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Evaluation of the Activity of Some Plants Extracts on Thyroid Gland Regulation in Female Albino Rats

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Abstract

This study sheds light on various drugs of plant origin which have shown action on thyroid and its functioning as well as on the various factors associated with thyroid dysfunction. Therefore, the aim of this study is to determine the activity of the aqueous extracts of *Fucus vesiculosus*, *Coleus forskohlii*, *Curcuma longa* L., *Rosmarinus officinalis* L., *Camellia sinensis* L. and *Melissa officinalis* L. in regulation of thyroid hormones in serum taken from rats. Fifty-seven female albino rats were divided into 19 groups, each group with 3 rats, and treated orally with an aqueous plant extract in three different doses, except the control group which was treated with normal saline only. Also, a histological study was conducted on the thyroid gland after short-term treatment with different doses of these extracts. The results demonstrated that 5mg/kg of *Curcuma longa* was the most powerful extract which increased T3 level in a rats serum by 25% compared with the control treatment. Also, the most effective dose which increased T4 level was 1000mg/kg of *Coleus forskohlii*, which increased the hormone level by 7% compared with the control. Meanwhile, 1000mg/kg of *Coleus forskohlii* was the effective extract which reduced TSH level by 61% compared with the control. While, the extract of *Rosmarinus officinalis* 220mg/kg reduced T3 and T4 levels in the serum of rats by 56% and 17% respectively. However, oral administration with *Camellia sinensis* 1.25mg/kg increased TSH level by 10% compared with the control. The obtained data demonstrated that *Curcuma longa* and *Coleus forskohlii*, at low doses, can be very effective for completely treating hypothyroidism in rats.The findings of this study propose that the extracts may have the property to regulate thyroid levels in rats.

Keywords: Thyroid gland, hyperthyroidism, hypothyroidism, plant extracts.

تقييم فعالية بعض مستخلصات النباتات الطبية في تنظيم هرمونات الغدة الدرقية في الجرذان

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الخلاصة

سلطت هذه الدراسة الضوء على العديد من الادوية ذات الاصل النباتي والتي أثبتت فعاليتها على الغدة الدرقية وأدائها وكذلك على العوامل المختلفة المرتبطة بضعف الغدة الدرقية. لذلك, الهدف من هذه الدراسة الى تحديد فعالية المستخلصات المائية لنبات الفيوكس, الكوليس, الكركم, اكليل الجبل, الشاي الاخضر والمليسا في

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تنظيم هرمونات الغدة الدرقية في دم الجرذان. تم تقسيم سبعة وخمسين من إناث الجرذان البيضاء في 19 مجموعة كل مجموعة تتالف من 3 جرذان تم تجريعها بثلاث جرع مختلفة عن طريق الفم بالمستخلصات المائية للنباتات المذكورة. عدا مجموعة السيطرة التي تم تجريعها بالنورمال سلاين فقط. ايضا, اجريت دراسة نسيجية للغدة الدرقية بعد التجريع لمدة قصيرة بجرعات مختلفة من هذه المستخلصات. اوضحت النتائج الى ان التجريع بنبات الكركم بجرعة 5 ملغم لكل كيلو له اكبر الاثر بزيادة مستوى هرمون T3 في مصل دم الجرذان بمقدار 25% مقارنة مع معاملة السيطرة. كذلك مستوى هرمون T4 ارتفع بمقدار 7% عند التجريع بمستخلص نبات الكوليس بجرعة 1000ملغم لكل كيلوغرام وفي الوقت نفسه خفض مستوى TSH بمقدار 61% مقارنة مع معاملة السيطرة. كما بينت النتائج ان مستخلص نبات اكليل الجبل 220ملغم لكل كيلو قد خفض مستوى كلا من T3,T4 بمقدار 56% و 17% على التوالي. في حين اشارت النتائج الى ان التجريع الفموي بمستخلص نبات الشاي الاخضر ادى الى ارتفاع مستوى TSH بمقدار 10% مقارنة مع معاملة السيطرة.اظهرت البيانات ان نباتي الكركم والكوليس وبجرع قليلة يمكن ان يكونا فعالين للغاية في علاج قصور الغدة الدرقية في الجرذان. تقترح نتائج هذه الدراسة أن هذه المستخلصات قد يكون لها اهمية في تنظيم مستويات الغدة الدرقية في الجرذان.

