

## HEMATOLOGICAL ALTERNATIONS AFTER PYRETHROIDS POISONING IN MICE

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**Abstract:** The aim of the study was evaluation of the effect of  $\alpha$ -cypermethrin, deltamethrin or fenvalerate poisoning on hematological parameters in male and female Swiss mice in sub-acute poisoning. All pyrethroids examined, irrespective of the dose and sex of animals, caused an increase in the number of leukocytes in peripheral blood. In  $\alpha$ -cypermethrin poisoning no changes in the hematological parameters were observed in male mice, whereas in female animals the administration of a lower  $\alpha$ -cypermethrine dose resulted in an inhibition, and a higher dose in mobilization of hemopoietic system. In male mice poisoned with deltamethrin or fenvalerate, mobilization of the hemopoietic system was noted. No changes in the hematological parameters were observed in female mice poisoned with a higher deltamethrin dose. In female animals which were administered a lower deltamethrin dose or fenvalerate a decrease was noted in the number of erythrocytes, as well as hemoglobin and hematocrit levels.

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**Key words:**  $\alpha$ -cypermethrin, deltamethrin, fenvalerate, hematological parameters, sub-acute poisoning, blood.

## INTRODUCTION

Hemopoietic and leukocytic are 2 dynamic systems which react quickly to environmental changes, and condition the maintenance of homeostasis by an organism.

Studies conducted by Luty *et al.* have shown that during the period of intense chemical plant protection, pesticides may cause a mobilization of the hemopoietic system in humans, manifested by a higher level of values of mean numbers of erythrocytes, hemoglobin, and hematocrit, as well as the general number of leukocytes and their subpopulations: neutrophils, lymphocytes and monocytes [18].

The studies pertaining to the changes in hematological parameters in pyrethroids poisoning are random and usually concern only one sex. In animals poisoned with pyrethroids both activation and suppression of granulocytic and erythrocytic system is observed. The reaction of peripheral blood erythrocytic and leukocytic systems to pyrethroids depends on the type and dose of the compound and sex of animals [6, 7, 9, 11, 19]. Apart from these experimental

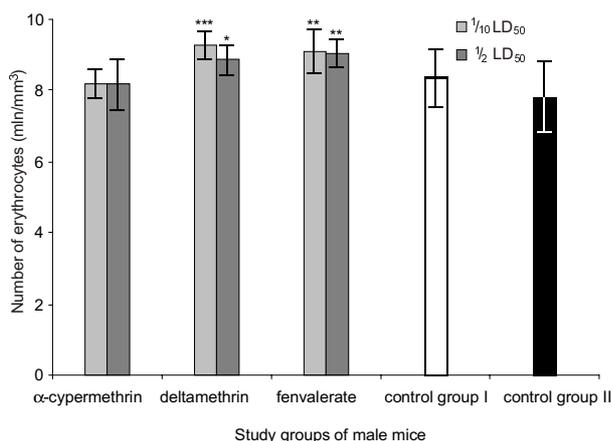
studies, there are data indicating the lack of any changes within the above-mentioned system.

Data concerning the body mass gain are also inconsistent and show a great variety according to the type of pyrethroid and duration of the experiment. Studies of the toxicity of pyrethroid compounds confirmed a decrease in body mass in animals poisoned with high doses of pyrethroids in sub-acute and sub-chronic experiment [13]. However, there are some reports where no significant differences in body weight gain were observed in animals poisoned with pyrethroids [4, 10].

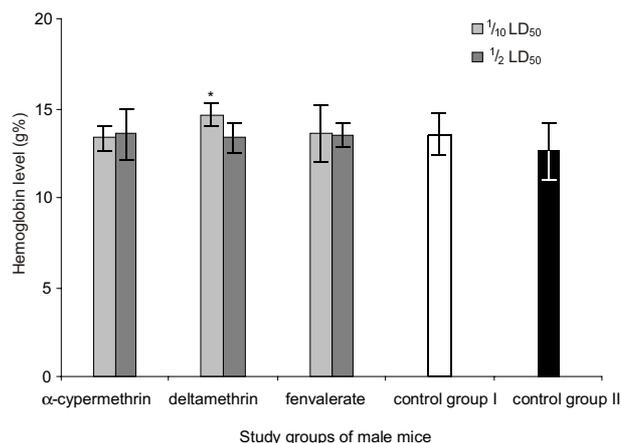
The aim of the study was the evaluation of the effect of 3 pyrethroids:  $\alpha$ -cypermethrin, deltamethrin and fenvalerate, on the selected hematological parameters in male and female Albinos Swiss mice in sub-acute poisoning *per os*.

## MATERIALS AND METHODS

The study covered 160 male and female Albinos Swiss mice aged 8–12 weeks, their body mass ranging from 20–30 g. The animals were fed with standard granulated fodder and watered *ad libitum* [1].



