



Research Article

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## ***Injury in Metabolic Gland Induced by Pyrethroid Insecticide Could Be Reduced by Aqueous Extract of *Sassura lappa****

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### ABSTRACT

**Aim:** The current study was undertaken to assess the protective effect of 70% methanolic extract of *Sassura lappa* (costus, CT) against oxidative stress and metabolic disorders caused by deltamethrin (DM) insecticide in rats

**Experimental Design:** Sixty adult male albino rats were divided into six groups : G1 control group; G2, plant extract treated group (300 mg/kg); G3 (DML), rats treated with a low dose of DM (1/30 LD50; 2 mg/kg) ; G4 (CTDML), rats treated with costus extract one hour prior the low dose of DM administration; G5 (DMH) , rats treated with a high dose of DM(1/15LD50;4 m/kg); G6 (CTDMH), rats treated with costus extract one hour prior the high dose of DM administration .

**Results:** The data revealed significant reduction in hemogram parameters (RBCs, Hb and PCV) accompanied with leukocytosis in both DML and DMH groups. The result also showed that a marked elevation in the oxidative stress biomarker, MDA, with concomitant decreases in the antioxidant enzymes, namely catalase (CAT), superoxide dismutase (SOD) and glutathione-s-transferase (GST) versus control group. A marked decrease in plasma triiodothyronine (T3) of both DML and DMH rat groups, while a reduction in thyroxin (T4) was recorded in plasma of DML rat group. These results were confirmed by degenerative changes in histomorphological architecture of the thyroid gland. A remarkable elevation in plasma glucose and lipid profile (total cholesterol, triglycerides, LDL-C and HDL-C) was observed in both DM intoxicated groups. Administration of costus extract successfully could mitigate the toxic impact of DM on most of the studied parameters.

**Conclusion:** The present study may suggest that the protective ingestion of costus extract could alleviate the oxidative stress as well as the metabolic and thyroid disorders induced in rats under the effect of DM toxicity

**Key words:** deltamethrin; thyroid; oxidative stress; hemogram; glucose; cholesterol.

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### INTRODUCTION

Pyrethroids are a group of pesticides extensively used outdoor and indoor [1, 2]. Oral exposure is the main source of pesticides due to the residue level of pyrethroids in different food commodities [3]. Exposure to indoor pyrethroids is through inhalation from spraying and vapour of household insecticides [4]. Deltamethrin (DM) is a type-II synthetic pyrethroid, widely used against household and agricultural insect and pest management programs. Application of deltamethrin helps to control the propagation of zoonotic disease vectors, including cockroaches, bedbugs, ants and spiders [5]. Propagation of pyrethroids applications induced adverse health effect on human and environment [6]. The adverse toxic impacts of pyrethroids on different biological organs and glands have been documented [7]. Pyrethroids have the ability to cause hormonal and metabolic disorders and suppress the antioxidant defense mechanism of the body vital organs [8-9]. It also could induce oxidative stress and generation of

free radicals which can cause serious effects on different cell components, including carbohydrates, lipids, proteins and nucleic acid [8-9].

Attenuation of metabolic and hormonal disorders as well as oxidative stress and its complications, using multifunctional natural products, may help in preventing organ damage in response to insecticide exposure [10]. Natural products of plant origin have been used widely due to their multi-activities. Many of these products have a prophylactic impact against the hazards of chemical pollutants.

Saussurea lappa roots (known as costus, family Asteraceae) is one of the therapeutic plants extensively used as a traditional medicine in Saudi Arabia. The plant contains many valuable ingredients with therapeutic activities, such as costunolide, dihydrocostunolide, 12-methoxydihydrocostunolide, dihydrocostus lactone, dehydrocostus lactone, Shikokiols [11]. These compounds can relieve smooth muscle spasms of the bronchi and gastrointestinal tract [12]. They have antibacterial and antitumor activities [13]. They prevent oxidation and remove free radicals [14]. Some authors reported that *S. lappa* extract decreases blood cholesterol and triacylglycerol [15].

