Effect of Saussurea costus on propylthiouracil induced hypothyroidism in rats

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ABSTRACT

The present study aims to evaluate the effect of *Saussurea costus*on on Propylthiouracil (PTU)-induced hypothyroidism in rats. The chemical composition, phenolic compounds and antioxidant activity in this plant were evaluated. Thirty male albino rats weighing about 170 ± 10 g was divided into five groups; negative control group, positive control group, and three treated groups with *S. costus* (100, 200 and 400 mg/kg bodyweight, respectively. The thyroid gland activity was evaluated utilizing biochemical and histopathological methods. The results indicated that the positive control group showed a significant increase in kidney and liver function biomarkers and a significant decrease in FT3, FT4, and TSH hormones. On the other hand, rats with induced hypothyroidism showed significant reduction in their body weight gain with different doses of *S. costus*. Also, the treated rats showed normal biochemical and hormonal levels, as well as normal histological results like the control group. This indicated that *S. costus* exhibits a promising effect in ameliorating PUT-induced hypothyroidism by regulating hormonal levels and restoring tissue damage, making it a potential natural candidate for future therapeutic studies.

Keywords: Thyroid gland, Saussurea costus, Propylthiouracil, histology.

INTRODUCTION

The thyroid gland is a small, butterfly-shaped endocrine organ situated in the anterior region of the neck. It plays a metabolic crucial role in regulating growth and thermogenesis processes, through the secretion of thyroid hormonesprimarily thyroxine (T4) and triiodothyronine (T3). Dysfunction of the thyroid gland can result in systemic disturbances that affect cardiovascular, neurological, and metabolic functions (Vitti and Hegedus, 2020). According to the World Health Organization (WHO), approximately 31% of the global population equivalent to 1,900.9 million individuals are estimated to have insufficient iodine intake. The most

affected regions include South-East Asia and Europe (WHO, 2001). There is a growing consensus among medical professionals that the prevalence of thyroid-related disorders is on the rise. Autoimmune thyroid diseases encompass both hyperthyroidism, such as Graves' disease (GD), and hypothyroidism, such as Hashimoto's thyroiditis (HT). GD is primarily driven by thyrotropin receptor antibodies (TRAbs), which target the thyroid-stimulating hormone receptor (TSHR), constituting the principal mechanism underlying disease the (Furmaniak et al., 2015). Conversely, HT is characterized by TH1 lymphocyte-mediated infiltration of the thyroid gland and the presence of autoantibodies against thyroid

peroxidase and thyroglobulin—key proteins involved in thyroid hormone synthesis (Walsh *et al.*, 2010).

Anti-thyroid agents such as 6-npropyl-2-thiouracil (PTU) and methimazole (MMI) have been utilized to suppress the thyroid axis to examine the role of thyroid hormone synthesis and metabolism during development larval and growth in (Campinho al.. vertebrates et 2015). Thyroras (Propylthiouracil or PTU) is a medication primarily used to manage hyperthyroidism: а condition characterized by excessive production of thyroid hormones. It works by inhibiting the synthesis of these hormones, thereby helping to alleviate symptoms such as rapid heartbeat, weight loss, and heat intolerance. As a member of the thiouracil family, Propylthiouracil is a heterocyclic compound known for its broad pharmacological and adaptability in chemical activity synthesis (Andersen et al., 2019).

Saussurea costus (Falc.) Lipsch, also known as Indian costus, has a long-standing history in traditional Saudi Arabian medicine and is recognized as a medicinal plant (Mujammami, 2020). It exhibits a wide range of biological activities, including antianti-urolithiasis. inflammatory, and antimicrobial properties (Soliman et al., 2022). Furthermore, it has demonstrated potential in improving thyroid tissue damage carbazole-related induced bv hypothyroidism (Fekry et al., 2023). The plant S. costus has been extensively investigated for its therapeutic efficacy in addressing various health conditions, offering multiple medicinal benefits that position it as a promising candidate for applications. pharmaceutical Its antiinflammatory and anti-urolithiasis effects, along with its capacity to mitigate thyroid disorders and tissue damage, have been the subject of numerous studies (Mammate et al., 2023). S. costus has also been thoroughly examined for its phytochemical composition and its traditional medicinal relevance (Rathore *et al.*, 2021). The therapeutic potential of its extracts has been validated in traditional medicine, where it has been employed to treat a broad spectrum of ailments (Idriss *et al.*, 2022). Therefore, the aim of this work is to determine the effect of *S. costus* in treatment of Propylthiouracil (PTU)-induced hypothyroidism rats.

MATERIALS AND METHODS Materials:

Saussurea costus were obtained from local market. Propylthiouracil (PTU) tablets were purchased from Amoun Pharmaceutical Co., Egypt. Each tablet contains 50 mg of PTU.

Analytical methods

Moisture, protein, fat, crude fiber and ash were determined according to the method of AOAC (2018). All determinations were made in triplicate. while the percentage carbohydrate was determined by the formula Carbohydrate= 100 - (moisture + crude fiber + ash + fat+ crude protein).