**Figure 1.** Number of erythrocytes in blood of male Swiss mice poisoned with pyrethroids. \* - statistically significant differences compared to Control Group I + II; \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.005$ ;



**Figure 2.** Hemoglobin level in male Swiss mice poisoned with pyrethroids. \* - statistically significant differences compared to Control Group I + II;  $p < 0.005$

The animals were divided at random into groups - 6 experimental and 2 control, 10 ( $n = 10$ ) animals in each group. Each group covered male or female mice, which were administered the pyrethroids examined ( $\alpha$ -cypermethrin, deltamethrin and fenvalerate) in 2 concentrations ( $1/10LD_{50}$  and  $1/2LD_{50}$ ) respectively:  $\alpha$ -cypermethrin and deltamethrin: 5 mg/kg b.m. and 25 mg/kg b.m.; fenvalerate: 10 mg/kg b.m. and 50 mg/kg b.m. The pyrethroids were suspended in emulsion and administered by stomach tube once daily for 28 days. Control Group I was intragastrically administered the emulsion applied for suspending pyrethroids, while Control Group II was kept only in the same breeding conditions.

$\alpha$ -cypermethrin was purchased from the Chemical Plant in Jaworzno, Poland, and deltamethrin and fenvalerate from the Institute of Organic Industry in Warsaw. The pyrethroids were chemically pure - min. 97.7%, and administered in the form of emulsion consisting of arabic gum, olive oil and water in the following proportion: 1: 2 : 1.5.

The following amounts of pyrethroids were suspended in 1 ml emulsion respectively:

- 0.5 mg and 2.5 mg  $\alpha$ -cypermethrin
- 0.5 mg and 2.5 mg deltamethrin
- 1 mg and 5 mg fenvalerate

The mice were weighed every day for 28 days prior to the administration of the pyrethroid in emulsion, or with emulsion only. The proper doses of the preparation were

administered by stomach tube in the amount of 0.1 emulsion per 10 g body mass of a mouse. The animals of Control Group I (male and female) were administered the emulsion only at the same time as the experimental animals.

Blood for the determination of selected hematological parameters was taken from the heart by heparinized syringes (heparine was obtained from Polfa, Poland).

Contrast analysis was selected as the basic method of analysis. The first stage of analyses was evaluation of the homogeneity of results in both control groups. Both control groups, i.e. Control Groups I and II, were joined by ascribing them mutual a weight in contrast analysis. Analysis was then carried out between experimental groups and the joint control group. Calculations were performed by means of SPSS statistical package.

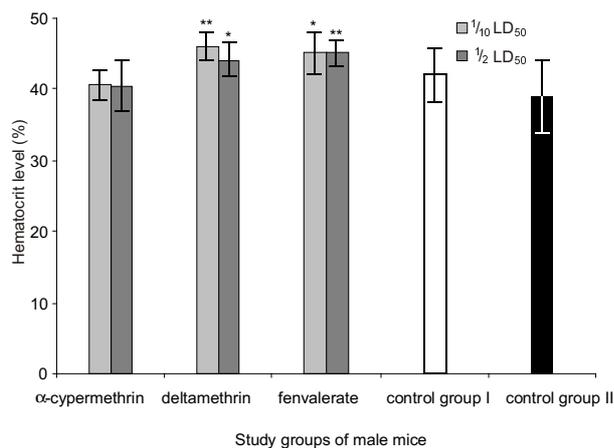
## RESULTS

**Number of erythrocytes in male mice:** In the group of mice poisoned with  $\alpha$ -cypermethrin, no significant differences in the number of peripheral blood erythrocytes were observed, compared to the control groups ( $p > 0.05$ ).

In deltamethrin poisoning, a statistically significant increase was noted in the number of erythrocytes in the blood of animals which were administered both doses of the pyrethroid, compared to the control groups.

**Table 1.** Number of leukocytes (thousand/ $mm^3$ ) in peripheral blood and leukogram in male Swiss mice poisoned with pyrethroids. \*-\*\*\* statistically significant differences compared to Control Group I + II: \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.005$

