

ORAL TOXICITY OF DELTAMETHRIN AND FENVALERATE IN SWISS MICE

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Abstract: The study was conducted on female and male Swiss mice with body mass of 20–30 g. The experimental animals were administered deltamethrin in concentrations of 5 mg/kg b.m. (1/10 LD₅₀) and 25 mg/kg b.m. (1/2 LD₅₀), or fenvalerate in the doses of 10 mg/kg b.m. (1/10 LD₅₀) and 50 mg/kg b.m. (1/2 LD₅₀). Pyrethroids were administered intragastrically once a day for 28 days. Parallel studies were conducted in two control groups. The following organs were taken for histologic examinations: liver, kidney, lung, heart and spleen. Blood was taken from the heart for hematologic tests. The total number of erythrocytes and leukocytes, the percentage of neutrophils and lymphocytes, as well as the level of hemoglobin and hematocrit were determined. Deltamethrin and fenvalerate caused degenerative changes in the liver and kidneys in Swiss mice. Changes were more intense in male mice which were administered deltamethrin, and in female mice which received fenvalerate. Irrespective of the dose, the pyrethroids examined stimulated erythropoiesis and synthesis of hemoglobin in male Swiss mice, while in female mice the administration of deltamethrin in the dose of 1/10 LD₅₀ resulted in the suppression of erythropoiesis and hemoglobin synthesis. Both in male and female mice, deltamethrin and fenvalerate - irrespective of the dose - caused a general increase in the number of leukocytes.

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INTRODUCTION

Pyrethroid insecticides show strong insecticidal properties, while their acute toxicity for humans and mammals is low.

Deltamethrin (S)-alpha-cyano-3-phenoxybenzyl-(1R,cis)-2,2-dimethyl-3-(2,2-dibromovinyl)-cyclopropanecarboxylate is the most toxic pyrethroid for vertebrates [18]. When administered *per os* in single doses of 20, 40 and 60 mg/kg b.m. this pyrethroid causes a significant decrease in cholinesterase activity in the blood and liver of rats, the inhibition of the enzyme being dependent not only on the dose but also on the vehiculum [6]. This preparation suspended in gum arabic, when administered to animals

per os, showed 100 times lower toxic effect compared to the use of oil or organic solvent. The effect of deltamethrin on CNS also depends on the route of administration and the substance in which it is suspended [18]. Deltamethrin shows an immunosuppressive effect [11], induces DNA fragmentation and necrotic changes in thymocytes [2].

Fenvalerate (RS)-alpha-cyano-3-phenoxybenzyl(RS)-2-(4-chlorophenyl)-3-methylbutyrate is highly toxic for fish and bees, while for birds and mammals its toxicity is low. The value of the oral LD₅₀ dose varies between 82–3200 mg/kg b.m., depending on the animal species and vehicle. Morphological changes were observed in nerve fibres in rats and mice which were administered lethal or sublethal

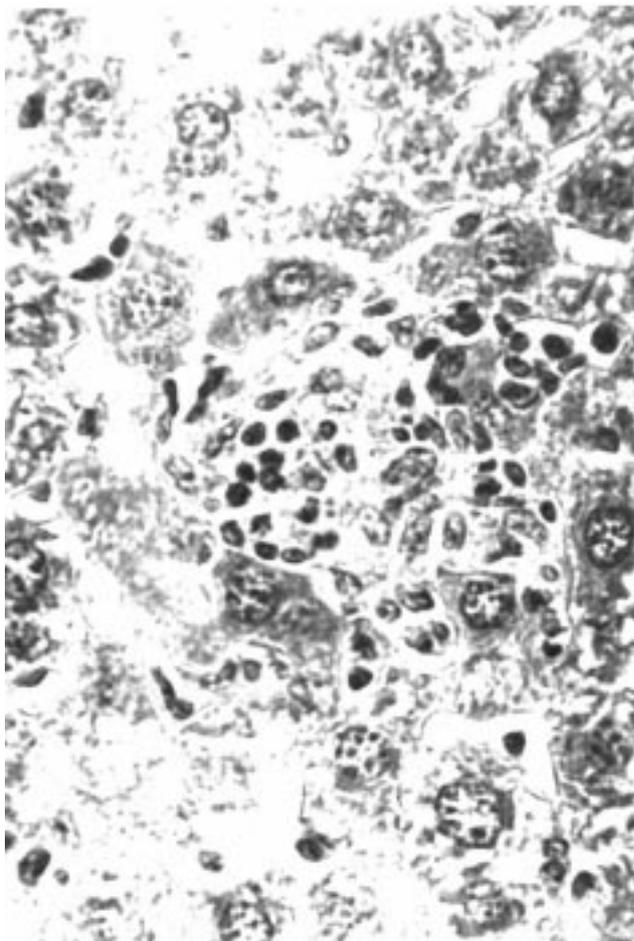


Figure 1. Liver. Fine inflammatory infiltration around individual necrotic hepatocytes and hyperplastic Kupffer cells. Deltamethrin - 25 mg/kg b.m., H+E, $\times 160$.

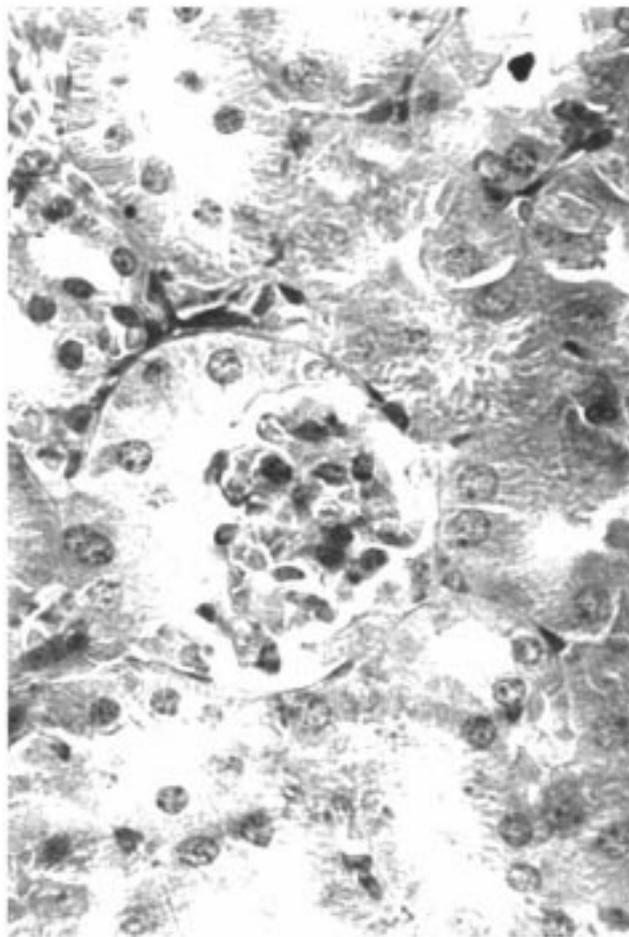


Figure 2. Kidney. Atrophy of the glomerule and hypertrophy of Bowman's capsule. Deltamethrin - 25 mg/kg b.m., H+E, $\times 160$.

