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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2020.510.517

Research Article
Naringenin Attenuates Toxicity and Oxidative Stress Induced by Lambda-cyhalothrin in Liver of Male Rats

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Abstract

Background and Objectives: Extensive use of Lambda-cyhalothrin (LTC), a synthetic pyrethroid insecticide, has been associated with serious health problems to the non-target organisms including mammals. The present study investigated the protective effect of naringenin (NGN), an antioxidant flavonoid, against the toxicity induced LTC in the liver of male rats. **Materials and Methods:** Five groups of rats were assigned as follows; control group, LTC group (6.12 mg kg^{-1}, 1/10 LD_{50}), LTC-NGN group (6.12 mg kg^{-1} LTC and 50 mg kg^{-1} NGN), NGN-LTC group (50 mg kg^{-1} NGN and 6.12 mg kg^{-1} LTC) and NGN group (50 mg kg^{-1}). Doses were administrated orally for 21 consecutive days. **Results:** Administration of LTC induced liver damage as indicated by the increase in the activities of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase and in the level of total bilirubin in serum. LTC also induced a significant elevation in the levels of serum total lipids, total cholesterol, triglycerides and low-density lipoproteins while high-density lipoproteins decreased. Furthermore, LTC significantly disturbed the oxidant/antioxidant balance in the liver as shown by the elevation in lipid peroxidation, lipid hydroperoxides, protein carbonyl content and conjugated dienes with a concomitant inhibition in the major antioxidants such as reduced glutathione and the activities of superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase. Both post-treatment and pre-treatment with NGN significantly modulated the LTC-induced hepatotoxicity and oxidative stress in rat's liver and pretreatment was found to be more effective in improving most of the studied parameters in both serum and liver tissue. **Conclusion:** NGN could be used as a safe dietary supplement to protect against the toxicity and oxidative stress associated with the use of LTC.

Key words: Lambda-cyhalothrin, naringenin, hepatotoxicity, oxidative stress, rats

Citation: Ahmed Mokhtar Abu El-Saad and Wessam Mohamad Abdel-Wahab, 2020. Naringenin attenuates toxicity and oxidative stress induced by lambda-cyhalothrin in liver of male rats. Pak. J. Biol. Sci., 23: 510-517.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Pyrethroids have been well recognized for their efficiency in control of insects and pests in agricultural and residential areas. They account for approximately one-fourth of the worldwide used insecticides[1]. Lambda-cyhalothrin (LTC) is a synthetic pyrethroid that is considered to be the first-choice insecticide compared with other organochlorines, organophosphates and carbamates[2]. The extensive use of LTC has been found to be associated with serious health problems to the non-target organisms including mammals[3]. LTC has been reported to induce neurotoxicity[4], nephrotoxicity[5], genotoxicity[6] and hepatotoxicity[7]. Excessive production of free radicals and induction of oxidative damage have been identified to be major mechanisms implicated in the toxicity of LTC[7]. Therefore, the use of natural antioxidants may be useful in preventing, or at least reducing, the toxicity of LTC through combating the formation of free radicals and inhibiting their reaction with cellular structures. Phytochemicals have gained much consideration in this regard because of their beneficial effects.

Naringenin (NGN) is a flavonoid that is found in grapes, citrus fruits and tomatoes. It has a wide range of pharmacological effects including anti-inflammatory, antiadipogenic, anticancer in addition to neuroprotective and cardioprotective properties[8]. Furthermore, NGN has been reported to be an effective antioxidant due to its ability to scavenge free radicals directly, chelate metal ions and to enhance the endogenous antioxidant system[9]. NGN protected against *in vivo* and *in vitro* liver damage induced by various agents such as carbon tetrachloride[10] and heavy metals[11]. The present study aimed to investigate the toxicity of LTC in the liver of male rats. Furthermore, the efficacy of pre-treatment and post-treatment with NGN in modulating the hepatotoxicity induced by LTC was investigated.

MATERIALS AND METHODS

Study area: The study was carried out at Zoology Department, Faculty of Science, University of Alexandria, Egypt from 15/06/2019 to 20/07/2019.