To the best of our knowledge, few or no *in vivo* studies are carried out on the effect of *S. lappa* extracts against oxidative stress, hematological, hormonal and metabolic disorders in experimental animals. Thus, measuring some oxidative stress and antioxidant markers as well as hematological, hormonal and metabolic parameters can be used as interesting markers for therapeutic ability of *S. lappa* extract against deltamethrin toxicity in rats.

This work was conducted to assess the effect of 70% methanolic extract of *Saussurea lappa* in attenuating hematological disorder, oxidative stress, thyroid hormone and metabolic disorders induced in rats under the effect of deltamethrin insecticide toxicity.

## MATERIALS AND METHODS

### Insecticide

Deltamethrin insecticide (formulated as agrodelta 25 EC/ULV contain 2.5%, deltamethrin) was purchased from the local market, Jeddah, KSA. Chemical formula: (S)-cyano-3-phenoxybenzyl (1R, 3R)-3-(2, 2- dibrom-ovinyl)-2, 2-dimethylcyclopropanecarboxylate.

### Preparation of *S. lappa* root extract

*S. lappa* dried roots were purchased from a local market in Jeddah, KSA. 100 g of the plant roots were grinded and then extracted using 70% methanolic solution. The supernatant of the root extract was separated by filtration using a filter paper and then concentrated into a thick semi solid paste by evaporation, using a rotary evaporator. The semi solid paste of the root extract was dissolved in bi-distilled water before administration to the experimental animals.

### Animals and Experimental Design

Male albino Wistar rats (150-180g) were used for this study. Animals were supplied by the breeding unit of King Fahd research center, King Abdulaziz University, Jeddah, KSA. Animals were acclimatized for experimental conditions (23-25°C and 50-60% humidity) two weeks before starting the experiment. Rats were fed a standard pellet chow and tap water *ad libitum* during the experimental period. The experiment was carried out according the guidelines of OECD protocol 407 (1992) for repeated dose 28 days oral toxicity study in rodents [16]. After acclimatization period, animals were arranged into six groups, each of five rats, as follows:

Group I: Control group, rats were orally ingested bi-distilled water (1ml/ rat)

Group II; Costus extract (CT): rats were orally given costus extract

Group III; Deltamethrin low dose (DML): rats were given 1/30 LD50 (2mg/ kg bw) of DM.

Group IV; DM low dose with costus extract (CTDML): rats were given costus extract one hour prior to the low dose of DM administration.

Group V; Deltamethrin high dose (DMH): rats were given 1/15 LD50 (4mg/ kg bw) of DM.

Group VI; Deltamethrin high dose with costus extract (CTDMH): rats were given costus extract one-hour prior to the high dose of DM administration.

All animals were intoxicated with an oral DM repeated dose for 28 successive days according to the standard procedures laid down by OECD guidelines 407 [16]. Costus extract was dissolved in bi-distilled water and administered (300 mg / Kg.bw) [17] to rats orally for 28 successive days, one hour prior to DM administration.

### **Sampling:**

At the end of the experimental duration, rats were kept fasting overnight (12-14 h) and then blood samples were collected from retro-orbital plexus vein on heparinized tubes [18]. Plasma samples were separated by centrifugation of the blood at 3600 rpm for 15 minutes and kept at -20 °C for biochemical analysis. After blood collection, animals were sacrificed and the thyroid glands from different animal groups were collected for histopathological investigation.

### **Histopathology**

The obtained thyroid glands were fixed in 10% formalin solution for 14–18 h, passed in a series of graded ethanol and embedded in a paraffin wax. Thyroid paraffin sections (5 µm in thickness) were stained with hematoxylin and eosin and examined, using Olympus light microscope (Olympus BX51, Tokyo, Japan) [19].

