OPEN ACCESS International Journal of Pharmacology

ISSN 1811-7775
DOI: 10.3923/ijp.2019.219.228

Research Article
Impact of Safflower Petals and Moringa Leaves Extracts in Experimental Hyper and Hypothyroidism in Rats

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Abstract

Background and Objective: Hyperthyroidism and hypothyroidism are the most common disorders of thyroid function. The current study aimed to evaluate the prophylactic effect of safflower petals and moringa leaves crude ethanol extracts against thyroid dysfunctions (hyper and hypothyroidism). **Materials and Methods:** Forty-two rats were divided into 7 groups, control normal, hyperthyroidism control, hyper-safflower, hyper-moringa, hypothyroidism control, hypo-safflower and hypo-moringa. L-Thyroxine (0.3 mg kg^{-1} b.wt.) and carbimazole (10 mg kg^{-1} b.wt.) were orally administrated for 3 weeks as hyperthyroid and hypothyroid inducer, respectively. Blood hemoglobin, plasma thyroid-stimulating hormone (TSH), glucose, catalase activity, lipid profile as well as liver and kidney functions were assessed. Histological examination of thyroid gland was carried out. **Results:** The results revealed that hyper and hypothyroidism mediated decrease and increase in TSH values, respectively. Oral administrations of either safflower petals extract or moringa leaves extract improve plasma levels of TSH. Oxidative stress and disturbance in plasma glucose, lipid profile as well as liver and kidney functions were occurred in conjunction with thyroid dysfunctions especially hypothyroidism. Administration of safflower petals extract or moringa leaves extract alleviates the reduction in catalase activity, hyperglycemia and disturbance in lipid profile as well as liver and kidney functions accompanied with thyroid dysfunctions especially hypothyroidism. **Conclusion:** The studied extracts have prophylactic potential against thyroid dysfunctions and the subsequent oxidative stress, hyperglycemia and changes in lipid profile. Crude ethanol extract of safflower petals was promising as prophylactic agents in hyper and hypothyroidism as observed by improving plasma levels of TSH, lipid profile and histopathological changes.

Key words: Thyroid dysfunction, hyperthyroidism, hypothyroidism, safflower petals, moringa leaves, prophylactic effect

Received: October 20, 2018 Accepted: November 23, 2018 Published: January 15, 2019

Citation: Doha A. Mohamed, Sherein S. Abdelgayed, Rasha S. Mohamed and Hend A. Essa, 2019. Impact of safflower petals and moringa leaves extracts in experimental hyper and hypothyroidism in rats. Int. J. Pharmacol., 15: 219-228.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Thyroid hormones play an important role in growth and metabolic control, therefore being necessary to normal development and energy expenditure[1]. Convenient thyroid function is necessary to physiological body functions[2]. Since growth, metabolism, development of cells and neurons, maturation of bone, metabolism of the oxidative and regulation of red blood cells production are affected by thyroid hormones[3]. Dysfunction in the thyroid gland either excessive secretion (hyperthyroidism or thyrotoxicosis) or low secretion (hypothyroidism) leads to impairment in the physiological body functions. Hypothyroidism leads to constipation, weight gain, decreased sweating, fatigue, lethargy, cold intolerance, change in voice, changes in cholesterol metabolism, cardiovascular diseases and decreased metabolic rate[1,4]. Hyperthyroidism is a catabolic syndrome and the most common symptoms associated with it are diarrhea, increased metabolic rate, hyperactivity, nervousness, polyuria, tachycardia and loss of lean body mass[1,5]. Hyperthyroidism and hypothyroidism are associated with oxidative stress and excessive production of free radicals[6]. These free radicals not only responsible for the DNA damage but also interfere with the intracellular signaling. Altered cellular functions can be caused by the change in the intracellular redox status[7]. Both hyperthyroidism and hypothyroidism are considered reversible causes of several health problems and diseases such as dementia and Alzheimer's disease[8], diabetes mellitus[9] and impairment in the reproduction especially in female[10]. Although, hypothyroidism can be treated using thyroid hormone replacement but this therapy exhibits various side effects among them, changes in the cardiovascular system, hypertrophy of the left ventricular and reduction in the mass and density of bone[11]. Agranulocytosis, a deficiency of granulocytes in the blood, causing increased vulnerability to infection is considered one of the most dangerous side effects of the thyroid dysfunction drugs and therapies[12]. Therefore, there is a need not only for safer modalities and therapies but also early protective agents for thyroid disorders and subsequent dysfunctions.

