RESEARCH PAPER

Evaluating The Antifertility Effects of Abamectin on Female Albino Rats

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ABSTRACT
Abamectin, a widely used macrocyclic lactone pesticide, has raised concerns regarding its potential toxic effects on mammalian systems. This study aimed to evaluate the impact of abamectin on reproductive hormones, hepatic and renal biomarkers, and oxidative stress parameters in female rats. Adult female Wistar albino rats were divided randomly into two groups of ten each. The first untreated group (control) was orally given distilled water. The second (treated) group was orally administered abamectin at 2.18 mg /kg for 21 days. Abamectin exposure significantly increased serum prolactin, FSH, LH, and testosterone ($p < 0.05$), indicating endocrine disruption. Hepatic and renal biomarkers (AST, ALT, ALP, GGT, urea, and creatinine) were markedly elevated, suggesting hepatotoxicity and nephrotoxicity. Furthermore, GSH content and activities of SOD and CAT were significantly reduced in all examined tissues, accompanied by a notable rise in MDA and NO levels ($p < 0.05$), confirming oxidative and nitrosative stress.These findings suggest that the abamectin has caused infertility in female rats. Abamectin induces multi-organ toxicity in female rats through endocrine disruption, hepatic and renal dysfunction, and oxidative/nitrosative stress. Therefore, it is recommended to highlight the need for stricter regulation of abamectin use and further research into protective strategies against its toxic effects
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INTRODUCTION

Abamectin is a naturally derived macrocyclic lactone that is frequently used in aquaculture, veterinary medicine, and agriculture as a broad-spectrum insecticide and anthelmintic ((Nie et al., 2022; Shimshoni and Barel, 2025). It exhibits potent activity against diverse pests, including insects, mites, and nematodes (Xu et al., 2020). Abamectin is a macrocyclic lactone formed by the fermentation of the soil bacterium Streptomyces avermitilis and consists mainly of avermectin B1a (≥80%) and B1b (≤20%) (Jankowska et al., 2024). It works by activating glutamate- and γ-aminobutyric acid (GABA)-gated chloride channels in invertebrates, leading to neurological inhibition, paralysis, and death ((Nie et al., 2022; Xu et al., 2020). Despite its efficiency, abamectin's widespread use has contributed to the establishment of resistance, raising worries about its toxicity to non-target organisms and potential environmental dangers (Hong et al., 2023).

Abamectin is very harmful to fish, bees, mammals, and aquatic invertebrates (Chen et al., 2024; Khaldoun et al., 2025; Sanches et al., 2017; Shrestha et al., 2025). There is evidence of potential organ damage, including hepatic, renal, reproductive, and neurological consequences (Abdelhafez et al., 2024; da Silva et al., 2018). Human exposure has been associated with gastrointestinal problems, including vomiting and diarrhea (Khaldoun et al., 2025). Long-term exposure can cause acute neurological problems and damage the reproductive and central nervous systems (Huang et al., 2024; Nie et al., 2022). The lipophilic features of abamectin and its gradual degradation facilitate tissue accumulation, resulting in an excess production of reactive oxygen species (ROS) (Shrestha et al., 2025). Abamectin causes oxidative stress by increasing reactive oxygen species (ROS), suppressing antioxidant defenses, and activating mitochondrial-mediated apoptosis (Abdelhafez et al., 2024; Tahir et al., 2025). It affects redox balance by affecting the expression and activity of major antioxidant enzymes (CAT, SOD, GPx) and depleting glutathione (GSH), while providing little effect on ROS-producing enzymes (Liang et al., 2019).

Abamectin is regarded as having comparatively low toxicity to mammals (with an oral LD_{50} of approximately 11 mg/kg in rats and a dermal LD_{50} exceeding 330 mg/kg; ingestion of around 100 mg/kg can be lethal in humans) (Khaldoun et al., 2025; Zia et al., 2022). The European Food Safety Authority (EFSA, 2008) reported that abamectin is almost entirely absorbed from the gastrointestinal tract after IV or oral administration (bioavailability ~86%), based on investigations conducted mostly in laboratory animals. It is then disseminated throughout the major tissues and organs but is not readily

