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The Impact of Mustard Oil (*Brassica Juncea*) Ingestion on Thyroid Gland Hormones in Experimental Rats

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THE present study was conducted to investigate the impact of mustard oil ingestion on thyroid hormones in experimental rats. Forty-two adult male albino rats (180± 5 g) were divided into 7 groups. Group (1) (-ve control) rats were fed on basal diet. Groups 2-4 were rendered hypothyroidism (injected with PTU, ip), where G2 fed on basal diet and G 3& 4 were given mustard oil at two levels (1&2 ml/Kg Bwt.), respectively. Groups 5-7 were rendered hyperthyroidism (injected with L-thyroxin, ip), where G5 was fed on basal diet and G6& 7 were given mustard oil at the same two levels, respectively. At the end of the experimental period (8 weeks), rats were sacrificed and blood samples were collected for serum. Thyroid hormones, liver and kidney functions were determined. Results indicated that, Ingestion of mustard oil at the two levels of intake improve in hypothyroid status as related to non-significant increase in FT3 and FT4 and significant reduction of the level of TSH. While hyperthyroid rats showed significant increase in FT4 and FT3 levels. TSH level was significantly increased. It was also observed that ingestion of mustard oil improves kidney function by reducing creatinine and urea concentrations in serum in the hypo and hyperthyroid rats. Results revealed that mustard oil had beneficial effect on AST, ALT and ALP activity in hypo and hyperthyroid rats, this was confirmed histopathologically. Finally, our results concluded that mustard oil ingestion improves thyroid hormones status, liver and kidney functions. Thus, it could be recommended for patients with thyroid dysfunctions.

Keywords: Mustard oil, Hypothyroidism, Hyperthyroidism, Thyroid hormone, Liver functions, Kidney functions.

Introduction

Mustard are seeds of various mustard plants, which is a cruciferous vegetable. Brassica juncea is known to deliver a few classes of bioactive phytochemicals including glycosides, terpenoids, sterols and flavonoids. (Ibrahim,2013)

Mustard oil (Brassica juncea) has been found to obtain important phytochemicals. Mustard seed oil has been used successfully both for medicinal use and as food spices (Sunday et al., 2014). Mustard oil (Brassica juncea) was widely used to downplays the severity of various health problems like asthma, lower high blood pressure and prevent heart attack in patient suffering from atherosclerosis (Al-Diwan et al., 2016).

Thyroid hormone release is under the control of the hypothalamus and anterior pituitary Thyroid disease is classically divided into hyperthyroidism and hypothyroidism, and goiter and other Iodine deficiency disorders, Hashimoto's thyroiditis and thyroid cancer. (Studer et al., 1989), The thyroid gland is unique among the endocrine organs as it maintains a large store of hormone. (Dunn, 1992 and Stanbury et al., 1998). Hyperthyroidism and hypothyroidism occurig overly due to autoimmune thyroid diseases . (Volpe,1988). Our endocrine system is a highly sophisticated hierarchical system that dictates efficiency as well as dynamic control of different processes in our body such as metabolism, growth, and sexual and emotional development. (Malik and Hodgson, 2002).

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Therefore, this study was conducted to investigate the impact of mustard oil supplementation on thyroid hormones in experimental rats with induced thyroid disorders.

Materials and Methods

Materials

1-Chemicals: Casein, vitamins, minerals, cellulose, choline chloride were purchased from El-Gomhoria Company – Cairo – Egypt. Propylthiouracil (PTU) and L-thyroxin were obtained from Sigma Company for Chemical, Cairo, Egypt. Kits for blood analysis were purchased from Gama Trade Company for Chemical, Cairo, Egypt.

2-Animals: Adult male albino rats (Sprague-Dawley strain) weighting approximately 180 ± 5 g were purchased from Helwan Experimental Animals Station.

3-Oil: Mustard seed oil (*Brassica juncea*) was obtained from Agriculture Research Center, Giza, Egypt.