oral doses of fenvalerate [21]. Fenvalerate also caused a slight increase in the number of mammary tumours in female rats [15]. Allergic reactions were noted among workers exposed to fenvalerate [5].

The aim of the study was to examine the toxicity of deltamethrin and fenvalerate administered intragastrically by stomach tube, based on histologic and hematologic tests.

Table 1. Degenerative changes in internal organs of Swiss mice poisoned intragastrically with pyrethroids, expressed as percent of total animals in a group.

Organs n=10	Deltamethrin				Fenvalerate			
	1/10 LD ₅₀		1/2 LD ₅₀		1/10 LD ₅₀		1/2 LD ₅₀	
	Male %	Female %	Male %	Female %	Male %	Female %	Male %	Female %
Liver	50	20	100	100	100	100	100	100
Kidneys	70	40	80	60	40	80	80	100
Spleen	40	30	50	50	30	50	40	60
Lungs	-	-	20	20	-	-	-	-
Heart	-	-	-	-	-	-	-	-

MATERIALS AND METHODS

The study covered 100 female and male Swiss mice, aged 8-12 weeks, with body mass of 20-30 g. The animals were fed with standard fodder LSM and watered *ad libitum* [7]. During the period of 14-days quarantine and 28 days of the experiment the mice were kept at the humidity of about 65% and a temperature of 21°C-24°C. The animals were divided into eight experimental groups and two control groups. The experimental animals (four groups of males and four groups of females) were administered deltamethrin in concentrations of 5 mg/kg b.m. (1/10 LD₅₀) and 25 mg/kg b.m. (1/2 LD₅₀), or fenvalerate administered in doses of 10 mg/kg b.m. (1/10 LD₅₀) and 50 mg/kg b.m. (1/2 LD₅₀). Pyrethroids suspended in an emulsion of gum arabic, olive oil and water in the proportion 1:2:1.5 were administered intragastrically by stomach tube in the amount of 1 ml of the solution per 100 g body mass of a mouse, once a day for a period of 28 days. The pyrethroids examined were chemically pure - min. 97.7%. Parallel studies were conducted on two control groups. One of them - Control Group I, was administered intragastrically the emulsion used for suspending the preparations examined, while the

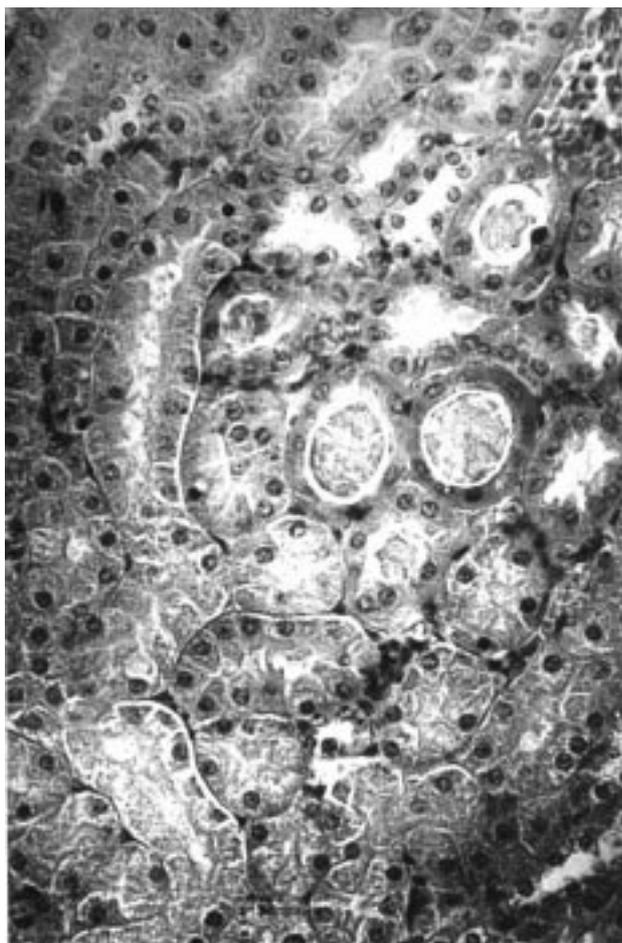


Figure 3. Kidney. Hyaline casts in nephric tubuli. Deltamethrin - 5 mg/kg b.m., H+E, $\times 80$.