Safflower dried petals (*Carthamus tinctorius* L., Asteraceae) have not been only used as a natural source of dyes in food[13] but also as a tea in India and China[14,15]. China, Egypt, India and Iran are among the most cultivated countries of this plant[16]. Flavones, serotonin derivatives, glycosides, steroids, alkandiols as well as polyacetylenes are among the photochemical in safflower petals[17,18]. Phyto-pharmaceuticals present in safflower petals possessed different biological activities such as anti-inflammatory, neurotropic, anti-oxidant, hepato-protective[19,20], diuretic agent[21] and improving blood circulation agent[17].

Moringa leaves (*Moringa oleifera*, Family Moringaceae) are the most used portion in the plant[22]. Moringa leaves powder can be utilized in the fortification of bakery products and to improve the gluten free bread[23]. Also the extract of moringa leaves can be used to elevate the nutritional value and the shelf life of food products[24]. Moringa is a good source of protein, essential amino acids and anti-oxidants as well as vitamins and minerals[25]. Flavonoids, isothiocyanates, glycosides, β-sitosterol, benzyl glucosinolates and saponins are among the phytochemicals in moringa[26]. The content of moringa leaves of such bioactive phytochemicals makes them of biological importance as anti-inflammatory, anti-cancer, anti-oxidant, hepato-protective and neuro-protective[25]. The current study was carried out to evaluate the prophylactic effect of crude ethanol extract of safflower petals and moringa leaves against the thyroid dysfunction (hyperthyroidism and hypothyroidism) induced in rats. Biochemical and nutritional changes associated with both hyperthyroidism and hypothyroidism were assessed in rats. The aim also included determination of total phenolic content of crude ethanol extract of safflower petals and moringa leaves.

MATERIALS AND METHODS

All the experimental work was done in the National Research Centre, Cairo, Egypt, except for the histopatological examination which done in Faculty of Veterinary Medicine, Cairo University, Egypt at the period from October, 2017 till February, 2018.

Materials

Plant materials: Safflower dried petals and moringa dried leaves were purchased from local market, grinded using electrical grinder and kept in polyethylene bags in the refrigerator until the extraction.

Animals: Male albino rats, of 183.57±12.35 g as Mean±SD were used. Animals were obtained from the animal house of National Research Centre, Cairo, Egypt. The animals were kept individually in stainless steel cages at room temperature. Water and food were given *ad-libitum*.

Diets: Balanced diet was prepared to contain 10% protein supplemented from casein, 10% corn oil, 23.5% sucrose, 47% maize starch, 5% fiber, 3.5% salt mixture provided by the AIN-93 formulation[27] and 1% vitamin mixture provided by the AIN-93 formulation[27].

Methods

Preparation of crude ethanol extract of the studying plants: The air-dried powdered of safflower petals and moringa leaves were extracted successively in a continuous extraction apparatus (Soxhlet) until exhaustion with ethanol for preparation of crude ethanol extract. The solvent was completely removed by evaporation under reduced pressure at a temperature not exceeding 40°C. Crude extract of safflower petals and moringa leaves were kept in deep-freeze till used.

Determination of phenolic compounds: Total phenolic compounds were determined in crude ethanol extract of safflower petals and moringa leaves using Folin-Ciocalteu reagent[28]. Absorbance was measured at 765 nm. The total phenolic content was expressed as gallic acid equivalents (GAE) in mg g^{-1} extract. The results were expressed as Mean±SE.