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absorbed into the bloodstream by mammals, and is rapidly removed from the body through the stool. However, numerous studies have indicated its potential to induce reproductive toxicity in both target and non-target organisms (Kolianchuk et al., 2023; Shrestha et al., 2025). Abamectin exposure in males has been linked to a dose-dependent reduction in sperm count, reduced motility, and structural damage to the seminiferous tubule (Bai and Ogbourne, 2016; Celik-Ozenci et al., 2011; Uwamahoro et al., 2025). Abamectin disturbs ATP homeostasis and compromises fertilization in swine spermatozoa via modifying protein kinase A (PKA) activity and tyrosine phosphorylation, disrupting important signaling pathways involved in fertilization (Uwamahoro et al., 2025). Elbetieha and Da'as, (2003) revealed that it causes testicular damage in male rats via oxidative stress, as demonstrated by enhanced oxidative stress indicators and activation of poly(ADP-ribose) polymerase (PARP).

Kolianchuk et al., (2023) conducted comprehensive investigations to evaluate the potential reproductive and developmental toxicity of abamectin. Their work included a two-generation study in rats to assess reproductive outcomes, alongside teratogenicity studies in both rats and rabbits to determine possible developmental effects. According to Kolianchuk et al., (2023), abamectin interferes with the estrous cycle, early gametogenesis, and embryonic development, all of which are extremely vulnerable to endocrine disruption. Teratogenic effects caused deformities in rats and rabbits, and developmental toxicity was observed at doses as low as 2 mg/kg/day. The European Food Safety Authority (EFSA, 2016) concluded that abamectin is unlikely to exert significant impacts on reproductive function. A No Observed Adverse Effect Level (NOAEL) of 0.4 mg/kg bw/day was pointed for reproductive toxicity, while a lower NOAEL of 0.12 mg/kg bw/day was determined for effects on offspring (EFSA, 2016). In contrast, Kolianchuk et al., (2023) reported a lower NOAEL of 0.1 mg/kg/day for reproductive toxicity and 1.0 mg/kg/day for developmental toxicity associated with fetotoxic effects.

Celik-Ozenc et al. (2016) executed a study on farmworkers in Antalya, Turkey, revealing diminished sperm maturation and motility correlated with exposure to abamectin. This is because plasma abamectin levels are higher, but serum testosterone, LH, and FSH levels stayed the same. Studies indicate that female rats appear more sensitive to abamectin toxicity than males (Abdelhafez et al., 2024; Tlili et al., 2025). Females observe greater body weight loss and oxidative stress, evidenced by elevated malondialdehyde (MDA) and reduced glutathione (GSH) and superoxide dismutase (SOD) activity (Kolianchuk et al., 2023). They also exhibit pronounced lipid peroxidation, mitochondrial dysfunction, and histopathological changes. These findings raise concerns about potential antifertility effects, which remain poorly characterized. This study aims to evaluate the antifertility potential of abamectin in female rats by assessing its impact on reproductive hormones, liver and kidney function, and oxidative/nitrosative stress across key organs, providing critical insights for comprehensive risk assessment and safer agricultural and veterinary applications.

MATERIALS AND METHODS

Chemicals

The chemical abamectin used in the current study was obtained from the company Sigma Aldrich (St. Louis, MO, USA).

Animals and Experimental Design

Adult female Wistar albino rats weighing between 150 and 200 g were recruited from the National Research Center's Animal Colony in Giza, Egypt. Initially, in the experiment, the animals were acclimated to a controlled environment in standard plastic cages for a week. Throughout the study, they were provided with a balanced rodent diet and free access to tap water. All animals were cared for by humans in accordance with the standard institutional requirements for the care and use of experimental animals established by the ethical committee of the Faculty of Science at Al-Azhar University (approval No. AZHAR 21/2024).

Adult female Wistar albino rats were divided randomly into two groups of ten each.

The first untreated group (control) was orally given distilled water for 21days.

The second (treated) group was orally treated with 2.18 mg Abamectin/kg for 21days.

Sample Collection and Serum Preparation

After the treatment period was complete, the animals were weighed and fasted during the night. Under anesthesia, blood samples were obtained from the retro-orbital plexus using sterile, heparinized glass capillaries. Whole blood was centrifuged at 3000 rpm for 10 minutes at 4 °C, and the resulting serum was aliquoted and stored at −80 °C until biochemical and hormonal analyses were performed. Following blood collection, the rats were quickly sacrificed. Afterward, the uterus, ovaries, liver, and kidneys were dissected. A sample of each organ (uterus, ovary, liver, and kidney) was rinsed with saline, dried, covered in aluminum foil, and stored at -80°C for biochemical analysis.