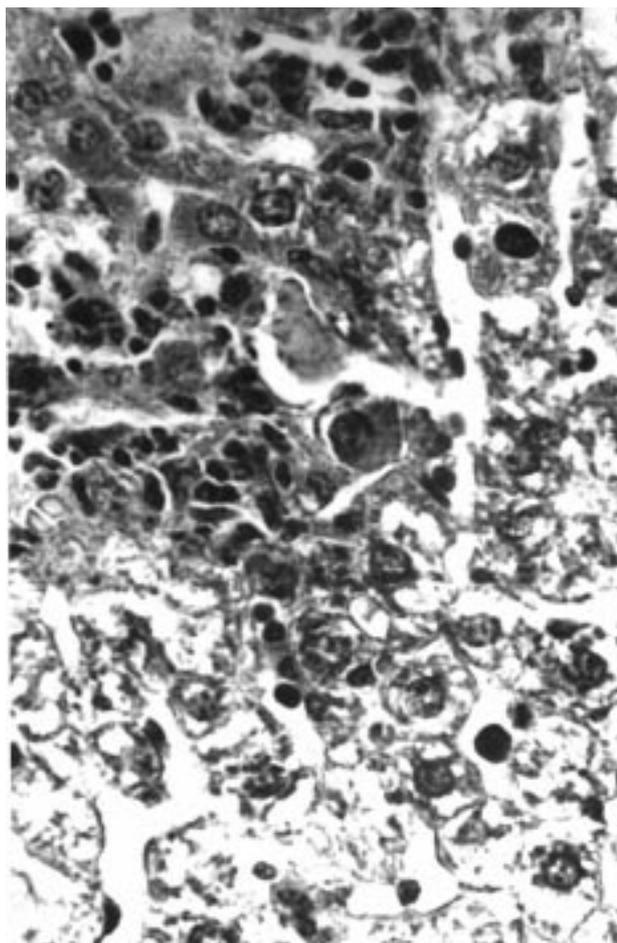


Figure 4. Liver. Degenerative changes of hepatocytes with infiltration of lymphocytes and Kupffer cells proliferation. Fenvalerate - 10 mg/kg b.m., H+E, $\times 160$.

other group - Control Group II, was not administered emulsion intragastrically during the experiment, and only kept in the same conditions as all the remaining experimental groups and Control Group I.

24 hours after the administration of the last dose of the preparation, or emulsion only, all animals were anaesthetised with ether and the following organs taken for histopathologic examinations: liver, kidney, lung, heart, and spleen. The material for the study was fixed in formalin and stained with H+E.

The blood for hematologic tests was taken from the heart. The total number of erythrocytes, leukocytes, percentage of neutrophils and lymphocytes, as well as the level of hemoglobin and hematocrit were determined.

For statistical evaluation of hematological results, independent contrast analysis was used.

RESULTS

Histologic studies

In the livers of mice exposed to a lower deltamethrin dose (5 mg/kg) degenerative changes in hepatocytes occurred in 50% of male mice and 20% of female mice

(Tab. 1). In individual animals of both sexes slight inflammatory foci were present. After administration of a higher dose of the preparation (25 mg/kg b.m.) degenerative changes in hepatocytes were observed in all animals in the study. There also occurred slight inflammatory infiltrations around single necrotic hepatocytes, composed of the hyperplastic Kupffer cells and single lymphocytes (Fig. 1).

In the kidneys, deltamethrin administered in a lower dose ($1/10 LD_{50}$) lead to the offuscatio parenchymatosa renis, both in male and female animals (70% of males, 40% of females). In single cases in male mice, hypertrophy of Bowman's capsules and hyaline deposits in renal tubuli were noted (Fig. 2, 3). After administration of a higher dose of preparation ($1/2 LD_{50}$) the above mentioned changes occurred in a slightly greater number of animals (80% of male mice and 60% of female mice).

In the lungs, after administration of a lower dose of deltamethrin ($1/10 LD_{50}$), no changes were observed. A higher dose ($1/2 LD_{50}$) led to the widening of intracellular septa and hyperaemia in 20% of mice of both sexes.

In the spleen, an obliteration of the outline of white and red pulp was noted in both sexes after administration of both doses of the preparation.

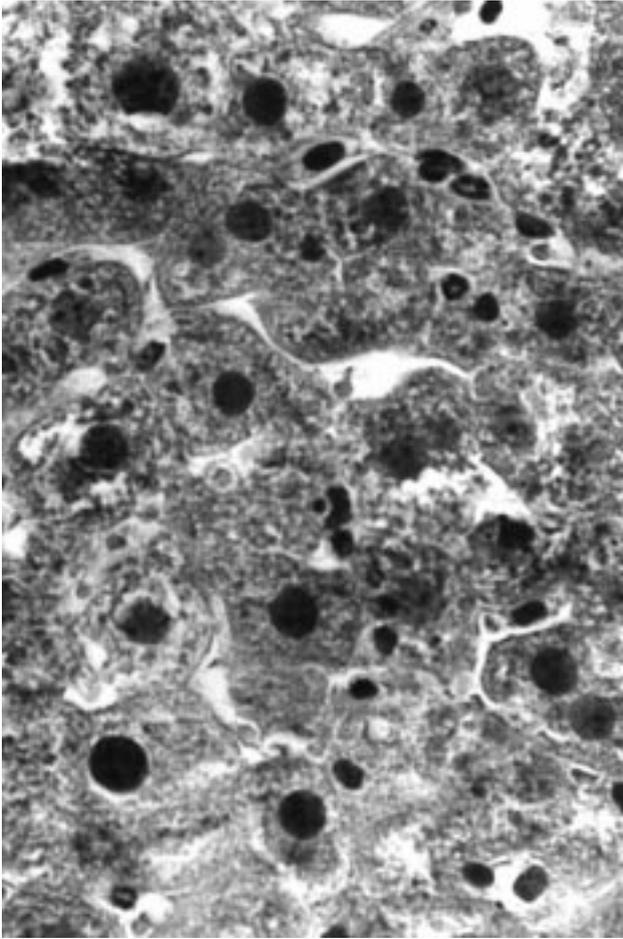


Figure 5. Liver. Nuclear anisocytosis in hepatocytes. Fenvalerate - 50 mg/kg b.m., H+E, $\times 160$.

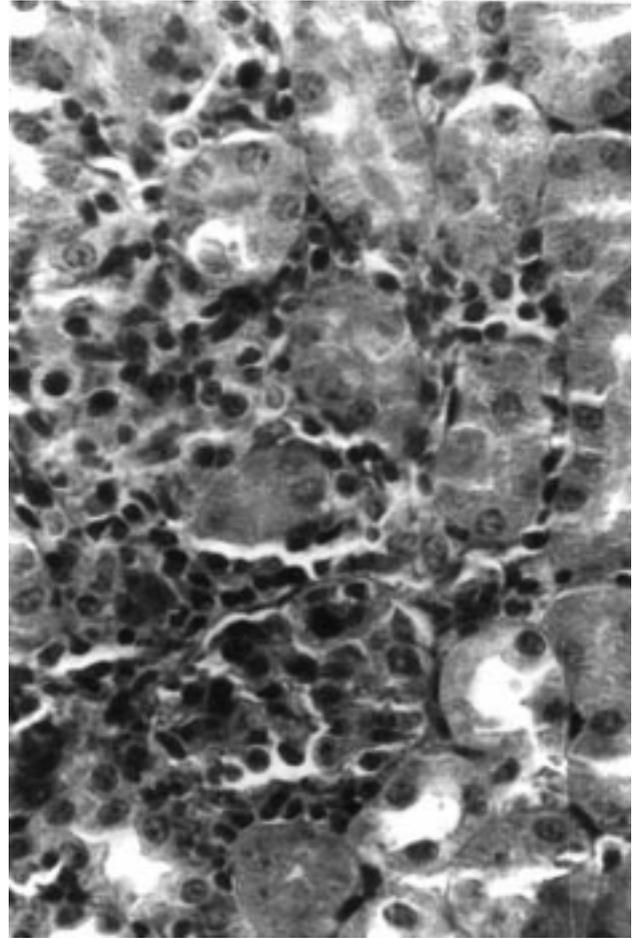


Figure 6. Kidney. Inflammatory infiltrations between the tubuli and parenchymatous degeneration of single cells. Fenvalerate - 10 mg/kg b.m., H+E, $\times 160$.