Methods

Chemical composition and phytochemical ingredients of the mustard oil were carried out at the National Research Center.

Induction of hypo- and hyperthyroidism: Hypothyroidism was induced in rats (n=42) according to Sener, et al., (2006) using PTU (10 mg/kg Bwt. IP) for 15 days. While rats were render hyperthyroidism by daily intraperitoneal injection (IP) using L-thyroxin at a dose of 300 µg/kg B.wt. according to Mogulkoc et al., (2006). Blood samples were collected from the eye of rats to determine TSH and T4 to insure thyroid disorders after injection with PTU or L-thyroxin.

C- Biological Study

The experimental study was carried out at the animal house, Faculty of Home Economic, Helwan University. The experimental procedure was applied for 8 weeks. Forty-two adult male rats were housed at well ventilated cages under hygienic requisites and fed on basal diet for one week for adaptation. The basal diet was admixes according to Reeves et al., (1993). After this week, rats were divided into 7 groups (6 rats each) as follows: Group (1) (negative control) rats were fed on basal diet. Groups 2-4 were rendered hypothyroidism, where G2 fed on basal diet and G 3& 4 were given mustard oil at two levels (1 and 2 ml/Kg Bwt.), respectively. Groups 5-7 were rendered hyperthyroidism, where G5 was fed on basal diet and G 6& 7 were given mustard oil at the same two tested levels, respectively.

At the end of the experimental period (8 weeks), rats were fasted overnight before scarifying and the blood samples were collected, then centrifuged to obtain serum. Feed intake (FI), body weight gain percent (BWG %) and feed efficiency ratio (FER) were determined.

Chemical analysis: were carried out at the Postgraduate Lab of Home Economics Faculty, Helwan University. Serum was analyzed to determine the levels of ALT and AST activities according to Henry et al., (1960) and ALP activity was assayed according Tietz et al., (1983). free thyroxin (FT4) ,Free triiodothyronine (FT3), and TSH hormones were gauged in serum using radioimmunoassay method provided by Ortho-Clinical Diagnostics, Inc, USA according to manufacturer's instruction Agharanya (1990); Frank et al., (1996) and Sachidhanandam et al., (2010).

Creatinine level was rimmed by the method of Tietz (1999). Urea level was rimmed by using the method of Reitman, and Frankel(1957).

Histopathological Examination: Thyroid gland was dissected from the tested rats, then immersed immediately in 10% neutral buffered formalin pH 7.4 (Gamble, 2008) for histopathological examination. Photographs were taken using light microscope provided with digital camera. The histopathological examination was carried out at Pathology Department, Faculty of Veterinary Medicine, and Cairo University.

Statistical Analysis: The obtained results were statistically analyzed according to SPSS program (version 18). ANOVA test were used to compare results among groups. Results were expressed as mean ± SE at $P < 0.05$ significancy (Bailey, 1994).

Results

The present work was designed to evaluate the effect of mustard oil ingestion at two levels of intake on thyroid hormones, kidney functions and liver functions in experimental induced hypo- and hyperthyroidism of adult male albino rats.

Effect of Mustard oil Ingestion on Body Weight Gain Percent (BWG %), Feed Intake (FI) and Feed Efficiency Ratio (FER) of Rats with Hypo and hyperthyroidism.

Results illustrate that body weight gain percentage (BWG)% of the hypothyroid rats (G2) was significantly ($p<0.05$) increased compared with the negative control group as seen in Table (1). However, BWG% was significantly decreased when rats became hyperthyroid compared with the negative control group. Data revealed that hypothyroid rats fed on mustard oil at any tested level of intake (G 3&4) had significant reduction in BWG% compared with the corresponding group (G2). The hyperthyroid rats' groups showed the same trends (G6 &7) compared to the hyperthyroid control group (G5).