Introduction:

The thyroid gland is one of the largest endocrine glands of the body that is situated outside of the central nervous system. It is characteristically shaped like a bowtie (or butterfly); the central isthmus joins together its two lateral lobes. It is situated in the midline, anterior to the larynx and trachea, and at the level of the C5 to T1 vertebrae. The normal adult gland has a weight of 20–25 gm [1]. The thyroid is responsible for regulation of oxygen use, basal metabolic rate, cellular metabolism, growth and development [2]. The thyroid gland secretes thyroxine (T4) and triiodothyronine (T3), which are needed for proper growth and development and primarily responsible for determining the basal metabolic rate [3]. The decreased levels of thyroid hormones lead to hypothyroidism, but hyperthyroidism is caused as a result of excessive thyroid function. Hyperthyroidism is often considered synonymous with thyrotoxicosis (a state of thyroid hormone excess) [4]. The World Health Organization has been encouraging countries to employ the traditional medicine in unresolved diseases. Therefore, there is a rising propensity toward application of herbal medicine in chronic diseases. There have been a growing interest to achieve the ability to reduce or cease taking medications for autoimmune thyroid diseases. Herbal medicines, alone or in combination with conventional medication, offer patients that option. Autoimmune diseases, including hyperthyroidism and hypothyroidism disease, are characterized by humeral or cell-medicated immune responses in the body.

The current medical therapies for hypothyroidism are often deemed inadequate because of difficulties in regulating the level of thyroid hormones through use of drugs. Thus, it is worth developing new plant-derived agents that enhance thyroid hormone in hypothyroidism and entail fewer adverse effects. Various herbal plants are available for hyperthyroidism, such as lemon balm (*Melissa officinalis*), rose marry *(Rosmarinus officinalis)* and green tea (*Camellia sinensis*) For treatment of hypothyroidism, herbal plants are also available, such as coleus *(Coleus forskohlii),* turmeric *(Curcuma longa)* and bladder wrack *(Fucus vesiculosus)* [5, 6]. Therefore, the aim of this study was to evaluate the effects of various herbal plants' extracts on the morphology and hormone levels of the thyroid gland in rats.

Materials and methods

1-Collection of plant samples

Plant samples included dry leaves of *Rosmarinus officinalis*, *Camellia sinensis, Melissa officinalis*, rhizome of *Curcuma longa*, roots of *Coleus forskohlii* and thallus of *Fucus vesiculosus* , obtained from local markets in Baghdad, Iraq. Each sample was air dried in shade and grinded by a blender to give small size pieces (2 mm), then stored in glass containers at room temperature in a dry dark place before the extraction step.

2-Preparation of plants aqueous extracts

An aqueous extract was prepared for each plant in different methods according to the plant parts [7]. Then each extract was stored in refrigerator until use. Different concentrations of each plant were prepared by dissolving a certain weight of each plant extract powder in D.W according to the needed

concentration. Then, different concentrations (mg/ml) of plant extracts were prepared according the following equation [8]:

Concentration mg/ml = weight/volume x 1000

3-Laboratory animals

Fifty-seven female albino rats in the age of 8-10 weeks and weight of 60-120g were purchased from the National Center for Drug Control and Research, housed with a temperature range of 27±2Cº, and subjected to the experimental protocol designed by OCED [9]. The experiments were performed in the Research and Production Center for Veterinary Drug which ethically approved all the experimental protocols. The rats were divided randomly into groups; each group was kept in a separate plastic cage. Rats were maintained under standard conditions of ventilations, temperature and humidity. Food and water were available *ad libitum.* All animals were sacrificed at the end of the study.

4-Experimental design

These experiments were designed to evaluate the effects of some medicinal plants on thyroid hormones in female albino rats. The parameters were examined after one month of experiments. Rats were divided into 19 groups, each group with 3 rats. and received three different oral doses (mg/kg) as in Table-1. The doses were diagnosed for each plant based on literatures.