Parameters	Control group I	Control group II	Pyrethroids (%)					
			$\alpha$ -cypermethrin		deltamethrin		fenvalerate	
			$1/10 LD_{50}$	$1/2 LD_{50}$	$1/10 LD_{50}$	$1/2 LD_{50}$	$1/10 LD_{50}$	$1/2 LD_{50}$
WBC (thousands/ $mm^3$ )	$3.86 \pm 1.68$	$4.86 \pm 2.01$	$8.1 \pm 2.97^{***}$	$5.75 \pm 2.25$	$4.31 \pm 0.92$	$7.42 \pm 2.4^{***}$	$8.5 \pm 4.38^{**}$	$6.14 \pm 2.02^*$
lymphocytes (%)	$70.10 \pm 16.80$	$74.73 \pm 9.2$	$72.8 \pm 8.09$	$75.44 \pm 4.67$	$73.2 \pm 9.46$	$85.2 \pm 8.3^{***}$	$80.3 \pm 8.73$	$72.2 \pm 10.76$
neutrophils (%)	$20.4 \pm 9.18$	$18.66 \pm 7.6$	$20.2 \pm 6.25$	$18.62 \pm 5.33$	$24.9 \pm 8.85^*$	$13.3 \pm 8.15^*$	$17.6 \pm 8.18$	$25.1 \pm 11.15$
monocytes (%)	$1.9 \pm 1.10$	$1.6 \pm 1.12$	$0.8 \pm 1.13^*$	$1.44 \pm 1.33$	$0.7 \pm 0.82^*$	$0.4 \pm 0.5^{***}$	$1.2 \pm 1.03$	$0.5 \pm 1.26^*$



**Figure 3.** Hematocrit level in male Swiss mice poisoned with pyrethroids. \*\_\*\*\* statistically significant differences compared to Control Group I + II: \* $p < 0.05$ ; \*\* $p < 0.001$ ; \*\*\* $p < 0.0005$ .

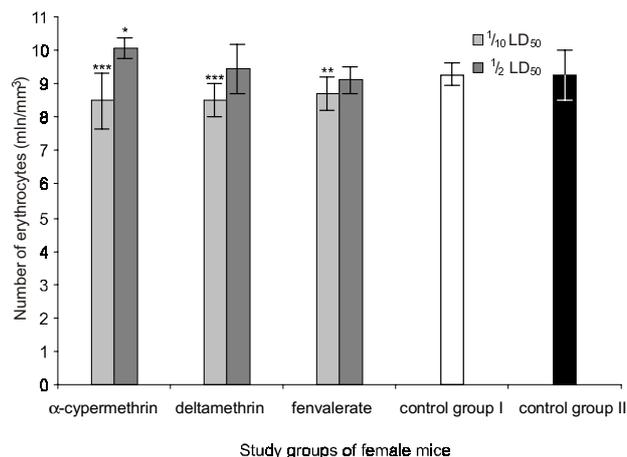
In male Swiss mice poisoned with fenvalerate, a statistically significant increase was noted in the number of erythrocytes in the blood of animals of both experimental groups, compared to the control groups ( $p < 0.005$ ) (Fig. 1).

**Hemoglobin level in male mice:** In the case of  $\alpha$ -cypermethrin and fenvalerate administration, no significant differences in the level of hemoglobin were observed between the control and experimental groups in male mice.

The deltamethrin poisoning caused a statistically significant increase in the level of hemoglobin in animals administered a lower dose of the compound, compared to the level noted in control groups ( $p < 0.05$ ). The administration of the dose of  $1/10LD_{50}$  deltamethrin did not affect the level of hemoglobin in the blood of the animals (Fig. 2).

**Level of hematocrit in male mice:** In the group of mice poisoned with  $\alpha$ -cypermethrin, no significant differences in the level of hematocrit were observed between animals of the experimental and control groups.

Poisoning with deltamethrin or fenvalerate was associated with the statistically significant elevation of hematocrit level in the blood of experimental mice, compared to the control groups (Fig. 3).



**Figure 4.** Number of erythrocytes in female Swiss mice poisoned with pyrethroids. \*\_\*\*\* statistically significant differences compared to Control Group I + II: \* $p < 0.05$ ; \*\* $p < 0.001$ ; \*\*\* $p < 0.0005$ .

**Number of erythrocytes in female mice:** The number of erythrocytes in mice poisoning with  $\alpha$ -cypermethrin was statistically significant increased after administration of  $1/2LD_{50}$  dose, and a statistically significant decreased after administration of the lower dose of the preparation, compared to the control groups. It was observed that the differences in the amount of erythrocytes in both experimental groups were also statistically significant ( $p < 0.0005$ ).

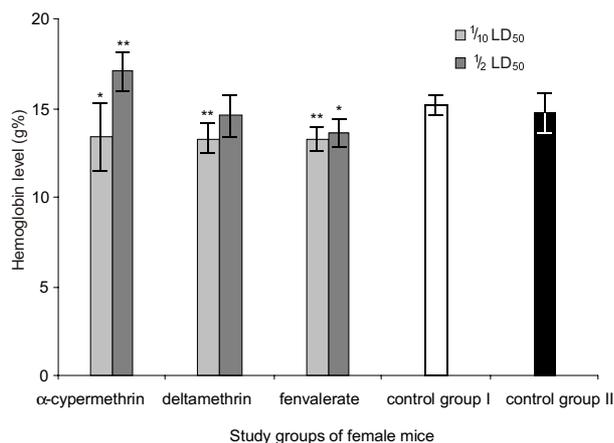
Only in mice poisoned with the lower deltamethrin dose was a decrease noted in the number of erythrocytes, compared to the level observed in the control groups ( $p < 0.0005$ ). After administration of a higher dose of the compound an insignificant increase was noted in the number of erythrocytes in peripheral blood.