No changes were observed in the heart muscle.

After oral administration of fenvalerate, the changes concerned mainly the parenchymatous organs. Degenerative parenchymatous changes of hepatocytes occurred in the liver, most frequently around the hepatic triad or in a form of foci disseminated in the whole parenchyma. These changes were observed in all animals in the study irrespective of sex and dose of the preparation, and were accompanied by stimulation of Kupffer cells (Fig. 4). In individual cases, nuclear anisocytosis and slight lymphatic infiltrations were noted (Fig. 5).

Foci of necrosis surrounded by slight infiltrations composed of lymphocytes, macrophages and Kupffer cells were observed, especially in female animals after administration of $1/2$ LD₅₀ of the preparation.

Atrophy of single renal glomerules and hypertrophy of Bowman capsules occurred in male animals after the administration of both doses of fenvalerate. Parenchymatous degeneration of the cells in renal proximal tubuli was present in both sexes and at both doses examined. In the case of a dose of $1/10$ LD₅₀, these changes occurred in 40% of male mice and 80% of female mice, whereas after the administration of a dose of $1/2$ LD₅₀, changes were observed in 80% of male animals and 100% of female

animals (Tab. 1). Morphological changes were more intense after the administration of the higher dose of fenvalerate. Slight inflammatory infiltrations were sporadically noted between the renal tubuli (Fig. 6).

In the groups of male and female animals, after the administration of both doses of fenvalerate, the changes in the spleen were manifested as disintegration of the lymphatic papules, hence the red pulp was filled with lymphocytes (Fig. 7).

No changes were noted in the lungs and heart.

Hematologic studies

Number of erythrocytes. In Swiss mice the number of erythrocytes depends on sex, being higher in the female and lower in the male (Fig. 8, 9).

After the 28-day experiment, the number of erythrocytes in female mice of Control Groups I and II was 9.27 ± 0.335 and 9.25 ± 0.727 mln/mm³ respectively, while in male animals of Control Groups I and II this number was 8.34 ± 0.798 and 7.80 ± 0.989 mln/mm³ respectively. In female mice, the number of erythrocytes in both control groups did not differ; however, in male animals which were administered the emulsion used for suspending

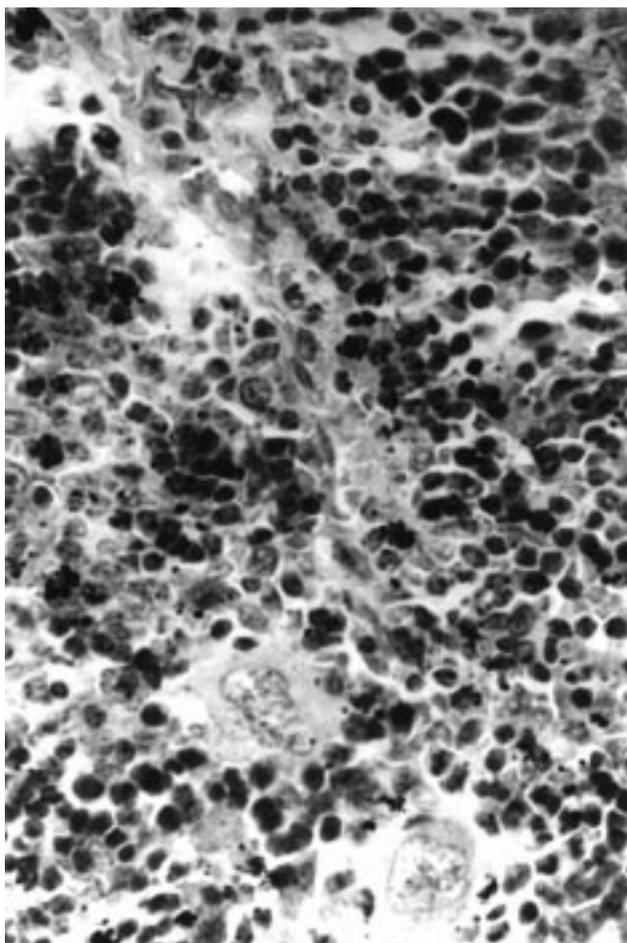


Figure 7. Spleen. Obliteration of the outline of white and red pulp with consistency of very large pale-staining cells. Fenvalerate - 50 mg/kg b.m., H+E, $\times 160$.

pesticides - Control Group I, this number was higher, compared to Control Group II. A higher number of erythrocytes in Control Group I may suggest a greater susceptibility of male animals to the stress associated with the experiment. This difference, however, was not statistically significant.

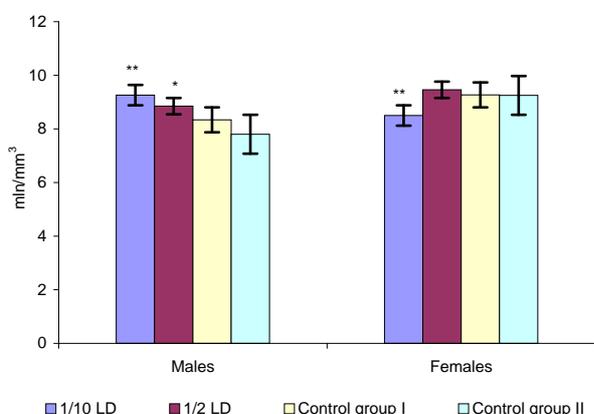


Figure 8. Number of erythrocytes in Swiss mice after deltamethrin poisoning (mean \pm S.D.). *_***: significant difference compared to Control Groups I + II; * $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$.