Concerning food intake (Table1), data show that hypothyroid rats had increased FI compared to the –ve control rats (12g (G2) vs 11g (G1), respectively). On the other hand, the food intake of the hypothyroid rats was decreased when rats were ingested the mustard oil at the two tested levels (G3&4). Meanwhile, hyperthyroid rats (G 5) showed reduced FI compare to the –ve control ones. However, when the hyperthyroid rats were ingested mustard oil at the two tested levels (G 6&7) FI were increased compared with the hyperthyroid control rats (G5).

Feed efficiency ratio (FER) of hypothyroid group show significant increases compared to the negative control group. However, the hyperthyroid control group illustrate a decrease in FER compared to negative control group. On the other hand, when hyperthyroid rats were ingested mustard oil at the two tested levels, showed significant increase in feed efficiency ratio (FER).

It could be concluded that the ingested mustard oil had beneficial effects on BW% of the hypo and hyperthyroid rats.

Effect of Mustard oil Ingestion on Thyroid Hormones Concentration in Serum of Rats with Hypo and Hyperthyroidism

Table (2) show the effect of mustard oil ingestion on thyroid hormones (FT3, FT4 and TSH) of rats with hypo & hyperthyroidism. Results revealed that serum concentration of FT3 and FT4 of rats with hypothyroidism were decreased significantly, however, their concentration were increased significantly when rats were become hyperthyroid compared with the normal negative group. When animals were fed on the mustard oil, leads to increase the level of FT3 and FT4 in serum (hypothyroid) but did not reach the normal levels for normal rats. The opposite trend was observed at the hyperthyroid rats (G5-7).

TABLE 1. Effect of Mustard oil Ingestion on Body Weight Gain Percent (BWG %), Feed Intake (FI) and Feed Efficiency Ratio (FER) of Rats with Hypo and Hyperthyroidism.

Groups \ Parameters		BWG%	FI (g/day)	FER
Group1 Negative control		67.113.25± b	11.00	0.1400.005± b
Hypothyroid rats	Group2 hypothyroidism	101.903.39± a	12.00	0.1970.006± a
	Group 3 (hypo+1ml oil)	10.941.89± c	9.00	-0.0310.005± c
	Group4 (hypo+2 ml oil)	24.371.04± b	8.25	-0.0750.004± d
Hyperthyroid rats	Group5 (hyperthyroidism)	26.122.56± b	8.50	-0.0770.007± d
	Group 6 (Hyper+1ml oil)	7.132.07± d	9.00	0.0160.006± c
	Group 7 (hyper+2ml oil)	16.861.51± c	10.75	0.0390.003± b

Mean values are expressed as means ± SE.
Means with different superscript letters in the column are significantly different at $P \leq 0.05$.

Concerning thyroid stimulating hormones (TSH) concentration for rats with hypothyroidism (Table 2), it was increased significantly when compared with the normal animals (0.3300.02± ng/dl for G2 vs 0.0230.008± ng/dl for G1). On the contrary, it was decreased significantly with ingestion of mustard oil compared with the hypothyroid group at the two levels of intake (0.2660.01± ng/dl for level 1, 0.1000.005± ng/dl, for level 2 and 0.3300.02± ng/dl for the hypothyroid control group (G2), respectively.

Regarding TSH concentration in serum for hypothyroid rat's data in Table 2 show that it was increased when rats were ingested the mustard oil (G6&7) compared to G5, but non-significant.

Effect of Mustard oil Ingestion on kidney function of Rats with Hypo and Hyperthyroidism

The effect of mustard oil ingestion on kidney functions of rats with hypo and hyper thyroidism was tabulated in Table (3). The creatinine concentrations in serum were increased for the hypothyroid rats (G2). However, no significant differences were detected between negative and the corresponding group representing 0.5330.04±mg/dl and 0.6260.05±mg/dl, respectively. All groups of hypothyroid rats had given mustard oil at all levels of intake showed non-significant differences (0.5760.02± mg/dl and 0.5660.03± mg/dl for level 1 and 2, respectively) compared to both negative and other control groups.