Fenvalerate poisoning in female animals was accompanied by a statistically significant decrease in the number of erythrocytes in the blood of mice administered the compound in the dose of  $1/10LD_{50}$ , compared to the control groups (Fig. 4).

**Hemoglobin level in female mice:** In mice administered  $1/10LD_{50}$   $\alpha$ -cypermethrin, a statistically significant decrease was observed in the level of hemoglobin in blood, compared to control groups. The dose of  $1/2LD_{50}$   $\alpha$ -cypermethrin caused a statistically significant elevation of the level of hemoglobin.

**Table 2.** Number of leukocytes in thousand/ $mm^3$  in peripheral blood, and leukogram in female Swiss mice poisoned with pyrethroids. \*\_\*\*\* statistically significant differences compared to Control Group I + II: \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.005$ ; \*\*\*\* $p < 0.0005$

Parameters	Control group I	Control group II	Pyrethroids (%)					
			$\alpha$ -cypermethrin		deltamethrin		fenvalerate	
			$1/10 LD_{50}$	$1/2 LD_{50}$	$1/10 LD_{50}$	$1/2 LD_{50}$	$1/10 LD_{50}$	$1/2 LD_{50}$
WBC (thousands/ $mm^3$ )	4.54 $\pm$ 2.87	4.18 $\pm$ 1.89	6.96 $\pm$ 2.82*	7.5 $\pm$ 2.2***	8.4 $\pm$ 2.6****	4.68 $\pm$ 2.44	5.94 $\pm$ 2.36*	7.2 $\pm$ 3.19*
lymphocytes (%)	86.3 $\pm$ 9.38	83.13 $\pm$ 5.3	84.4 $\pm$ 5.75	90.3 $\pm$ 4.54*	90.2 $\pm$ 3.08*	86.5 $\pm$ 6.67	91 $\pm$ 5.37*	90 $\pm$ 8.12*
neutrophils (%)	10.1 $\pm$ 6.09	11.66 $\pm$ 5.4	10.1 $\pm$ 4.60	7.8 $\pm$ 4.44	7.5 $\pm$ 2.95	12 $\pm$ 7.07	7.1 $\pm$ 4.53	8.2 $\pm$ 8.25
monocytes (%)	1.6 $\pm$ 2.2	2.9 $\pm$ 3.1	1.2 $\pm$ 1.54	0.6 $\pm$ 0.84*	0.8 $\pm$ 0.78*	0.2 $\pm$ 0.4***	1.4 $\pm$ 1.7	0.8 $\pm$ 1.3**



**Figure 5.** Level of hemoglobin in female Swiss mice poisoned with pyrethroids. \*-\*\*\* statistically significant differences compared to Control Group I + II: \* $p < 0.01$ ; \*\* $p < 0.0005$ .

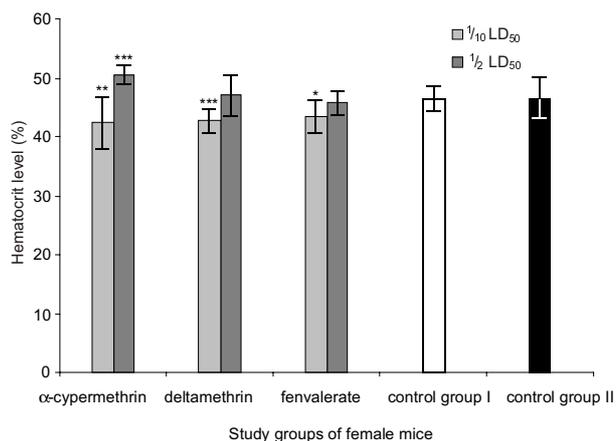
In the group of animals poisoned with a lower dose of deltamethrin a decrease was observed in the level of hemoglobin, compared to control groups.

Fenvalerate poisoning was accompanied by a statistically significant decrease in the level of hemoglobin in blood, compared to the level noted in the control groups (Fig. 5).

**Level of hematocrit in female mice.** In the group of mice poisoned with  $1/10$ LD<sub>50</sub> α-cypermethrin, a statistically significant decrease in the level of hematocrit was observed, whereas in those poisoned with the dose of  $1/2$ LD<sub>50</sub> of this compound, this level significantly increased statistically, compared to the control groups.

