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Nephroprotective and Anti-Apoptotic Effects of Selenium Nanoparticles in Deltamethrin-Treated Albino Rats

Mona Ragheb [1*], Afaf A. Shalaby [1], Areej Yaseen[2] and Ahmed A. Baiomy[3]

[1] *Research Institute of Medical Entomology (RIME), General Organization of Teaching Hospitals and Institutes (GOTHI), P.O. Box 12311 Dokki, Cairo, Egypt.*
[2] *National Hepatology and Tropical Medicine Research Institute (NHTMRI), General Organization of Teaching Hospitals and Institutes (GOTHI), General Kasr Eleiny, Cairo, Egypt.*
[3] *Zoology Dept., Faculty of Science, Cairo University, Giza, Egypt.*

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Abstract

Our aim is to evaluate selenium nanoparticles (SeNPs) protective potency towards renal tissues which were exposed to deltamethrin sub lethal dose for one month using corn oil as a solvent. Four groups were assigned (10 rats per group). In the control group rats were fed on corn oil while in the other groups rats were administered SeNPs, deltamethrin and SeNPs along with deltamethrin respectively. Histopathological investigations revealed induced significant renal damage characterized by mononuclear cell infiltration which led to induced marked vacuolar degeneration of epithelial and endothelial lining of renal tubules, glomerular tuft and widening of the Bowman's space in deltamethrin treated rats meanwhile, SeNPs showed protective effect on such tissues. These findings were emphasized by the increased antioxidant activities of superoxide dismutase, catalase and glutathione reductase enzymes among SeNPs treated groups. On the other hand, lipid peroxidase and nitric oxide activities along with urea and creatinine levels showed significant increase in deltamethrin treated groups which was mitigated in SeNPs administered groups. Immunohistochemical detection of BAX protein (BCL-2- Associated X protein) showed its over expression pattern in deltamethrin group which was also mitigated upon SeNPs treatment. In conclusion, SeNPs exhibit a protective effect against deltamethrin-induced renal damage.

1. Introduction

Nanoscience scholars regarded selenium nanoparticles (SeNPs) to attract great attention in the upcoming few years owing to their promising protective effects at the cellular and tissue levels **[1,2]** and to their lower toxicity and higher bioavailability compared to their forms of the organic and inorganic forms **[3,4]**. One advantage of

* **Corresponding author E-mail:** mona.ragheb@yahoo.com

SeNPs is the availability of administering selenium in its elemental selenium which confers excellent bioavailability and low toxicity when compared to the other oxidation states **[5].** Undeniable, SeNPs exhibit wide range of biomedical applications the most popular of which is their effect on mitigating the oxidative stress and protecting the reproductive cells **[6].** Meanwhile, SeNPs also exhibit potential role as being a chemo-preventive agent **[3].** Nano science studies have revealed that SeNPs are also beneficial in cancer chemo-prevention owing to their magnificent characters as a potential anticancer drug **[7],** as well as a delivery carrier for anticancer drugs **[8]**. SeNPs high efficiency showed effective medicinal impacts as antibiotic **[9],** anti-diabetic **[10]** and cytotoxic medicines **[11]** compared to the traditional therapeutic medicines. Moreover, the immuno-stimulatory effect of SeNPs was recently elucidated **[1].** SeNPs implied beneficial effects on a number of physiological functions **[3,12]**. Adding to the all mentioned capabilities of SeNPs, their parasitic effect has also been described **[13]**. Moreover, they are currently explored for their potency as anti-viral and anti-tuberculosis drugs **[1]**. In mice, SeNPs are known to enhance the effects of instigated toxicity thereby, decrease the reactive oxygen species and glutathione levels, rebuild the cell reinforcement protein activity and decrease the chromosomal variations in bone marrow as well as DNA damage declination **[14].**

