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The Impact of Neocidol on Hematological Parameters in Swiss Albino Mice

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Abstract

Neocidol, containing Diazinon, stands as a prevalent compound in the fields of plant protection and insect control for public health. Despite its historical prominence, Neocidol, classified as a non-systemic organophosphate, exerts its effects by inhibiting cholinesterase, a pivotal enzyme in nerve transmission. In light of the widespread use of Neocidol in Libya and the absence of local studies, this research endeavors to assess its impact on blood parameters and the biochemistry of female white mice. The study involves prolonged tests wherein a sublethal concentration of 15 µl Neocidol per kg of body weight is introduced through the mice's drinking water. Toxicity assessments reveal noteworthy distinctions in various blood parameters between treated and untreated mice. Treated mice exhibit elevated leukocyte and erythrocyte values, coupled with diminished MCHC and MCV values. While blood chemistry results generally align between the control and treatment groups, an exception is observed in the form of heightened Alk-phosphatase values in treated mice. In summary, despite Neocidol's historical favorability in agricultural and public health pest control, this study underscores emerging criticisms concerning its identified health and environmental implications.

Keywords: Neocidol, Diazinon; Blood parameters; Blood chemistry; Organophosphorus pesticides; Acetylcholinesterase

1 Introduction

Pesticides are chemical products intended to combat the attack of various pests of agricultural and horticultural crops as well as pests affecting livestock. Many well-known poisons have been applied at one time or another to control insects and other pests [1] sometimes quite effectively, despite the risk to operators and non-target organisms.

Organophosphate insecticides, such as Diazinon, have been recognized as highly significant within the realm of organic insecticides. Early examples of these compounds include systemic insecticides effective against aphids and spider mites, as well as the contact insecticide parathion [2]. However, both compounds have been shown to be highly toxic to humans and other mammals. Thus, research has been directed toward finding a safer, more selective, and less toxic compounds. In 1950, malathion was synthesized to represent the first example of a broad-spectrum OP insecticide associated with very low mammalian toxicity. Safer compounds such as menazon, selective systemic bedbugs, and acaricides were then monitored [1].

Diazinon stands out as a key organophosphate (OP) insecticide, introduced by the Geigy company in 1952, gaining significant prominence and ranking as the third most widely used insecticide in the United States by the 1970s. Notably, Diazinon exhibits relatively low toxicity in mammals and maintains a broad safety margin. Despite the success in developing pesticides, whether chemical or biological, for pest control, concerns arise regarding the potential for human

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and non-target organism exposure to reach unacceptable levels. The intricate ways in which humans, especially, may come into contact with pesticides create a scenario where the toxic effects of these substances have repercussions for both consumers of food products and individuals involved in pesticide production. This includes workers engaged in pesticide dispensing, farming activities, and spraying applications [3,4,5].

The impact of pesticide residues in food and water is perhaps the greatest public concern. Many insecticides, including diazinon, affect the nervous system of insects, and many also have some activity against the mammalian nervous system.

Because of its relative safety, diazinon has been used effectively against a number of soil, fruit, vegetable, and rice pests such as cabbage, carrots and fungal maggots, aphids, spider mites, thrips, and thrips. and scale insects as well as household and livestock pests. However, in most formulations, a minimum period of two weeks is required between the last application and the harvest of the edible crop. Misuse of this compound by repeated use or overuse leads to human exposure. As a result, government regulators in many countries are increasingly likely to restrict its use due to concerns about its neurotoxicity. Diazinon acts as a contact, gastrointestinal and respiratory poison. Like other OPs, the toxic effect of diazinon is achieved by inhibiting acetylcholinesterase, an enzyme required for the normal transmission of nerve impulses [6].

Although diazinon and other related compounds have been used for more than five decades, concern remains high about its possible effects on humans and other non-target organisms as well as other non-target organisms. the environment in general. Studies targeting acute toxicity, chronic toxicity, carcinogenicity, neurological effects, environmental effects, wildlife effects, and residues in food and water will continue. continue and continue [7,8,9].

Diazinon may have been around in Libya for more than three decades now, spanning a wide range of uses including household insects, public health insects, agricultural insects, poultry, and animal insects. feed. Meanwhile, with the exception of limited research on field efficacy or ecotoxicity on beneficial soil animals, very little work has been done to evaluate locally available formulations in models. vertebrate animals.

