the diphenyl ether linkage and further hydroxylation of the benzene ring.

The liver is believed to be the principle site for degradation, but the kidney is very active in deiodinating, conjugating and deaminating

T_4 and T_3. It is known that the rate of thyroid hormone degradation is decreased in hypothyroidism and increased in hyperthyroidisim (Williams and Bakke, 1963).

Inhibition of Iodine Metabolism

Metabolism of the thyroid gland and thyroid hormone are readily altered by a wide variety of goitrogens are of two classification, those that block uptake of inorganic iodide and those which inhibit binding organic iodide by the thyroid gland (Wright and Sinclair, 1958). The most common inhibition of iodine metabolism is the lack of iodine, and the compounds known as goitrogens make up the lesser part. Any substance that can produce a form of goiter is described as being goitrogenic. These include chemicals, drugs, and herbicides, and there are data indicating vegetable oils contain a goitrogenic substance (Kaunitz and Johnson, 1967). Calcium, cobalt, potassium, arsenic and possibly vitamins and minerals in excess are said to be goitrogenic (Sampson and Putzki, 1952; Taylor, 1954; Kriss et al., 1956; Paley et al., 1958; Williams and Bappe, 1963; Sharpless and Metzger, 1941; Steyn, 1938). Vitamin A might be considered to be goitrogenic either in abscence or in excess. In vitamin A deficiency the weight of the thyroid is known to increase, indicating a decreased rate of thyroxine formation (Lipsett et al., 1947). Sadhu and Brody (1947) proposed that the iodine which normally joins tyrosine is bound by the double bond of excess Vitamin A decreasing the formation of thyroxine. Then the iodinated vitamin A acts as thyroxine acting on the pitituary to decrease TSH levels. Deficiency of vitamin E

results in hypofunction of the thyroid gland (Anderson, 1956). It has long been known that peanuts have goitrogenic activity which is thought to be due to the phenolic compounds in the red skin which are iodinated in the thyroid gland (Virtanen, 1963). The competition for binding of iodide is the mechanism responsible for this goitrogenic activity in peanuts, which results in a similar situation to that of excess vitamin A. Many goitrogenic compounds are concentrated by the iodine trap, including monovalent anions such as thiocyanate, perchlorate, hypochlorite, iodate, periodate, chlorite and nitrate (Williams and Bakke, 1963). Of these anions two are used to treat hyperthyroidisin, namely thiocyanate and perchlorate. These monovalent anions are competitive with iodide on an equilmolar basis even though they are not concentrated in the thyroid tissue.

After the high gradient of iodide maintained by the iodide trap is abolished, the thyroid must depend on simple diffusion of iodine for thyroxine snythesis. Diffusion is inadequate to supply sufficient iodide for normal thyroxine synthesis, resulting in depletion of the thyroxine stored in the thyroid. When the thyroxine level falls in the blood, increased amounts of TSH are released resulting in the formation of goiter. By increasing the iodide intake the effect of goitrogens can be overcome. Rall et al., (1964) reported high levels of iodide inhibit radiation damage to the thyroid from ^{131}I. It is suggested by Williams and Bappe (1963) that high levels of serum iodide do not impair the thyroid-iodide trap, but appear to because they dilute the radioisotope resulting in less uptake.

The other method of inhibiting the production of thyroid hormone is by inhibiting the organic binding of iodide once it is trapped by the gland. Williams and Bakke (1968) suggest goitrogens acting in this way could inhibit at different sites such as:

1) The conversion of iodide to iodine which is needed to iodinate the tyrosine.

2) By inhibiting coupling of diiodotyrosine molecules to form the thyroxine.

Thiocarbamides and thioureylenes are the most prominent members of this category of goitrogens. These would include thiourea, methimazole, trumil and tapazole. Virtanen (1963) reported thiourea, thiouracil and a number of sulfur bearing substances obstruct oxidation of the iodide to iodine inside the thyroid gland. He also suggested aromatic goitrogens such as aminobenzene may be iodinated in the thyroid instead of tyrosine, thus replacing it and inhibiting formation of thyroxine. These goitrogenic substances can be overcome and goiter prevented by increasing dietary iodine.