Chemicals: Lambda-cyhalothrin ($C_{23}H_{19}ClF_3NO_3$, commercial formulation named KARATE® 5EC) was obtained from Syngenta agrochemicals (Greensboro, USA). The dose selected in the present study was 6.12 mg kg^{-1} (1/10 of LD_{50}) which was reported to be toxic but not lethal to rats[12]. Naringenin was purchased from Sigma Chemical Co (St. Louis, MO, USA) and was administered at a dose of 50 mg kg^{-1} according to Jain *et al.*[13]. All other chemicals and kits used in this study were purchased from Sigma Chemical Co. (St. Louis, MO., USA) and were of analytical grade.

Animals and experimental protocol: Forty male Sprague-Dawely rats (weighing 120-140 g) were obtained from the animal house of Faculty of Agriculture, University of Alexandria, Egypt. Animals were housed 4/cage and kept on commercial standard pellet diet and tap water provided *ad libitum*. The rats were maintained under standard laboratory conditions (Temperature 24±2°C and natural light-dark cycle). All animals received human care which complies with the institutional instructions and guidelines. After 2 weeks of acclimation, the effect of LTC on the toxicity and oxidative stress biomarkers in the liver of male rats and the role of NGN were studied by randomly dividing the animals into 5 groups (eight animals in each) as follows: Group 1 served as control group and received 1 mL kg^{-1} 0.5% dimethyl sulfoxide (DMSO) once/day via gavage. Group 2 (LTC group) was given LTC at a dose of 6.12 mg kg^{-1} (1/10 LD_{50}) once/day via gavage. Group 3 received NGN at a dose of 50 mg kg^{-1} 30 min after the administration of LTC (6.12 mg kg^{-1}) and was used as post-treatment group. Group 4 was given NGN (50 mg kg^{-1}) 30 min before the administration of LTC (6.12 mg kg^{-1}) and served as pre-treatment group. Group 5 received NGN only (50 mg kg^{-1}) once/day via gavage. Both LTC and NGN were dissolved in 0.5% DMSO and were orally administrated daily for 21 consecutive days.

Blood collection and tissue preparation: After the administration of the last doses of LTC and NGN, rats were fasted overnight. Rats of each group were euthanized and the trunk blood samples were collected from the animals and centrifuged at (860×g for 20 min) for serum separation which was stored at -60°C till measurements. The liver was removed quickly, weighed and placed in ice-cold 0.9% NaCl solution, perfused with the physiological saline solution to remove blood cells and blotted on filter paper. The gall bladder was then carefully dissected away and the excised liver was minced and homogenized (10%, w/v) in appropriate buffer (pH 7.4) using a mechanically driven Teflon fitted Potter-Elvehjem homogenizer and centrifuged (3000×g for 10 min). The resulting clear supernatant was used for estimation of different biochemical parameters.

Determination of liver function parameters: The activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and total bilirubin level were estimated spectrophotometrically according to the standard procedures using commercially available diagnostic kits (Sigma diagnostics (I) Pvt. Ltd., Baroda, Gujarat, India).

Assay of serum lipid and lipoprotein profiles: The concentrations of total lipids in serum were determined by the method of Knight *et al.*[14] and that of cholesterol and triglycerides were assayed by the method Carr *et al.*[15]. High density lipoprotein-cholesterol (HDL-C) was detected according to the methods of Warnick *et al.*[16]. Serum LDL-cholesterol (LDL-C) level was calculated according to Friedewald *et al.*[17] equation:

$$\text{LDL-C} = \text{Total cholesterol concentration} - \left(\frac{\text{Triglyceride concentration}}{5}\right) - \text{HDL-C concentration}$$

Estimation of lipid and protein oxidation indices: Lipid peroxidation was determined calorimetrically by measuring thiobarbituric acid reactive substances (TBARS) and hydroperoxides (HPs) as reported by Niehaus and Samuelsson[18] and Jiang *et al.*[19], respectively. Also, total protein carbonyl content (PCC) content was determined spectrophotometrically according to the method of Levine *et al.*[20]. The level of conjugated dienes (CD) was estimated using the method of Rao and Recknagel[21].

Determination of antioxidants in the liver tissue: Reduced glutathione (GSH) was detected by the described method of Ellman[22]. Superoxide dismutase (SOD) activity was estimated spectrophotometrically by the method of Kakkar *et al.*[23]. Colorimetrically, catalase (CAT) activity was assayed as described by Sinha[24]. Also, the activity of glutathione peroxidase (GPx) was assayed by the method reported by Rotruck *et al.*[25]. Glutathione S-transferase (GST) activity was assayed spectrophotometrically according to the method of Habig *et al.*[26]. Glutathione reductase (GR) was determined by the method of Horn and Burns[27].