2 Material and methods

2.1. Animals

78 female Swiss albino Mus musculas mice used in the experiments were generated from several parents obtained from the animal house of the Benghazi University Faclty of Medicine. Animals were kept under laboratory conditions, where the temperature was 27 ± 2 °C and the relative humidity was 71 ± 11%. The current regulator was set up to adjust the photoperiod in the laboratory at 14 h light and 10 h dark throughout the animal rearing and experimental period.

The animals were kept in plastic cages, size (50 x 30 x 19cm), each cage kept from 4 to 6 animals. At the bottom of each cage, a little bit of sawdust is sprinkled before the mice are taken care of. The animals received the diet two to three times per day to meet their dietary needs. Clean bottles of about 350 cc are used for irrigation. Cages are washed with soap and water every two days, and fresh sawdust is placed in the cage to replace old ones that have been discarded [10].

2.2. Chemicals

The main chemical is the organophosphate pesticide, Diazinon, manufactured by Novartis Inc. Basel, Switzerland under the trade name Neocidol. This commercial preparation is designated as "600" emulsable concentrate and is obtained from the local pesticide market. The other chemicals used in this study were of technical grade with known structures and functions.

2.2.1 Prepearing the Neocidol dose, Blood collecting and testing

The female mice were divided into 13 groups of six each, their ages ranged from 21 days to one month and their weights ranged from 13 to 20 grams at the start of the experiment. Each group was housed in a separate cage. The dose of chemical chosen for this study was 15 µl/kg body weight (ppm) Neocidol. Neocidol was administered to each group in 300 ml of water in a regular mice drinking bottle. The average daily water intake for the test animals has been estimated to be about 4 ml of water, so a required daily dose of 15 µl/kg has been calculated on this basis. A total of 42 females were placed exclusively on treated water, while another 36 females continued to drink controlled water. The test animals were allowed to drink the treated water for 13 weeks during which precise observations were registerd.

At the end of week 13, the animals were weighed and anesthetized and humaenly sacrificed, and the samples were collected. 15 treated and 25 control blood collected in vials with potassium EDTA to prevent blood clotting, and was collected to measure RBC, WBC, HB, HCT, MCV, MCVH, and PLT.

The rest of the blood samples from the remaining animals were collected in a single tube with no coagulant, blood here collected and then separated into the serum center for serum urea, creatinine, electrolytes (Na+, K+) measurements AST, ALT, ALK-Phosphatase and total protein.

3 Results

3.1. Blood parameters

Means ± SD of blood parameters including WBC, RBC, HB, HCT, MCV, MCHC, and control PLT and 15 µl/kg female treated with neocidol for 13 weeks are presented in (Table 1). The treated female appeared to have significantly higher WBC values than their control female ($t = 3.49$ $p < 0.05$), where the mean ± SD of WBC were, respectively. 11.75 ± 3.11 and 7.10 ± 3.65 for treated and control female (Figure 1). In addition, the treated female also showed significantly higher RBC values ($t=3.39$ $p<0.05$) than the control RBC. The mean ± SD of erythrocytes for treated and control female mice were 9.17 ± 0.587 and 8.151 ± 0.953, respectively (Figure 2). Meanwhile, the MCV value of the female intervention group was significantly lower ($t = 3.34$ $p < 0.5$) compared to the control group.

The mean ± SD of MCV for treated and control females were 45.7 ± 2.81 and 50.54 ± 4.54 respectively (Figure 3). In the same direction, the values of MCHC were significantly higher in the control ($t = 4.25$ $p < 0.05$) 16.96 ± 1.84 compared with 14.78 ± 0.63 in the control group ($t = 4.25$ $p < 0.05$) (Figure 4).

The remaining blood parameters, HB, HCT, and PLT did not show any significant difference between the control and neocidol-treated female. The calculated t value for HB was ($t = -1.27$ $p > 0.05$) where the means ± SD were 13.28 ± 0.81 and 13.69 ± 0.80 for females, respectively treatment and control.

The calculated t value for HCT values of the control group and the treated group ($t=-0.474$ $p > 0.05$) while the mean ± SD was 40.9 ± 2.92 for the control and 41.43 ± 2.7 for the treated female. PLT was also not significant between control and treated females ($t=-0.43$ $p > 0.05$). The PLT value of treated females was slightly higher than that of means ± SD, was 1396.3 ± 224.73 for the female treated versus mean ± SD, 1343.50 ± 371.85 for control females.