Animal and Experimental Design

Thirty male albino rats weighing about 170±10 g was obtained from Agricultural Research Center, Giza, Egypt. The animal groups were kept in an atmosphere of filtered, pathogen-free air, water, and a temperature of 20-25°C for 8 weeks, with a 12-hour light/dark cycle and a light cycle (8-20 h) and a relative humidity of 50%. For one week, all rats were fed a basal diet. The basal diet was designed to contain 14% casein, 10% sucrose, 4% corn oil, 5% fiber (cellulose), 3.5 percent mineral mixture, 1% vitamin mixture, 0.25 percent choline chloride, 0.3 percent D-L methionine, and 61.95 percent corn starch

(Reeves et al., 1993). After becoming acclimated to the circumstances of the experimental room, the animals were randomly separated into five groups of six rats each: The first main group (6 rats) was the negative control group and given distilled water. The second was the hypothyroid groups (24 rats): fed on a basal diet with received daily oral dose of propylthiouracil (15mg/kg body weight) by gastric tube for (17 days) and the tablet was dissolved in 10ml water to induce hypothyroid state according to (Hatem and AL- Mayali, 2018). A sample was taken from the eyes of rats at the end of the seventeenth day to confirm the occurrence of hypothyroidism. FT4 and FT3 were determined to ensure the hypothyroidism.

Afterward, administrated rats (n=24) were divided into 4 equal subgroups (6 rats) as follows: Subgroup (1): Rats were fed on a basal diet only and kept as a positive control group. Subgroup (2): Rats were fed on a basal diet containing *S. costus* (100mg/kg bodyweight). Subgroup (3): Rats were fed on a basal diet containing *S. costus* (200mg/kg bodyweight). Subgroup (4): Rats were fed on a basal diet containing *S. costus* (400mg/kg bodyweight). The intervention continued for 8 weeks.

Sampling

At the end of the experiment, rats were allowed to fast for 12 to 14 hours before blood samples were collected (Williams *et al.*, 2020). Blood samples were collected into evacuated tubes, and serum was separated by centrifugation at 3000 rpm for 10 min at 4°C.

Biochemical analysis

Thyroid hormone concentrations were analyzed by colorimetric competitive enzyme immunoassay using individual ELISA kit. Triiodothyronine (FT3) levels in plasma were determined according to the

method described by Braverman et al. (1996), while thyroxin (FT4) levels in plasma were estimated following the method outlined by Mazzafferi et al. (1998). Thyroid stimulating hormone (TSH) was assessed based on the method detailed by Shamsian et al. (2016). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were determined calorimetrically using spectrophotometer (model DU 4700) at 505 nm according to the method of Reitman and Frankel (1957). Alkaline phosphatase (ALP) activity was determined calorimetrically using spectrophotometer (model DU 4700) at 510 nm according to the method by Belfield and Goldberg (1971). Serum urea nitrogen was determined according to the method of Batton and Crouch, (1977) using spectrophotometer (model DU 4700) adjusted nm 550 nm. Serum creatinine was determined by Tietz (1986)using spectrophotometer (model DU 4700) adjusted at 510 nm.

Histopathological examination

Tissue specimens were collected from thyroid, heart, liver and kidney and fixed in 10 % neutral buffer formalin. Tissues were then processed by paraffin embedding technique using ascending concentration of alcohol and xylene, embedded in paraffin wax, sectioned into 4 um thick sections and stained bv hematoxylin and eosin stain. Light microscope with installed digital camera is used for examination (Banchroft et al., 1996).

Statistical analysis

The obtained values were given as means \pm S.D of the mean. The comparisons between different groups were carried out by one-way analysis of variance (ANOVA) according to Snedecor and Cochran (1980) followed by Duncan's Multiple Range test for post hoc analysis using SPSS software version 24. The level of significance was set at $P \le 0.05$.

RESULTS AND DISCUSSION Chemical composition of *Saussurea costus*

The chemical composition of S. costusas expressed in Table (1) showed that it contains 0.60g/100g moisture, 2.74g/100g of proteins, 5.33g/100g of crude lipid, 84.91g/100g of carbohydrates, ash content 3.74g/100 g and crude fiber 1.68g/100g. The low moisture content indicates effective post-harvest drying, which is critical for preserving bioactive compounds and preventing microbial degradation. This aligns with studies showing that low moisture (<10%) in S. costus roots enhances shelf life and concentrates phytochemicals like sesquiterpene lactones (Binobead et al., 2024).

Table (1): Chemical constituent ofSaussurea costus Constituents.

Chamical composition	Samples g/100g		
Chemical composition	Saussurea costus		
Moisture	0.60±0.1		
Crude Protein	2.74 ± 0.22		
Lipids	5.33±0.15		
Crude fiber	$1.68{\pm}0.08$		
Total Ash	3.74±0.36		
Carbohydrates	84.91±0.73		

Protein content may be relatively low, the substantial presence of crude lipids and carbohydrates, along with the mineral composition, underscores the potential nutritional and medicinal value of the roots of S. *costus*. The relatively high presence of crude lipids suggests the presence of fats, which could be important for energy storage and the absorption of fat-soluble vitamins. The carbohydrate content provides information on the energy potential of these roots, and the ash content reflects the mineral composition, which is important for both nutritional and medicinal considerations, as minerals play a crucial role in various physiological functions (Tungmunnithum *et al.*, 2018)

Biological evaluation of *S. costus* on experimental rats induced by Propylthiouracil

Body weight, body weight gain (BWG) and weight of the organs

Data in Table (2) indicated that the initial weight of all groups had similar values to that of the negative control group. The initial weights ranged from 170.02 to 180.83 g, where there was none statistically significant difference among groups.

