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Behavioral and Neurochemical Consequences of Subacute Acetamiprid Administration in a Mice Model

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ABSTRACT

Acetamiprid, a neonicotinoid insecticide, effectively controls a wide range of crop pests and fleas on livestock and pets. This research examined the neurobehavioral and biochemical consequences of subacute, low-dose oral exposure to acetamiprid in adult mice. The study population was divided into four groups (5 mice/group), including one control group, while the remaining groups received 3.14, 6.29, and 12.59 mg/kg acetamiprid orally three times per week for a duration of 28 days. Behavioral evaluations indicated a clear dose-dependent decline in motor performance, spatial learning, and memory. Reduced rearing activity in the open-field test, poorer outcomes in the negative geotaxis assessment, and fewer head-poking events were indicative of these impairments. Animals treated with higher doses (6.29 and 12.59 mg/kg) also exhibited shorter wire-hanging endurance times and reduced alternation in the T-maze, pointing to deficits in working memory. Biochemical investigations revealed notable reductions in cholinesterase activity in both plasma and brain tissues, coupled with pronounced oxidative stress, as evidenced by increased malondialdehyde levels and decreased glutathione content. Such alterations emerged as early as the 14th day of treatment and persisted until the 28th day. Collectively, the results indicate that subacute acetamiprid exposure can interfere with cholinergic signaling, promote oxidative injury, and compromise both cognitive and motor abilities in mice. Additional studies are needed to clarify the long-term neurodevelopmental risks associated with neonicotinoid exposure in mammals.

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INTRODUCTION

Neonicotinoids are a group of insecticides whose chemical structure closely resembles that of nicotine. They have gained extensive application in agriculture because of their ability to selectively affected nicotinic acetylecholine receptors (nAChRs) and perceived lower risk to mammals**(Tomizawa and Casida, 2005)**. However , growing evidence suggests that these compounds may adversely affect mammalian neurodevelopment and cognitive function, raising concerns about their safety (**Mitsushima *et al*.,2013**).

Among neonicotinoids, acetamiprid (a chloronicotinyl insecticide) is commonly employed as an alternative to organophosphates and carbamates, yet its potential neurotoxicity in mammals remains insufficiency characterized. Acetamiprid acts as an agonist at nAChRs, disrupting synaptic transmission and neuronal excitability in insects **(Terayama *et al*.,2016; Kutlu, and gould 2015)**. While its insecticidal mechanism is well understood, Acetamiprid enter the body through the gastrointestinal tract, it then passes across the BBB in mammals, build-up in the brain tissue , and interfere with cholinergic signaling- a critical regulator of learning , memory , and motor function(**Shamsi *etal.*, 2021**).

Experimental models have linked acetamiprid exposure to oxidative stress, neuroinflammation, and behavioral abnormalities , including defect in spatial memory and reduced exploratory activity (**Dhouïb *et al*., 2017; Gasmi *et al.*, 2017)**. Despite these findings, the dose-response effects of prolonged , low-dose acetamiprid exposure on neurobehavioral and biochemical parameters remain underexplored(**Mitsushima *et al*.,2013; Ballinger *et al.*,2016**). Given that neonicotinoids are regulated in numerous countries, including those of the European Union, it is important to gather comprehensive data on their potential toxicity to mammalian neurodevelopment from a precautionary perspective **(Ballinger *et al.*,2016; Sano *et al.*, 2016; Saito *et al.*, 2023**).

This work investigated the sub-acute neurotoxic effects of acetamiprid in mice, focusing on motor activity, cognitive performance, and biochemical markers of oxidative stress and cholinesterase inhibition. We hypothesized that repeated oral administration of acetamiprid would induce dose dependent deficits in neurobehavioral function, accompanied by oxidative damage and disrupted cholinergic activity. Our finding aims to contribute to the growing body of evidence on neonicotinoid toxicity, informing risk assessments and regulatory decisions regarding their agricultural and public health use.

MATERIALS AND METHODS

Animals

Forty white Swiss laboratory mice (male and female, 8–12 weeks old, 24–36 g) were procured from the breeding unit of the College of Veterinary Medicine, University of Mosul. They were maintained in plastic cages under standardized environmental conditions (22 ± 2 °C, 10 hours light/14 hours dark) with free access to food and water. All experimental protocols received approval from the college's Animal Care (Code: UM.VET.2024.007).

Acetamiprid Preparation and Administration

Acetamiprid (20%, Golan, Holanda) was diluted daily in distilled water to obtain the target concentrations. Doses (3.14, 6.29, and 12.59 mg/kg) were derived from preliminary studies and administered orally at 10 mL/kg body weight(**Al-Najmawi And Al-Zubaidy 2022**).

Experimental Design

Forty mice were randomly allocated into four experimental groups:

Group 1 (Control): Received 10 mL/kg of distilled water orally.

Groups 2–4: Received acetamiprid at 3.14, 6.29, or 12.59 mg/kg, respectively.

