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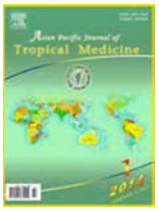

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Oxidative damage and nephrotoxicity induced by prallethrin in rat and the protective effect of *Origanum majorana* essential oil

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ABSTRACT

Objective: To investigate the effects of prallethrin on renal dysfunction biomarkers, antioxidant enzyme activities and lipid peroxidation (LPO) in rats and the protective effect of *Origanum majorana* essential oil.

Methods: Rats were divided into four groups of seven rats in each group: (I) received only olive oil, (II) treated with 64.0 mg/kg body weight prallethrin (1/10 LD_{50}) in olive oil via oral route daily for 28 d, (III) treated with 64.0 mg/kg body weight prallethrin (1/10 LD_{50}) and essential oil (160 μL/kg body weight) in olive oil and (IV) received essential oil (160 μL/kg body weight) in olive oil via oral route twice daily for 28 d.

Results: Prallethrin caused significant increase in LPO and decrease in superoxide dismutase, glutathione peroxidase and glutathione reduced. Consistent histological changes were found in the kidney of prallethrin treatment. Co-administration of essential oil attenuated the prallethrin induced renal toxicity and oxidative stress by decreasing LPO in kidney, creatinine, urea and uric acid levels in serum. In addition, superoxide dismutase, glutathione peroxidase activity and glutathione reduced level were increased in kidney in prallethrin-essential oil groups.

Conclusions: We can conclude that prallethrin induced oxidative damage and renal toxicity in male rat. The administration of essential oil provided significant protection against prallethrin-induced oxidative stress, biochemical changes and histopathological damage.

1. Introduction

Synthetic pesticides have made valuable contributions to human health by increasing food, fiber production and by reducing the occurrence of vector-borne diseases[1]. Large amounts of these pesticides are released daily into the environment and, hence, they represent a potential hazard not only to human and mammalian nervous system, but also to their genetic material and to the function of their livers and kidneys, since their residues and derivatives are known to contaminated field crops[2].

Introduced commercially about 30 years ago, synthetic pyrethroids account for more than 30% of insecticides used worldwide in agricultural, domestic and veterinary applications and have a high potential for human exposure[3,4]. Pyrethroids are more hydrophobic than other classes of insecticides and this feature indicates that the site of action is in the biological membrane[5]. In fact, the principal target site for pyrethroids is defined as the voltage-dependent sodium channel in the neuronal membrane[6,7]. prallethrin is the most popular Type I synthetic pyrethroid that produces a rapid knockdown in household insect pests[8]. It has prevalent household presence in the form of mosquito repellant mats, coils, liquid vaporizers, *etc.* and therefore there could be direct and indirect exposure in pets and humans through accidental continued contamination of feed/food[9]. Consistent with its lipophilic nature, it has been found to accumulate in body fat, skin, liver, kidneys,

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adrenal glands, ovaries and brain[10].

Kidney plays an essential role in health, disease and overall development and growth. The main function of kidney is to maintain total body fluid volume, its composition and acid base balance. A number of environmental variables including certain xenobiotics (*e.g.* pesticides) influence these functions[11,12]. In fact, oxygen free radicals are reportedly involved in toxicity of numerous chemicals including pesticides and in pathogenesis of many diseases[13-15]. Reactive oxygen species (ROS) such as superoxide anions ($O_2^{\bullet-}$), hydroxyl radicals ($HO^{\bullet-}$) and H_2O_2 enhance oxidative process and produce lipid peroxidative damage to cell membranes. The $HO^{\bullet-}$ radical has been proposed as an initiator of lipid peroxidation through an iron-catalyses Fenton reaction[16].