On the other side, data in table (3) illustrated that serum urea concentration was significantly increased as a result of rats become hypothyroidism with mean value of 43.331.66± mg/dl compared with the negative healthy control group fed normal diet (37.660.33±mg/dl). Non-significant differences in urea concentrations of rats group fed on mustard oil at all levels of intake and that of negative control group representing (40.002.08±mg/dl for level and 39.331.45±mg/dl for level 2 vs 37.660.33±mg/dl. Also, the hyperthyroid rats showed the same trends.

In general, ingestion of mustard oil had reduced the elevation of creatinine and urea concentrations in serum for animals suffering from hypo and hyperthyroidism, but non-significant.

TABLE 2. Effect of Mustard oil Ingestion on Thyroid Hormones Concentration in Serum of Rats with Hypo and Hyperthyroidism.

Groups \ Parameters		Free triiodo thyronine (FT3) (pg/dl)	Free thyroxine (FT4) (ng/dl)	Thyroid stimulating hormone (TSH) (ng/dl)
Group1 Negative control		10.961.01± a	8.200.40± a	0.0230.008± d
Hypothyroid rats	Group2 hypothyroidism	1.340.24± d	1.740.03± c	0.3300.02± a
	Group 3 (hypo+1ml oil)	3.570.06± c	2.650.31± c	0.2660.01± b
	Group4 (hypo+2 ml oil)	5.400.33± b	4.460.36± b	0.1000.005± c
Hyperthyroid rats	Group5 (hyperthyroidism)	13.500.44± a	11.370.55± a	0.0010.000± b
	Group 6 (Hyper+1ml oil)	10.961.01± b	8.200.40± b	0.0530.008± b
	Group 7 (hyper+2ml oil)	7.660.31± c	7.230.59± b	0.0900.005± b

Mean values are expressed as means ± SE.
Means with different superscript letters in the column are significantly different at $P \leq 0.05$.

TABLE 3. Effect of Mustard oil Ingestion on Kidney Function of Rats with Hypo and Hyperthyroidism.

Groups \ Parameters		Creatinine (mg/dl)	Urea (mg/dl)
Group1 Negative control		0.5330.04± a	37.660.33± b
Hypothyroid rats	Group2 hypothyroidism	0.6260.05± a	43.331.66± a
	Group 3 (hypo+1ml oil)	0.5760.02± a	40.002.08± ab
	Group4 (hypo+2 ml oil)	0.5660.03± a	39.331.45± ab
Hyperthyroid rats	Group5 (hyperthyroidism)	0.7030.047± a	43.001.73± a
	Group 6 (Hyper+1ml oil)	0.6130.047± a	41.331.45± ab
	Group 7 (hyper+2ml oil)	0.5630.061± a	43.331.76± a

Mean values are expressed as means ± SE.
Means with different superscript letters in the column are significantly different at $P \leq 0.05$.

Effect of Mustard oil Ingestion on Liver Functions of Rats with Hypo and Hyperthyroidism.

Results in Table (4) showed the effect of ingestion of mustard oil on the activity of liver functions of rats with hypo and hyperthyroidism. Rats group suffering from hypothyroidism exhibited significant increase in the level of ALT and AST in serum compared with the negative control group (healthy). However, rats fed on levels (1) and (2) of mustard oil showed significant reduction in ALT and AST concentration compared with the corresponding control groups of rats with either hypo and hyperthyroidism. Thus, we could conclude that mustard oil ingestion improves the ALT and AST activity.

No significant changes in Alkaline phosphatase (ALP) concentration in serum (Table 4) between the control groups (hypo and hyperthyroidism) when compared with the negative control group. Moreover, data showed that when rats were given mustard oil at the two tested levels of intakes (G3&4), reduced the elevated level of ALP that happens in the rats suffering from hypothyroidism(G2) but non-significant difference compared with corresponding rats group. On the contrary, ingestion of different levels of mustard oil in hyperthyroid rats (G6&7) showed significant decrease in ALP concentration compared to the hyperthyroid group fed on the basal diet (G5).