In female animals, which were administered deltamethrin or fenvalerate a statistically significant decrease in the level of hematocrit in blood was observed only in mice poisoned with the lower dose of the preparation (Fig. 6).

**Number of leukocytes in male mice:** In the experimental mice, an increase in the number of leukocytes (WBC - white blood cells) in peripheral blood occurred only after



**Figure 6.** Level of hematocrit in female Swiss mice poisoned with pyrethroids. \*-\*\*\* statistically significant differences compared to Control Group I + II: \* $p < 0.01$ ; \*\* $p < 0.005$ ; \*\*\* $p < 0.001$ .

administration of the lower dose of α-cypermethrin, compared to the control groups.

Deltamethrin poisoning in animals, which were administered  $1/2$ LD<sub>50</sub> deltamethrin resulted in a statistically increase in the number of leukocytes in peripheral blood, compared to the control groups and animals poisoned with the lower dose of the pesticide ( $p < 0.001$ ). After poisoning with both doses of fenvalerate, a statistically significant increase was observed in the number of leukocytes in peripheral blood in experimental animals, compared to the control groups (Tab. 1).

**Percentage of lymphocytes, neutrophils and monocytes in male mice:** No statistically significant differences were noted in the percentage of lymphocytes and neutrophils in peripheral blood of mice poisoned with α-cypermethrin or fenvalerate, compared to the level noted in the control groups.

Only in the case of administration of the higher dose of deltamethrin was a statistically significant increase observed in the percentage of lymphocytes in the blood, compared to the control groups and animals which were administered  $1/2$ LD<sub>50</sub> deltamethrin ( $p < 0.05$ ).

**Table 3.** Body mass of Swiss mice poisoned with α-cypermethrin.  $p < 0.05$  - the level of significance adopted for the study; ns - no statistical significance; Results obtained in the experimental groups were compared to the Control Group I+II

Animal examined	Dose	Type of compound	Mean body mass of animals (g)		Body mass gain (g)	Statistical significance	
			Day of the experiment				
sex	n		0	28			
male	10	$1/10$ LD <sub>50</sub>	α-cypermethrin	23.23 ± 2.68	28.85 ± 2.86	5.62	ns
	10	$1/2$ LD <sub>50</sub>	α-cypermethrin	24.42 ± 2.33	27.38 ± 2.72	2.96	$p < 0.05$
	10	Control group I		23.10 ± 1.44	29.10 ± 1.79	6.00	ns
	10	Control group II		22.85 ± 2.34	29.35 ± 2.00	6.50	ns
female	10	$1/10$ LD <sub>50</sub>	α-cypermethrin	22.70 ± 2.43	25.80 ± 1.57	3.10	$p < 0.005$
	10	$1/2$ LD <sub>50</sub>	α-cypermethrin	23.16 ± 2.15	24.5 ± 2.58	1.36	$p < 0.0001$
	10	Control group I		23.40 ± 2.92	28.10 ± 2.38	4.70	ns
	10	Control group II		23.10 ± 3.35	27.55 ± 1.76	4.45	ns

**Table 4.** Body mass of Swiss mice poisoned with deltamethrin.  $p < 0.05$  - the level of significance adopted for the study; ns - no statistical significance; Results obtained in the experimental groups were compared to the Control Group I+II.

Animal examined		Dose	Type of compound	Mean body mass of animals (g)		Body mass gain (g)	Statistical significance
sex	n			Day of the experiment			
				0	28		
male	10	$1/10$ LD <sub>50</sub>	deltamethrin	23.36 ± 1.73	26.26 ± 1.88	2.90	$p < 0.0005$
	10	$1/2$ LD <sub>50</sub>	deltamethrin	23.42 ± 1.56	28.04 ± 1.71	4.62	$p < 0.05$
	10	Control group I		23.10 ± 1.44	29.10 ± 1.79	6.00	ns
	10	Control group II		22.85 ± 2.34	29.35 ± 2.00	6.50	ns
female	10	$1/10$ LD <sub>50</sub>	deltamethrin	21.55 ± 1.27	25.60 ± 2.43	4.05	$p < 0.01$
	10	$1/2$ LD <sub>50</sub>	deltamethrin	22.80 ± 1.60	27.25 ± 2.29	4.45	ns
	10	Control group I		23.40 ± 2.92	28.10 ± 2.38	4.70	ns
	10	Control group II		23.10 ± 3.35	27.55 ± 1.76	4.45	ns

Poisoning with a lower dose of deltamethrin resulted in a statistically significant elevation of the percentage of neutrophils in peripheral blood, compared to the control groups. Poisoning with the higher deltamethrin dose ( $1/2$ LD<sub>50</sub>) was accompanied by a statistically significant decrease in the number of neutrophils, compared to the control groups ( $p < 0.05$ ). In animals which were administered the lower dose of  $\alpha$ -cypermethrin and the higher dose of fenvalerate, the percentage of monocytes in the peripheral blood was significantly lower statistically, compared to control groups (Tab. 1).