Preparation of dosage form: Crude ethanol extract of safflower petals and moringa leaves were dispersed separately in water using gum acacia powder to be given orally to rats.

Design of the animal study: Forty two rats were used in the current study. L-Thyroxine (0.3 mg kg^{-1} b.wt.) was used to induce hyperthyroidism, while carbimazole (10 mg kg^{-1} b.wt.) was used to induce hypothyroidism. After one week of acclimation, rats were divided into 7 groups of six rats each as follows:

- **Group one:** Normal healthy group (control normal)
- **Group two:** Where rats were kept untreated for 1 week then given daily oral dose of L-thyroxine (0.3 mg kg^{-1} b.wt.) (hyperthyroidism control) for 3 weeks
- **Group three:** Where rats were given daily oral administration of crude ethanol safflower petals extract (300 mg kg^{-1} b.wt.) for 1 week then post-treated orally with L-thyroxine (hyper-safflower) along with the safflower petals extract for further 3 weeks
- **Group four:** Where rats were administered orally with moringa leaves crude ethanol extract (300 mg kg^{-1} b.wt.) for 1 week then post-treated orally with L-thyroxine (hyper-moringa) along with the safflower petals extract for further 3 weeks
- **Group five:** Where rats were kept untreated for 1 week then treated orally by carbimazole (10 mg kg^{-1} b.wt.) (hypothyroidism-control) for 3 weeks
- **Group six:** Where rats were administered orally by safflower petals crude ethanol extract (300 mg kg^{-1} b.wt.) for 1 week then post-treated orally with carbimazole (hypo-safflower) along with the safflower petals extract for further 3 weeks
- **Group seven:** Where rats were given daily oral dose of moringa leaves crude ethanol extract (300 mg kg^{-1} b.wt.) for 1 week then post-treated orally with carbimazole (hypo-moringa) along with moringa leaves extract for further 3 weeks

All rats groups were fed on balanced diet all over the study period (4 weeks). During the experiment, body weight and food intake were recorded weekly. At the end of the study total food intake, body weight gain and feed efficiency ratio were calculated. Blood samples were collected from all rats after an overnight fast. A portion of the whole blood was analyzed for hemoglobin (Hb) concentration[29]. The remaining blood was centrifuged and the plasma was analyzed for thyroid-stimulating hormone (TSH) using Enzyme Linked Immunosorbent Assay (ELISA), fasting blood glucose levels[30], total cholesterol (T-Ch)[31], high-density lipoprotein cholesterol (HDL-Ch)[32], low-density lipoprotein cholesterol (LDL-Ch)[33] and triglycerides[34]. Plasma levels of creatinine and urea were determined depending on Larsen[35] and Fawcett and Scott[36] in succession as indicators of kidney function. The activities of aspartate transaminase (AST) and alanine transaminase (ALT) were determined according to Reitman and Frankel[37] as liver function indicator. Catalase activity[38] was determined as indicator of oxidative stress. Rats were dissected and thyroid gland was immediately separated from each rat then immersed in 10% formalin solution for histological examination. This study has been carried out according to the Ethics Committee, National Research Centre, Cairo, Egypt and followed the recommendations of the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985).

Statistical analysis: The results of animal experiments were expressed as the Mean±SE and they were analyzed statistically using the one-way analysis of variance ANOVA followed by Duncan's test. In all cases $p<0.05$ was used as the criterion of statistical significance.

RESULTS

Total phenolic compounds (Table 1) were present in crude ethanol extract of safflower petals by 133.2 mg GAE/g extract and in moringa leaves by 74.3 as mg GAE/g.

