International Journal of Design & Nature and Ecodynamics
Vol. 18, No. 3, June, 2023, pp. 747-752
Journal homepage: http://iieta.org/journals/ijdne

Effect of Sub Lethal Dose of Pyrethroids Insecticide on Hepatocyte of Female Albino Mice

Saphia Ali[1*], Maysoon Hussein Zain[2]

[1] Department of Dental Industry, Basra University College of Science and Technology, Basra 61001, Iraq
[2] Community Health Department, Health and Medical Techniques College, Southern Technical University, Basra 61006, Iraq

Corresponding Author Email: saphia.aitte@stu.edu.iq

https://doi.org/10.18280/ijdne.180329

Received: 28 January 2023
Accepted: 10 May 2023

Keywords:
albino mice, hepatocytes, sub-lethal, pesticide, pyrethroids

ABSTRACT

Agricultural pesticides play an important and pivotal role in agricultural production processes in all their stages, and the superior success shown by agricultural pesticides in controlling agricultural pests has led to greater dependence on them. Pesticides accumulate in the food chain and the human environment over time in both cases, including the overuse or misuse of many of them in various fields at times. However, they are also used to treat agricultural biting and sucking insects. The current paper aims to investigate the effect of a sub lethal dose of pyrethiored insecticide on the hepatocytes of male albino mice. Based on the current results, the hepatocyte structure and tissues section clarify the effect of Permethrin insecticide, including changes such as necrosis, venous hypertrophy, and increased vacuoles. The hepatic portal and vacuoles show vacuolar degeneration, which means that the changes are severe and an indication of the toxicity of insecticide, and this difference appears to be significant compared to the control.

1. INTRODUCTION

Pesticides are chemicals that are used to protect cattle from diseases brought on by fungi, insects, mites, and rodents, to protect agricultural plants against competition from plentiful sources, and to protect humans against the insect vectors of disease-causing infections [1].

Pesticides are chemicals that are used to combat agricultural pests. Agricultural groups are exposed to pesticides when they contract various forms of worms, insects, and fungus. Pesticide use meets the needs of population increase while enhancing soil productivity and agricultural production [2].

Agricultural technology is aiming to maximise their use because the targeted pests are these pesticides' primary targets. The fact that numerous creatures, including fish, birds, and rodents, that are not the pests that are the objective of the treatment are killed by and adversely affected by most pesticides is another issue. When using pesticides with a wide toxicity spectrum, it is crucial to keep this in mind [3, 4]. Additionally, it helps to get rid of mice and rats by employing the pesticide spraying approach. As a result, these poisons build up on the plant's leaf surfaces, where mice and rats feed [5].

The liver is one of the most crucial organs since it regulates fundamental bodily functions like digestion and introduces the idea of pesticide toxicity and its potential for harm. However, because of the accumulation of pesticides in the liver, which is distinguished by its capacity to accumulate quickly and the effectiveness of this accumulation is estimated to cause pathological damage to the animal's tissues, this pesticide unfortunately undergoes toxic changes that cause it to lose its ability to store sugar, build proteins, and maintain cholesterol levels in the body [6, 7]. It has been found that the effects of permethrin on albino mice can be used as a predictor of the consequences of short- or long-term exposure on human health, which extends the harm it causes to various physiological systems.

Permethrin is an insecticide that has been studied by a number of writers [8, 9]. Synthetic substances called pyrethroids, such as 3-phenoxybenzyl and 3-(2, 2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, mimic the effects of chrysanthemum flower extracts.

Previous studies have shown the use of pesticides on a large scale to preserve agricultural yields, and their use constitutes a kind of technology for chemical compounds because they eliminate all insects that transmit disease [10]. In another report, residues of pesticides were found in water and plants; therefore, the toxicity of pesticides increased in bioaccumulation over the long term [11].