In general, the mustard oil ingestion improved the activities of ALT, AST and ALP in serum of hypo and hyperthyroid rats.

Histopathological Examination of Thyroid Gland:

Microscopically, thyroid gland of the normal (-ve) control rats fed on basal diet revealed normal histopathological structure of thyroid gland (normal follicles lined by flattened epithelium and filled with colloid) (Photo1). Meanwhile, thyroid gland of hypothyroidism positive control group showed obvious changes such as inactivation of follicles in the lobules characterized by flattened lining epithelium, wide lumen which were impacted by massive eosinophilic colloid. (Photo 2).

TABLE 4. Effect of Mustard oil Ingestion on Liver Function of Rats with Hypo and Hyperthyroidism.

Groups / Parameters		Alanin Transaminase (ALT) (U/L)	Aspartate Amino transferase (AST) (U/L)	Alkaline Phosphatase (ALP) (U/L)
Group1 Negative control		48.001.52± b	144.662.33± c	165.663.17± a
Hypothyroid rats	Group2 hypothyroidism	68.001.15± a	210.6610.17± a	179.005.00± a
	Group 3 (hypo+1ml oil)	53.332.40± b	191.005.03± b	177.336.06± a
	Group4 (hypo+2 ml oil)	50.330.88± b	174.332.18± b	172.332.02± a
Hyperthyroid rats	Group5 (hyperthyroidism)	67.001.73± a	167.661.45± a	179.002.64± a
	Group 6 (Hyper+1ml oil)	57.662.84± b	157.331.76± b	171.001.73± b
	Group 7 (hyper+2ml oil)	57.662.02± b	152.331.66± b	168.001.52± b

Mean values are expressed as means ± SE.
Means with different superscript letters in the column are significantly different at $P \leq 0.05$.

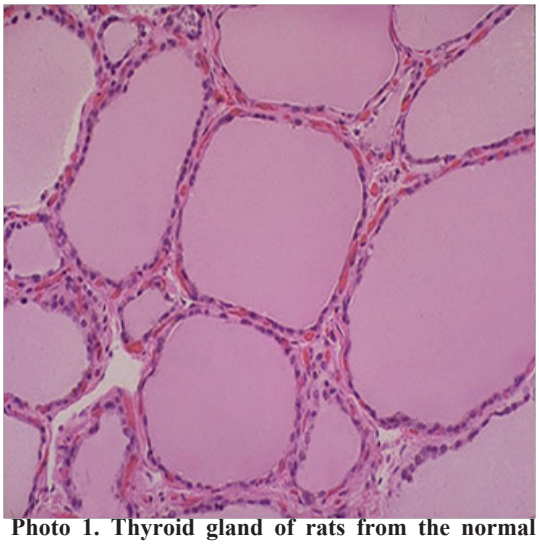

Photo 1. Thyroid gland of rats from the normal negative control group.

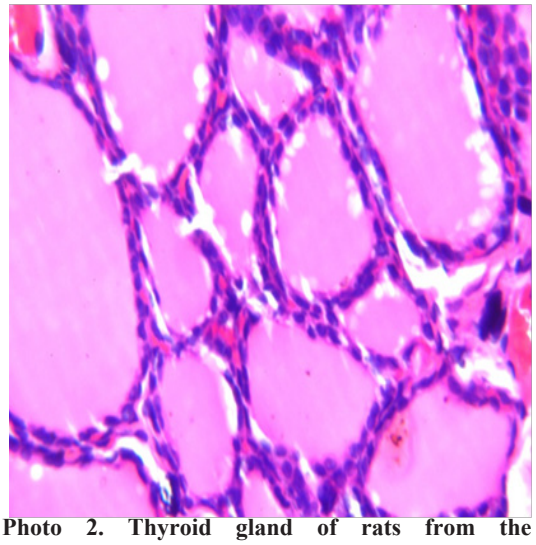

Photo 2. Thyroid gland of rats from the hypothyroidism positive control group.