The edible portions of most members of the Brassica family contain some goitrin (Underwood 1962). When raw brassica are chewed, hydrolysis of progoitrin by the enzyme myosin yields glucose and goitrin. Although myosin is destroyed by cooking, progoitrin can be hydrolyzed by other enzymes, possible bacterial, in the digestive tract (Williams and Bakke, 1963). Goitrin can be released by enzymatic hydrolysis in the rumen when ruminants consume members of the brassica family. Progoitrin can also

yield thiocyanate and isothiocyanate. The compound glucobrassica found in members of the brassica family also yields thiocyanate when attacked by myosin (Grimelin and Virtamen, 1960). Cattle can consume large quantities of goitrogen when members of the brassica (Cabbage, rutabaga) and cruaferous (rape, kale, turnip, radish) families are fed (Virtamen, 1963).

The goitrogenic agent in soybeans has not been isolated or identified. Many investigators have produced goitrogenic effects by high losses of iodine in feces with soy bean products (Van Middlesworth, 1957; Beck, 1958; Block et al., 1961; Richert et al., 1964). The goitrogen in soybeans can be partially deactivated by heat. The substance could be volatile and driven off by heat, or an enzyme or protein that undergoes denaturization. If one goitrogen is present it may be partially destroyed, but if two are present, one may be heat resistant, and the other not. Wilgus et al., (1941) reported the goitrogenic factor in soybeans was not extractable with chloroform, acetone, ethyl alcohol or ethyl ether, so this would eliminate it being an oil soluble factor, although it has been linked at times to vegetable oils. Infants receiving soy protein as a replacement of milk protein in their diet have developed goiter prior to the addition of iodine to the formula. The goitrogenic factor of soybeans seem to differ from most other goitrogens. Beck (1958) reports soy flour diets increase thyroxine excretion in the feces due to decreased reabsorption of the thyroxine and its breakdown products from the intestine. McPherson and Albert (1961) reported that a cereal diet such as "Friskies" caused even a greater fecal excretion of organic iodide by rats than soybean meal.

Urinary and Fecal Loss

The kidney is an important excretory route for iodine in the form of iodide. This is derived from blood iodine and from T_3 and T_4 degradation by the kidney (Williams and Bakke, 1963). The kidney is in competition with the thyroid for plasma iodide (Underwood, 1962). It appears if there is a renal threshold for iodine it is very low. Since high levels of dietary iodine greatly increase urinary iodine levels, renal excretion appears to be an overflow mechanism for excess iodide (Van Middlesworth, 1963).

Long et al., (1956) showed that supplemental iodine at 11 and 22 mg per day did not effect serum iodide in non-lactating dairy cattle. This would indicate a homeostatic mechanism, possible involving the kidney, for keeping serum iodide levels constant at these low levels of iodide intake. When cows in the same study were given 44 to 2,816 mg of KI per day, serum iodide levels doubled approximately in direct proportion to the quantity fed. When KI feeding was discontinued, serum iodide levels fell rapidly. These results indicate a fairly low upper threshold for iodide excretion in the dairy cow.

Fecal iodine is primarily organically bound degradation products from thyroid hormones or the hormones themselves and is secreted into the gut with bile. Van Middlesworth (1957) suggests the ability of the intestine to reabsorb thyroxine secreted into the intestine may be altered chemically by some substance. He also suggested that prolonged retention of thyroid hormone breakdown products may result in bacterial destruction releasing thryoxine iodine which becomes available for reuse by the thyroid.

CHAPTER III

PROCEDURE

Experiment 1

Initially, six calves with a beginning average weight of 144 kg were assigned to treatments as in Table 1. However, one calf failed to adjust to the metabolism stall, did not eat normally, and lost weight. After period 1 the experiment was continued with the remaining five. The pretreatment ration contained 74.5% ground yellow corn, 5% molasses, 5% alfalfa meal, 14% soybean meal, 1% dicalcium phosphate and 0.5% noniodized salt. Grass-clover mixed hay and noniodized salt were offered free choice before and throughout the experiment.

Experiment 1 consisted of five periods (Table 1). The treatment schedule was as follows:

Period 1: This 4 week period was intended to stabilize the animals and to obtain excretory, secretory, and circulatory measurements of iodine losses and retention with all calves fed hay only.