### **Biochemical blood plasma assay**

Different hematological parameters were investigated according to Schalm, [20]. Malondialdehyde (MDA) as an index of lipid peroxidation, was measured according to Ohkawa *et al.* [21], using thiobarbituric acid. The pink color of MDA produced by these reactions was measured spectrophotometrically at 532 nm. Total thiol proteins were determined using 5,5-dithiobis (2-nitrobenzoic acid) (DTNB) [22]. Activities of superoxide dismutase (SOD) [23], catalase (CAT) [24] and glutathione s-transferase (GST) [25] were measured as antioxidant markers. Plasma glucose level was determined using the commercial diagnostic kit of stanbio Co., Spain [26]. Both TCh and HDL-C were estimated in plasma according to the method described [27]. Triglycerides (TGs) were measured by the method of [28]. From The results, LDL-C was calculated as follows:  $LDL-C = \text{total cholesterol} - HDL-TGs/5$  [29]. Triiodothyronine (T3) and thyroxin (T4) hormones were also measured in plasma [30].

### **Statistical Analysis:**

Statistical analysis was based on comparing the values between the treated groups. The results are expressed as mean  $\pm$  SD of 5 animals/group. The statistical significance of the data has been determined using one way analysis of variance (ANOVA-LSD) using SPSS statistical software package version 10. The level of significance taken as  $p < 0.05$ .

## **RESULTS**

### **Biochemical Results:**

The obtained results in Table (1) revealed that intoxication of rats with DM with either of the low dose (DML) or the high dose (DMH), induced significant reduction in RBCs, Hb and PCV accompany with an elevation in WBCs in both intoxicated groups versus control group ( $p < 0.05$ ). The blood index (MCV) showed a pronounced elevation in DH group compared with control rats ( $p < 0.05$ ). Ingestion of costus extract (300 mg/kg b.w) to both intoxicated groups (CTDML and CTDMH) caused improvements in most of the above studied parameters compared with intoxicated counterpart animal group ( $p < 0.05$ ). The plant extract was effective in restoring RBCs and Hb to normal levels in rats intoxicated by either of the two doses of DM.

Table (1): Effect of coustus extract on hemogram biomarkers of rats intoxicated with deltamethrin.

Groups	RBCs X106	WBCs X103	Hb Mg/dl	PCV %	MCV fl	MCH pg	MCHC %
Cont	5.19 ±0.21	8.32 ±0.64	16.45 ±0.93	40.73 ±1.15	78.61 ±1.50	31.84 ±2.04	38.25 ±1.42
CT	5.07 ±0.27	7.98 ±0.93	15.93 ±0.44	40.99 ±0.9	81.78 ±4.38	31.75 ±1.75	38.93 ±1.46
DML	4.92 ±0.29 <sup>ab</sup>	24.23 ±0.73 <sup>ab</sup>	14.87 ±0.72 <sup>a</sup>	38.84 ±0.39 <sup>a</sup>	77.50 ±2.33	31.04 ±1.63	38.31 ±1.93
CTDML	5.03 ±0.19 <sup>c</sup>	17.8 ±1.38 <sup>abc</sup>	16.14 ±0.57	37.93 ±0.69 <sup>ab</sup>	76.71 ±3.87	32.50 ±1.12	41.29 ±0.68
DMH	4.24 ±0.26 <sup>abc</sup>	18.29 ±1.23 <sup>abc</sup>	14.45 ±0.32 <sup>a</sup>	37.76 ±0.58 <sup>ab</sup>	90.11 ±2.57 <sup>ac</sup>	34.64 ±2.32	38.31 ±1.11
CTDMH	4.92 ±0.29	13.51 ±1.07 <sup>ae</sup>	17.05 ±0.62 <sup>e</sup>	37.74 ±0.49 <sup>a</sup>	77.60 ±3.70 <sup>e</sup>	35.04 ±2.04	43.43 ±0.94 <sup>ae</sup>

CT= costus +ve cont. DML= 1/30LD50. CTDML= costus + delta 1/30LD50  
DMH= delta 1/15LD50. CTDMH= costus + delta 1/15LD50.

