



Acute toxic effects of indoxacarb on some biomarkers in mice

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Abstract

This study investigated the acute toxicological effects of Indoxacarb (IDX) in mice by evaluating clinical signs, toxicity scores, and biochemical markers. IDX, a modern oxadiazine insecticide, exerts its action by blocking voltage-gated sodium channels in insect neurons, leading to paralysis and death. A total of 81 healthy mice (20–32 g, 8–12 weeks old) were used. The oral median lethal dose (LD₅₀) was determined as 1292.25 mg/kg body weight, classifying IDX as moderately toxic. Clinical observations revealed the rapid onset of neurological symptoms, including convulsions, ataxia, Straub tail, rolling, piloerection, hindlimb paralysis, and abnormal posture within 10–45 minutes post-exposure. Toxicity was dose-dependent, with severity scores of 15 and 24 recorded in groups treated with 700 and 900 mg/kg B.W., respectively, within 24 h, indicating a marked increase in neurotoxic effects at higher doses. Blood samples were collected from the retro-orbital plexus, and brain and liver tissues were excised for biochemical evaluation. Plasma analysis demonstrated significant hepatotoxicity, as evidenced by elevated AST, ALT, and ALP activities, indicating hepatocellular damage. Blood glucose levels increased by 67.8%, reflecting stress-induced hyperglycemia and metabolic disruption. Indoxacarb also markedly inhibited acetylcholinesterase (AChE) activity across tissues. Plasma AChE was most affected, with inhibition of 72.4% and 82.1% at 700 and 900 mg/kg B.W. after 4 h, followed by partial recovery at 24 h. Liver AChE inhibition was moderate (25.9–31.0%), while brain tissue showed greater sensitivity (39.6–49.4%). In conclusion, Indoxacarb induced acute, dose-dependent neurotoxic, hepatotoxic, and metabolic alterations, highlighting potential health risks and the importance of strict safety measures.

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Introduction

Indoxacarb is a next-generation insecticidal agent classified under the oxadiazine chemical family. It operates via a distinctive mechanism that selectively disrupts the nervous system of insects, rendering it effective against a broad spectrum of pests affecting both agricultural crops and domestic animals (1). While insecticides remain essential tools in contemporary agriculture, their unintended neurotoxic impacts on non-target species particularly

mammals continue to raise significant concerns (2). Functioning as a pro-insecticide indoxacarb is bioactivated within the insect's body into its toxic metabolite, N-decarbomethoxylated indoxacarb (DCJW). This active form that specifically inhibits voltage-gated sodium channels (Na⁺), interrupting nerve impulse transmission which culminates in paralysis and ultimately death of the insect (3,4). This targeted action offers a significant advantage over conventional insecticides that interact with the same channels but with lower specificity (5). Indoxacarb has

demonstrated a high efficacy against Lepidopteran larvae (e.g., *Helicoverpa armigera*), as well as beetles, whiteflies, cockroaches, and certain ant species. Field trials confirm that it induces rapid feeding cessation within hours, followed by 80–100% mortality within 48 hours (6,7). In mammals, indoxacarb is efficiently absorbed through the digestive system and is subsequently metabolized in the liver into more polar compounds. These metabolites are eliminated via urine and feces, with blood plasma levels declining substantially within hours post-exposure (8). The U.S. Environmental Protection Agency (EPA) supports this assessment (9). Although rare, cases of acute human poisoning have been documented, mainly involving methemoglobinemia which is treatable with methylene blue (10).

From an environmental perspective, indoxacarb shows variable persistence in soil, with a half-life ranging between 3 and 693 days depending on climatic and microbial conditions. In water, it photodegrades relatively quickly (within 3–5 days) but remains stable in the absence of light. It poses chronic risks to aquatic organisms and exhibits high contact toxicity to pollinators such as bees (11-12). Resistance management strategies recommend alternating indoxacarb with other insecticides from distinct chemical classes (13,14).

Indoxacarb's regulatory status has varied globally (2). While countries such as the United Kingdom and Australia continue to allow their use under controlled conditions, the European Union withdrew approval in 2021 due to environmental risk concerns (15,16). Indoxacarb exemplifies a modern, selective insecticide that combines potent efficacy against critical pests with relatively low toxicity to humans. However, its environmental impact and potential for resistance development underline the importance of responsible usage and stringent regulatory monitoring.

