

EFFECT OF SOYBEAN ON THYROID HORMONES

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ABSTRACT

There has been much discussion of late over the possible adverse effect of soy consumption on thyroid function in both infants and adults. Recently, several studies have provided insight into the relationship between soy and thyroid function. Many researchers indicates that the consumption of isoflavone – rich soy protein had little effect on thyroid hormone level. So, it is important to study the effect of soybean on thyroid hormones.

Three formulas of soybean, i.e., whole meal, low fat flour and dehulled ones, were used in this study and chemically analyzed. Female rats were fed on soybean (whole meal, low fat flour and dehulled) for six weeks with or without exo-thyroid hormone. Biological evaluation of the experimental rats such as: body weight gain, weight of some organs, thyroid hormones, (T_3 , T_4), TSH, prolactin and progesteron hormones were estimated. Data showed that feeding soybean resulted in loss weight of animals and weight of organs and affected TSH, T_3 secretion followed by T_4 . Also, it increased progesterone hormone, but no effect on prolactin hormone.

Keywords: Soybean, biological effect, T_3 , T_4 , TSH, prolactin, progesteron.

INTRODUCTION

Soybean is a legume increasingly consumed for economical and nutritional reasons (Garcia *et al.*, 1997). In fact, soybean products are an important low – cost sources of protein, minerals and vitamins. Soybean is grown for food, feed, fodder, oil and green manure purpose. Soybean food such as tofu, miso, shoyu, soy milk, temph and immature green pod are very popular in China, Taiwan, Japan, Thailand and Malaysia. Soybean contained 40 – 45% protein, so, it is called "meat of the field" and produced about three times more protein than rice, wheat or maize. It is also an excellent source of good quality unsaturated oil (Sapkota, 2003). As increasing numbers of consumers embrace soyfoods, health professionals need to understand both the benefits and the potential challenges of soy consumption. There has been much discussion of late over the possible adverse effects of soy consumption on thyroid function in both infants and adults (Messina, 2001). The thyroid gland is the body's thermostat and catalyst. It regulates the temperature of the body by secreting two hormones that control how quickly the body burns calories and uses energy. The normal healthy thyroid gland produced about 80% T_4 (3,5,3',5'-tetraiodothyronine) and 20% T_3 (3,5,3'-triiodothyronine). Thyroid Stimulating Hormone (TSH) stimulates thyroid gland to produce T_3 and T_4 . In addition, liver converts T_4 into T_3 . The primary cause of goiter and hypothyroidism around the world is inadequate iodine intake. Approximately one billion people are considered to be iodine deficient worldwide (Delange, 1994). Over consumption of goitrogenic foods such as soy, broccoli, cabbage, kale, radishes, etc. cause goiter. Recently, (Divi and Doerge, 1996 and Divi *et al.*, 1997), at the National Center for Toxicology Research (NCTR)

in Arkansas, concluded that the isoflavones in soybean are goitrogenic. In fact, they suggest that flavonoids are responsible for goiter associated with the consumption of large amounts of millet in certain developing countries (Gaitam *et al.*, 1995 and Elnour *et al.*, 2000). *In vitro* research clearly shows that genistein, the primary isoflavone in soy, is able to inhibit the activity of thyroid peroxidase, the enzyme involved in the synthesis of thyroid hormone (Divi *et al.*, 1997). More importantly, a recent study in rats found that dietary genistein inhibited thyroid peroxidase activity by up to 60 percent (Chang and Doerge, 2000). Ishizuki *et al.* (1991) suggested that the addition of 30 g/day of pickled soybean to the diet significantly increased TSH levels and caused goiter. (Duncan *et al.* 2000) from the university of Minnesota indicated that the consumption of isoflavone-rich soy protein, that intake in Japan, had little effect on thyroid hormone levels in either pre – or postmenopausal women over a three – month period. In addition, a recently conducted double – blind study six months in duration, that involved 38 postmenopausal women who were not on hormone therapy, found no differences in thyroid function, based on measures of thyroid stimulating hormone (TSH), total T_4 and T_3 , between subjects given daily either a placebo or a soybean isoflavone extract that provided 90 mg (equal to approximately three servings of soy) of isoflavones (Bruce *et al.*, 2000).

This investigation was conducted to show the effect of soybean on thyroid hormones (T_3 and T_4), TSH, progesterone and prolactin in the presence or absence of exo-thyroid hormone, and to restrict over consumption of soy products for infants and adults.