Table 1-Doses of plant aqueous extracts in mg/kg

Plants	Groups	Doses (mg/kg)	References
Fucus vesiculosus	1	50	[10]
	2	100	
	3	150	
Melissa officinalis	4	50	[11]
	5	100	
	6	150	
Coleus forskohlii	7	100	[12]
	8	300	
	9	1000	
Rosmarinus officinalis	10	170	[13]
	11	220	
	12	270	
Camellia sinensis	13	1.25	[14]
	14	2.5	
	15	5	
Curcuma longa	16	5	[15]
	17	10	
	18	20	
Control	Rats treated with normal saline only		

5- Collection of blood samples and organs

Five milliliters (ml) of blood were withdrawn from the heart of the animals directly by cardiac puncture using a medical syringe. Each blood sample was placed in a tube containing a gel free anticoagulant to obtain the serum and centrifuged at 3000 rpm for 15 minutes to ensure a sufficient amount of serum free of red blood cells. The serum was then withdrawn and placed in a special plastic tube, which was kept clean and stored at -20 ° C until used [16].

Biochemical analysis

Previously reported methods were applied to determine the levels of thyroid stimulating hormone (TSH) and Triiodothyronine (T3) [17] in addition to thyroxine (T4) [18].

Histopathological study of thyroid gland

At the end of the studies, all animals were sacrificed by cervical dislocation. Thoracic and neck cavity was cut open to isolate the thyroid gland from each animal. Isolated glands were cleaned off the extraneous tissue and kept in freshly prepared 10% formalin for histopathological analysis [19]. The animals in the histological examination were orally administration with the most effective concentration of each plant extract obtained from the above tests.

Statistical analysis

All data are presented as the mean ±SD (standard deviation). The data were analyzed by one-way ANOVA followed by student t-test using SPSS software package version 17.0 (SPSS Inc., Chicago, IL, USA). The differences were considered significant at $P<0.05$.

Results and Discussion

Thyroid profile assay of the studied groups

1. Effects of *Fucus vesiculosus* on thyroid hormones

The results in Table-2 show the thyroid profile for rats treated with *F. vesiculosus*. The oral administration of *F. vesiculosus* for four weeks indicated that the levels of T3 and T4 were increased, while the level of TSH was decreased. The results indicated that the highest T3 and T4 increases were of 21, 4%, respectively, for 150mg/kg of the same treatment, while the highest TSH reduction was by 13% for 150mg/kg treatment, as compared with the control treatment.

Table 2-The effects of *Fucus vesiculosus* on T3, T4 and TSH levels in rats blood serum

Concentration (mg/kg)	Mean ± SE		
	TSH	**T3**	**T4**
50	2.13 ± 0.08	2.02 ± 0.03	114.33 ± 7.21
100	1.98 ± 0.01	2.13 ± 0.08	119.33 ± 3.71
150	1.89 ± 0.03	2.50 ± 0.06	121.33 ± 2.02
Control	2.16 ± 0.17	2.07 ± 0.08	127.00 ± 1.73
LSD value (P<0.05)	0.116	0.229	6.081

Thyroid hormones are essential for normal body functions, including metabolism, growth, maturation, and reproduction. Thyroid hormone levels are controlled by feedback regulation to the pituitary and hypothalamus [20], which bears primary responsibility for integrating thyroid function with body needs. These results are in agreement with those of a previous study [21], which concluded that the use of algae extract may regulate the thyroid hormones levels and improve the function of the thyroid gland in sera of hypothyroidism animals. The above results may be due to the effects of *F. vesiculosus,* which is rich in iodine and that might help in the metabolism of thyroid hormones [22]. The thyroid gland actively absorbs iodine; it combines iodine with tyrosine in enzymatic reactions to synthesize thyroxine and triodothyronine, the active thyroid hormone. Also, *F. vesiculosus* is rich in fucoidan and polyphenols (phlorotannins), both of which showed powerful antioxidant and anti-inflammatory activities [23] and inhibited lipid peroxidation [24].

2- Effects of *Curcuma longa* on thyroid hormones

The results of thyroid profile assay for treatment with *C. longa* that are shown in Table-3 demobstrate that the level of TSH was decreased, while the levels of T3 and T4 were increased. The results revealed that the highest T3 and T4 increases were by 25 and 5%, respectively, for 5mg/kg of the same treatment, while the maximum reduction in TSH was 58% for 5mg/kg treatment as compared with the control.