In the meantime, deltamethrin, a synthetic pyrethroid used globally as an insecticide and acaricide **[15]**, belongs to the second type pyrethroid family and is extensively used in house hold and agriculture pest control concerns. It is categorized by the WHO **[16]** as a moderately hazardous insecticide, the LD_{50} value of oral exposure was estimated at 135 mg / kg b.w. (on the basis of LD_{50} value of deltamethrin in corn oil, **[17]**). Deltamethrin mode of action was known to decrease the activities of the antioxidants and increasing the lipid peroxidases leading to cellular toxicity **[18].** Thus, exposure to deltamethrin could lead to damages of internal organs via toxic metabolites **[15]**, nervous system imbalance and eventually neural death **[19]**. In addition, deltamethrin could induce impaired kidney function **[15]**, disruption in the endocrine system of the body, changing in blood morphology **[20]** and definitely could lead to oxidative stress **[21]**. Since the oxidative stress and cell metabolism are strongly correlated with toxicity **[22],** exposure of rats for one month to the pesticide deltamethrin was found to produce toxicity in kidney cells **[15]**. Worthy to mention, the nephrotoxic effect of deltamethrin could be resulted from a single toxic dose of deltamethrin confirmed with changes in the histology of kidneys which eventually led to kidney dysfunction **[23].** Kidney function impairment could be detected via residual products like urea and creatinine which are formed in the rat body as a consequence of a series of metabolic reactions for the ingested body substances which should be removed from the blood by the kidneys. Intact kidneys should filtrate and remove toxic materials and the excess liquid through urination process, they also perform many vital functions such as regulation of water balance in the body and protection of the acidity and alkalinity of body liquids **[24]**. Meanwhile, apoptosis or programmed cell death, is a vital mechanism that function in both physiological and pathological aspects. Two main apoptotic pathways are concerned with either death-receptors or mitochondrial pathways. Mitochondrial pathway apoptosis is defined by the mitochondrial outer membrane permeabilization (MOMP) and the consequent release of apoptotic factors such as Bcl-2 family proteins and the cytochrome c **[25].** In this concern, Bax (BCL-2-Associated X protein) and Bak, are the two pro-apoptotic proteins with multiple Bcl-2 homology domains which are the main gate-keeper molecules of MOMP. MOMP could be prohibited via antagonizing Bax and Bak by means of the anti-apoptotic Bcl-2 proteins, such as Bcl-2 and Bcl- XL. On the other hand, MOMP could be initiated by the BH3-domain only proteins such as Puma, Bim and Bid that consequently activate Bax and Bak to form oligomers in the mitochondrial outer membrane **[25]**. Thereby, both Bax and Bak could provide mitochondrial activation resulting in MOMP and the consequent release of apoptotic factors. Apoptosis via Bax/Bak-mediated mitochondrial pathway was found to play crucial roles in many diseases including AKI, acute kidney injury which is a kidney disease manifested by the rapid impairment of kidney functions associated with the wide-spread of renal tubular cell death by means of necrosis or apoptosis **[26,27]**.

Accordingly, the main aim of this study is to investigate the protective role of SeNPs towards the nephrotoxic effect induced as a consequent of deltamethrin exposure in albino rats at a sub-lethal dose of 27 mg/Kg bwt deltamethrin corresponding to its 1/5 LD_{50} using corn oil as a solvent for 30 days.

2. Materials and Methods

2.1. Animals:

This study was carried out on mature Swiss albino rats (223+/- 3.5 g) at ages ranged from 12 to 14 weeks old. Forty adult rats were used in this study. They were obtained from the existed bred strain at the animal house of Research Institute of Medical Entomology (RIME), Egypt. Studies were performed following the standards of animal care set out in Egyptian rules and the National Institutes of Health (NIH) Guidelines for the care and use of laboratory animals.

2.2. Materials:

1- Technical grade deltamethrin (98%) from which 27mg/Kg bwt deltamethrin was obtained by dilution with corn oil according to the estimated rat weights.

2- Preparation and Characterization of SeNPs were prepared from sodium selenite salt via simple precipitation method using the reducing capacity of ascorbic acid. Ascorbic acid was dissolved in distilled water (0.8g in 100ml) and was added in drop wise manner to 1.3 gm of sodium selenite dissolved in 50 ml distilled water while steering at

temperature adjusted at 50^0C till light orange solution was formed [**28].** The prepared SeNPs were characterized by their distinctive absorption band displayed by UV-visible spectrophotometer **[29].**

2.3. Methods:

Four groups of rats (n = 10 per group) were used in this study.

1- The negative control group includes rats that were fed only on corn oil.
2- The Second group includes rats that were orally injected with SeNPs (0.5 mg/kg) b.w. **[30]**.
3- The Third group includes rats that were orally administered 1/5 of LD_{50} of deltamethrin (27mg/kg b.w. dose) **[17,31]**.
4- The fourth group includes rats that were exposed to deltamethrin at dose of 27mg/ kg and SeNPs at dose of o.5 mg/ kg b.w. Deltamethrin was orally injected after one hour of SeNPs administration.