MATERIALS AND METHODS

Materials:

Soybean:

Soybean (whole meal), low fat soybean flour and dehulled soybean were obtained from soybean pilot plan, Food Technology Research Institute (FTRI), Agricultural Research Center, Giza, Egypt.

Experimental animals:

Thirty five albino female rats, Sprague Dawley strain (weighed 180 ± 5 g) were obtained from the experimental animal house, Crops Technology Department, FTRI, Giza, Egypt.

Methods:

Chemical composition:

Chemical composition of soybean (whole meal, dehulled and low fat soy flour) were determined according to A.O.A.C. (2000). Total hydrolyzable carbohydrates were calculated by difference.

Biological evaluation:

Experiment design:

The animals (35 albino female rats) were housed in clean cages under healthy conditions at room temperature ($25 \pm 2^\circ\text{C}$) and fed on basal diet for 7 days (adaptation period). After this period, animals were divided into seven groups as following scheme: ($n = 5$)

Group (1):	Rats fed on basal diet (control).
Group (2):	Rats fed on whole meal soybean and take daily orally exo-thyroid hormone (eltraxin, 50 µg) using stomach tube for six weeks.
Group (3):	Rats fed on low fat soybean flour and orally exo – thyroid hormone (50 µg) using stomach tube for six weeks.
Group (4):	Rats fed on dehulled soybean and orally exo – thyroid hormone (50 µg) using stomach tube for six weeks.
Group (5):	Rats fed on whole meal soybean.
Group (6):	Rats fed on low fat soybean flour
Group (7):	Rats fed on dehulled soybean.

The basal diet, minerals and vitamins mixtures were prepared as recommended by A.O.A.C. (2000). During the experimental period, the rats were weighed. At the end of the experiment (6 weeks), the final weight of body and organs were recorded. The blood samples were obtained from the orbital plexus of each rat after 3 and 6 weeks, then centrifuged to separate the serum. Then the serum was frozen and kept until analysis.

Biochemical analysis:

1) Determination of T₃ and T₄:

Serum 3, 5, 3' triiodothyronine (T₃) and 3, 5, 3', 5' tetraiodothyronine (T₄) were determined after three weeks and after six weeks according to the method described by Wayne (1998).

2) Determination of TSH:

Thyroid stimulating hormone (TSH) was determined according to the method described by Wada *et al.* (1982).

3) Determination of progesterone and prolactin:

Progesterone and prolactin hormones were determined according to the methods outlined by Bojanic *et al.* (1991) and Houdebine (1983), respectively.

4) Statistical analysis:

Statistical analysis was carried out according to Fisher (1970). The Statistical Package for Social Science S.P.S.S. (1999) program version 10 was used for all analysis.

RESULTS AND DISCUSSION

Chemical composition of soybean:-

Table (1) shows the chemical composition of soybean (whole meal, low fat and dehulled). From the obtained data, low fat soybean recorded the highest value of protein content (50.42%), followed by dehulled soybean (42.16%) then whole meal (24.37%). On the other hand, the lowest value of oil content was observed for low fat soybean (6.00%), but whole meal and dehulled soybean were higher (21.65 and 23.56%, respectively). Concerning fiber content, it decreased due to dehulling of soybean, but ash content resulted in the highest value at low fat soybean. Regarding total carbohydrates, it decreased from 34.89 to 24.58 and 21.74 for whole meal, dehulled and low fat soybean, respectively.

Table (1): Chemical composition of soybean

Sample	Protein %	Oil %	Fiber %	Ash %	T.C* %
Whole meal	24.37	21.65	12.19	6.90	34.89
Low fat	50.42	6.00	14.01	7.83	21.74
Dehulled	42.16	23.56	2.50	7.20	24.58

* T.C. = Total carbohydrate

Effect of soybean on body weight gain, feed intake and feed efficiency in the presence or absence of exo – thyroid hormone:

Table (2) shows the body weight gain, feed intake and feed efficiency of the experimental animals fed soybean in the presence or absence of exo – thyroid hormone in the amount of 50 µg, compared with control. The data revealed that all treatments resulted in loss weight except that of low fat soy flour and orally thyroid hormone feeding. The highest loss was found due to feeding soy whole meal either in the presence or absence of exo – hormones being -35 ± 6.43 and -26.33 ± 3.76 g, which equal of -19.26 and -14.50 than the initial weight, respectively. The presence of thyroid hormone resulted in loss more than that orally induced by about 25%. Concerning food intake, it could be noticed that no significant differences were found due to all treatments compared with control. On the other hand, the negative values of feed efficiency reflected the losing body weight gain. It is well known that certain foods have the ability to suppress the functioning of the thyroid such as beans, peanut, raw proccoli, cauliflower, cabbage, animal protein, poly unsaturated oil and β -carotene (Ridha, 1999).