The PTU group exhibited minimal body weight gain $(7.6\pm0.15g)$ compared to the negative control $(38.7\pm3.09g)$, aligning with the profound metabolic slowdown characteristic of hypothyroidism (Kyriacou *et al.*, 2019). PTU inhibits thyroid peroxidase, disrupting thyroxine (T4) and triiodothyronine (T3) synthesis and reducing basal metabolic rate (BMR). This suppresses lipolysis, gluconeogenesis, and thermogenesis, collectively curtailing weight gain (Khaled *et al.*, 2022).

All root extract S. costus treated groups showed significant recovery in weight gain, with near-complete normalization at 400 mg/kg (35.8±1.74g to control 38.7±3.09g). negative This demonstrates the significant effect of S. counteracting PTU-induced costus in metabolic dysfunction.

Body weight (g) /wk	Groups				
	Negative	Negative D	Treated with Saussurea costus		
	control	Positive controll	100mg	200mg	400mg
Initial body weight	170.02±2.34 ^a	174.17±2.18 ^a	172.67±2.42 ^a	180.83±3.28 ^a	179.83±3.94 ª
Final body weight	271.3±2.26 ^a	197.29±5.98 °	267.0±3.05 ^b	270.0±2.77 ^a	273.7±2.33ª
Body Weight gain	38.70±3.09 ^a	7.6±0.15 ^e	34.1±1.79°	34.8 ± 1.67^{d}	35.8±1.74 ^b

 Table (2): Body weight and body weight gain (%) of experimental rats which treated with Saussurea costus.

Values are means \pm SD, n=6. Means in the same row with different superscripts (a,b,c and d) are statistically significant (p \leq 0.05). WK: Week.

Thyroid hormones analysis

Results in Table (3) showed thyroid hormones analysis and the group induced with PTU alone exhibited the classical biochemical hallmarks of hypothyroidism: significantly depressed levels of Free Triiodothyronine (FT3: 0.8±0.06 ng/ml) and Free Thyroxine (FT4: 1.5±0.1 ng/ml) coupled with a substantial elevation in Thyroid Stimulating Hormone (TSH: $3.41 \pm$ 0.3 mIU/l) compared to the negative control (FT3: 4.5±0.4 ng/ml; FT4: 6.4±0.5 ng/ml; TSH: 0.08±0.003 mIU/l). This pattern (low FT3/FT4, high TSH) is the definitive signature of diagnostic primary hypothyroidism (De Groot et al., 2012). PTU achieves this by inhibiting thyroid peroxidase (TPO), the enzyme critical for iodine organification and the coupling of iodotyrosines to form T3 and T4 (Cooper & Biondi, 2012). The resulting decrease in thyroid hormone synthesis triggers а compensatory rise in TSH secretion from the pituitary via the negative feedback loop of the hypothalamic-pituitary-thyroid (HPT) axis (Brent, 2012). Treatment with S. costus root extract at all tested doses (100, 200, 400 mg/kg) effectively ameliorated the hypothyroid state induced by PTU. This was evidenced by a dose-dependent increase in FT3 and FT4 levels and a corresponding

decrease in TSH levels compared to the PTU-induced hypothyroid group. PTUinduced hypothyroidism is associated with increased oxidative stress in thyroid tissue. S. costus is rich in sesquiterpene lactones (e.g., costunolide, dehydrocostus lactone) and flavonoids known for potent antioxidant (Chen et al., properties 2016). By scavenging free radicals and reducing oxidative damage to thyroid follicular cells, the extract may protect thyroid tissue integrity and enhance its synthetic capacity, as demonstrated in studies with other antioxidants (Erdamar et al., 2008). Some phytochemicals may directly stimulate thyroidal iodine uptake or TPO activity or protect the gland from the inhibitory effects of PTU. While specific data on S. costus and TPO is limited, its overall hepatoprotective and tissue-regenerative properties (Pandey et al., 2007) could extend to the thyroid. The significant restoration of FT3 and FT4, especially at 400 mg/kg, strongly suggests enhanced thyroidal synthesis and/or secretion. These findings corroborate and extend previous research highlighting the thyroid-modulator potential of medicinal plants. especially those with strong antioxidant and anti-inflammatory profiles (Saeed et al., 2022; Sharma et al., 2019).

Thuroid	Groups				
Thyroid hormones	Negative control	Positive control	Treated with Saussurea costus		
			100mg	200mg	400mg
FT3 (ng/ml)	4.5±0.4 ^a	$0.8{\pm}0.06^{d}$	3.5±0.09 ^b	3.05±0.04°	3.7±0.1 ^b
FT4 (ng/ml)	6.4±0.5ª	1.5±0.1 ^d	3.2±0.1 ^{bc}	3.4±0.07°	4.6±0.2 ^b
TSH (mlu/l)	$0.08{\pm}0.003^{d}$	3.41±0.3 ^a	1.49±0.3°	1.01±0.1 ^{bc}	$0.08{\pm}0.001^{d}$

 Table (3): Thyroid hormones analysis of experimental rats induced by Propylthiouracil and treated with Saussurea costus.