Oral administration for all subjects and all treatments lasted for one month two times per week. Thereafter, rats were sacrificed and the kidneys were removed, blood was collected from the abdominal aorta from which serum was isolated. The obtained kidneys and sera were used in the Immunohistological, histological and biochemical studies. The animal weights were recorded prior to the different types of treatment and prior to death along with the weights of kidneys upon sacrificing.

2.3.1. Estimation of the kidneys weight Index of Rats

The relative weight of kidneys was estimated according to [**32].**

2.3.2. Estimation of kidney functions

The serum urea and creatinine levels were estimated following the instruction manual of Biomed diagnostics CAT NO: URE 120240 and CRE 106240 respectively**.**

2.3.3. Preparation of kidneys Homogenates

The kidneys were homogenized in ice-cold medium of phosphate buffer solution (PBS, pH 7.4). Kidney homogenates were centrifuged and the supernatants were collected to be involved in biochemical, oxidative stress and antioxidant enzyme activities investigations **[33].**

2.3.4. Oxidative Stress of kidneys

Lipid peroxidation (LPO) and nitric oxide (NO) levels in kidneys and urine of all subjects were determined using the instruction manual of Biodiagnostics kit accessories Cat No.: MD2529 and 190309 respectively.

2.3.5. Antioxidant Status

Superoxide dismutase (SOD), catalase (CAT), which is important for eliminating the hydrogen peroxide produced by SOD and glutathione reductase (GR) activities were estimated as described by the methods of **[34,29,35]** respectively.

2.3.6. Histological Investigations

Kidney tissues were fixed using 10% neutral buffered formalin for 24 hours and dehydrated with ethanol. Post fixation step; tissues were cleared by xylene and mounted in molten paraplast. Tissues were Sliced into thin sections ranged from 4to5 um. Such tissue Sections were stained with H&E stain in order to visualize nephrotic cells using Olympus microscope **[6].**

2.3.7. Immunohistochemistry

To evaluate the immunohistochemical reactions in kidney tissues, the peroxidase/anti-peroxidase (PAP) method was conducted. kidney tissue sections were embedded in formaldehyde-fixed, paraffin and incubated with methanol and normal goat serum for 30 minutes. The tissue sections were incubated with the first antibody that recognize the BAX protein (BCL-2- Associated X protein) and subsequently with HRP-conjugated goat anti-mouse IgG as a secondary antibody. Thereafter, tissue sections were incubated with the PAP complex for 60 minutes using Diaminobenzidine as a chromogen. Sections were counterstained with haematoxylin and examined under a light microscope **[36].**

2.3.8. Statistical analysis

Statistical analyses were carried out using the Statistical Package for Social Science (SPSS) version 25 (SPSS Inc., Chicago, IL, USA.). Data were displayed as means ± SD. Differences in the various parameters in more than 2 groups were evaluated by a one-way analysis of variance (ANOVA). Differences between groups were regarded as significant at $p < 0.05$**.** Bonferroni post hoc test was conducted at 95% Confidence Interval **[6].**

3. Results

Relative kidney weights estimations revealed a reduction in kidney weight in deltamethrin treated rats compared to control rats (Table1). On the other hand, the kidney weight of rats treated with deltamethrin and SeNPs showed a slight increase in kidney weight compared to the control group (Table1).

Table 1: Average of relative kidney weights among different experimental groups

Groups	Average total body weight (g) ± SE	Average kidney weight (g) ± SE	Average of relative kidney weight index ± SE
Control (corn oil only)	223±3.483	0.728±.0.007	0.32±.0067
0.5 nanoselenium mg/Kg	227±3.726**	0.75±.0.011**	0.33±.0.0067**
27 deltamethrin mg/kg	173±2.752**	0.47±.0.007**	0.27±.0.0047**
27 deltamethrin mg/kg + 0.5 nanoselenium mg/Kg	217±4.284**	0.688±.0.009**	0.31±.0.0066**

Values are represented as mean± SE, ** is highly significant= P< 0.001, * is significant = P<0.005, NS is non-significant= P>0.005

Upon estimating the Sera levels of urea and creatinine as kidney function biochemical markers, results showed significant ($p < 0.005$) increase in deltamethrin treated rats. Interestingly, SeNPs significantly decreased serum urea and creatinine levels in rats treated with SeNPs along with deltamethrin administration (Table2).