Period 2: During weeks 5-15 of the experiment, two calves each received 2.7 kg cottonseed meal (CSM) and three were fed 2.7 kg soybean meal (SBM) each daily in addition to hay.

Period 3: Protein supplements were removed from the ration during weeks 16-25 of the experiment. This 10 week period was to allow treatment effects due to CSM of SBM to disappear.

TABLE 1

(EXPERIMENT 1). PROTEIN SUPPLEMENTS FED IN ADDITION TO GRASS-MIXED HAY

Period	Week	Calf 312	314	315	316	317
1	1-4	None	None	None	None	None
2	5-15	CSM[a]	SBM[b]	SBM	SBM	CSM
3	16-25	None	None	None	None	None
3a	22-23	8 mg. iodine given orally as KI every other day				
4	26-36	SBM	CSM	CSM	CSM	SBM

[a]Cottonseed Meal, 41% Protein

[b]Soybean Oil Meal, 44% Protein

Period 3a: This consisted of the 7th and 8th weeks of Period 3. After 6 weeks on Period 3, it became apparent that blood plasma changes indicating iodine depletion during Period 2 had not been alleviated. Apparently the hay did not contain sufficient iodine to replete the calves after protein supplements were discontinued. Before treatments were reversed in period 4, the calves were given 8 mg of iodine as potassium iodide (KI) for two more weeks.

Period 4: Protein supplements fed during Period 2 were reversed during weeks 26-36 of the experiment. Three calves received 2.7 kg CSM and the other two 2.7 kg SBM daily in addition to hay.

Treatment averages were obtained as follows: Two calves from Period 2 along with three calves from Period 4 were averaged for the CSM treatment. The SBM treatment average consisted of three calves from Period 2 and two calves from Period 4. All five calves from Period 1 and the last two weeks of Period 3 were averaged for the hay only treatment. The second week of Period 3a (week 23 of the experiment) during which all calves were fed hay and given KI by capsule, was considered the hay plus supplemental iodide treatment.

Calves were maintained in metabolism stalls equipped for separate collection of feces and urine (Hansard, 1951) during the last two weeks of each period. In the last week of each period, each calf was given 150 μCi of ^{125}I as sodium iodide orally and 150 μCi of ^{131}I labelled thyroxine intravenously. Jugular blood was collected in heparinized tubes and feces and urine were weighed and sampled daily for 6 days.

Blood plasma was analyzed for protein bound iodine (PBI) (Lennon and Mixner, 1957) and thyroxine (T_4) by a competitive binding procedure using materials and methods from a commercial kit.[1] These measurements were performed at the beginning and end of the week when ^{125}I and ^{131}I collections were made.

Thyroxine secretion rate was measured by a modification of the procedure described by Post and Mixner (1961). At 24, 48, 72 and 96 hours after intravenous dosing with ^{131}I labeled thyroxine, blood samples were drawn from the opposite jugular vein. Plasma protein in each sample was precipitated (Lennon and Mixner, 1957) and ^{131}I determined to obtain the rate of thyroxine disappearance (fractional turnover rate) from plasma. The extrathyroidal thyroxine pool was calculated from the specific activity of plasma thyroxine at time of injection with T_4 measured directly using a commercial kit[2] rather than as 0.653 x PBI (Post and Mixner, 1961). The extrathyroidal thyroxine pool and thyroxine fractional turnover rate were multiplied to obtain thyroxine secretion rate.

Experiment 2

Nine calves of dairy beef cross with an average weight of 136 kg were assigned to three replicates of the latin square design (Table 2). Soybean meal and cottonseed meal were compared with a more pure low residue

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[1]Tetrasorb 125, Abbott Laboratories, North Chicago, Ill. 60064.

[2]Tetrasorb-125, Abbott Laboratories, North Chicago, Ill. 60064.

TABLE 2

(EXPERIMENT 2). CALVES AND EXPERIMENTAL LATIN SQUARE DESIGN

	Calf and Square								
	1			2			3		
Period	357	352	355	353	351	361	354	353	363
1	SBM	ISP	CSM	SBM	CSM	ISP	CSM	SBM	ISP
2	ISP	CSM	SBM	ISP	SBM	CSM	SBM	ISP	CSM
3	CSM	SBM	ISP	CSM	ISP	SBM	ISP	CSM	SBM

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protein source, that of isolated soy protein (ISP). Amounts of the protein supplement (Table 3) were calculated to make the three rations iosnitrogenous. The concentrates were fed at the rate of 2.7 kg per calf daily with free choice hay during three four week periods. Treatment periods were separated by three week periods when corn meal was fed as the only concentrate. Blood plasma samples obtained during the last two weeks of each period were assayed for thyroxine (Abbott Laboratories) and protein bound iodine (Lennon and Mixner, 1957).