Treatments were administered three times weekly for 28 days. Behavioral and biochemical assessments were conducted on days 14th and 28th (5 mice were sacrificed per group at each time point (14th and 28 th) day.

eurobehavioral Tests

Open-Field Test

Locomotor activity (squares crossed) and rearing frequency were recorded for 3 min in a 35 × 35 × 25 cm arena(**Al-Zubaidyand Mohammad, 2013; Al-Hamadany and Al-Zubaidy,2023; Al-Zubaidy, 2021).**

Negative Geotaxis

Mice were placed head-down on a 45° inclined surface, and the time to complete a 180° turn (max 60 s) was recorded (**Al-Hamadany and Al-Zubaidy,2023**).

Head-Pocking Test

Exploratory behavior was assessed by counting head pokes into holes (2 cm diameter) on a circular platform over 3 min(**Al-Hamadany and Al-Zubaidy,2023**).

T-Maze Test

The spontaneous alternation task is a well-established method for assessing spatial working memory, while the T-maze provides insights into short-term memory, locomotion, and repetitive behavioral patterns (**Onaolapo *et al.,* 2012**). T- maze consist of 3 equally spaced arms The length of the left, right, and starting arms is 35 cm. The central selection area is a square of 7 cm by 7 cm. the maze's overall width is 77 cm (between the distal ends of the left and right arms). The maze's total length is 42 cm (from the northern wall to the distal end of the start arm). After placing each mouse into one of the maze arms, it was allowed to explore freely until its tail completely crossed into a different arm. The sequence of arm entries was recorded manually. An alternation was considered when the mouse entered all three arms consecutively without repetition. For example, if an animal made 15 arm entries, 5 of these would count as successful alternations.

The percentage of alternation was determined using the formula: {(number of correct alternations ÷ total arm entries) × 100}. Each mouse underwent the T-maze test for a duration of 3 minutes (**Onaolapo *et al.,* 2012**).

Hanging Test

Hang tests are simple and cheap methods to detects neuromuscular abnormalities of muscle strength in mice. The inverted screen consists of a 43 cm by 43 cm wire mesh, composed of 12 mm square grids formed by 1 mm diameter wires. To prevent mice from climbing over, the apparatus is bordered by a 4 cm deep wooden frame that effectively restricts escape attempts (**Deacon, 2013**).

Procedure

Initial Placement: Position the mouse at the center of a wire mesh screen (43 cm square with 12 mm grid spacing).

Test Initiation: Start a stopwatch and gradually invert the screen over a 2-second period, ensuring the mouse's head is oriented downward.

Positioning: Preserve the inverted screen steadily at a height of 40-50 cm above a padded surface to prevent injury upon falling.

Observation: Record the latency time until the mouse drops or remove it upon reaching the 2-minute cutoff time (adjustable for specific experimental needs).

Scoring System (2-minute trial):

Score 1: Drop occurs within 1-10 seconds
Score 2: Drop occurs between 11-25 seconds
Score 3: Drop occurs between 26-60 seconds
Score 4: Drop occurs between 61-90 seconds
Score 5: Mouse maintains grip beyond 90 seconds

Biochemical Analyses

On days 14 and 28 post-treatment, blood samples were obtained from the mice via the ophthalmic venous plexus into heparinized tubes. Immediately afterward, the animals were euthanized by cervical dislocation, and whole brains promptly removed for further analysis. Blood samples were centrifuged at 3000 rpm for 15 minutes to separate plasma, which, along with brain tissues, was stored at –20°C until cholinesterase (ChE) activity assays were conducted within one week.

Brain Homogenization

Whole brain tissues were homogenized using an Omni Bead Ruptor 24 omogenizer (USA) in a barbital-phosphate buffer solution at pH 8.1, prepared by dissolving 0.309 g of $C_8H_{11}N_2NaO_3$, and 0.040 g of $KH_2PO_4$and 8.768 g of NaCl were added in 225 ml of distilled water, then the pH of the final solution was adjusted to 8.1 using hydrochloric acid (0.1 M). Homogenization was carried out using 3 mL of buffer for every 100 mg of wet tissue (**Al-Hamadany, and Alzubaidy., 2023).**

Cholinesterase Activity Assay

Buffer phosphate solution with a pH of 8.1 and prepared as follows: 0.309 g of sodium barbital, 0.040 g of dihydrogen potassium phosphate and 8.768 g of sodium chloride were added in 225 ml of distilled water, then the pH of the final solution was adjusted to 8.1 Using hydrochloric acid (0.1 M) and measuring the pH with a pH meter, complete the volume to 250 ml by adding distilled water. The aqueous solution of acetylcholine iodide 7.1% was prepared as follows: 0.375 mg of acetylcholine iodide was added in 5 ml of distilled water, and prepared on the same measurement day (**Mohammad, 2007; Mousa,2009; Al-Zubaidy And Amin, 2018**; **Al-Shalchi and Mohammad, 2024; Al-Zubaidy).**

Oxidative Stress Markers

Glutathione (GSH) and malondialdehyde (MDA) levels in plasma and brain were quantified using commercial kits (Shanghai Ideal Medical Technology Co., China)(**El-Gendy *et al.*, 2022**).