Table 1 Means ± SD of blood parameters WBC, RBC HB , HCT , MCV, MCHC and PLT for control and 15µL/kg Neocidol Treated female mice after 13 weeks of exposure

Parameters	Control	Treated	T	P
WBC	7.10 ± 3.65 *	11.75 ± 3.11 *	3.49	<.05
RBC	8.15 ± 0.95*	9.17 ± 0.58 *	3.39	<.05
HB	13.69 ± 0.80	13.28 ± 0.81	-1.27	>.05
HCT	40.90 ± 2.92	41.43 ± 2.76	-0.47	>.05
MCV	50.54 ±4.54*	45.71 ± 2.81*	3.34	<.05
MCHC	16.96 ± 1.84*	14.78 ± 0.63 *	4.25	<.05
PLT	1343.50±371.8	1396.33 ± 244.7	-0.43	>.05

Means followed by the same sing are significantly different (T - test , P < .05)

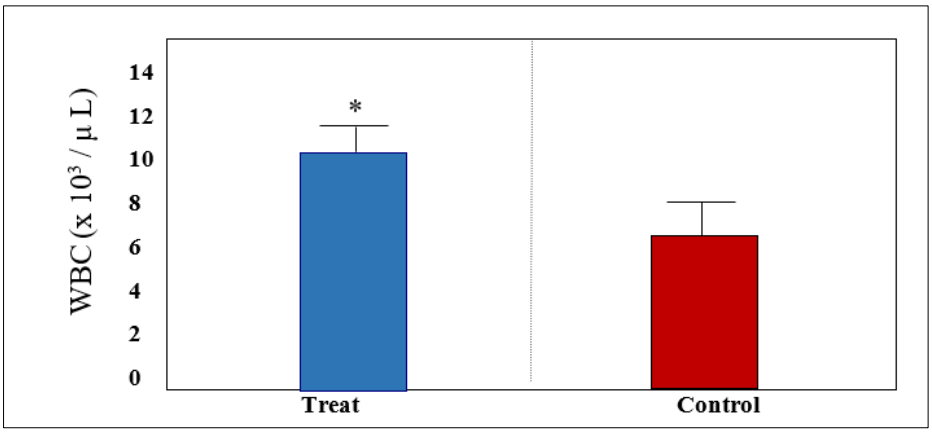

Figure 1 Means ± SD of WBC after exposure for 13 weeks.

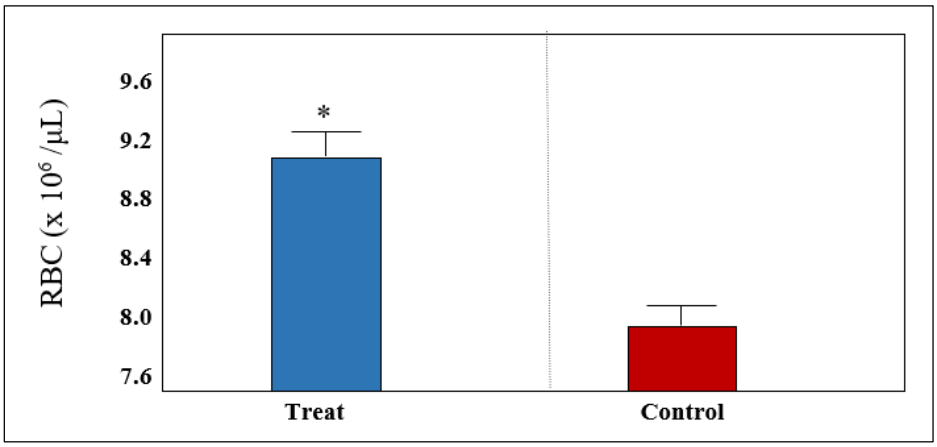

Figure 2 Means ± SD of RBC after exposure for 13 weeks.