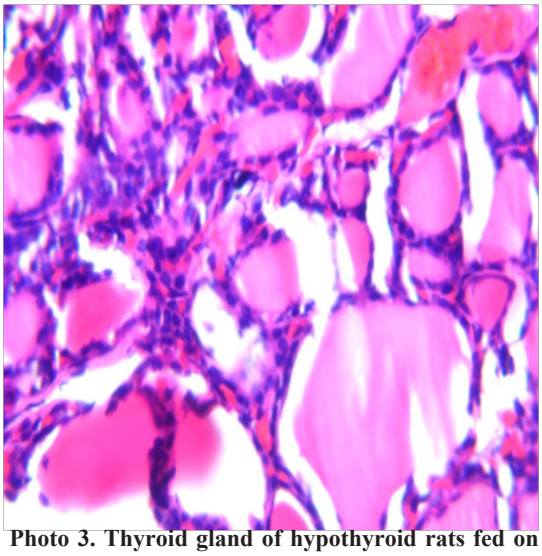

Photo 3. Thyroid gland of hypothyroid rats fed on Mustard oil at level (1).

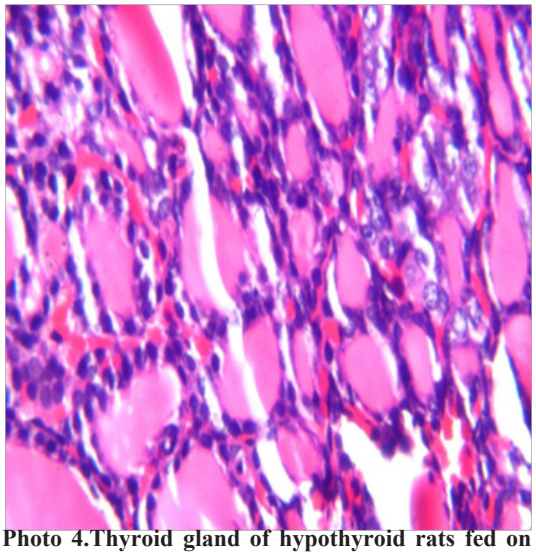

Photo 4.Thyroid gland of hypothyroid rats fed on mustard oil at level (2).

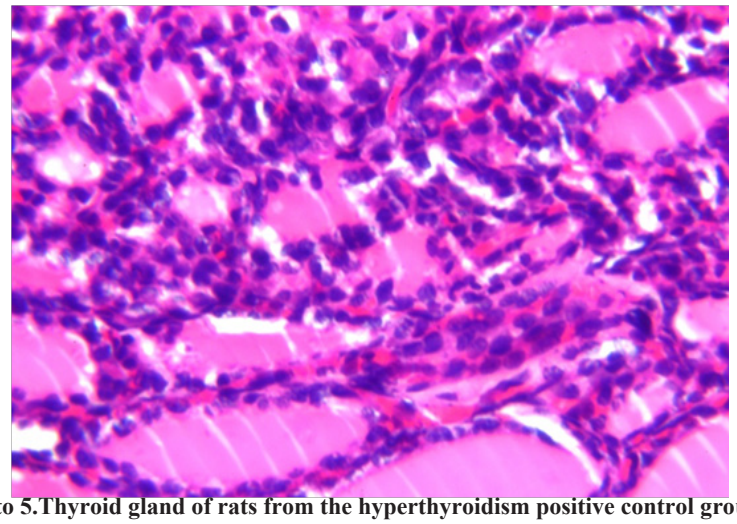

Photo 5.Thyroid gland of rats from the hyperthyroidism positive control group.