Effect of soybean on some organs weight in the presence or absence of exo – thyroid hormone:

Table (3) shows the liver, kidney and heart weight and their relation to body weight as affected by feeding soybean in different formulas in the presence or absence of exo–thyroid hormone. The data revealed that liver weight decreased by about 40–60% than that of control as a result of all treatments. Similar trend was found for kidney and heart. In fact, these results may be reflect the weight loss of the animal and therefore a decreasing in the organs were found. From the view point of relative weight of organs, data revealed that a slight variation was found in the organs due to the soybean formulas in the presence or absence of exo–thyroid hormone. (50 µg).

Effect of soybean on thyroid hormones:

Table (4) shows the effect of feeding soy whole meal, low fat soy flour and dehulled ones either orally administered with exo – thyroxin or without. After 3 weeks of feeding, data revealed that administration with exo – thyroid hormone increased serum hormone T_4 by about 2 and 3.5 fold as that of control, while in the absence of exohormone, it recorded an amount similar to that of control except that of low fat flour which showed a slight increase. Concerning T_3 , a remarkable increase was found and this increase was independent of exo – thyroid hormone administration.

Table (2): Effect of soybean on body weight gain, feed intake and feed efficiency in the presence or absence of exo-thyroid hormone.

Treatments	Initial weight	Final weight	B. wt. gain		Feed intake	Feed efficiency
	(g)	(g)	(g)	%	(g)	
Control	182.33 ^a ±8.88	252.33 ^a ±15.21	70 ^a ±23.71	38.38	810 ^a ±25.98	0.085±0.03
Whole meal + Ex	181.66 ^a ±9.28	146.66 ^d ±3.28	-35 ^c ±6.43	-19.26	840 ^a ±39.69	-0.041±0.01
Low fat flour + Ex	182.66 ^a ±5.81	197 ^b ±8.14	14.33 ^b ±13.96	7.84	855 ^a ±25.98	0.0157±0.02
De-hulled + Ex	182.00 ^a ±5.57	169 ^{bcd} ±8.51	-13 ^{bc} ±6.43	-7.14	825 ^a ±39.69	-0.0153±0.01
Whole male	181.66 ^a ±6.39	155.33 ^{cd} ±5.33	-26.33 ^c ±3.76	-14.50	795 ^a ±15.00	-0.033±0.00
Low fat flour	182.33 ^a ±5.78	181.33 ^{bc} ±12.84	-1 ^{bc} ±9.87	-0.65	810 ^a ±45.00	-0.002±0.01
De-hulled	182.33 ^a ±4.70	182 ^{bc} ±7.81	-0.33 ^{bc} ±3.71	0.18	825 ^a ±39.69	-0.0004±0.00
LSD at 5%	20.699	28.89	35.61		104.60	0.042

Each value represents the mean of 3 rats (Mean ± SE)

B. wt.= Body weight

- Feed efficiency = B. wt. gain / Feed intake

* Ex = Exo thyroid hormone

Table (3): Effect of soybean on some organs weight in the presence or absence of exo-thyroid hormone.

Treatments	Final body weight	Liver		Kidney		Heart	
	(g)	(g)	%	(g)	%	(g)	%
Control	252.33 ^a ±15.21	9.57 ^a ±0.39	3.79	1.94 ^a ±0.21	0.77	0.86 ^a ±0.06	0.34
Whole meal + Ex	146.66 ^d ±3.28	4.33 ^e ±0.16	2.95	0.96 ^c ±0.10	0.65	0.59 ^c ±0.00	0.40
Low fat flour + Ex	197 ^b ±8.14	6.76 ^b ±0.20	3.43	1.38 ^b ±0.06	0.70	0.69 ^{bc} ±0.03	0.35
De-hulled + Ex	169 ^{bcd} ±8.51	4.43 ^{de} ±0.18	2.62	1.19 ^{bc} ±0.06	0.70	0.61 ^{bc} ±0.01	0.36
Whole male	155.33 ^{cd} ±5.33	4.63 ^{de} ±0.11	2.98	1.08 ^{bc} ±0.04	0.70	0.63 ^{bc} ±0.02	0.41
Low fat flour	181.33 ^{bc} ±12.84	5.45 ^c ±0.36	3.01	1.15 ^{bc} ±0.05	0.63	0.65 ^{bc} ±0.03	0.36
De-hulled	182 ^{bc} ±7.81	5.14 ^{cd} ±0.09	2.82	1.27 ^{bc} ±0.09	0.70	0.70 ^b ±0.03	0.38
LSD at 5%	28.89	0.728		0.313		0.095	