Table 3-The effects of *Curcuma longa* on T3, T4 and TSH levels in rats serum

Concentration (mg/kg)	Mean ± SE		
	TSH	**T3**	**T4**
5	0.910 ± 0.03	2.59 ± 0.24	133.67 ± 2.18

10	1.31 ± 0.19	2.54 ± 0.08	131.00 ± 4.35
20	1.52 ± 0.44	2.23 ± 0.18	132.33 ± 2.18
Control	2.16 ± 0.17	2.07 ± 0.08	127.00 ± 1.73
LSD value (P<0.05)	0.841	0.543	9.159

These findings are in agreement with a previous study [25], which found that curcumin induced hypothyroidism in rats by its antioxidant property. Curcumin in turmeric is primarily accumulated in rhizomes and considered to be an effective antioxidant against oxidative tissue damage [26]. Also, curcumin scavenges or neutralizes free radicals by oxygen quenching, making it less available for oxidative reaction [27]. Although, curcumin was found to inhibit cell viability and assist cell apoptosis in a dose-dependent manner in papillary thyroid cancer cells [28].

3- Effects of *Coleus forskohlii* on Thyroid hormones

The results presented in Table-4 demonstrate the that, following treatment with *C. forskohlii* , the level of TSH was decreased, while the levels of T3 and T4 were increased. The results indicated the levels of T3 and T4 were increased to 24 and 7% for 100mg/kg and 1000mg/kg treatments, respectively, while the maximum reduction in TSH level was by 61% for 1000mg/kg treatment as compared with the control.

Table 4-The effects of *Coleus forskohlii* on T3, T4 and TSH levels in rats serum

Concentration (mg/kg)	**Mean ± SE**		
	TSH	**T3**	**T4**
100	0.953 ± 0.14	2.56 ± 0.12	132.67 ± 1.76
300	1.32 ± 0.06	2.30 ± 0.11	130.33 ± 0.88
1000	0.840 ± 0.02	2.50 ± 0.05	136.00 ± 0.57
Control	2.16 ± 0.17	2.07 ± 0.08	127.00 ± 1.73
LSD value (P<0.05)	0.385	0.319	4.382

These results are possibly due to the presence of forskolin in the roots of *C. forskohlii*, which is a diterpene that directly activates adenylate cyclase enzyme and raises cyclic AMP levels in many tissues. This is important because TSH stimulates all steps in the synthesis and secretion of T3 and T4. The first step is the binding of TSH to TSH receptors located on the basal membrane of the thyroid epithelial cells, followed by elevation of cyclic AMP levels, and a subsequent cascade of phosphorylation reactions via activation of protein kinase A (PKA). The final step is the secretion of thyroid hormones T4 and T3, which again could not happen without cAMP [29].

4- Effects of *Melissa officinalis* on thyroid hormones

The obtained results in Table-5 show that, following the administration of *M. officinalis*, the level of TSH was increased, while the levels of T3 and T4 were decreased. The highest increase in TSH level was by 21% for 50mg/kg treatment, while the maximum reduction for T3 and T4 were 11 and 9 % for 100mg/kg and 50mg/kg treatments, respectively, as compared with the control.

Table 5-The effects of *Melissa officinalis* on T3, T4 and TSH levels in rats serum

Concentration (mg/kg)	**Mean ± SE**		
	TSH	**T3**	**T4**
50	2.61 ± 0.10	1.99 ± 0.02	115.33 ± 0.88
100	2.53 ± 0.21	1.85 ± 0.05	116.67 ± 1.45
150	1.92 ± 0.07	2.12 ± 0.09	124.00 ± 2.08
Control	2.16 ± 0.17	2.07 ± 0.08	127.00 ± 1.73
LSD value (P<0.05)	0.503	0.225	5.213

These results indicate the reducing effects of *M. officinalis* on T3 and T4 and the stimulatory effect on TSH. This may be due to the fact that *M. officinalis* is considered as a thyrosuppressive agent and used in treatment of hyperthyroidism. It effectively blocks TSH binding to the receptor by acting on

the hormones and the receptor itself. The main role of *M. officinalis* is inhibiting cAMP production to stimulating by TSH receptor as antibodies. The chemical analysis of an aqueous extract of *M. officinalis* reveals the presence of high concentration of rosmarinic acid which affects Immunoglobuline G (IgG) antibodies. They have the ability of creating a receptor response on the thyroid gland and affecting the response of the immune system by reducing the loading of IgG. Because of that IgG antibodies cannot have a direct action on the thyroid gland. According to this result, *M. officinalis* is used to treat the symptoms associated with hyperthyroidism, such as insomnia, tachycardia and hyperactivity [6].