Many studies dealt with the effect of pesticides on albino mice, which are considered harmful rodents that kill plants and agricultural groups. In return, many aspects of the effect of these pesticides on mice were studied, whose effects were similar to the human effects of these toxic substances in terms of physiological, chemical, genetic, and histological aspects. For example, Onur et al. [12] indicated the effect of Parquet rodenticide, where significant changes were found in the biochemical values of AST, ALT, and creatinine, leading to an increase in these values and a decrease in erythrocytes and leukocytes in albino mice. In another study, Ali and Ibrahim [13] found the effect of malathion pesticide on the reproductive system of male laboratory albino mice, where physiological changes were observed, including necrosis, filtration, and inflammation, during treatment with pesticides. Mahgoub and El- Medany [14] also indicated that malathion caused a decrease in sperm count. As well, Mohamed et al. [15] found that physiological changes, including necrosis and degeneration in the epithelial tissue of the rat testes, occurred in the male organs of the rat during exposure to the pesticide sulfoxaflor.

There are many ways to manage insects with permethrin. Programs for controlling mosquitoes in public areas may employ products containing permethrin. Permethrin-containing products can come in the form of liquids, powders, dusts, aerosols, sprays, etc.

According to Liang et al. [16] and Hughes et al. [17], pregnant mice fed pyrethroids had offspring that weighed less and some of them more frequently acquired additional ribs than control rats. Permethrin-fed pregnant rabbits lost their foetuses more frequently, and the children who survived had less bone growth [18, 19].

This choice was made in light of permethrin's chemical makeup, how it interacts with the body, studies in which it induced tumours in mice, and indications of tumours in animals.

2. MATERIALS AND METHODS

2.1 Test samples

Female albino mice samples were purchased from the animal housing centre in the biology department and delivered to the facility Figure 1 (a). The experiment investigation was conducted in the animal house of Southern Technical University's department of community health technologies, where the samples were acclimated in a lab setting at 25°C and 12 hours of daylight. It's very important to mention here that the sun shines in the winter to renew the vitality of the animal by making it feel warm, with no side effects on the test results. The test samples were trained for two weeks in special cages and fed water from some available libitum Figure 1 (b).

Figure 1. Samples of albino mice (a) In the animal house; and (b) For adaptation to injection of dose from pesticide

2.2 Experimental design

The samples obtained from the albino mice were distributed across specialised cejats, with each cejat containing six samples distributed across five replicates (n=30 total). The samples were treated with sub-lethal concentrations of the insecticide methrin (3.5 and 5.5 mg/kg), and the treatment lasted for five weeks. The dose is given as two to three injections given intracardiacally and intraperitoneally on a weekly basis; the control group also got doses of insecticide; however, these doses were given as injections of distilled water. In preparation for a hepatic section: After the allotted amount of time has elapsed, the samples are given anaesthesia, and then they are placed on a dish for dissection. During the autopsy, the liver is removed, meticulously cleansed to remove any trace of blood, and then placed through multiple layers of ethyl alcohol that has been diluted to 70%. In addition, the completion of the tissue section method according to Hu et al. [20]. Swiss albino mice are used in studies and research because they are small in size and easy to adapt to new environmental conditions due to their rapid reproduction. They are also bred for scientific research, so they are considered an important animal model in all medical experiments and other research fields.

3. RESULTS AND DISCUSSION

In general, the histological changes that were observed in the laboratory albino mice during their exposure to the pesticide Permethrin were in as depicted in Figures 2-5. and treatment with low and high doses, where different degrees of alterations were observed in hepatocytes compared with the control, as it was determined from this study that small variations were associated with low doses.

Changes in necrosis, haemorrhage in the hepatic veins, and an increase in lipid vacuoles are indicative of the pesticide's toxicity. This study concurs with the findings of Danaei et al. [21] regarding the effect of diazinon on the liver and kidneys of rodents. In addition to what was observed in the case study, similar changes in heterotrophy, degeneration, and swelling were observed in Sun et al. [22] investigation on the effect of permethrin on rat liver cells and kidneys.

The first thing that was done when analyzing hepatocytes that had not been treated with the chemical was to look at them using an electron microscope with a magnification of (H&E) 400x and (H&E) 100x induction. This was the initial step in the examination process. The control sample, in which the liver cells are arranged as slices in a radial pattern, did not display any symptoms of modification at any point in time throughout the experiment. These strips are kept apart from one another by a series of minute spaces that are meant to represent the sinuses. The lining consists of a single layer of epithelial cells that are not linked to one another and cover the interior of the gaps. Both an increase in the number of Kupffer cells as well as Kupffer cells themselves have been recognized as indications of the illness Figure 2 (a) and (b).

