

**The Potential Protective Roles of *S.costus* (*Saussurea costus*)
Root in Thyroiditis Induced by Amiodarone-Hydrochloride in
Experimental Rats**

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Abstract

Aim: *S.costus* root is one of the most medicinal plants that are high in antioxidants. The aim of this work was to investigate the roles of an aqueous extract of *S.costus* root a portative effect for thyroiditis in rats.**Material and Methods:** Thirty six rats were randomly divided into six groups (n = 6). The group1 (G1) received only distill water for ten days; group 2 was treated alone with amiodarone hydrochloride 40 mg/kg b.wt. per day for ten days. Groups 3 & 4 were treated orally with an aqueous extract of *S. costus* alone in two doses (L₁ & L₂) (50 & 100 mg/kg body weight/day). Groups 5 and 6 were given an aqueous extract of *S. costus* at two doses (L₁ & L₂), respectively plus administrated the amiodarone hydrochloride 40 mg/kg body weight and continued for ten days. **Results:** The results showed the levels of SOD and total anti-oxidant were decreased significantly ($p \leq 0.01$) in (G2) rats with thyroiditis compared to all treated groups and the control group. Animals in groups (3-6) ingested extracts *S. costus* improved and decreased significantly ($p \leq 0.01$) in CRP, TNF-a, T3, and T4 hormone levels compared to rats had amiodarone alone. **Conclusion:** We can conclude that using the *S.costus* extract considers the potential effect against amiodarone and the side effects. Also, the aqueous extract of *S.costus* may offer benefits as a treatment to decrease thyroiditis and hyperthyroidism.

Key words: thyroiditis, amiodarone hydrochloride, *Saussurea lappa*,Hyperthyroidism,T3,T4 .

Introduction

The thyroid gland produces many hormones and regulates the body's metabolism. Hypothyroidism and hyperthyroidism are also common types of thyroid disease. (Mikos, et al .2017 and Skarulis & Stack, 2015) Thyroid hormone levels in the blood are either abnormally high or low. It generates hormones that regulate the growth and metabolism of the body. These hormones regulate heart rhythm and body temperature, as well as convert food into energy to keep the body running. Thyroiditis can reason differently. It is caused by antibodies that assault the thyroid gland. As a result, thyroiditis, like (type 1) diabetes and rheumatoid arthritis, is often an autoimmune disease (Plomp,et al.,1989 and Rios-Prego et al., 2019).

Thyroid cells can also be damaged by medications like interferon or amiodarone, as well as radiation, resulting in thyroiditis. Symptoms of hypothyroidism occur when thyroiditis causes slow and chronic destruction of thyroid cells, low levels of thyroid hormones in the blood. Fatigue, weight gain, constipation, leanness, depression, and poor exercise tolerance are all common symptoms of hypothyroidism. Thyroid hormone which is stored in the gland escapes, thyroid hormone levels in the blood, so causes rapid damage and loss of cells. These patients will develop thyrotoxicosis symptoms, which are identical to those of hyperthyroidism. It is characterized by the overproduction of the thyroxine hormone. Anxiety, sleeplessness, fast heart rate, exhaustion, weight loss, and irritability are common complaints and liver damage is a common side effect of hyperthyroidism (Rios-Prego et al., 2019). This is noticed in people with sub-acute, painless blood cause the symptoms of thyrotoxicosis and hyperthyroidism. Further thyroid cancer can be caused by an imbalance in the regulation of these hormones, which can range from a minor goiter to life-threatening conditions as thyroid cancer (Ratini, 2015; Skarulis and Stack, 2015, and Rios-Prego et al., 2019)

Saussurea costus (*S. costus*) (also known as *Saussurea lappa*) is a member of the *Asteraceae* family, however, many species are found in India, specifically in Jammu and Kashmir, a few parts of the

Himalayas, and Pakistan. The plant was well-known about 2500 years ago. *S. costus* has well known in Islamic medicine, which is enlisted in the Holy Ahadith told by the Prophet Muhammad (Peace be upon him). It's known in Arab countries as "Al-Kost Al-Hindi (Ahmad, et al, 2009). It is used to treat various ailments, viz., ulcers, rheumatism, throat infections, etc. (Pandey et al.,2007). *S.costus* is one of the most medicinal plants that are high in antioxidants, antidiabetic, anti-inflammatory, anti-tumor, anti-fungal, immunostimulant, antihelminthic, antimicrobial, and antiseptic (Lin et al., 2016; Hasson, et al, 2013; Kalid, et al,2011, and Ail, et al.,2020)). It also affects serum parameters in both hypo-and hypertension in mice (Bolkin et al.2019&Ail, et al., 2020). Tian et al., 2017 dedicated *S. costus* to anticancer prostate cells.

Various compounds isolated from the plant have medicinal properties, including terpenes, alkaloids, anthraquinone, and flavonoids Lee et al. (1995). *S.costus* extract prevents cytokine-induced neutrophil chemotactic factor induction and tumor necrosis factor-alpha production (Cho et al., 1998). The biological activities of the roots of *S. costus* have been widely investigated, costunolide, dihydrocostunolide, 12-methoxydihydrocostunolide, dehydrocostus lactone, dihydrocostus lactone, lappadilactone, -hydroxydehydrocostus lactone, -hydroxydehydrocostus lactone, reynosin, santamarine, caryophyllene oxide, myrcene, octanoic acid, pycmene (Cho et al., 1998 & Choi et al., 2012).