Values are means \pm SE, n=6. Means in the same row with different superscripts (a,b,c and d) are statistically significant (p \leq 0.05). FT₃, Threonine; FT₄, Thyroxine, TSH Thyroid stimulating hormone

Biochemical investigations of liver function biomarkers

Data in Table (4) indicated that administration of PTU resulted in a pronounced significant increase (p < 0.05) of all measured liver enzymes compared to the negative control (AST: 47.6 ± 0.6 vs 81.6 ± 1.2 ; ALT: 25.6 ± 0.2 vs 67.3 ± 1.4 ; ALP: 40.90 ± 1.1 vs 82.13 ± 1.13). PTU is known to cause liver injury through mechanisms involving oxidative stress, mitochondrial dysfunction, and direct cellular damage, leading to hepatocyte necrosis and potential cholestatic changes (Woeber, 2002; Heidari et al., 2012). These results align with previous studies showing PTU significantly raises serum AST, ALT, and ALP levels in experimental models (Abd El-Twab et al., 2016).

After the treatment with root extract of S. costus at doses of 100, 200, and 400mg alongside PTU induction resulted in a significant, dose-dependent attenuation of the PTU-induced enzyme elevations for all parameters. The dose-dependent normalization of AST, ALT, and ALP strongly suggests that S. costus possesses potent hepatoprotective properties against PTU-induced damage. This protection is likely mediated through several mechanisms previously attributed to SC and its bioactive constituents (such as sesquiterpene lactones, flavonoids, and essential oils) also, S. costus is rich in antioxidants capable of scavenging PTU-generated reactive oxygen species

(ROS) and enhancing endogenous antioxidant defenses (e.g., glutathione, superoxide dismutase) (Al-Yahya et al., 2015). Oxidative stress is a primary mechanism of PTU hepatotoxicity; thus, counteracting it is crucial (Heidari et al., 2012). Hepatic inflammation often accompanies toxin-induced injury. Constituents like dehydrocostus lactone in S. costus have demonstrated significant antiproperties. inflammatory potentially reducing inflammatory cytokine release and subsequent hepatocyte damage (Cho et al., 2000; Lee et al., 2011).

Gilani et al., (2007) and Pandey et al., (2007) reported significant reductions in AST, ALT, and ALP in CCl4-intoxicated rats treated with S. costus root extract, attributing it to antioxidant and antiinflammatory effects. Also, Al-Yahya et al. (2015) demonstrated S. costus is efficient in protecting against paracetamol-induced liver damage, correlating reduced enzyme levels with improved histopathology and enhanced antioxidant status. The dose-dependent response observed here (particularly the superior effect of 400mg) is consistent with findings by Rasool et al., (2010) who noted increasing hepatoprotection with higher S. doses of costus extract against thioacetamide.

liver enzymes (mg/dl)	Groups				
	Negative	Positive control	Treated with Saussurea costus		
	control		100mg	200mg	400mg
AST	47.6±0.6 ^e	81.6±1.2 ^a	51.6±1.4 ^d	57.6±0.9 ^b	56.6±0.3°
ALT	25.6±0.2 ^e	67.3±1.4 ^a	43.6±0.8 ^b	42.6±0.8°	39±1.5 ^d
ALP	40.90±1.1e	82.13±1.13 ^a	56.74±1.16 ^b	48.60±1.40°	43.00±1.15 ^d

 Table (4): liver enzymes of experimental rats induced by Propylthiouracil and treated with Saussurea costus.

Values are means \pm SD, n=6. Means in the same row with different superscripts (a,b,c and d) are statistically significant (p \leq 0.05). AST, aspartate amino transferase; ALT, Alanine amino transferase.ALP: serum alkaline phosphatase

Biochemical investigations of kidney function biomarkers

It was obvious from data in Table (5) that the group induced with PTU alone exhibited a significant elevation (p<0.05) in all measured kidney function parameters compared to the negative control group. Urea increased from 31.29 ± 0.7 mg/dL to 61 ± 0.7 mg/dL, creatinine increased from $0.4 \pm 0.07 \text{ mg/dL}$ to $1.4 \pm 0.08 \text{ mg/dL}$, and uric acid increased from $2.2 \pm 0.2 \text{ mg/dL}$ to 4.5 ± 0.3 mg/dL (Table 5). These marked increases indicate severe impairment of kidney function, specifically glomerular filtration rate (GFR) and tubular handling. aligns established This finding with evidence of PTU's adverse effects on renal

function. Studies suggest PTU nephrotoxicity may involve direct tubular damage, induction of oxidative stress, generation of free radicals, and potential immune-complex mediated glomerulonephritis. The drastic rise in creatinine, a direct indicator of GFR, strongly suggests reduced filtration capacity (Al Asmari et al., 2015; Wiles et al., 2019). Similarly, elevated urea levels reflect impaired nitrogenous waste clearance. Increased uric acid could result from reduced excretion due to tubular damage or potentially increased production linked to metabolic disruption or oxidative stress (Kang et al., 2002).

 Table (5): Serum kidney functions of experimental rats induced by Propylthiouracil and treated with Saussurea costus.

kidney functions (mg/dl)	Groups				
	Negative	Positive control	Treated with Saussurea costus		
	control		100mg	200mg	400mg
Urea	31.29 ± 0.7^{d}	$61{\pm}0.7^{a}$	38.7±0.9 ^b	34.4 ± 1.4^{b}	29.3±1.8°
Creatinine	$0.4{\pm}0.07^{d}$	$1.4{\pm}0.08^{a}$	0.54±0.1°	$0.44{\pm}0.07^{b}$	$0.43{\pm}0.03^{d}$
Uric acid	2.2 ± 0.2^{b}	4.5±0.3 ^a	3.2±0.1 ^b	3.2±0.1 ^b	2.9±0.2°

Values are means \pm SD, n=6. Means in the same row with different superscripts (a,b,c and d) are statistically significant (p \leq 0.05).

