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Research Article
Sub-Acute 28-Days Oral Toxicity Study of Deltamethrin on Female Rats and the Protective Role of Moringa Tea

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Abstract

Background and Objective: Pyrethroid insecticides are extensively used in agriculture and public health sectors to control insects. It accumulates in fatty tissues, food and environment and caused several adverse effects to mammals and ecosystem. The current research was designed to study the sub-acute oral toxicity "28 days" of deltamethrin (DLM) on female rats and to evaluate the protective effect of moringa tea. **Materials and Methods:** Rats were divided into four groups of five rats each, control group, moringa tea group, deltamethrin group and deltamethrin-moringa tea group. After 28 days of exposure, serum and tissues samples were used for biochemical and histopathological investigations. All data were analyzed using one-way analysis of variance (ANOVA) followed by *post hoc* multiple comparisons. **Results:** Deltamethrin-induced significant alterations in the liver dysfunction biomarkers such as AST (aspartate aminotransferase), ALT (alanine aminotransferase) and ALP (alkaline phosphatase) in the serum of female rats. It caused also, significant changes in oxidative stress markers such as lipid peroxidation (LPO), glutathione (GSH) and catalase (CAT) and histological alteration in the liver tissues of treated female rats. Deltamethrin induced a significant reduction ($p<0.05$) in body weights and relative liver weights compared to untreated female rats. Co-administration of moringa tea to deltamethrin-intoxicated female rats improved liver functions and restored the liver and oxidative stress biomarkers to within normal ringing. **Conclusion:** DLM-induced oxidative stress, lipid peroxidation and liver damage in female rats. Administration of moringa tea could prevent the adverse and toxic effects of pyrethroid insecticides. Moringa tea may be useful, easy and economical to protect human against the adverse toxic effects of pesticides exposure, especially of agriculture workers.

Key words: Deltamethrin, moringa tea, liver damage, sub-acute toxicity, histopathology

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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

In modern pesticides, pyrethroid insecticides are the most active class for control insects in agriculture and public health sectors. It is extensively used worldwide for control mosquito, housefly and other insects in domestic animals. Due to the lipophilic in natural and widely used of pyrethroid insecticides, it accumulates in fatty tissues, food and environmental and caused adverse effects to human health and their ecosystem[1]. Pyrethroid insecticides are neurotoxic to insects and the mechanism of action refers to action on axon in the nervous system through interference with the sodium channel and effect in nerve impulse[2]. It induced an alteration in the permeability of nerve cells that lead to changes in the control of sodium passages and nerve impulses. It affects and blocks the gamma-amino butyric acid (GABA), noradrenergic, dopaminergic and cholinergic neurotransmission[3]. Deltamethrin, [(S)-cyano-(3-phenoxyphenyl)methyl] (1R,3R)-3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropane-1-carboxylate, one of the important insecticides in agriculture for insect pest control and plays key role in public health for control.

Deltamethrin had acute oral toxicity (LD_{50}) for rats ranged from 30 in oil to >5000 mg kg^{-1} b.wt., in an aqueous vehicle[4]. The different in LD_{50} is due to the effect of vehicle, which enhanced the absorption of deltamethrin[5].

Pyrethroid insecticides such as deltamethrin[6,7], β-cyfluthrin[8], lambda-cyhalothrin[9], cypermethrin[10], prallethrin[11,12] can induced toxicity to human and experimental animals. It caused alteration in the liver[12,13], oxidative stress biomarkers[9,14] and induced genotoxic effect[15,16].

The ability of pesticides to induce oxidative stress is one of the most important mechanisms to explain the toxic effect of exposure to pesticides for a long time at low doses[17]. Therefore, natural antioxidants are important to protect and minimize the adverse effects induced by exposure to pesticides[18].

Moringa oleifera (*M. oleifera*) is growing in tropics and subtropics countries with a wide range of the beneficial uses in medicine and nutrition[19]. The plant has biological activities as antioxidant, antitumor, antiinflammatory and antipyretic. *M. oleifera* plant can be used to treat diabetes, asthma, hepatorenal and hematological disorders[20,21].

It is speculated that there are no studies regarding the hepatoprotective activity of *M. oleifera* tea against the toxic effect of deltamethrin in female rats. Therefore, the current study was designed to study the sub-acute "28 days" oral toxicity of deltamethrin (DLM) on female rats and to evaluate the protective effect of moringa tea.

MATERIALS AND METHODS

All experiments were carried out of the year 2016 and 2017 in the laboratories of Pesticide Chemistry Department, National Research Centre (NRC), Dokki, Giza, Egypt.