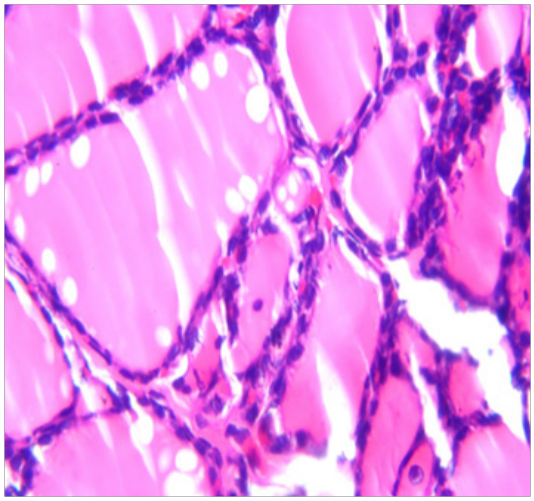

Photo 6.Thyroid gland of hyperthyroid rats fed on Mustard oil at level (1).

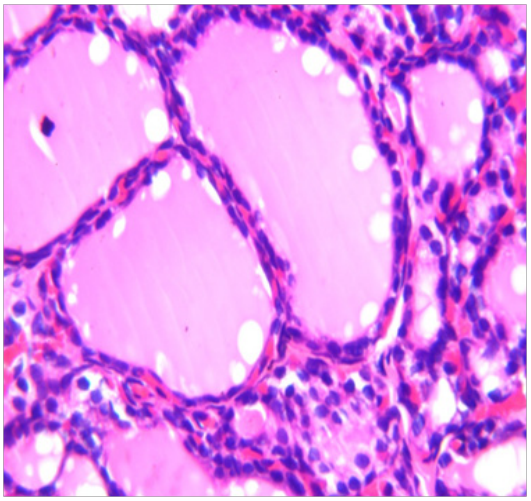

Photo 7. Thyroid gland of hypothyroid rats fed on Mustard oil at level (2).

Discussion

Mustard seed oil has been found to get important phytochemicals like tannins, flavonoids and alkaloids (Rosengarten, 1989). Mustard (Sinapis alba) commonly called yellow or white mustard; they are widely used over the world as spices and condiments in daily cooking. They are recognized for their antioxidant properties (El-Ghorab et al., 2010).

In the present study, the amount of food intake (FI) and the body weight gain percent of hypothyroid rats were increased more than the normal control group. In addition, the BWG% of hypothyroid rats was increased (34.79 %) than the negative control rats. Cadnapaphornchal et al., (2003) illustrated that hypothyroidism (HT) is a metabolic disorder, which is generally associated with disturbance in FI which is reflected by body weight of individual.

Our study showed that the hyperthyroid rat group had significant reduction in body weight. These results are in agreement with a study by El-Kotb et al., (2014) who found that hyperthyroidism rats showed significant decreases in body weight and the strength of skeletal muscle contraction. Also, excess thyroid hormone affects many different organ systems .Commonly reported symptoms are symptoms include ophthalmopathy, thyroid dermopathy, and thyroid acropachy in Graves' disease; globus sensation, dysphagia, or orthopnoea due to oesophageal or tracheal compression in nodular goitre.

Ophthalmopathy, also known as Graves' orbitopathy, occurs in 25% of patients with Graves' disease. (Goichot et al., 2015, and Boelaert et al., 2010).

Results of our study revealed that there was a significant increase in the serum concentration of TSH in hypothyroid rats compared with control group, while, there was a significant decrease in the serum concentration of T4, T3 compared with the control, these are in agreement with the finding of Sener, et al., (2006) and Kandir and keskin (2016).

