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Selenium Nanoparticles Ameliorate Apoptotic Pathways and DNA Neural Damage in Deltamethrin-Treated Rats

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Abstract

Our aim is to look into selenium nanoparticles (SeNPs) potency in mitigating DNA and cellular damages that lead to cell apoptosis in brains of rats treated with deltamethrin. Four groups of adult Wister albino rats were orally adminstered for four successive weeks, a control group of corn oil feeding, other groups of SeNPs, deltamethrin and SeNPs with associated doses of deltamethrin. In SeNPs treated rats, histological studies confirmed an improvement in neural tissue architecture associated with an increase in the relative brain weight index. Also, antioxidant enzymes estimation revealed an increase in the activities of catalase, superoxide dismutase and glutathione reductase and a cut down in lipid peroxidation and nitric oxide levels. Meanwhile, Immunohistological studies indicated an increased expression of Caspase 3 in tissues treated with deltamethrin however, such expression was mitigated upon SeNPs treatment which was visually confirmed by evaluating the comet assay patterns of such cells which implied decreased DNA damages. In conclusion, deltamethrin insecticide exhibited sever toxic influences on brain tissues regarding their architecture, their cellular structures and functions which would eventually directed them to apoptotic pathways. However, SeNPs may provide protective actions that could mitigate such influences and strengthen the neural potency to encounter such neural damage.

Keywords: Brain DNA damage, Brain histology, Caspase 3 in brains, Neural apoptosis, Selenium nanoparticles, Comet assay in brain tissues.

Introduction

Currently used pesticides are capable of disturbing different organs of vital functions in the human body systems as in the reproductive, respiratory and nervous systems [1]. Their capability to induce such disorders may occur via several mechanisms the most significant of which are either chronic inflammations, prominent oxidative stress or irreversible mitochondrial dysfunctions and bargained cell death [2]. Deltamethrin as a synthetic pyrethroid insecticide, is considered to be of severe toxicity [3].Owing to its hazardous effects to the target organisms, World Health Organization (WHO) adopted it as an artificial pyrethroid of the second type which can be counted on as an insecticide for house- hold, agriculture and public health concerns [4]. Since then, deltamethrin was extensively used for controlling vector disease insects via paralyzing their nervous system [5]. However, its toxicity on non-target subjects was reported [3]. Being lipophilic in nature, deltamethrin can penetrate the brain cells in trace quantities that are could be harmful[6]. The main adverse effect manifested upon deltamethrin exposure is that neurodegenerative disorders progression that could end up to nerve impulse inhibition by causing vital changes in the kinetics of the voltage-sensitive sodium channel and in the ligand-gated ion channels (GABA receptors, nicotinic acetylcholine receptors and glutamate receptors) as well [7]. Deltamethrin acts to bind to GABA-gated chloride channels causing their inhibition [8] which turn up the risk of neurodegenerative diseases [9]. In rats, deltamethrin brain toxicity was demonstrated through the inhibition of acetyl cholinesterase activity [10]. Furthermore, Deltamethrin was brought up to cause oxidative stress and to give in reactive oxygen species (ROS) inside the body [7].

Meanwhile, SeNPs are capable to confer protective and therapeutic effect to cells and tissues [11,12]. Owing to their insignificant toxicity and their higher bioavailability compared to their mates of the organic and inorganic forms [13], they were regarded as important agents for cellular protection

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regimens. One of their popular biomedical applications is their effect on mitigating the oxidative stress [14]. In addition, their role in immuno-stimulation and other various physiological functions was recently reported [11, 15]. In mice, SeNPs were capable to decrease the reactive oxygen species, the variations of bone marrow chromosomes and the DNA damage [16]. SeNPs could regulate various functions of brains metabolism relying on their selenoproteins activities [17]. SeNPs can deplet the accumulation of amyloid β plaque by turning down the development of ROS [18]. SeNPs showed to cut down the expression of mRNA of pro-inflammatory cytokines encompassing nitric oxide synthase which is one marker of oxidative stress in animal and human tissues [19]. Accordingly, this investigation aimed at highlighting SeNPs protective effect in restoring DNA and cellular damages in rat brains exposed to deltamethrin.

Material and Methods

Albino western rats 9-13 weeks age were selected from the available strain in the Research Institute of Medical Entomology. The study procedures were conducted following the animal care standardizations declared by Egyptian rules and National Institutes of Health guidelines and was ethically approved by the scientific committee of General Organization of teaching hospitals and institutes. Ethical approval number: IME00062).