Chemicals and reagents: Deltamethrin (98%) was obtained from Gharda Chemicals Ltd., Bombay. Kits of catalase, glutathione reduced, malondialdehyde (MDA) as a biomarker of lipid peroxidase, aspartate aminotransferases, alanine aminotransferases, alkaline phosphatase, total protein and albumin were purchased from Biodiagnostic Company, 29 Tahrir Street, Dokki, Giza, Egypt. All other chemicals were of reagent grades and were obtained from the local scientific distributors in Egypt.

Preparation of moringa tea extract: Moringa tea was purchased from moringa unit at National Research Centre, Dokki, Giza, Egypt. Similarly, the crude aqueous extract of moringa tea was prepared by soaking 15 g of moringa tea leaves in 1 L of distilled water whose temperature did not exceed 90°C, for 5 min to obtain soluble polyphenols dissolved in the aqueous extract[22]. The solution was filtered, adjusted by water to obtain 1.5% (w/v) moringa tea extract (1.5 g L^{-1} extract water). This solution was substituted in the place of water as the sole source of drinking fluid.

Animals and treatments: Female albino rats of the Wistar strain (*Rattus norvegicus*) weighing 100±5 g obtained from Animal Breeding House of the National Research Centre (NRC), Dokki, Cairo, Egypt. Animals were feed in standard pellet diet and allowed distillate water *ad libitum*. Rats were kept in clean plastic cages at 22±3°C with 44% a minimum relative humidity and a 12 h dark/light cycle. Rats were divided into four groups, five rats of each. Rats in Group I served as control group and given corn oil (0.5 mL/rat). Rats in Group II were given deltamethrin in corn oil at a dose 13.5 mg kg^{-1} b.wt. (1/10 LD_{50}) via oral gavage for 28 consecutive days[5]. Rats in Group III were given deltamethrin at the same dose in Group II simultaneously allowed to an aqueous moringa tea extract as the sole source of drinking fluid. Rats in Group IV were given aqueous moringa tea extract as the sole drinking fluid during the 28 days at a concentration of 1.5% (w/v). Body weights were recorded every week and the doses were modulated accordingly.

Samples preparation: At the end of experimental period, the animals fasted overnight and blood samples were withdrawn from the retero-orbital venous plexus. Then, blood samples

were left to coagulate in clean dry tubes, centrifuged at 3000 rpm for 10 min using Heraeus Labofuge 400R, Kendro Laboratory Products GmbH, Germany to obtain the serum. Serum was stored at -20°C and used for liver dysfunction biomarkers measurements (ALT, AST, ALP, total protein and albumin) within 2 weeks. Then, female rats were killed by cervical dislocation, the liver was dissected out, cleaned and weighed. Small pieces of liver were cut and kept in formalin solution (10%) for histological studies. Other portions of liver washed with saline solution, weighed, cut in small parts, homogenized in 10% (w/v) ice cold 100 mM phosphate buffer (pH 7.4) and centrifugation at 10,000 rpm for 15 min at 4°C. The supernatant was obtained and used for oxidative stress biomarkers measurements (CAT, GSH and LPO).

Liver dysfunction biomarkers: All liver biomarkers AST, ALT, ALP, albumin and total protein were measured spectrophotometrically according to the details given in the kit's instructions using Shimadzu UV-VIS Recording 2401 PC (Japan).

Oxidative stress biomarkers: Oxidative stress biomarkers such as CAT, GSH and MDA were determined in liver homogenate using a spectrophotometer Shimadzu UV-VIS Recording 2401 PC (Japan). All biomarkers were performed according to the details given in the kit's instructions.

Histological study: Liver pieces were dehydrated in alcohol and embedded in paraffin wax. Liver sections (5 m hick) were stained with haematoxylin and eosin (H and E). Two slides were prepared for each rat, each slide contains two sections. Ten field areas for each section were selected and examined for histopathological changes (160×) under the light microscope. The liver fields were scored as normal appearance (–), minimal cellular disruption (+), mild (++), moderate (+++), severe (++++) and very severe cellular disruption (++++)[17].

Statistical analysis: The Statistical Package for Social Sciences program (SPSS 18.0 for windows, SPSS Inc. 233 South Wacker Drive, 11th Floor Chicago, IL 60606-6412) used for statistical analysis of the results. The results were analyzed using one-way analysis of variance (ANOVA) followed by using *post hoc* multiple comparisons ($p<0.05$). All results were expressed as means±standard error (S.E.).