In mice intoxicated with deltamethrin, the effect of the pyrethroid on the number of erythrocytes differed according to sex. In male animals deltamethrin stimulated erythropoiesis, whereas in female mice it had an inhibitory effect (Fig. 8). A statistically significant increase in the number of erythrocytes was observed in male mice which were administered both doses of the pyrethroid, compared to the control groups. For the dose of 1/10 LD₅₀, a statistically significant increase in the number of erythrocytes was noted, compared to the dose of 1/2 LD₅₀ deltamethrin ($p < 0.05$).

In the group of female animals, poisoning with deltamethrin was accompanied by a statistically significant decrease in the number of erythrocytes in blood of the animals which received the dose of 1/10 LD₅₀ ($p < 0.001$). For the dose of 1/2 LD₅₀, however, the poisoning was accompanied by a slight increase in the number of erythrocytes.

Similar to deltamethrin poisoning, in poisoning induced by fenvalerate, various responses of the animals was observed depending on sex. In male mice, fenvalerate stimulated erythropoiesis, whereas in female animals it had an inhibitory effect (Fig. 9). In male Swiss mice poisoned with fenvalerate a statistically significant increase in the number of erythrocytes in blood was noted in both experimental groups.

In female animals, the poisoning with fenvalerate was accompanied by a statistically significant decrease in the number of erythrocytes in blood of all the animals which received the dose of 1/10 LD₅₀. The administration of a higher dose of the preparation resulted in only a slight decrease in the number of erythrocytes.

Hemoglobin level. The clear effect of deltamethrin poisoning in mice according to sex was also observed for hemoglobin. In male animals a stimulatory effect of the pyrethroid was noted, while in female mice - an inhibitory effect (Fig. 10).

Deltamethrin poisoning caused in male mice which received a lower dose of the preparation, a statistically

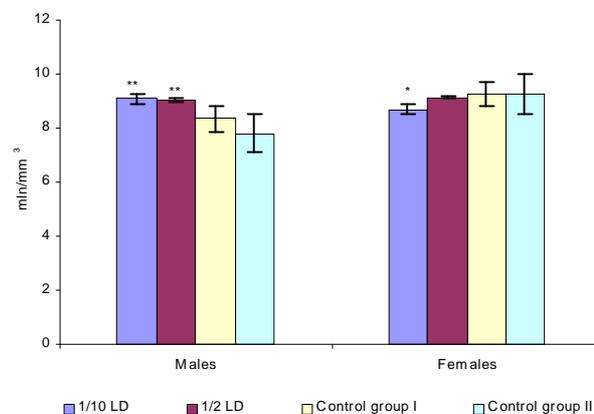


Figure 9. Number of erythrocytes in Swiss mice after fenvalerate poisoning (mean \pm S.D.). *_***: significant difference compared to Control Groups I + II; * $p < 0.01$, ** $p < 0.005$.

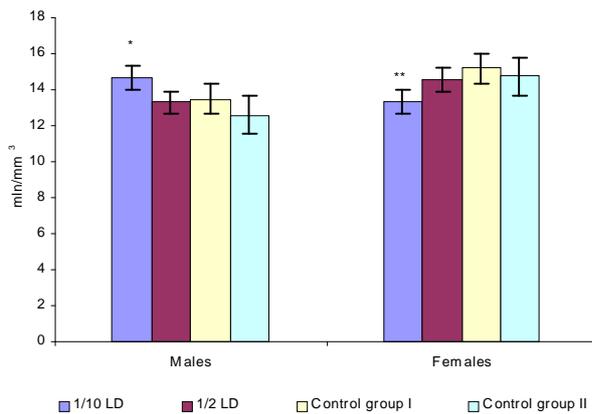


Figure 10. Hemoglobin level in Swiss mice after deltamethrin poisoning (mean \pm S.D.). *-***: significant difference compared to Control Groups I + II; * $p < 0.005$, ** $p < 0.0005$.

significant increase in the level of haemoglobin in blood, compared to the level observed in male animals of the control groups, and those poisoned with a lower dose of deltamethrin ($p < 0.05$). The administration of the dose of 1/2 LD₅₀ deltamethrin to male mice had no effect on the level of hemoglobin.

In female mice which were administered deltamethrin, a decrease in the level of hemoglobin was observed, compared to those noted in control groups, but the differences were statistically significant only after administration of a lower dose of the preparation.

The effect of fenvalerate on the hemoglobin level in mice poisoned with this pyrethroid differed according to sex. In this case, male mice seemed to be more resistant to the effect of fenvalerate than female animals, in which this pyrethroid caused a decrease in the hemoglobin level in blood (Fig. 11). No significant differences in hemoglobin level were observed between male mice of the control groups, and male animals of the experimental groups. In female mice, however, the administration of both lower and higher dose of fenvalerate was accompanied by a statistically significant decrease in the level of hemoglobin.

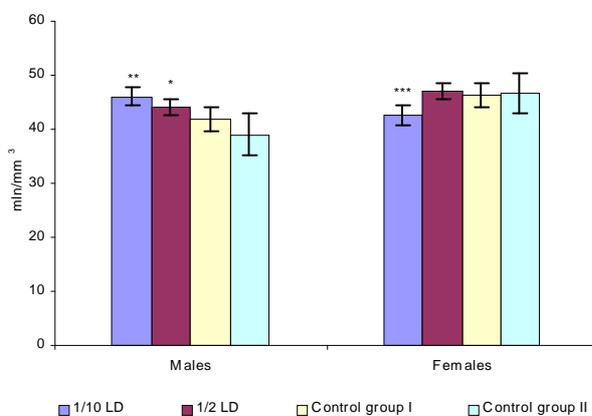


Figure 12. Level of hematocrit in Swiss mice after deltamethrin poisoning (mean \pm S.D.). *-***: significant difference compared to Control Groups I + II; * $p < 0.05$, ** $p < 0.001$, *** $p < 0.0005$.

