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Research Article:

Detecting the Effect of Melatonin Against Deltamethrin-Induced Neurotoxicity Using Adult Male Rats Model

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Abstract

Background and Objectives: Deltamethrin (Delta), a widely used insecticide, is associated with neurotoxic effects primarily due to its ability to induce oxidative stress. To date, no specific antidote is available for deltamethrin poisoning. This study aimed to investigate the potential protective effects of melatonin, a potent antioxidant, against deltamethrin-induced neurotoxicity. **Methods:** The median lethal dose (LD_{50}) of deltamethrin was determined to be 106.6 mg/kg (p.o.) in adult male rats. Twenty rats were divided into four groups (n = 5 per group): Group A received deltamethrin alone (75 mg/kg, p.o.); Group B was pretreated with melatonin (12.5 mg/kg, i.p.) 15 minutes prior to deltamethrin administration; Groups C and D received melatonin alone and distilled water, respectively. Neurotoxic signs, onset time, and toxicity scores were recorded, and antioxidant enzyme (glutathione peroxidase) levels were measured. **Results:** Rats treated with deltamethrin alone exhibited severe neurotoxic signs within 55 ± 0.7 seconds, with a toxicity score of 24. Pretreatment with melatonin significantly delayed the onset of neurotoxicity (720 ± 0.2 seconds) and reduced the overall toxicity score to 4. This group also showed a marked decrease in the incidence of individual neurotoxic signs and a significant increase in serum glutathione peroxidase levels compared to the deltamethrin-only group. **Conclusion:** Melatonin demonstrated a protective effect against deltamethrin-induced neurotoxicity, likely due to its potent antioxidant properties. These findings suggest the potential use of melatonin as a therapeutic agent in managing insecticide-induced oxidative stress and neurotoxicity.

1. Introduction

The huge increase in demand for effective insecticides, whether for household, agricultural, or veterinary use, has led to an increase in the chances of poisoning in humans after prolonged exposure to these insecticides (1), this is confirmed by the detection of residues of some insecticidal pyrethroids in the urine of some pregnant women and children (2). Deltamethrin is a very effective insecticide. It belongs to the second type of synthetic pyrethroid pesticides, which is characterized by containing a cyanide group which increases the effectiveness of the insecticide by ten times. It works through its effect on the nervous system of insects by modulating sodium channels (1).

Melatonin (N-acetyl-5-methoxy tryptamine) is an endogenous neurohormone secreted by the pineal gland that regulates the biological clock (3). Melatonin attracts the attention of researchers because it has broad pharmacological effects such as antioxidant, anti-inflammatory, and anti-apoptotic (4-7). These pharmacological effects have confirmed the effectiveness of the melatonin molecule in detoxifying harmful reactions, thereby reducing molecular damage to cell contents such as (cell membrane, proteins, and nucleus) (8).

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Regarding the mechanism of melatonin as an antioxidant, it is either directly through its effect as a potent scavenger of free radicals of oxygen and nitrogen, including hydroxyl radical, hydrogen peroxide, singlet oxygen, nitric oxide, and peroxynitrite anion, or indirectly through stimulating the gene expression of antioxidant enzymes by activating the nuclear factor erythroid 2-related factor 2 (Nrf2) (5, 8, 9). The lipophilic nature of melatonin helps it achieve the effects mentioned above by crossing all cellular membranes and spreading rapidly to all cellular tissues (10).

Deltamethrin induces potent neurotoxicity which is linked to its ability to destroy antioxidant enzymes, leading to an imbalance between oxidants and antioxidants, followed by oxidative stress and the release of high concentrations of free radicals that attack cellular macromolecules such as the cell membrane, proteins, and nucleus, causing cellular damage (11). The question that arises is whether melatonin, based on what was mentioned above about its possession of anti-oxidative stress mechanisms, can reverse the neurotoxicity of deltamethrin caused by oxidative stress.

2. Materials and methods

2.1 Ethical considerations

All procedures were approved by the Committee for the Ethics on Animal Care and Experiments of the University Mosul/College of Veterinary Medicine (Approval No.UM.VET.2024.053).