- Each value represents the mean of 3 rats (Mean ± SE)

* Ex = Exo thyroid hormone

Similar trend was observed regarding thyroid stimulating hormone (TSH) as that of T_4 . After 6 weeks of feeding, a slight variation was found, but in the same trend as that of 3 weeks of feeding. It is worth to mention that the normal value of TSH, T_4 and T_3 was 0.4 – 5 μ IU/ml, 5 – 12 μ g/dl and 80 – 180 ng/dl, respectively (Bunevicius *et al.*, 1999).

From the above mentioned data, it could be concluded that feeding soybean affected TSH and T_3 secretion followed by T_4 . It is well known that thyroxin hormone promotes growth and oxidative metabolism. These hormones regulate numerous key biochemical reactions, especially protein synthesis and enzymatic activity. Adequate amounts of thyroid hormones are especially important to the development of brain, muscles, heart and kidney in the fetus and young child. TSH control the amount of thyroglobulin secreted. Pituitary TSH in turn, is regulated by TSH releasing factor (TRF), which is secreted by the hypothalamus (Carol, 2001).

In this connection, iodine must be present in sufficient quantities for the body to produce adequate amounts of thyroid hormones when the diet containing foods affected thyroid hormone reaction (Dunn, 1998).

Table (4): Effect of soybean on thyroid hormones and TSH in the presence or absence of exo-thyroid hormone.

Treatments	T_4 μ g/dl	T_3 ng/dl	TSH μ IU/l
After 3 weeks			
Control	5.6 ^{cd} ±0.35	68 ^d ±2.309	0.06 ^d ±0.017
Whole meal + Ex*	12.7 ^b ±0.23	60 ^e ±1.732	0.12 ^c ±0.012
Low fat flour + Ex*	17 ^a ±1.73	88 ^d ±2.309	0.17 ^c ±0.017
De-hulled + Ex*	15 ^a ±0.40	62 ^e ±1.270	0.08 ^{cd} ±0.012
Whole male	5.2 ^d ±0.23	95 ^a ±0.635	0.22 ^a ±0.017
Low fat flour	7.8 ^c ±0.29	80 ^c ±2.309	0.1 ^{cd} ±0.012
De-hulled	5.7 ^{cd} ±0.23	72 ^d ±1.155	0.08 ^{cd} ±0.003
LSD at 5%	2.15	5.42	0.041
After 6 weeks			
Control	4.8 ^d ±0.23	60 ^{de} ±5.77	0.18 ^{ab} ±0.012
Whole meal + Ex*	14 ^b ±0.23	80 ^c ±2.89	0.05 ^c ±0.012
Low fat flour + Ex*	12.2 ^c ±0.29	68 ^d ±1.15	0.11 ^{bc} ±0.052
De-hulled + Ex*	21 ^a ±0.23	112 ^a ±1.15	0.12 ^{bc} ±0.012
Whole male	4.4 ^{de} ±0.29	95 ^b ±2.89	0.24 ^a ±0.012
Low fat flour	3.6 ^e ±0.35	54 ^e ±1.15	0.14 ^b ±0.017
De-hulled	5.2 ^d ±0.29	88 ^{bc} ±2.31	0.14 ^b ±0.012
LSD at 5%	0.84	8.8	0.07

Each value represents the mean of 3 rats (Mean ± SE)

- * Ex = Exo thyroid hormone

Effect of soybean on prolactin and progesterone hormones:

Table (5) shows the prolactin and progesterone hormones as affected by feeding different soybean formulas either administered with orally chemical thyroid hormone or in absence of it. Data showed that no adverse effect, due to all treatment, on prolactin hormone during 6 weeks of the experiment. The prolactin content ranged from 0.7 to 1.3 mg/ml. Concerning

progesterone, it is well known that soy bean increases progesterone due to containing hormone like substance or that of isoflavones. The amount of progesterone was 14.4 ± 0.17 mg/ml for the control fed basal diet. It is increased by about 3.9, 2.3, 3.5, 3.0, 2.2 and 4.4 fold as that of control when fed whole meal + exo – thyroid hormone (EX), low fat flour + EX, dehulled + EX, whole meal, low fat flour and dehulled soybean, respectively, after 3 weeks of feeding. After 6 weeks of feeding, there were a slight differences between the treatments and control, except that of whole meal + EX, low fat flour + EX and dehulled which decreased by about 48%, 25% and 37.5%, respectively. This may be due to the aging or the accumulation of the hormone, the adverse effect of the increasing of hormone which affected some other hormones or the interaction between the chemical and feeding material.