RESULTS

Active ingredient of deltamethrin (98% purity) was used (Fig. 1) in the present study. No mortality was recorded in rats exposed to DLM during the experimental period. In contrast, DLM caused signs of toxicity in female rats including a change in activity, convulsion, unsteady gait and emaciated appearance. As shown in Fig. 2, there was a significant ($p<0.05$) decrease in body weight of DLM-intoxicated rats compared to the control group. The decreases in body weight account -13.05% of DLM-group and restored to -1.60% after administration moringa tea (DLM-moringa group) compared to control animals. In contrast, body weight was an increase in rats administrated moringa tea by 1.35% compared to control (Fig. 2a). DLM caused significant ($p<0.05$) decrease in relative liver weight in DLM-treated rats (Fig. 2b). The decrease account -15.24% of DLM-treated rats and increase to 9.04% of DLM-moringa group compared to untreated animals.

As presented in Table 1, a significant ($p<0.05$) elevation in the liver dysfunction biomarkers in serum of DLM-treated female rats. For example, the activity of liver enzyme AST, ALT and ALP account 40.02, 29.01 and 40.48 U L^{-1} in control and increased to 70.99, 80.14 and 90.90 U L^{-1} in DLM-treated rats, respectively. Administration of moringa tea to DLM-intoxicated rats caused significant ($p<0.05$) decreases in liver dysfunction biomarkers and restored these enzymes to the normal values. The same effect was recorded in total protein and albumin concentrations but with significant decreases. There is no significant difference in all liver biomarkers were recorded in moringa tea treated group.

Table 2 show the results of oxidative stress biomarkers in rats exposed to DLM for 28 days and the protective role of moringa tea. DLM caused significant alteration in all oxidative stress biomarkers in liver tissue of female rats. DLM induced significant increase in MDA to 2.42 nmol mg^{-1} protein vs. 0.87 nmol mg^{-1} protein of control animals (Fig. 3 a).

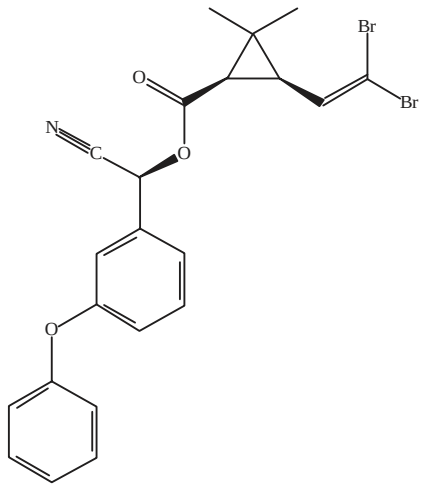

Fig. 1: Chemical structure of deltamethrin

Table 1: Liver dysfunction biomarkers in serum of female rats exposed to deltamethrin for 28 days and the protective effect of moringa tea

Treatments	AST (U L^{-1})	ALT (U L^{-1})	ALP (U L^{-1})	Total protein (g dL^{-1})	Albumin (g dL^{-1})
Control	40.02±0.49^{c}	29.01±0.32^{c}	40.48±0.29^{c}	7.59±0.12^{a}	3.20±0.14^{a}
DLM	70.99±3.58^{a}	80.14±1.79^{a}	90.90±2.49^{a}	6.06±0.36^{b}	2.78±0.30^{b}
DLM+moringa tea	45.57±0.32^{b}	52.02±0.77^{b}	51.13±1.33^{b}	7.15±0.44^{a}	3.10±0.28^{a}
Moringa tea	39.30±0.34^{c}	28.17±0.27^{c}	41.56±1.67^{c}	7.04±0.13^{a}	3.16±0.31^{a}

DLM: Deltamethrin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, Each value is a Mean±SE, n = 5, ^{a,b,c}Values differ significantly at p<0.05

Table 2: Severity damage in the liver of female rats exposed to deltamethrin for 28 days and the protective effect of moringa tea

Histological observation	Control	DLM	DLM+moringa tea	Moringa tea
Inflammatory cells in the portal area	--	+++	+	-
Focal necrosis in the hepatic parenchyma	-	+++	+	-
Diffuse Kupffer proliferation	-	+++	+	-