L-thyroxin was used to induce hyperthyroidism in rat, the mechanism for this response is a decrease in TSH levels due to the increases in FT3 and FT4 levels as stated by Mogulkoc et al., (2006). In hypothyroidism state, the level of free T4 (FT4) is decreased and TSH is increased. In hyperthyroidism is opposite (Kostoglou-Athanassiou, Ntalles, 2010). In our study induction of hypothyroidism, leads to reduction in serum thyroid hormones level of FT3 and FT4 with increase in serum TSH level compared to the normal control rats. These results are in agreement with Alkalby, and Alzerjawi, (2013),. They found that there was a significant increase in the serum concentration of TSH in hypothyroid treated group compared with the control one, while, there was a significant decrease in the serum concentration of T4 and T3.

Hyperthyroidism is a pathological disorder in which excess thyroid hormone is synthesised and secreted by the thyroid gland. It is characterised by normal or high thyroid radioactive iodine uptake (thyrotoxicosis with hyperthyroidism or true hyperthyroidism (Leo, et al., 2016). In a study by Kravets, (2016) illustrated that hyperthyroidism state exhibited an excessive concentration of thyroid hormones in tissues caused by increased synthesis of these hormones.

In the present study the kidney functions (urea, creatinine) in both groups of hypo and the hyperthyroidism, exhibited significant increases in both urea and creatinine concentration in serum compared to normal control group. In addition, the ingestion of mustard oil at level2 showed significant decreases in hypo and hyperthyroid animals. These results are in agreement with the finding of El-Shenawy et al., (2014) who showed that mustard oil significantly lower kidney functions in the tissues by 52.7%, as compared to corn oil.

Chronic kidney disease (CKD) redounds both hypothalamus–pituitary–thyroid axis and thyroid hormones peripheral metabolism. Uremia impacts the function and size of the thyroid. Uremic patients suffer from increase in thyroid volume compared with subjects with normal renal function and a higher deployments of goiter, mainly in women. (Iglesias and Dı´ez ,2009).

Relation liver functions, data in our study showed that the hypo and hyperthyroid rats groups showed significant excess compared to the negative control group. These results are in agreement with Pinter et al., (2017) who find that thyroid hormone substitution was more often noticed in patients with decreases (TSH) concentration .Another study by Al-Diwan et al., (2016) should that patients with high TSH had larger tumors, while the antonym was true for patients with low TSH concentrations.

Thyroid dysfunction might inconvenience liver function as stated by Khan et al., 2010). Carrion et al., (2010) recorded a positive relation between liver enzymes and thyroid hormones. These findings obtain along with ours.

Histopathological changes in the thyroid gland of PTU-treated rats were observed in the present study. There were characterized by The follicles in the lobules showed inactivation characterized by flattened lining epithelium, wide lumen which were impacted by massive eosinophilic colloid. Hypothyroidism was evidenced histopathological by the hugely follicles over distended with colloid with minimal scalloping (El-Mehi and Amin, 2012). In our study after rats ingested mustared oil, the most of the follicles of thyroid gland were lined by columnar epithelium with round nuclei, narrow lumen and scant colloid. (Cakic-milosevic, et al., 2004). AL – Saeed and Anas (2017) showed that induction of hyperthyroidism with L-T4 characterized by follicular cells and depletion of parafollicular cells, some follicle presents a variety in size of thyroid follicles**.**in the present study. Most of the follicles were active and lined by high columnar epithelium with round nuclei, narrow lumen and scant colloid but after ingestion the rats mustard oil most of the follicles were inactive with flattened lining epithelium, massive colloid and wide cystic lumen. These finding get along with our results.

In conclusions, ingestion of the mustard oil resulted in improvement of biochemical and histopathological changes resulted from hyperthyroidism. Biochemically by significant increase in serum thyroid hormone levels with significant decrease in serum TSH level compared to the hypothyroid rats and opposite in hyperthyroid rats.

Our results concluded that, mustard oil ingestion improves thyroid hormones status as well as liver and kidney functions. Thus, it could be recommended for patients with thyroid dysfunctions due to its beneficial effects.

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