2.2 Animals

This study used adult albino male rats that were raised in the animal house of the College of Veterinary Medicine/University of Mosul, and their weight was limited to between (195 and 280) grams, taking into account that the weights of the rats were similar in the experiment. The animals were raised in special laboratory conditions characterized by a photo period of 12 hours of light and 12 hours of darkness, and the laboratory temperature was 22 ± 2 °C. The rats were placed in plastic cages 41x24 x19.5 cm, an average of 5 rats in one cage, food and water were available ad libitum.

2.3 Determination of the median lethal dose (LD_{50}) of deltamethrin

The acute (24 hrs) median lethal dose (LD_{50}) of deltamethrin (Deltarin, 2.5%, Emulsifiable - Concentrate, Vapco-Jordan) was determined in the adult male rats by the up-and-down method (12). Six adult male rats were used in this experiment, and an initial dose of deltamethrin (150 mg/kg, p.o.) was given. This dose was arrived at based on preliminary experiments. After 24 hours, the result was read: the animal remained alive, symbolized by O, or its death, symbolized by X, in addition to recording the signs of toxicosis and the time of their appearance. This method was repeated up or down after the change occurred for three adult male rats.

2.4 Preparing doses of deltamethrin and melatonin

A deltamethrin dose (75 mg/kg, p.o.) was prepared using the original insecticide solution. Melatonin (10 mg/equivalent per capsule—Green Field Nutrition's Company -USA) dose (12.5 mg/kg, i.p.) was prepared by dissolving melatonin in a 1% vehicle solution (ethanol in physiological saline solution).

2.5 Effect of melatonin on deltamethrin-induced neurotoxicity

To examine the effect of melatonin against deltamethrin-induced neurotoxicity in adult male rats. Twenty adult male rats were divided into four groups (A, B, C, and D), with (5 rats/ group). The animals in group A (positive control) were dosed with deltamethrin alone (75 mg/kg, p.o.), which represents 70.3% of (LD_{50} 106.6 mg/kg, p.o.). The animals in group B were injected with melatonin (12.5 mg/kg, i.p.) 15 minutes before the deltamethrin dosing (75 mg/kg, p.o.). It is worth noting that the melatonin dose was chosen based on preliminary experiments. The animals in groups C and D (negative control) administered melatonin alone (12.5 mg/kg, i.p.) and distilled water (2 ml/kg, p.o.) respectively.

After completing the treatment of the adult male rats in groups (A, B, C, and D), they were transferred to the cages to be monitored individually by installing a color digital camera to record video and recording. After completing the 180 minutes of monitoring the animals, the video is transferred to the computer and displayed to observe the effect of melatonin on neurotoxicity induced by insecticide deltamethrin in relation to the severity of the signs of toxicosis, the time of their appearance, the time of death, percentages of occurrence of signs of toxicosis and a score of toxicity.

The toxicity score was calculated for each group by giving each percentage of the occurrence of signs of acute neurotoxicosis (convulsion, salivation, itching, licking, escape behavior, tremor, and restlessness) that appeared on the rats within 180 minutes in a score. These scores are summed up to obtain the toxicity score, which is as follows (13).

Table 1. Explains how to calculate the scores of toxicities in rats

Percentages of occurrence of signs of toxicosis %	Score of toxicity
1-25	1
26- 50	2
51-75	3
76-100	4

A value of 28 is considered the highest level of toxicosis for one group (when all signs of acute toxicities appear in all animals of the group), so the percentage of signs of toxicosis becomes 100% **Table 1**.

2.6 The effect of melatonin against deltamethrin-induced oxidative stress

After 24 hours of treatment in groups (A, B, C, and D) mentioned above, blood samples were collected from the vascular plexus of the eyes of adult male rats to obtain blood serum to measure the concentration of the antioxidant enzyme (glutathione peroxidase) and malondialdehyde by using a GPX KIT and MAD Kit respectively, according to the manufacturer's instructions (GPX, Elabscience-USA).

2.7 Statistical analysis

Frequency data were statistically analyzed using Fisher's exact probability test (14). Other data were subjected to analysis of variance (ANOVA) followed by the least significant difference test (15). The level of significance was at $p<0.05$.

3. Results

The acute (24 hrs) median lethal dose (LD_{50}) for deltamethrin in adult male rats was (106.6 mg/kg, p.o.), which showed signs of acute toxicosis within 45-300 seconds after dosing, including convulsion, salivation, itching, licking, escape behavior, tremor, restlessness, gasping, paralysis, and recumbency and then death **Table 2**.