Protein determination: Protein assay was determined according to the method of Lowry *et al.*[28].

Statistical analysis: Results are expressed as the Mean±SE. Treated group size was eight animals. Statistical analysis were performed using ANOVA, followed by Duncan's multiple range test[29]. The data were compared against those from the proper control animals. Differences were considered significant at $p<0.05$.

RESULTS

No death was observed in any of the experimental groups. Also, no statistically significant changes in all tested parameters were observed in the group treated with NGN alone compared with the control group.

Effect of LTC and NGN on liver function biomarkers: In the present study, administration of LTC induced liver dysfunction. Data in Table 1 showed a significant ($p<0.05$) increase in the activities of serum hepato-specific enzymes. The activities of AST, ALT, ALP and in the level of bilirubin were found to be increased by 70.3, 60.5, 55.2 and 62.4%, respectively, as compared to the control. Pre-treatment with NGN in LTC-intoxicated rats significantly reduced the activities of AST and ALT when compared with LTC group while; post-treatment could not improve the activities of these enzymes as indicated by the significant difference with the control group. However, post-treatment with NGN in LTC-intoxicated rats significantly reduced the ALP activity. Pre-treatment and post-treatment with NGN showed a significant decrease in the level of bilirubin as compared to LTC-intoxicated rats, although not reaching the value of the control group (Table 1).

Table 1: Effect of lambda-cyhalothrin, naringenin and their combination on the levels of hepatic biomarkers in serum of rats

	Treatment (dose kg^{-1})				
Parameters	Control	LTC (6.12 mg)	LTC/NGN (6.12 mg/50 mg)	NGN/LTC (50 mg/6.12 mg)	NGN (50 mg)
AST (U L^{-1})	34.24±3.32	58.30±4.25*	52.74±3.53*	41.25±4.15#	37.12±3.02#
ALT (U L^{-1})	21.62±2.04	34.71±3.25*	29.22±3.05*	26.36±2.64#	22.11±2.11#
ALP (U L^{-1})	62.22±7.41	96.57±9.21*	75.21±6.22#	88.31±6.48*	64.54±6.82#
Bilirubin (mg dL^{-1})	0.93±0.04	1.51±0.07*	1.23±0.05*,#	1.18±0.05*,#	0.87±0.04#

LTC: Lambda-cyhalothrin, NGN: Naringenin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, data are expressed as Mean±SE for 8 rats in each group, *Significant difference ($p<0.05$) from the control group, #Significant difference ($p<0.05$) from LTC-treated group

Table 2: Serum lipid and lipoprotein profiles of male rats treated with lambda-cyhalothrin, naringenin and their combination

Lipid profile (mg dL^{-1})	Treatment (dose kg^{-1}) Control	LTC (6.12 mg)	LTC/NGN (6.12 mg/50 mg)	NGN/LTC (50 mg/6.12 mg)	NGN (50 mg)
TL	563.26±13.41	734.33±17.54*	602.64±14.11$^{\#}$	591.32±13.34$^{\#}$	552.43±11.72$^{\#}$
Cholesterol	192.56±4.73	234.72±6.82*	206.41±5.62$^{\#}$	223.82±4.22*	184.72±3.75$^{\#}$
TG	113.63±2.51	152.42±7.21*	125.22±3.61$^{\#}$	138.72±4.77*	108.42±3.42$^{\#}$
HDL-C	63.46±5.32	41.53±2.51*	60.11±3.22$^{\#}$	56.31±4.36$^{\#}$	68.63±4.33$^{\#}$
LDL-C	96.62±3.81	127.63±3.85*	112.52±2.83$^{\#}$	106.22±3.44$^{\#}$	92.52±3.72$^{\#}$

LTC: Lambda-cyhalothrin, NGN: Naringenin, TL: Total lipids, TG: Triglycerides, HDL-C: High density lipoprotein-cholesterol, LDL-C: Low density lipoprotein-cholesterol, data are expressed as Mean±SE for 8 rats in each group, *Significant difference ($p<0.05$) from the control group, $^{\#}$Significant difference ($p<0.05$) from LTC-treated group