Materials

Used chemicals

Deltamethrin powder (98%), Al-nasr Company for Chemicals. Sodium selenite., Ascorbic acid.

Selenium nanoparticles preparation

SeNPs were prepared following the simple precipitation method [20]. SeNPs unique absorption bands portrayed by UV-visible spectrophotometer confirmed their syntheses [21].

Experimental methods

The study regarded a total number of 32 selected rats which were set into four categories, eight rats/group, and treatments last for four successive weeks:

1- The control group fed on corn oil.
2- Group I: rats were orally administered with 27 mg/Kg b.w. deltamethrin corresponding to 1/5 LD_{50} referring to the LD_{50} value of deltamethrin solved in corn oil, [22].
3- Group II: SeNPs were orally administered (0.5 mg/ kg b.w.) [23].
4- Group III: rats were orally administered with deltamethrin with SeNPs with the same addressed doses.

Post experimental oral administrations, rats were sacrificed and their brains were removed and weighed, part of them were preserved in 10% formalin to be included in the histological concerns. The other part was kept in phosphate buffer solution to be homogenized. Animals' weights were estimated before and after treatments and sacrifice.

Estimation of brain indices

Relative brain weights were computerized referring to the total body weights by substitution in the equation: brain weight/ body weight X 100 [14].

Preparation of brain homogenates

Brains parts which were preserved in cold phosphate buffer solution were homogenized in PBS (pH 7.4). The homogenates were subjected to cool centrifugation at 5 C^o for quarter of an hour. Supernatants were preserved to be involved in the biochemical aspects [14].

Determination of antioxidant enzymes

The activities of Superoxide dismutase (SOD) catalase (CAT) and glutathione reductase (GR) were assessed in brain homogenates following the instruction manual of Bio-daignostics, Egypt, kit.

Oxidative stress status

The levels of lipid peroxidase enzyme along with nitric oxide were measured in brain tissue homogenates as indicators of brains cellular damage following the instruction manual of Bio-diagnostics, Egypt, kit for both tests.

Histological Studies

Histological sections were prepared and examined following the method described by Mohamed and Hussein [24].

Immunohistochemistry

Immunohistochemical studies were conducted following Figueira *et al.,* [25].

Single cell electrophoresis (Comet assay)

Alkaline comet assay was managed following the method brought up in a previous publication [26].

Statistics

Statistical Package for Social Science (SPSS) version 21 (SPSS Inc., U.S.A.). Outputs were portrayed in forms previously published by Ragheb *et al.* [14].

Results

Deltamethrin treated group showed reduction in brain weights compared to the control rat set (Table1). On the other hand, such weights were restored in deltamethrin and SeNPs exposed group as those in the control set (Table1).

Meanwhile, the average activities of the SOD, CAT and GR were turned down in deltamethrin

administered set as demonstrated in table 2. Meanwhile, the average activities of such enzymes were significantly restored in rats where SeNPs were administered.

On the other hand, peroxidation of lipids and levels of nitric oxides showed an observed rise in tissue homogenates of rats treated with deltamethrin (Table 3). Meanwhile, the average levels of such markers were significantly decreased in rats where SeNPs were administered alone or in combination with deltamethrin.

Histological investigations of the cerebrum revealed normal astrocytes with granules and normal pyramidal layer of pyramidal cells with dark stained cytoplasm and normal blood vessels (Fig. 1A&B). In rats treated with deltamethrin neural histopathological investigations showed vasodilatation, glial cell degeneration with deep staining and shrunk nuclei, neuronal degeneration(pyknosis), distorted granular cells with deep stained shrunken nuclei and cytoplasm and neurophil vacuolization (Fig. 1C). However, such histopathological pattern was improved upon SeNPs intervention (Fig. 1D).

Meanwhile, immunohistochemical investigations showed great Caspase 3 gene expressional discriminations in neural tissues among different experimental groups. Caspase 3 expression was turned up in neural tissues treated with deltamethrin (Fig. 2C) while, their expression was suppressed with SeNPs treatment (Fig. 2Band D).

Comet assay revealed DNA damages in neural cells exposed to deltamethrin (Fig. 3C) in contrast to control group. Indeed, SeNPs mitigate such damages (Fig. 3D) as it was confirmed by the discriminations in the comet parameters as tail length, DNA damage percent , percent of tail DNA and percent of DNA in the head.