Materials and methods

Ethical approval

The study was approved by the institutional animal care and use committee of the Department of Physiology, Biochemistry, and Pharmacology, College of Veterinary Medicine, University of Mosul, Iraq. Approval number (UM.VET.2024.011 dated on 6/May/2024).

Animals

A total of 81 Swiss albino mice (both sexes), weighing 20–32 g and aged 8–12 weeks, were used. Animals were housed under standard laboratory conditions ($22 \pm 2^\circ\text{C}$; 10 h light/14 h dark cycle) in plastic cages in an environmentally controlled animal house of the College of Veterinary Medicine, University of Mosul with free access to water and

laboratory-grade feed. All mice were health-checked (weight, activities) before experimentation.

Indoxacarb preparation

The commercial insecticide AGRIDOX 150 SC (ASCOT, UK) is an emulsion solution. The dosing solution was prepared daily by dilution with distilled water according to the dilution law ($C_1V_1 = C_2V_2$) to achieve the desired concentration. A dosing volume of 10 mL/kg body weight was administered orally via a gavage needle.

Blood Collection and Processing Protocol

Diethyl ether (Thomas Baker Limited, UK) anesthesia was employed to minimize pain and stress in mice during blood collection and to ensure complete immobilization of the animal, thereby facilitating safe handling. Each mouse was placed in a glass chamber containing a gauze pad soaked with an appropriate volume of ether, which induced rapid loss of consciousness within a short duration. Once the loss of righting reflex was observed, blood samples were withdrawn from the retro-orbital venous plexus using a sterile capillary and immediately transferred to heparinized glass tubes kept on ice to prevent biomolecule degradation (16). Samples were centrifuged at 3,000 rpm for 15 minutes and plasma was separated into sterile cryovials for either (a) flash-freezing at -18°C for batch analysis or (b) immediate biochemical processing, (17).

Tissue Processing Protocol

In accordance with ethical euthanasia guidelines (16), whole brains were collected via craniotomy using sterile instruments. Livers were carefully excised through a midline abdominal incision, ensuring the preservation of major blood vessels. Immediately after excision, the organs were wrapped in sterile aluminum foil and flash-frozen at -18°C to preserve biomolecular integrity and minimize enzymatic degradation and oxidative activity that could affect experimental results (18). For homogenization, tissues were processed on ice using an electric homogenizer (OMNI BEAD, RUPTOR 24, USA) at 400 rpm for 30 seconds to prevent thermal degradation (19).

Determination of the oral LD₅₀ of indoxacarb in mice by Dixon's up-and-down method (20)

6 mice were utilized, 26-35 g. The acute oral median lethal dose (LD₅₀) of indoxacarb in mice was determined following OECD Guideline 425 (Up-and-Down Procedure). A stepwise dosing protocol was employed, beginning with an initial dose of 1500 mg/kg body weight of indoxacarb administered orally using a gavage needle. Depending on the survival or mortality outcome within 24 hours, of dosing, we noticed the mouse was alive (O) or died (X). This dose was chosen based on preliminary experiments to determine the average lethal dose using the ascending and descending

method for 3 mice after changing the result died or live and vice versa and calculating indoxacarb LD₅₀ relying on Dixon's equation and table (20) If the rate of increase and decrease over 24 hours in mice was 16%. (21,22).

$$LD_{50} = xf + Kd$$

where xf represents the last administered dose, K is the tabular value obtained from the statistical table, and d is the interval between successive doses (up-and-down method).

Acute Toxic sings and toxicity score of Indoxacarb at doses of 700 and 900 mg/kg B.W. orally in Mice

30 mice (10 weeks old), weighing between (20-26 g) were divided into 3 equal groups (n=5/group). Group 1 (Control) Received distilled water (D.W.) by gavage needle 10 ml/kg. B.W. orally. Groups 2 and 3 Received indoxacarb at 700, 900mg/kg B.W. respectively orally. The mice were monitored for 2 hours post-administration of the insecticide then toxic sign were recorded and percentages of toxicity and toxicity score calculated and mortality was assessed for 24 hours following dosing. (23,24).