Saif-Al-Islam, 2020 who, reported the therapeutic potential of *S. costus* in the treatment of COVID-19, so is worthy to separate the bioactive compounds from the roots of *S. costus* to get new natural and effective drugs.

Our previous literature suggests that *S. costus* contains bioactive compounds that might act as a potential therapeutic agent to treat thyroiditis. Data on the role of *S. costus* in thyroid disorders are lacking, and a few studies represent the effect of *S.costus* in treating thyroiditis. The current study was, therefore, designed to evaluate the pretreatment and curative effects of an aqueous extract of *S.costus* root at two doses (50 & 100 mg/kg body weight/day) a portative

effect for thyroiditis induced by amiodarone hydrochloride and histopathology abnormalities in Waster male rats.

2-Material and Methods

2-1. Animals

Thirty-six adult male Wistar rats weighing 153–165 g in age 8–12 weeks were gained from the lab creature generation unit of the Food Technology Research Institute, Agricultural Research Centre, Giza, Egypt. Animals were housed in individual plastic pens with bedding. Rats were given unlimited access to water and fed a standard pelleted diet, as recommended by Reeves et al. (1993). The rats were kept in 22 ± 2 °C with a 12/12 h light/dark cycle.

2-2. Preparation of *S. costus* an aqueous extract.

The aqueous concentrates of *S. costus* were prepared by boiling 100 mL of distilled water and soaking 10 g of *S. costus* root powder for 2 hrs. At that point, the solution was filtered through a filter three times and stored in a refrigerator at 4 °C.

2-3 Prescription drugs and kits

A 200 mg tablet of amiodarone hydrochloride (Sanofi-Aventis) was used. Amiodarone was administered by giving in a daily dose of 1 mL solution (40 mg/kg body weight) orally, as according to Repetto (1989). Commercial kits were used to determine liver and kidney function, total antioxidant capacity, malondialdehyde (MDA) concentration, glutathione peroxidase (GSH-Px) , superoxide desmids (SOD) , C-reactive protein (CRP) , alpha tumor necrosis factor (TNF-a), interleukin-1 alpha (IL-1 alpha), interleukin L-6 (IL-6), and thyroid hormone. All synthetic compounds were acquired from Sigma Chem. Organization, Cairo, Egypt. *S. costus* root was obtained from I Herb Pharmacy, a natural treatment department export outside the US.

2-4. Induction of thyroiditis and treatment protocol

The rats were randomly divided into six groups (n = 6). The negative control group (G1) received only distill water for ten days; group 2 was treated alone with amiodarone hydrochloride 40 mg/kg body

weight per day for ten days. Groups 3 & 4 were treated alone orally with an aqueous extract of *S. costus* at two doses (L1 & L2) (50 & 100 mg/kg body weight/day), respectively. Groups 5 and 6 were given an aqueous extract of *S. costus* at two doses (L1 & L2) (50 & 100 mg/kg body weight/day, respectively plus administrated the amiodarone, hydrochloride 40 mg/kg body weight and continuing for ten days. Following the last treatment, all rats fasted for 12 hours but had free arrival to water. The creatures were then forfeited by cervical separation. Blood specimens were collected and the thyroid gland was excised. Blood specimens were collected from the orbital sinus veins were carried to dry centrifuge tubes (for serum) and ethylenediaminetetraacetic acid (EDTA) tubes (for whole blood). After clotting, the blood was centrifuged for 20 min at 2500 rpm to separate plasma, which was transferred to plastic vials and frozen (-20 °C) until analysis. Each sample undergoes only one freeze-thaw cycle before being assayed. Serum samples and thyroid tissues were kept at 20C before assessment of IL-1b, IL-6, TNF-a, and sent in dry ice. Levels of these cytokines were measured using a multiplexed particle-based flow cytometric cytokine assay (Vignali, 2000), Thyroid glands were cleaned in saline and fixed in 10% neutral buffered formalin for 24 hours and embedded in paraffin for histological examination according to the method of Bancroft et al., (1996).

2-5 Nutritional and biochemical analysis

The body weight gain (BWG) = final wt.(g) – starting wt.(g) as well as thyroid relative weight (%) = thyroid wt. (g) ÷ final body wt. (g) × 100 were calculated according to Hsu et al., 1978, Red blood cell (RBC) and white blood cell (WBC) counts were measured according to Natt and Herrick (1952), and hemoglobin (Hb) according to the International Committee for Standardization in Hematology (1967). The malondialdehyde (MDA) in plasma was estimated according to the method of Yoshioka, et al. (1979), as well as total antioxidant capacity according to the method of Koracevic et. al.,(2001). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured as described by the International Federation of Clinical Chemistry (1980); Friedman *et al.*,(1980. Glucose was determined colorimetrically in serum using (Tietz 1986).

Determination of the creatinine and urea concentration in blood, according to Henry, (1974) and Fawcett, Soctt (1960). Concentrations of thyroid stimulation hormone (TSH), free triiodothyronine (T3), and thyroxine (T4) were determined by autoanalyzer (ADVIA Centaur XP Immunoassay System, Siemens, USA) and selected cytokines IL-1 β (Cat. No. BMS630), IL-6 (Cat. No. BMS625) and, TNF- α (Cat. No. BMS622) were determined by ELISA (Bio-tek Instruments, Inc.) using sandwich enzyme-linked immunosorbent method according to manufacturer's (BioVision) instructions (Vignali,2000).

