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Toxic effects of Lambda-cyhalothrin, on the rat thyroid: Involvement of oxidative stress and ameliorative effect of ginger extract

Wael M. Al-Amoudi

Department of Biology, Faculty of Applied Sciences, Umm Al-Qura University, Makkah 21955, Saudi Arabia

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ABSTRACT

Lambda-cyhalothrin (LCT) is a synthetic pyrethroid that is widely used to control insecticide. Ginger is a traditional plant that is widely used as a spice or folk medicine. This study evaluates the antioxidant effect of ginger extract on thyroid toxicity induced by LCT in albino rats. Adult Rats were divided into 4 experimental groups: Group 1: control, Group 2: oral ginger treatment (24 mg/ml, 3 days/week for 4 weeks), Group 3: oral LCT treatment (1/100 LD_{50}, 3 days/week for 4 weeks), Group 4: oral LCT and ginger mixture treatment. The histological results of LCT group showed degenerated follicles with reduced colloids, congestion of blood vessels and hyperaemia between the follicles. Histochemically, depletion of glycogen and proteins was recorded in follicular cells and colloids. The biochemical results of LCT treated group revealed a decrease in T3, T4, SOD and CAT, while TSH and MDA were increased. The comet assay showed that LCT significantly induced DNA damage in the thyroid gland. However, treating rats with LCT plus ginger led to an improvement in the histological structure of the thyroid, with noticeable increases in glycogen and protein deposition. Also, LCT plus ginger increase in T3, T4 and the antioxidant enzymes SOD and COT were detected concomitantly with a decrease in TSH and MDA as well as a significant reduction in DNA damage. LCT affected the thyroid function and structure. On the other hand, ginger has a preventative effect against the histological damage and biochemical toxicity caused by the (LCT) insecticide.

1. Introduction

Pyrethroid pesticides are used worldwide as insecticides in pest control by disrupting the normal function of sodium channels. Pyrethroid pesticides are known to be less harmful to mammals, birds and less toxic to the environment than other insecticides [40]. Based on the mechanism of action chemical structure, we have two classification of pyrethroid pesticides namely: type I and type II. Type I pyrethroids have been reported to influence sodium channels in nerve membranes thereby causing a continuos neuronal discharge and leading to an after-potential in a prolonged negative way [40,50,77]. Type II pyrethroids are a modified version of type I pyrethroids that are formed by adding an α-cyano to phenoxybenzoic constituents in order to enhance their photostability [90]. These pyrethroids causes a longer delay in sodium channel inactivation and inhibit sodium channel-dependent activity of rat cortical neurons *in vitro* [45,67]. In addition, pyrethroid pesticides have been found in environmental samples, such as water and sediments [66,85,86]; food [95]; and they can also be found in Urine and breast milk under human samples, metabolites of pyrethroids have also been shown to exert adverse effects on different physiological functions in the body [21,65]. In connection to the exposure of this pesticide, it was reported that diseases such as reproductive disorders, cancer, neurological disorders, allergies, mental disorders could be connected [61,87,93].

Moreover, it has been revealed that many pyrethroids and other insecticides are potential endocrine-disrupting chemicals. They have been shown to develope a negative impact on the reproductive, immune and hormonesystems of humans and animals [10,63,87]. Normal secretion of thyroid hormones is essential for some physiological processes as a controller of metabolic activity, including bone remodeling, cardiovascular activities, and abnormal behaviour. Hence, maintaining normal activities of thyroid is imperative for normal physiological and psychological health [10,49]. It has been reported that opening to thyroid-disrupting chemicals can cause a reduction of serum hormone

Abbreviations: LCT, Lambda-cyhalothrin; SOD, superoxide dismutase; CAT, catalase; TSH, thyroid-stimulating hormone; MDA, malondialdehyde; AD, Alzheimer's disease; PD, Parkinson's disease; PCO, protein carbonyl; T3, triiodothyronine, T4, thyroxine; PAS, Periodic acid–Schiff; ALT, plasma alanine aminotransferase; AST, aspartate aminotransferase; GPx, glutathione peroxidase; GR, glutathione reductase; GST, glutathione-S-transferase; CC14, carbon tetrachloride; DMBA, 7,12-dimethylbenz(a)anthracene; DMA, lipid peroxidan marker; ALK-P, alkaline phosphatase; GSH, glutathione; ROS, reactive oxygen species; TL, distance of DNA migration from the center to the nuclear core; TI, percent of genomic DNA that migrated during electrophoresis from the nuclear core to the tail

E-mail address: wmamoudi@uqu.edu.sa.