All data are expressed as means ± SE five rats.

a Significant difference versus control group at  $p < 0.05$ .

b Significant difference versus CT group at  $p < 0.05$ .

c Significant difference versus DML group at  $p < 0.05$ .

d Significant difference versus CTDML group at  $p < 0.05$ .

e Significant difference versus DMH group at  $p < 0.05$ .

Significant elevation in the oxidative stress biomarker (MDA) was observed in DMH rat group versus control group, however, reduction in antioxidant markers (SH –proteins, GST, CAT and SOD) were recorded in both DML and DMH rat intoxicated groups with respect to control group ( $p < 0.05$ , Table 2). These changes were severe in DMH rat group compared with DML intoxicated group. Administration of costus extract to both DM intoxicated groups, markedly modulates the deviations in the level of oxidative stress and antioxidant markers compared with intoxicated counterpart rat group ( $p < 0.05$ ). The plant extract could beneficially normalize MDA, SH proteins and SOD levels in DML rat group, meanwhile this extract could restore MDA, SH proteins to normal levels in DMH intoxicated rats.

The results of T3 and T4 hormones of different experimental groups are expressed in Table (3). The data demonstrated that intoxication with both DM doses, significantly decreased level of T3 hormone versus control groups; however, T4 recorded significant decrease in DML group and elevation in DMH group versus control rats ( $p < 0.05$ ). Table (3) also demonstrated that elevation in blood glucose, total cholesterol (Tch), triglycerides (TGs), high and low lipoproteins (HDL-C and LDL-C) were observed in both DM intoxicated groups. Administration of costus extract, markedly modulated the deviations in these parameters in both DM intoxicated groups compared with the counterpart group ( $p < 0.05$ ).

**Histopathological observation of thyroid gland**

Light microscopic observation of the thyroid glands from normal control animals revealed normal thyroid follicles filled with eosinophilic colloid and normal follicular epithelial lining (Fig. 1a). Rats treated with costus extract showed also normal histomorphologic structure of thyroid follicles (Fig.1b). Rats intoxicated with DM low repeated dose for 28 consecutive days showed obvious histomorphologic lesions in the thyroid structure, including reduction in the size of some follicles with a reduction in the amount of colloid, other follicles showed vacuolated colloid and degeneration in the epithelial lining (Fig 1c). These histological changes were more severe in rats intoxicated with the high dose of DM. Disorganization and severe degenerative changes of follicular architecture were shown in most follicles, other follicles showed detachment and desquamated of epithelial lining (Fig 1d). Pre-treatment of low DM dose intoxicated rats with costus extract showed more or less normal thyroid architecture with normal follicles (Fig 1e). Supplementation of a high DM dose intoxicated rats with costus extract revealed a pronounced improvement in thyroid follicles compared with intoxicated counterpart group except some colloid vacuolation still appear in some follicles (Fig 1f) .

Table (2): Effect of coustus extract on oxidative stress biomarkers in plasma of rats intoxicated with deltamethrin

Groups	MDA ( $\mu\text{mol/ml}$ )	SH protein ( $\mu\text{mol/dl}$ )	GST ( $\text{mM/min/ml}$ )	CAT (U/ml)	SOD (U/ml)
Cont	41.15 $\pm 2.24$	395.22 $\pm 20.76$	674.37 $\pm 16.09$	12.02 $\pm 0.49$	99.85 $\pm 2.16$
CT	41.20 $\pm 1.62$	486.77 $\pm 22.12^a$	603.66 $\pm 17.62^a$	13.97 $\pm 1.15$	113.07 $\pm 2.40$
DML	43.45 $\pm 1.43$	366.66 $\pm 5.10^{ab}$	630.22 $\pm 12.6^a$	8.39 $\pm 0.98^{ab}$	80.99 $\pm 3.84^{ab}$
CTDL	42.32 $\pm 2.11^c$	446.43 $\pm 20.42^c$	593.56 $\pm 16.82^{abc}$	11.86 $\pm 0.36^{abc}$	98.71 $\pm 2.08^c$
DMH	51.62 $\pm 1.40^{abc}$	315.32 $\pm 8.21^{abc}$	581.15 $\pm 13.88^{abc}$	5.67 $\pm 0.51^{abc}$	87.35 $\pm 2.55^{ab}$
CTDMH	42.68 $\pm 1.60^e$	410.42 $\pm 20.52^e$	610.98 $\pm 14.66^{ae}$	9.10 $\pm 0.22^{ae}$	93.38 $\pm 2.13^{ae}$