2-6 Statistical analysis

Statistical analysis was carried out using the SPSS, PC statistical software (version 8.0 SPSS Inc., Chicago, USA). The results were presented with mean \pm SD. Data were analyzed by using a one-way examination of change (ANOVA) test. The differences between mean were tested for significance using Tukey's test at $P \leq 0.01$.

Results

The nutritional status, blood picture, and glucose of rats with thyroiditis

The impact of two doses of *S. costus* on BWG, feed intake, and thyroid relative wt. for thyroiditis rats presented in table (1) the results indicated that BWG, feed intake were decreased significantly ($P \leq 0.01$) in group 2 of rats ingesting the amiodarone alone or groups (5 & 6) fed amiodarone plus *S.coast* compared to the negative control group (G1). Correspondingly, weight gain and thyroid relative wt. were also normally in groups (3 & 4) fed *S. costus* only compared to the negative control group. However, G 5 & G6 (feed amiodarone plus *S. costus* at two doses) results showed that BWG, FI, and thyroid wt. ratio were improved significantly ($p \leq 0.01$) compared to the rats that ingested the drug alone (G2). Table 2 reported the effects of the *S. costus* on the blood pictures and sugar levels of rats with thyroiditis. Rats in groups treated with *S. costus* (G3 to G6) improved significantly ($p \leq 0.01$) in hemoglobin, RBC, and WBC levels compared with rats with thyroiditis in G2. The group of animals treated with *S. costus* at dose two (G6) showed the best improvement

in blood pictures. The platelet count represented in table 2 showed all groups treated with *S. costus* only seemed at normal levels. However, groups fed amiodarone plus *S. costus* improved significantly ($p \leq 0.01$) compared to G2. The glucose results are also shown in table 2, the data revealed that the group2 that ingested amiodarone drugs only have high levels of glucose significantly ($p \leq 0.01$) compared to all groups. Also, G 5 & G6 (feed amiodarone plus *S. costus* at two doses) results showed improved significantly ($p \leq 0.01$) in glucose levels compared to control negative but doesn't in a normal range. Concerning, animals treated with *S. costus* at two doses (G3&G4) that have the normal range in glucose levels compared to control negative.

Changes in serum kidney and liver functions

The results of the effect of the *S. costus* at doses on the kidney and liver functions of rats with thyroiditis are reported in table (3). The data showed that the urea, creatinine, ALT, and AST levels increased significantly ($p \leq 0.01$) in the group ingesting amiodarone alone (G2) compared to all other groups. On the other hand, improved significantly ($p \leq 0.01$) in the group (G3 to G6) treated with *S. costus* at two doses, compared to G2.

The oxidative process and antioxidant levels of rats with thyroiditis

The effect of the *S. costus* at two doses on the oxidative process and antioxidant levels in the blood and thyroid tissue of rats with thyroiditis were represented in the table (4). The MDA level in blood and thyroid tissue increased significantly ($p \leq 0.01$) in group 2 fed amiodarone alone compared to all other groups, and vice versa, treated with *S. costus* at two doses caused a decrease in MDA levels significantly ($p \leq 0.01$) compared to the control positive. The results of superoxide desmids (SOD) and total antioxidant levels in blood and thyroid tissues were reported in the table (4). The results showed the levels of SOD in blood and thyroid tissues were decreased significantly ($p \leq 0.01$) in (G2) of rats with thyroiditis compared to all treated groups and the control group. Conversely, animals treated with *S. costus* at two doses (G5&G6) caused increased and improved significantly ($p \leq 0.01$) in SOD levels compared to (G2). The rats of

groups 3 and 4 fed *S. costus* at two doses were seemed normally concentrated in MDA, SOD, in blood, and thyroid tissues compared to control negative. The results indicated the total antioxidant levels in blood increased and improved significantly ($p \leq 0.01$) in groups treatment with *S. costus* at two levels compared to control positive (G2).

The cytokine levels and inflammation factor of rats with thyroiditis

The impact of the *S. costus* at two doses on the serum levels of cytokine in rats with thyroiditis is shown in table (5). In this regard, we have investigated the serum levels of the TNF-a, IL-1 alpha, IL-6, and CRP in rats. The results indicated TNF-a, IL-1 alpha, IL-6, and CRP levels were increased significantly ($p \leq 0.01$) in (G2) rats with thyroiditis compared to all treated groups with *S. costus* and control negative. Conversely, animals in groups (3-6) ingested the *S. costus* at two doses improved and decreased significantly ($p \leq 0.01$) in CRP, TNF-a, IL-1 alpha, and IL-6 levels compared to rats had amiodarone alone, however, the result of dose two of the *S. costus* was significantly more effective. Our finding is that groups of rats fed the *S. costus* at two doses alone have normal levels of CRP, TNF-a, IL-1 alpha, and IL-6 in blood compared to control negative.

Change in the thyroid hormone levels

The results of the thyroid hormone groups and GSH were reported in Figures (A&B). The results showed hyperthyroidism that represented the elevated levels of triiodothyronine (T3) and thyroxine (T4) hormones significantly ($p \leq 0.01$) with the rats ingested amiodarone drug alone (G2) compared to control negative. The groups were treated with the *S. costus* at two doses (G5 & G6) improved and decreased significantly ($p \leq 0.01$) in T3 and T4 hormone levels, respectively, compared with control positive (G2). As well as rats ingested the aqueous extract of *S. costus* at two doses (G3 & G4), they showed normal levels compared with control negative (G1). Furthermore, the result of the hormone TSH level was represented in Fig. (A) The data showed the rats ingested with amiodarone drug alone (G2) decreased significantly ($p \leq 0.01$) in TSH level compared

to all groups. The vice versa occurred in G5 and G6. The results showed improved and increased significantly ($p \leq 0.01$) in the TSH levels compared to G2.