At the end of the Latin square comparison, calves receiving rations containing SBM or CSM were each fed 2.7 kg respectively of SBM or CSM as the only concentrate. Calves fed rations containing ISP were then fed hay only. These treatments were continued for 15 weeks (Experiment 2b). During the last two weeks, each calf was given 8 mg supplemental iodine.

Experiment 3

Nine 200-300 kg calves were selected from experiments in which the daily ration had not been changed in at least five weeks. Three were fed forage only, three 2.7 kg of cottonseed meal plus forage and three 2.7 kg soybean meal plus forage. The calves were sacrificed and the digestive tracts removed quickly and divided into rumen-reticulum, omasum, abomasum, six equal length sections of the small intestine, cecum and two equal length sections of the large intestine. Contents were weighed, mixed separately and sampled. Butanol extracts of the contents from each section were assayed for thyroxine (T_4) using a commerically available kit (Abbott Laboratories).[3]

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[3]Tetrasorb-125, Abbott Laboratories, North Chicago, Ill. 60064.

TABLE 3

(EXPERIMENT 2). CONCENTRATE MIXTURE FED TO CALVES TO COMPARE EFFECTS OF PROTEIN SOURCE ON PLASMA THYROXINE

Ingredient	SBM	CSM	ISP
	----------(percent)----------		
Corn	70.5	68.5	86.5
44% soybean oil meal (SOM)	28	----	----
41% cottonseed meal (CSM)	----	30	----
Isolated soy protein (ISP)[a]	----	----	12
Ca_2PO_4	1	1	1
Plain salt	.5	.5	.5

[a]C-1 assay protein, Skidmore Enterprises, Cincinnati, Ohio.

CHAPTER IV

RESULTS

Experiment 1

After 8-15 weeks of feeding either CSM or SBM, plasma protein-bound iodine (PBI) was reduced to 35% of the original level (Table 4). There was a similar 60% reduction of plasma thyroxine (T_4). These measurements remained low, even six weeks after the protein supplement had been discontinued, indicating a depletion of body iodine stores. After one week of supplementation with iodine, the measurements had returned to slightly above 60% of the preliminary level. Thyroxine secretion rate (TSR) was reduced to 24% of the initial value during 8 weeks of feeding either CSM of SBM. The reduced TSR after Period 2 increased to 60% of the initial (Period 1) level after two weeks of supplemental iodine feeding.

Van Middlesworth, (1957) suggested that soybean meal in the digestive tract of the rat depletes the animal of iodine by reducing reabsorption of thyroxine. Thyroxine labeled with ^{131}I was given intravenously to determine the effects of SBM and CSM on the thyroxine excretory losses, Although about 4% more ^{131}I from the thyroxine dose was lost in the feces when calves were fed CSM or SBM, the increase was not statistically significant. Urinary excretion of ^{131}I was reduced about 40% when CSM and SBM were fed, possibly signifying an effort for iodine conservation.

TABLE 4

(EXPERIMENT 1). EFFECT OF DIETARY PROTEIN SOURCE ON MEASUREMENT OF THYROID FUNCTION

Treatment and period[a]	Plasma (PBI) µg/100 ml	Plasma (T_4) µg/100 ml	Thy. Sec. Rate (TSR) mg/100 kg/day	Thyroxine Fractional Turnover Rate mg/day
Hay only				
Period 1	6.01 ± 0.60[b]	9.18 ± 1.49	0.34 ± 0.06	0.39 ± 0.04
Period 3	4.90 ± 1.11	5.93 ± 0.67		
Period 1 & 3	5.45 ± 1.02	7.56 ± 2.03		
Hay + supplemental iodide				
Period 3a	3.64 ± 0.42	5.56 ± 0.66	0.20 ± 0.04	0.35 ± 0.03
Hay + SBM				
Period 2 & 4	1.64 ± 0.49	3.19 ± 0.57	0.08 ± 0.02	0.30 ± 0.02
Period 2	1.52	3.44	0.08	0.28
Period 4	2.67	2.73	0.07	0.33
Hay + CSM				
Period 2 & 4	2.22 ± 0.70	2.99 ± 0.36	0.07 ± 0.01	0.34 ± 0.03
Period 2	1.10	2.74	0.07	0.32
Period 4	2.96	3.07	0.08	0.35

[a]See Table 1, page 14.