Table 2. Determination of the median lethal dose (LD_{50}) of deltamethrin administered orally (p.o.) in adult male rats by the up-and-down method

Variable	Results
The extent of the doses used	125-150 = 25 mg/kg
Initial dose	150 mg/kg,
Last dose	125 mg/kg
Number of rats used	XXOXOX (6)
The extent of the increase or decrease in dose	25 mg/kg
Extent of latency to onset of poisoning	45-300 seconds
Signs of acute toxicosis	convulsion, salivation, itching, licking, escape behavior, tremor, restlessness, gasping, paralysis and recumbency and then death

X: The animal remains alive within 24 hours, while O: The animal dies within 24 hours. To detect the effect of melatonin on the neurotoxicity of the insecticide deltamethrin, the dose of the insecticide (75 mg/kg, p.o.) was chosen based on its (LD_{50}), which represents (70.3%) of the LD_{50} (106.6 mg/kg, p.o.), to use it in the interaction experiment between melatonin and deltamethrin **Table 2**.

Group A treated with the insecticide deltamethrin alone at a dose of (75 mg/kg, p.o.) showed signs of severe neurotoxicosis at a mean of (55 ± 0.7) seconds **Figure 1**. after treatment with insecticide, represented by convulsion, salivation, itching, licking, escape behavior, tremor, restlessness in percentages of occurrence of signs of toxicosis % (100, 100, 60, 100, 60, 40 and 100%), which led to raising the score of toxicities in this group to 24 **Table 3**. While injection of adult male rats in group B with melatonin (12.5 mg/kg, i.p.) 15 minutes before the administration of deltamethrin (75 mg/kg, p.o.) resulted in a significant prolongation of the time for the appearance of acute toxicosis signs to (720 ± 0.2) seconds compared to the group treated with deltamethrin alone (55 ± 0.7) seconds **Figure 1**.

In addition, it was accompanied by a significant decrease in the percentages of occurrence of signs of toxicosis such as convulsion, salivation, licking, and restlessness from 100, 100, 100 and 100 % in the group treated with deltamethrin alone to 20, 20, 0 and 20% in the group pre-treated with melatonin 15 minutes before the administration of deltamethrin **Table 3**.

It is important to mention that pre-treatment with melatonin also prevented the appearance of itching, licking, and escape behavior, so that the percentages of occurrence of these signs reached zero, and thus the score of toxicity in the animals group B was significantly reduced from 24 in the group treated with deltamethrin alone to 4 in group pre-treated with melatonin 15 minutes before the administration of deltamethrin **Table 3**. The animals in group C that were treated with melatonin alone (12.5 mg/kg, i.p) did not show any signs of acute toxicities, for this reason, it was not included in **Table 3**. Note: Group C (melatonin alone) and Group D (negative control - distilled water) were not included in Table 3 because the animals belonging to these groups did not show signs of toxicosis.

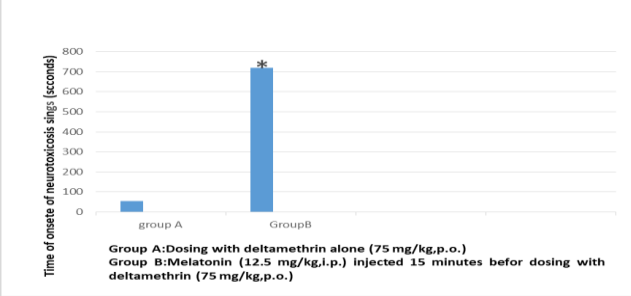

Figure 1. The effect of melatonin on the time to onset of signs of neurotoxicosis induced by deltamethrin. Values are mean ± S.E. of 5 rats/group.
* Significantly compared to the group treated with deltamethrin alone, level $p< 0.05$.