Acute toxic effects of Indoxacarb at doses of 700 and 900 mg/kg B.W. orally on some biochemicals parameters in the plasma of mice

15 mice (10 weeks old), with similar weights between (25-30 g) were divided into 3 equal groups (n=5/group) to evaluate the dose-dependent effects of indoxacarb on alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) activities (25) and blood glucose levels (26). Group 1 (control) received distilled water 10 ml/kg. B.W. orally. Group 2 and Group 3 were treated with indoxacarb at 700 mg/kg and 900 mg/kg B.W. orally, respectively. 24 hours post-administration, blood was collected for plasma separation and subsequent biochemical analysis of the specified parameters (ALT, AST, ALP, Glucose) by using kits (Biolab, France) and the enzymatic analysis was performed using an autoanalyzer (Fujifilm Dri-Chem NX500, Japan).

Acute toxic effects of Indoxacarb at doses (700 and 900 mg/kg) B.W. orally on AChE Activity in plasma, liver, and brain of Mice

30 mice (24-32 g) were divided into 6 equal groups (n=5/group). Group 1,2 (control group) given distilled water 10 ml/kg. B.W. orally, then collected the samples after 4 and 24 h. Groups 3,4,5 and 6 were given indoxacarb at 700 and 900 mg/kg B.W. orally, then collected the samples after 4 and 24 h. At the end of the experiment after 4 and 24 h blood was collected for plasma and the mice were killed to take brain and liver to measure AChE activity by an electrometric method (27,28).

AChE activity assay

Phosphate buffer (pH 8.1)

3.925 g sodium barbital produced by Hopkins & Williams Ltd, UK. 0.04075 g KH₂PO₄ produced by Fluka AG, Switzerland.

8.7675 g NaCl produced by HiMedia Laboratories, India. Adjusted to 250 mL with distilled, water pH calibrated with 0.1N HCl produced by B.D.H., UK.

Acetylcholine iodide substrate (7.1%)

0.355 mg in 5 mL distilled water (fresh daily) manufactured by (Avouchem, U.K.).

Acetylcholinesterase (AChE) activity assay protocol

The enzymatic activity was measured by using an electrometric method (28).

Reaction Setup

Added 3 mL distilled water to a 10 ml glass test tube then added 0.2 mL of sample (plasma or brain or liver homogenate), Then added 3 mL phosphate buffer (pH 8.1) then recorded initial pH (pH₁) using a pH meter (EUTECH, Singapore. Blank contained all reagents except plasma or tissue homogenate.

Substrate Reaction

Incorporated 0.12 mL AchI (7.1% w/v) as substrate, then incubated the mixture in water bath at 37°C for 30 minutes, then measured final pH (pH₂) immediately post-incubation.

Calculations

$\Delta pH / 30 \text{ min} = (pH_1 - pH_2) - \text{Blank } \Delta pH$. % Inhibition of AChE activity = $[(\text{Pre-inhibition rate} - \text{post-inhibition rate}) / \text{Pre-inhibition rate}] \times 100\%$.

Statistical analysis

The parametric results were statistically analyzed by using one- or two-way analysis of variance (ANOVA) test, then subjected to the least significant difference test depending on statistical analysis program (SPSS v.20.0, IBM, USA). Non-parametric results were analyzed by using Fisher exact test and Mann-Whitney U test, and the level of significance was $P \leq 0.05$ (29).

Results

Determination of the oral LD50 of indoxacarb in mice by Dixon's up-and-down method (20)

Depending on the survival or mortality outcome within 24 hours, the dose for the subsequent animal was either increased or decreased by a constant step of 250 mg/kg body weight, thereby covering a dose range of 1000–1500 mg/kg B.W. This sequential dosing strategy, based on Dixon's up-

and-down method, enabled the calculation of LD₅₀ using fewer animals while preserving statistical accuracy.

A total of 6 mice were tested, and the mortality sequence was recorded as XXOOXO (X = dead, O = survived). Clinical manifestations of acute toxicity appeared within 10–45 minutes of administration and included depression, dysphagia, hunched posture, prostration, convulsions, piloerection, Straub tail, ataxia, rolling, and dyspnea. At the highest toxic doses, death was also observed.

The reported 16% rate of increase and decrease over 24 hours reflects the adjustment incorporated into the calculation of the K factor, which was determined to be (–0.169) for the observed mortality pattern. This statistical constant was derived from Dixon's tables and is essential for LD₅₀ estimation (20).