**Percentage of lymphocytes, neutrophils and monocytes in female mice:** In mice poisoned with  $\alpha$ -cypermethrin or fenvalerate a statistically significant increase was observed in the number of leukocytes in peripheral blood, compared to the control groups. In the groups of animals poisoned with deltamethrin, the administration of the lower dose of the compound resulted in a statistically significant elevation of the level of leukocytes in blood, compared to the control groups and the higher dose of the pyrethroid ( $p < 0.01$ ).

In female mice administered with  $1/2$ LD<sub>50</sub>  $\alpha$ -cypermethrin,  $1/10$  deltamethrin, and those poisoned with both doses of

fenvalerate, a statistically significant increase was noted in the percentage of lymphocytes in peripheral blood, compared to the control groups.

No statistically significant differences in the level of neutrophils in peripheral blood were observed between the experimental groups poisoned with  $\alpha$ -cypermethrin, deltamethrin or fenvalerate and control groups.

In the experimental animals poisoned with  $1/10$ LD<sub>50</sub>  $\alpha$ -cypermethrin, the higher dose of deltamethrin and fenvalerate, a decrease was observed in the percentage of monocytes, compared to the control groups (Tab. 2).

**Body mass gain in mice:** In mice which were administered  $\alpha$ -cypermethrin *per os*, lower values of body mass gain were noted compared to the control groups, especially after the administration of the lower dose of the compound ( $p < 0.05$ ). In the group of female animals poisoned with  $\alpha$ -cypermethrin, a statistically significant decrease was observed in body mass during 28-day experiment, especially after poisoning with the higher dose of the pyrethroid (Tab. 3).

In male Swiss mice poisoned with deltamethrin, especially with the lower dose of this compound, the body mass gain

**Table 5.** Body mass of Swiss mice poisoned with fenvalerate.  $p < 0.05$  - the level of significance adopted for the study; ns - no statistical significance; Results obtained in the experimental groups were compared to the Control Group I+II.

Animal examined		Dose	Type of compound	Mean body mass of animals (g)		Body mass gain (g)	Statistical significance
sex	n			Day of the experiment			
				0	28		
male	10	$1/10$ LD <sub>50</sub>	fenvalerate	23.23 ± 2.68	28.80 ± 2.96	5.57	ns
	10	$1/2$ LD <sub>50</sub>	fenvalerate	24.89 ± 1.88	27.84 ± 2.43	2.95	$p < 0.05$
	10	Control group I		23.10 ± 1.44	29.10 ± 1.79	6.00	ns
	10	Control group II		22.85 ± 2.34	29.35 ± 2.00	6.50	ns
female	10	$1/10$ LD <sub>50</sub>	fenvalerate	23.40 ± 2.28	27.10 ± 2.75	3.70	ns
	10	$1/2$ LD <sub>50</sub>	fenvalerate	21.00 ± 2.07	26.20 ± 2.70	5.20	ns
	10	Control group I		23.40 ± 2.92	28.10 ± 2.38	4.70	ns
	10	Control group II		23.10 ± 3.35	27.55 ± 1.76	4.45	ns

was significantly statistically lower, compared to the control groups. In female Swiss mice poisoned with  $1/10LD_{50}$  deltamethrin, the increase in the body mass was significantly lower compared to the control group (Tab. 4).

The lower dose of fenvalerate caused a statistically insignificant inhibition in body mass gain among male Swiss mice, compared to the control groups. The higher dose of the compound caused a considerable inhibition of body mass increase in male animals ( $p < 0.05$ ). In female mice poisoned with fenvalerate the increase in body mass was similar in animals of both experimental and control groups (Tab. 5).

## DISCUSSION

The number of erythrocytes, levels of hemoglobin and hematocrit in Swiss mice depend on the sex of the animals, which is clearly observed in control groups. In female mice all the parameters analyzed are higher, compared to male animals.

Results of own studies of the effect of pyrethroids on the hemopoietic system clearly show that the reaction of this system depends on sex of animals. Only female mice poisoned with  $\alpha$ -cypermethrin reacted by very clear changes in the number of erythrocytes, as well as levels of hemoglobin and hematocrit, in male mice no significant changes were observed in the values of hematological parameters analyzed. In deltamethrin or fenvalerate poisoning, very significant changes were noted concerning the analyzed erythrocytic parameters both in male and female animals. In all male mice a mobilization of the erythrocytic system was observed, while in the groups of female animals inhibition was noted.