Table 3. Effect of melatonin (12.5 mg/kg i.p.) against deltamethrin (75 mg/kg o.p.) induced neurotoxicity in adult male rats

Signs of toxicosis	Groups			
	(Group A) n=5		(Group B) n=5	
	Dosing with deltamethrin alone		Melatonin was injected 15 minutes before dosing with deltamethrin.	
	Percentages of occurrence of signs of toxicosis %	Score of toxicity	Percentages of occurrence of signs of toxicosis %	Score of toxicity
Convulsion	100 (5/5)	4	20* (2/5)	1
Salivation	100 (5/5)	4	20* (2/5)	1
Itching	60 (3/5)	3	0 (0/5)	0
Licking	100 (5/5)	4	0* (0/5)	0
Escape behavior	60 (3/5)	3	0 (0/5)	0
Tremor	40 (2/5)	2	20 (1/5)	1
Restlessness	100 (5/5)	4	20* (1/5)	1
Total scores of toxicities	__	24	___	4*
Death within 24 hours	0	__	0	__

[a] Melatonin was injected 15 minutes before the administration of deltamethrin, each animal was monitored individually for 180 minutes after treatment using a video camera to record the time of appearance of signs of toxicosis, their severity, and death within 24 hours, percentages of occurrence of signs of toxicosis % and score of toxicity.
*The value differs significantly compared to the group treated with deltamethrin alone at a significant level of p< 0.05

Regarding the effect of melatonin against deltamethrin-induced oxidative stress, the group treated with deltamethrin alone at a dose of (75 mg/kg, p.o.) showed a significant decrease in the concentration of the enzyme glutathione peroxidase (antioxidant enzyme) to (538.4 ± 0.1) U/ml compared to the B, C and D groups (negative control) with values of (614.3 ± 0.6), (663 ± 0.1) and (620 ± 0.3) U/ml respectively. This significant decrease in the enzyme concentration in the group treated with deltamethrin alone confirms the occurrence of oxidative stress **Table 4**.

While pretreatment with melatonin, 15 minutes before dosing with deltamethrin, led to a significant increase in the concentration of the enzyme glutathione peroxidase to (614.3 ± 0.6) U/ml compared to the group treated with deltamethrin alone (538.4 ± 0.1) U/ml, this result proves that melatonin has antioxidant effects **Table 4**.

It is important to mention that the group treated with melatonin alone showed a significant increase in the concentration of the antioxidant enzyme glutathione peroxidase (663 ± 0.1) U/ml compared to the A, B, and D groups (538.4 ± 0.1), (614.3 ± 0.6), (620 ± 0.3) U/ml respectively, this result is a second confirmation that melatonin has powerful antioxidant effects Table 4. No significant differences were observed between groups A, B, C, and D) in the concentration of malondialdehyde **Table 4**.

Table 4. The effect of melatonin against deltamethrin-induced oxidative stress is based on changes in the concentration of antioxidant enzyme (glutathione peroxidase) and malondialdehyde in the serum of rats.

Groups		Glutathione peroxidase concentration (U/ml)	Malondialdehyde concentration (nmol/ml)
A	Administration of deltamethrin alone (positive control)	538.4 ± 0.1 abc	12.7 ± 0.1
B	Melatonin was injected 15 minutes before dosing with deltamethrin	614.3 ± 0.6*	9.8 ± 0.2
C	Melatonin injected alone	663 ± 0.1*a c	14.72 ± 0.3
D	Administration of distilled water alone (negative control)	620 ± 0.3*	14.95 ± 0.5

[a] Values represent the (mean ± standard error) for 5 animals/group. After 24 hours of treatment in groups (A, B, C, and D), blood samples were taken to measure the concentrations of glutathione peroxidase and malondialdehyde in the serum of the rats.
*The value differs significantly compared to the group treated with deltamethrin alone at a significant level of P< 0.05
a- The value differs significantly compared to the group injected with melatonin 15 minutes before dosing with deltamethrin at a significant level of P< 0.05.
b- The value differs significantly compared to the group injected with melatonin alone at a significant level of *p*< 0.05
c- The value differs significantly compared to the group administration of distilled water alone (negative control) at a significant level of *p*< 0.05.

4. Discussion

One of the worst toxic effects of the insecticide deltamethrin, which is widely used in household use, agricultural, and veterinary fields, is neurotoxicity which results from inhibition of the neurotransmitter (GABA), leading to hyperexcitability of the central nervous system (1) and it is also linked to the occurrence of oxidative stress (11). For this reason, melatonin was chosen in our current study as a powerful antioxidant and reactivator for neurotransmitter (GABA) (4 - 6). Based on these effects of melatonin, the question arises as to whether it can reverse the neurotoxicity induced by the insecticide deltamethrin.