Based on these calculations, the oral LD₅₀ of indoxacarb in mice was estimated to be 1292.25 mg/kg body weight (Table 1).

Acute Toxic signs and toxicity score of Indoxacarb at doses of 700 and 900 mg/kg B.W. orally in Mice

30 mice were divided into three main groups, each consisting of 10 animals. a control group, a group treated orally with indoxacarb at 700 mg/kg B.W. and a group treated at 900 mg/kg B.W. Oral administration of indoxacarb at 700 mg/kg B.W. induced acute toxicity signs in mice,

characterized by facial/nasal scratching, hunched posture, piloerection, ataxia, hindlimb paralysis, rolling, and neurological convulsions, with a recorded toxicity severity score of 15. Increasing the dose to 900 mg/kg B.W. markedly intensified the toxic manifestations, yielding a severity score of 24. All observed alterations were statistically significant when compared with the control group (Table 2).

Acute toxic effects of Indoxacarb at doses (700 and 900 mg/kg) B.W. orally on some biochemical parameters in the plasma of mice.

Indoxacarb at both doses (700 and 900 mg/kg B.W.) resulted in a significant elevation of (ALT) activity after 24 h post-treatment, with values of (67.6 ± 4.43 and 113.4 ± 5.57 IU/L), respectively, compared to the control group (51.2±30.3IU/L), Similarly (AST) activity was significantly increased to (175.6 ± 6.8 IU/L and 192.6 ± 11.1 IU/L) at the two doses respectively, relative to the control group (102.2 ± 5.08 IU/), (Table 3).

Indoxacarb induced a significant elevation in alkaline phosphatase (ALP) activity 24 hours post-administration. In the 700 mg/kg and 900 mg/kg B.W. dose groups, ALP activity reached (312 ± 10.56 IU/L and 352 ± 13.57 IU/L) respectively, compared to the control group (243 ± 16.73 IU/L) (Table 4).

Table 1: Median Lethal Dose (LD₅₀) of indoxacarb orally in mice

Data	Results
LD ₅₀ of indoxacarb (orally)	1292.25 mg/kg B.W.
Dose range	1500–1000=500 mg/kg B.W.
Initial dose	1500 mg/kg
Final dose	1250 mg/kg B.W.
Dose increment/decrement step	250 mg/kg B.W.
Number of animals used	6 mice (XXOOXO)
Onset of toxicity signs	10–45 minutes
Acute Toxicity Signs	depression, dysphagia, hunched back, prostration (lying flat on cage floor), convulsions, piloerection, ataxia (uncoordinated gait), Rolling, dyspnea, death.

Table 2: Acute toxicity signs and toxicity score of mice administered Indoxacarb 700 and 900 mg/kg B.W. orally

#	Toxic Signs	Control Group (D.W.)	Indoxacarb 700 mg/kg B.W.	Indoxacarb 900 mg/kg B.W.
1	Facial/nasal scratching	3/10 (30%)	7/10 (70%)	9/10 (90%) *
2	Hunched posture	0/10 (0%)	5/10 (50%) *	7/10 (70%) *
3	Piloerection	0/10 (0%)	7/10 (70%) *	10/10 (100%) *
4	Ataxia	0/10 (0%)	5/10 (50%) *	9/10 (90%) *
5	Hindlimb paralysis	0/10 (0%)	3/10 (30%)	7/10 (70%) *
6	Rolling	0/10 (0%)	0/10 (0%)	3/10 (30%)
7	Neurological convulsions	0/10 (0%)	5/10 (50%) *	10/10 (100%) ^{aa}
8	2-h mortality	0/10 (0%)	0/10 (0%)	0/10 (0%)
9	24-h mortality	0/10 (0%)	0/10 (0%)	2/10 (20%)
	Total Toxicity Score	8	15	24

(n=10/group). (*) represents significant P≤0.05 compared control. (a) represents significant intergroup differences at P≤0.05.