--: Severity, -: Normal, +: Minimal, ++: Mild, +++: Moderate, DLM: Deltamethrin

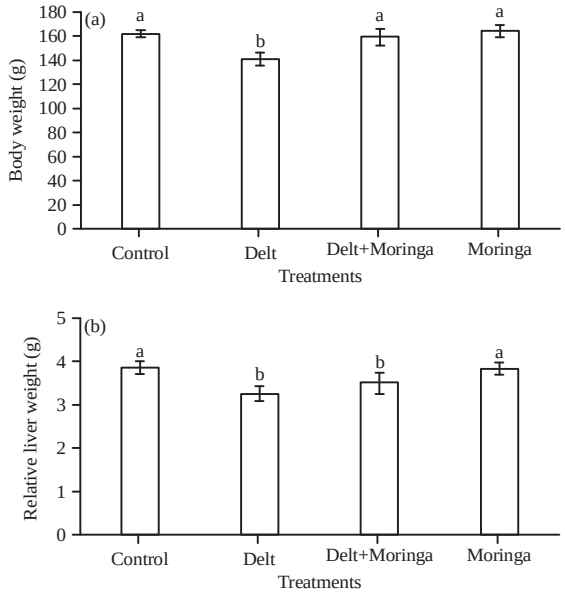

Fig. 2(a-b): Body weights and relative liver weights of female rats exposed to deltamethrin for 28 days and the protective effect of moringa tea
Each value is a Mean±SE, ^{a,b,c}values differ significantly at p<0.05

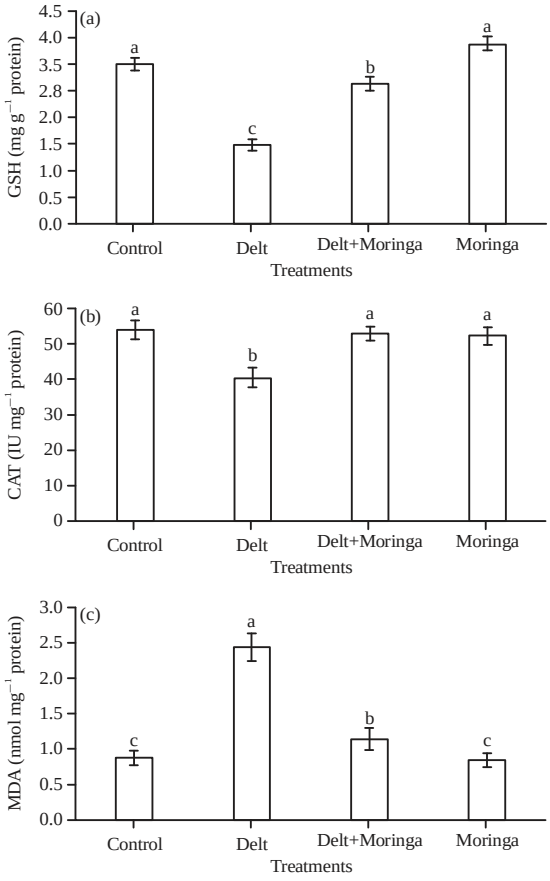

Fig. 3(a-c): Oxidative stress biomarkers, GSH, CAT and MDA in liver of female rats exposed to deltamethrin for 28 days and the protective effect of moringa tea.
Each value is a Mean±SE, ^{a,b,c}values differ significantly at p<0.05

Administration of moringa tea to DLM-intoxicated female rats decrease the level of MDA to 1.13 nmol mg^{-1} protein (-46.69% of DLM value).

Results showed that a significant (p<0.05) decrease in GSH level (Fig. 3b) and CAT activity in DLM treated rats (Fig. 3c). The GSH account 1.66 mg g^{-1} protein of DLM vs 2.95 mg g^{-1} protein of DLM along with moringa tea compared to 3.37 mg g^{-1} protein of control while, CAT account 40.25 IU mg^{-1} protein of DML vs 52.85 IU mg^{-1} protein of DLM along with moringa tea compared to 53.90 IU mg^{-1} protein of control, respectively.

Histopathological investigation in the liver sections of female rats exposed to DLM showing moderate severity in liver tissue with loss of normal cellular pattern, irregular dilated central vein, congestion, inflammatory cells in the portal area, focal necrosis in the hepatic parenchyma and diffuse Kupffer proliferation (Fig. 4). Administration of moringa tea to DLM-treated female rats improved the liver function and