Statistical Analysis

Data were analyzed using SPSS v20 (IBM) via One way analysis of variance and, the results were subjected to the LSD test, and Mann-Whitney U test for non-parametric data. The results are expressed as mean ± SE; with significance defined at $p \leq 0.05$ (**Petrie and Watson, 2013).**

RESULTS

Repeated oral doses of acetamiprid for 14 days 3 times per week at doses (3.14.6.29,12.59) mg/kg causes a significant reduction was observed in open field activity (rearing), time spent in the negative geotaxis test, and the number of head pokes, all compared to the control group **(Table 1).** Administration of acetamiprid at a dose of 6.29 and 12.59 mg/kg orally resulted in significantly reduction in the duration mice remained attached to the wire compared to controls. Additionally, at the 12.59 mg/kg dose, a significant reduction was observed in the percentage of correct alternations in the T-maze test **(Table 1).**

Table 1: Effect of oral acetamiprid administration at doses of 3.14, 6.29, and 12.59 mg/kg for 14 days (3 times per week) on motor activity and neurobehavioral activity in mice.

groups	Control (Distilled water)	3.14 Mg/Kg	6.29 Mg/Kg	12.59 Mg/Kg
Negative geotaxis Test/Sec	12.60±1.16	11.00±1.37	5.80±1.88*	4.20±1.01*
Head pocking Test /3 min	35.40±5.56	18.80±3.24*	15.20±0.73*	10.80±0.37*
Open-field rearing frequency over a 3-minute period	28.80±1.01	21.00±0.44*	16.40±0.92*	9.40±2.31*
Squares crossed in open-field test (3 min)	117.00±10.19	97.60±13.95	88.20±4.67	50.00±9.43*
Hanging test/2min	4.6±0.24	3.6±0.24	3.00±0.0*	2.20±0.37*
% Number of correct rotations/3 minutes	87%	80%	35%	24%*

Mean ± standard error (5 mice/group). * Values differ significantly from distilled water group at *P ≤0.05.*

Following 28 days of oral administration of acetamiprid at doses of 3.14, 6.29, and 12.59 mg/kg, causes a significant reduction in open field activity (crossing squares and rearing), decreased time spent in the negative geotaxis test, and a notable decline in head poking compared to the control group **(Table 2).** Oral administration of acetamiprid at doses of 6.29 and 12.59 mg/kg significantly reduced the time mice remained suspended on the wire compared to controls. At the 12.59 mg/kg dose, a marked decrease was also observed in the percentage of correct alternations in the T-maze test **(Table 2).**

Table 2: Effect of oral acetamiprid administration at doses of 3.14, 6.29, and 12.59 mg/kg for 28 days on otor activity and neurobehavioral activity in mice.

Groups	Control (Distilled water)	Acetaiprid 3.14 mg/Kg	Acetamiprid 6.29 mg/Kg	Acetamiprid 12.59 mg/Kg
Negative geotaxis Test/Sec	17.20±1.15	11.20±3.42*	7.00±0.89*	4.80±1.20*
Head pocking Test /3 min	30.00±1.64	13.60±1.50*	5.80±0.66*	3.00±0.83*
Open-field rearing frequency over a 3-minute period	15.60±1.28	9.40±1.83*	1.80±1.56*	0.20±0.20*
Squares crossed in open-field test/ 3min	64.00±8.57	36.20±5.80*	17.00±6.95*	9.20±2.78*
Hanging test/2min	4.8±0.20	4.20±0.49	3.00±0.0*	1.60±0.40*
% of Number of correct rotations/3min	85%	50%	33%	20%*

* Values differ significantly from distilled water group at $P \leq 0.05$. Values mean ± standard error (5 mice/group).

Oral administration of acetamiprid after 14 days at doses (3.14.6.29,12.59) mg/kg resulted in significant reduction in glutathione concentration in plasma and brain at ratio 8%,13%,20%, respectively and 15%,25%, and 28% respectively in brain **(Fig.1).** As well as the ratio of glutathione inhibition in plasma and brain after 28 days of treatment 4%,3%, 14%, and 9%,4%, and 15% respectively **(Fig.2).**

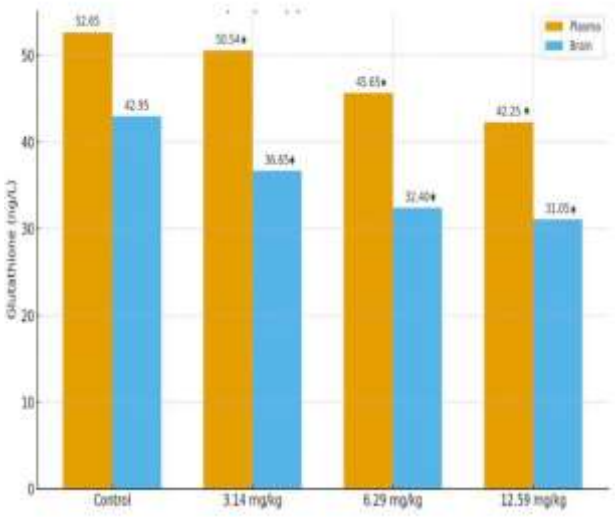

Fig. 1: Effect of acetamiprid on glutathione levels in plasma and brain of mice (14 days).