CT= CT= costus +ve cont. DML= 1/30LD50. CTDMH= costus + delta 1/30LD50  
DMH= delta 1/15LD50. CTDMH= costus + delta 1/15LD50.

All data are expressed as means  $\pm$  SE five rats.

a Significant differences versus control group at  $p < 0.05$ .

b Significant difference versus CT group at  $p < 0.05$ .

c Significant difference versus DML group at  $p < 0.05$ .

d Significant difference versus CTDL group at  $p < 0.05$ .

e Significant difference versus DMH group at  $p < 0.05$ .

Table (3): Effect of costus extract on thyroid hormones and some metabolic biomarkers in plasma of rats intoxicated with deltamethrin

Groups	T3 nmol/L	T4 ng/L	Glucose mg/dL	T.Ch mg/dL	TGs mg/dL	HDL-C mg/dL	LDL-C mg/dL
Cont	2.29 ±0.07	96.56 ±1.99	80.35 ± 1.69	97.08 ±3.41	117.01 ±5.52	64.86 ±0.97	32.12 ±0.77
CT	1.97 ±0.03	100.15 ±1.83	70.53 ± 1.72 <sup>a</sup>	119.99 ±5.04	110.20 ±2.47	64.70 ±1.12	55.29 ±1.03
DML	1.90 ±0.10 <sup>a</sup>	90.53 ±2.49 <sup>ab</sup>	91.16 ± 0.97 <sup>ab</sup>	158.3 ±3.54 <sup>ab</sup>	± 8.99 <sup>ab</sup>	69.58 ±1.03 <sup>ab</sup>	89.22 ±1.20 <sup>ab</sup>
CTDML	2.33 ±0.08 <sup>bc</sup>	107.53 ± 4.24 <sup>ac</sup>	77.14 ± 1.55 <sup>bc</sup>	71.07 ±3.55 <sup>ac</sup>	115.84 ±6.38 <sup>c</sup>	56.27 ±1.50 <sup>abc</sup>	14.80 ±1.34 <sup>abc</sup>
DMH	1.79 ±0.09 <sup>a</sup>	111.30 ± 3.69 <sup>ab</sup>	92.35 ± 1.42 <sup>ab</sup>	160.44 ±5.32 <sup>ab</sup>	227.41 ±3.94 <sup>abc</sup>	114.14 ±1.45 <sup>abc</sup>	56.30 ± 1.03 <sup>ab</sup>
CTDMH	2.54 ±0.11 <sup>abe</sup>	103.68 ±3.82	79.33 ± 1.75 <sup>e</sup>	97.57 ±2.45 <sup>e</sup>	116.76 ±6.85 <sup>e</sup>	58.17 ±1.93 <sup>abe</sup>	39.40 ±1.67 <sup>abe</sup>

CT= costus +ve cont. DML= 1/30LD50. CTDML= costus + delta 1/30LD50  
DMH= delta 1/15LD50. CTDMH= costus + delta 1/15LD50.

Data are expressed as means ± SE of five rats.

a Significant differences versus control group at  $p < 0.05$ .

b Significant difference versus CT group at  $p < 0.05$ .

c Significant difference versus DML group at  $p < 0.05$ .

d Significant difference versus CTDML group at  $p < 0.05$ .

e Significant difference versus DMH group at  $p < 0.05$ .