[b]Standard Deviation.

Similar results occurred when the animals were dosed with ^{125}I given as the iodide (Table 5). Urinary ^{125}I loss was reduced by SBM or CSM 25-33% and fecal ^{125}I excretion was increased 6-33%.

Insufficient available iodine could result in the reduced TSR observed. However, the reason for the iodine shortage was not explained by total radioiodine excretion which remained relatively unchanged. As is usually observed when animals are changed from an inadequate iodine intake, urinary excretion of ^{125}I almost doubled when an 8 mg iodine supplement was given every other day.

Experiment 2

During the periods covered by the Latin square design experiment, no statistically significant effects of protein source on plasma T_4, or gain in body weight were noted (Table 6). However, when supplemental protein was fed, plasma T_4 averaged 5.4 µg/100 ml which was only 72% of the pre-treatment values.

Mean squares for the various sources of variation in the Latin Square design are presented in Table 7. In Table 7 none of the sources of variation was significant for weight gain. For plasma thyroxine, rows in squares, which represents time period in the experimental design, was the only statistically significant source of variation. This resulted from decreases in plasma thyroxine with time independent of protein source (Table 8). Although iodine status of calves in experiment 2b as measured by plasma T_4, was not reduced nearly as much as in Experiment 1, the rations without supplemental iodine may have been marginally deficient in

TABLE 5

(EXPERIMENT 1). EXCRETION OF ORAL $Na^{125}I$ AND INTRAVENOUS ^{131}I-THYROXINE DURING 144 HOURS AFTER ADMINISTRATION TO CALVES FED DIFFERENT RATIONS

	Hay only	Hay + supplemental I[a]	Hay + SBM	Hay + CSM
	percent of dose			
Urine				
Oral $Na^{125}I$	27.5 ± 2.1	46.3 ± 6.2	20.7 ± 4.9	18.4 ± 4.3
Intravenous ^{131}I-thyroxine	19.2 ± 2.9	16.2 ± 2.2	12.0 ± 2.1	11.5 ± 2.4
Feces				
Oral $Na^{125}I$	22.3 ± 7.1	33.9 ± 7.2	29.8 ± 5.4	23.6 ± 3.0
Intravenous ^{131}I-thyroxine	57.5 ± 3.2	57.1 ± 4.6	59.2 ± 5.2	59.9 ± 4.4
Total				
Oral $Na^{125}I$	49.8 ± 7.2	80.2 ± 6.2	50.5 ± 2.7	42.0 ± 4.2
Intravenous ^{131}I-thyroxine	76.7 ± 3.2	73.3 ± 4.0	71.2 ± 4.8	71.4 ± 5.2

[a] 8 mg I given as KI by capsule every other day.

TABLE 6

(EXPERIMENT 2). EFFECTS OF PROTEIN SOURCE ON WEIGHT GAIN AND PLASMA THYROXINE IN CALVES

Measurement	Protein Source		
	SCM	CSM	ISP
Weight gain (kg/day)	.73	.86	.73
Plasma thyroxine (µg/100 ml)	5.5	5.2	5.6

TABLE 7

(EXPERIMENT 2a). SOURCES OF VARIATION AND MEAN SQUARE ASSOCIATED WITH MEASUREMENT OF EFFECTS OF PROTEIN SOURCE ON WEIGHT GAIN AND PLASMA THYROXINE IN CALVES

Source of Variation	Measurement and mean square	
	Weight gain	Plasma thyroxine
Squares	.16	.64
Periods	.22	2.16[a]
Calves	.07	.45
Treatments	.24	.48
Treatments x squares	.42	.38
Residual	.17	.38

[a]Statistically significant (P<.01).