Table 3: Changes in the levels of thiobarbituric acid reactive substances, hydroperoxides, protein carbonyl content and conjugated dienes in the liver of male rats treated with lambda-cyhalothrin, naringenin and their combination

Parameters	Treatment (dose kg^{-1}) Control	LTC (6.12 mg)	LTC/NGN (6.12 mg/50 mg)	NGN/LTC (50 mg/6.12 mg)	NGN (50 mg)
TBARS (mg g^{-1})	8.32±0.35	21.13±1.83*	17.42±1.31$^{*,\#}$	11.32±1.72$^{\#}$	8.62±0.37$^{\#}$
HPs (mmol g^{-1})	1.32±0.22	2.55±0.16*	1.76±0.15$^{\#}$	1.58±0.11$^{\#}$	1.12±0.13$^{\#}$
PCC (nmol mg^{-1})	3.54±0.32	5.52±0.65*	3.46±0.46$^{\#}$	3.81±0.25$^{\#}$	3.74±0.33$^{\#}$
CD (mmol mg^{-1})	41.05±0.52	72.34±0.46*	53.72±0.41$^{*,\#}$	44.33±0.32$^{\#}$	38.75±0.47$^{\#}$

LTC: Lambda-cyhalothrin, NGN: Naringenin, TBARS: Thiobarbituric acid reactive substances, HPs: Hydroperoxides, PCC: Protein carbonyl content, CD: Conjugated dienes, data are expressed as Mean±SE for 8 rats in each group, *Significant difference ($p<0.05$) from the control group, $^{\#}$Significant difference ($p<0.05$) from LTC-treated group

Table 4: Changes in the enzymatic and non-enzymatic antioxidants in the liver of male rats treated with lambda-cyhalothrin, naringenin and their combination

Parameters	Treatment (dose kg^{-1}) Control	LTC (6.12 mg)	LTC/NGN (6.12 mg/50 mg)	NGN/LTC (50 mg/6.12 mg)	NGN (50 mg)
GSH (μg mg protein^{-1})	6.72±0.30	3.56±0.24*	4.28±0.37*	5.21±0.23$^{\#}$	6.20±0.36$^{\#}$
SOD (U mg protein^{-1})	5.82±0.31	3.43±0.52*	3.82±0.36*	4.42±0.33$^{\#}$	6.22±0.44$^{\#}$
CAT (μmol min^{-1} mg protein^{-1})	78.82±4.05	51.39±3.84*	63.27±2.85$^{*,\#}$	66.11±2.44$^{*,\#}$	81.53±3.16$^{\#}$
GPx (μg min^{-1} mg protein^{-1})	9.16±0.37	5.17±0.43*	7.34±0.41$^{\#}$	7.81±0.25$^{\#}$	9.75±0.41$^{\#}$
GST (μmol min^{-1} mg protein^{-1})	8.33±0.46	4.77±0.22*	6.33±0.35$^{\#}$	6.91±0.37$^{\#}$	8.82±0.62$^{\#}$
GR (nmol min^{-1} mg protein^{-1})	0.58±0.05	0.51±0.02	0.53±0.03	0.55±0.02	0.56±0.04

LTC: Lambda-cyhalothrin, NGN: Naringenin, GSH: Reduced glutathione, SOD: Superoxide dismutase, CAT: Catalase, GPx: Glutathione peroxidase, GST: Glutathione-S-transferase, GR: Glutathione reductase, data are expressed as Mean±SE for 8 rats in each group, *Significant difference ($p<0.05$) from the control group, $^{\#}$Significant difference ($p<0.05$) from LTC-treated group

Effect of LTC and NGN on serum lipid profile: Relative to the control, LTC treatment induced a significant ($p<0.05$) increase in serum levels of total lipids, total cholesterol, triglycerides and LDL-C by 30.4, 21.9, 34.13 and 32.09%, respectively when compared with the control group while the level of HDL-C decreased significantly by 34.55%. Pre-treatment and post-treatment with NGN in with LTC-intoxicated rats could alleviate the adverse effects of LTC and the alterations in total lipids, HDL-C and LDL-C and restored their normal values. Interestingly, the levels of cholesterol and triglycerides were significantly decreased in post-treatment with NGN, while pre-treatment with NGN does not show any significant change in their levels when compared with the LTC-treated group (Table 2).