Discussion

Deltamethrin is capable of passing the brain barriers thereby it could exert its effect by disrupting the central nervous system [27]. In doing so, it affects neurons of non-target subjects which are the managing centres that receive and send sensory inputs and outputs from and to the surrounding medium thereby affecting their vital activities[28]. In the mean time, pyrethroids usage causes various hazardous [28] that could lead to neuro-toxic imbalance induction starting with inflammations passing through oxidative stresses and mitochondrial dysfunctions and ending with DNA damages and cell deaths [1,29]. Evaluation of brain weight changes upon reporting body weight differences could help in using brain-to-body weight index to evaluate treatment effects in toxicological studies [30]. In this concern, results implied significant decrease in the total body weights, average brain weights and average brain weight indices in rat group orally administered with deltamethrin compared to the other experimental groups. However, SeNPs exhibit protective effect towards such decreasing weights. These results are in accordance with recent studies who reported the severe effect of deltamethrin oral injection in reducing body weights and the SeNPs protective effect confered [31,14,30]. One elucidation of such manifested decreased brain weight indices in deltamethrin treated groups is the developing oxidative stress. Oxidative stress is the master key of pesticide toxicity where a state of an uneven rates of developed free radicals and the available antioxidant defence potency is generated[30]. Oxidative stress are expecting to be directed to brains owing to their high capacity of consuming oxygen and many declarations were published for that concern [32, 33, 34]. At present, this work brought up SOD, CAT and GR reduced activities in rats that were orally administered with deltamethrin in contrast to the control set. Nevertheless, SeNPs exhibited protective potency towards such decreasing activities. Substantially, in critical oxidative challenges as in pesticide intoxications [35], nature antioxidants body machineries are exhausted in neutralizing vulnerable subjects and free radicals which are produced via pyrethroids metabolism [36]. Many studies have reported the severe effect of deltamethrin of being capable of reducing the anti oxidative actions of SOD, CAT, and GR in rat brain tissues [1, 10, 37]. In this context Kahtani [38] showed that increased activity of SOD, CAT, and GR enzymes of groups treated with SeNPs could walk through the antioxidant role of SeNPs. The improvement may be due to the formation of seleno proteins which are capable of improving the antioxidant potency of the brain, such elucidation is almost in accordance with the results of this study. Furthermore, results in this study showed significant elevated levels of lipid peroxidation and nitric oxide among groups that were treated with deltamethrin in contrast to the control group. These results are in the line with many publications that described the effect of deltamethrin in increasing nitric oxide and lipid peroxidation [1, 35, 32] However, SeNPs exhibited protective potency towards such increasing levels which was also described by Yuan *et al.* [39], and others [40,41]. They indicated that SeNPs exhibited neuro-protective potency which they exerted on the functional properties of brain cells where, they act on their survival by managing their antioxidant systems thereby conferring adequate cellular metabolism and abolishing inflammatory reactions. In addition to the role of SeNPs as an essential component of the antioxidant system in the brain, studies have demonstrated that SeNPs can attenuate oxidative