TABLE 8

(EXPERIMENT 2). MONTHLY CHANGES AND EFFECT OF SUPPLEMENTAL IODINE ON PLASMA THYROXINE CONCENTRATIONS IN CALVES USED IN THREE REPLICATES OF LATIN SQUARE

Month	Square 1	Square 2	Square 3
	(ug/100 ml)		
Experiment 2a			
May[a]	7.1	6.5	6.7
June[a]	5.0	5.1	4.8
July[a]	4.8	4.9	5.0
August[a]	4.8	4.4	5.3
September[a]	5.0	4.8	5.3
Experiment 2b	Treatment CSM	Treatment SBM	Treatment Hay
October[b]	6.0	4.6	5.8
November-December[b]	5.1	4.2	5.0
December-January[b,c]	7.4	6.1	8.2

[a]The Latin square comparison (Table 3, page 19) took place during May-September.

[b]Calves fed hay alone or with 2.7 kg of SBM or CSM as the only concentrate.

[c]Calves each given 8 mg supplemental iodine daily.

iodine. The lesser effect during Experiment 2a may have resulted from the much lower levels of SBM or CSM fed. Although as much SBM or CSM was fed in Experiment 2b as in Experiment 1, the calves were older when Experiment 2b was begun and may have been less subject to iodine depletion. During the 10 week period when the three groups were fed hay only or hay with 2.7 kg per day of CSM or SBM as the only concentrate, (Experiment 2b) thyroxine concentration was not affected by protein source. As in experiment 1, plasma thyroxine concentrations were increased in all treatments when 8 mg supplemental iodine per day were fed to each calf for 2 weeks.

TSR (Table 9) was also unaffected by protein source, but with thyroxine concentration, it was increased with feeding supplemental iodine as in Experiment 1.

Experiment 3

Digestive tract thyroxine contents from calves fed CSM or no supplemental protein were compared to determine why TSR was reduced but excretory loss or radiothyroxine was not increased in Experiment 1.

A limiting factor of the experiment is that the efficiency of the thyroxine extraction for the digestive tract contents was not determined. While absolute levels of thyroxine in digestive tract contents were not obtained, it is hoped that the results will be comparable for the treatments.

Although blood plasma T_4 concentration in animals fed SBM or CSM averaged only 39% that of animals on forage only, T_4 in butanol extracts

TABLE 9

(EXPERIMENT 2b). EFFECT OF SUPPLEMENTAL IODINE ON THYROXINE SECRETION RATE AND PLASMA THYROXINE CONCENTRATIONS IN CALVES

Treatment and measurement	Supplemental protein		
	SOM	CSM	NONE
No supplemental iodine			
Thyroxine secretion rate (mg/100 kg/day)	.17	.21	.20
Plasma thyroxine (µg/100 ml)	4.6	5.3	5.1
8 mg/day supplemental iodine			
Thyroxine secretion rate (mg/100 kg/day)	.32	.31	.36
Plasma thyroxine (µg/100 ml)	6.9	7.2	7.5

of the small intestine contents averaged about twice that of animals fed no supplemental protein (Table 10). The treatment differences were most apparent in small intestine but were non-significant statistically because of the large variations within treatments.

TABLE 10

(EXPERIMENT 3). CONCENTRATION OF THYROXINE IN BLOOD PLASMA AND DIGESTIVE TRACT CONTENTS OF CATTLE FED DIFFERENT SOURCES OF SUPPLEMENTARY PROTEIN

Sample	Ration		
	Hay + SOM	Hay + CSM	Hay + pasture
	---(μg T_4 per 100 g sample)----------		
Blood plasma	2.7	3.1	7.5
Rumen	8.6	10.2	3.4
Omasum	9.7	11.5	6.1
Abomasum	9.7	10.7	3.6
Small intestine 1	41.7	51.8	36.4
Small intestine 2	75.3	90.5	19.9
Small intestine 3	53.1	32.8	21.4
Small intestine 4	13.4	26.0	13.9
Small intestine 5	12.6	14.6	8.0
Small intestine 6	8.8	25.5	6.0
Cecum	8.0	17.0	3.8
Large intestine 1	6.9	7.7	4.6
Large intestine 2	13.4	22.8	5.6