Table 2: Average levels of serum urea and creatinine in kidney

Groups	Serum urea mean levels (mg/ml) ±SE	Serum creatinine mean levels (U/g) ±SE
Control (corn oil only)	2325±11.1	0.42±0.0089
0.5 nanoselenium mg/Kg	1988±3.57**	0.4±0.013**
27 deltamethrin mg/kg	6783±4.47**	0.66±0.0089**
27 deltamethrin mg/kg + 0.5 nanoselenium mg/Kg	1991±3.57**	0.46±0.013**

Values are represented as mean± SE, ** is highly significant= P< 0.001, * is significant = P<0.005, NS is non-significant= P>0.005

Regarding the oxidative damage studies indicated by Superoxide dismutase (SOD), catalase (CAT) and glutathione reductase (GR) enzyme activities, results revealed significant reduction in the activities of Superoxide dismutase (SOD) and glutathione reductase (GR) enzyme in kidney tissue homogenates of rats treated with deltamethrin. However, deltamethrin resulted in non-significant reduction in the activity of Catalase (CAT) enzymes (Table3). In the meantime, administration of deltamethrin and SeNPs increased the activities of such markers significantly compared to deltamethrin treated rats (table 3).

Estimation of cellular toxicity biomarkers indicated significant increase in lipid peroxidation, LPO, activities along with nitric oxide, NO, levels in both kidney tissues and urine of rats treated with deltamethrin however, SNPs administration mitigate such influence significantly (Tables 4&5).

Table 3: Average activities of oxidative status enzymes in kidney tissues

Groups	Super oxide dismutase means levels in kidney tissues (U/ml tissue) ±SE	Catalase mean levels in kidney tissues (U/g) ±SE	Glutathione reductase mean levels in kidney tissues (mg/g tissue) ±SE
Control (corn oil only)	332±2.23	1.19±0.026	2.0±0.268
0.5 nanoselenium mg/Kg	355±2.23**	1.23±0.017NS	3.0±0.223^{NS}
27 deltamethrin mg/kg	239±2.68**	1.0±0.134NS	1.68±0.008^{NS}
27 deltamethrin mg/kg + 0.5 nanoselenium mg/Kg	343±1.34**	1.21±0.0089NS	2.5±0.089^{NS}

Values are represented as mean± SE, ** is highly significant= P< 0.001, * is significant = P<0.005, NS is non-significant= P>0.005

Table 4: Average of lipid peroxidase and nitric oxide in kidney tissues of treated groups

Groups	Lipid peroxidase mean levels in kidney tissues (U/ml tissue) ±SE	Nitric oxide means levels in kidney tissues (U/g) ±SE
Control (corn oil only)	54.3±0.447	14±1.34
0.5 nanoselenium mg/Kg	52.1±0.89**	11±0.89**
27 deltamethrin mg/kg	67.7±3.13**	30±1.34**
27 deltamethrin mg/kg + 0.5 nanoselenium mg/Kg	55.2±1.78**	25±0.89**

Values are represented as mean± SE, ** is highly significant= P< 0.001, * is significant = P<0.005, NS is non-significant= P>0.005

Table 5: Average of lipid peroxidase and nitric oxide in urine among different control and treated groups

Groups	Lipid peroxidase mean levels in urine (U/ml tissue) ±SE	Nitric oxide means levels in urine (U/g) ±SE
Control (corn oil only)	42.5±0.89	104±1.78
0.5 nanoselenium mg/Kg	39.6±1.34**	65±0.89**
27 deltamethrin mg/kg	72.2±0.89**	230±1.78**
27 deltamethrin mg/kg + 0.5 nanoselenium mg/Kg	60.9±1.78**	199±1.78**

Values are represented as mean± SE, ** is highly significant= P< 0.001, * is significant = P<0.005, NS is non-significant= P>0.005

Histological studies revealed normal histo architecture of the renal cortex in both the control group and nano selenium treated group which could be distinguished by its characteristic renal corpuscles, each renal corpuscles consists of an outer envelope of simple squamous epithelium

(Bowman's capsule) surrounding a fluid-filled space (Bowman's space) within which is suspended a glomerulus of normal size (figure 1a&b). However, in deltamethrin treated group (figure1c) renal cortex histological deteriorations was observed implying karyomegaly in proximal tubular cells at the proximal tubules along with marked vacuolar degeneration of renal tubular epithelium with focal tubular necrosis, nuclear pyknosis and inflammatory cell infiltration. Moreover, marked improved picture was seen in kidneys of rats treated with deltamethrin along with SeNPs exhibited mild histopathological changes (figure 1d) appeared in more or less normal architecture of the renal cortex with glomeruli which tend to be of normal size and with smaller sub-capsular spaces.