The Glutathione peroxidase (GSH-Px) in blood and thyroid tissue is reported in Fig. (B). The results showed that GSH-Px concentrated in the blood and thyroid tissue decreased significantly ($p \leq 0.01$) in rats with thyroiditis (G2) compared to all other groups. Treatment with *S. costus* at two doses improved and significantly increased ($p \leq 0.01$) the GSH-Px concentration in thyroid tissues of (G3-G6) compared to control negative.

The results of histopathological examination of thyroid glands

Microscopical examination of the thyroid gland of normal control rats revealed the normal histological structure, which exhibited normal thyroid follicles lined by a cuboidal follicular cells epithelium and the follicles filled with colloids (Photo 1) On the contrary, thyroid glands of control positive rats exhibited histopathological alterations described as follicular cell vacuolation, necrosis, and desquamation of follicular epithelium (Photo 2). Meanwhile, sections from group 3 & group 4 showed no histopathological alterations, examined sections revealed the normal histology of thyroid follicles and filled with deeply stained colloids (Photos 3&4). On the other hand, the thyroid glands of rats from group 5 showed some improvement as examined sections revealed vacuolation of some follicular cells (Photo 5). Moreover, the thyroid glands of rats from group 6 revealed no histopathological alterations (Photo 6).

Discussion

Heart disease was considered the first reason for death in the world according to statistics WHO, (2019). The amiodarone hydrochloride medication drug was written in doctor prescription to treat fatal irregular heartbeat like persistent ventricular fibrillation. It is used to restore normal heart rhythm and maintain a regular. Thyrotoxicosis or thyroid dysfunction may also result from the administration of amiodarone, which contains high levels of iodine (Zhao, et al., 2020 and Narayana, et al., 2011).

Thyroid dysfunction, hyperthyroidism, as well hypothyroidism can affect the circulatory system by affecting output or contractility cardiac, blood pressure, and vascular resistance, which can all lead to heart failure, fibrillation, congestive heart failure, and high blood pressure (Klein and Danzi, 2007 & Gionfra et al., 2019). The current study revealed the amiodarone hydrochloride drug effects on the thyroid gland tissue structure, excretion the hormones T3, T4, and TSH secreted with thyroid gland caused hyperthyroidism, moreover, proinflammatory cytokines, such as interleukin IL-1b, IL-6, and TNF-a and the acute phase reactant C-reactive protein was elevated above normal levels.

The current study appeared that amiodarone caused hyperthyroidism, impact to decrease all the body weight gain and thyroid gland weight in rats, hemoglobin, RBC, WBC, Plates count, SOD, total antioxidant levels, TSH, and Glutathione peroxidase in blood and thyroid tissue these decreased it significantly. As well as, raises the levels of glucose, kidney and liver enzymes, TNF, IL-1 alpha, IL-6, and C-reactive protein, T3 and T4 hormone levels. These results agree with Zhao et al. 2020, who illustrated that the amiodarone drug may induce thyroiditis in people treated with it to treat cardiac arrhythmias. Amiodarone and its major metabolite, desethylamiodarone, are preferentially distributed in the thyroid gland, lungs, kidneys, liver, heart, adipose tissue, skeletal muscle, and brain (Riva et al. 1995; Plomp et al. 1989; Brien et al. 1987, and Kannan et al. 1991).

According to Rios-Prego et al., (2019), thyroid dysfunctions are linked to rat weight loss or gain. These agree with our results so rats with thyroids have low BWG, feed intake significantly ($P < 0.01$), also groups treated with amiodarone plus *S. costus* showed that BWG, FI, and thyroid wt. ratio were improved but not in the normal range. In addition, thyroid hormone disruption is a primary target that plays a role in body weight management (Gionfra et al., 2019).

Furthermore, the groups of rats (G3&G4) treated with two doses of *S. costus* alone didn't observe any abnormality parameters and examined the thyroid tissue were seen naturally. *S. costus* possesses

many natural compounds with an immunostimulant effect, it is hyperbolic to the leukocytes count, body function process, and antibody-secreting cells, and it is prevent-up the oxidation of reduced glutathione (Zahara,2014; Choi , et al,2012; pandy,2012, and Shati, et al,2020)

From another aspect, our finding also confirmed the groups of rats (G5&G6) that treatment with the *S. costus* lowers the side effects of amiodarone and thyroiditis in rats. Furthermore, improved the body weight of rats, thyroid gland weight, hemoglobin, RBC, WBC, Plates count, SOD, and total antioxidant levels, TSH, and (GSH-Px) in blood and thyroid tissue. These results agree with Saif-Al-Islam, 2020 who, reported *S. costus* is employed for the treatment of chronic inflammation of the lungs, chest congestion, respiratory organ inflammation. In addition, Ali et al., 2020 reported the *S. costus* extract is the potential source of secondary metabolites that could be used as an anticancer agent to treat diverse cancers of the breast, colon, and liver. Amina, et al., 2020 reported that the formation of nanoparticles with *S. costus* was screened for antimicrobial and toxicity against totally different infective microbes as well as MCF-7 cancer cells. It is a comparison with the biomass of *S. costus*

Conclusion: We can conclude that using the *S.costus* extract considers the potential effect against amiodarone and the side effects. Also, the aqueous extract of *S.costus* may offer benefits as a treatment to decrease thyroiditis and hyperthyroidism. Our results suggest that subjects treated with amiodarone may benefit from incorporating natural *S.costus* root as part of their diet during treatment.