5- Effects of *Rosmarinus officinalis* on thyroid hormones

The results of thyroid profile assay after treatement with *R. officinalis* are shown in Table-6, indicating that the level of TSH was increased, while the levels of T3 and T4 were decreased. The highest increase in TSH level was by 15% for 170mg/kg treatment, while the maximum reductions in T3 and T4 levels were by 56% and 17% for 220mg/kg of the same treatment, as compared with the control.

Table 6-The effects of *Rosmarinus officinalis* on T3, T4 and TSH levels in rats serum.

Concentration (mg/kg)	Mean ± SE		
	TSH	T3	T4
170	2.49 ± 0.08	1.29 ± 0.40	108.67 ± 0.88
220	2.43 ± 0.20	0.916 ± 0.03	105.33 ± 4.05
270	2.09 ± 0.10	2.11 ± 0.06	120.67 ± 7.05
Control	2.16 ± 0.17	2.07 ± 0.08	127.00 ± 1.73
LSD value (P<0.05)	0.307	0.681	13.643

These findings can be explained by the chemical analysis of theaqueous extract of the plant by high performance chromatography HPLC, which showed the presence of high concentrations of rosmarinic acid, which is used in the treatment of hyperthyroidism. Previous research demonstrated that rosmarinic acid affects TSH on the receptor site. It also inhibits the effects of the immunoglobins on TSH receptor and decreases the peripheral conversion of T3. Rosmarinic acid may also be beneficial in the treatment of Grave's diseases [6, 30].

6- Effects of *Camellia sinensis* on thyroid hormones

The results of thyroid profile assay after treatment with *C. sinensis* are shown in Table-7, which reveals that the level of TSH was increased, while the levels of T3 and T4 were decreased. The highest increase in TSH level was by 10% for 1.25mg/kg treatment, while the maximum reductions of T3 and T4 levels were by 20 and 3%, respectively, for 1.25 mg/kg of the same treatment, compared with the control.

Table 7-The effects of *Camellia sinensis* on T3, T4 and TSH levels in rats serum

Concentration (mg/kg)	Mean ± SE		
	TSH	T3	T4
1.25	2.38± 0.12	1.65 ± 0.11	123.67 ± 4.02
2.50	2.31 ± 0.08	1.71 ± 0.09	125.67 ± 2.92
5.00	2.23 ± 0.11	1.87 ± 0.06	127.67 ± 4.37
Control	2.16 ± 0.09	2.07 ± 0.08	127.00 ± 4.28
LSD value (P<0.05)	0.409	0.329	14.285

These findings are in agreement with a previous study [14] which found that catechin present in green tea has an antithyroidal potential and reduced the levels of triiodothyronin and thyroxine, while the level of TSH was increased. These results are related to the chemical composiition of *C. sinensis* with the presence of wide range of phytochemicals that are digested, absorbed and metabolized by the body. Tea constituents such as flavonoids, quercetin, kaempferol, caffeine and catechin exert their effects at the cellular level [31]. The inhibitory effect of green tea is due to its high content of catchens which has antithyroidal and goitrogenic potentials [32].

Histopathology of the thyroid gland in different groups

1. Control group rats

Histopathological studies were undertaken on tissue section of the thyroid gland of different experimental groups of rats. The figure below shows the histopathological results. Thyroid gland of normal rats showed numerous follicles, some of which containing colloid, which varies from thick to thin with occasional scalloping. In the control treatment, the sections of thyroid gland were surrounded by a thin connective tissue capsule, consisting of a thin collagenous, while their thin septa were extended into the glandular parenchyma, subdividing it into lobules. Each lobule composed of a group of follicles; the follicles were cyst-like structures, measure 62.6 ± 2.4 µm in diameter and 9.9 ± 0.21 µm in height (Table-8). The follicles at the periphery of the gland were a few of larger follicles which store much of colloid, while those at the center of the glandular parenchyma were smaller and showed an active resorption process. Each follicle was lined by a simple cuboidal epithelium (follicular cells). Capillaries surrounded each follicle but are separated from the follicular and Para follicular cells (C-cells) by a thin basal lamina (Figure-1a)**.**