Table (5): Effect of soybean on prolactin and progesterone hormones in the presence or absence of exo-thyroid hormone.

Treatment	Prolactin mg/ml	progesteron mg/ml
After 3 weeks		
Control	$1.1^a \pm 0.17$	$14.4^1 \pm 0.17$
Whole meal + Ex	$0.9^a \pm 0.17$	$56^b \pm 1.15$
Low fat flour + Ex	$0.8^a \pm 0.17$	$33.6^c \pm 0.35$
De-hulled + Ex	$1.2^a \pm 0.12$	$50.4^c \pm 0.81$
Whole meal	$1.2^a \pm 0.06$	$43.2^d \pm 0.69$
Low fat flour	$1.0^a \pm 0.12$	$32^e \pm 0.58$
De-hulled	$0.9^a \pm 0.12$	$64^a \pm 0.81$
LSD at 5%	0.42	2.18
After 6 weeks		
Control	$0.71^b \pm 0.01$	$96^a \pm 2.31$
Whole meal + Ex	$1.2^a \pm 0.12$	$49.6^e \pm 0.35$
Low fat flour + Ex	$1.3^a \pm 0.17$	$72^c \pm 1.73$
De-hulled + Ex	$1.05^a \pm 0.03$	$97^a \pm 1.73$
Whole meal	$1.1^a \pm 0.08$	$96^a \pm 1.15$
Low fat flour	$1.3^a \pm 0.04$	$80^b \pm 3.46$
De-hulled	$1.05^a \pm 0.04$	$60^d \pm 0.58$
LSD at 5%	0.26	5.75

Each value represents the mean of 3 rats (Mean \pm SE)

- * Ex = Exo thyroid hormone

In conclusion, there is no reason to restrict soy consumption over concerns about the impact on thyroid function. When counseling patients consuming large amounts of soy, it is important to make sure iodine intake in adequate amount. But of course, all people, regardless of their dietary pattern, need to consume sufficient amount of iodine. The American Thyroid Association recommends that all people have their thyroid hormone levels checked every five years beginning at the age of thirty – live (Ladenson *et al.*, 2000).

Also, it could be concluded that soy could cause goiter, but only in animals or humans consuming diets marginally adequate in iodine, or who were predisposed to develop goiter.

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تأثير فول الصويا على هرمونات الغدة الدرقية

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هناك مناقشات كثيرة في الآونة الأخيرة حول إمكانية تأثير فول الصويا على وظائف الغدة الدرقية في حالات الرضع والبالغين وقد قامت دراسات كثيرة لمعرفة العلاقة بين فول الصويا ووظائف الغدة الدرقية. وقد أوضحت الدراسات أن استهلاك بروتين الصويا الغني بالأيزوفلافون له تأثير بسيط على هرمونات الغدة الدرقية. ولذلك كان لابد من دراسة تأثير فول الصويا على هذه الهرمونات. استخدم في هذه الدراسة ثلاثة صور لفول الصويا (حبة كاملة – دقيق منزوع الدهن – بذور منزوعة القشرة) وقد تم تحليله كيميائياً. وقد تم تغذية إناث الفئران على فول الصويا بصورة الثلاثة بدون إضافة خارجية لهرمون الغدة الدرقية (الإلثروكسين) أو بإضافة هذا الهرمون.

وكانت مدة التجربة حوالي 6 أسابيع. تم إجراء التحاليل البيولوجية منها: وزن الفئران – وزن بعض الأعضاء – تقدير هرمونات T₃, T₄, TSH وكذلك الهرمونات الأنثوية وهي البرولاكتين، والبروجسترون. وقد أوضحت النتائج أنه بتغذية الفئران على فول الصويا أدى إلى فقد في وزن الجسم وكذلك وزن الأعضاء. كما أدى أيضاً إلى خلل في إفراز هرمونات الغدة الدرقية (T₃, T₄, TSH) أما بالنسبة للهرمونات الأنثوية فأدت التغذية على فول الصويا إلى زيادة كبيرة في هرمون البروجسترون، أما هرمون البرولاكتين فلم يتأثر.