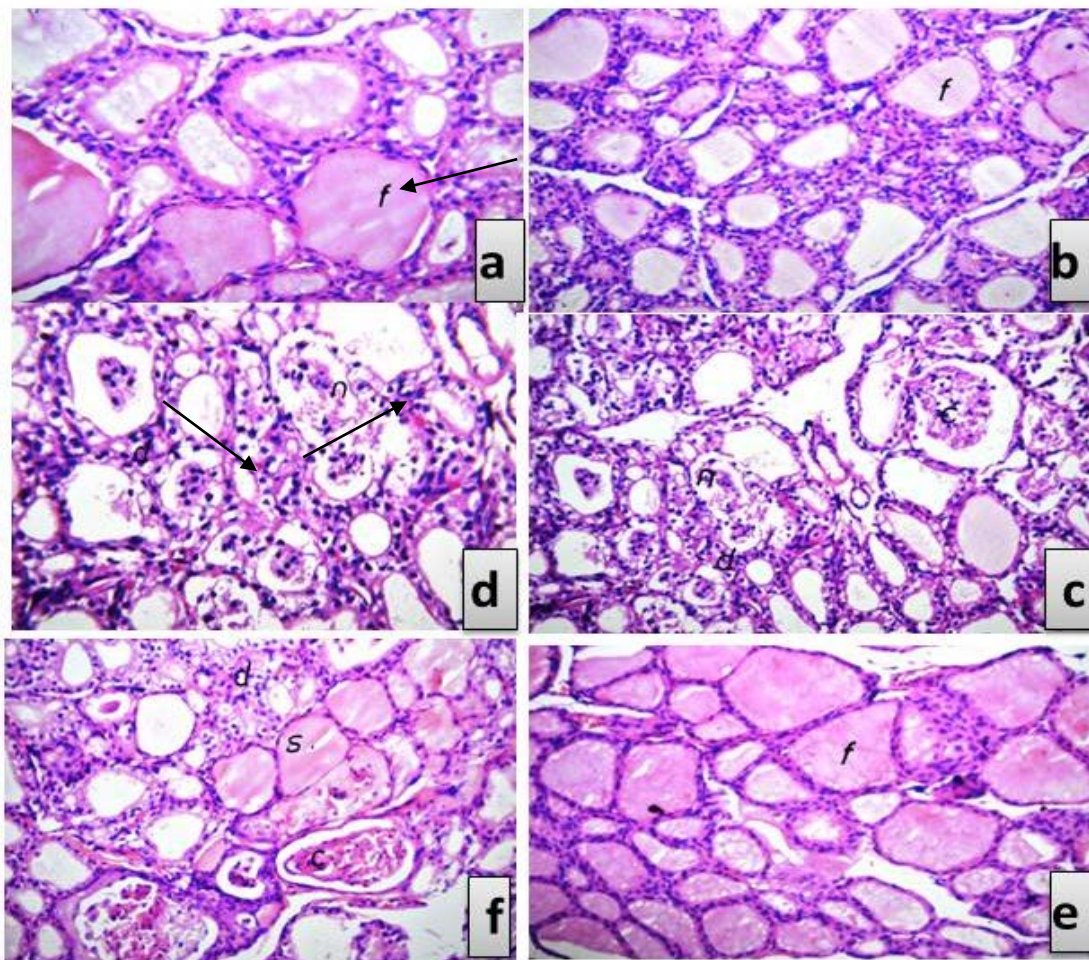


Fig 1: Effect of costus extract on histopathological pictures of thyroid glands of rats intoxicated with deltamethrin: (a) Section of a thyroid gland of control rat, showing normal interfollicular C-cells (arrow), normal follicles (f) lined with epithelial cells and filled with eosinophilic colloid. (b) Section of a thyroid gland of costus extract treated rat, showing normal follicles and C-cells. (c) Section of a thyroid gland of rat intoxicated with the low dose of DM, showing reduction in the size of thyroid follicles with a reduction in the amount of colloid. Notice that some follicles showed vacuolated colloid and degeneration in the lined follicular cells. (d) Section of a thyroid gland of rat intoxicated with the high dose of DM, showing disorganization and severe degenerative changes of follicular architecture. Most follicles showing severe reduction in their sizes, degeneration of epithelial lining and a minimum amount of colloid. Other follicles showing detachment and desquamated of epithelial lining in the lumen (arrows). (e) Section of a thyroid gland of rat pre-treated with costus extract and intoxicated with the low dose of DM, showing more or less normal thyroid architecture with normal follicles. (f) Section of a thyroid gland of rat pre-treated with costus extract and intoxicated with the high dose of DM, showing an obvious improvement in the thyroid architecture, but some colloid vacuolation still appear in some follicles (H& E  $\times$  400)

## DISCUSSION

With extensive use of pyrethroids, progressive adverse health problems have recorded in an environment and humans [31]. The aim of the present study was to explore the potential impacts of *S lappa* (costus) extract in reducing the toxic impacts of DM on hemogram parameters, oxidative stress and antioxidant markers, metabolic parameters and thyroid gland function.

Assessing of hemogram markers is significant in evaluating the toxicity of hazard environmental pollutants. The results of the current study showed that administration of either the low or the high dose of DM to rats caused marked decreases in RBCs, Hb and PCV coupled with an elevation in WBCs in both intoxicated groups versus control group. Similar result has been obtained by some authors [32]. The decrease in RBCs of rats by DM