Table 8-Follicular diameters and heights of follicular cells in control and treated groups

Groups	Height of follicular cells/ µm	Follicular diameter/ µm
Control	9.9 ± 0.21	62.6 ± 2.4
Fucus vesiculosus	7.6 ± 0.13	81.4 ± 4.1
Coleus forskohlii	6.2 ± 0.2	79.0 ± 2.5
Curcuma longa	7.1 ± 0.18	66.6 ± 3.9
Melissa officinalis	10.2 ± 0.10	57.4 ± 1.6
Rosmarinus officinalis	10.0 ± 0.07	50.8 ± 4.1
Camellia sinensis	10.5 ± 0.08	45.4 ± 3.7

2. Rats treated with *Fucus vesiculosus* (150mg /kg)

Histopathology studies of the thyroid organ of the hyperthyroid rats was conducted and contrasted with the control rats. Hyperthyroidism was observed in positive control animals due to the increase of colloid in the follicular epithelial cells and the luminal colloids. The treated rats demonstrated normal follicles lined by follicular epithelial cells. The findings indicate that the aqueous extract of *Fucus* plants is stimulant to thyroid functions. After 4 weeks of administration of *F. vesiculosus* extract at a concentration of 150mg/kg b.w., thyroid gland sections revealed that there were enlarged follicles at the center and periphery of the gland, which measured 81.4 ± 4.1µm in diameter and 7.6 ± 0.13µm in height as compared with the control (Table-8). These were associated with hyper vascularized connective tissue capsule. Most of the follicles revealed an active re-absorptive form characterized by a foamy appearance between the colloid and the apical surface of the follicular cells (Figure-1b). These results are in agreement with the findings of Hameed *et al.* [21] who found that the aqueous extract from algae stimulates hyperactivity of the thyroid gland, where thyroid follicles became larger and contained dense colloid. Connective tissues in between thyroid follicles along with blood vessels could be observed. The gland tissue appeared in a natural function with a good response to *F. vesiculosus,* without deformation in the gland tissue that may cause growth of several follicles with different sizes containing colloid, according to a study that described the effects of treatment with 35 mg/ kg *F. vesiculosus* for 42 days to male rats [33].

3. Rats treated with *Coleus forskohlii* (1000mg/kg)

Thyroid sections from rats treated with a high dose of *C. forskolhlii* extract (1000mg/kg b.w.) also showed an enlarged follicles at the center and the periphery of the gland, which measured 79.0 ± 2.5 µm in diameter and 6.2 ± 0.20 µm in height, as compared with the control as in Table- 8. These were associated with a hyper vascularized connective tissue capsule, while most of the follicles revealed active re-absorptive form characterized by a foamy appearance between the colloid and the apical surface of the follicular cells (Figure-1c). These results are possibly due to the fact that *C. forskohlii* has high content of forskolin which increases the production and secretion of the thyroid hormones. It may be recommended for the treatment of hypothyroidism through stimulation of adenylate cyclase

which binds to TSH receptor and leads to reducing TSH release with increasing the synthesis of T4 through thyroid follicles. This may lead to enlarged follicles at the center and periphery of the gland [34, 35].

4. Rats treated with *Curcuma longa* (5mg/kg)

Sections of the thyroid gland from rats treated with *C. longa* extract at a concentration of 5mg/kg b.w. demonstrated highly active colloid resorption with many small follicle (Figure-1d). The follicular diameter measured 66.6 ± 3.9 µm while the follicular height measured 7.1 ± 0.18 µm, compared with the control, as in Table-8. The presence of polyphenolic compounds like curcumin may reduce the oxidative damage of oxidative materials, which leads to an activated thyroid gland in female rats [15, 36]. Hence, the observed variable densities of colloid staining might explain the variable follicular activities [37]. In addition, most of the thyroid follicles were filled with colloid that was combined with an increase in follicular diameter and a decrease in follicular cell height. These findings could be attributed to the protective effects of curcumin due to its antioxidant and anti-inflammatory properties, leading to regression of alterations caused by oxidative stress [38].