The use of natural antioxidants for curing pesticide induced kidney toxicity or injury is being studied extensively[12]. Also, there are several reports on oils indicating that it results in alterations of pharmacologic responses to drugs[17]. Our previous study, gas chromatography-mass spectrometer (GC-MS) analysis of *Origanum majorana* (*O. majorana*) essential oil revealed the presence of 4-terpineol (29.97%), γ-terpinene (15.40%), trans-sabinene hydrate (10.93%), α-terpinene (6.86%), and 3-cycolohexene-1-1 methanal, a, a4-trimethyl-, (S)- (CAS) (6.54%) were identified as main constituents. It exhibited concentration-dependent inhibitory effects on DPPH$^{\bullet}$, hydroxyl radical, hydrogen peroxide, reducing power and lipid peroxidation[18].

At this time, a very little, unsatisfactory information is available in literature on oxidative stress and nephrototoxicity of prallethrin in mammals and protective effect of *O. majorana* essential oil. Therefore, this study aims to investigate the effects of prallethrin on renal dysfunction biomarkers, antioxidant enzyme activities and lipid peroxidation in rats and the protective effect of *O. majorana* essential oil.

2. Materials and methods

2.1. Chemicals and reagent

Prallethrin (96.2%) was obtained from Jiangsu Yangnong Chemical Co., Ltd, China. The assay kits used for biochemical measurements of glutathione reduced (GSH), superoxide dismutase (SOD), glutathione peroxidase (GPx) and lipid peroxidation were obtained from Biodiagnostic Co., Dokki, Giza, Egypt. Kits of creatinine, urea and uric acid were obtained from Stanbio Laboratory, Texas, USA. All other chemicals were of reagent grades and obtained from the local scientific distributors in Egypt.

2.2. Essential oil

O. majorana essential oil was obtained from leaves by hydro distillation in a Clevenger apparatus. The distillation continued until no more condensing oil could be seen. The oil was permitted to stand undisturbed so that a good separation from water could be obtained. The essential oil was separated from the aqueous solution, dried over anhydrous sodium sulfate, transferred into an amber glass flask, and kept at a temperature of −20 °C until used. *O. majorana* essential oil was analyzed by gas chromatograph (Thermo Trace 2000) equipped with a mass spectrophotometer (Finnigan SS-7000) (GC-MS system, Central Laboratory of the National Research Centre, Cairo, Egypt) as described in our previous study[18].

2.3. Animals

Healthy male Wistar rats were obtained from Animal Breeding House of the National Research Centre, Dokki, Cairo, Egypt. Rats were housed in clean plastic cages with free access to food (standard pellet diet) and tap water *ad libitum*, under standardized housing conditions [12 h light/dark cycle, the temperature was (23±2) °C and a minimum relative humidity of 44%] in the laboratory animal room. Animals received humane care according to the criteria outlined in the "Guide for the Care and Use of Laboratory Animals." The local ethics committee at the National Research Centre, Dokki, Cairo, Egypt approved the experimental protocols and procedures. The rats attained a body weight range of 145-155 g before being used for this study.

2.4. Treatments

Dosages of prallethrin and *O. majorana* essential oil were freshly prepared in olive oil, given via oral route for 28 consecutive days and adjusted weekly for body weight changes. The animals were acclimatized for a minimum of 7 d before treatment and randomly assigned into four groups of seven rats each as follows: Group I received olive oil and served as control; Group II received prallethrin at a dose 64.0 mg/kg body weight (1/10 LD_{50}) daily; Group III received the same as group II+*O. majorana* essential oil (0.16 mL/kg body weight twice daily); Group IV received *O. majorana* essential oil at a dose 0.16 mL/kg body weight twice daily. The selective dose of prallethrin based on published LD_{50} (640 mg/kg body weight)[19], and dose of *O. majorana* essential oil (0.16 mL/kg body weight twice daily) based on Ashmawy *et al*[20]. At the end of the administration, the animals were fasted for 12 h and sacrificed by ether anesthesia on 29th day.