Biochemical determinations

Biochemical analyses were conducted using a Shimadzu UV–Vis spectrophotometer (Model 1201, Japan). Serum alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) activity were measured using accessible reagent kits from Human Gesellschaft für Biochemica and Diagnostica mbH (Germany). Serum urea, creatinine, and uric acid concentrations have been determined utilizing kits from Biodiagnostic (Dokki, Giza, Egypt).

Oxidative stress markers of utres, ovary, liver and kideny tissue

ELISA was used to measure the level of malondialdehyde (MDA), reduced glutathione (GSH), and nitric oxide (NO) in uterine, ovarian, hepatic, and renal tissues as well as the activities of superoxide dismutase (SOD) and catalase

(CAT). A Dynatech Microplate Reader (Model MR 5000; Midland, ON, Canada) was used for the measurement process. SinoGeneClon Biotech Co., Ltd. (Hangzhou, China) provided rat-specific ELISA kits, and all assays were carried out in accordance with the manufacturer's guidelines.

Determination of testosterone, LH, FSH and PRL

ELISA has been employed (Dynatech Microplate Reader Model MR 5000; Midland, ON, Canada) to measure the levels of testosterone

, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin (PRL) in serum. Rat-specific ELISA kits were obtained from SinoGeneClon Biotech Co., Ltd. (Hangzhou, China), and all processes were carried out in compliance with the manufacturer's guidelines.

Statistical analysis

One-way analysis of variance (ANOVA) was used to analyze the data, and Duncan's multiple range test was used for post hoc comparisons. At $p \leq 0.05$, differences have been considered statistically significant. Following the steps outlined by Steel and Torrie (1980), statistical analyses were carried out using the SAS software package (SAS Institute Inc., Cary, NC, USA; Copyright © 1998).

Results

Effect of abamectin on hormonal fertility

Figure 1 highlights that administration of abamectin led to a significant rise in serum reproductive hormones of adult female rats, including testosterone, LH, FSH, and prolactin, compared with the control group.