stress in the brain through monitoring the gates of calcium channels and the biogenesis of mitochondrial concerns. The real hazardous effects of free radicals accumulations could lead to almost macromolecules damages including critical cellular compartments like proteins, lipids, and nucleic acids which is considered the causative effect of many neurodegenerative manifestations [42]. Generally and as formerly mentioned, pesticides exert their toxic effects via generating a state of oxidative stress by extreme free radicals liberation and induction of peroxidation of lipids in tissues of vulnerable subjects [35,37] this could be elaborated by bringing up deltamethrin's molecules lipo-philic form by means of which they could penetrate the lipid bilayer of the cell membrane and exert their damaging effects on the cell integrity lifting behind a lot of oxidant free radicals that could randomly enter into various irreversible oxidation reactions which end up to undesirable chemical alterations of the cell biological processes [37]. The elevation of lipid peroxidase and nitric oxide concentrations observed in this study, pointed out that deltamethrin causes brain cells damage owing to extreme free radicals liberation and generation of oxidative stresses which have the lion share in the aetiology of brain injuries[43, 37]. Indeed, accumulation of deltamethrin in brains turn up the ROS production and edging out the antioxidant tools [35]. Even, lipid peroxides that do accumulate in brain cells out of lipid peroxidation are so harmful to their viability. On the other hand, SeNPs with their antioxidant properties could augment the seleno proteins which support cells endogenous anti-oxidant systems [30]. What made SeNPs fit for their role in neuro-protection, is their capability to attenuate free radicals development exploiting their antioxidant potency through preventing lipid peroxidation and scavenging undesirable free radicals. They also act to inhibit oxidative stresses and maintain the integrity and function of neural cells [38]. Studies confirming the neuro-protective properties of SeNPs in various neurodegenerative diseases confirmed the mechanisms of the neuro protective action of SeNPs as an effective neuro protector that could easily penetrate the blood brain barriers [44]. Histological investigations in the current study showed marked improvement of SeNPs treated groups compared to the deltamethrin treated groups. Where, deltamethrin exposure induced severe histological manifestations in the hippocampus observed as spongi-form or vacuolizations, pyknotic changes and granular cell layer thickness reduction of astrocytes. such histopathological findings were also described by Ali *et al.*, [37] who declared that oral administrations of deltamethrin resulted in neuronal degenerations with vacuolizations, glial cells degenerations and necrosis. While, SeNPs treated groups showed mitigation to such histopathological effects. These manifestations were also in agreement with Kahtani [38]. Furthermore, the developed oxidative stresses and the excess ROS formed due to deltamethrin consumption [39], led to imbalance in cellular physiologic functions which ends up to apoptosis [30]. Substantially, apoptosis and SOD activity in nervous tissue are close couples. Oxidative stresses elevation and antioxidants attenuation ends up to extrinsic apoptotic pathways[38]. Neuronal apoptotic pathways were elaborated by augmented pro-apoptotic markers and attenuated anti- apoptotic markers [30]. However, interventions of nanostructures that exhibit therapeutic concerns could do away with neuronal oxidative stresses, neuro inflammation, and neuronal apoptosis as well [15]. Apoptosis or programmed cell death like any other cellular imbalance state, could be triggered by toxins, oxidative stress, and DNA damage [45]. The mitochondrial (intrinsic) pathway and death receptor (extrinsic) pathway are the two main signaling pathways inducing apoptosis. Both pathways eventually merge in the terminal portion of the so-called caspase cascade which act to activate caspase-3 in the final step thereby triggering activation of cell content proteolysis, cytoskeleton collapse and eventually lead to DNA fragmentation [45]. Therefore, caspase-3 is considered a universal indicator of an apoptotic cell [45]. Pyrethroids can trigger apoptosis through ROS and cytotoxins [1, 44]. Meanwhile and being toxic to neuronal cells, deltamethrin could also trigger apoptosis in the striatum, cerebral cortex and in the hippocampus as well [10]. In a study by Gasmi *et al.*, [6] exposure to deltamethrin resulted in higher caspase-3, followed by apoptosis, which confirmed mitochondrial damage (swelling and permeability). In this study; immuno histological investigations revealed over expression of caspase3 in neural tissues of rats treated with deltamethrin however administration of SeNPs greatly ameliorate this induction. Such results come in the line with data reported by Galal *et al.*, [35] and Mohammadi *et al.*, [1] who described that the accumulation of deltamethrin in body systems increases ROS production leading to oxidative stress and apoptotic cell death. Results of this study were also in harmony with that of Ibrahim *et al.*, [46] and Ebokaiwe *et al.*, [40] who studied the effect of SeNPs on neural cells. They showed that SeNPs could completely inhibit the activation of caspase-3, -8, and -9 and consequently, suppress apoptosis. Additionally, Hossain and Richardson [47] reported that exposure to the deltamethrin caused apoptosis via increased caspase-3 activity as it was demonstrated by the intrinsic pathway, caspase-9 is activated by cytochrome c from the mitochondria into the cytosol then, caspase-9 could activate caspase-3 as the final effector of apoptosis. Ibrahim *et al.* [46] also declared that the increase in the number of stained neurons of caspase-3 reaction

indicated a rise in the number of cells who show positive reactions to caspase-3. The immunohistochemical results also revealed that SeNPs reduced the area percentage of caspase-3 reaction in the group exposed to deltamethrin and SeNPs. SeNPs are able to cross the blood–brain barrier, accumulate in the brain and prevent the development of apoptosis in cells owing to the uniqueness of such nanoparticles properties mediated by their small in size, high surface area, having surface charge, having surface chemistry, solubility and multi-functionality. The mechanisms of the protective action of SeNPs involved the processes of restoration of calcium homeostasis, inhibition of mitochondrial and endoplasmic reticulum stress pathways which ultimately lead to inactivation of caspase-3 and inhibition of apoptosis [41].