5. Rats treated with *Melissa officinalis* (100mg/kg)

Compared to the control, the sections of thyroid glands from rats treated with *M. officinalis* extract at a concentration of 100mg/kg b.w. showed small salivary lobes composed of few of normal sized follicles measured 57.4 ± 1.6 µm in diameter and 10.2 ±0.10 µm in height , as in Table- 8. These were surrounded by a thick layer of adipose connective tissue **(**Figure-1e). These results show that *M. officinalis* extract possesses strong antioxidant properties due to the phenolic compounds [39]. These plants are rich in rosmarinic acid that is beneficial for various thyroid conditions. These plants also block the antithyroid effects of immunoglobulins and reduce the conversion of T4 to T3 [40]. Polyphenolic compounds are considered as most important anti-oxidants [41] and these compounds, particularly flavonoids, have defensive effects against any damage induced by free radicals [42]. Therefore, the tissue appeared as normal, mainly in that dose [43].

6. Rats treated with *Camellia sinensis* (1.25 mg/kg)

Thyroid sections from rats treated with a *C. sinensis* extract at a concentration of 1.25mg/kg b.w. also revealed the same results as in sections treated with *Melissa officinalis.* They showed small salivary lobes composed of few of normal sized follicles, which measured 45.4 ± 3.7 µm in diameter and 10.5 ± 0.08 µm in height, in comparison with the control as in Table- 8. These were surrounded by a thick layer of adipose connective tissue (Figure-1f). These results are in agreement with Chandra *et al.*, (2014) who found that the thyroid appeared normal both grossly and microscopically using a mild dose (1.25 mg/kg), but the changes appeared with a moderate dose of 2.5 mg/kg daily for 30 days. These changes were represented by diffused hypertrophy and/or hyperplasia of the thyroid follicular epithelial cells, with less amount of colloidal material and irregularly shaped follicles that have decreased luminal spaces with tall cuboidal follicular epithelium. A high dose (5mg/kg daily) caused large colloid-filled follicles with tall columnar epithelium that occupied most of the thyroid tissue. In another study of Badr El Dine *et al.* [44], structural changes were shown in the thyroid tissue, like augmentation of thyroid follicles and swollen vacuolated follicular cells. The excessive vacuolation of the colloid may be a response to hypersecretion of TSH.

7. Rats treated with *Rosmarinus officinalis* (220mg/kg)

In comparison with the control, thyroid sections from rats treated with *R. officinalis* extract at a concentration of 220mg/kg b.w. showed normal sized glandular lobes. The glandular follicles at the periphery of the glandular lobules appeared active, while at the center of the gland the follicles appeared smaller in size and containd few colloids that measured 50.8 ± 4.1µm in diameter and 10.0 ± 0.07 µm in height, compared with the control (Table-8). They also displayed thick interstitial tissue (Figure-1g). These results can be correlated to the presence of high amounts of rosmarinic acid in the plant, which is used to treat hyperthyroidism. This acid influences TSH on the receptor site and prevents the effect of immunoglobulins on TSH receptor. Also, it reduces the peripheral change in T3 [45].