الادوار الوقائية المحتملة للجذور نبات القسط الهندي في التهاب الغدة الدرقية المستحث بواسطة عقار اميدوين كلوريد في فئران التجارب .

الملخص باللغة العربية

الهدف : تعتبر جذور نبات القسط الهندي من النباتات الطبية التي تحتوي علي مضادات اكسدة بكميات كبيرة . لذلك الهدف من هذه الدراسة هو فحص الادوار الوقائية لمستخلصات جذور نبات القسط الهندي للتهاب الغدة الدرقية في فئران التجارب . **المواد والطرق:** تم تقسيم ستة وثلاثين من ذكور الفئران إلى ست مجموعات (ن = 6). تلقت (G1) ماء مقطر لمدة عشرة أيام فقط ؛ عولجت المجموعة الثانية بأميودارون هيدروكلوريد بمفرده بجرعه تقدر 40 مجم / كجم من وزن الجسم يومياً لمدة عشرة أيام. عولجت المجموعتان 3 و 4 عن طريق الفم بالمستخلص المائي لنبات القسط الهندي بجرعتين 50 و 100 مجم / كجم من وزن الجسم / يوم). أعطيت المجموعتين 5 و 6 المستخلص المائي من نبات القسط الهندي بجرعتين بالإضافة إلى إعطاء الأميودارون هيدروكلوريد 40 مجم / كجم لمدة عشرة أيام. **النتائج** ان مستويات انزيم سوبر أكسيد ديسميوتاز ومضادات الاكسدة الكلية انخفضت معنويا ($P < 0.01$) في المجموعة الثانية مقارنة مع جميع المجموعات المعالجة ومجموعة التحكم السليبي . الفئران في المجموعات (3-6) التي تناولت مستخلصات القسط الهندي تحسنت وانخفضت بشكل ملحوظ ($p \leq 0.01$) في مستويات عامل مضاد الالتهاب والسيطوكينات CRP و (TNF-a) و هرمونات الغدة الدرقية T3 و T4 (مقارنة بالفئران التي تغذت بالأميودارون بمفرده . **الخلاصة :** يمكننا ان نستنتج ان استخدام المستخلص المائي لجذور القسط الهندي يقلل من التأثيرات المحتملة والاثار الجانبية لعقار الأميودارون ، وقد يقدم المستخلص المائي من القسط الهندي فوائد كعلاجية لتقليل التهاب الغدة الدرقية وفرط نشاطها.

الكلمات المفتاحية:

التهاب الغدة الدرقية , عقار اميدوين كلوريد, القسط الهندي , فرط نشاط الغدة الدرقية , هرمون ثلاثي يود الثيرونين, الثيروكسين

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Table (1): The impact of *S. costus* extracts on Body weight gain “BWG” Feed Intake “FI”, and thyroid relative wt. for rats have thyroiditis

Groups	BWG*	Thyroid relative wt. %	Feed intake (g)
G1(-)	49.50 ±6.32 ^a	0.05±0.01 ^{ac}	9.50±1.12 ^{as}
G2 (+) (amiodarone)	16.17 ±5.23 ^b	0.56±0.07 ^{bb}	٦,١٧±0.41 ^{bd}
G3 L ₁ <i>S.coast</i>	40.67±7.71 ^a	0.03±0.02 ^{ac}	١٠,٤٢ ±0.49 ^{as}
G4L ₂ <i>S.coast</i>	43.25±5.98 ^a	0.04±0.02 ^{ac}	9.08±0.20 ^{es}
G5L ₁ <i>S.coast</i> + amiodarone	22.33±7.71 ^c	0.39±0.05 ^f	٧,٨٣± 0.45 ^c
G6 L ₂ <i>S.coast</i> + amiodarone	39.33±4.93 ^c	0.13±0.06 ^{ec}	8.25±0.41 ^{es}

* Each value represents the mean ± SD. Means in the same column with different superscript letters are significantly different at p≤0.01. * (BWG)= Final wt. – initial wt. Thyroid relative weight (%) = Thyroid weight (g) ÷ final body weight (g) * 100

Table (2) The effect of the *S. costus* extracts on blood pictures and glucose levels of rats who had thyroiditis

	Hemoglobin (gm/dl)	RBC (mil/μl)	WBC (10 ³ /ul)	Platelets 10 ³ /cmm	Glucose (mg/dL)
G1(-)	16.32 ±0.30 af	4.75 ± 0.30 as	15.65 ±0.47 o	578.33 ± 21.37 d	90.00 ±2.10 h
G2 (+) (amiodarone)	8.33 ± 0.21b	3.15 ± 0.21 b	23.27 ± 1.30 b	277.50 ±24.03 b	199.50 ±7.58 b
G3 L ₁ <i>S.coast</i>	15.65 ±0.21af	3.15 ± 0.21 c	13.10 ±0.75 c	568.00 ±34.83 d	82.50 ±1.87 h
G4L ₂ <i>S.coast</i>	15.55 ±0.19 af	4.75 ± 0.19 as	14.35 ±0.76 o	568.67 ± 33.15 d	84.92 ±2.84 h
G5L ₁ <i>S.coast</i> + miodarone	12.26 ± 0.19 c	4.20 ± 0.19 d	18.47 ± 1.03 d	408.33 ± 39.20 c	155.50 ±4.64 c
G6 L ₂ <i>S.coast</i> + amiodarone	14.24 ± 0.46 ef	4.60 ± 0.46 d	17.60 ± 0.60 d	534.17 ± 40.30 d	119.67±7.42 e

* Each value represents the mean ± SD. Means in the same column with different superscript letters are significantly different at p≤0.01.