Indeed, comet assay confer valuable data that could assess various forms of damages and repairs in DNA molecules which could be beneficial in the genetic toxicology fields [37]. In this study, exposure to deltamethrin lead to significantly marked DNA damage in brain rat tissues; as evidenced by significant increase in the mean values of comet tail length, tail DNA% and tail moment among the deltamethrin, groups .This discrepancy might be explained by the fact that brain tissues are of lipophilic nature which tend to attract deltamethrin which affect their nature rendering them in great challenge with ROS which lead eventually to tissue damages [44]. Mustafa *et al.,* [45] also found that chronic exposure to deltamethrin cause significant oxidative damage in rat brain, which is associated with marked disturbance in antioxidant defense system in addition to genotoxicity. The possible mechanism of deltamethrin genotoxicity is either due to its reaction with DNA or by the generation of ROS, nitric oxide and enhancement of lipid peroxidation which end up to cease cellular respiration causing DNA damages and induction of DNA breaks [28,37]. The oxidative stress induced by deltamethrin causes depletion of mitochondrial energy and the induction of radical mediated injury through the extracellular release of superoxide ions which are cytotoxic [1]. In the meantime, Yuan *et al.,* [39] showed that SeNPs exhibit high antioxidant properties and was able to enhance the seleno proteins-based endogenous antioxidant system.

Conclusion

In brief, deltamethrin is a potential neuro-toxic pesticide that if swallowed orally by non-target subjects could induce brain tissues deteriorations, increase in cellular damage enzymes activities, reduce the anti-oxidant enzymes activities, increase cellular damage, over express Caspase 3 enzyme and cause cellular and molecular neural damages which was visualized as DNA comets. However, SeNPs exhibit potent, protective and effective antioxidant potency which ameliorates the adverse effects triggered by deltamethrin.

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Declaration of Conflict of Interest

None

TABLE 1. Average of relative weights of brains

Groups	Average body weights (g) ± SE	Average brain weights(g) ± SE	Average of relative brain weight index ± SE
Control	221±0.47	1.4±.0.047	0.63±.0.0047
SeNPs	230±0.47**	1.5±.0.047**	0.65±.0.0047**
Deltamethrin	158±0.39**	1.2±.0.047**	0.615±.0.00047**
Deltamethrin + SeNPs	212±0.35**	1.35±.0.04**	0.627±.0.00047**

Mean are ± SE, ** is highly significant= P< 0.001, n=8

TABLE 2. Average activities of anti-oxidant enzymes

Groups	Average levels of SoD (U/ml tissue) ± SE	Average levels of CAT (U/g)± SE	Average levels of GR (mg/g tissue) ± SE
Control	1400±47.1	0.58±0.00471	2.95±0.0043
SeNPs	1440±4.7**	0.69±0.00471**	3.53±0.0047**
Deltamethrin	399±0.39**	0.18±0.00471**	1.7±0.00471**
Deltamethrin + SeNPs	602±0.471**	0.41±0.00471**	2.2±0.0471**

Means are ± SE, ** is highly significant= P< 0.001, n=8

TABLE 3. Cellular toxicity markers

Groups	Average activities of lipid peroxidase (U/ml tissue) ± SE	Average levels of nitric oxide (U/g) ± SE
Control	32±0.47	24±0.471
SeNPs	17±0.47**	21±0.471**
Deltamethrin	151±1.196**	62±0.471**
Deltamethrin + SeNPs	75±0.471**	31±0.471**

Means are ± SE, ** is highly significant= P< 0.001, n=8

TABLE 4. Scores of histological changes in brain tissues

Organ	Histopathological findings	Control	SeNPs treated group	Deltamethrin treated group	SeNPs + deltamethrin treated group
Brain	Vacuolar degeneration of neurons	0	0	3	2
	Neuronal cell degeneration (pyknosis)	0	0	3	1
	Granular cells distortion	0	0	3	2

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

TABLE 5. Scores of immune- histological staining in brain tissues

Organ	Immunohistopathological findings	Control	SeNPs	Deltamethrin	SeNPs + deltamethrin
Brain	Intensity of neural staining	Moderate	Weak	Deep	Moderate
	Score	2	1	3	2