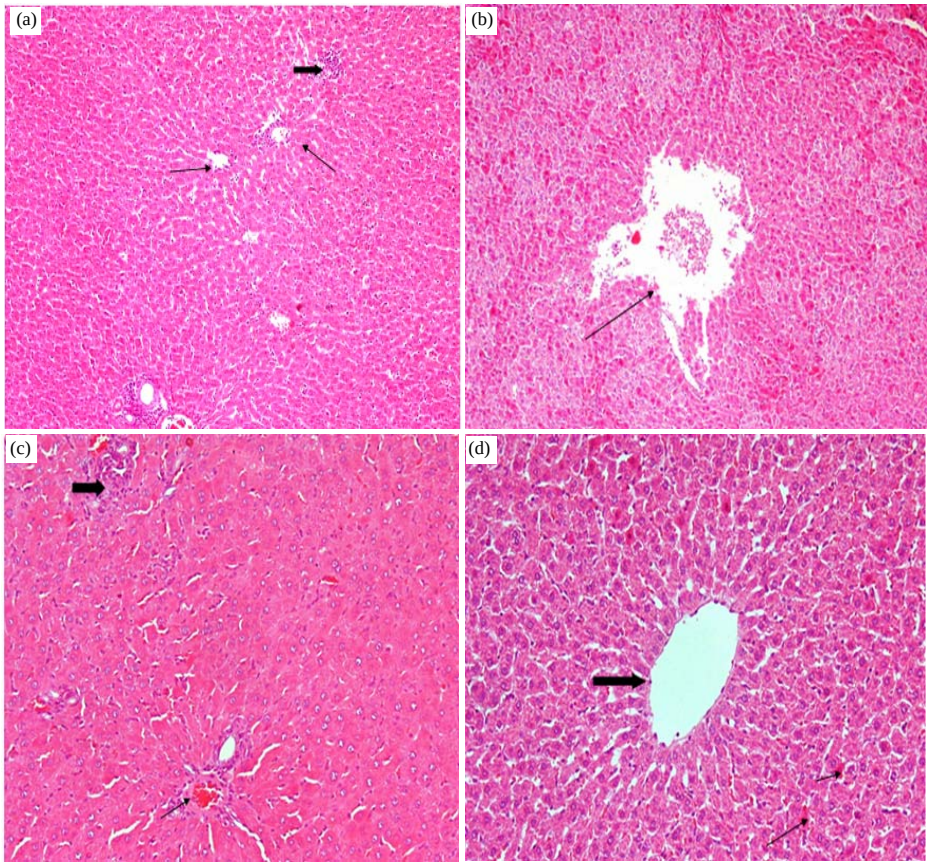

Fig. 4(a-d): Photomicrography of liver sections (H and E, 100X) showing normal liver tissue in (a) Control group with normal hepatocytes and central vein (thin arrow), (b) Deltamethrin treated group showing liver tissue with loss of normal cellular pattern, irregular dilated central vein, congestion (thin arrow), Inflammatory cells in the portal area, focal necrosis in the hepatic parenchyma and diffuse Kupffer proliferation, (c) DLM+Moringa tea group showing mild dilated bile duct with mild fibroses and (d) Moringa tea group showing normal liver tissue

histopathological structure of the liver. Both control and moringa tea showed the normal histopathological structure in the liver sections.

DISCUSSION

In the current study, DLM caused signs of toxicity in female rats after 1 week of exposure time including a change in activity, convulsion, unsteady gait and emaciated appearance. While no mortality was observed. Other study reported that the important role of vehicle in the toxicity of DLM. Signs of toxicity including motor incoordination, convulsion, respiratory defects and hypomotilty were recorded in rats given DLM in sesame oil[23]. In contrast, no mortality or signs of toxicity in rats given DLM as an aqueous suspension in methylcellulose (1% w/v) at dose 5000 mg kg^{-1}. b.wt.[24]. DLM in peanut oil caused moderate to severe salivation in male rats at dose 10 mg kg^{-1} b.wt., while mild salivation was observed in female rats at the same dose[25,26]. No signs of toxicity or mortality were recorded in DLM-moringa tea treated group.

A DLM-treated group showed lost significant body weight during the experimental period. Relative liver weight also was decreased in DLM-treated female rats. Administration of moringa tea restored body weight in DLM-treated groups to normal weight while significantly ($p<0.05$) reduction in relative liver weight was noted. The decrease in body weight and relative weight could be due to the hepatotoxic effect of DLM or due to the decrease in food consumption and the neurotoxicity of DLM[11]. DLM caused lost in food consumption in rats compared to control group which resulting in reduced body weight gain. Other studies reported change in body

weight and relative organs weights in experimental animals after exposure to pesticides[8,9-12,26].

The liver is a man organ in the body, which plays an essential role in xenobiotic metabolism and detoxification. Therefore, changes in liver biomarkers is correlating to liver dysfunction, hepatic damage and cell injury. The increase in liver enzymes such as AST, ALT and ALP, for example, is one marker of hepatotoxicity and liver damage[27,28] . In the present study, DLM caused a significant increase in liver function enzymes (AST, ALT and ALP) of female rats. It has been reported that aminotransferases (AST and ALT) are responsible for metabolism, detoxification and biosynthesis of energetic macromolecules[29]. They play an essential role in amino acids catabolism and biosynthesis and used for specific biomarkers for hepatic and liver injuries[11,17]. The ALP mostly reaches the liver from bone, execrated into the bile; so an increase in serum can be associated with hepatobiliary disease[35].The increase in liver enzymes in DML-treated female rats could be due to the change in hepatic cells permeability, the hepatotoxicity and liver damage. Results showed a decrease in total protein and albumin concentrations in serum of DLM-treated rats. This decreased could be due to the toxic effect of DLM on hepatocytes that caused a change in protein biosynthesis and live function[30,31].