2.5. Samples preparation

At the end of experimental period, blood samples were withdrawn from the animals under light ether anesthesia

by puncturing the retero-orbital venous plexus of the animals with a fine sterilized glass capillary. Blood samples were taken and left to clot in clean dry tubes, and then centrifuged at 3 000 r/min for 10 min using Heraeus Labofuge 400R (Kendro Laboratory Products GmbH, Germany) to obtain the sera. The sera was then stored frozen at −20 °C for the biochemical analysis (creatinine, urea and uric acid). After blood collection, rats were then killed by decapitation, and kidneys were dissected out and cleaned. Small pieces of kidney were cut and kept in 10% formalin solution for histological studies. Other portions of kidneys washed with saline solution, weighed, cut in small parts, homogenized in 10% (w/v) ice cold 100 mmol/L phosphate buffer (pH 7.4) and centrifuged at 4 500 r/min for 15 min at 4 °C, then the supernatant was obtained and used for antioxidant enzyme measurements (SOD, GSH, GPx) and lipid peroxidation.

2.6. Serum kidney dysfunction markers

Serum creatinine was measured as described by Tietz *et al.*[21], urea by Henry[22], and uric acid was measured by the method of Teitz[23].

2.7. Kidney lipid peroxidation and antioxidant enzymes

Antioxidant enzyme activities and lipid peroxidation were determined in kidney homogenate using a spectrophotometer Shimadzu UV-vis recording 2401 PC7 (Japan). The biochemical measurements were performed according to the details given in the kit's instructions. The principals below of different methods are given for each concerned biochemical parameter.

2.7.1. Lipid peroxidation

lipid peroxidation was estimated by measuring thiobarbituric acid reactive substances and was expressed in terms of malondialdehyde (MDA) content by a colorimetric method according to Satoh[24]. The MDA values were expressed as nmol of MDA/g tissue.

2.7.2. Antioxidant enzymes and GSH

Superoxide dismutase activity was determined according to the method of Nishikimi *et al*[25]. The method is based on the ability of SOD enzyme to inhibit the phenazine methosulphate-mediated reduction of nitroblue tetrazolium dye. Briefly, 0.05 mL sample was mixed with 1.00 mL buffer (pH 8.5), 0.10 mL nitroblue tetrazolium and 0.10 mL reduced form of nicotinamide-adenine dinucleotid. The reaction was initiated by adding 0.01 mL phenazine methosulphate, and then the increase in absorbance was read at 560 nm for 5 min. SOD activity was expressed in μmol/g tissue.

GPx activity was determined according to the method of Paglia and Valentine[26]. The assay is an indirect measure of the activity of c-GPx. Oxidized glutathione (GSSG), produced upon reduction of organic peroxide by c-GPx, is recycled to its reduced state by the enzyme glutathione reductase (GR):

$$R\text{-}O\text{-}O\text{-}H + 2GSH \xrightarrow{c\text{-}GPX} R\text{-}O\text{-}H + GSSG + H_2O$$

$$GSSG + NADPH + H \xrightarrow{GR} 2GSH + NADP$$

The oxidation of NADPH to NADP is accompanied by a decrease in absorbance at 340 nm providing a spectrophotometric means for monitoring GPx enzyme activity. The rate of decrease in the absorbance at 340 nm is directly proportional to the GPx activity in the sample. GPx activity was expressed in μmol/g tissue.

GSH level in the kidney was assessed spectrophotometrically according to the method of Beutler *et al*[27]. The method was based on the reduction of 5,5 dithiobis (2-nitrobenzoic acid) with glutathione to produce a yellow compound. The reduced chromogen was directly proportional to GSH concentration and its absorbance could be measured at 405 nm. GSH activity was expressed in nmol/g tissue.

2.8. Histological study

At the end of the treatment period, rats were killed, kidney samples were dissected and fixed in 10% neutral formalin, dehydrated in ascending grades of alcohol and imbedded in paraffin wax. Paraffin sections (5 μm thick) were stained for routine histological study using haematoxylin and eosin (H&E). Two slides were prepared for each rat; each slid contain two sections. Ten field areas for each section were selected and examined for histopathological changes (×160) under light microscope. The kidney fields were scored based on tubular injury as follows: no tubules injury (−), mild tubules injury in less than 10% of tubules injury (+), moderate tubules injury in 10% to 25% of tubules injury (++) and extensive tubules injury in greater than 25% of tubules injury (+++). Such quantitative assessment of histopathological injury has been performed by previous investigators[28].