After treatment with *S. costus* extract at all doses (100, 200 and 400mg) significantly improved (p<0.05) the PTUinduced elevations in urea, creatinine, and uric acid levels compared to the untreated PTU group. The dose-dependent attenuation of renal dysfunction by *S. costus* strongly supports its nephroprotective potential. This aligns with numerous studies on medicinal plants rich in antioxidants and antiinflammatory compounds. *S. costus* root is known to contain potent bioactive constituents like sesquiterpene lactones (costunolide, dehydrocostus lactone), alkaloids, and flavonoids (Pandey et al., 2007). Previous research on S. costus and related species has demonstrated significant antioxidant activity (scavenging free radicals, boosting endogenous antioxidants like SOD and GSH), anti-inflammatory (inhibiting pro-inflammatory effects cytokines like TNF- α , IL-6), and potential anti-fibrotic properties (Singh et al., 2017; Kumar al., 2019). PTU-induced et nephrotoxicity is heavily mediated by oxidative stress and inflammation. By counteracting these pathways, S. costus likely protects renal tubular cells from damage, preserves glomerular integrity, and improves overall excretory function. The significant reduction in creatinine. particularly at 200mg and 400mg doses, highlights its potential to protect or restore glomerular filtration. The reduction in uric acid suggests improved tubular handling or reduced oxidative stress burden (Butterworth et al., 2008). The efficacy of S. costus was clearly dose-dependent across all parameters. The 400mg/kg dose consistently produced the most significant improvements. consistent with It is pharmacological principles where higher concentrations of active compounds exert greater biological effects. Similar dosedependent nephroprotective effects have been observed with other plant extracts in models of drug-induced toxicity (Atessahin et al., 2005).

Histopathological studies:

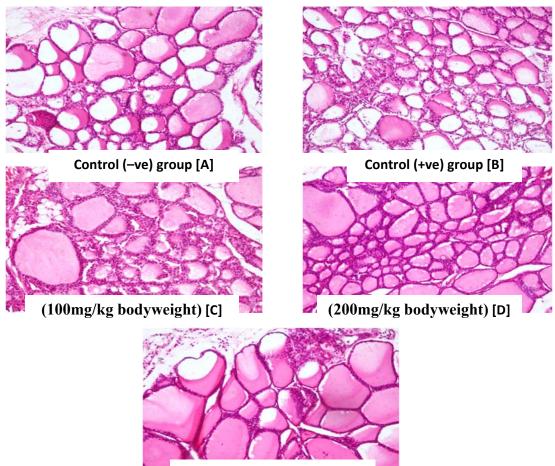
Microscopy of the thyroid gland revealed normal histological structures in the negative control group. It is characterized by follicles, which are the functional units, and the colloid they contain. These follicles are lined by a single layer of thyroid follicular epithelium formed

of cuboidal cells, with moderate amounts of eosinophilic cytoplasm and round. hyperchromatic nuclei. The follicles are embedded in connective tissue stroma, which includes capillaries and lymphatic vessels. The colloid is a homogeneous, eosinophilic, protein-rich fluid in the thyroid follicles and containing thyroid hormones by the thyroid produced follicular epithelium. (Fig.1A).

In positive control group, the thyroid gland microscopy showed less organized follicles which were hyper cellular, with occluded or small lumen having little colloid. Few desquamated cells were seen in the lumen (Fig.1B). Oxidative stress is implicated in various thyroid pathologies (Mancini *et al.*, 2016).

In S. costus (100mg/kg body weight) group, few large thyroid follicles lined by flattened epithelium and containing colloid were observed (Fig.1C). In S. costus (200mg/kg bodyweight) group, the thyroid gland, showed mild histopathological alteration (Fig.1D). In S. costus (400mg/kg bodyweight) group, the microscopy of thyroid gland, showed normal histological structure as seen in (Fig. 1 E).

S. costus is renowned for potent antioxidant properties due to sesquiterpene lactones (costunolide, dehydrocostus flavonoids, and phenolic lactone), compounds (Pandey et al., 2007; Kumar et 2015). Some phytochemicals can al.. influence deiodinase enzymes, thyroid hormone transport, or even feedback at the hypothalamic-pituitary-thyroid axis (HPT axis) (Deiana et al., 2020).



(400mg/kg bodyweight) [E]

- Fig. (1): Histopathological changes in thyroid gland of experimental rat (control -ve and +ve groups) and other groups treated by *Saussurea costus*. Stained with H and E stain X 200).
- A- Showing multiple thyroid follicles lined by squamous epithelium and containing colloid.
- **B-** Showing less organized follicles which were hypercellular, lined by columnar epithelium and with occluded or small lumen having little colloid.
- C- Showing few large follicles lined by flattened epithelium and containing colloid.
- **D-** Showing many large follicles lined by flattened epithelium and containing colloid

Showing many large follicles lined by flattened epithelium and containing colloid

E- Showing many large follicles lined by flattened epithelium and containing colloid