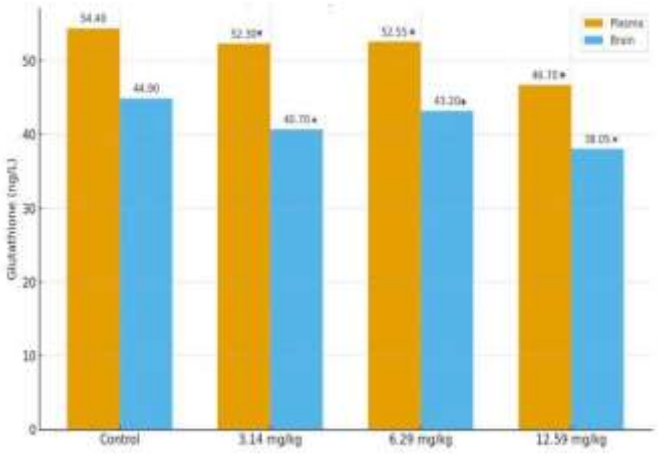

Fig. 2: Effect of acetamiprid on glutathione levels in plasma and brain of mice (28 days).

This was accompanied by a significant elevation in the level of malondialdehyde in the blood plasma and brain of mice given acetamiprid after 14 and 28 days, the elevation ratios were 16%,28%,62% in plasma and 8%,21%, and 35% in brain after 14 days **(Fig.3),** and 12%,29%,40% in plasma and 40%,63%, and 76% in brain after 28 days **(Fig.4).**

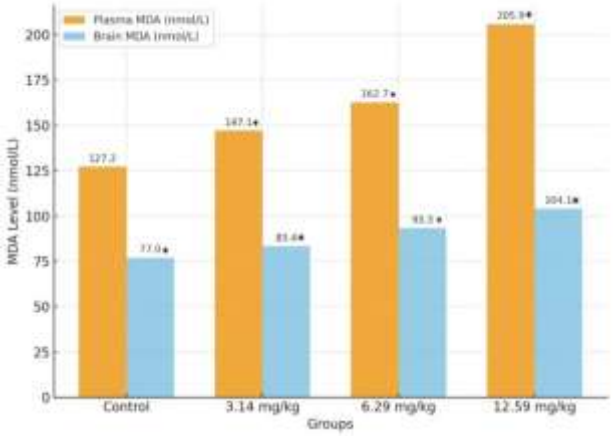

Fig. 3: Effect of acetamiprid on MDA levels in plasma and brain of mice (14 days).

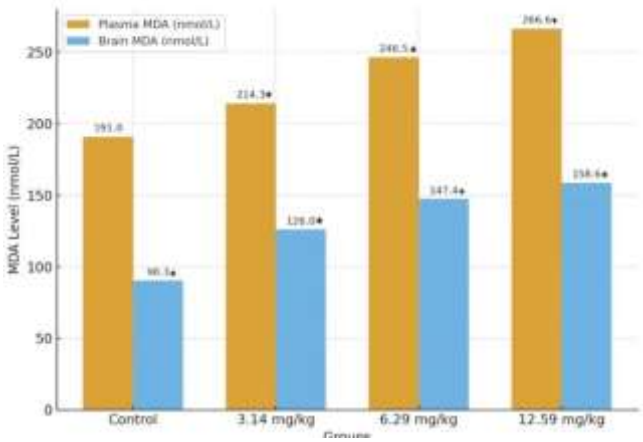

Fig. 4: Effect of acetamiprid on MDA levels in plasma and brain of mice (28 days).

Giving acetamiprid at doses (3.14.6.29,12.59) mg/kg after 14 days of treatment led to significant inhibition in the concentration of cholinesterase in plasma and brain of mice and the ratios of inhibition were 27%,37%,50% and 14%, 19%,28% respectively **(Table 3).** While the ratios of inhibition were 8%,10%,25% in plasma and 19%,23%, 34% in brain after 28 days of acetamiprid treatment **(Table 4).**

Table 3: Effect of oral acetamiprid administration at doses of 3.14, 6.29, and 12.59 mg/kg for 14 days on cholinesterase activity.