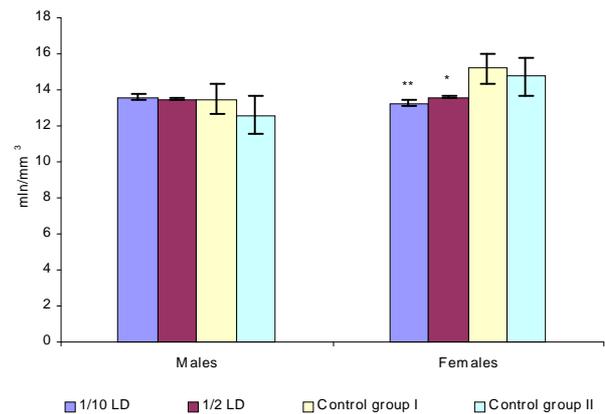


Figure 11. Hemoglobin level in Swiss mice after fenvalerate poisoning (mean \pm S.D.). *-***: significant difference compared to Control Groups I + II; * $p < 0.001$, ** $p < 0.0005$.

Level of hematocrit. The effect of deltamethrin on the level of hematocrit differed according to sex. A clear increase in the level of hematocrit was observed in male mice, while in female animals a decrease was noted (Fig. 12).

In male mice which were administered deltamethrin a significantly elevated level of hematocrit was observed, especially for the lower dose. In female animals, a statistically significant decrease in the level of hematocrit in blood was noted for the lower dose of deltamethrin, compared to the control groups and animals which received the higher dose ($p < 0.01$).

Similarly, in animals poisoned with fenvalerate, various effects of pyrethroid administration on hematocrit level were observed according to sex. In male animals a significant increase in the level of hematocrit was noted, while in female mice a significant decrease was observed, but only in the case of a lower dose. In females, statistically significant differences were also noted between both doses of fenvalerate ($p < 0.05$) (Fig. 13).

Number of leukocytes. A clear increase in the number of leukocytes in blood of mice poisoned with

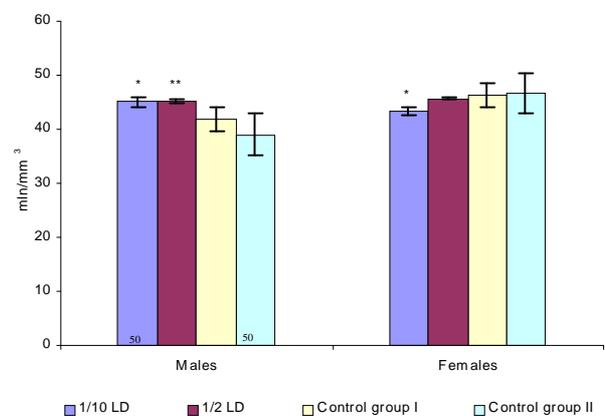


Figure 13. Level of hematocrit in Swiss mice after fenvalerate poisoning (mean \pm S.D.). *-***: significant difference compared to Control Groups I + II; * $p < 0.01$, ** $p < 0.005$.

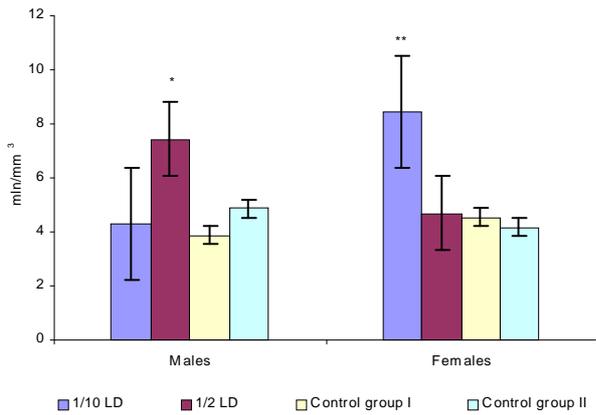


Figure 14. Number of leukocytes in Swiss mice after deltamethrin poisoning (mean ± S.D.). *_**_: significant difference compared to Control Groups I + II; * $p < 0.005$, ** $p < 0.0005$.

deltamethrin was the result of stimulation of the process of lymphopoiesis. Hence, lymphocytes constituted a dominant population of leukocytes. The stimulation of myelopoiesis was smaller.

A considerable decrease in the number of leukocytes in male mice which were administered only the emulsion (Control Group I) was mainly due to the inhibition of the process of lymphopoiesis (Fig. 14).

In male mice poisoned with a higher dose of deltamethrin, a statistically significant increase in the number of leukocytes in peripheral blood was noted, compared to the control groups and the animals which received a lower dose of the pesticide ($p < 0.001$). Among female animals, however, only a lower deltamethrin dose induced a statistically significant elevation of the number of leukocytes, compared to the animals of the control groups, as well as to those poisoned with a higher dose of the pyrethroid.

Both in male and female mice, fenvalerate poisoning was accompanied by a statistically significant elevation of

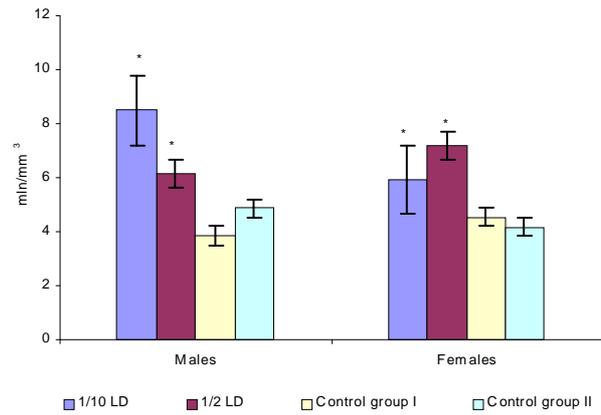


Figure 15. Number of leukocytes in Swiss mice after fenvalerate poisoning (mean ± S.D.). *: significant difference compared to Control Groups I + II; * $p < 0.05$

the number of leukocytes in peripheral blood, which was caused by the stimulation of lymphopoiesis and/or myelopoiesis, depending on sex (Fig. 15). A lower dose of fenvalerate in male mice, and a higher dose in female mice, exerted a stronger stimulatory effect.

Percentage of lymphocytes. Lymphopoiesis in mice is stimulated by deltamethrin poisoning. Stress may cause an inhibition of this process (Fig. 16).

A higher deltamethrin dose of 1/2 LD₅₀ caused a significant increase in the percentage of lymphocytes in leukocyte population of male mice, compared to the control groups and the animals which received 1/10 LD₅₀ ($p < 0.05$). In female mice, only a lower dose of deltamethrin caused a statistically significant increase in the percentage of lymphocytes.