REFERENCES

- Abd El-Twab, S.M.; Hussein, O.E. and Hozayen, W.G. (2016). Protective effects of chicoric acid on propylthiouracil-induced hepatotoxicity in rats. Environmental Toxicol. Pharmacol., 41:129-137.
- Al Asmari, A.K.; Al Sadoon, K.T.; Obaid,
 A.A.; Yesunayagam, D. and Tariq,
 M. (2015). Protective effect of quinacrine against glycerol-induced acute kidney injury in rats. BMC Nephrology, 16(1):1-11.
- Al-Rasheed, N.M.; Attia, H.A.; Mohamed, R.A.; Al-Rasheed, N.M. and Al-Amin, M.A. (2017). Preventive effects of selenium yeast, chromium picolinate, zinc sulfate and their combination on oxidative stress, inflammation, and impaired hepatorenal function in propylthiouracil-induced hypothyroid rats. Biological Trace Element Res., 178(1): 33-42.
- Al-Yahya, M.A.; Mothana, R.A.; Al-Said, M.S.; El-Tahir, K.E.; Al-Sohaibani, M.O. and Rafatullah, S. (2015). Hepatoprotective effect of *Saussurea costus* against paracetamol-induced liver damage in rats. Afr. J. Traditional, Complementary and Alternative Medicines, 12(1): 1-6.
- Andersen, S.L.; Knøsgaard, L.; Olsen, J.; Vestergaard, P. and Andersen, S. (2019). Maternal thyroid function, use of antithyroid drugs in early pregnancy, and birth defects. The J. Clin. Endocrinol. Metabolism, 104(12): 6040-6048.
- Ateşşahin, A.; Çeribaşı, A.O.; Yüce, A.; Bulmuş, Ö. and Çikim, G. (2005). Role of ellagic acid against cisplatininduced nephrotoxicity and oxidative stress in rats. Basic Clin. Pharmacol. Toxicol., 100(2):121-126.

- Bancroft, J.D. and Stevens, A. (1996). The haematoxylin and eosin. Theory and practice of histological techniques.
 4th ed, Ch. 6, pp.99–112. Churchill Livingstone, London, New York & Tokyo.
- Binobead, M.A.; Ibrahim M.A.; Sobhy, M.I. and Reem, M.A. (2024). Chemical composition and bioactivities of the methanol root extracts of *Saussurea costus*. Open Chemistry, 22: 20240002
- Brent, G.A. (2012). Mechanisms of thyroid hormone action. J. Clin. Investigation, 122(9):3035–3043.
- Butterworth, P.J.; Sallis, J.D. and Simmons, N.L. (2008). Evidence for a sodiumindependent transport system for urate in human kidney proximal tubule brush-border membrane vesicles. J. Pharmacol. Experimental Therapeutics, 324(1):139-144.
- Campinho, M.A.; Silva, N.; Roman-Padilla, J.; Ponce, M.; Manchado, M. and Power, D.M. (2015). Flatfish metamorphosis: a hypothalamic independent process?. Mol. Cell. Endocrinol., 404: 16-25.
- Chen, H.C.; Chou, C.K.; Lee, S.D.; Wang, J.C. and Yeh, S.F. (2016). Active compounds from *Saussurea lappa* Clarke that suppress hepatitis B virus surface antigen gene expression in human hepatoma cells. Antiviral Res., 123:131-138.
- Cho, J.Y.; Baik, K.U.; Jung, J.H. and Park, M.H. (2000). In vitro antiinflammatory effects of cynaropicrin, a sesquiterpene lactone, from *Saussurea lappa*. European J. Pharmacol., 398(3):399-407.
- Cooper, D.S. and Biondi, B. (2012). Subclinical thyroid disease. The Lancet, 379(9821):1142-1154.

- DeGroot, L.J.; Beck-Peccoz, P.; Chrousos, G.; Dungan, K.; Grossman, A.; Hershman, J.M. and Weickert, M.O. (2012). Hypothyroidism. In: Endotext. MDText.com, Inc.
- Deiana, M.; Piras, A.; Rosa, A. and Dessì, M.A. (2020). Natural products targeting the synthesis/function of thyroid hormones and their effects on thyroid homeostasis. Planta Medica, 86(02):73-86.
- Erdamar, H.; Demirci, H.; Yaman, H.; Erbil, M.K.; Yakar, T.; Sancak, B. and Yetkin, I. (2008). The effect of hypothyroidism, hyperthyroidism, and their treatment on parameters of oxidative stress and antioxidant Chemistry status. Clinical and (CCLM). Laboratory Medicine 46(7):1004-1010.
- Fekry, E.; Awny, M.; Refaat, G. and Arafat, H. (2023). Ameliorative Role of Saussurea Lappa Root Extract. Zagazig J. Forensic Med. Toxicol., 21(1):172-189.
- Gilani, A.H.; Yaeesh, S.; Jamal, Q. and Ghayur, M.N. (2007). Hepatoprotective activity of aqueous-methanol extract of *Saussurea lappa*. Phytotherapy Res., 21(2):170-172.
- Heidari, R.; Babaei, H. and Eghbal, M.A. (2012). Ameliorative effects of taurine against methimazole-induced cytotoxicity in isolated rat hepatocytes. Scientia Pharmaceutica 80(4):987-99. DOI:10.3797/scipharm.1205-16
- Hatem, R.M. and AL-Mayali, H.K. (2018): The effect of *Fucus vesiculosus* on the function and structure of the thyroid gland of male rats treated with propylthiouracil. J. Pharm. Sci. Res., 10(10):2669-2673
- Idriss, H.; Siddig, B.; Maldonado, P.G.; Elkhair, H.M.; Alakhras, A.I.;

Abdallah, E.M. and Elzupir, A.O. (2022). Phytochemical discrimination, biological activity and molecular docking of watersoluble inhibitors from *Saussurea costus* herb against main protease of SARS-CoV-2. Molecules, 27(15): 4908.