It was notable from the results (Table, 2) that oral administration of L-thyroxine (0.3 mg kg^{-1} b.wt.) as hyperthyroidism inducer was accompanied with decreasing of body weight gain, while carbimazole (10 mg kg^{-1} b.wt.) as hypothyroidism inducer was accompanied with increasing of body weight gain. Since the hyperthyroid control group showed the lowest final body weight (197.50 g) and the lowest body weight gain (13.83 g) compared to the other groups, while the hypothyroid control group showed the highest final body weight (222.67 g) and the highest body weight gain (38.83 g) compared to the other groups. Administration of either safflower petals extract or moringa leaves extract combated the decreasing of body weight gain subsequent to hyperthyroidism induction. On the other hand, administration of either safflower petals extract or moringa leaves extract combated the increasing of body weight gain subsequent to hypothyroidism induction.

Results of blood hemoglobin, plasma TSH, plasma glucose and plasma catalase are tabulated in Table 3. With regard to TSH, the results declared that significant decrease in TSH values occurred subsequent to hyperthyroidism induction, while an increase in TSH values occurred subsequent to hypothyroidism induction. Oral administration with either safflower petals extract or moringa leaves extract combated the decreasing in TSH values caused by hyperthyroidism induction. On the other side, treatment orally with either safflower petals extract or moringa leaves extract combated the increasing in TSH values caused by hypothyroidism induction. As for hemoglobin values, there were not significant changes between the different groups. Elevation in the glucose values occurred subsequent to either hyperthyroidism or hypothyroidism induction. Oral treatment with either safflower petals extract or moringa leaves extract diminished these elevations in the glucose values. Significant decreasing in the catalase activity values occurred subsequent to either hyperthyroidism or hypothyroidism induction though this decreasing was higher in the hypothyroid control group (617.22 U L^{-1}) than hyperthyroid control group (724.44 U L^{-1}). Both safflower petals extract and moringa leaves extract limit of the decreasing in the catalase activity values, although the safflower petals extract was significantly more effective.

Results in Table, 4 illustrated that hyperthyroidism showed non-significant changes in plasma lipid profile in all the experimental groups, while significant elevation in the

Table 1: Total phenolic content (mg GAE/g extract) of safflower petals and moringa leaves crude ethanol extract

Extracts	Total phenolic content (mg GAE/g extract)
Safflower petals crude ethanol extract	133.2±4.532
Moringa leaves crude ethanol extract	74.3±5.146

Table 2: Nutritional parameters of different experimental groups

Groups	Initial body weight (g)	Final body weight (g)	Body weight gain (g)	Total food intake (g)	Feed efficiency ratio
Control normal	183.67±4.61^{a}	221.00±6.440^{ab}	37.33±4.50^{b}	367.83±12.98^{a}	0.10±0.01^{b}
Hyper-control	183.67±5.06^{a}	197.50±10.25^{a}	13.83±9.50^{a}	391.00±20.14^{ab}	0.03±0.02^{a}
Hyper-safflower	183.33±7.00^{a}	215.67±6.370^{ab}	32.33±6.43^{ab}	393.33±2.810^{ab}	0.08±0.02^{ab}
Hyper-moringa	183.50±3.84^{a}	212.83±3.730^{ab}	29.33±3.74^{ab}	409.00±8.420^{b}	0.07±0.01^{ab}
Hypo-control	183.83±5.49^{a}	222.67±5.790^{b}	38.83±3.00^{b}	403.00±3.000^{ab}	0.08±0.03^{ab}
Hypo-safflower	183.33±7.39^{a}	200.17±10.92^{ab}	16.83±6.35^{a}	374.33±10.36^{ab}	0.04±0.02^{a}
Hypo-moringa	183.67±3.62^{a}	215.17±5.140^{ab}	31.50±5.47^{ab}	401.17±8.410^{ab}	0.08±0.01^{ab}

In each column same letter means non-significant difference while different letter means significant difference at 0.05 probability. The data are expressed as mean values±standard error

Table 3: Blood hemoglobin, plasma TSH, glucose and catalase of different experimental groups