Previous studies have shown that pesticides can change the oxidant and antioxidant status in the cells, cause oxidative stress, lipid peroxidation (LPO) and cell damage. LPO also is implicated in the pathogenesis induced liver damage due to the disturb the integrity of cellular membranes[32,33]. It can be used as a specific marker in insecticides caused oxidative damage and considered as one of the molecular mechanisms involved in insecticides-induced toxicity[33,34]. In the current study, increase malondialdehyde (MDA) level in liver of DLM-treated female rats could be due to increase production of free radicals especially hydroxyl radicals, alter oxidant and antioxidant statues and changes in antioxidant defense system[35].

Support for this hypothesis, CAT was significantly decreased in DLM-intoxicated female rats in the present study. CAT is considered one of the first defenses that protect cell membrane and macromolecules from oxidative damage especially against reactive oxygen species. Superoxide anion is converted to hydrogen peroxide (H_2O_2) by superoxide dismutase (SOD), the latter is converted to water by CAT[36]. Reduced in GSH concentration also, in DLM-treated rats support the formation of free radicals and induce oxidative stress. The results of the present study supported by previous studies which have confirmed that exposure to insecticides e.g., pyrethroids caused hepatotoxicity, liver injury and changes in antioxidant defense mechanisms and enhanced LPO in the liver[7,13,37] . The changes in liver marker enzymes and oxidative stress in female rats in the present study was characteristic of initial hepatic cell injury that appeared in liver sections of histopathological investigation. The histological changes could be due to production of free radicals that lead to liver tissue damage as shown by enhanced hepatic LPO which plays a vital role in hepatic cellular membrane injury[13].

Administration of *M. oleifera* tea to DLM-intoxicated female rats decreased liver function enzymes and lipid peroxidation. It caused a significant ($p<0.05$) increase in total protein, albumin, AST, GSH and reduced histopathological lesions in the live tissue from moderate to mild alterations. The ameliorative effect of moringa tea could be due to the presence of antioxidant compounds that play an essential role to scavenge free radical and induced balance of oxidant/antioxidant status in hepatocytes lead to reduced oxidative stress and lipid peroxidation. Previous studies showed that *M. oleifera* had antioxidant activity due to the content of many active phenolic and flavonoids active compounds e.g., rutin, kaempferol, rhamnetin, isoquercitrin and kaempferitrin[38,39]. It content oleic acid, L-(+)-ascorbic acid- 2, 6-dihexadecanoate and 9-octadecenoic acid[40]. Hepatoprotective of moringa was reported by other studies[41,42].

CONCLUSION

Deltamethrin induced oxidative stress, lipid peroxidation and liver injury in female rats. It caused decrease in body weight and relative liver weights. The administration of moringa tea prevents the hepatotoxic effect of deltamethrin. This effect could be due to the antioxidant and free radical scavenging properties of *M. oleifera*. The results showed that moringa tea might be useful, easy and economical to protect human against the adverse toxic effects of pesticides exposure, especially of agriculture workers.

SIGNIFICANCE STATEMENTS

The current research was carried out to study the adverse effects of deltamethrin on female rats and the protective role of moringa tea. The administration of moringa tea prevents the hepatotoxic effect of deltamethrin. This study will help the researcher to use moringa tea for protecting human against the adverse toxic effects induced by pesticides.