Groups	Plasma	%Inhibition	Whole brain	%Inhibition
Control (Distilled Water)	0.90±0.04	0	0.72±0.04	0
3.14 mg/kg	0.66±0.03*	27	0.62±0.03*	14
6.29 mg/kg	0.57±0.03*	37	0.58±0.03*	19
12.59 mg/kg	0.45±0.03*	50	0.52±0.02*	28

* Values differ significantly from distilled water group at $P \leq 0.05$. Mean± SE (5 mice/ group)

Table 4: Effect of oral acetamiprid administration at doses of 3.14, 6.29, and 12.59 mg/kg for 28 days on the cholinesterase activity.

Groups	Plasma	%Inhibition	Whole brain	%Inhibition
Control (Distilled Water)	0.99±0.02	0	0.64±0.01	0
3.14 mg/kg	0.91±0.01*	8	0.52±0.05*	19
6.29 mg/kg	0.89±0.01*	10	0.49±0.02*	23
12.59 mg/kg	0.74±0.03*	25	0.42±0.03*	34

* Values differ significantly from distilled water group at $P \leq 0.05$. Mean± SE (5 mice / group).

DISCUSSION

Acetamiprid, a next-generation chloronicotinyl insecticide, is widely used as an alternative to organophosphates and carbamates for controlling insect pests (**Phogat *et al*., 2022**). Although designed to selectively bind to nicotinic acetylcholine receptors in insects, its extensive application has been associated with adverse effects on non-target organisms, including mammals. (**Phogat *et al*., 2022**).

Continuous and extensive application of acetamiprid has led to its recognition as an environmental toxin. It can cause organ system toxicity that negatively impacts behavior, oxidative stress, and biochemical alteration.

Acetamiprid enters the body through the gastrointestinal tract; it then passes across the BBB and moves throughout the brain, particularly to the

hippocampus. Upon exposure, the brain may serve as a vulnerable target for acetamiprid due to its neurotoxic properties and propensity to accumulate within neural tissue. (**Shamsi *et al.,* 2021**). The results of our study on mice exposed to acetamiprid at a low level for 28 days show significant decreases in open-field activity, head poking, and negative geotaxis. These behavioral changes are identical in cases of neonicotinoid poisoning in subacute exposure (**Gasmi *et al.*, 2017)** and are in agreement with **Singh *et al.* (2012).** Acetamiprid has also been shown to impair locomotor function, induce tremors, and create diseases related to the neurological system. Its neurotoxic effects may be related to decreased efferent nerve transmission and aberrant afferent transmission production at neuromuscular synapses (Kara ***et al*., 2015).** Exposure to acetamiprid has been demonstrated to impact rat hippocampal synaptic strength, desensitize ionic receptors **(Szyndler *et al*., 2006; Gasmi *et al.*, 2019),** and cause neuronal degeneration. According to **Dhouïb *et al*., (2017),** acetamiprid administration is known to change rats' sociosexual and anxiety-associated behaviors, cause memory loss, learning impairment, and shorten their activity latency time **(Shamsi *et al.,* 2021**; **Dhouïb *et al*., 2017; Phogat *et al*., 2022**).

Mice are an ideal model animal for assessing muscular strength problems and possible treatments since they are naturally able to hold onto items tightly (Deacon, **2013**). When acetamiprid was administered for 28 days, the mice's time needed to stay connected to the wire was much less than that of the control group. Our research produced findings that were comparable to those of other studies (**Tomizawa and Casida, 2005)**.). Acetamiprid's action on acetylcholine and nicotinic receptors directly explains muscle weakness. Tissues, including the head, thorax, and abdomen, that have a high density of nicotinic acetylcholine receptors have the greatest amounts of it **(Tomizawa and Casida, 2005; Kara *et al*., 2015).**

Neonicotinoids have been shown to impact mammalian brain functions, including cognitive behaviors. Exposure to these pesticides during prenatal and early postnatal stages has been linked to neurobehavioral deficits such as increased anxiety, impaired learning, memory, and altered social interactions (**Dhouïb *et al*., 2017; Karaca *et al*., 2019**). This is what our current results in the maize T-test have proven, where exposure to acetamiprid resulted in a significant reduction in the number of correct rotations compared to the control group. Our results were consistent with what the researchers had reported **(El-Bialy *et al.*, 2020**; **Alemdar *et al*., 2025)**.

The formation of memory depends critically on glutamate, an excitatory neurotransmitter in the glutamatergic system. Prior research has demonstrated that memory consolidation is hampered by a reduced glutamate concentration in the hippocampus **(Cammarota *et al.*, 2004**). Decreased glutamate levels in the hippocampal regions are therefore thought to be the cause of exhibited deficits in memory consolidation in all groups treated with acetamiprid. The malfunction of the hippocampus's glutamatergic system at low dosages and the death of neural cells in the hippocampus's dentate gyrus area at high levels were the causes of this behavioral deficiency (**Olajide *et al*., 2021**).

When acetamiprid is exposed to live tissues, free radicals are produced inside the tissues. Through the oxidation of structural molecules and the reduction of antioxidant capacity, the interaction between free radicals and cellular components sets off a series of events that harm tissue. Numerous disease processes and the development of oxidative stress are linked to these free radicals.