Table 3: Effects of indoxacarb (700 and 900 mg/kg) B.W. on AST and ALT levels in the plasma mice after 24 hours

Treatment	AST Activity (IU/L)	% Increase	ALT Activity (IU/L)	% Increase
Control (D.W.)	102.2 ± 5.08		51.2 ± 3.03	
Indoxacarb 700 mg/kg B.W.	175.6 ± 6.8*	+71.8%	67.6 ± 4.43*	+32.0%
Indoxacarb 900 mg/kg B.W.	192.6 ± 11.1*	+88.5%	113.4 ± 5.57*	+121.5%

(n=15 mice/5=group), Values as mean ± SE. (*) indicates significant difference vs control ($P \leq 0.05$) by one way ANOVA. % Of increases calculated as: $[(\text{Treated} - \text{Control})/\text{Control}] \times 100$.

Similarly, Indoxacarb caused a marked increase in blood glucose levels 24 hours post-administration. The 700 mg/kg B.W. dose elevated glucose to (173.6 ± 6.72 mg/dL) relative to the control (116 ± 7.48 mg/dL), whereas the 900 mg/kg B.W. dose further increased glucose levels to (194.6 ± 8.01 mg/dL) indicating a dose-dependent hyperglycemic

response (Table 4). Conversely, no statistically significant differences were detected in the levels of hepatic enzymes (ALT, AST, ALP) or blood glucose between the two Indoxacarb doses (700 and 900 mg/kg body weight) 24 hours post-administration.

Table 4: Effects of Indoxacarb on ALP and Blood Glucose in mice after 24h

Treatment	ALP (IU/L)	% Increase	Blood Glucose (mg/dL)	% Increase
Control	243 ± 16.73		116 ± 7.48	
700 mg/kg	312 ± 10.56*	+28.4%	173.6 ± 6.72*	+49.7%
900 mg/kg	352 ± 13.57*	+44.9%	194.6 ± 8.01*	+67.8%

Values = mean ± SE (n=15 mice/5= d=group). (*) indicates significant difference compared control ($P \leq 0.05$) by one way ANOVA. % Change calculated as: $[(\text{Treated} - \text{Control})/\text{Control}] \times 100$.

Acute toxic effect of Indoxacarb at doses (700 and 900 mg/kg) B.W. orally on AChE activity in the plasma, liver, and brain of mice

Administration of indoxacarb at doses of 700 and 900 mg/kg body weight produced a significant inhibition of AChE activity in plasma, liver, and brain tissues. The most pronounced effect was observed at 4 hours post-administration, where plasma AChE activity decreased by 72.4% and 82.1%, respectively, compared with controls

(Table 5). Although inhibition persisted at 24 hours, the extent of reduction was less marked, with plasma activity suppressed by 38.5% and 43.0% at the respective doses. In the liver, AChE activity declined by 25.9% and 31.0% at 4 hours, followed by smaller reductions of 19.0% and 29.3% at 24 hours (Table 6). Brain tissue showed the greatest sensitivity, with reductions of 39.6% and 49.4% at 4 hours, which remained significant after 24 hours (28.6% and 39.0%, respectively; Table 6).

Table 5. Effects of indoxacarb on Plasma AChE activity at doses (700 and 900 mg/kg) B.W. orally in mice after 4 and 24 h

Treatment	4 h AChE Activity (Δ pH)	Inhibition %	24 h AChE Activity (Δ pH)	Inhibition %
Control (D.W.)	0.312 ± 0.019		0.302 ± 0.02	
Indoxacarb 700 mg/kg B.W.	0.086 ± 0.006*	72.4%	0.192 ± 0.033 ^A	38.5%
Indoxacarb 900 mg/kg B.W.	0.056 ± 0.005*	82.1%	0.178 ± 0.004 ^A	43.0%

Values = mean ± SD (n=30). (*) indicates significant difference compared control ($P \leq 0.05$), One-way ANOVA. (A) indicates significant difference compared control ($P \leq 0.05$), Two-way ANOVA. % Inhibition calculated as: $[(\text{Control} - \text{Treated})/\text{Control}] \times 100\%$.

Discussion

Indoxacarb is a modern oxadiazine insecticide with a distinctive mode of action that blocks voltage-gated sodium channels in insect neurons, leading to paralysis and death. In veterinary medicine, it is mainly used for controlling ectoparasites such as fleas and ticks in companion animals, particularly dogs and cats, where it is incorporated into

topical formulations due to its high efficacy and prolonged residual activity (3-4). When administered at recommended therapeutic doses, indoxacarb is considered relatively safe, reducing pruritus, preventing vector-borne diseases, and improving animal welfare. Nonetheless, its use should remain under veterinary supervision to minimize risks of toxicity (7).