Scores evaluation; 4;very deep, 3; deep, 2; moderate, 1; week, 0; negative

TABLE 6. Comet parameters of neural cells

Comet parameters	Control	SeNPs	Deltamethrin	Deltamethrin + SeNPs
Comet length(um) ± SE	30.96±0.35	52.2±0.47**	32.04±0.009**	29.88±0.004**
Head diameter (um) ± SE	30.96±0.035	52.2±0.047**	18.72±0.47**	23.76±0.087**
% DNA in head	95.86±0.074	99.64±0.0086**	47.27±0.139**	87.02±0.161**
Tail length (um) ± SE	0±0.00	0±0.00**	13.32±0.066**	6.12±0.0047**
%of DNA in tail	0.414±0.004	0.354±0.0087**	52.72±0.0047**	12.97±0.0076**
Tail moment (um) ± SE	0±0.00	0±0.00**	7.023±0.0047**	0.793±0.0047**

Means are ± SE, ** is highly significant= P< 0.001, n=10

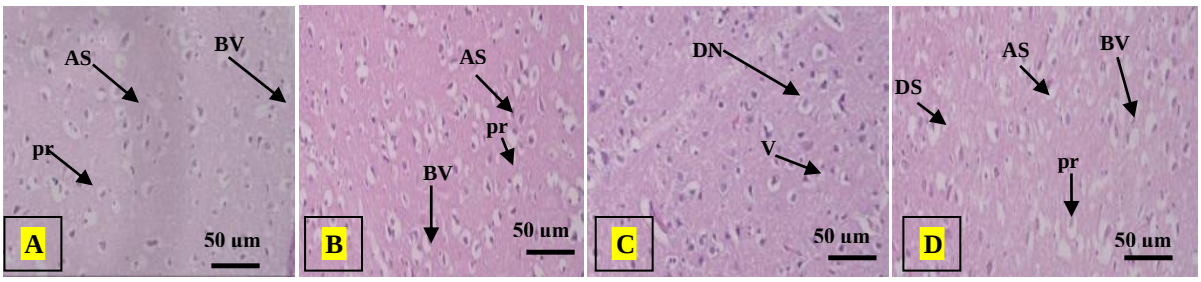

Fig. 1. Photomicrograph (H&E X40) in brains of rats demonstrating ; A: control group with astrocytes (granular cells) (AS) (astrocyte), pyramidal cells (pr) with vesicular nuclei and normal blood vessels (BV).B: nanoselenium treated group with the same control findings, C: deltamethrin treated group showing vacuolization (V), distorted granular cells with deep stained shrunken nuclei and cytoplasm (DS) and degenerated neurons (DN) and D: deltamethrin and nanoselenium treated groups which showed improved histological pattern (scale bar 50 µm).

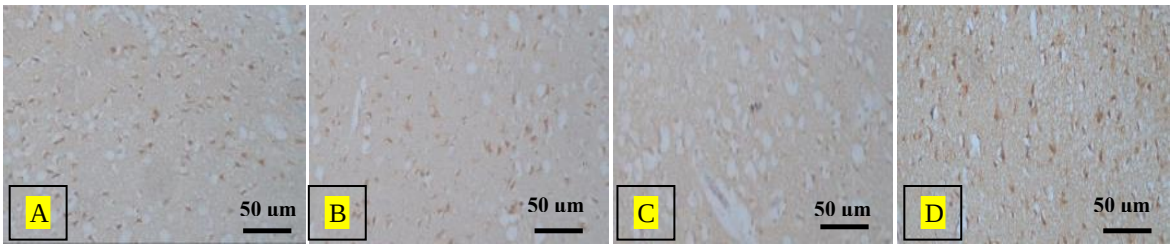

Fig. 2. demonstrates brain cells that were immune-reactive positive to the Caspase 3 for all groups where, Fig. 2A showed normal neural tissues that exhibit normal expression of Caspase 3 in the control group and Fig. 2B had the lowest content of Caspase 3 in SeNPs treated groups. While, in deltamethrin treated group (Fig. 2 C) the number of Caspase-positive neural cells was markedly increased in contrast to those for groups A&B. On the other hand, SeNPs and deltamethrin treated rats showed fewer positive nuclei for Caspase 3 in the neural cells (Fig. 2D) in contrast to those exposed to deltamethrin alone (Fig. 2C) (scale bar 50 µm).