- Kang, D.H.; Nakagawa, T.; Feng, L.; Watanabe, S.; Han, L.; Mazzali, M. and Johnson, R.J. (2002). A role for uric acid in the progression of renal disease. J. Am. Soc. Nephrology, 13(12):2888-2897.
- Khaled, G.A.; Fathia, A.M.; Doaa, G.E.;
 Fatma, A.M. and Heba F.G. (2022).
 Effect of oral administration of methanolic root extract of *Saussurea costus* to rats after propylthiouracilinduced hypothyroid obesity.
 Comparative Clin. Pathol., (31):377– 390,
- Kumar, S.; Sharma, S. and Chattopadhyay, S.K. (2015). The potential benefits of *Saussurea costus* (Falc.) Lipsch. roots cultivated in the western Himalaya. Industrial Crops and Products, 63:165-190.
- Kumar, V.; Sharma, N.; Sourirajan, A. and Khosla, P.K. (2019). Phytochemical and pharmacological review on genus *Saussurea*. J. Pharm. Pharmacol., 71(11):1595-1625.
- Kyriacou, A.; Alexis, K.; Konstantinos, C.M.; Akheel A.S. and Petros, P. (2019). Weight gain following treatment of hyperthyroidism-A forgotten tale. Clin. Obes., 9(5): e12328. doi: 10.1111/cob.12328.
- Lee, M.G.; Lee, K.T.; Chi, S.G. and Park, J. H. (1999). Costunolide induces apoptosis by ROS-mediated mitochondrial permeability transition and cytochrome C release. Biolog. Pharmaceutical Bull., 24(3):303-306.

- Lee, M.G.; Lee, K.T.; Chi, S.G. and Park, J.H. (2011). Costunolide induces apoptosis by ROS-mediated mitochondrial permeability transition and cytochrome C release. Biolog. Pharmaceutical Bull., 24(3), 303-306.
- Mammate, N.; El Oumari, F.E.; Imtara, H.; Belchkar, S.; Benjelloun, T.G.; Al-Zharani, M., ... and Sqalli, H.T. (2023). Anti-struvite, antimicrobial, and anti-inflammatory activities of aqueous and ethanolic extracts of *Saussurea costus* (Falc) Lipsch Asteraceae. Molecules, 28(2):667.
- Mancini, A.; Di Segni, C.; Raimondo, S.; Olivieri, G.; Silvestrini, A.; Meucci, E. and Currò, D. (2016). Thyroid hormones, oxidative stress, and inflammation. Mediators of Inflammation, 2016:1–12.
- Mujammami, M. (2020). Clinical significance of Saussurea Costus in thyroid treatment. Saudi Medical J., 41(10), 1047.
- Mazzafferi , E.L. and Gharib, H. (1998).Thyroxine superessive therapy in patients with nodular thyroid disease . Ann. Intem. Med., 128:386-394.
- Pandey, M.M.; Rastogi, S. and Rawat, A.K. (2007). *Saussurea costus*: botanical, chemical and pharmacological review of an ayurvedic medicinal plant. J. Ethnopharmacol., 110(3): 379-390.
- Rasool, M.; Iqbal, J.; Malik, A.; Ramzan, H.S.; Qureshi, M.S.; Asif, M. and Kamal, M.A. (2010). Hepatoprotective effects of *Saussurea lappa* extract on thioacetamide-induced liver cirrhosis in rats. J. Med. Plants Res., 4(24):2657-2665.
- Rathore, S.; Debnath, P. andKumar, R. (2021). Kuth Saussurea costus

(Falc.) Lipsch.: A critically endangered medicinal plant from Himalaya. J. Appl. Res. Med. Aromatic Plants, 20:100277.

- Reeves, P.G.; Nielsen, F.H. and Fahey, Jr, G.C. (1993). AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. J. Nutrition, 123(11):1939-1951.
- Saeed, M.A.; Sabir, A.W. and Khan, I.U. (2022). Phytochemistry and pharmacological activities of *Saussurea costus*: A review. J. Ethnopharmacol., 298:115598.
- Sharma, A.K.; Basu, I. and Singh, S. (2019).
 Efficacy and safety of Ashwagandha root extract in subclinical hypothyroid patients: a double-blind, randomized placebo-controlled trial.
 J. Alternative and Complementary Medicine, 25(9):950-957.
- Shamsian, A.A.; Ghazvini, K.; Sokhtanloo, M.; Moghaddam, M.S. and Vakili, R. (2016). Which quantitative method in determination of the thyroid hormone levels is more consistent with the clinical symptoms of the thyroid disorders? Comp. Clin. Pathol., 25(1):101–106. DOI: 10.1007/s00580-015-2148-2.
- Singh, A.; Malhotra, S. and Subban, R. (2017). Anti-inflammatory and analgesic agents from Indian medicinal plants. Int. J. Integrative Biol., 8(3):159.
- Snedecor, G.W. and Cochran, W.G. (1980). Statistical Methods, 7 Th. IBIT Public. Co, Oxford
- Soliman, M.F.; Shetaia, Y.M.; Tayel, A.A.; Munshi, A.M.; Alatawi, F.A.; Alsieni, M.A. and Al-Saman, M.A. (2022). Exploring the antifungal activity and action of *Saussurea*

Effect of Saussurea costus on propylthiouracil induced hypothyroidism in rats

costus Root extracts against Candida albicans and non-albicans species. Antibiotics, 11(3):327.