According to Figure 2 (a), which illustrates the anatomy of the liver segment in the mice that were part of the control group, the arrows point to the central vein, hepatic sinusoidal cells, and Kupffer cells. This is based on the fact that the figure represents the anatomy of the liver segment. Also, take a look at Figure 2 (b), which illustrates the hepatocytes of mice that were part of the control group alongside the anatomy of the liver segment. Note the hepatic sinusoidal cells as well as the Kupffer cells, which are represented by the arrows and arrowheads.

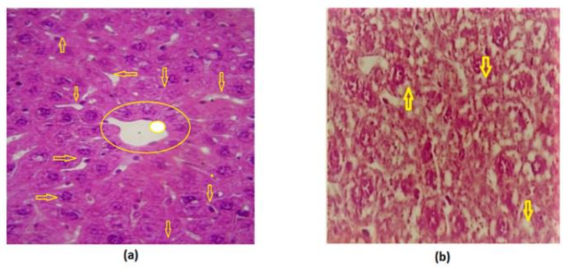

Figure 2. (a) the liver structure of mice in the control groups hepatocytes, and (b) Albino mice liver of the low dose group with vacuole degeneration in the cytoplasm of smoe hepatocytes

With reference to Figure 3, lobules in the nucleus of some hepatocytes serve as the building blocks for the formation of vacuoles in the cytoplasm of those cells. It was discovered that some hepatocytes' cytoplasm contained vacuoles Figure 3 (a) and Figure 3 (b), and that the vacuoles were surrounded by widespread necrosis (shapes). The necrosis that had developed in some of the hepatocytes extended throughout the portal area and the degenerative cells as they died off. It would appear that vacuolation in the cytoplasm of the cell is the point of origin for the chain of modifications at the level of the nucleus and cytoplasm that ultimately result in the death of the cell in those who are affected by necrosis.

In certain instances, it was seen that the shape of the nuclei shifted and became irregular, as depicted in Figure 3 (c) and Figure 3 (d), or took on the appearance of a lobule. After the cytoplasm has completely disintegrated, the nucleus may appear to be swimming in the middle of the cell or on one of its sides. At this same instant, the nuclear material inside the nucleus is decomposing and moving outward from the core towards the nuclear envelope. The membrane eventually deteriorates, which results in some hepatocytes having lobules in their nuclei, other hepatocytes developing vacuoles in their cytoplasm, larger hepatocytes, and expanded central veins, as seen in Figure 4 (a) and Figure 4 (b).

The plasma necrosis episodes stopped when the cell totally disintegrated, leaving behind the skeletal remains of dead cells Figure 3 (c) and substantial bleeding in the portal region. In addition, the emergence of additional cells that are drawn to the acid pigment (form), along with obvious necrosis and degeneration, the presence of vacuoles in the cytoplasm of hepatocytes, the enlargement of some of them (form), the loss of some of the typical shapes of hepatocytes, and the enlargement of others; and finally, the development of new cells that are drawn to the acid pigment. In compared to the group that served as the control, the histological examination of the livers of the animals that were given the high dose revealed pathological abnormalities. The congested blood vessels shown in Figure 3 (d) serve as a visual picture of the aforementioned modifications.

The cytoplasm has entirely disintegrated, as seen in Figure 4, and the nucleus may be seen swimming either in the centre of the cell or along one of its sides. Because of this process, the nuclear material of the nucleus degrades from the centre outward towards the nuclear envelope. This happens in the opposite direction of how it initially formed. Then, a piece of the membrane starts to split, which results in the formation of lobules in the nuclei of some hepatocytes and vacuoles in the cytoplasm of others, as well as the expansion of the central vein and the growth of all of the hepatocytes Figure 4 (a) and Figure 4 (b).

Figure 3 (c) depicts severe bleeding in the portal space, the formation of vacuoles in the cytoplasm of hepatocytes, and the growth of some of these vacuoles. The occurrence of plasma necrosis events led to the complete disintegration of the cell, which resulted in the formation of the remnants of dead cells.