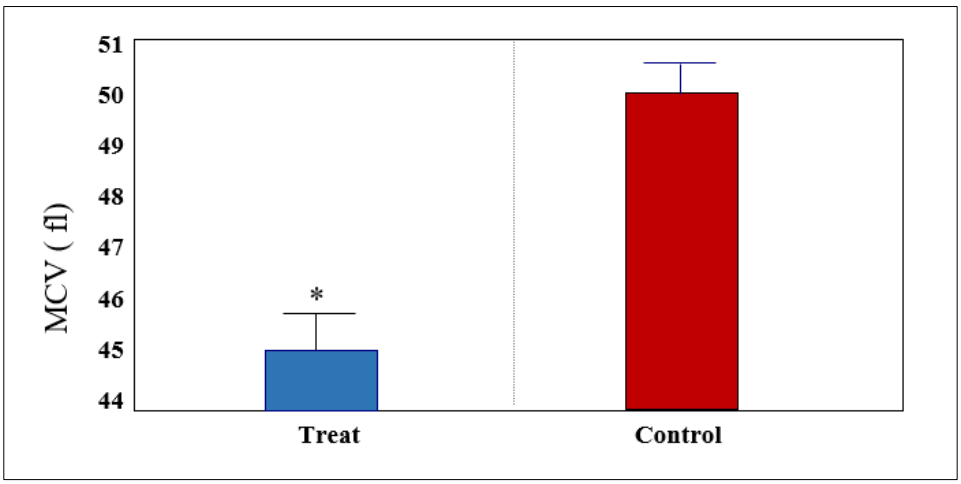

Figure 3 Means ± SD of MCV after exposure for 13 weeks.

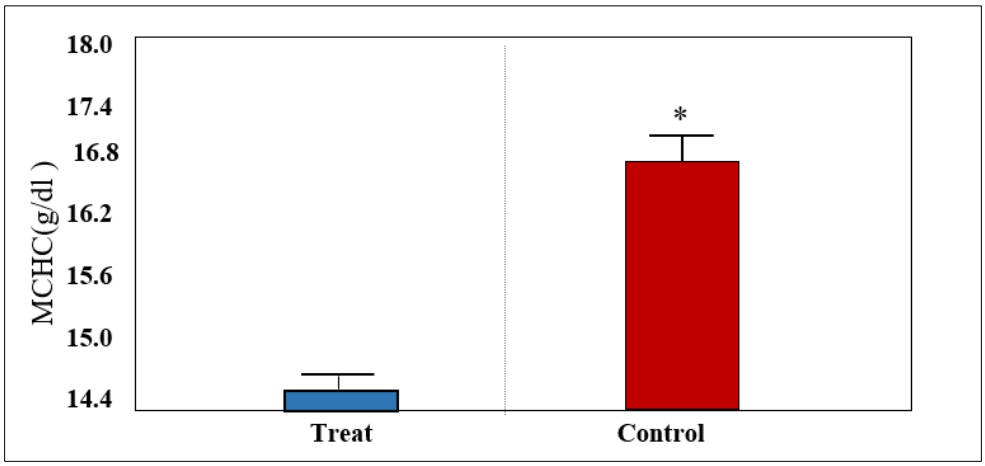

Figure 4 Means ± SD of MCHC after exposure for 13 weeks

3.2. Blood Chemistry

Means ± SD of control and blood chemistry of female mice treated with 15 µl/kg of neocidol are presented in (Table 2). Only Alk-phosphatase reported a significant difference (t = 2.22, P < 0.05) (Figure 5) between the control and treated groups of females. The mean ± SD of the control group was 126.6 ± 55.38, while that of the control group was 168.94 ± 55.45.

All other blood chemistry levels were more or less comparable in controlled and treated female. The mean ± SD of urea in the control and control groups were 33.60 ± 9.25 and 37.56 ± 7.58, respectively, showing no significant difference (t = -1.307 P > 0.05), however, the treatmemt group had a slightly higher value than the control. Creanin values were also similar in control and treated females, as the mean ± SD for both were 0.32 ± 0.11 and 0.29 ± 0.099, with (t = 0.68) at P > 0.05). the The mean ± SD of potassium (K) in the treatment females was also found to be similar to the mean ± SD of the potassium level in the control group (6.87 ± 0.71 compared with 7.23 ± 0.91), the t-value is (t-1.07P > 0.05). Blood sodium (Na) showed the same trend as (K) because no significant difference (t -1.59P > 0.05) was reported between the control mean 155.16 ± 7.38 and the mean of the treated group 160.66 ± 9.40. Potassium (K) and sodium (Na) concentrations appear to be slightly higher in treated female compared with control female.