Following exposure to acetamiprid, oxidative stress has been confirmed by our study. Sub-acute exposure to acetamiprid has been demonstrated to significantly elevate malondialdehyde (MDA) levels and injury biomarkers while reducing glutathione concentrations in both plasma and brain tissues of mice. These findings align with previous research conducted on rats and mice (**Khovarnagh and Seyedalipour, 2021**; **El-Gendy *et al.*, 2022).** The rise in MDA levels alongside the depletion of glutathione suggests that oxidative stress is induced, potentially due to lipid peroxidation. Consequently, the brain becomes particularly vulnerable to free radical-induced damage. Because of its high lipid content and oxygen requirement, it is more vulnerable to oxidative damage **(Blokhina *et al*., 2003; PREISER, 2012).**

Specific studies directly measuring cholinesterase activity in response to acetamiprid exposure in mice are limited; our findings indicate that sub-acute exposure to acetamiprid can result in decreased AChE levels in plasma and brain mice, and our results corroborate previous research. conducted by researcher **Pothu *et al.* (2019).** Acetamiprid has been shown to affect acetylcholinesterase (AChE) activity in the plasma and brain of mice. This occurs because acetamiprid mimics nicotine and interacts with nicotinic acetylcholine receptors (nAChRs), leading to disruptions in neurotransmitter balance **(Phogat *et al*., 2022; Alemdar *et al*., 2025**). Studies indicate that exposure to acetamiprid can result in decreased AChE levels, which may contribute to neurotoxicity and behavioral changes. Additionally, research suggests that acetamiprid accumulates in different brain regions, potentially influencing AChE activity **(Saito *et al.*, 2023**).

CONCLUSIONS

Sub-acute oral exposure to low doses of acetamiprid over 28 days causes dose-dependent neurobehavioral impairments and biochemical disruptions in adult mice, including oxidative stress and cholinergic dysfunction. These findings reinforce concerns about neonicotinoid neurotoxicity and underscore the need for further research to inform regulatory policies and safeguard health.

Conflict of interest: None.

REFERENCES

ABDUL HAMEED, Y. M., and NASER, A. S., 2025. Exploring The Anxiolytic and Neurobehavioral Benefits of Serratiopeptidase in Mice. Journal of Applied Veterinary Sciences, 10 (1): 57-63. https://dx.doi.org/10.21608/javs.2024.330246.1455

ALEMDAR, N. T., DEMIR, S., YULUG, E., KULABER, A., DEMIR, E. A., ERDOGAN, N. S., BALKAN, B., and YILMAZ, O., 2025. Acetamiprid-induced testicular toxicity in mice: ameliorative effect and potential mechanisms of morin. BMC Complementary Medicine and Therapies, *25*(1): 1–12. https://doi.org/10.1186/s12906-025-04983-y

AL-HAMADANY, N. S., and AL-ZUBAIDY, M. H., 2023. Evaluating the toxic oral doses of iron oxide nanoparticles in mice. Iraqi Journal of Veterinary Sciences, 37(4):801–811 https://doi.org/10.33899/ijvs.2023.138368.2796

AL-HAMADANY, N. A., and ALZUBAIDY, M. H., 2023. Sub-acute Effects of α-Fe2O3 Nanoparticles on Some Biochemical Parameters in Mice**.** Journal of Applied Veterinary Sciences, 8 (3): 46-53. https://dx.doi.org/10.21608/javs.2023.210749.1232

AL-NAJMAWI, T. K., and AL-ZUBAIDY, M. H., 2022. Acute toxicity events of ivermectin in chicks' model. Iraqi Journal of Veterinary Sciences, 36(4): 1119– 1124. https://doi.org/10.33899/ijvs.2022.133188.2188

AL-SHALCHI, R. F., and MOHAMMAD, F. K., 2024. Alterations of neurobehavioral performance, blood and brain cholinesterase activities and cholesterol levels by repeated statin treatments in mice. Bulletin of Pharmaceutical Sciences Assiut University, *47*(1): 415–425.https://doi.org/10.21608/bfsa.2024.270145.2033

AL-ZUBAIDY, M. H. I. 2021. Acute neurotoxicity of acetaminophen in chicks. Veterinarski Arhiv, *91*(4): 379–387. https://doi.org/10.24099/vet.arhiv.0950

AL-ZUBAIDY, M. H., I., and AMIN, S. M., 2019. Cholinesterase inhibition in chicks treated with manganese chloride. Iraqi Journal of Veterinary Sciences. 32(2):37-42. https://doi.org/10.33899/ijvs.2019.153875

AL-ZUBAIDY, M. H. I., and MOHAMMAD, F. K., 2007. Metoclopramide protection of diazinon-induced toxicosis in chickens. Journal of Veterinary Science, *8*(3): 249–254. https://doi.org/10.4142/jvs.2007.8.3.249