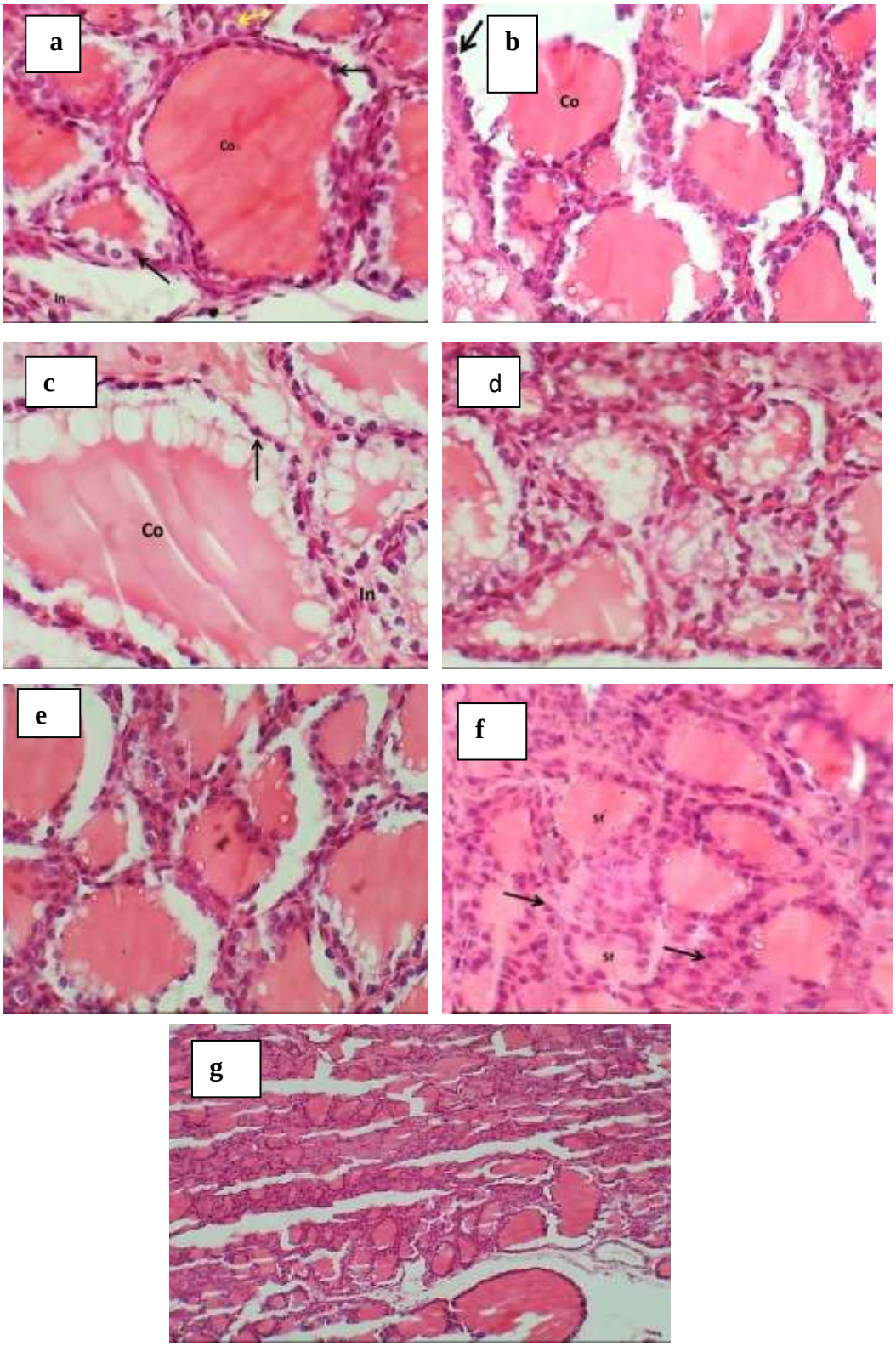

Figure 1-a) Magnified section of thyroid gland (Control) shows: C-cells (C), follicles (yellow arrow), follicular cells (Black arrows) colloid (Co) & inter follicular connective tissue (In).H&E.400x. **b)** Magnified section of thyroid gland (*F. vesiculosus*) shows: follicular cells (Black arrows) colloid (Co).H&E.400x. **c)** Magnified section of thyroid gland (*Coleus forskohlii*) shows: follicular cells (Black arrows) colloid (Co) & inter follicular connective tissue. **d)** Magnified section of thyroid gland

(*Curcuma longa*) shows: small follicles with active resorption .H&E.400x. **e)** Magnified section of thyroid gland (*Melissa officinalis*) shows: large active follicle .H&E.400x. **f)** Section of thyroid gland (*Camellia sinensis*) shows: trachea (T), small thyroid lobe (Th), & Adipose connective tissue (At).H&E.40x. **g)** Magnified section of thyroid gland (*Rosemarinus officinalis*) shows: smallest inert follicles (Sf) with thick interstitial tissue (arrows).H&E.400x.

Conclusion:

Thyroid hormones have an important role in the growth and development of the body and regulate metabolism. Many factors can influence the concentration of these hormones and therefore disturb the general body metabolism. The outcomes of the present study exhibited that the aqueous extracts of *Curcuma longa* and *Coleus forskohlii* are the most effective against hypothyroidism, while *Rosmarinus officinalis* could possibly overcome hyperthyroidism in albino rats. Our preliminary results are encouraging, but further studies are needed to clarify the exact mechanisms behind the anti-thyroid activities of medicinal plant extracts.

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