Degeneration is also accompanied by severe necrosis, the loss of particular hepatocytes' usual shape, and the formation of new cells that adore the acid pigment (form). Necrosis is the death of healthy tissue. A histological examination of the livers of the animals who were given the high dose revealed pathological changes, which could be separated from the group that served as a control due to the presence of blood congestion Figure 3 (d).

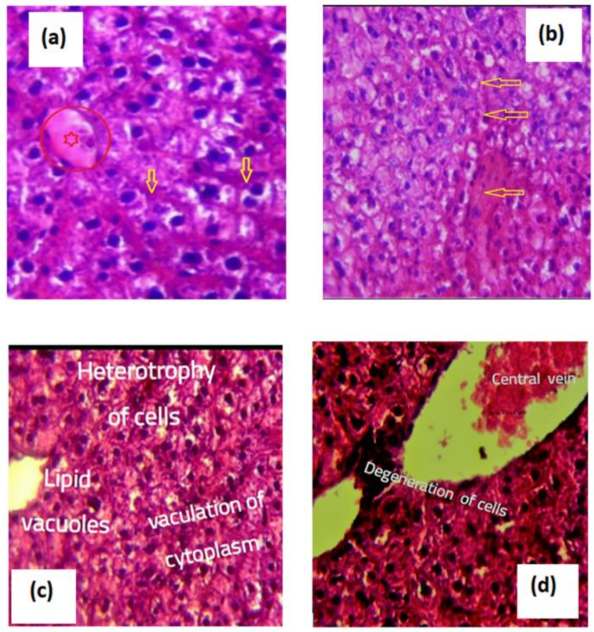

Figure 3. Hepatocytes of the low dose group with: (a) Congestion of the follicles (arrows); (b) Congestion of the follicles (arrows) and fluid in the central vein; (c) Dilatation of the central vein and infiltration of infiltration cells; and (d) Dilatation and infiltration of inflammatory cells

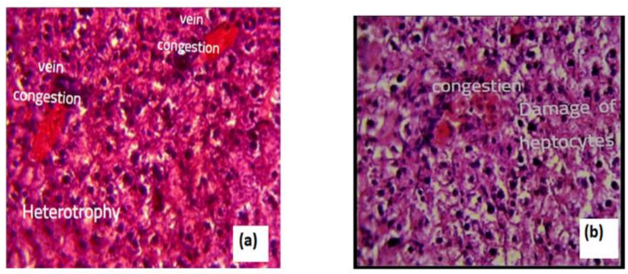

Figure 4. Mice of hepatocytes of the low dose group with hypertrophy of hepatocytes and central vein congestion (a); and (b) The cells of the liver of female mice of high-dose group with the congestion of the hepatic portal vein

The hepatocytes of mice that had been given high doses of the pesticide are shown to have swollen in Figure 5 (a). This can be attributed to the toxic effect of the pesticide, as it causes vein congestion and cell swelling. This finding is in line with the findings of Green et al. [23], who discovered that toxic substances can cause a variety of different types of cell damage. Because of its impact on the efficiency of enzymes that are responsible for the removal of toxins from the hepatocytes, in addition to the fact that it influences the analysis of the detoxification system that is present in the hepatocytes. In addition, a large number of studies provided evidence that the long-term consequences, which may be seen in their connection to a variety of cancers. It has been backed up by Noaishi and Abd Alhafez [24].

Necrosis in the cells and the appearance of some acid blood cells are indications of blood connective tissue disintegration and hemorrhagic stasis and an increase in vein congestion, and hepatocytes lose many functions for plasma protein synthesis and storage. This is a clear appearance in the destruction that occurs in the hepatocyte and many deformities that are found in it due to damage to its cellular structure, as shown in Figure 5 (b).