The dose of the preparation also plays an important role in the response of the erythrocytic system. In  $\alpha$ -cypermethrin poisoning, the higher dose of the pyrethroid stimulated the hemopoietic system, whereas the lower dose causes its inhibition in female animals. In poisoning with deltamethrin, there occurred various relationships between the dose of the pyrethroid and the changes observed. In male mice, the administration of the lower dose of deltamethrin ( $1/10LD_{50}$  - 5 mg/kg b. m.) was accompanied by a stronger stimulation of the hemopoietic system, compared to the higher dose ( $1/2LD_{50}$  - 25 mg/kg b.m.). In female animals, only the lower dose of the pyrethroid caused a clear inhibition of the hemopoietic system, whereas the higher dose of deltamethrin was not manifested by changes in the number of erythrocytes, levels of hemoglobin and hematocrit. The analysis of hematological parameters in Swiss mice in fenvalerate poisoning showed the smallest differences in the hemopoietic system response according to the dose of the pyrethroid applied.

Similar relationships were described by other authors who observed in mice poisoned with pyrethroids various effects on the number of erythrocytes according to sex and dose of the compound [20, 21, 22]. The effect of pyrethroids poisoning in mice, according to sex and dose, was also noted with respect to the hemoglobin level [2, 8].

However, no significant changes in the erythrocytic system parameters were observed, irrespective of the fluvalinate dose [6]. In mice poisoned with fenvalerate a decrease in hemoglobin level and the number of erythrocytes were noted, with a clear increase in the number of thrombocytes [22, 23]. Studies conducted by Desi *et al.* showed a decrease in hematocrit level and an increase in the level of hemoglobin in animals poisoned with cypermethrin [2].

Based on own studies, it may be presumed that  $\alpha$ -cypermethrin does not exert an effect on the hemopoietic system in male animals. While in female mice the effect of poisoning with this compound is observed according to dose - stimulatory after administration of a higher dose, and inhibitory after a lower dose of  $\alpha$ -cypermethrin. Deltamethrin and fenvalerate exert a stimulatory effect on the erythrocytic system in male mice, while in female animals anemia was observed, especially after poisoning with the higher dose of the compound. Based on the above, it may be presumed that female mice are particularly sensitive to poisoning, especially with low doses of pyrethroids administered for a relatively long period of time. This may be associated with the known hormonal potential of synthetic pyrethroids [3, 5, 6]. Although male mice react to pyrethroid poisoning by an increase in erythropoiesis, but contrary to female animals this increase is not accompanied by an increase in hemoglobin level, which may suggest the damaging effect of pyrethroids on the synthesis of hemoglobin. At the same time, it was confirmed that the character of the changes observed with respect to erythrocytic system parameters is connected not only with the sex, but also within the same sex is associated with the type of compound and of the dose.

With respect to the number of leukocytes, the groups examined differed according to the pyrethroid dose. No significant differences were noted according to sex. All the pyrethroids in the study:  $\alpha$ -cypermethrin, deltamethrin and fenvalerate, irrespective of the sex of mice, caused an increase in the number of leukocytes in peripheral blood. In animals poisoned with  $\alpha$ -cypermethrin or fenvalerate, the lower dose of the pyrethroid exerted a stronger effect on male mice, while on female mice - the higher dose. Deltamethrin caused a greater increase in the number of leukocytes in male animals administered the higher dose ( $1/2LD_{50}$ ), whereas in female animals it was the opposite - the administration of the lower dose caused a significant increase in the number of leukocytes. The data obtained may suggest that only poisoning with fenvalerate has a mobilizing effect on the leukocytic system in both male and female animals. In the case of  $\alpha$ -cypermethrin, female mice seem to be more sensitive, in which both doses applied caused leukocytosis, while in male animals only the lower dose of the preparation exerts a mobilizing effect. In deltamethrin poisoning, male animals are more sensitive to the higher dose of the compound, whereas female mice to the lower dose. The percentage of white morphotic elements of peripheral blood in mice poisoned with pyrethroids shows variation according to the sex of

animals and type of pyrethroid. In male mice poisoned with  $\alpha$ -cypermethrin or fenvalerate, no significant changes were observed with respect to the percentage of peripheral blood lymphocytes, whereas in female animals an increase was noted in the percentage of peripheral blood lymphocytes. In deltamethrin poisoning in male animals, an increase in the percentage of lymphocytes was observed only after the administration of the higher dose of the compound, while in female mice - after the lower pyrethroid dose ( $p < 0.005$ ).

A decreased percentage of monocytes in peripheral blood observed in animals poisoned with pyrethroids, especially intensified in poisoning with higher doses of the compounds, may suggest either an impairing effect of pyrethroids directly on monocytes or myelopoiesis. It cannot be excluded that this is caused by shifts in the pool of cells circulating and resting - macrophages.