Groups	TSH (ng mL^{-1})	Hb (g dL^{-1})	Glucose (mg dL^{-1})	Catalase (U L^{-1})
Control normal	0.53±0.04^{a}	14.94±0.39^{a}	50.96±1.90^{a}	763.40±8.050^{d}
Hyper-control	0.30±0.01^{a}	14.59±0.23^{a}	78.19±3.78^{cd}	724.44±6.310^{c}
Hyper-safflower	0.44±0.02^{a}	14.82±0.11^{a}	62.81±3.65^{b}	742.65±4.990^{cd}
Hyper-moringa	0.33±0.02^{a}	14.56±0.19^{a}	56.63±1.38^{ab}	725.44±14.72^{c}
Hypo-control	15.69±0.64^{d}	14.59±0.42^{a}	80.04±1.64^{cd}	617.22±10.65^{a}
Hypo-safflower	6.95±0.35^{b}	14.67±0.21^{a}	75.95±1.79^{c}	659.60±4.950^{b}
Hypo-moringa	9.03±0.39^{c}	14.69±0.27^{a}	76.30±1.64^{c}	629.44±14.11^{a}

In each column same letter means non-significant difference while different letter means significant difference at 0.05 probability. The data are expressed as mean values±standard error. TSH: Thyroid stimulating hormone, Hb: Hemoglobin

Table 4: Lipid profile of different experimental groups (Mean±SE)

Groups	T-Ch (mg dL^{-1})	TG (mg dL^{-1})	HDL-Ch (mg dL^{-1})	LDL-Ch (mg dL^{-1})
Control normal	59.75±1.03^{b}	70.80±1.29^{a}	22.38±0.53^{b}	23.21±0.83^{a}
Hyper-control	58.38±1.40^{b}	69.80±1.54^{a}	21.97±0.66^{b}	22.44±1.28^{a}
Hyper-safflower	57.63±2.05^{b}	70.71±2.46^{a}	22.71±0.62^{b}	20.77±2.19^{a}
Hyper-moringa	51.29±1.12^{a}	66.87±1.54^{a}	21.87±0.58^{b}	16.04±0.90^{a}
Hypo-control	80.63±2.06^{d}	79.65±2.35^{b}	20.00±0.58^{a}	44.70±2.38^{c}
Hypo-safflower	69.37±1.58^{c}	78.71±1.78^{b}	22.38±0.25^{b}	31.25±1.90^{b}
Hypo-moringa	68.53±3.64^{c}	80.90±1.36^{b}	21.38±0.51^{ab}	30.97±3.13^{b}

In each column same letter means non-significant difference while different letter means significant difference at 0.05 probability. The data are expressed as mean values±standard error. T-Ch: Total cholesterol, TG: Triglycerides, HDL-Ch: High density lipoprotein-cholesterol, LDL-Ch: Low density lipoprotein-cholesterol

Table 5: Liver and kidney functions of different experimental groups (Mean±SE)

Groups	ALT (U L^{-1})	AST (U L^{-1})	Urea (mg dL^{-1})	Creatinine (mg dL^{-1})
Control normal	31.67±0.84^{a}	26.50±2.55^{a}	23.20±0.54^{ab}	0.44±0.01^{ab}
Hyper- control	33.83±2.04^{ab}	32.33±1.28^{a}	28.31±1.54^{bc}	0.47±0.06^{abc}
Hyper- safflower	34.00±1.95^{ab}	24.83±4.69^{a}	26.90±1.91^{abc}	0.49±0.09^{abc}
Hyper- moringa	33.00±2.11^{ab}	24.50±0.85^{a}	22.47±1.93^{a}	0.42±0.05^{a}
Hypo- control	38.50±1.50^{b}	26.50±1.93^{a}	28.71±2.46^{c}	0.62±0.02^{c}
Hypo- safflower	38.00±2.32^{b}	28.00±4.42^{a}	22.28±1.52^{a}	0.57±0.04^{abc}
Hypo- moringa	39.17±2.30^{b}	26.50±2.74^{a}	26.16±1.50^{abc}	0.59±0.05^{bc}

In each column same letter means non-significant difference while different letter means significant difference at 0.05 probability. The data are expressed as mean values±standard error. AST: Aspartate transaminase, ALT: Alanine transaminase

total cholesterol, triglycerides and LDL-Ch values occurred subsequent to hypothyroidism induction, while HDL-Ch plasma levels significantly decreased in the hypothyroid control group (20.00 mg dL^{-1}). Oral administration of either safflower petals extract or moringa leaves extract limit of both the increasing of total cholesterol and LDL-Ch values and the decreasing of HDL-Ch caused by hypothyroidism induction.