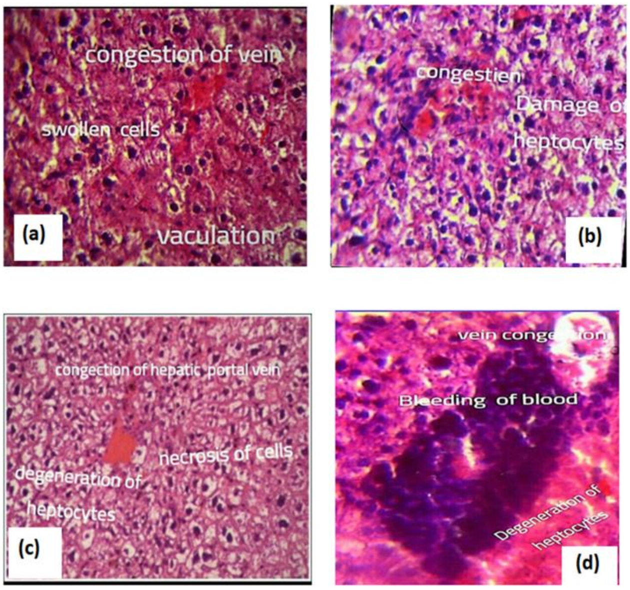

Figure 5. Hepatocytes of the high dose group shows vacuolar degeneration in the cytoplasm (a); (b) Hepatocytes of the high dose group including acid-loving liver cells; (c) Section of the liver of female mice of the high-dose group including congestion of the hepatic portal vein (asterisk) and vacuolar degeneration around the portal space (arrows) and necrosis of some hepatocytes (arrowheads); and (d) liver of female mice in high group including heptic portal vein congestion and hemorrhage (asterisk) and basophils

The hepatocytes of female laboratory albino mice that were given a high dose of the pesticide are depicted in Figure 5 (c). as having the appearance indicated there. As a result of the multiple alterations that were visible, including the death of hepatic cells and the development of necrosis, as well as congestion in the hepatic portal vein and filtration in the hepatocytes, it was clear that many changes had taken place. The author investigated how exposure to the insecticide malathion affected hepatocytes in female subjects.

Physiological activities and their negative impact on them, as well as the emergence of necrosis in the hepatocytes as a result of the effectiveness and effect of the toxic and harmful pesticide on the cellular structure of the hepatocytes, as it affects the lack of physiological function, which is the active organ for energy supply for the animal's body and also has an active immunity system, so the resistance of the animal's weight body decreased, which led to the death of the animal. Physiological.

As for the histological changes of the low dose of female mice in Figure 5 (d), they are haemorrhage, degeneration, and necrosis due to the change caused by the toxic chemical in the structural makeup of the hepatocytes, which leads to physiological ineffectiveness, which causes hepatotoxic cells, as shown by Sangha et al. [25]. These changes were caused by the change caused by the toxic chemical in the structural makeup of the hepatocytes.

Because of their striking resemblance to people, mice employed in research frequently serve as proxies for human subjects in clinical trials and scientific investigations in the fields of medicine and the biological sciences. Because of this, the environmental contaminants in which these animals live, such as weeds, fields, and other areas that feed on them, such as the leaves and roots of some plants that are routinely treated with pesticides to protect them from fungi and hazardous insects, have an effect on them. This is because these creatures live in environments that feed on them. Because of this, these animals are influenced by the food chain in some way, which is why researchers chose to utilise them in this study on the effect of the pesticide permethrin on hepatic cells in general.

Pyrethroid insecticides are often used as an insecticide in large-scale industrial agriculture applications. Permethrin is not only highly toxic to animals, such as laboratory mice, which were used to demonstrate the pesticide's effects as a biomarker for its effects on humans, but it is also highly toxic to people; it has negative effects on human health [20], including causing skin itching and eye irritation. In addition, it has been shown to have negative effects on animals, such as laboratory mice, which were used to demonstrate the pesticide's effects as a biomarker for its effects on humans.

Animals, fish, bees, Pesticides clearly affect the hepatocytes' tissues and cells after being administered in low and high doses for a total of five weeks in albino mice.

The tissue sections of the pesticide-free control exhibit no alterations to their normal structure Figure 2. (a). These alterations in male and female albino mice were depicted in Figures 3b and c and included congestion in the hepatic sinuses, hepatocyte infiltration, an increase in Kupffer, and vitreous fluid accumulation in the hepatocyte cells.

The results of the current investigation demonstrated that the risks brought on by pesticide toxicity vary in their effects depending on the dose to which an animal is exposed when compared to a control. This showed a major difference since it started with the emergence of cells with vacuolar degeneration and hypertrophy, as seen in Figure 3 (b).