The acute (24 hrs) median lethal dose (LD_{50}) of deltamethrin obtained in this study was (106.6 mg/kg, p.o.) in adult male rats, and thus it is close to the LD_{50} found by Frank and Kellner (16). In addition, the neurotoxic symptoms that appeared in the animals of the group treated with deltamethrin alone in the LD_{50} experiment included (convulsion, salivation, itching, licking, escape behavior, tremor, restlessness, gasping, paralysis, recumbency, and then death) were consistent with Symington et al., (2007) study (17) **Table 2**.

Among the symptoms of toxicity that appeared severely in the group treated with the deltamethrin alone was salivation, with an incidence of 100% (Table 3) can be attributed to the inhibition of the enzyme serum acetylcholinesterase (AChE), which leads to an increase in acetylcholine, which stimulates muscarinic receptors, and an increase in salivation, which is considered a characteristic sign of Type II pyrethroid poisoning (18).

Neurotoxic signs, including convulsions appearing in animals treated with deltamethrin alone, which reflect a hyperexcitation, may be due to the inhibition of the neurotransmitter GABA (gamma-aminobutyric acid), and this is confirmed by Manna et al., (2006) (19) findings a significant decrease in the concentration of the neurotransmitter GABA in the central nervous system from (1065 ± 88.00) ppm in the control group to (168 ± 24.46) ppm in the group treated with deltamethrin at a dose of (150 mg/kg) in the rats, this decrease in this neurotransmitter leads to strong stimulation of the nervous system (hyperexcitation) in the rats.

Pretreatment with melatonin at a dose of (12.5 mg/kg, i.p.) 15 minutes before dosing with deltamethrin (75 mg/kg, p.o.) led to a significant decrease in the percentage of convulsion occurring to 20% compared to the group treated with the insecticide alone (100%), this may be related to the ability of melatonin through positive activation of GABA receptors, which increases the influx of Cl− ions by binding to high-affinity benzodiazepine sites of GABA-A receptors (20), which in turn calms the rats. This interpretation confirms the success of our study in choosing melatonin against deltamethrin-induced neurotoxicity in adult male rats, based on the scientific references mentioned above (20), which proved that melatonin has an activating effect on GABA-A receptors, and thus melatonin will reverse the inhibitory effects of these receptors (GABA) by deltamethrin.

In addition, the effect of melatonin as an anticonvulsant may also be attributed to its stimulating effect on Adenosine triphosphate (ATP)-sensitive potassium (KATP) channels and efflux of potassium, which leads to hyperpolarization of the nerve potential, which results in inhibition of the influx of calcium, and this inhibits the release of excitatory neurotransmitters such as glutamate (excitatory) which leads to reduced neuroexcitation of the nervous system of rats (convulsions) (21, 22).

The rats in the group treated with deltamethrin alone showed escape behavior, with an incidence rate of 60% **Table 3**. This behavior can be attributed to the insecticide's anxiogenic effects (23), deltamethrin also stimulates nerves in the central nervous system, such as noradrenergic, dopaminergic, and cholinergic neurotransmission (24).

The group treated with deltamethrin alone recorded signs of nervousness such as tremors that may be due to modifications in the kinetics of Na+ channels, excitatory glutamate receptors, and nicotinic and acetylcholine receptors (25).

The apparent decrease in scores of toxicities, especially neurotoxic signs in the group pre-treated with melatonin, such as escape behavior Table 3, may be due to melatonin having anxiolytic effects (26), through facilitating the function of the GABA neurotransmitter (facilitates the inhibitory aminobutyric acid (GABA)-ergic neurotransmitter) function (27), as this neurotransmitter has inhibitory effects on the central nervous system.

Proudfoot (2005) (28) found that deltamethrin causes dermatitis, conjunctivitis, and rhinitis, and can develop in some cases into hypersensitivity reactions caused by the fact that deltamethrin is an allergen. This scientific reference can be relied upon to explain the appearance of

severe itching on adult male rats in the group treated with the insecticide alone, with an incidence rate of 60% (Table 3). While the group pre-treated with melatonin recorded a significant decrease in the percentage of itching occurrence to 0%, the reason for this may be attributed to melatonin having anti-inflammatory effects (4, 29).

The group treated with deltamethrin alone recorded a significant decrease in the level of the antioxidant enzyme glutathione peroxidase (PGX) in the serum of rats **Table 4**, this decrease may be due to deltamethrin destroying the antioxidant enzymes, leading to the accumulation of free radicals in tissues and the occurrence of oxidative stress (30).