administration may attribute to the suppression of their formation by bone marrow and/or their destruction by the insecticide toxicity [33]. The remarkable leukocytosis of intoxicated rats may result from an induction of rat immune system due to an inflammation caused by the exposure to the insecticide. This result is corroborated by a clinical study revealed an elevation in white blood cells of farm workers under the effect of pesticide exposure that may create a relationship between chronic lymphocytic leukemia and pesticide exposure [32].

Administration of costus extract to rats intoxicated with either of DM dose, markedly modulated the deviations in hemogram parameters (RBCs, Hb and WBCs) in relation to the control counterpart group. The modulating effect of the plant extract on RBCs and Hb may confirm its ability to inhibit DM toxicity. The ameliorating impact of the used extract on WBCs may indicate its immunomodulatory beneficial action. The immunomodulatory of hydroalcoholic extract from costus roots was previously proved [34].

The current data revealed that intoxication of rats with the high or the low dose of DM caused an increase in oxidative stress biomarker, MDA (index of lipid peroxidation), in plasma of intoxicated rats versus control ones. This adverse effect of DM on oxidative stress marker was accompanied by marked decreases in the plasma antioxidant markers, namely protein thiol, GST, CAT and SOD. The induction of reactive free radicals, promotion of lipid peroxidation, and alteration in the antioxidant defense are considered mechanisms of pyrethroids toxicity [35]. Exposure of organic molecules to free radical species can induce irreversible oxidation of these molecules and cause alterations of many metabolic reactions that in turn can lead to cellular dysfunction [36-37]. The decrease in SH-protein has been found in animals intoxicated with Lambda cyhalothrin for 90 days [38]. Also, a previous study stated that significant decreases in antioxidant enzymes, including CAT, GST and SOD in experimental animals exposed to low doses of DM [39]. In addition, cypermethrin, as one of pyrethroids, has been reported to promote lipid peroxidation and repress the activities of antioxidant enzymes, including SOD, CAT, GST, glutathione reductase and glutathione peroxidase [40].

Administration of costus extract to either DM intoxicated rat group, significantly reduced the lipid peroxidation and attenuated the deviations in the antioxidant defense markers compared with intoxicated counterpart rat group. This result may imply the beneficial antioxidant capacity of costus extract. Few studies have investigated the antioxidant effect of costus extracts. The present study suggests that the antioxidant capacity of costus extract may relate to its active ingredients, namely flavonoids, anthraquinone, and various terpenes [41-42].