- Tungmunnithum, D.; Thongboonyou, A.;
 Pholboon, A. and Yangsabai, A.
 (2018). Flavonoids and other phenolic compounds from medicinal plants for pharmaceuticaland medical aspects: an overview. Med. (Basel, Switz.) 5 (3), 93. doi:10.3390/medicines5030093
- Vitti, P. and Hegedus, L. (2020). Thyroid diseases: pathogenesis, diagnosis and treatment (No. 180913). Springer. International Council for Control of Iodine Deficiency Disorders, UNICEF.
- Wiles, K.; Chappell, L.C. and Lightstone, L. (2019). Update on the diagnosis and management of hypertensive disorders of pregnancy. Clinical Medicine, 19(2):160–163.
- World Health Organization. (2001). Assessment of iodine deficiency disorders and monitoring their

elimination: a guide for programme managers. 2nd. Geneva: World Health Organization.

- Walsh, J.P.; Bremner, A.P.; Feddema, P.; Leedman, P.J.; Brown, S.J. and O'Leary, P. (2010). Thy-rotropin and thyroid antibodies as predictors of hypothyroidism: a 13-year, longitudinal study of a communitybased cohort using currentimmunoassay techniques. J Clin. Endocrinol Metab., 95:1095– 1104
- Williams, S.C.; Linske, M.A. and Stafford, K.C. (2020). Humane use of cardiac puncture for non-terminal phlebotomy of wild-caught and released Peromyscus spp. Animals,10:826.

https://doi.org/10.3390/ani10050826

Woeber, K.A. (2002). Methimazole-induced hepatotoxicity. Endocr. Pract., 8:222-224.

تأثير أستخدم نبات القسط الهندى على قصور الغدة الدرقية المحدث بالبروبيل ثيور اسيل فى فنران التجارب

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تهدف الدراسة الحالية إلى تحديد تأثير نبات القسط الهندى Saussurea costuson على قصور الغدة الدرقية المحدث بعقار البروبيل ثيور اسيل (PTU) في فئران التجارب. وقد تم تحليل التركيب الكيميائى , والمركبات الفينولية ونشاط مضادات الأكسدة في النبات. كما تم تقسيم 30 فأر ذكر البينو وزن كل واحد (170 ±10 جرام) إلى خمس مجموعات. مجموعة ضابطة سالبة, مجموعة ضابطة موجبة أحدث فيها قصور في الغدة الدرقية بواسطة (PTU), ثلاث مجموعات مصابة بقصور الغذة الدرقية بواسطة (PTU), ثلاث مجموعات مصابة بقصور الغذة الدرقية واسطة (PTU), ثلاث مجموعات مصابة بقصور في الغدة الدرقية بواسطة (PTU), ثلاث مجموعات مصابة بقصور الغذة الدرقية واسطة (PTU), ثلاث مجموعات مصابة بقصور الغذة الدرقية وتم علاجها بجرعات 100, 200, 400 ملجم/كجم من وزن الجسم) على التوالي. تم تقييم وظيفة الغدة الدرقية باستخدام التحاليل البيوكميائية والفحص النسيجى. أظهرت نتائج القسط الهندى أنخفاض معنوى في وزن الفئران. كما أظهرت نتائج الموعنة المجموعة الضابطة الموجبة زيادة جوهرية في مؤسرات وظائف الكبد والكلى وأنخفاض كبير جوهرى في مستويات هرمونات 10, 713 المحموعة الضابطة الموجبة زيادة السيجى. أظهرت النتائج عودة النتائج البيوكميائية ونتائج الهرمونات وظائف الكبد والكلى وأنخفاض كبير جوهرى في مستويات هرمونات ولمونات المجموعة الضابطة. أظهرت التائج أن مرمونات 10, 100 معنوى أون الفيران. كما أظهرت التائج المورنات 10, 713 بعنوى أون الفيران. كما أظهرت التائج ألى مونات وراست المجموعة الضابطة الموجبة للغذة الدرقية لتصبح مشابه للمجموعة الضابطة. أظهرت التائج أن هرمونات المتوى المجموى المورات وأخرار النتائج ورفات التروبي ألهرين التائج، ألهرت التائج، ألهرت التائج، ألهرمونات إلى المجموعة الصابطة. أظهرت التائج، ألهرت التائج، ألهرت التائج، ألهرت التائج، وألكلى وألمران التولية المروبي في ألهرات التائج، وألكلى وألخون المحموعة الضابطة. (170 معنوى ألهرت التائم، والتال وإلمان التائم، والحمور اليل ولينية الستوى المحموى وألمرت العندى ألمرمولية ألهرار النائم، والحموم ألميي والعا. (و10 م), والملاح الأضرار النسيجة, مما

الكلمات الدالة: الغدة الدرقية، القسط الهندي، البروبيل ثيور اسيل (PTU) ، علم الأنسجة.