Effect of LTC and NGN on LPO and protein oxidation indices: The alterations in the level of lipid and protein oxidation product in liver of control and experimental rats were reported in Table 3. The levels of TBARS, HPs, PCC and CD were significantly ($p<0.05$) increased in rats treated with LTC by 154, 93.2, 55.9 and 76.2%, respectively compared to the control. Pretreatment with NGN was able to recover the elevation in liver LPO to the control group level. Statistically, there were significant differences between LTC-treated group and post-treated with NGN and the control group. The same scenario was repeated for hepatic CD, where pre-treatment with NGN to the rats intoxicated with LTC normalized the LTC effect and post-treatment with NGN decreased the effect of the pesticide, without reaching the control level. Interestingly, treatment with NGN either before or after the administration of LTC caused significant reductions in the levels of HPs and PCC in liver when compared to LTC-intoxicated animals.

Effect of LTC and NGN on non-enzymatic and enzymatic antioxidants in the liver: Changes in the liver antioxidant status are illustrated in Table 4. The level of GSH in the liver

of rats treated with LTC was significantly ($p<0.05$) decreased by 47% when compared to the control group. A significant elevation of hepatic GSH content was observed in rats pre-treated with NGN and intoxicated with LTC, while post-treatment could not modulate the change in GSH level. The activities of the main antioxidant enzymes were found to be significantly ($p<0.05$) decreased by 41, 34.8, 43.55 and 42.73% for SOD, CAT, GPx and GST, respectively when compared with the control group. The activity of SOD was significantly increased upon pre-treatment with NGN while post-treatment induced a non-significant change compared with the LTC-treated group. Both regimens of treatment with NGN partially improved the activity of CAT as compared to control group, Both regimens of treatment with NGN rats significantly increased the activities of GPx and GST and brought their values near the control group value. No change in the activity of GR in rats administered LTC or NGN or both when compared with the control group.

DISCUSSION

Environmental pollutants, including pesticides, are hazardous to health because of their toxicological effects and their ability to induce multiorgan dysfunctions. In the current study, the hepatotoxic effect of LTC, a synthetic pyrethroid insecticide, was studied through monitoring the liver function biomarkers, the lipid profile and the oxidant/antioxidant status of the liver. Also, the efficiency of pre-treatment and post-treatment with NGN against the toxic effect of LTC was evaluated. Results illustrated that LTC altered the liver function markers and the lipid profile, induced oxidative stress and suppressed the antioxidant status of the liver. Both regimen of treatments with NGN significantly attenuated the toxicity of LTC and mostly restored the proper function of the liver and its normal oxidant/antioxidant status.

The liver is a major target organ for xenobiotic compounds because of its role in detoxification and biotransformation reactions; therefore, it is more susceptible to toxic effects of these compounds[30]. The current study revealed a significant elevation in serum activities of AST, ALT and ALP and in the level of total bilirubin in response to administration of LTC. The disturbance in liver function markers reflects hepatocellular damage and dysfunction. This may be attributed to increased leakage of the enzymes into the circulation due to loss of integrity and/or increased permeability of cell membrane due to LTC-induced hepatocellular damage[31]. These results are in accordance with Fetoui *et al.*[31], Ramadhas *et al.*[32] and Moustafa and Hussein[33].

Pre-treatment with NGN prevented the elevation in the activity of ALT an AST while post-treatment could improve the activity of ALP. The level of bilirubin was partially improved in both pre-treatment and post-treatment. These results agree with Yen *et al.*[34] who reported similar results concerning liver enzymes. The protective effect of NGN may be mediated through its ability to decrease membrane fluidity and therefore prevent the leakage of the enzymes as discussed later.

Dysregulation of lipid metabolism may indicate hepatotoxicity. The present study showed a disturbance in lipid and lipoprotein profiles in response to LTC administration. These changes may be attributed to the increase in fat catabolism. LTC was found to be associated with up-regulation of lipogenic genes and to increase the number of lipogenic factors involved in fat metabolism and fatty acid synthesis[33]. Post-treatment with NGN significantly improved LTC-induced alterations in lipid profile. Also pre-treatment improved the lipid profile except for total lipids and triglycerides. NGN has been shown to be effective in regulating lipid metabolism and modulating the synthesis and oxidation of lipids and cholesterol in nonalcoholic fatty liver disease[35]. It is also able to modulate signaling pathways involved in fatty acids metabolism which enhance oxidation of fatty acids and impairs accumulation of lipids in liver[36].