On the other hand, this decrease in antioxidant enzyme glutathione peroxidase concentration may be related to the inhibitory effect of deltamethrin on the factor nuclear erythroid 2-related factor 2 (Nrf2), which is responsible for the gene expression of antioxidant enzymes (31), which results in a decrease in the concentration of this enzyme. Pretreatment with melatonin 15 minutes before dosing with deltamethrin led to a reversal of the inhibitory effect of deltamethrin on the factor (Nrf2) by activating this factor (32), which led to a significant increase in the concentration of the antioxidant enzyme (PGX) **Table 4**.

The appearance of neurotoxic signs in rats treated with deltamethrin alone in our current study can be linked to a decrease in the concentration of the antioxidant enzyme (PGX), because the function of this enzyme is to convert free radicals, including H_2O_2, into water (33), when this enzyme decreases, H_2O_2 will accumulate and promote the formation of OH, which is the most toxic molecule, leading to an increase in the oxidant load on the central nervous system and the occurrence of neurotoxicity (34).

It is worth noting that there was no depletion in the concentration of the enzyme glutathione peroxidase in the group pre-treated with melatonin compared to the group treated with deltamethrin alone. Because melatonin reduces the release of free radicals, it maintains the enzyme concentration in addition to stimulating the gene expression of antioxidant enzymes (8).

5. Conclusion

We conclude from our results the ability of melatonin to reverse deltamethrin neurotoxicity because it has potent antioxidant effects.

Conflicts of interest

The authors declare there is no conflict of interest.

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References

1. Panwar M, Usha G, Kumath M. Status epilepticus: An association with pyrethroid poisoning. *Indian Journal of Critical Care Medicine* 2013;17:119-20.
2. Hardt J, Angerer J. Biological monitoring of workers after the application of insecticidal 492 pyrethroids. *International archives of occupational and environmental health* 2003;76:492-498.
3. Reiter RJ, Rosales-Corral SA, Manchester LC, Tan DX. Peripheral reproductive organ health and melatonin: ready for prime time. *International Journal of Molecular Sciences* 2013;14:7231-72.
4. Mayo JC, Sainz RM, Tan DX, Hardeland R, Leon J, Rodriguez C, et al. Anti-inflammatory actions of melatonin and its metabolites, N1-acetyl-N2-formyl-5-methoxykynuramine (AFMK) and n1-acetyl-5-methoxykynuramine (AMK), in macrophages. *Journal of Neuroimmunology* 2005;165:139–49.
5. Tanabe M, Tamura H, Taketani T, Okada M, Lee L, Tamura I, et al. Melatonin protects the integrity of granulosa cells by reducing oxidative stress in nuclei, mitochondria, and plasma membranes in mice. *Journal of Reproduction and Development* 2015;61:35–41.
6. Remiao MH, Lucas CG, Domingues WB, Silveira T, Barther NN، Komninou ER, et al. Melatonin delivery by nanocapsules during in vitro bovine oocyte maturation decreased the reactive oxygen species of oocytes and embryos. *Reproductive Toxicology* 2016;63:70–81.
7. Hussein A, Ahmed M, Mustafa N. Biochemical and histological investigation of azathioprine and melatonin in rats. *Journal of the Hellenic Veterinary Medical Society* 2024;75(1):6779–6786.
8. Reiter RJ, Mayo JC, Tan DX, Sainz RM, Alatorre-Jimenez M, Qin L. Melatonin as an antioxidant: under promises but over delivers. *Journal of Pineal Research* 2016;61:253–278.