Other studies show similar data: in fluvalinate poisoning in rats of both sex [7] an increase was noted in the number of leukocytes in peripheral blood, especially of neutrophilic granulocytes, whereas in  $\alpha$ -cypermethrin poisoning in female mice [9] an increase in the number of monocytes was observed. According to some authors, the administration of  $\alpha$ -cypermethrin causes a decrease in the number of leukocytes [2, 19]. Sub-acute poisoning with  $\alpha$ -cypermethrin in female Swiss mice, however, results in an increase in the general number of leukocytes (monocytes and lymphocytes) and does not cause changes in the erythrocytic system [9]. In sub-acute poisoning with fluvalinate in female rats, a decrease was observed in the number of leukocytes after the administration of lower doses of this compound (17.5 and 35 mg/kg b.m.), but an increase was noted at the dose of 70 mg.kg b.m.

An increase in the number of leukocytes in the blood of animals - irrespective of the pyrethroid applied for poisoning - may result from the mobilization of the immunological system and/or a shift in the leukocytic pool from the spleen to peripheral blood. Pyrethroids may disturb the processes of production of effector cells of the immunological system [14] as a result of changes in neurohormone activity [11, 16, 17]. According to Santoni *et al.* [16], pyrethroids causes shifts in the pool of spleen and peripheral blood lymphocytes, which is manifested by lymphocytosis in the blood of rats poisoned with cypermethrin, and the decrease in the subpopulation of T lymphocytes in the spleen [15, 16]. Immunohistologic studies of spleens of animals poisoned with pyrethroids [7, 13, 17] indicate a disturbed development of lymphatic follicle and decreased number of lymphocytes in the cortex and subcortical region of the spleen, suggesting that pyrethroids contribute to disturbances of the process of lymphocytes production in the spleen. In own studies [8] in male mice poisoned with  $\alpha$ -cypermethrin, a decrease was observed in the number of T lymphocytes in the spleen, which was not accompanied by its increase in the peripheral blood, which suggests the disturbing effect of the compound directly concerning the processes of lymphopoiesis.

Based on the results of the studies, it may be presumed that all of the tested pyrethroids mobilize the lymphocytic system.  $\alpha$ -cypermethrin exerts an effect mainly in female mice poisoned with high doses of the preparation, while in deltamethrin poisoning male animals seem to be more sensitive to higher, and female mice to lower doses of the preparation. Fenvalerate intoxication exerts a stronger effect in female than male mice, irrespectively of the dose.

In studies of the toxicity of compounds the observation of body mass gain is one of the basic parameters. Numerous studies confirmed a decrease in body mass in animals poisoned with high doses of pyrethroids in sub-acute and sub-chronic experiments [7, 9, 10, 12, 13]. In the course of the studies conducted by Madsen, a statistically significant decrease in body mass was observed in animals poisoned with deltamethrin at the dose of 10 mg/kg b.m. during the first and the third week of the experiment, and lasted throughout the whole period of the study [12]. Studies concerning the toxic effect of fluvalinate also showed a significant decrease in body mass of mice poisoned with the dose of 15 mg/kg b. m., compared to the animals of the control groups [7]. Similar data were obtained in the studies carried out by Luty *et al.*, where during a 28-day intoxication with  $\alpha$ -cypermethrin a decrease in body mass of animals was noted during the first week of the experiment, and a slight increase in body mass during the further 3 weeks [9]. However, Łukowicz-Ratajczak *et al.* and Enan *et al.* did not observe a similar effect of deltamethrin and cypermethrin in rats during a 4-week experiment, or in mice poisoned intraperitoneally with the dose of 25 mg/kg deltamethrin [4, 10]. Own studies provided similar data; in  $\alpha$ -cypermethrin poisoning male mice seem to be more sensitive, while in poisoning with deltamethrin female animals are the more sensitive. Fenvalerat inhibited body mass increase to the smallest degree. The inhibition in body weight increase of animals exposed to pyrethroids may confirm a general toxic effect of pyrethroids.

## CONCLUSIONS

Intoxication of male Swiss mice with deltamethrin or fenvalerate has a mobilizing effect on the erythrocytic system.

In female animals the character of disturbances in the erythrocytic system depends on the dose of the pyrethroids. Lower doses of  $\alpha$ -cypermethrin, deltamethrin or fenvalerate cause anemia, while after the administration of higher doses of these compounds a mobilization of the erythrocytic system is observed.

Leukocytosis in blood of Swiss mice - irrespective of the type of pyrethroid applied for intoxication - may result from the mobilization of the immunological system and/or shift of the leukocytic pool from the spleen to peripheral blood.

An inhibition of the body mass gain in Swiss mice poisoned with  $\alpha$ -cypermethrin, deltamethrin or fenvalerate may suggest a general toxic effect of pyrethroids.

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