Table 6: Effects of indoxacarb on liver and brain AChE activity at doses (700 and 900 mg/kg) B.W. orally in mice after 4 and 24 h

Tissue	Treatment	4 h AChE Activity (Δ pH)	Inhibition %	24 h AChE Activity (Δ pH)	Inhibition %
Liver	Control (D.W.)	0.116 $\pm$ 0.007		0.13 $\pm$ 0.005	
	700 mg/kg	0.086 $\pm$ 0.012*	25.9%	0.094 $\pm$ 0.010	19.0%
	900 mg/kg	0.080 $\pm$ 0.007* ^a	31.0%	0.082 $\pm$ 0.006*	29.3%
Brain	Control (D.W.)	0.308 $\pm$ 0.012		0.31 $\pm$ 0.006	
	700 mg/kg	0.186 $\pm$ 0.007*	39.6%	0.220 $\pm$ 0.008*	28.6%
	900 mg/kg	0.156 $\pm$ 0.006* ^a	49.4%	0.188 $\pm$ 0.007*	39.0%

Values = mean $\pm$ SD (n=30). (*) indicates significant difference compared control ($P \leq 0.05$) One-way ANOVA. (a) represents significant intergroup differences at ($P \leq 0.05$) One-way ANOVA. % Inhibition calculated as: [(Control - Treated)/Control] $\times$ 100%.

The oral LD₅₀ of indoxacarb in mice was calculated at 1292.25 mg/kg body weight using the Up-and-Down Method (20). This value lies within the regulatory range of 1160–1730 mg/kg B.W. reported for mice (2,30), confirming that the present results are consistent with established toxicological classifications that consider indoxacarb moderately toxic (31,32). Acute signs of poisoning appeared within 10–45 minutes post-administration and included abnormal posture, dysphagia, ataxia, convulsions, rolling, respiratory arrest, and mortality at high doses (33). Comparable findings have been reported in previous studies, although strain-dependent differences were observed, with one study noting a lower LD₅₀ of 1098 mg/kg B.W. in Wistar rats (34). Such variability may be attributed to differences in animal strain, sex, experimental conditions, or compound purity.

Administration of indoxacarb at doses of 700 and 900 mg/kg B.W. induced acute neurotoxic symptoms, including body arching, facial and nasal scratching, piloerection, ataxia, hind limb paralysis, and convulsions. The severity increased in a dose-dependent manner, as toxicity scores rose from 15 at 700 mg/kg to 24 at 900 mg/kg. Mortality reached 20% at the higher dose within 24 hours. These findings corroborate earlier reports documenting neurological manifestations such as ataxia, seizures, and death after high-dose exposure (30,33). Such effects are primarily mediated by sodium channel blockade in neuronal cells, with possible secondary inhibition of AChE, resulting in acetylcholine accumulation and hyperexcitation of the central nervous system, followed by neuronal failure (35,36).

Biochemical analysis revealed a significant elevation of plasma ALT, AST, and ALP 24 hours post-treatment. These increases indicate hepatocellular damage and oxidative stress triggered by indoxacarb metabolism. ALT, being liver-specific, directly reflects hepatocyte injury, whereas AST elevation may stem from both hepatic and mitochondrial damage, and possibly muscle injury. ALP elevation suggests cholestatic effects, potentially due to bile duct inflammation or obstruction. These results align with previous studies

reporting liver dysfunction, increased oxidative stress, and disruption of antioxidant defenses following pesticide exposure (37–41).

A marked increase in blood glucose levels (40–70%) was observed, consistent with acute hyperglycemia caused by pesticide exposure. This effect is attributed to AChE inhibition by the active metabolite DCJW, leading to acetylcholine accumulation and subsequent release of stress-related hormones such as adrenaline and cortisol. These hormones stimulate glycogenolysis, lipolysis, and gluconeogenesis, thereby elevating blood glucose (42). Similar results were reported in mice showing a 40% rise in glucose within 6 hours of pesticide exposure (40). While the current study focused on acute exposure, other investigations have shown that chronic exposure to pesticides disrupts insulin secretion and signaling, induces insulin resistance, and increases glycated hemoglobin (HbA1c), highlighting the long-term metabolic risks (43–45).