As notable from the results in Table 5, either hyperthyroidism or hypothyroidism induction resulted in both liver and kidney dysfunctions though the hypothyroidism was more effective in the liver and kidney dysfunctions. Oral treatment with either safflower petals extract or moringa leaves extract limit of the elevations in the urea and creatinine values caused by either hyperthyroidism or hypothyroidism induction.

Histopathological examination of the thyroid gland: The histopathological examination of thyroid gland of rat of normal control group showed normal and healthy follicles, normal epithelium and intact basement membrane was noted (Fig. 1a). Thyroid gland of hyperthyroidism control group showing hyperplastic follicles, infolding epithelium was noted (Fig. 1b). In Fig. 1c, thyroid gland of hyperthyroidism rats given safflower petals crude ethanol extract showed healthy follicles and absence of infolding epithelium. Thyroid gland of hyperthyroidism rats given moringa leaves crude ethanol extract showed healthy follicles and absence of infolding epithelium (Fig. 1d). Thyroid gland of hypothyroidism control group showed atrophied follicles. The thickening of inter and intralobular stroma connective tissue with leucocytic cells infiltrations were noted (Fig. 1e). Thyroid gland of hypothyrodisim rats given safflower petals crude ethanol extract showed normal histological features. Normal sized follicles and normal thickening of inter and intra-lobular stroma connective tissue together with absence of leucocytic cells were noted (Fig. 1f). Thyroid gland of hypothyrodisim rats given moringa leaves crude ethanol extract showed normal histology. Normal sized follicles and the decreased thickening of inter and intra-lobular stroma connective tissue together with absence of leucocytic cells were noted (Fig. 1g).

DISCUSSION

In the current research total phenolic content of crude ethanol extract of safflower petals was 133.2±4.532 mg GAE/g extract. This result is less than the results of Kruawan and Kangsadalampai[39] who reported that water extract of safflower flowers contains 139.98±18.02 mg GAE/g. Crude ethanol extract of moringa leaves contain 74.3±5.146 as mg GAE/g extract as observed in the present study. This result is in agreement with the results of Castillo-López *et al.*[40], who reported that moringa leaves contain 76.63±10.63 and 71.08±12.05 as mg GAE/g in moringa long and short pod, respectively.