Total protein was also comparable in the control and neocidol-treated females for 13 weeks (t = 1.79 P > 0.05), indicating a non-significant difference between the mean values. of controls was 6.50 ± 0.57 and the mean of treated female was 6.15 ± 0.48. The AST value was also not significantly different (t=1.31 P>0.05) between the control group and the neocidol-treated group after 13 weeks. However, the treated females showed a higher relative mean ± SD of 162.60 ± 80.87 compared with the mean ± SD of the control of 136.00 ± 26.93.

Table 2 The mean ± SD of blood chemistry for control and 15 µl /Neocidol Treated female mice after 13 weeks of exposure

Blood chemistry	Control / mean ± SD	Treatment / mean ± SD	T	P
Alk – phosph	126.64 ± 55.38 *	168.94 ± 55 .45*	2.22	<.05
Urea	33.60 ± 9.25	37.56 ± 7.58	1.3	>.05
Createnin	0.32 ± 0.11	0.29 ± 0.099	0.68	>.05
Potassium (K)	6.87 ± 0.71	7.23 ± 0.91	1.07	>.05
Sodium (Na)	155.16 ±7.38	160.66 ±9.40	1.59	>.05
T-protien	6.50 ± 0.57	6.15 ± 0.48	1.79	>.05
AST	136.00 ±26.93	162.60 ± 80.87	1.31	>.05
ALT	61.86 ± 10.85	65.07 ±10.65	0.80	>.05

Means followed by the same sign are significantly different.

Similar trends were also found for ALT for control and treated females, where there was no significant difference (t = 0.80 P > 0.05) between the groups. The ALT of the treated female was 65.07 ± 10.65 compared with the ALT of the control female relatively smaller than 61.86 ± 10.85.

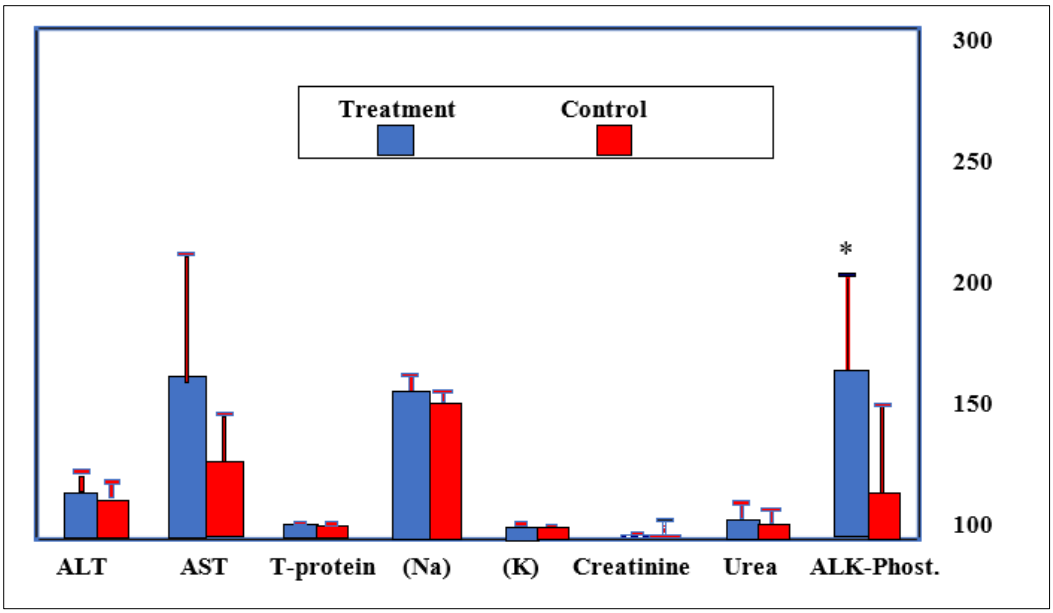

Figure 5 Means ± SD of Blood chemistery for control and Neocidol treated female mice after 13 weeks of exposure.

4 Discussion

The toxicity of diazinon as an OP compound was described by [11]. These compounds are toxic because they inhibit the enzyme acetylcholinesterase present in the nervous system. Inhibition of this enzyme leads to the accumulation of acetylcholine in nervous tissue and effectors, the main site of action being the peripheral nervous system "PNS". Diazinon itself is a moderate cholinesterase inhibitor, however, in animals, it is converted to the strong diazoxide (the oxone form) substituting oxygen for the sulfur molecule), Diazoxon is a compound that is an enzyme inhibitor strong [6].