Table (3) The effect of the *S. costus* extracts on the kidney and liver functions of rats, thyroiditis

Groups	Urea(mmol/ml)	Creatinine (μmol/ml)	ALT (u/ml)	AST (u/ml)
G1(-)	3.12 ± 0.43 ^{aa}	43.38 ± 2.08 ^{cc}	39.15 ± 0.70 ^{ai}	44.07 ± 1.32 ^{ae}
G2 (+)amiodarone	24.55 ± 0.88 ^{bs}	81.92 ± 1.96 ^b	86.73 ± 1.77 ^{bb}	96.70 ± 1.61 ^{bb}
G3 L₁ <i>S.coast</i>	3.07 ± 0.42 ^{aa}	46.35 ± 2.95 ^{cc}	29.55 ± 1.13 ^{ci}	43.58 ± 0.52 ^{ae}
G4L₂ <i>S.coast</i>	3.11 ± 0.47 ^{aa}	45.39 ± 2.50 ^{cc}	38.80 ± 0.58 ^{ai}	43.99 ± 0.93 ^{ae}
G5L₁ <i>S.coast</i> + amiodarone	14.36 ± 0.98 ^{ce}	42.61 ± 3.18 ^{ad}	70.04 ± 2.12 ^{dd}	76.83 ± 1.91 ^{cc}
G6 L₂ <i>S.coast</i>+ amiodarone	6.64 ± 0.71 ^{da}	51.31 ± 3.15 ^{dc}	47.28 ± 1.94 ^{fi}	51.72 ± 1.15 ^{af}

* Each value represents the mean ± SD. Means in the same column with different superscript letters are significantly different at $p \leq 0.01$.

Table (4) The effect of the *S. costus* extracts on the oxidative process and antioxidant levels in the blood and thyroid tissue of rats with hydroiditis.

Groups	MDA in Blood (n. mol/ml)	MDA in Thyroid ((n. mol/mg/ protein)	SOD in Blood (u/ml)	SOD in Thyroid (u/mg/ protein)	Total anti-oxidant in Blood (mM/ml)
G1(-)	*0.30 ± 0.04 ^{ar}	0.50 ± 0.07 ^a	1.48 ± 0.12 ^f	2.17 ± 0.21 ^a	1.53 ± 0.09 ^{ad}
G2 (+)amiodarone	4.27 ± 0.27 ^b	5.39 ± 0.25 ^b	0.38 ± 0.10 ^g	0.45 ± 0.12 ^b	0.06 ± 0.01 ^b
G3 L ₁ <i>S.coast</i>	0.30 ± 0.01 ^{ar}	0.56 ± 0.05 ^a	0.97 ± 0.08 ^f	1.95 ± 0.13 ^a	1.51 ± 0.24 ^{ad}
G4L ₂ <i>S.coast</i>	0.28 ± 0.06 ^{ar}	0.53 ± 0.09 ^a	1.32 ± 0.27 ^f	2.20 ± 0.26 ^a	1.57 ± 0.16 ^{ad}
G5 L ₁ <i>S.coast</i> + amiodarone	2.66 ± 0.12 ^{ce}	3.89 ± 0.42 ^d	0.94 ± 0.06 ^{fr}	1.42 ± 0.14 ^c	0.69 ± 0.11 ^c
G6 <i>S.coast</i> L ₂ + amiodarone	0.87 ± 0.20 ^{er}	0.95 ± 0.08 ^f	1.21 ± 0.22 ^{fe}	0.91 ± 0.08 ^d	1.20 ± 0.06 ^d

* Each value represents the mean ± SD. Means in the same column with different superscript letters are significantly different at p≤0.01.

Table (5) Impact of the *S. costus* extracts on the cytokine levels of rats with thyroiditis

Groups	CRP(ng/ml)	L1B IL-1 pg/mg	L6B IL-6 (pg/ml)	TNF -a (pg/ml)
G1(-)	*33.12 ± 1.91 a	82.81 ± 5.70 ^{ad}	49.60 ± 2.18 ^{af}	67.27 ± 2.76 aa
G2 (+) amiodarone	163.72 ± 7.70 b	199.90 ± 5.96 b	180.85 ± 1.54 b	211.90 ± 4.27 c
G3 L ₁ <i>S.coast</i>	36.58 ± 4.75 ^a	81.11 ± 4.32 ad	46.24 ± 2.30 ^{af}	72.85 ± 2.98 ^{aa}
G4L ₂ <i>S.coast</i>	35.95 ± 3.77 ^a	81.94 ± 4.80 ad	47.84 ± 3.79 af	68.93 ± 5.39 aa
G5L ₁ <i>S.coast</i> + amiodarone	104.46 ± 6.19 c	111.33 ± 6.65 c	125.21 ± 5.35 c	164.80 ± 1.44 e
G6 L ₂ <i>S.coast</i> + amiodarone	68.50 ± 6.64 ^e	91.83 ± 3.43 ^d	73.22 ± 6.31 ef	118.78 ± 3.98 d

* Each value represents the mean ± SD. Means in the same column with different superscript letters are significantly different at $p \leq 0.01$.