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REFERENCES

1. Pauluhn, J., 1999. Hazard identification and risk assessment of pyrethroids in the indoor environment. Toxicol. Lett., 107: 193-199.
2. Aldridge, W.N., 1990. An assessment of the toxicological properties of pyrethroids and their neurotoxicity. Crit. Rev. Toxicol., 21: 89-104.
3. Michelangeli, F., M.J. Robson, J.M. East and A.G. Lee, 1990. The conformation of pyrethroids bound to lipid bilayers. Biochem. Biophys. Acta-Biomembranes, 1028: 49-57.
4. McGregor, D.B., 2000. Pesticide residues in food 2000: Deltamethrin. http://www.inchem.org/documents/jmpr/jmpmono/v00pr04.htm
5. Tomlin, C.D.S., 2005. The Pesticide Manual-A World Compendium. 13th Edn., British Crop Protection Council, Hampshire, UK.
6. Atif, F., S. Parvez, S. Pandey, M. Ali and M. Kaur *et al*., 2005. Modulatory effect of cadmium exposure on deltamethrin-induced oxidative stress in *Channa punctata* Bloch. Arch. Environ. Contam. Toxicol., 49: 371-377.
7. Abbassy, M.A. and A.T.H. Mossa, 2012. Haemato-biochemical effects of formulated and technical cypermethrin and deltamethrin insecticides in male rats. J. Pharmacol. Toxicol., 7: 312-321.
8. Mohafrash, S.M.M., H.F. Abdel-Hamid and A.H. Mossa, 2017. Adverse effects of sixty days sub-chronic exposure to β-cyfluthrin on male rats. J. Environ. Sci. Technol., 10: 1-12.
9. El-Demerdash, F.M., 2007. Lambda-cyhalothrin-induced changes in oxidative stress biomarkers in rabbit erythrocytes and alleviation effect of some antioxidants. Toxicol. *In vitro*, 21: 392-397.
10. Mossa, A.T.H., F.M. Ibrahim, S.M. Mohafrash, D.H. Abou Baker and S. El Gengaihi, 2015. Protective effect of ethanolic extract of grape pomace against the adverse effects of cypermethrin on weanling female rats. Evidence-Complement. Altern. Med. 10.1155/2015/381919.
11. Mossa, A.T.H., A.A. Refaie, A. Ramadan and J. Bouajila, 2013. Amelioration of prallethrin-induced oxidative stress and hepatotoxicity in rat by the administration of *Origanum majorana* essential oil. Biomed. Res. Int. 10.1155/2013/859085.
12. Refaie, A.A.E.R., A. Ramadan and A.T.H. Mossa, 2014. Oxidative damage and nephrotoxicity induced by prallethrin in rat and the protective effect of *Origanum majorana* essential oil. Asian Pac. J. Trop. Med., 7: S506-S513.
13. Giray, B., A. Gurbay and F. Hincal, 2001. Cypermethrin-induced oxidative stress in rat brain and liver is prevented by vitamin E or allopurinol. Toxicol. Lett., 118: 139-146.
14. El-Gengaihi, S.E., E.M. Hassan, H.F. Aly, A.A. Refaee, M.A. Mohammed and H.M. Abdel-Tawab, 2016. Hepatoprotective of *Taraxacum officinale* against liver damage induced by carbon tetrachloride in male rats. J. Chem. Pharm. Res., 8: 538-545.
15. Chauhan, L.K.S., S. Chandra, P.N. Saxena and S.K. Gupta, 2005. *In vivo* cytogenetic effects of a commercially formulated mixture of cypermethrin and quinalphos in mice. Mutat. Res./Genet. Toxicol. Environ. Mutagen., 587: 120-125.
16. Patel, S., A.K. Pandey, M. Bajpayee, D. Parmar and A. Dhawan, 2006. Cypermethrin-induced DNA damage in organs and tissues of the mouse: evidence from the comet assay. Mutat. Res./Genet. Toxicol. Environ. Mutagen., 607: 176-183.
17. Mossa, A.T.H., E.S. Swelam and S.M.M. Mohafrasha, 2015. Sub-chronic exposure to fipronil induced oxidative stress, biochemical and histopathological changes in the liver and kidney of male albino rats. Toxicol. Rep., 2: 775-784.
18. Mossa, A.T.H., T.M. Heikal, S.M.M. Mohafrash and A.A. Refaie, 2015. Antioxidant potential and hepatoprotective activity of *Origanum majorana* leaves extract against oxidative damage and hepatotoxicity induced by pirimiphos-methyl in male mice. J. Applied Sci., 15: 69-79.
19. Sinha, M., D.K. Das, S. Datta, S. Ghosh and S. Dey, 2012. Amelioration of ionizing radiation induced lipid peroxidation in mouse liver by *Moringa oleifera* Lam. leaf extract. Indian J. Exp. Biol., 50: 209-215.
20. Paliwal, R., V. Sharma, Pracheta and S. Sharma, 2011. Elucidation of free radical scavenging and antioxidant activity of aqueous and hydro-ethanolic extracts of *Moringa oleifera* pods. Res. J. Pharm. Tech., 4: 566-571.
21. Toppo, R., B.K. Roy, R.H. Gora, S.L. Baxla and P. Kumar, 2015. Hepatoprotective activity of *Moringa oleifera* against cadmium toxicity in rats. Vet. World, 8: 537-540.
22. Heikal, T.M., A.T.H. Mossa, M.A. Abdel Rasoul and G.I.K. Marei, 2013. The ameliorating effects of green tea extract against cyromazine and chlorpyrifos induced liver toxicity in male rats. Asian J. Pharm. Clin. Res., 6: 48-55.
23. Manna, S., D. Bhattacharyya, T.K. Mandal and S. Dey, 2006. Neuropharmacological effects of deltamethrin in rats. J. Vet. Sci., 7: 133-136.
24. Myer, J.R., 1989. Acute oral toxicity study of deltamethrin in rats. Hoechst-Roussel Agri-Vet Company Study No. 327-122.
25. Kavlock, R., N. Chernoff, R. Baron, R. Linder and E. Rogers *et al*., 1979. Toxicity studies with decamethrin, a synthetic pyrethroid insecticide. J. Environ. Pathol. Toxicol., 2: 751-765.