Excessive production of free radicals and induction of oxidative damage have been suggested to be major mechanisms involved in many pathological conditions. In the present study, LTC enhanced LPO as indicated by the significant increase in the levels of TBARS, HPs and CD in the liver. Peroxidation of lipids is a metabolic process resulting from the oxidation of polyunsaturated fatty acids (PUFA) which are the main components of membrane lipids. LTC may be involved in the generation of reactive oxygen species (ROS) that may react with the PUFA to form LPO by-products. It may induce the release of the unstable cyanohydrins that further decompose to cyanides and aldehydes which are sources for free radicals[37]. Pyrethroids, including LTC, are known to be lipophilic which enables them to easily cross the plasma membrane and induce peroxidation of the membrane lipids[38]. In addition to peroxidation of lipids, PCC is used as a marker for protein oxidation. The present study revealed a significant increase in PCC in the liver of LTC-treated rats which further confirm the oxidative damage in the liver tissue. Similar increase in PCC was recorded using the deltamethrin, a synthetic pyrethroid[6]. Administration of NGN attenuated the oxidation of lipid and protein as indicated by a significant decrease in the levels of TBARS, HPs, CD and PCC. These results are in accordance with Jayaraman *et al.*[39]. The

ameliorative effect of NGN may be attributed to its direct antioxidant activity and its ability to scavenge free radicals through its three hydroxyl substituents[40]. Also, NGN has the ability to chelate the Fe^{+2} by suppression of iron-dependent reaction thus decrease the formation of hydroxyl radical[41]. NGN has been reported to decrease membrane fluidity and increased rigidity of the membrane. In this way, NGN reduces the interaction between the free radicals and membrane lipids and subsequently, the membrane LPO is decreased[42].

Administration of LTC in the current study induced a significant decrease in the level of GSH and in the activity of the antioxidant enzymes SOD, CAT, GPx and GST in the liver while the activity of GR remains unchanged. The decline in the enzymatic antioxidant status together with the elevation in the oxidation by-products indicate the failure of antioxidant defense system to overcome the excessive production of reactive species generated by LTC. Inhibition of these enzymes leads to exacerbation of the reactive species which promote oxidation of lipids and proteins. These results corroborate with Moustafa and Hussein[33] and Abdallah *et al.*[43]. Results indicated that the antioxidant status was significantly enhanced upon NGN treatment when compared with LTC group. Similarly, Chtourou *et al.*[44] found that NGN averts the depletion in SOD, CAT and GPx activities. The improvement in the antioxidant status upon treatment with NGN may be related, at least in part, to its antioxidant activity. It may directly scavenge free radicals through its chemical structure as mentioned before and therefore preserves the antioxidant system. Furthermore, NGN was found to induce the expression of endogenous antioxidants[35]. A limitation of the present study is the lack of molecular studies such as investigation of the gene expression of the antioxidant enzymes under the influence of NGN. Therefore, future studies are needed to confirm the biochemical results obtained in the present study using molecular techniques.

CONCLUSION

Use of 1/10 LD_{50} of LTC impaired the liver function, altered lipid profile in the serum, increased lipid and protein oxidation and suppressed the antioxidant status of the liver. Both post-treatment and pre-treatment with NGN significantly modulated LTC-induced hepatotoxicity and oxidative stress in rat's liver and pre-treatment was found to be more effective in improving most of the studied parameters in both serum and liver tissue. The hepatoprotective effect of NGN is largely attributed to its ability to combat free radicals and enhance the antioxidant system. Therefore, NGN could be used as a safe dietary supplement to protect against the toxicity and oxidative stress associated with the use of LTC.

SIGNIFICANCE STATEMENT

This study discovered that pre-treatment and post-treatment with naringenin was effective in attenuating the toxic effects of lambda-cyhalothrin in the liver of rats. The protective effect of naringenin is largely attributed to its ability to scavenge free radicals and to enhance the antioxidant system. This study will help the researcher to uncover the area of using natural flavonoid antioxidants to overcome the side effects associated with the use of lambda-cyhalothrin as a commonly used pyrethroid insecticide.

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