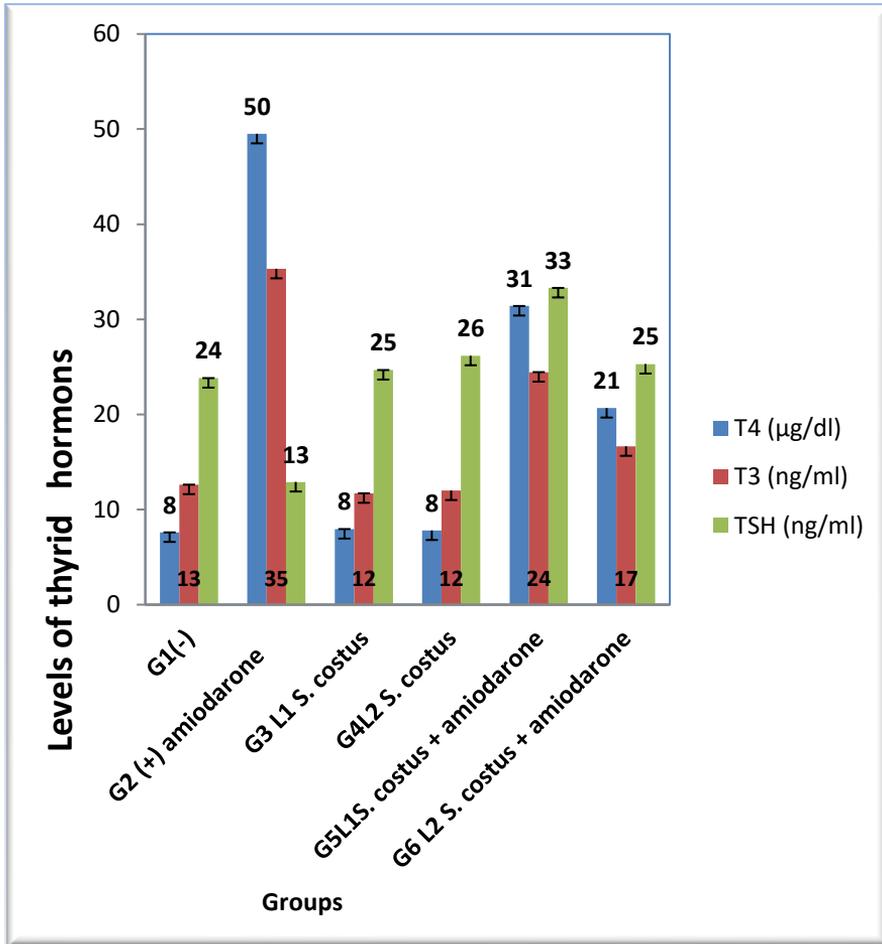


Fig (A) The effect of the *S. costus* extracts on the groups of thyroid hormone levels of rats with thyroiditis

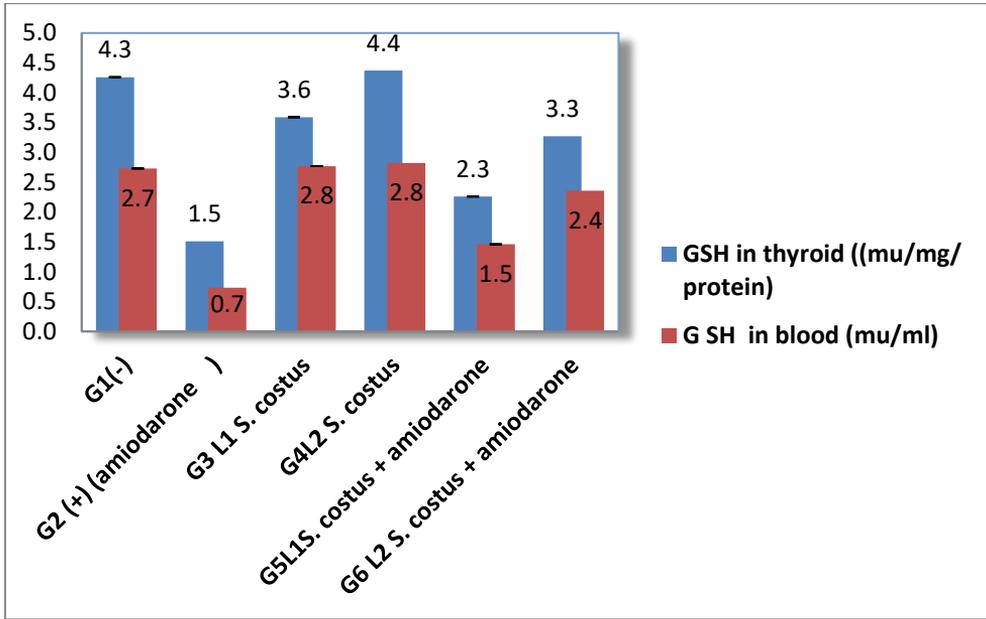


Fig.(B) The effect *S. costus* extracts on the groups of GSH in blood and thyroid tissue of rats with thyroiditis

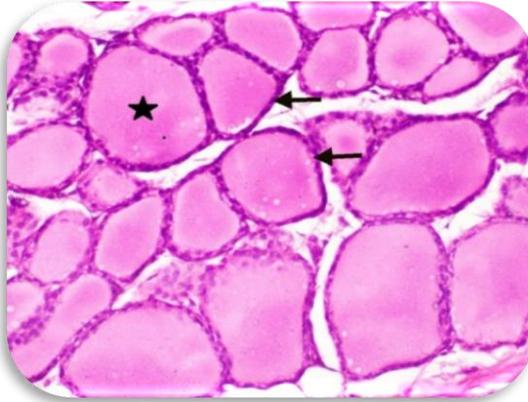


Photo (1): Photomicrograph of thyroid gland of normal control rats showing the normal histological structure, which exhibited normal thyroid follicles lined by a cuboidal follicular cells epithelium (arrows) and the follicles filled with colloids (asterisk). (H & E, x 200).