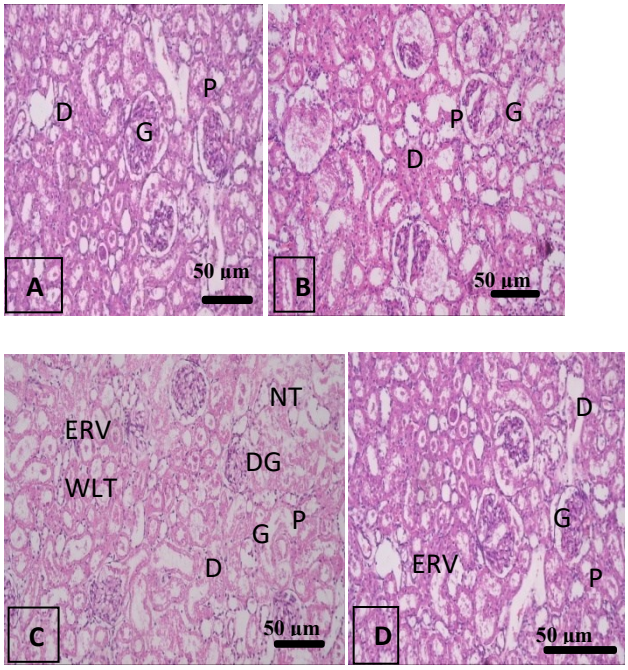

Figure 1: Eosin &Hematoxyline stained photomicrograph revealing the effect of SeNPs on kidney tissuesmedulla of wistar rats treated with deltamethrina; control kidney, b; SNPs treated kidney, c; Deltamethrin treated kidney, d; Deltamethrin and SNPs treated kidney Glomerulus**(G);** proximal tubules (P); distal tubule (D); Enlarged Renal vein (ERV), Degenerated tubules (DG), Enlarged renal vein (RV), necrosis of tubuler epithelium (NT) and Wide lumen tubule (WLT).

Table 6: Scores of histopathological changes among different experimental groups

Organ	Histopathological lesion	Control	SeNPs treated group	Deltamethrin treated group	SeNPs + deltamethrin treated groups
Kidney	Vacuolar degeneration of renal tubular epithelium	0	0	3	1
	Necrobiotic changes of tubular epithelium	0	0	3	1
	Congestion of renal blood vessels	0	0	3	2
	Mononuclear cell infiltration	0	0	3	1

Scores evaluation; 3 is the highest score, 2 is the moderate score and 1 is the lowest score.

Immuno-histochemical expression of BAX protein in the experimental kidney group tissues were demonstrated. Immuno-histochemical sections revealed normal expression in the control group (figure 2a) while, decreased BAX protein is revealed in tissues treated with SeNPs (figure 2b). The highest levels of expression were revealed in deltamethrin exposed tissues (figure2c) while co administration of SeNPs with deltamethrin attenuated BAX expression (figure 2d).

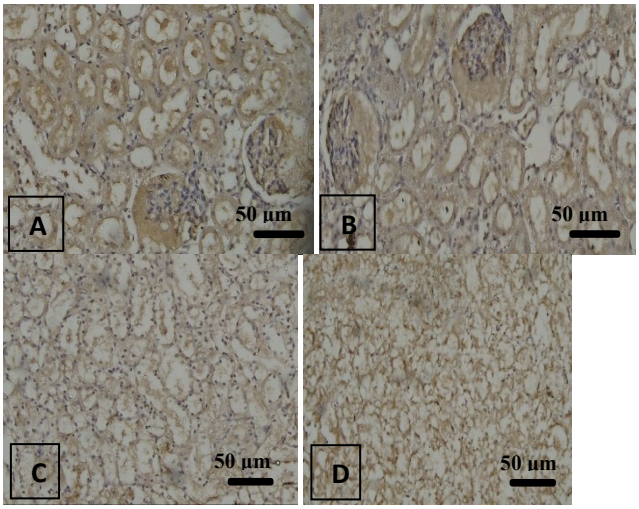

Figure 2: Immuno histo chemical effect of SNPS for BAX protein among different groups, a; control kidney, b; SNPs treated kidney, c; deltamethrin treated kidney, d; deltamethrin and SNPs treated kidney