In fenvalerate poisoning, the degree of the stimulation of lymphopoiesis may depend on the sex of the animals. Female mice show a greater activity of the lymphocytic system (Fig. 17).

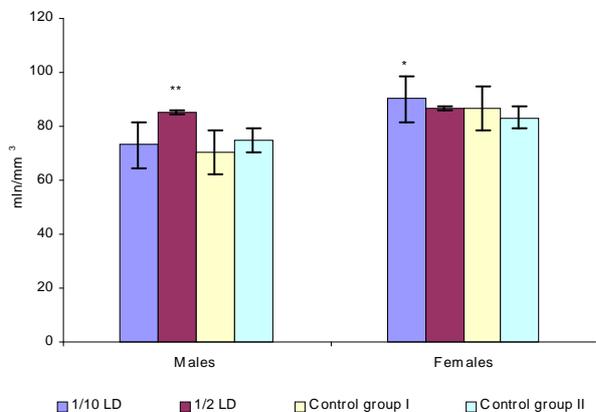


Figure 16. Percent of lymphocytes in leukocyte population of Swiss mice after deltamethrin poisoning (mean ± S.D.). *: significant difference compared to Control Groups I + II; * $p < 0.05$, ** $p < 0.005$.

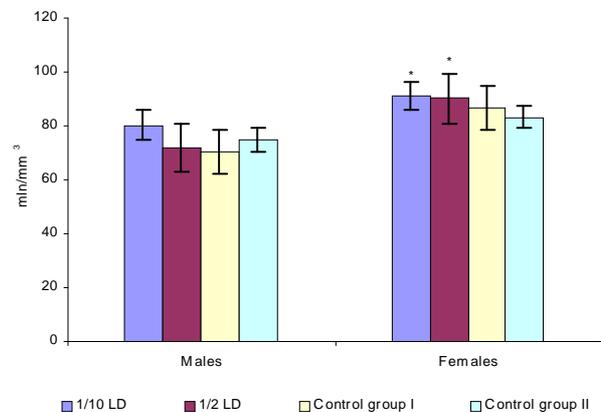


Figure 17. Percent of lymphocytes in leukocyte population of Swiss mice after fenvalerate poisoning (mean ± S.D.). *: significant difference compared to Control Groups I + II; * $p < 0.05$.

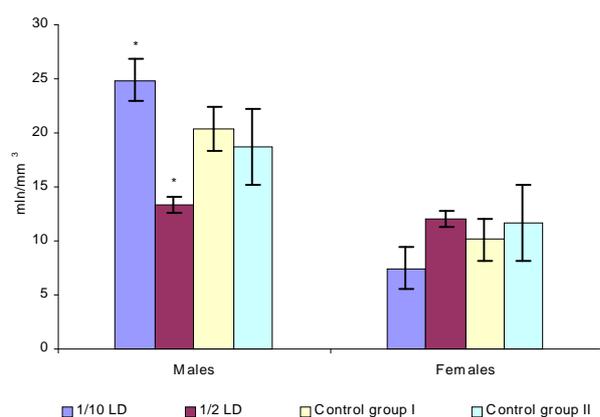


Figure 18. Percent of neutrophilic granulocytes in leukocyte population of Swiss mice after deltamethrin poisoning (mean \pm S.D.). *: significant difference compared to Control Groups I + II; * $p < 0.05$

In male mice, poisoning with a lower dose of fenvalerate was accompanied by an increase in the percentage of lymphocytes, while the administration of a higher dose resulted in a slight decrease. These differences, however, were not statistically significant. In female mice poisoned with fenvalerate, a statistically significant increase in the percentage of lymphocytes was observed for both doses.

Percentage of neutrophils. In deltamethrin poisoning, a great difference in sensitivity according to sex was manifested by a clear intensification of myelopoiesis in male mice and the lack of such an intensification among female animals (Fig. 18).

In male mice poisoned with a lower deltamethrin dose, a significant elevation of the percentage of neutrophils in leukocyte population was observed. Poisoning with a higher dose (1/2 LD₅₀) was accompanied by a significant decrease in the number of neutrophils ($p < 0.05$).

In female mice, an insignificant decrease in the percentage of neutrophils was noted for a lower deltamethrin dose, whereas a higher dose caused an insignificant increase.

In fenvalerate poisoning, a weakening of the process of myelopoiesis may occur, which was observed in female mice (Fig. 19).

In male animals poisoned with a lower dose of fenvalerate an insignificantly lower percentage of neutrophils was noted, while poisoning with a higher dose resulted in an insignificant increase.

In female mice poisoned with fenvalerate in doses of 1/10 LD₅₀ or 1/2 LD₅₀, an insignificant decrease was observed in the percentage of neutrophils.

DISCUSSION

Pyrethroids, which belong to highly active insecticides, show relatively low toxicity for humans. The studies conducted on animals indicate that the toxicity of the preparation depends on many factors, such as body

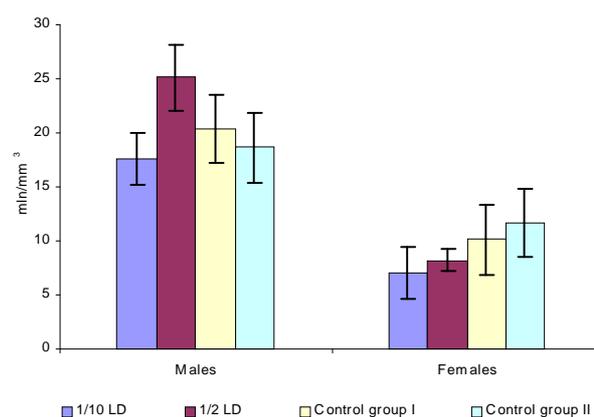


Figure 19. Percent of neutrophilic granulocytes in leukocyte population of Swiss mice after fenvalerate poisoning (mean \pm S.D.).

construction, route of administration, period of administration, substance in which the preparation was administered, etc.

In subacute and subchronic studies of pyrethroids toxicity in experimental animals which received high doses of the preparations, a decrease in body mass, as well as hypertrophy in the liver and kidneys were observed [17]. In rats poisoned with labelled pyrethroids, 90% of the initial dose was recovered from urine and faeces after 48 hours. Total excretion took place 2–4 days after administration of deltamethrin, and six days after administration of fenvalerate [13, 16]. The studies by Łukowicz-Ratajczak and Krechniak [12] showed that deltamethrin and cypermethrin did not exert a nephrotoxic effect.