CHAPTER V

DISCUSSION

The most apparent changes in iodine utilization during periods when large amounts of SBM or CSM were fed were reductions in PBI, T_4 and TSR. No appreciable effects of SBM or CSM on excretion of radioiodine given either orally as iodide or intravenously as thyroxine could be detected although plasma T_4 was reduced by about half when these protein sources were fed in Experiment 1. Plasma T_4 remained low even when protein supplementation was discontinued and hay only was fed for 6 weeks, but plasma T_4 approached normal within a week after 8 mg of supplemental iodine was fed on alternate days. It was observed, in agreement with many other reports, that addition of supplemental iodine to a previously inadequate diet markedly increased iodine excretion. These results suggest depletion of body iodine stores but the mechanism is not clear.

In Experiment 1, SBM and CSM were compared in the same period followed by periods of hay without supplemental protein. It was not determined whether an extended period of feeding hay only without supplemental iodine would result in a similar depletion of iodine. Experiment 2 was designed to more adequately account for period effects. The rations were also kept isonitrogenous by comparing CSM and SBM with a low residue protein source, isolated soy protein.

No statistically significant effects of protein sources were found in Experiment 2. There are at least two possible reasons for the lack of treatment differences in plasma T_4 or body weight gain: 1) The smaller intakes of the protein sources when fed in concentrate mixtures were insufficient to produce measurable effects, or 2) all protein sources, including isolated soy protein, affected these measurements to the same degree.

The only statistically significant component of variation for T_4 measurements in Experiment 2 was rows in squares (Table 7, page 25) which represents periods in the experimental design. This indicates as also shown by Experiment 1, that prolonged feeding of low iodine rations eventually reduced plasma T_4 which did not return to normal without supplemental iodine.

Van Middlesworth (1957) suggested that soy flour diets depleted the rat of iodine by reducing reabsorption of thyroxine from the digestive tract. However, fecal losses of endogenous thyroxine in calves, as estimated by intravenously injected ^{131}I-labeled hormone, were increased only about 4% by SBM or CSM (Table 5, page 23), a statistically nonsignificant difference. A lack of sufficient available iodine could result in the reduced TSR observed (Table 4, page 21). However, the cause of an iodine shortage was not explained by increased excretory losses (Table 5, page 23).

Although blood plasma T_4 concentrations of animals fed SBM or CSM in Experiment 3 averaged only 39% of those fed forage only, T_4 concentration in their small intestine contents were substantially elevated. Since

efficiency of extracting T_4 from digesta was not determined, it is not known whether these values are absolute measurements. However, unless extraction efficiency was influenced by treatments, the measurements should have comparative value. Results in Table 10, page 30, suggest that thyroxine or iodine from thyroxine may have been tied up temporarily in the small intestine, then later absorbed in the large intestine. Such a temporary tie up could increase the iodine requirement without it being evident in the fecal excretion. If soy flour delayed reabsorption of thyroxine from the rat intestine (Van Middlesworth, 1957), the prolonged exposure of thyroxine to bacterial and enzymatic action in the intestine could have increased its destruction.

However, Van Middlesworth's results with rats may not be applicable to ruminants for the following reasons: 1) cattle normally consume a high residue diet and addition of SBM or CSM to a forage ration would more likely decrease rather than increase dietary residues in the digestive tract; 2) only about 10-15% of the thyroxine secreted into the bovine digestive tract is normally reabsorbed (Miller et al., 1975) so this mechanism for conserving thyroxine is relative minor; 3) even if thyroxine degradation in the digestive tract were increased, the resulting free iodine could still be absorbed and reutilized by the thyroid.

A possibility that has not been considered is an effect of dietary protein on plasma proteins causing a decrease in the thyroxine binding capacity. This type of change has been observed in dairy cattle fed thyroprotein (Etta and Reineke, 1971).

These experiments show that prolonged feeding of low iodine rations may eventually reduce amounts of thyroid hormone secreted. Concentrations of thyroid hormone in digestive tract contents may be higher when SBM or CSM are fed, but excretary loss of iodine is not greatly increased. Adequate dietary iodine appears to be more important than source of supplemental protein for maintaining normal thyroid function. Although certain natural feed ingredients may increase retention of iodine in the digestive tract to some extent, iodine recycling together with moderate iodine supplementation should permit adequate thyroid hormone production.

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