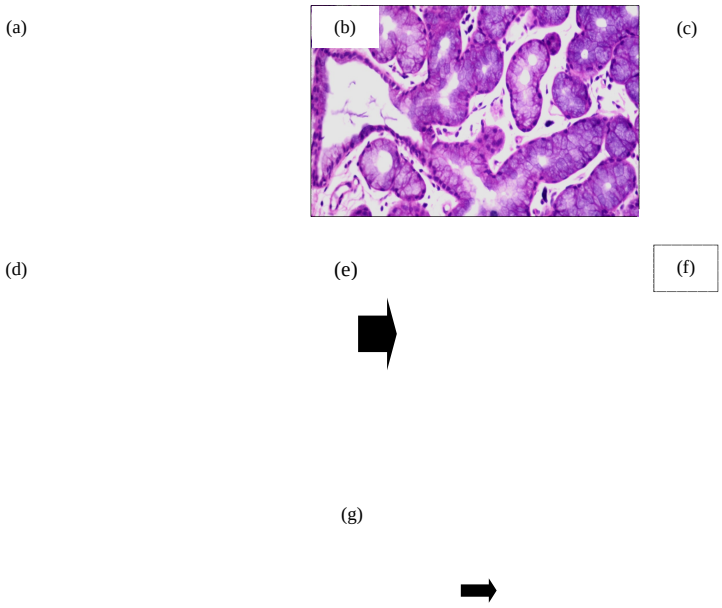

Fig. 1(a-g): (a) Thyroid gland of control normal (H and E X 400), (b) Thyroid gland of hyperthyroidism control group (H and E X 400) arrows = hyperplastic follicles, infolding epithelium, (c) Thyroid gland of hyperthyroidism rats given safflower petals crude ethanol extract (H and E X 400) arrows = healthy follicles and absence of infolding epithelium, (d) Thyroid gland of hyperthyroidism rats given moringa leaves crude ethanol extract (H and E X 400) arrows= healthy follicles, and absence of infolding epithelium, (e) Thyroid gland of hypothyroidism control group (H and E X 400) arrow head = thickening of inter and intralobular stroma connective tissue, arrows = leucocytic cells infiltrations, (f) Thyroid gland of hypothyroidism rats given safflower petals crude ethanol extract (H and E X 400) arrows = normal sized follicles and (g) Thyroid gland of hypothyroidism rats given moringa leaves crude ethanol extract (H and E X 400) arrows = normal sized follicles

Hyperthyroidism and hypothyroidism are the most common disorders of thyroid function[41]. Hypothyroidism may be without clinical signs or obvious symptoms which is defined as subclinical hypothyroidism (SH) as stated by Jain *et al.*[42] or may be accompanied by some symptoms (overt hypothyroidism). In the current research hyperthyroid rat model was induced by oral administration of thyroxin (eltroxin) while hypothyroid rat model was induced by oral administration of carbimazole (anti-thyroid agent). The increase in body weight gain associated with hypothyroidism present in the current study may be a consequence of elevated energy availability related to the slow metabolic processes in hypothyroidism state[43]. Thyroid stimulating hormone (TSH) or thyrotropin was considered one of the pituitary glycoprotein hormones family. It is secreted from the hypothalamus and stimulates the production of thyroid hormones from the thyroid gland by binding its receptor which is known as TSH receptor[44]. American thyroid association and American Association of Clinical Endocrinologists guidelines recommend serum TSH measurement as the single most reliable test to diagnose all common forms of hypothyroidism and hyperthyroidism particularly in the ambulatory setting[45]. The results of the present study declared that the experimentally induced hyperthyroidism could decrease plasma TSH values while the experimentally induced hypothyroidism could increase plasma TSH values. Oral administration of either safflower petals extract or moringa leaves extract to hyperthyroid rats could attenuate the reduction of plasma TSH. On the other hand, oral administration of either safflower petals extract or moringa leaves extract to hypothyroid rats could attenuate the elevation of plasma TSH. The beneficial effect of plants