Prolonged exposure (13 weeks) of female mice to sublethal doses of Neocidol through drinking water showed mild to moderate toxicity. The 15 µl/kg Neocidol used in this study was clearly higher than the ineffectual fixed dose of Diazinon. This discovery subsequently confirmed that of the National Research Council (1977) related to the chronic toxicity of Diazinon. As they concluded, chronic effects of the compound were observed at doses ranging from 10 µl/kg/day for pigs to 1000 µl/kg/day for rats [12].

Some effects such as inhibition of erythrocyte AchE and enzymatic reactions occur at much lower doses. Doses with no effect ranged from 0.02 mg/kg/day in humans to 0.1 mg/kg/day in rats. However, these values are based on inhibition of the enzyme - ACHE.

Therefore, the ADI (Acceptable Daily Intake) of Diazinon was set at 0.002 mg/kg/day, which was obtained by considering an inactive dose of 0.02 mg/kg/day. multiplied by a factor of safety of 10% is generally considered safe contact with humans. Sensitivity to diazinon and other diazinon analogs and their oxygen analogs may vary between individuals depending on their serum paraoxonase (PONI) concentrations [3]. PONI is an enzyme that binds to high-density lipoprotein (HDL) particles in the serum. The main role of this enzyme appears to be protection against vascular disease. However, PONI has an alternative function, namely it neutralizes toxic forms of pesticides as well as some neurotoxins such as sarin and soman.

The female blood chemistry showed a significant increase in Alk-phosphatase, with slightly higher values of urea, potassium, sodium, AST, and ALT in the treated women compared with the control, while creatine and total protein were slightly higher in the control than in the treated women. These results are in part consistent with the results of the National Research Council (1977), where they found that the values of alanine and aspartate aminotransferase, alkaline creatine kinase, and acid phosphatase were comparable in test and control, while total protein and lactate

concentrations were significantly lower in the experimental groups. On the other hand, potassium, calcium, and phosphorus showed higher concentration values in treated animals compared with controls. These plasma profile findings reveal a wide range of pronounced neurotoxic effects [12].

In another study, EPA scientists (2000) reported higher sodium and potassium values and significantly lower calcium and phosphorus concentrations in treated females compared with controls. Calcium and phosphorus ions are functionally involved in maintaining the normal excitability of the myocardium and nerves, as well as the selective permeability of cell membranes. Thus, a significant reduction in the concentration of these ions may be included in the diagnosis of symptoms caused by the toxic effects of diazinon [13].

Diazinon is classified as a restricted-use insecticide and is intended for use by professional pest control professionals. In 1988, the US EPA revoked the registration for use on golf courses and lawns due to mass bird deaths that often congregate in these areas [13].

Residential and commercial diazinon products for home use were phased out in 2001. Sales of diazinon products for home use were exceeded in 2001, in the United States, with a small supply delivered in 2002. In addition, an update on the reassessment of diazinon in Canada [14] revealed that residential and commercial diazinon products for home use will be phased out beginning in 2001, with a limited number of Small Delivered in 2002. On the other hand, domestic grade products intended for home use on lawns will be virtually phased out by the end of 2002 with a small amount carried over to 2003. At the same time, products A domestic commercial product for pest control operators to use on homes and lawns will be completed by the end of 2003, with a small amount remaining to be carried over to 2004 [14].

Diazinon will no longer be used in the United States and Canada by the end of 2004 due to its health and environmental impacts. However, the compound still seems to be widely used in many other countries, including Libya, and the author predicts that the pesticide regulator will act to limit its use in the country.

5 Conclusion

Several blood parameters of the treated females were found to be increased or decreased compared with the control females, which may indicate significant dysbiosis due to diazinon toxicity. The chemical composition of the treated females' blood showed significantly increased Alk-phosphate levels and relatively higher AST values compared with the control. Although the observed results of this study were not entirely conclusive regarding the effects of Diazinon, it is recommended that diazinon should no longer be used close to livestock or humans due to a number of reports on its impact on health and the environment.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest between the authors.

Statement of ethical approval

Animal experiments were designed and conducted in accordance with the guidelines of institutional animal ethical committee.

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