2.9. Statistical analysis

The results were expressed as mean±SE. All data were done with the SPSS 17.0 for windows. The results were analyzed using One way analysis of variance followed by Duncan's test for comparison between different treatment groups. Statistical significance was set at $P \leqslant 0.05$.

3. Results

Serum kidney biomarkers including uric acid, urea and creatinine were mainly used in the evaluation of renal damage. As shown in Figures 1, 2 and 3, significant increases in uric acid, urea and creatinine concentrations were

observed in serum in prallethrin-treated rats, in comparison with the control values. The increase in uric acid, urea and creatinine concentrations accounted to 1.84, 22.33 and 0.67 mg/dL in prallethrin-treated rat compared to 1.35, 18.75 and 0.56 mg/dL in untreated rats, respectively. Results indicated that co-administration of *O. majorana* essential oil with prallethrin modulated significantly the level of uric acid and creatinine concentrations to normal control. Compared to controls, uric acid and creatinine concentrations returned to control values of *O. majorana* essential oil+prallethrin-treated group (1.51 mg/dL *vs.* 1.35 mg/dL and 0.57 mg/dL *vs.* 0.56 mg/dL).

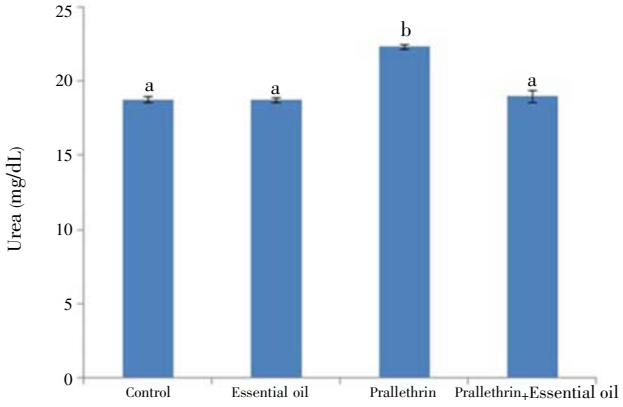

Figure 1. Urea concentration in the sera of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a,b]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

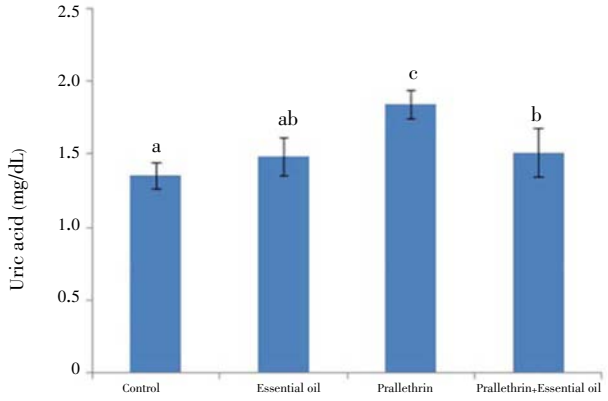

Figure 2. Uric acid concentration (mg/dL) in the sera of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a, b, c]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

The effects of prallethrin treatment on the activities of SOD and GPx in kidney tissue were shown in Figures 4 and 5. Activities of SOD (215.80 μmol/g tissue *vs.* 259.22 μmol/g tissue) and GPx (70.41 μmol/g tissue *vs.* 81.33 μmol/g tissue) in kidney homogenate were significantly decreased compared to control group. *O. majorana* essential oil administrated in prallethrin-treated rats improved significantly the activities of SOD and GPx compared with control values. The activity of SOD and GPx was returned to control values in essential oil+prallethrin treated group (Figures 4 and 5).