especially in hypothyroid rats may be attributed to selenium (Se) and zinc (Zn) since Moyo *et al*.[46] reported that the dried leaves of moringa contained selenium (363 mg kg^{-1}) and zinc (13.03 mg kg^{-1}). Ibrahim *et al*.[47] suggested that Zn and Se could be utilized as good therapies for hypothyroid patients and also stated that thyroid function not only affected by iodine but also with selenium which has an important effect in the control of thyroid hormones metabolism. Selenium is important not only for iodothyronine deiodinase (selenoprotein), the enzyme which controls of the conversion of T_4 hormone to its active form T_3 hormone but also for glutathione peroxidases which are involved in the protection of thyroid gland[48]. The biologically active confirmation of T_3 receptor depends on Zinc[49]. The results of the present study declared that hyperglycemia was promoted by both hyperthyroidism and hypothyroidism. Wang[50] stated that type 2 diabetes may be occur in patients suffering from thyroid dysfunction due to the disturbance in genetic expression of various genes in conjunction with physiological abnormality resulted in impairment of the glucose consumption by muscles, elevation of hepatic glucose output and increasing in the glucose absorption from intestine. Lyu *et al*.[51] suggested that the function of pancreatic β cells may be modified by TSH via TSH receptor. Either subclinical hypothyroidism or overt hypothyroidism results in insulin resistant (IR) thus hyperglycemia can be promoted[52]. It is noteworthy that oral administration of either safflower petals extract or moringa leaves extract could attenuate the elevation of plasma glucose values either in hyperthyroid rats or hypothyroid rats. This effect may be due to prophylactic effect of these extracts against hyperthyroidism and hypothyroidism caused hyperglycemia. The studied extracts contain phenolic compounds as shown in the present results. Phenolic compounds plays an important role in protect and treat human from illness[53]. Also the studied plants contain several phytochemicals such as flavones and polyphenols either in safflower petals[54] or in moringa leaves[46]. Phytochemicals possess beneficial effect as hypoglycemic agents[55]. Also safflower petals and moringa leaves contain several phytochemicals which possess anti-oxidant activities since Salem *et al*.[56] reported the anti-oxidant activities of the carthamin dye extracted from safflower petals. Safflower petals also contain quercetin, kaempferol, 6-hydroxykaempferol and chalcones such as hydroxysafflor yellow A, safflor yellow A and safflamin A and C[57]. Moringa leaves contain several anti-oxidants such as β-carotene[46], vitamin C and E[58]. The studied plant content of anti-oxidants interprets their role in attenuation of the reduction in plasma catalase activity which occurred subsequent to thyroid dysfunction especially in hypothyroidism state. Poncin *et al*.[59,60] reported that TSH is implicated in the excessive production of H_2O_2 which results in increased formation of free radicals. Peepre *et al*.[61] recommended with utilization of vitamin C and E as potent antioxidants to prevent thyroid disorders. The results of the present study indicated to that there were not significant changes in plasma lipid profile occurred subsequent to hyperthyroidism induction while hypothyroidism induction resulted in elevations in the total cholesterol, triglycerides and LDL-Ch values in association with reduction in HDL-Ch values. Either overt or subclinical hypothyroidism are associated with lipid profile abnormalities since the genes expression of the key enzymes involved in lipid metabolism can be increased by thyroid dysfunctions[62]. HMG-CoA reductase (the first step in cholesterol biosynthesis) and the upregulation of LDL receptors that mediate the uptake of LDL-Ch are affected by elevated TSH[63]. The effective role of studied plants in attenuation of the disturbed lipid profile may be attributed to above mentioned phytochemicals and anti-oxidants. The results of the present study indicated that the hypothyroidism was more effective in the liver and kidney dysfunctions may be due to the increased oxidative stress and disturbed lipid profile that accompanied to hypothyroidism. Rabeh and El-Ghandour[64] reported that the basal metabolic rate of hepatocytes as all the cells of the body can be regulated by the thyroid hormones and thereby any modulation in the thyroid hormones may be modify liver functions.

CONCLUSION

It was concluded that both crude ethanol extract of safflower petals and moringa leaves has prophylactic potential against thyroid dysfunctions and the subsequent oxidative stress, hyperglycemia and changes in lipid profile. These prophylactic effects of safflower petals and moringa leaves may be due to presence of phenolic compounds and their hypoglycemic, hypolipidemic as well as anti-oxidant properties. Crude ethanol extract of safflower petals was the most promising in the present research. So, crude ethanol extract of safflower petals and moringa leaves may be recommended as nutraceuticals or dietary supplement for protection from thyroid dysfunctions especially hypothyroidism.

SIGNIFICANCE STATEMENT

This study discovers that crude ethanol extract of safflower petals and moringa leaves could be beneficially used as prophylactic for thyroid dysfunction (hyperthyroidism

and hypothyroidism). Both extract contain high content of phenolic compounds. Both extracts showed promising effect against thyroid dysfunction, especially hypothyroidism and their deterioration. This study will help the researcher to find new extracts that may be used as nutraceuticals for prevention of hyper or hypothyroidism. Thus a new strategy on the treatment of thyroid disorders may be used.

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