4. Discussion

One of the primary mechanisms by which deltamethrin affects cells as a potent insecticide is to cause oxidative stress that led to marked impair kidney functions **[15]**. Meanwhile, SeNPs exhibit an antioxidant effect that could reduce such developed oxidative stress and the consequent renal functions impairment **[6].** Results of this study indicated a relative decrease in kidney weights in rats treated with deltamethrin compared to the control group. However, such weights showed slight increase in rats treated with deltamethrin and SeNPs. Several studies had shown a

reduction in organ weights in intoxicated rats compared to control rats **[37-39]**. Although, the increase in organ masses may indicate active inclusion of these organs to clear and remove deltamethrin from the blood of the tested rats **[40],** in case of this study the increase in kidney weights in the groups treated with deltamethrin along with SeNPs might be attributed to the active role of SeNPs in expelling deltamethrin and its metabolites which definitely lead to active kidney inclusion. However, the rate of eradication of deltamethrin alone without any supplements was lower than that supplemented with SeNPs thus, a decrease in kidney weight was also observed.

The main action of the antioxidant defense mechanisms is to restrain the developed free radicals. For a body system to function in a proper manner, reduction of hydrogen peroxide and lipid hydroperoxides is a mandatory defense target which could be achieved via seleno proteins and seleno enzymes **[41].** In this study, results showed a decrease in the activities of SOD, CAT and GR in groups treated with deltamethrin. Such results were in accordance with that recorded by **[18]**. However, the intervention of SeNPs in rats treated with deltamethrin restored these enzyme activities. This was attributed to the role of SeNPs in scavenging the developed free radicals directly by means of increasing the amount of seleno proteins and seleno enzymes activities and thereby lower the degree of toxicity as it was reported by **[41,42].** The proposed scenario for the obtained results is that; rats treated with deltamethrin suffered from insufficient SOD activity rate which is responsible for scavenging the hydro peroxides radicals in a way that it cannot cope with the increasing hydro peroxides radicals that were produced in response to the intoxication state induced by deltamethrin administration **[18]**. On the other hand, the initially existed SOD is insufficient to neutralize the hydro peroxides radicals to hydrogen peroxide thus it was accumulated in the kidney tissues. Moreover, and owing to the decreased catalase activity which is responsible for hydrogen peroxide neutralization to water and oxygen inside the cells such hydrogen peroxide were accumulated in the kidney cells leading to great cellular injuries **[18].** Such decrease in SOD and CAT activities were also reported by **[43].** Meanwhile, results of this study showed decreased activities of GR in rats administered with deltamethrin however, SeNPs intervention mitigate this effect. The decrease in the GR activity in kidneys of rats exposed to deltamethrin may be due to changes in the structure of the enzyme caused by such pesticide. These findings were supported by **[18,44].**

In the meantime, results in this study implied increased levels of lipid peroxidation, LPO and nitric oxide, NO in rats treated with deltamethrin. On the other hand, SeNPs exert their protective effect to reduce such levels. The observed increase in LPO levels leads to the initiation of peroxidation cascade reactions of the unsaturated fatty acids in the cell membranes. This lipid peroxidation eventually leads to loss of the membrane structure and consequently its function **[45].** The increase in LPO and generation of reactive oxygen species, ROS eventually stand for reduction in cell viability. Hence, the oxidative stress developed by deltamethrin administration resulted in elevated LPO levels in kidney tissues. This increase in LPO was previously reported in kidneys exposed to deltamethrin **[18].** Nitric oxide, a free radical molecule produced by many cells endogenously, participate in many physiological mechanisms including neurotransmission, regulation of vasomotor tone and immune system functions **[46].** However, investigators had demonstrated that endogenously generated nitric oxide initiate cytotoxic reactions and can act as a potent oxidant that initiate biochemical pathways associated with cellular toxicity **[46].** In this study, the elevated values of NO in both tissue homogenates and urine of rats treated with deltamethrin came in accordance to such increased peroxidation reactions which were formally mentioned indicating cellular toxicity, which was mitigated by SeNPs upon their intervention via exerting their antioxidant properties.