9. Reiter RJ, Tan DX, Galano A. Melatonin: exceeding expectations. *Physiology* 2014;29:325–333.
10. García JJ, Lopez-Pingarrón L, Almeida-Souza P, Tres A, Escudero P, Garcia Gil FA, Tan DX, Reiter RJ, Ramirez JM, Bernal-Perez M. Protective Effects of Melatonin in Reducing Oxidative Stress and in Preserving the Fluidity of Biological Membranes: A Review. *Journal of Pineal Research* 2014;56(3):225–237.
11. Li HY, Wu SY, Ma Q, Shi N. The pesticide deltamethrin increases free radical production and promotes nuclear translocation of the stress response transcription factor Nrf2 in rat brain. *Toxicology and Industrial Health* 2011;27:579–590.
12. Dixon WJ. Efficient analysis of experimental observations. *Annual Review of Pharmacology and Toxicology* 1980;20:441.
13. Al-Baggou BK, Mohammad FK. Antagonism of methomylinduced toxicosis by diphenhydramine in rats. *Environmental Toxicology and Pharmacology* 1999;7:119-125.
14. Runyon RP. Nonparametric Statistics. Addison-Wesley, Reading 1977;42.
15. Bruning JL, Kintz BL. Computational Handbook of Statistics. *Scott Foresman, Glenview* 1977:18.
16. Frank JP, Kellner TP. Deltamethrin Risk Characterization. Vol. 1, Health Assessment Section Medical Toxicology Branch, Edited by Department Pesticide Regulation California Environmental Protection Agency, USA. 2000.
17. Symington SB, Frisbie RK, Lu KD, Clark JM. Action of cismethrin and deltamethrin on functional attributes of isolated presynaptic nerve terminals from rat brain. *Pesticide Biochemistry and Physiology* 2007;87(2):172–181.
18. Abdel-Daim MM, Abd Eldaim MA, Mahmoud MM. Trigonella foenum-graecum protection against deltamethrin-induced toxic effects on haematological, biochemical, and oxidative stress parameters in rats. *Canadian Journal of Physiology and Pharmacology* 2014;92(8):679-685.
19. Manna SD, Bhattacharyya TK, Mandal S. Neuropharmacological effects of deltamethrin in rats. *Journal of Veterinary Science* 2006;7(2):133–136.
20. Hosseinzadeh A, Kamrava S, Moore B, Reiter R, Ghaznavi H, Kamali M. et al. Molecular Aspects of Melatonin Treatment in Tinnitus; a Review. *Current drug targets* 2019;20(11):1112-1128.
21. Hernández-Sánchez C, Basile AS, Fedorova I, Arima H, Stannard B, Fernandez AM, et al. Mice transgenically overexpressing sulfonylurea receptor 1 in forebrain resist seizure induction and excitotoxic neuron death. *Proceedings of the National Academy of Sciences* 2001;98:3549-3554.
22. Mohammadi F, Shakiba S, Mehrzadi S, Afshari K, Rahimnia AH, Dehpour AR. Anticonvulsant effect of melatonin through ATP-sensitive channels in mice. *Fundamental & clinical pharmacology* 2020;34(1):148-155.
23. Kalueff AV, Tuohimaa P. Experimental Modeling of Anxiety and Depression. *Acta Neurobiologiae Experimentalis* 2004;64(4):439–448.
24. Meng Li, Zhang TI, Yi QJ, YuMeng S, Shao ZZ, Ping Mi, ZeYang F, Xin Z, DongYan C, XiZeng F. Combined treatment of melatonin and sodium tanshinone IIA sulfonate reduced the neurological and cardiovascular toxicity induced by deltamethrin in zebrafish. *Chemosphere* 2020;243:125373.
25. Mani MV, Asha S, Sadiq AM. Pyrethroid Deltamethrin-Induced Developmental Neurodegenerative Cerebral Injury and Ameliorating Effect of Dietary Glycoside Naringin in Male Wistar Rats. *Biomedical Aging Pathology* 2020;4:1–8. doi: 10.1016/j.biomag.2013.11.001.
26. Golombek DA, Pevet P, Cardinali DP. Melatonin effects on behavior: possible mediation by the central GABAergic system. *Neuroscience & Biobehavioral Reviews* 1996;20:403–412.
27. Wan Q, Man HY, Liu F, Braunton J, Niznik HB, Pang SF, Brown GM, Wang YT. Differential modulation of GABAA receptor function by Mel1a and Mel1b receptors. *Nature Neuroscience* 1999;2:401–403.
28. Proudfoot AT. Poisoning due to pyrethrins. *Toxicological Reviews* 2005;24:107‐13.
29. Carloni S, Favrais G, Saliba E, Albertini MC, Chalon S, Longini M, Gressens P, Buonocore G, Balduini W. Melatonin modulates neonatal brain inflammation through endoplasmic reticulum stress, autophagy, and miR-34a/silent information regulator 1 pathway. *Journal of Pineal Research* 2016;61:370–380.
30. Küçükler, S., Kandemir, F. M., Özdemir, S., Çomaklı, S., & Caglayan, C. Protective effects of rutin against

deltamethrin-induced hepatotoxicity and nephrotoxicity in rats via regulation of oxidative stress, inflammation, and apoptosis. *Environmental Science and Pollution Research* 2021;28:62975-62990.