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levels leading to unusual activities of the thyroid gland by disrupting the TSH receptor since normal diffusion of thyroid-stimulating hormone (TSH) invigorates all the steps of hormone secretion [49]. In turn, this may have substantial consequences for the healthy metabolic function of the biosystem. Some clinical studies have demonstrated that pyrethroids hamper endocrine functions [76]. Furthermore, oxidative stress effects of pyrethroid-induced toxicity have been reported by some investigators [64,94]. A growing number of studies have indicated that oxidative stress plays critical roles in various toxicities associated with pyrethroid insecticides [84].

Lambda-cyhalothrin (LCT) is a manufactured pyrethroid insecticide that is being used in home pest control, agriculture, protection of food production and disease vector control [33,88]. LCT has been widely used to control pests, including aphids, Colorado beetles and lepidopteran larvae, [81] and was detected in milk, the blood of dairy cows [17] and cattle meat [43]. It has been reported that exposing rats to LCT leads to hepatotoxicity and severe renal structure injury due to its toxicity in rats [83]. Another study indicated that renal activities, tissue malondialdehyde (MDA), histopathology, protein carbonyl (PCO) levels, reduced glutathione (GSH) levels and antioxidant enzyme activities were significantly affected by LCT [33]. The use of LCT to treat rats can result to an uprising in the number of structural chromosomal aberrations and frequency of micronucleated erythrocytes [19]. LCT expanded the generation of reactive oxygen species and DNA damaged levels, inducing adverse immune effects [96]. In addition, other results revealed that LCT caused significant increases in the kidney, brain and liver weight as well as plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Additionally, the decreased Alk-P and brain activity has been found in rats. However, the plasma content of bilirubin, urea, creatinine, and glucose were significantly increased. By contrast, plasma total protein and albumin was decreased [91]. The was aim of this study is to investigate the propensity of Lambda-cyhalothrin (LCT) to prompt oxidative pressure and changes in the biochemical parameters and the movement of enzyme in the thyroid gland of male rats as well as its conceivable weakening by Ginger extract.

Synthetic chemical drugs are expensive and cause genetic and metabolic alterations in biosystems. Botanical medicines have traditionally been used to treat disease development and progression. In this regard, medicinal plants and their components have important roles in disease control by modulating the activity of biological systems [37,51]. Ginger, the rhizome of the Zingiber officinale, a standout amongst the most commonly utilized traditional food types and has been shown to have a therapeutic role in overall health and well-being. Many studies have shown that ginger plays a noteworthy part in the avoidance of many diseases by means of a tweak of hereditary and metabolic activities in human and animal model [24,36,97].

Ginger is publicly described and has been used for thousands of years as an anti-vomiting, diabetes mellitus, and cancer treatment, especially in Asian and other Eastern cultures [22,51]. It likewise has anti-inflammatory and anti-oxidative properties for controlling the way towards maturity [37,56]. The analyzed chemical composition of aqueous extracts of ginger root includes polyphenols, vitamin C, B, C, β carotene, flavonoids and tannins [60,70]. It has at least 14 bioactive compounds, including [4]-gingerol [6],-gingerol [8],-gingerol [10],-gingerol [6],-paradol [14],-shogaol [6],-shogaol, 1-dehydro- [10]-gingerdione [10],-gingerdione, hexahydrocurcumin, tetrahydrocurcumin, gingerenone A, 1,7-bis-(4′hydroxyl-3′methoxyphenyl)-5-methoxyhepthan-3-one, and methoxy- [10]-gingerol [16,46,83]. HPLC analysis of Zingiber officinale ethanolic extracts showed that shogaol and gingrol were the most abundant phenolic components [12].