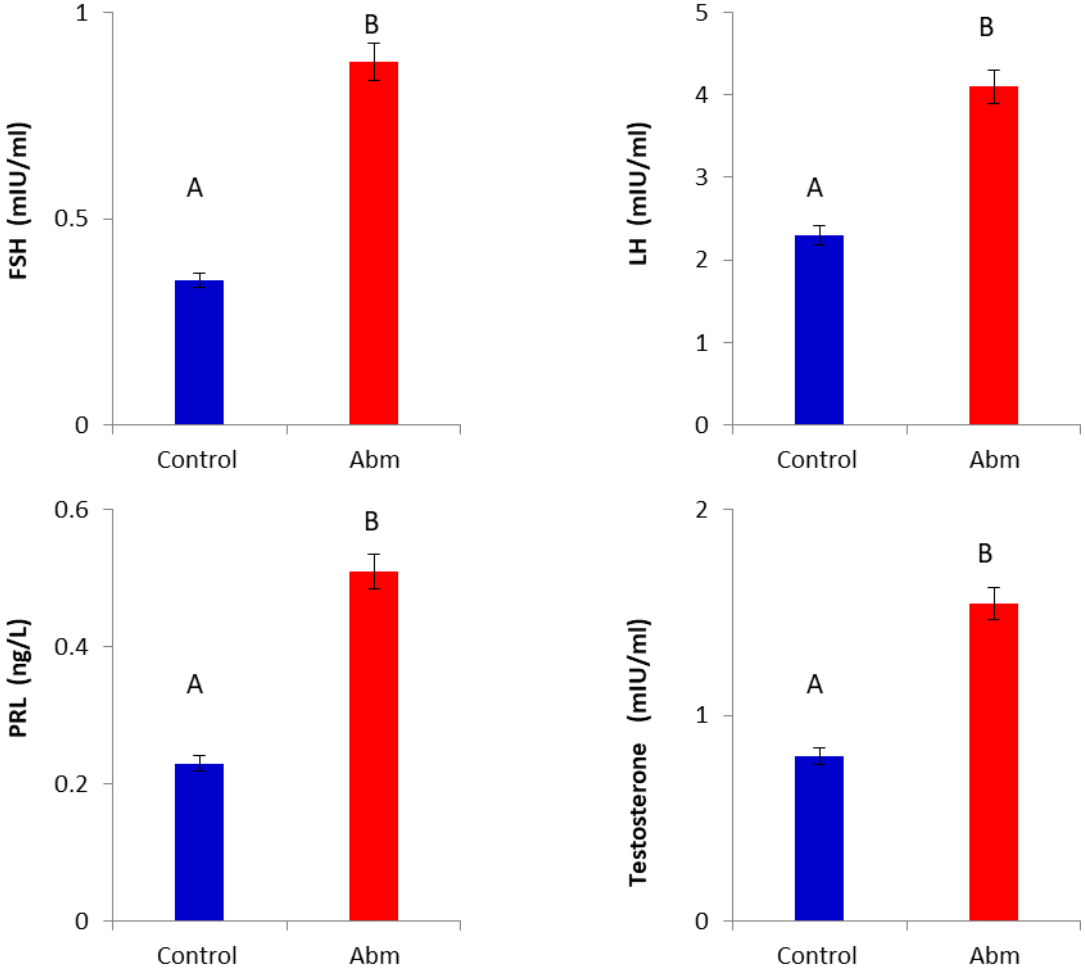

Figure (1) Figure 3. Serum hormonal fertility markers testosterone, LH, FSH and prolactin of normal and Abamectin treated female rats. The data are displayed as mean ± SE. One-way ANOVA and Duncan's post hoc test are used to determine significant differences, which are denoted by various superscript letters at p≤0.05.

Effect of abamectin on liver and kidney function

Abamectin administration significantly increased serum biochemical markers of renal and hepatic function, as shown in Table 1. In particular, there was a significant increase in ASAT, ALAT, GGT, and ALP activities when compared to the control group ($p < 0.05$). Similarly, after being exposed to abamectin, serum levels of urea and creatinine significantly increased ($p < 0.05$).

Table 1. Serum biochemical markers of normal and abamectin traeted female albino rats

	Liver and kidney function					
	ALAT	ASAT	ALP	GGT	Urea	Creatinine
Control	34.50±8.00^{A}	40.50±6.00^{A}	256±12.4^{A}	8.5±1.11^{A}	39.05±5.15^{A}	0.48±0.06^{A}
Abamectin	90.65±16.2^{B}	81.45±18.1^{B}	456±22.4^{B}	18.4±2.1^{B}	55.95±0.35^{B}	0.905±0.04^{B}

The data are displayed as mean ± SE. One-way ANOVA and Duncan's post hoc test are used to determine significant differences, which are denoted by various superscript letters at $p \leq 0.05$.

Effect of abamectin on utres, ovary, liver and kidney oxidative stress

Abamectin administration significantly altered the oxidative balance in the uterus, ovary, liver, and kidney, as Table 2 shows. This was demonstrated by a significant increase in MDA and nitric oxide NO levels ($p < 0.05$) in all tissues studied, indicating increased nitrosative stress and lipid peroxidation. In addition to a significant decrease in reduced GSH content when compared to the control group, the activities of important antioxidant enzymes, such as SOD and CAT, were also significantly decreased ($p < 0.05$).

Table 2. Utres, ovary, liver and kidney oxidative stress markers of normal and abamectin treated female rats

Hepatic oxidative stress					
	MDA	NO	SOD	CAT	GSH
Control	4.165±3.98^{C}	133.5±3.98^{C}	66.24±1.95^{C}	7.065±0.48^{C}	220.8±6.50^{C}
Abamectin	16.030±0.12^{A}	270.4±2.89^{A}	20.17±3.28^{A}	2.885±0.07^{A}	63.78±7.45^{A}
Renal oxidative stress					
	MDA	NO	SOD	CAT	GSH
Control	5.450±2.24^{A}	220.2±16.9^{A}	78.84±7.96^{A}	11.92±1.09^{A}	280.8±45.5^{A}
Abamectin	14.20±0.55^{B}	456.0±20.4^{B}	49.46±0.77^{B}	2.860±0.08^{B}	119.3±20.9^{B}
Ovary oxidative stress					
	MDA	NO	SOD	CAT	GSH
Control	4.450±0.96^{A}	174.3±42.8^{A}	54.18±10.5^{A}	10.49±2.67^{A}	263.9±48.3^{A}
Abamectin	14.94±2.38^{B}	744.2±101^{B}	39.08±7.51^{B}	2.890±0.22^{B}	130.3±25.0^{B}
Utres oxidative stress					
	MDA	NO	SOD	CAT	GSH
Control	8.015±2.25^{A}	125.3±21.0^{A}	104.0±6.44^{A}	10.09±2.59^{A}	496.8±71.5^{A}
Abamectin	69.48±15.2^{B}	827.5±38.1^{B}	35.44±3.11^{B}	2.640±0.21^{B}	187.3±11.0^{B}