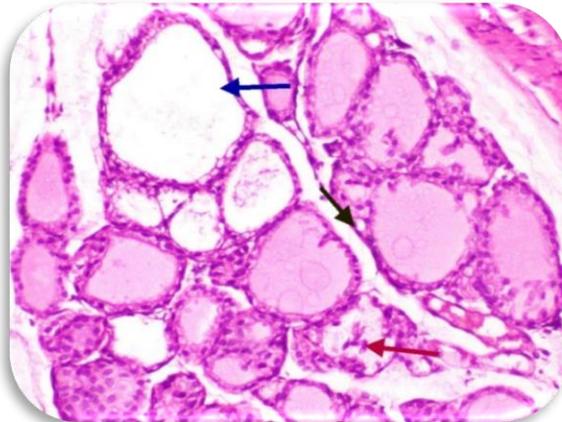


Photo (2): Photomicrograph of the thyroid gland of G2 showing follicular cell vacuolation (black arrow), necrosis and desquamation of follicular epithelium (red arrow), and absence of the colloid within some follicles (blue arrow) (H & E, x 200).

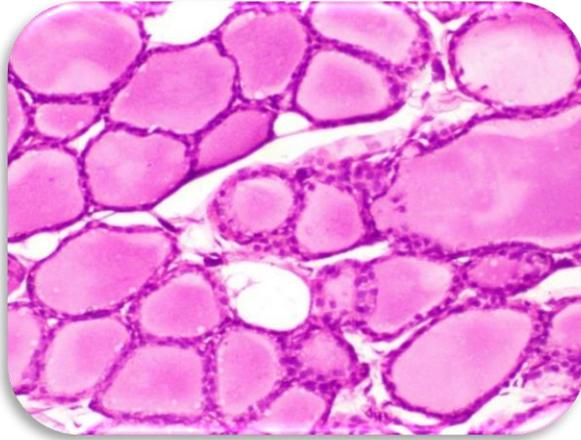


Photo (3): Photomicrograph of the thyroid gland of mice from group 3 showing no histopathological alterations. Note the normal histology of thyroid follicles and filled with deeply stained colloids (H & E, x 200).

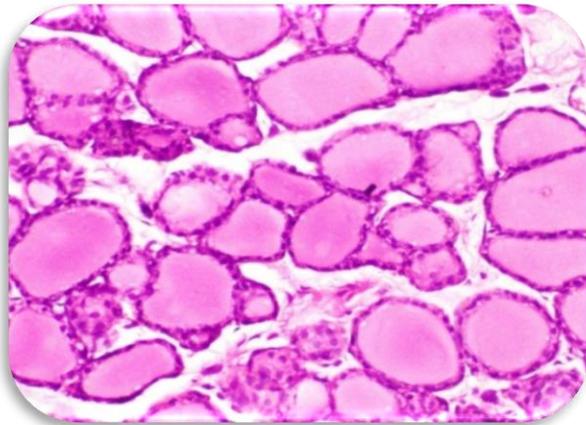


Photo (4): Photomicrograph of the thyroid gland of mice from group 4 showing no istopathological alterations. Note the normal histology of thyroid follicles and filled with deeply stained colloids (H & E, x 200).

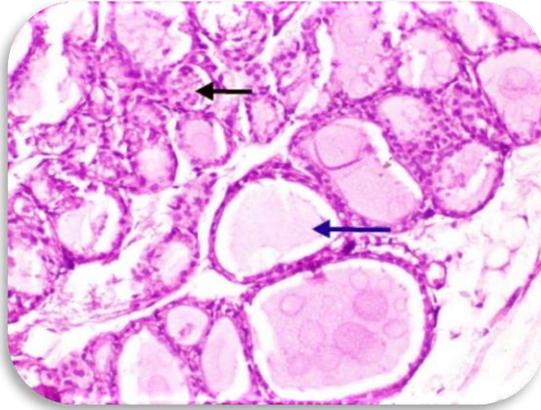


Photo (5): Photomicrograph of the thyroid gland of rats from group 5 showing necrosis of follicular cells lining some follicles (black arrow) and lightly stained colloid within the follicles (blue arrow) (H & E, x 200).

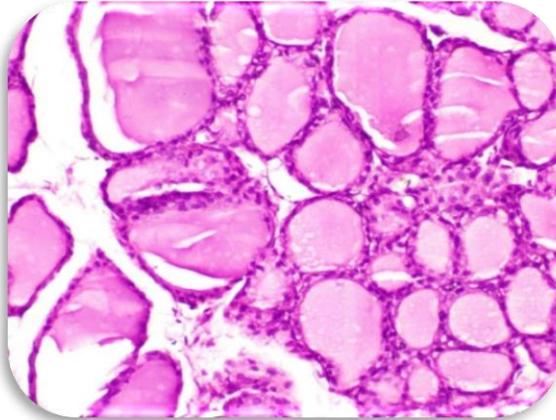


Photo (6): Photomicrograph of the thyroid gland of mice from group 6 showing no histopathological alterations. Note the normal histology of thyroid follicles and filled with deeply stained colloids (H & E, x 200).