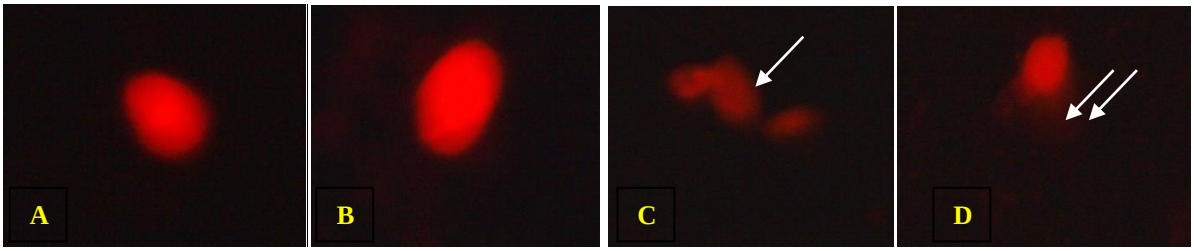

Fig. 3. DNA comet assay on neural cells. (A) is the control group where the neural nuclei are undamaged and are almost normal condensed type nuclei, (B) is nanoselenium treated group where neural nuclei are more condensed compared to control group nuclei, (C) is deltamethrin treated group where damaged cells with abnormal tailed nuclei(white arrow) are shown and (D) is deltamethrin and nanoselenium treated group where the abnormal tail group are much shorter compared to group (C) that were treated with deltamethrin only (double arrow short tail).

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جزيئات السيلينيوم النانويه تحد من مسارات الإستماته الخلويه و تلف الأحماض النوويه لخلايا المخ فى الجرذان المعالجه بالدلتامثرين

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الملخص

تعنى هذه الدراسة إلى الوقوف على الفاعلية المضاده للإستماته الخلويه للجسيمات النانوية للسيلينيوم للحد و التقليل من التأثير الخلوى المميت على خلايا المخ الناتج عن التعرض للجرعات التحت مميتة لمبيد الحشرات الدلتامثرين، وهو من أشهر المبيدات المستخدمة للمكافحة في قطاعات الصحة العامة والزراعة في مصر.و قد تم فى هذا البحث بانتخاب الجرذان المعمليه الغربيه البالغه و التى تتروح أعمارهم من 9 إلى 13 أسبوع حيث تم تقسيمهم إلى أربع مجموعات كل مجموعه تضم 8 جرزان . مجموعه منهم مثلت القسم الضابط للتجارب والتى لم تتعرض لاى معامله و المجموعات الاخرى تم تعريض الجرذان بهم إما لجزيئات السلينيوم النانويه فقط أو للدلتامثرين فقط اوللدلتامثرين مصحوبا بجزيئات السلينيوم النانويه عن طريق البلع بالفم ولفترات تعريض لمدة أربعه أسابيع متتاليه. بعد التعريض للمده المذكوره تم سحب عينات دم منهم و ذبحهم و استخراج الكتله المخيه من الجمجمه و حفظها . و قد تم فصل عينات الدم و استخراج السيرم الذى تم عمل اختبارات الكيمياء الحيويه عليه. إما بالنسبه للكتله المخيه فقد تم التعامل معها حسب الأبحاث السباقه المنشوره فى هذا الصدد و تحضير شرائح نسيجيه منها لفحصها و عمل شرائح نسيجيه مناعيه لتحديد كمية انزيم الكاسبيز3 و عمل اختبار الكوميت للوقوف على نسبة التلف فى الجزيئات الوراثيه بالخلايا و قد تم مقارنة جميع النتائج بالقسم الضابط لمعرفة تأثير كل هذه العوامل على الخلايا محل الدراسه. وقد أوضحت النتائج قدرة وفاعلية جزيئات السيلينيوم النانويه على حماية خلايا المخ من الأخطار الناجمه عن التعرض للمبيد الحشرى الدلتامثرين عن طريق رفع نشاط انزيمات مضادات الأكسده و خفض معدل نشاط انزيمات التسمم الخلوى و قد تأكدت هذه النتائج عن طريق فصح لمقاطع النسيج المخى لكل مجموعه و عمل اختبارت تلف الحمض النووى.

الكلمات الدالة: تلف الأحماض النوويه بالمخ، النسيج المخى، كسباس 3فى المخ، الموت المبرمج فى خلايا المخ، جزيئات السلسنيوم النانونيه، تقنية الكوميت فى أنسجة المخ.