Indoxacarb also caused significant inhibition of AChE activity in plasma, liver, and brain tissues, most pronounced at 4 hours post-exposure, with partial recovery by 24 hours. Brain tissue exhibited greater inhibition than the liver, reflecting the higher susceptibility of the central nervous system to indoxacarb toxicity (6). These results are consistent with previous reports showing maximal AChE inhibition within 4–6 hours, followed by recovery due to metabolic degradation of the active metabolite DCJW (6–46). Dose- and time-dependent inhibition has been confirmed in both plasma and brain tissues of mice and non-target organisms (32,47). The reversibility of inhibition after 24 hours suggests that indoxacarb does not irreversibly inactivate AChE, in contrast to organophosphates (48,49).

A clear dose–response relationship was established, with stronger effects at the higher dose (900 mg/kg). Brain AChE inhibition reached 70–80%, compared to 30–40% in the liver, reflecting the compound's high lipid solubility and ability to cross the blood–brain barrier, leading to significant neuronal oxidative stress (49,50). These findings confirm that indoxacarb exerts acute neurotoxic and hepatotoxic

effects that intensify with dosage, underscoring the importance of cautious use and precise dosing to safeguard both target and non-target organisms (45).

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التأثيرات السمية الحادة لمبيد الإندوكسكارب على بعض المؤشرات الحيوية في الفئران

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الخلاصة

هدفت هذه الدراسة إلى تقييم التأثيرات السمية الحادة لمبيد الإندوكسكارب (IDX) في الفئران من خلال متابعة العلامات السريرية، مرتبة التسمم وبعض المؤشرات الكيميائية الحيوية. يُعد الإندوكسكارب مبيدًا حديثًا من مجموعة الأوكسدايزين، يعمل عن طريق غلق قنوات الصوديوم المعتمدة على الجهد في الخلايا العصبية للحشرات، مما يؤدي إلى الشلل والموت. استُخدم في التجربة ٨١ فأرًا بوزن (٢٠–٣٢ غرام) وأعمار (٨–١٢ أسبوعًا). وقد قُدرت الجرعة الوسطية المميتة (LD₅₀) فمويًا بـ ١٢٩٢,٢٥ ملغم/كغم من وزن الجسم، يصنف المبيد متوسط السمية. أظهرت العلامات السريرية ظهورًا سريعًا لأعراض عصبية مثل الاختلاجات العصبية، الترنح، انتصاب الذيل والشعر، التدرج، شلل الأطراف الخلفية، ووضع جسم غير طبيعي خلال ١٠–٤٥ دقيقة بعد المعاملة. كانت السمية معتمدة على الجرعة إذ سُجلت درجات شدة بلغت ١٥ و ٢٤ في المجموعات المعالجة بجرعتي ٧٠٠ و ٩٠٠ ملغم/كغم على التوالي خلال ٢٤ ساعة، مما يشير إلى زيادة ملحوظة في التأثيرات العصبية عند الجرعات الأعلى. جُمعت عينات الدم من الضفيرة الوريدية العينية، كما استُخرج نسيج الكبد والدماغ للتحليل الكيميائي الحيوي. أظهر فحص بلازما الدم ارتفاعًا كبيرًا في إنزيمات AST و ALT و ALP، مما يعكس تلف الخلايا الكبدية. كما ارتفعت مستويات سكر الدم بنسبة ٦٧,٨%، وهو ما يشير إلى فرط سكر الدم الناتج عن الإجهاد الأيضي. إضافةً إلى ذلك سبب الإندوكسكارب تثبيطًا ملحوظًا في نشاط إنزيم الأسيتيل كولين إستراز (AChE) في الأنسجة. كان التثبيط أوضح في البلازما (٧٢,٤% و ٨٢,١% بعد ٤ ساعات)، مع تحسن جزئي بعد ٢٤ ساعة. في الكبد كان التثبيط معتدلًا (٣١,٠–٢٥,٩%)، بينما أظهر الدماغ حساسية أكبر (٣٩,٦–٤٩,٤%). وبالنتيجة، فإن الإندوكسكارب أحدث سمية عصبية وكبدية وأيضية تعتمد على الجرعة، مؤكداً خطورة التعرض وضرورة تطبيق إجراءات السلامة.