Furthermore, other investigators have reported that ginger extract has hypolipidaemic [78] and anti-hypercholesterolemic [35] effects, hepatoprotective [31] and antioxidant properties [28,83] and it is protected against dyslipidaemia in diabetic rats [15]. It has been revealed that ginger extract has a protective effect against cyclophosphamide, which induces chromosomal abnormalities in the somatic cells of mice [89], and also has chemopreventive and chemotherapeutic activities against cancer development [59]. It has been showed that ginger has anti-mutagenic effects against genotoxicity induced by the anti-cancer drug Taxol [9]. Recent studies have suggested that Ginger can reduce the risk of some chronic diseases, such as fatty liver disease, asthma, cancer growth and arthritis through its anti-inflammatory, immunoregulatory and antioxidative properties [8,69]. The present work was designed to evaluate the preventive effect of aqueous extracts of *Zingiber officinale* on thyroid toxicity and oxidative pressure initiated by Lambda-cyhalothrin in albino rats. Evaluating the bioactivity and histopathological alterations of ginger are necessary to completely understand its potential therapeutic effects.

2. Materials and methods

2.1. Lambda-cyhalothrin

Lambda-cyhalothrin (α-cyano-3-phenoxy -benzyl-3-(2-chloro-3, 3, 3-trifluoro-1-propenyl)-2, 2-dimethylcyclopropanecarboxylate) is a synthetic pyrethroid that is 99.8% active. The product was obtained from the faculty of Agriculture, King Abdulaziz University, Jeddah, KSA. Water was added to the chemical to dilute it for a final concentration that was appropriate for dosing. LCT was used at a dosage of $1/100^{th}$ LD_{50} (0.79 mg/kg b.wt), 3 days/week for 4 weeks, diluted in water according to a previous report [27].

2.2. Ginger extract

Ginger (*Z. officinale* Roscoe) rhizome was purchased from a local market. One kilogram of ginger rhizome was cleaned, washed under running water, cut into small pieces and air dried. The dried rhizomes were powdered and stored at lab temperature (20–23 °C) for oral feeding. One-hundred-twenty-four grams of this powder was macerated in 1000 ml of distilled water (dH_2O) for 12 h at room temperature and filtered. The concentration of the concentrate was 24 mg/ml. The rats under study were given 1 ml of this fluid concentrate orally [42].

2.3. Experimental animals

The ethics committee of Umm Al-Qura University approved the animal under experiments. In this study, male albino rats (Wistar) were used, they were seven-week old rats with an average body weight of 160–180 g were used. The cages that rats were housed was (23–25 °C) under identical laboratory conditions. Food and water were provided ad libitum amid the trial/experimental time frame (30 days). Animals were provided with monetarily accessible dry food pellets. Animals were kept up in a controlled climate with a 12-hour dark/light cycle at an encompassing temperature of 22 ± 2 °C. Following one week of acclimation, animals were divided randomly into four experimental groups (n = 10 in each group).

Group I: was used as a control and got the standard diet and water *ad libitum*.

Group II: was used to study the effect of ginger and was orally given ginger extract (powder) dissolved in water at a measurement level of 24 mg/ml 3 days/week for 4 weeks by using the intragastric gavage technique.

Group III: was utilized to evaluate the impact of a low oral dose of Lambda-cyhalothrin (0.79 mg/kg b.wt. $1/100^{th}$ of the LD_{50}) and was orally given Lambda-cyhalothrin 3 days/week for 4 weeks by using the intragastric gavage technique.

Group IIII: was utilized to evaluate the impact of the mixture of a low dose of Lambda-cyhalothrin of $1/100^{th}$ of the LD_{50} and ginger (24 mg/ml) and was orally administered 3 days/week for 4 weeks by using the intragastric gavage technique.

the total body weight of each animal was recorded at the end of the