The data are displayed as mean ± SE. One-way ANOVA and Duncan's post hoc test are used to determine significant differences, which are denoted by various superscript letters at $p \leq 0.05$.

DISCUSSION

Xenobiotics and environmental contaminants, particularly pesticides, represent a major threat to human health and ecological integrity. These compounds exert their harmful effects through diverse mechanisms, including direct cytotoxicity, endocrine disruption, neurodevelopmental interference, and persistent bioaccumulation (Gamil et al., 2025).

Female reproductive hormones play a crucial role in understanding pesticide toxicity, as they regulate the reproductive system and are susceptible to disruption by various pesticides. The present study demons(Kandil, 2015)trates that administration of abamectin led to statistically significant elevations in serum prolactin, FSH, LH, and testosterone in female rats. These results are in line with those of Bretveld et al., (2006); Rattan et al., (2017), who showed that abamectin can disrupt the hormonal equilibrium necessary for healthy reproduction. Multiple levels of hormone regulation, including hormone synthesis, release, transport, receptor binding, and post-receptor activation, may be affected by this interference. Abamectin's endocrine-disrupting properties and its capacity to affect the hypothalamic-pituitary-gonadal (HPG) axis, which is crucial for regulating reproductive hormones (Parandin and Behnam-Rassouli, 2017). An alteration in feedback regulation within the HPG axis is suggested by the concurrent rise in FSH and LH. Kolianchuk et al., (2023) demonstrated that exposure to abamectin in female Wistar rats resulted in changes to estrous cyclicity, suggesting a potential mechanism involving gonadotropin dysregulation. The literature describing abamectin's effect on dopaminergic pathways, which control prolactin secretion, is consistent with

elevated prolactin levels after exposure. Reproductive dysfunction, such as irregular estrous cycles and poor ovulation, is frequently linked to elevated prolactin (Kandil, 2015). Furthermore, abnormal steroidogenesis is implied by the significant rise in testosterone. In females, abnormal follicular development and ovarian function are frequently linked to elevated androgens. Abamectin in particular was demonstrated to dramatically increase testosterone and progesterone in rats in a comparison study of endocrine-disrupting insecticides, supporting its potential to disrupt steroidogenic pathways (Nassar, 2016). The notion that abamectin acts as an endocrine disruptor in female rats, influencing gonadotropin release and steroidogenesis, is substantiated by these hormonal anomalies. The current results are in line with previous evaluations of reproductive and developmental toxicity that found ovarian dysfunction and disturbed estrous cycles at comparable exposure levels (Kolianchuk et al., 2023).

The current study observed that administering abamectin significantly raised the levels of ASAT, ALAT, ALP, and GGT in treated rats compared to controls. These enzymes are well known as sensitive indicators of liver integrity and function. Their rise indicates hepatic damage, increased membrane permeability, and potential cholestatic alterations (Elgohary et al., 2025; Rahib et al., 2024). The simultaneous rise of ALAT and ASAT strongly indicates hepatocellular involvement (Mobeen et al., 2022; Rohmah et al., 2022). An increase in ALP and GGT often indicates cholestasis or bile duct blockage. GGT, in particular, is regarded as a particularly sensitive marker for hepatobiliary dysfunction and oxidative stress-induced damage (Lonardo and Ndrepepa, 2022). Several recent studies reinforce these findings. Karaboduk et al., (2025) reported that abamectin-treated rats exhibited significant increases in ALT, AST, ALP, and LDH levels. Moreover, Rahib et al., (2024) evaluated Citrus reticulata peel extract's protective effects against abamectin-induced hepatotoxicity and observed marked elevation in these enzymes along with histopathological evidence of liver injury. The rising levels of these enzymes are due to hepatocyte membrane breakdown, necrosis, and intracellular enzyme leaking into the blood (Mobeen et al., 2022). Variations in sex have been identified, with female rats being more susceptible to abamectin-induced hepatic enzyme changes and oxidative stress than male rats (Abdelhafez et al., 2024).