Deltamethrin accumulation can ultimately lead to nephro-toxicity **[47]**. Such nephro toxicity is the main cause of kidney dysfunction. Kidney function disorders are manifested by the accumulation of toxic substances in the blood that nephrons should normally eliminate from the body **[24].** Organ functionality is closely linked to the efficacy of antioxidant defense mechanisms. Results in this study implied an increase in the levels of urea and creatinine biomarkers in deltamethrin treated rats while, reduction in the levels of such biomarkers was observed in SeNPs treated rats These results were in accordance with those described by **[15,48]** who mentioned that the increased urea levels are attributed to the increased protein catabolism to urea. High Creatinine level indicates impairment of renal function and it reflects a decline in glomerular filtration rate which confer an index for the general evaluation of the renal damage severity developed due to deltamethrin exposure **[24]**. The oxidative stress which is the imbalance between the ROS and the antioxidants can damage the kidney cell constituents including DNA, lipids and proteins. This would lead to a change in the cell's metabolism and would eventually affect the gene expression and the posttranslational processing of proteins thereby enhance kidney cells dysfunctions **[15]**. On the other hand, the antioxidant defense system is spread not only inside the cells but also in the extracellular environments to confer complete scanned protection mechanism which would provide better environment to the cell to act in a proper way, such role that was seen to SeNPs to achieve **[49].** These suggestions might elucidate the protective role that SeNPs exert on kidney cells to function in a proper way and this was revealed in the observed reduced urea and creatinine levels in groups treated with SeNPs. According to **[15]** the increased levels of creatinine and urea gives an indication to glomeruli and tubules deterioration owing to the damaging effect of deltamethrin on kidneys **[50].** Such deteriorations

were visualized histologically as indicated by the glomerular congestion, tubular degeneration, necrosis and swelling of tubules and vacuolization at different foci throughout the cortex in renal tissues of rats treated with deltamethrin. Such findings are in accordance with **[51,52]**, who found degenerative changes in renal tissues of adult rats exposed to methidathion and methyl parathion and the nephropathic changes observed in rats treated with deltamethrin**.**

Cell apoptosis significantly impacts endothelial function, glomerular filtration rate and may ultimately lead to renal failure **[53]**. Some studies suggest that DNA is easily targeted for apoptosis and as a result, the stability of the cellular genomic machinery is compromised by a wide range of toxicants leading to the generation of DNA lesions **[54].** In addition, the high ROS concentrations formally implied, contribute to the apoptotic cell death **[55]**. Accordingly, Bax, a pro-apoptotic protein in proximal tubular cells, plays a critical role in tubular cell injury, ischemic acute renal injury and ultimately cell death **[27]**. Hence, immuno- histological reports of this study revealed over expression of Bax in rat cells influenced with deltamethrin while, such expression was attenuated by the protective effect of SeNPs. This implies that the toxic effect of deltamethrin was encountered by the cells in a way that they were obliged to undergo programmed cell death or apoptosis thereby elevating renal functions and cellular toxicity pathways and decreasing the anti- oxidant defense mechanism in such cells leading to acute kidney injury **[3]**. However, upon SeNPs intervention, this clinical picture was improved confirming the protective role of SeNPs on kidney cells. These findings were also described by **[3,15,27]** concerning acute kidney injury, AKI, the effect of deltamethrin on renal cells and the beneficial role of SeNPs on such cells respectively.

Conclusion

SeNPs exhibit protective role towards renal cells that were influenced with deltamethrin insecticide in a way that they not only improved kidney function and the anti-oxidant machinery of the cells, but also decrease the markers of cellular toxicity and Bax expression thereby protecting the cells from undergoing apoptosis. Structurally, they were capable to improve the histological architecture of the cells. Hence, SeNPs were recommended to be involved in the diet of individuals who are suspected to be exposed to deltamethrin as a prophylactic action to prevent acute kidney injuries after further studies concerning their metabolic, accumulation and excretory concerns.

Ethical issues declarations:

This work was not concerned with any clinical trials. An ethical approval was obtained from the scientific research ethical committee of the General Organization of Teaching Hospitals and Institutes (GOTHI, Egypt) with registered approval number: IME00088/2024.

Declaration of interest's statement:
The authors declare no conflict of interests.

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