An oral administration of alphacypermethrin to mice for 28 days in the doses of 1/5 and 1/2 LD₅₀ led to degenerative changes and inflammatory infiltrations in the liver and kidneys, especially after a higher dose of the preparation [10].

Our previous studies of toxicity of the mixture of deltamethrin and chlorpyrifos [8], as well as alphacypermethrin [9] administered to the skin of rats in two doses for four weeks, showed that these preparations cause parenchymatous degenerative changes in hepatocytes and offuscatio parenchymatosa renis, especially after the administration of higher doses. Changes were observed by light and electron microscopes. This study shows that deltamethrin administered intragastrically to mice in a lower dose led to the degeneration of hepatocytes in 50% of male and 70% of female animals. In individual animals of both sexes fine inflammatory foci were noted. After the administration of the dose of 1/2 LD₅₀ of the preparation, degenerative changes in hepatocytes were observed in all animals in the study. Fine inflammatory infiltrations were noted around single necrotic hepatocytes, these included hyperplastic Kupffer cells and single lymphocytes.

The administration of a lower dose of deltamethrin (1/10 LD₅₀) tends to offuscatio parenchymatosa renis both

in male and female mice - 70% and 40% respectively. In single cases in male animals hypertrophy of Bowman capsules and hyaline casts of the renal cortex were observed. After administration of a higher dose of the preparation, the above-mentioned changes occurred in a slightly larger number of animals (80% of male mice and 60% of female mice).

The administration of fluvalinate to mice in the dose of 15 mg/kg b. m. resulted in a decrease in spleen mass, and histologic changes were manifested as the obliteration of the outline of white and red pulp and disintegration of the lymphatic papules. Moreover, histologic changes were observed in the kidneys in the form of hypertrophic renal glomerule, total obliteration of Bowman capsules, and hyalinization of the renal tubules. Changes in the liver concerned fatty degeneration of hepatocytes [4]. In the studies conducted on rats, the administration of fluvalinate in the doses of 35 and 70 mg/kg b. m. caused a decrease in spleen mass, and an increase in the mass of the adrenal glands and liver [3].

Okuno *et al.* [14] in their studies of fenvalerate observed the presence of numerous microgranulomas in the liver and kidneys of mice and rats. In chronic experiments conducted on mice and rats, high doses of fenvalerate caused reduction of body mass, increase in liver mass, and proliferation of the smooth endoplasmic reticulum, affected by the enzymes which metabolize kynurenine and ribonucleic acid in hepatic cells, as well as by the induction of the activity of microsomal enzymes [1, 20, 21].

In this study, after oral administration of fenvalerate, the changes concerned mainly the parenchymatous organs. In the liver, degeneration of hepatocytes occurred, most frequently around the hepatic triad or in the form of foci spread all over the parenchyma. These changes were observed in all animals in the study irrespective of sex and preparation dose, and were accompanied by the stimulation of the Kupffer cells. In individual cases nuclear anisocytosis and fine lymphocytic infiltrations were noted. After administration of $1/2$ LD₅₀ of the preparation, necrotic foci were observed, especially in female mice, with clear infiltrations composed of lymphocytes, macrophages and Kupffer cells.

Atrophy of single renal glomerules and hypertrophy of Bowman capsules occurred in male mice after poisoning with both doses of fenvalerate. Offuscatio parenchymatosa renis was present in both sexes and after exposure to both doses examined. For the dose of $1/10$ LD₅₀, changes occurred in 40% of male and 80% of female animals, whereas after the administration of the dose of $1/2$ LD₅₀ changes were observed in 80% of male and 100% of female mice. Morphological changes were more intense after the administration of a higher dose of fenvalerate. Clear inflammatory infiltrations between the tubuli were sporadically observed.

In the spleen, the administration of fenvalerate caused the disintegration of lymphatic papules, which resulted in the obliteration of the structure of the organ in mice of both sexes.

Haematologic changes in mice poisoned with pyrethroids are manifested by a decrease in the level of hemoglobin and number of erythrocytes, and by thrombocytosis [19, 20].

In this study, in mice poisoned with deltamethrin or fenvalerate, the stimulation of erythropoiesis in male animals and its inhibition in female mice were observed. The number of erythrocytes in male mice was significantly higher, while in female mice - significantly lower, compared to the control groups. In deltamethrin poisoning, a significant increase in the level of hemoglobin was noted in male mice, and a significant decrease in female animals, whereas in fenvalerate poisoning a significant decrease in the level of hemoglobin was observed in female mice, while in male animals no changes in this level occurred.

The elevation of the haematocrit level in male mice and its decrease in female mice was noted both in deltamethrin and fenvalerate poisoning.

The number of leukocytes and the percentage of the cells of the leukocytic system were subject to various changes in deltamethrin and fenvalerate poisoning, depending on the sex of mice. An increase in the number of leukocytes resulted from the stimulation of lymphopoiesis, and to a smaller degree - myelopoiesis.

CONCLUSIONS

1. Deltamethrin and fenvalerate caused degenerative changes in the liver, kidney and the spleen of Swiss mice. In deltamethrin poisoning greater intensity of changes was observed in male animals and in fenvalerate poisoning - in female animals.

2. Irrespective of the dose, in male mice deltamethrin and fenvalerate caused:

- stimulation of erythropoiesis and synthesis of haemoglobin;
- statistically significant increase in the level of haematocrit;
- increase in the total number of leukocytes, with stimulation of myelopoiesis.

3. Irrespective of the dose, in female mice fenvalerate led to:

- suppression of erythropoiesis and synthesis of hemoglobin;
- statistically significant decrease in the level of haematocrit;
- increase in the number of leukocytes, with stimulation of lymphopoiesis.

4. In female mice deltamethrin caused:

- increase in the number of leukocytes, with stimulation of lymphopoiesis (in $1/10$ LD₅₀ and $1/2$ LD₅₀ doses);
- suppression of erythropoiesis and synthesis of hemoglobin (in a $1/10$ LD₅₀ dose);
- statistically significant decrease in the level of haematocrit (in a $1/10$ LD₅₀ dose);
- statistically significant increase in the level of haematocrit (in a $1/2$ LD₅₀ dose).

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