The current data show that abamectin administration caused a substantial increase in serum urea and creatinine levels in treated rats compared to controls, indicating compromised renal function. Urea and creatinine are traditional indicators of renal health; elevated levels usually indicate a lower glomerular filtration rate (GFR) and decreased renal clearance. Elevated levels indicate that the kidneys are unable to adequately filter and eliminate these waste products, implying compromised renal function (Rahib et al., 2024). These alterations in kidney function are consistent with prior observations. Moqbel et al., (2017) found that rats receiving intraperitoneal abamectin showed significant increases in urea and creatinine levels, as well as histological changes such as glomerular shrinkage and tubular degeneration. Similarly, Abdel-Daim and Abdellatief, (2018) found that abamectin-treated rats had significantly higher levels of kidney biomarkers and oxidative stress indicators. Furthermore, in combination pesticide studies, urea and creatinine concentrations increased considerably in rat models, indicating that abamectin contributes to renal impairment (Nasr et al., 2016). In both mammalian and aquatic models, abamectin exposure is linked to elevated serum urea and creatinine levels, indicating decreased kidney function via pathways involving oxidative stress, inflammation, and apoptosis (Rahib et al., 2024; Wu et al., 2023).

The present study provides strong evidence that abamectin exposure induces oxidative and nitrosative stress in female rats. Specifically, significantly elevated levels of MDA and NO, a marker of lipid peroxidation and nitrosative stress. Furthermore, GSH level was depleted, and the activities of SOD and CAT, key antioxidant enzymes, were reduced in the uterus, ovary, liver, and kidney. These alterations reflect a disruption of cellular redox homeostasis and increased susceptibility to oxidative damage (Abdelhafez et al., 2024; Kotb et al., 2021). GSH is a major intracellular antioxidant responsible for neutralizing reactive oxygen species (ROS) and maintaining cellular integrity. Its depletion suggests excessive ROS generation and impaired detoxification capacity (Tahir et al., 2026, 2025; Wu et al., 2023). Similarly, SOD and CAT are critical enzymatic antioxidants that protect against oxidative injury by converting superoxide radicals and hydrogen peroxide into less harmful molecules (Tahir et al., 2026; Wang et al., 2025). The observed decline in their activities indicates enzymatic inactivation or downregulation under oxidative stress conditions. Raised MDA is a well-known indicator of membrane lipid damage, but increased NO indicates reactive nitrogen species participation, which can worsen oxidative injury involving peroxynitrite production and protein nitration (Gao et al., 2023; Wang et al., 2025). These results align with prior research indicating that abamectin and other macrocyclic lactones cause oxidative stress via ROS overproduction, mitochondrial dysfunction, and lipid peroxidation. Kotb et al., (2021) found that abamectin exposure resulted in significant reductions in hepatic GSH, SOD, and CAT activity, as well as increased MDA. Aioub et al., (2022) verified similar oxidative changes in hepatic and renal tissues, whilst Adiguzel et al., (2024) found oxidative damage in reproductive organs.

CONCLUSION:

The findings of this study clearly demonstrate that abamectin exerts multi-organ toxicity in female rats through endocrine disruption, hepatotoxicity, nephrotoxicity, and oxidative/nitrosative stress. Significant alterations in reproductive hormones, elevation of liver and kidney function biomarkers, depletion of antioxidant defenses (GSH, SOD, CAT), and increased levels of malondialdehyde (MDA) and nitric oxide (NO) collectively indicate that abamectin compromises physiological

homeostasis and induces cellular damage. These effects are likely mediated by excessive reactive oxygen and nitrogen species generation, leading to lipid peroxidation, mitochondrial dysfunction, and inflammatory responses. Further research should encompass histological analysis of impacted organs, quantification of supplementary oxidative and nitrosative stress indicators, and evaluation of antioxidant gene expression to clarify the molecular underpinnings of abamectin-induced toxicity.

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