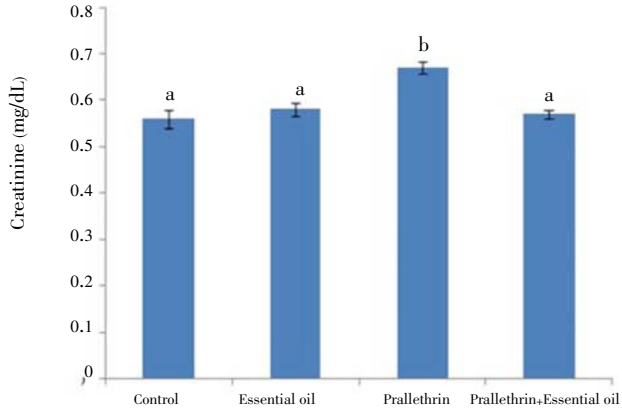

Figure 3. Creatinine concentration (mg/dL) in sera of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a,b]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

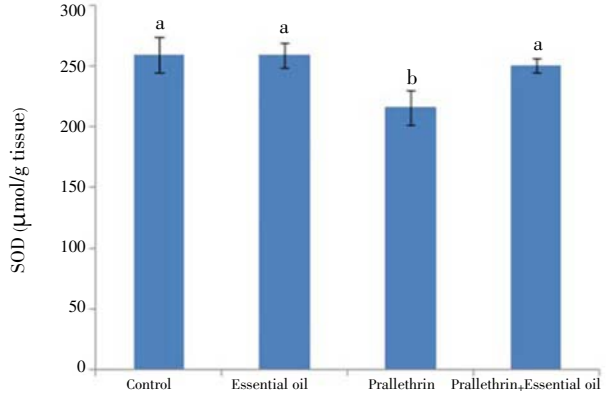

Figure 4. SOD activity in kidney tissue of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a,b]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

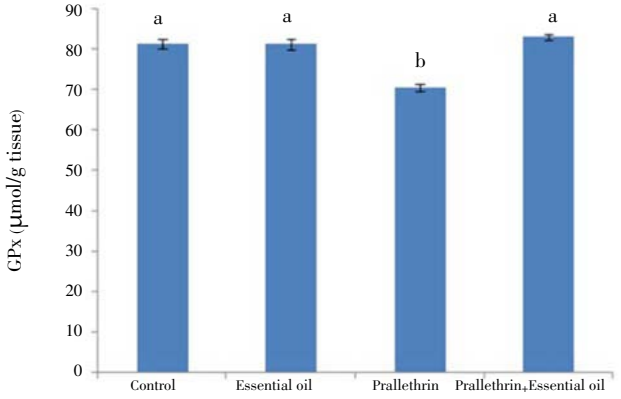

Figure 5. GPx activity in kidney tissue of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a,b]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

As shown in Figure 6, significant change in GSH was observed after prallethrin-treatment compared to control group (2.58 nmol/g tissue *vs.* 3.26 nmol/g tissue). Co-administration of *O. majorana* essential oil with prallethrin

modulated significantly the level of GSH to normal control. Compared to controls, GSH returned to control values of *O. majorana* essential oil+prallethrin-treated group (3.34 nmol/g tissues *vs*. 3.26 nmol/g tissues). Kidney MDA level was markedly increased by prallethrin administration as compared to control group (Figure 7). The difference between the two groups was statistically significant (17.42 nmol MDA/g tissues *vs*. 12.52 nmol MDA/g tissues). *O. majorana* essential oil administered to rats of prallethrin group alleviated lipid peroxidation induced by prallethrin treatment and modulated significantly (14.16 nmol MDA/g tissues *vs*. 12.52 nmol MDA/g tissues) the levels of MDA compared to control.

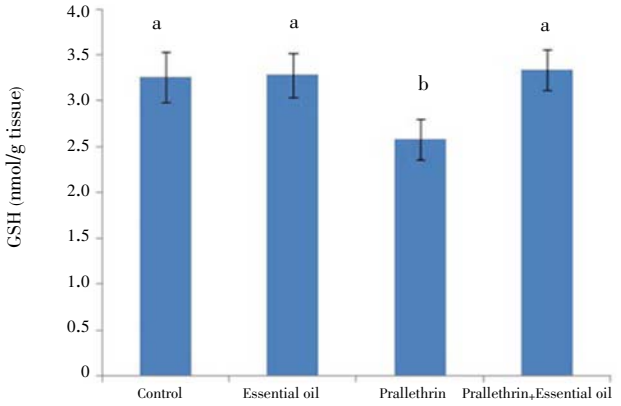

Figure 6. GSH level in kidney tissue of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a,b]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