AL-ZUBAIDY, M. H. I., and MOHAMMAD, F., K., 2013. Effects of acute manganese neurotoxicity in young chicks. Arhiv za Higijenu Rada i Toksikologiju, *64*(1): 69–75. https://doi.org/10.2478/10004-1254-64-2013-2222

BALLINGER, E., C., ANANTH, M., TALMAGE, D., A., and ROLE, L., W. 2016. Basal forebrain cholinergic circuits and signaling in cognition and cognitive decline. Neuron, *91*(6): 1199–1218. https://doi.org/10.1016/j.neuron.2016.09.006

BLOKHINA, O., VIROLAINEN, E., and FAGERSTEDT, K., V., 2003. Antioxidants, oxidative damage and oxygen deprivation stress: a review. Annals of Botany, *91*(2): 179–194. https://doi.org/10.1093/aob/mcf118

CAMMAROTA, M., BEVILAQUA, L. R. M., BONINI, J. S., ROSSATTO, J. I., MEDINA, J., H., and IZQUIERDO, N., 2004. Hippocampal glutamate receptors in fear memory consolidation. Neurotoxicity Research, 6: 205–211. https://doi.org/10.1007/bf03033222

DEACON, R. M. J. 2013. Measuring the strength of mice. Journal of Visualized Experiments, (76): e2610. https://doi.org/10.3791/2610

DHOUÏB, I. B., ANNABI, A., DOGHRI, R., REJEB, I., DALLAGI, Y., BDIRI, Y., JAMOUSSI, K., ABID-ESSEFI, S., and BÉJAOUI, S., 2017. Neuroprotective effects of curcumin against acetamiprid-induced neurotoxicity and oxidative stress in the developing male rat cerebellum: biochemical, histological, and behavioral changes. Environmental Science and Pollution Research, 24: 27515–27524. https://doi.org/10.1007/s11356-017-0331-5

EL-BIALY, B. E. S., ABD ELDAIM, M. A., HASSAN, A., and ABDEL-DAIM, M. M., 2020. Ginseng aqueous extract ameliorates lambda-cyhalothrin–acetamiprid insecticide mixture for hepatorenal toxicity in rats: role of oxidative stress-mediated proinflammatory and proapoptotic protein expressions. Environmental Toxicology, 35:(2), 124–135. https://doi.org/10.1002/tox.22848

EL-GENDY, K. S., ALY, N. M., MAHMOUD, F. H., and ALLAH, D. A., 2022. Toxicological assessment of sublethal dose of acetamiprid in male mice and the efficacy of quercetin. Pesticide Biochemistry and Physiology, 184: 105078. https://doi.org/10.1016/j.pestbp.2022.105078

GASMI, S., CHAFAA, S., LAKROUN, Z., ROUABHI, R., TOUAHRIA, C., KEBIECHE, M., CHERIF, H., and BOUKHALF, A. A., 2019. Neuronal apoptosis and imbalance of neurotransmitters induced by acetamiprid in rats. Toxicological and Environmental Health Sciences, 11: 305–311. https://doi.org/10.1007/s13530-019-0417-1

GASMI, S., KEBIECHE, M., ROUABHI, R., TOUAHRIA, C., LAHOUEL, A., LAKROUN, Z., CHERIF, H., and BOUKHALFA, A., 2017. Alteration of membrane integrity and respiratory function of brain mitochondria in the rats chronically exposed to a low dose of acetamiprid. Environmental Science and Pollution Research, 24: 22258–22264. https://doi.org/10.1007/s11356-017-9901-9

KARA, M., YUMRUTAS, O., DEMIR, C. F., OZDEMIR, H. H., BOZGEYIK, I., COSKUN, S., KAZAZ, S. N., KAZAZ, N., and ALTUNAY, S., 2015. Insecticide imidacloprid influences cognitive

functions and alters learning performance and related gene expression in a rat model. International Journal of Experimental Pathology, 96(5): 332–337. https://doi.org/10.1111/iep.12139

KARACA, B. U., ARICAN, Y. E., BORAN, T., BINAY, S., OKYAR, A., KAPTAN, E., AYDIN, M. S., KILINC, A., and AKSOY, M., 2019. Toxic effects of subchronic oral acetamiprid exposure in rats. Toxicology and Industrial Health, 35 (11–12): 679–687. https://doi.org/10.1177/0748233719893203

KHALIL, H. A., and FARIS, G. A., 2025. A Study Investigating the Synergistic Analgesic Effects of Nefopam and Medetomidine in a Multimodal Pain Management Approach in Mice. Journal of Applied Veterinary Sciences, 10 (3): 129 136. https://doi.org/10.21608/javs.2025.389940.1628

KHOVARNAGH, N., and SEYEDALIPOUR, B., 2021. Antioxidant, histopathological and biochemical outcomes of short-term exposure to acetamiprid in liver and brain of rat: The protective role of N-acetylcysteine and S-methylcysteine. Saudi Pharmaceutical Journal, *29*(3): 280–289. https://doi.org/10.1016/j.jsps.2021.02.004