Also, it should be mentioned that modest dosages also lead to alterations in tissue composition through hepatic cell degeneration and cytoplasmic congestion. Low and high dose hypertrophy of hepatocytes and vascular cytoplasmic of hepatocyte cells in female and male albino mice, follicles and fibrous, are considered indicators of pesticide toxicity in the liver tissues and the damage to the vitality of this active organ in the body, which is the centre of the majority of metabolic and immune processes and stores glycogen energy. Figure 4 (a), Figure 4 (b), and Figure 4 depicts congestion in the central vein and the infiltration of some infilimantory cells. When the congestion is brought on by an accumulation of blood in the liver as a result of the hepatic vessel that transports blood to the outside, the lowered blood pressure brought on by the congestion damages the hepatic cells because they are unable to obtain their needs from the blood.

As mentioned earlier, permethrin was administered to albino mice in low and high doses for 5 weeks; this altered the structure of their tissues and resulted in hepatocytosis in their liver organs.

As seen in Figure 5 (a), the tissue samples from the untreated control exhibit a natural structure that exhibits no alterations. Figure 4 depicts changes in the hepatocyte cells of male and female albino mice in the 3.5mg/kg dosing group, including congestion in the hepatic sinuses, hepatocyte infiltration, an increase in Kupffer, and vitreous fluid accumulation in the hepatocyte cells (a, b). This is what is implied because it started when cells with vacuolar degeneration and hypertrophic cells first appeared, as seen in Figure 5 (a) and Figure 5 (b).

On the other hand, this low dose is likewise connected to alterations in tissue composition brought on by hepatic cell death and cytoplasm buildup. Additionally, in male and female albino mice, the follicles, the fibrous tissue, and the low and high dose hypertrophy of hepatocytes are all considered indicators of the toxicity of pesticides in the liver tissues and the damage to the vitality of this active organ in the body, which is the centre of the majority of metabolic and immune processes and stores glycogen energy. This was also noted by Sangha et al. [25] in their study on the effects of pesticides on the liver, which showed congestion of blood vessels, haemorrhage, infiltration, vasodilatation, and hypertrophy, where the congestion is caused by the congestion of blood in the liver as a result of the hepatic vessel that carries blood to the outside. Figure 4 (a, b) shows congestion in the central vein and infiltration in Figure 5 (b, c).

Because the hepatic cells do not acquire their nutrition from the blood, they become destroyed. Hepatocyte enlargement, central vein dilatation, and the infiltration of inflammatory cells, certain hepatocytes, and some cell types' micronucleus lobes are all effects of congestion (Figure 5d). The findings by Sayed and Zidan [26] and Afshar et al. [27] are similar to the current outcomes. Histopathological alterations such as hepatocyte enlargement and hepatocellular degeneration were discovered by Özgöçmen and TOĞAY [28] when they examined the effects of fluopyram dosages on the liver and kidney tissues of albino mice.

4. CONCLUSIONS

In this study, which dealt with the effect of sub lethal doses of permethrin pesticide on the hepatocytes of Swiss albino mice, it was found that histological changes such as hepatotrophy and an increase in haemorrhage and congestion of the veins occurred. The study showed that low and high doses cause severe damage to the normal structure of the hepatic cells. Also, the effect depends on the amount of response, as the study showed that the toxicity of the pesticide has a clear effect on the hepatocytes of mice as an indicator of the effect on human health, especially for farmers who work on spraying pesticides on plants in addition to pesticide factory workers. Because of the use of laboratory mice as samples, they are qualified to carry out more scientific research because of their response to toxins or drugs, which are taken into account in scientific and medical research.

Pesticide toxicity is the term used to describe the presence of tissues in hepatocytes, including hepatic portal vein congestion, acute haemorrhage (asterisk), basal staining, and vacuole degeneration in mice hepatocytes from a high-dose group. The study demonstrated how pesticide poisoning affects hepatocytes. The consequences were significant in terms of damages based on the dose. Additionally, it revealed modifications to the liver cells' nuclei as well as the emergence of cytoplasmic vacuoles. Mice are therefore employed as concrete evidence of human influence with these pesticides, which reach them directly or indirectly, as chemical pollutants are thought to cause severe long-term damage.