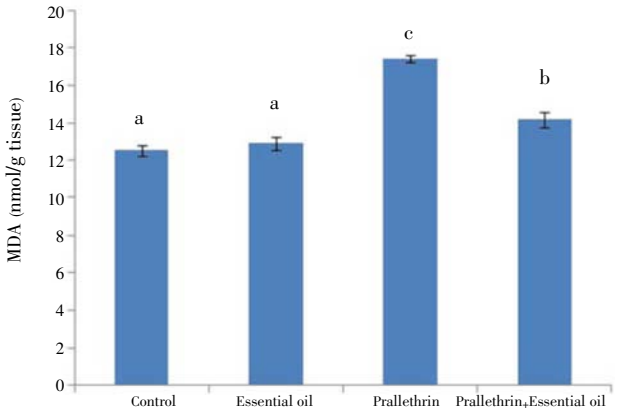

Figure 7. MDA content in kidney tissue of rats exposed to prallethrin and the protective effect of *O. majorana* essential oils.
Bars represent the group means±SE; [a,b,c]: data not sharing a common letter are significantly different ($P \leq 0.05$) after One-way ANOVA and Duncan's multiple-range test.

The histopathological findings on kidney for various treatment groups are presented in Figure 8 and Table 1. In light microscopic examinations, histopathological changes were observed in kidney of prallethrin and essential oil-prallethrin-treated groups compared to untreated group. The kidney in the control animals showed normal histological structure (Figure 8A). With respect to the renal histoarchitecture of the prallethrin-treated animals, oedema, inflammatory cells and severs dilation of cortical blood are shown in Figure 8B1; swelling and vacuolization of the endothelial cells lining the glomeruli tuft are shown in Figure 8B2. Normal histological structure was observed in *O. majorana* essential oil-treated group (Figure 8C). Administration of *O. majorana* to prallethrin-treated group showed degeneration in lining epithelium of the tubules (Figure 8D). Quantitative evaluation of histopathological injury of renal based on scoring the severity of injury is presented in Table 1. The kidneys of male rats exposed to prallethrin showed sever injury in kidney tissue compared to normal control. In contrast, the histopathological alterations in kidney were improved after essential oil supplementation to prallethrin-treated group.

Table 1
Histopathological changes in the kidneys of male rats exposed to prallethrin and the ameliorative effect of *O. majorana* essential oil.

Histopathological alterations	Treatment			
	Control	Prallethrin	Essential oil	Prallethrin + Essential oil
Focal inflammatory reaction in between the glomeruli and tubules	–	+++	–	–
Glomeruli affchns	–	++	–	–
Tubular degeneration	–	++	–	++

–: Normal; +: Mild; ++: Moderate; +++: Extensive.