26. Naumann, K., 2012. Synthetic Pyrethroid Insecticides: Chemistry and Patents. Vol. 5, Springer Science and Business Media, New York, ISBN: 9783642748523, Pages: 390.
27. Hocine, L., H. Merzouk, S.A. Merzouk, H. Ghorzi, M. Youbi and M. Narce, 2016. The effects of alpha-cypermethrin exposure on biochemical and redox parameters in pregnant rats and their newborns. Pesticide Biochem. Physiol., 134: 49-54.
28. Lankoff, A., A. Banasik and M. Nowak, 2002. Protective effect of melatonin against nodularin-induced oxidative stress in mouse liver. Arch. Toxicol., 76: 158-165.
29. Seven, A., S. Glizel, O. Seymen, S. Civelek, M. Bolayrh, M. Unca and G. BurCak, 2004. Effects of vitamin E supplementation on oxidative stress in streptozotocin induced diabetic mice: Investigation of liver and plasma. Yonsei Med. J., 45: 703-710.
30. Mansour, S.A. and A.H. Mossa, 2010. Adverse effects of lactational exposure to chlorpyrifos in suckling rats. Hum. Exp. Toxicol., 29: 77-92.
31. Mansour, S.A. and A.T.H. Mossa, 2010. Oxidative damage, biochemical and histopathological alterations in rats exposed to chlorpyrifos and the antioxidant role of zinc. Pestic. Biochem. Physiol., 96: 14-23.
32. Sharma, D. and G.K. Sangha, 2014. Triazophos induced oxidative stress and histomorphological changes in liver and kidney of female albino rats. Pestic. Biochem. Physiol., 110: 71-80.
33. Kehrer, J.P., 1993. Free radicals as mediators of tissue injury and disease. Crit. Rev. Toxicol., 23: 21-48.
34. Kelly, K.A., C.M. Havrilla, T.C. Brady, K.H. Abramo and E.D. Levin, 1998. Oxidative stress in toxicology: Established mammalian and emerging piscine model systems. Environ. Health Perspect., 106: 375-384.
35. Banerjee, B.D., V. Seth, A. Bhattacharya, S.T. Pasha and A.K. Chakraborty, 1999. Biochemical effects of some pesticides on lipid peroxidation and free-radical scavengers. Toxicol. Lett., 107: 33-47.
36. Peixoto, F., J. Vicente and V.M.C. Madeira, 2004. A comparative study of plant and animal mitochondria exposed to paraquat reveals that hydrogen peroxide is not related to the observed toxicity. Toxicol. *In Vitro*, 18: 733-739.
37. Abbassy, M.A., A.E.S.M. Marei, M.A.M. Al-Ashkar and A.T.H. Mossa, 2014. Adverse biochemical effects of various pesticides on sprayers of cotton fields in El-Behira Governorate, Egypt. Biomed. Aging Pathol., 4: 251-256.
38. Iqbal, S. and M.I. Bhanger, 2006. Effect of season and production location on antioxidant activity of *Moringa oleifera* leaves grown in Pakistan. J. Food Comp. Anal., 19: 544-551.
39. Dehshahri, S., M. Wink, S. Afsharypuor, G. Asghari and A. Mohagheghzadeh, 2012. Antioxidant activity of methanolic leaf extract of *Moringa peregrina* (Forssk.) Fiori. Res. Pharm. Sci., 7: 111-118.
40. Aja, P.M., N. Nwachukwu, U.A. Ibiam, I.O. Igwenyi, C.E. Offor and U.O. Orji, 2014. Chemical constituents of *Moringa oleifera* leaves and seeds from Abakaliki, Nigeria. Am. J. Phytomed. Clin. Therapeut., 2: 310-321.
41. Pari, L. and N.A. Kumar, 2002. Hepatoprotective activity of *Moringa oleifera* on antitubercular drug-induced liver damage in rats. J. Med. Food, 5: 171-177.
42. Das, N., K. Sikder, S. Ghosh, B. Fromenty and S. Dey, 2012. *Moringa oleifera* Lam. leaf extract prevents early liver injury and restores antioxidant status in mice fed with high-fat diet. Indian J. Exp. Biol., 50: 404-412.