REFERENCES

[1] Mossa, A.T.H., Mohafrash, S.M., Chandrasekaran, N. (2018). Safety of natural insecticides: Toxic effects on experimental animals. BioMed Research International, 2018. https://doi.org/10.1155/2018/4308054

[2] Klich, D., Łopucki, R., Stachniuk, A., Sporek, M., Fornal, E., Wojciechowska, M., Olech, W. (2020). Pesticides and conservation of large ungulates: Health risk to european bison from plant protection products as a result of crop depredation. PLoS One, 15(1): e0228243. https://doi.org/10.1371/journal.pone.0228243

[3] Hill, I.R. (1989). Aquatic organisms and pyrethroids. Pesticide Science, 27(4): 429-457. https://doi.org/10.1002/ps.2780270408

[4] Günal, A.Ç., Tunca, S.K., Arslan, P., Gül, G., Dinçel, A.S. (2021). How does sublethal permethrin effect non-target aquatic organisms? Environmental Science and Pollution Research, 28(37): 52405-52417. https://doi.org/10.1007/s11356-021-14475-4

[5] Okoroiwu, H.U., Iwara, I.A. (2018). Dichlorvos toxicity: A public health perspective. Interdisciplinary Toxicology, 11(2): 129. https://doi.org/10.2478%2Fintox-2018-0009

[6] Abd Ali, I.K., Ibrahim, T.A., Farhan, A.D., Abbas, M.N. (2018). Study of the effect of pesticide 2, 4-D on the histological structure of the lungs in the albino mice (Mus musculus). Journal of Pharmaceutical Sciences and Research, 10(6): 1418-1421.

[7] Basal, W.T., Ahmed, A.R.T., Mahmoud, A.A., Omar, A.R. (2020). Lufenuron induces reproductive toxicity and genotoxic effects in pregnant albino rats and their fetuses. Scientific Reports, 10(1): 1-24. https://doi.org/10.1038/s41598-020-76638-6

[8] Zhu, Q., Yang, Y., Lao, Z., Zhong, Y., Zhang, K., Zhao, S. (2020). Acute and chronic toxicity of deltamethrin, permethrin, and dihaloacetylated heterocyclic pyrethroids in mice. Pest Management Science, 76(12): 4210-4221. https://doi.org/10.1002/ps.5978

[9] Mamun, M.A.A., Rahman, A., Belal, S.H., Islam, M.A., Sarker, M.E.H., Arman, M.S.I., Ekram, A.E., Hoque, K.M.F. (2015). Histological study of the effect of malathion on liver and kidney tissues of mice model. International Journal of Pharmaceutical Sciences and Research, 6(3): 1043. http://dx.doi.org/10.13040/IJPSR.0975-8232.6(3).1043-48

[10] Hadi Chegni, S., Taghizadeh, M., Goliaei, B. (2020). A systematic review of the biophysical aspect of the effect of pesticides on the structural changes in HSA protein: the analysis of experimental and computational studies. Journal of Arak University of Medical Sciences, 22(6): 136-169.

[11] Xu, L., Guo, L., Wang, Z., Xu, X., Zhang, S., Wu, X., Kuang, H., Xu, C. (2020). Profiling and identification of biocatalyzed transformation of sulfoxaflor in vivo. Angewandte Chemie, 132(37): 16352-16358. https://doi.org/10.1002/ange.202007079

[12] Onur, B., Çavuşoğlu, K., Yalçin, E., Acar, A. (2022). Paraquat toxicity in different cell types of Swiss albino mice. Scientific Reports, 12(1): 4818. https://doi.org/10.1038/s41598-022-08961-z

[13] Ali, R.I., Ibrahim, M.A. (2018). Malathion induced testicular toxicity and oxidative damage in male mice: The protective effect of curcumin. Egyptian Journal of Forensic Sciences, 8: 1-13. https://doi.org/10.1186/s41935-018-0099-x