KUTLU, M., G., and GOULD, T., J. 2015. Nicotinic receptors, memory, and hippocampus. In Neurobiology of Nicotine and Tobacco, 137–163. https://doi.org/10.1007/978-3-319-13665-3_6

MITSUSHIMA, D., SANO, A., and TAKAHASHI, T., 2013. A cholinergic trigger drives learning-induced plasticity at hippocampal synapses. Nature Communications, 4(1): 2760. https://doi.org/10.1038/ncomms3760

OLAJIDE, O. J., GBADAMOSI, I. T., YAWSON, E. O., AROGUNDADE, T., LEWU, F. S., OGUNRINOLA, K. Y., ABUBAKAR, O. L., and SULEIMAN, M., 2021. Hippocampal degeneration and behavioral impairment during Alzheimer-like pathogenesis involves glutamate excitotoxicity. Journal of Molecular Neuroscience, 71: 1205–1220. https://doi.org/10.1007/s12031-020-01747-w

ONAOLAPO, O. J., ONAOLAPO, A. Y., MOSAKU, T. J., AKANJI, O. O., and ABIODUN, O., R., 2012. Elevated plus maze and Y-maze behavioral effects of subchronic, oral low dose monosodium glutamate in Swiss albino mice. Journal of Pharmacy and Biological Sciences, *3*(4): 21–27. http://dx.doi.org/10.9790/3008-0342127

PETRIE, A., and WATSON, P., 2013. Statistics for veterinary and animal science. 3rd ed. John Wiley & Sons.

PHOGAT, A., SINGH, J., KUMAR, V., and MALIK, V., 2022. Toxicity of the acetamiprid insecticide for mammals: a review. Environmental Chemistry Letters, 1–26. https://doi.org/10.1007/s10311-021-01353-1

POTHU, U. K., THAMMISETTY, A. K., and NELAKUDITI, L. K., 2019. Evaluation of cholinesterase and lipid profile levels in chronic pesticide exposed persons. Journal of Family Medicine and Primary Care, *8*(6): 2073–2078. https://doi.org/10.4103/jfmpc.jfmpc_440_19

PREISER, J. 2012. Oxidative stress. Journal of Parenteral and Enteral Nutrition, *36*(2): 147–154. https://doi.org/10.1177/0148607111434963

SAITO, H., FURUKAWA, Y., SASAKI, T., KITAJIMA, S., KANNO, J., and TANEMURA, K., 2023. Behavioral effects of adult male mice induced by low-level acetamiprid, imidacloprid, and nicotine exposure in early life. Frontiers in Neuroscience, 17:1239808. https://doi.org/10.3389/fnins.2023.1239808

SANO, K., ISOBE, T., YANG, J., WIN-SHWE, T. T., YOSHIKANE, M. NAKAYAMA, S., F., NAKAJIMA, D., KASHIWA, H., and SHINKAI, Y., 2016. In utero and lactational exposure to acetamiprid induces abnormalities in socio-sexual and anxiety-related behaviors of male mice. Frontiers in Neuroscience, 10: 228. https://doi.org/10.3389/fnins.2016.00228

SHAMSI, M., SOODI, M., SHAHBAZI, S., and OMIDI, A., 2021. Effect of acetamiprid on spatial memory and hippocampal glutamatergic system. Environmental Science and Pollution Research, 28: 27933–27941.https://doi.org/10.1007/s11356-020-12314-6

SINGH, T. B., MUKHOPADHAYAY, S. K., SAR, T. K., and GANGULY, S., 2012. Acetamiprid induces toxicity in mice under experimental conditions with prominent effect on the hematobiochemical parameters. Journal of Drug Metabolism and Toxicology, *3*(6): 134. http://dx.doi.org/10.4172/2157-7609.1000134

SZYNDLER, J., PIECHAL, A., BLECHARZ-KLIN, K., SKÓRZEWSKA, A., MACIEJAK, P., WALKOWIAK, J., TURZYŃSKA, D., LEWANDOWSKA, A., and WISŁOWSKA, A., 2006. Effect of kindled seizures on rat behavior in water Morris maze test and amino acid concentrations in brain structures. Pharmacological Reports, *58*(1): 75–82.PMID: 16531633

TERAYAMA, H., ENDO, H., TSUKAMOTO, H., MATSUMOTO, K., UMEZU, M., KANAZAWA, T., MITSUHASHI, T., SHIMIZU, T., KAKUTANI, H., and TANAKA, M., 2016. Acetamiprid accumulates in different amounts in murine brain regions. International Journal of Environmental Research and Public Health, 13(10): 937.https://doi.org/10.3390/ijerph13100937

TOMIZAWA, M., and CASIDA, J. E., 2005. Neonicotinoid insecticide toxicology: mechanisms of selective action. Annual Review of Pharmacology and Toxicology, 45(1): 247–268. https://doi.org/10.1146/annurev.pharmtox.45.120403.095930

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