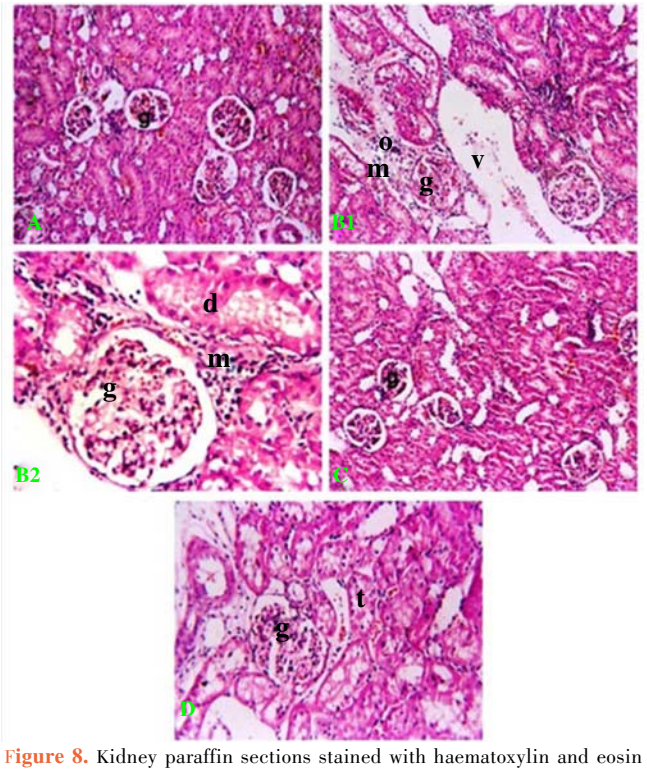

Figure 8. Kidney paraffin sections stained with haematoxylin and eosin (H&E) for histopathological changes.
Control group A: showing the intact histological structure of the glomeruli (g) and tubules (t) in cortex (×40). Prallethrin group B1: showing oedema (o) with inflammatory cells infiltration (m) in between the glomeruli and tubules with sever dilatation of cortical blood vessels (v) (×40) and B2: swelling and vacuolization of the endothelial cell lining the glomeruli tuft (g), inflammatory cells infiltration (m) and tubular degeneration (d) (×80). *O. majorana* essential oil group C: showing normal histological structure of the glomeruli (g) and tubules (t) (×40). Essential oil-prallethrin-treated group D: showing degeneration in lining epithelium of the tubules (×64).

4. Discussion

The kidneys perform two major important functions, first, they excrete most of the end products of bodily metabolism, and second, they control the concentrations of most of the constituents of the body fluids[29]. As markers of renal function uric acid, urea and creatinine are for routine analysis. Uric acid is the end product of nucleic acid catabolism, *i.e.* purine and pyrimidine bases metabolism[30]. Urea is major nitrogenous end product of protein and amino acid catabolism, produced by liver and distributed throughout intracellular and extracellular fluid. In kidneys, urea is filtered out of blood by glomeruli and is partially being reabsorbed with water[31]. Creatinine is a breakdown product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body depending on muscle mass[32].

In the present study, serum uric acid and urea levels exhibited a significant increment in prallethrin-treated rats. This increase in uric acid level may be due to degradation of purines and pyrimidines, overproduction or inability of its excretion[30]. Also, our results revealed that the concentration of creatinine was significantly elevated in prallethrin-treated group compared to the control value. The creatinine excretion is dependent almost on the process of glomerular filtration, though tubular secretion contributes slightly[33]. The slight and significant rise in the serum creatinine level of male rats may be due to the impairment of the glomerular function and tubular damage to the kidneys. The increased levels of these end products in blood especially serum creatinine and serum urea indicate poor clearance of these substances by the kidneys, rather than excessive production. Interestingly, our results indicated that co-administration of essential oil to prallethrin-treated group restored uric acid and creatinine concentrations within normal limits. Abbassy and Mossa[34] reported that deltamethrin and cypermethrin treatments caused significant increases in serum uric acid and creatinine concentrations in treated rats. Rodwell[35] found an elevated level of urea in blood correlating with an increase of protein catabolism in the mammalian body. It may due to a more efficient conversion of ammonia to urea as a result of increased synthesis of enzyme involved in urea production[35,36]. Other investigations[37,38] showed an increase of urea and creatinine in the serum of chicks and rats-treated with acute and chronic doses of 2, 4-D and cypermethrin. Because creatinine is a metabolite of creatine and is excreted completely in urine via glomerular filtration, an elevation of its level in the blood is thus an indication of impaired kidney function[39]. The change in its concentration together with the histological results indicates a reduction in the glomerular filtration rate as a result of prallethrin intoxication.