[14] Mahgoub, A.A., El-Medany, A.H. (2001). Evaluation of chronic exposure of the male rat reproductive system to

the insecticide methomyl. Pharmacological Research, 44(2): 73-80. https://doi.org/10.1006/phrs.2001.0816
[15] Mohamed, W.H., Ali, M.F., Yahia, D., Hussein, H.A. (2022). Reproductive effects of sulfoxaflor in male sprague dawley rats. Environmental Science and Pollution Research, 29(30): 45751-45762. https://doi.org/10.1007/s11356-022-19006-3
[16] Liang, Y.J., Wang, P., Long, D.X., Wang, H.P., Sun, Y.J., Wu, Y.J. (2020). The progressive alteration of urine metabolomic profiles of rats following long-term and low-dose exposure to permethrin. Biomarkers, 25(1): 94-99. https://doi.org/10.1080/1354750X.2019.1697755
[17] Hughes, M.F., Ross, D.G., Starr, J.M., Scollon, E.J., Wolansky, M.J., Crofton, K.M., DeVito, M.J. (2016). Environmentally relevant pyrethroid mixtures: A study on the correlation of blood and brain concentrations of a mixture of pyrethroid insecticides to motor activity in the rat. Toxicology, 359: 19-28. https://doi.org/10.1016/j.tox.2016.06.013
[18] Boumezrag, A., Hemida, H., Boumezrag, F.A., Smail, F., Cisse, S. (2021). Pathological and biological effects of treatments with lambda-cyhalothrin in rabbits. Iraqi Journal of Veterinary Sciences, 35(3): 443-450.
[19] Shah, M.K., Khan, A., Rizvi, F., Siddique, M. (2007). Effect of cypermethrin on clinico-haematological parameters in rabbits. Pakistan Veterinary Journal, 27(4): 171-175.
[20] Hu, J.X., Li, Y.F., Li, J., Pan, C., He, Z., Dong, H.Y., Xu, L.C. (2013). Toxic effects of cypermethrin on the male reproductive system: With emphasis on the androgen receptor. Journal of Applied Toxicology, 33(7): 576-585. https://doi.org/10.1002/jat.1769
[21] Danaei, G.H., Amali, A., Karami, M., Khorrami, M.B., Riahi-Zanjani, B., Sadeghi, M. (2022). The significance of thymoquinone administration on liver toxicity of diazinon and cholinesterase activity; a recommendation for prophylaxis among individuals at risk. BMC Complementary Medicine and Therapies, 22(1): 1-8. https://doi.org/10.1186/s12906-022-03806-8
[22] Sun, Y.J., Liang, Y.J., Yang, L., Long, D.X., Wang, H.P., Wu, Y.J. (2022). Long-term low-dose exposure of permethrin induces liver and kidney damage in rats. BMC Pharmacology and Toxicology, 23(1): 46. https://doi.org/10.1186/s40360-022-00586-2
[23] Green, T., Toghill, A., Lee, R., Waechter, F., Weber, E., Noakes, J. (2005). Thiamethoxam induced mouse liver tumors and their relevance to humans: Part 1. mode of action studies in the mouse. Toxicological Sciences, 86(1): 36-47. https://doi.org/10.1093/toxsci/kfi124
[24] Noaishi, M.A., Abd Alhafez, H.H. (2016). Hepatotoxicity and nephrotoxicity evaluation after repeated dose of acetamiprid in albino rats. Egyptian Journal of Chemistry and Environmental Health, 2(2): 439-452. https://doi.org/10.21608/ejceh.2016.254597
[25] Sangha, G.K., Kaur, K., Khera, K.S., Singh, B. (2011). Toxicological effects of cypermethrin on female albino rats. Toxicology International, 18(1): 5. https://doi.org/10.4103%2F0971-6580.75844
[26] Sayed, H.Y., Zidan, A.H. (2016). Histopathological and biochemical effects of acute and chronic tramadol drug toxicity on liver, kidney, and testicular function in adult male albino rats. J Forensic, 1(2): 41.
[27] Afshar, S., Farshid, A.A., Heidari, R., Ilkhanipour, M. (2008). Histopathological changes in the liver and kidney tissues of wistar albino rat exposed to fenitrothion. Toxicology and Industrial Health, 24(9): 581-586. https://doi.org/10.1177/0748233708100090
[28] Özgöçmen, M., Toğay, V.A. (2021). The effect of different doses of fluopyram on the kidney tissues of mice. Erzincan University Journal of Science and Technology, 14(3): 970-978. https://doi.org/10.18185/erzifbed.969104