Pesticides are among the chemicals that have endocrine disruption effect [43]. The present study recorded a significant reduction in the plasma triiodothyronine (T3) in both DM intoxicated groups, while plasma thyroxin (T4) recorded a significant decrease in the low intoxicated group and an elevation in DM high dose treated group. This result indicated that the toxicity of the used pesticide induced disorders in the thyroid hormones. This is supported by previous study reported that exposure to pesticides could lead to disruptions of the thyroid gland [43]. The molecular mechanisms by which the pesticides could induce thyroid disturbances include inhibition of iodine uptake by the thyroid follicular cells, interference in thyroid hormone receptor or inhibition of the thyroperoxydase enzyme involved in the biosynthesis of thyroid hormones [44]. Some authors concluded that pesticides may have a direct toxic effect on the thyroid by inhibiting the synthesis of thyroxin or accelerating its deiodination [45]. Histopathological study confirmed these findings as observed by degenerative changes of thyroid follicular architecture in both DM intoxicated. These changes were more severe in animals exposed to the high dose of DM. This histopathological observation may indicate that the thyroid gland is one of the sensitive target organs to DM toxicity. Similar thyroid histopathological changes have been documented in rats exposed to DM [46]. The damaging impact of DM on the thyroid gland may attribute to the oxidative stress and lipid peroxidation which have the major role in tissue damage [35]. Pretreatment of DM intoxicated rats with costus extract, effectively up-modulated the thyroid hormones and improved the histomorphological changes of thyroid gland. This may indicate that the used costus extract contributes to the protection against the damaging impact of DM toxicity. The prophylactic impact of the used plant extract may relate to the antioxidant ability of its constituents [41-42].

Hyperglycemia and hyperlipidemia are metabolic disorders caused by the adverse impacts of pesticide toxicity in human [47-49]. The present study illustrated that intoxication of rats with the low or the high dose of DM, induced hyperglycemia and dyslipidemia as shown by significant increases in the plasma fasting glucose and lipid profile, including TCh, TGs, HDL- C and LDL-C in DM treated rats with respect to control ones. Some authors reported



that hyperglycemia and hyperlipidemia are the major complications of DM toxicity [47-49]. The induced hyperglycemia by DM may reflect that this toxin has a deleterious effect on pancreatic  $\beta$ -cells. A previous study has suggested that the diabetic state induced in response to pesticide toxicity is a result of dysfunction of pancreatic  $\beta$  cell, causing a deficient in insulin secretion [50]. Hyperlipidemia may be related to hypothyroidism induced by DM [51]. Previous reports demonstrated that hypothyroidism is associated with a decrease in LDL-receptors' activity, resulting in a suppression in LDL catabolism [52]. Also, hypothyroidism is contributed to the inhibition of lipoprotein lipase activity which is responsible for the catabolism of TG-rich lipoproteins, thus decreasing its clearance [53].

In our study, treatment with costus extract significantly reversed the levels of both plasma glucose and lipids in both DM intoxicated rat groups, implying its potential hypoglycemic and hypolipidemic beneficial actions. The regulatory effects of costus extracts on blood glucose level and lipid profile have been previously confirmed [54-55]. The antidiabetic potential of costus extract may be due to the increased secretion of insulin from the pancreatic  $\beta$  cells and /or stimulation of glucose utilization by peripheral tissues. On the other hand, the hypolipidemic impact of the plant extract may be due to its modulating beneficial impact on the thyroid hormones.

### CONCLUSION

The present investigation may suggest that early ingestion of *S lappa* hydro-alcoholic extract could mitigate the alteration in hemogram parameters, oxidative stress, thyroid and metabolic disorders caused by deltamethrin intoxication. The beneficial effect of the used costus extract may be due to the immunomodulatory, antioxidant, hypoglycemic and hypolipidemic of its active constituents.

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