Pesticides induce oxidative stress as well as alter the defense mechanisms of detoxification and scavenging enzymes[12,15,40-42]. These toxic compounds impair the cellular function, enzymes activity and produce cytotoxic changes through generation of ROS[12,15,34]. These free radicals also damage the cell components including proteins, lipids and DNA[43]. In fact, the antioxidant enzymes *e.g.* SOD, CAT and GPx are the main enzymes that act as defenses with non-enzymatic *e.g.* GSH[19]; they protect against the adverse effects of ROS. SOD is responsible for catalytic dismutation of highly reactive and potentially toxic superoxide radicals to hydrogen peroxide and O_2. CAT and GPx are responsible for the catalytic decomposition of hydrogen peroxide to molecular oxygen and water[19]. GSH participate in the elimination of ROS, acting both as non enzymatic oxygen radical scavenger and as a substrate for various enzymes such as GSHPx[44]. In the present study, prallethrin treatment induced significant decrease in the activity of SOD (215.8 μmol/g tissue vs. 259.22 μmol/g tissue) and GPx (70.41 μmol/g tissue vs. 81.33 μmol/g tissue) in kidney homogenate compared to control group. Also, significant changes in GSH and MDA in kidney tissue were observed after prallethrin-treatment compared to control rats. The change in SOD, GPx, GSH and MDA might be in response to increased oxidative stress and lipid peroxidation. According to Halliwell and Gutteridge[45], when a condition of oxidative stress strongly establishes, the defense capacities against ROS become insufficient; in turn ROS also affects the antioxidant defense mechanisms, reduces the intracellular concentration of GSH, increases lipid peroxidation and alters the activity of antioxidant enzymes *e.g.*, SOD, CAT, GPx and GST. The changes in these oxidative stress biomarkers have been reported to be an indicator of tissue's ability to cope with oxidative stress[34,40,46].

With respect to the renal histoarchitecture of the prallethrin-treated animals, oedema, inflammatory cells, severs dilation of cortical blood; swelling and vacuolization of the endothelial cells lining the glomeruli tuft were recorded in kidney. The present findings are in consequence with the results of the previous investigations after exposure to different types of pyrethroid insecticides[47-49]. Previous study Mossa *et al.*[50] reported that pyrethroid induced oxidative stress as well as changes in cell morphology, tissue injury and in the cytoskeleton occured during cell injury. Oxidative stress is generated by stimulated leucocytes in the areas of inflammation associated with tissue injury[49]. Mongi *et al.*[51] reported an increase in the serum urea and creatinine in rats exposed to deltamethrin and this toxicity are attributed to its free radical induced oxidative damage.

Our results revealed that co-administration of *O. majorana* essential oil with prallethrin- treated rats returned the level of GSH and the activity of SOD and GPx at the control values. While, essential oil administered

to prallethrin-treated rat modulated significantly (14.16 nmol MDA/g tissues *vs*. 12.52 nmol MDA/g tissues) the levels of MDA compared to control. The observed normalization trend of GSH, SOD and GPx following *O. majorana* essential oil treatment could possibly due to scavenging effect of *O. majorana* essential oil. The high potential of phenolics components to scavenger radicals might be explained by their ability to donate a hydrogen atom from their phenolic hydroxyl groups. Previous studies showed *O. majorana* contained phenolic terpenoids (thymol, carvacrol), flavonoids (diosmetin, luteolin, and apigenin), tannins, hydroquinone, phenolic glycosides (arbutin, methyl arbutin, vitexin, and orientinthymonin), triacontane, sitosterol, oleanolic acid and cis-sabinene hydrate[52,53]. GC-MS analysis of *O. majorana* essential oil used in the present study contained 4-terpineol (29.97%), γ-terpinene (15.40%), trans-sabinene hydrate (10.93%), α-terpinene (6.86%), and 3-cycolohexene-1-1 methanal,a,a4-trimethyl,(S)-(CAS) (6.54%)[18]. According to Singh *et al.*[54], the antioxidant activity of essential oils could not be attributed to the major compounds, and minor compounds might play a significant role in the antioxidant activity, and synergistic effects were reported. Therefore, the possible mechanisms of *O. majorana* essential oil renal protective activity could arise from the free radical scavenging effect, preventing lipid peroxidation and improvement of the antioxidant/detoxification system in kidney.

We can conclude that prallethrin induced oxidative damage and renal toxicity in male rat. The administration of essential oil provided significant protection against prallethrin-induced oxidative stress, biochemical changes and histopathological damage.

Conflict of interest statement

We declare that we have no conflict of interest.

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