31. Li S, Zheng X, Zhang X, Yu H, Han B, Lv Y, Liu Y, Wang X, Zhang Z Exploring the liver fibrosis induced by deltamethrin exposure in quails and elucidating the protective mechanism of resveratrol. *Ecotoxicology and Environmental Safety* 2021;207:111501.
32. Dehdashtian E, Mehrzadi S, Yousefi B, Hosseinzadeh A, Reiter RJ, Safa M, et al. Diabetic retinopathy pathogenesis and the ameliorating effects of melatonin; involvement of autophagy, inflammation and oxidative stress. *Life Sciences* 2018;193:20–33.
33. Wilcox CS. Reactive oxygen species: roles in blood pressure and kidney function. *Current Hypertension Reports* 2002;4:160–166.
34. Ishrat T, Hoda MN, Khan MB, Yousuf S, Ahmad M, Khan MM, Ahmad A, Islam F. Amelioration of cognitive deficits and neurodegeneration by curcumin in rat model of sporadic dementia of Alzheimer's type (SDAT). *European Neuropsychopharmacology* 2009;19:636–647.

الكشف عن تأثير الميلاتونين المضاد للسمية العصبية المحدثة بالمبيد الحشري الدلتامثرين باستخدام نموذج ذكور الجرذان البالغة

الخلفية والاهداف: واحد من أخطر تأثيرات المبيد الحشري الدلتامثرين هو السمية العصبية والناجمة عن احداثه للإجهاد التأكسدي مع عدم وجود ترياق خاص له لحد الان لذلك وقع الاختيار على الميلاتونين بسب امتلاكه تأثيرات مضادة للأكسدة قوية. في بداية حددت الجرعة المميتة الوسطية للدلتامثرين (106.6 ملغم/كغم، عن طريق الفم) لغرض الاستفادة منها في تصميم الدراسة **الطرق:** قسمت 20 من ذكور الجرذان البالغة إلى أربع مجاميع (5/مجموعة) (أ وب وجـ ود)، جرعت الحيوانات في المجموعة أ بالدلتامثرين لوحده (75 ملغم/كغم ،عن طريق الفم) في حين حقنت الحيوانات في المجموعة ب بالميلاتونين (12.5 ملغم / كغم، داخل البريتون) قبل 15 دقيقة من تجريع الدلتامثرين، الحيوانات في المجموعة جـ و د اعطيت الميلاتونين (12.5 ملغم / كغم، داخل البريتون) والماء المقطر (2 مل / كغم، عن طريق الفم) على التوالي. **النتائج** ادى تجريع الحيوانات في المجموعة أ بالدلتا لوحده الى ظهور علامات التسمم وخلال 0.7 ± 55 ثانية والتي شملت على الاختلاجات العصبية والألعاب والحكة ولعق أصابع اليد وسلوك الهرب والرجفة وعدم الراحة، وبنسب حدوث (100%, 40, 60, 100, 60, 100, 100) وعلى التوالي مما أدى الى وصول مرتبة التسمم الى 24 في حين أدى حقن الميلاتونين قبل 15 دقيقة من تجريع الدلتامثرين في المجموعة ب الى حدوث إطالة معنوية في زمن ظهور علامات التسمم الى 0.2 ± 720 ثانية مع انخفاض معنوي في النسب المئوية لحدوث هذه العلامات الى 20,20% ,0 ,0 ,0 ,20 ,20 وعلى التوالي مؤديا الى حدوث انخفاض معنوي في مرتبة التسمم الى 4 صاحبها حدوث ارتفاع معنوي في مستوى الانزيم المضاد للأكسدة (الكلوتاثيون بيروكسيديز) في المصل بالمقارنة بالمجموعة المعاملة بالدلتامثرين لوحده .**الاستنتاج** :نستنتج من نتائجنا قابلية الميلاتونين على عكس التاثيرات السمية العصبية للدلتامثرين .

الكلمات المفتاحية: المبيد الحشري، الدلتامثرين، الميلاتونين، مضاد الاكسدة، السمية العصبية