ANIMAL PATHOLOGY, MORPHOLOGY, PHYSIOLOGY, PHARMACOLOGY AND TOXICOLOGY

ПАТОЛОГИЯ ЖИВОТНЫХ, МОРФОЛОГИЯ, ФИЗИОЛОГИЯ, ФАРМАКОЛОГИЯ И ТОКСИКОЛОГИЯ

УДК 615

Original Empirical Research

https://doi.org/10.23947/2949-4826-2025-24-3-26-33

Subchronic Toxicity of D-Cyphenothrin-, Piperonyl Butoxide- and Pyriproxyfen-Based Insecticide-Acaricide upon Its External Use in Laying Chickens

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Abstract

Introduction. Implementation of safe and efficient insecticides-acaricides suitable for using in the presence of poultry infected with ectoparasites is particularly relevant for poultry farming specializing in egg production. The development and implementation of new medicinal products into veterinary practice is a complicated process requiring comprehensive preclinical studies. The objective of this research is to investigate the subchronic toxicity of a new D-cyphenothrin-, piperonyl butoxide-, and pyriproxyfen-based antiparasitic product and the effect of its external use on homeostasis in egg-laying chickens.

Materials and Methods. A subchronic toxicity study of the D-cyphenothrin-, piperonyl butoxide- and pyriproxyfen-based medicinal product was conducted in 2024 at Podolsk Experimental and Production Base of the All-Russian Research Institute of Fundamental and Applied Parasitology of Animals and Plants – Branch of the Federal State Budgetary Scientific Institution "Federal Scientific Center – All-Russian Research Institute of Experimental Veterinary Medicine (VIEV) of the Russian Academy of Sciences. Fifteen Hisex White chickens were divided into three groups of five birds each. Before each treatment, a 5.0% solution of the product was diluted in water at a ratio of 1:1000. A dose of 10.0 ml per 0.3 kg of body weight was assumed to be a therapeutic dose. Birds in the two experimental groups were treated in dosage of 33.3 ml/kg and 100.0 ml/kg, respectively, using a fine-mist spray pump. Chickens from the third control group were not treated. Treatment with a 0.005% aqueous emulsion of the medicinal product was carried out 6 times with an interval of 48 hours. The dynamics of changes in chicken weight, body temperature, some hematological and biochemical blood parameters was monitored, along with the features of behavior, feed and water intake.

Results. No significant changes in body weight in birds from the two experimental groups were recorded. Compared to the control group, no statistically significant changes in body temperature of chickens were revealed throughout the experiment. Six-fold application of the increased dose of the medicinal product resulted in destabilization of red blood cell parameters and decrease of protein metabolism in chickens from the second experimental group; however, these changes were reversible. Accordingly, a dose of 100.0 ml/kg can be assumed a threshold dose of no observed adverse effect level (NOAEL), and 33.3 ml/kg can be assumed a safe one of no observed effect level (NOEL).

Discussion and Conclusion. Statistically significant changes in some blood parameters in chickens were observed after six applications of a 0.005% aqueous emulsion of the new combined insecticide-acaricide at a dose of 100.0 ml/kg. However, these changes were reversible. Taking into account the threefold increase of the therapeutic dose in the experiment, the product proved to have a wide range of safe dosages for external use. Therefore, the antiparasitic treatment with the 0.005% aqueous emulsion of the combined product in dosage of 33.3 ml/kg can be ascertained safe for poultry.

Keywords: insecticide-acaricide product, subchronic toxicity, D-cyphenothrin, piperonyl butoxide, pyriproxyfen, chickens, preclinical studies

For Citation. Indyuhova EN. Subchronic Toxicity of D-Cyphenothrin-, Piperonyl Butoxide- and Pyriproxyfen-Based Insecticide-Acaricide upon Its External Use in Laying Chickens. *Russian Journal of Veterinary Pathology.* 2025;24(3):26–33. https://doi.org/10.23947/2949-4826-2025-24-3-26-33

Оригинальное эмпирическое исследование

Субхроническая токсичность инсектоакарицидного средства на основе D-цифенотрина, пиперонилбутоксида и пирипроксифена при наружном применении у яичных цыплят

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Аннотация

Введение. Внедрение безопасных и эффективных инсектоакарицидных средств с возможностью их применения в присутствии птиц при эктопаразитозах особенно актуально для яичного птицеводства. Разработка и внедрение новых препаратов в ветеринарную практику — сложный процесс, требующий всесторонних доклинических исследований. Цель работы — изучение субхронической токсичности нового противопаразитарного средства на основе D-цифенотрина, пиперонилбутоксида и пирипроксифена и его влияния на гомеостаз яичных цыплят при наружном применении.

Материалы и методы. Исследование субхронической токсичности средства на основе D-цифенотрина, пиперонилбутоксида и пирипроксифена было проведено в 2024 г. на Подольской опытно-производственной базе ВНИИП – филиала ФГБНУ ФНЦ ВИЭВ РАН (г. Москва). 15 цыплят кросса Хайсекс Уайт были разделены на три группы по пять голов в каждой. Перед каждой обработкой 5,0 %-ный препарат разводили водой в соотношении 1:1000. Условно за терапевтическую дозу принимали 10,0 мл на 0,3 кг массы тела птицы. В двух опытных группах птиц обрабатывали мелкокапельным опрыскиванием с помощью помпового опрыскивателя в дозах 33,3 мл/кг и 100,0 мл/кг соответственно. Цыплят из третьей контрольной группы не обрабатывали. Обработки 0,005 %-ной водной эмульсией лекарственного препарата проводили 6 раз с интервалом 48 ч. Контролировали у цыплят в динамике массу, температуру тела, некоторые гематологические и биохимические показатели крови, а также учитывали особенности поведения, приема корма и воды.

Результаты исследования. Достоверные изменения массы тела у птиц из двух опытных групп отсутствовали. Статистически значимых изменений не выявлено при анализе температуры тела у цыплят в течение всего эксперимента по сравнению с контролем. У цыплят из второй опытной группы в результате 6-кратного применения увеличенной дозы препарата выявлены дестабилизация показателей системы красной крови и снижение интенсивности белкового обмена, однако указанные изменения носили обратимый характер. Соответственно, дозу 100,0 мл/кг можно считать пороговой, а 33,3 мл/кг — недействующей (безопасной).

Обсуждение и заключение. На фоне 6-кратного применения 0,005 %-ной водной эмульсии нового комбинированного инсектоакарицидного средства в дозе 100,0 мл/кг описаны статистически значимые изменения некоторых показателей крови у цыплят, однако они носили обратимый характер. Учитывая трехкратное увеличение терапевтической дозы в эксперименте, у препарата имеется гарантия безопасного наружного применения в широком диапазоне доз. Исходя из этого можно утверждать, что при противопаразитарных обработках использование 0,005 %-ной водной эмульсии комбинированного препарата в дозе 33,3 мл/кг будет безопасно для птиц.

Ключевые слова: инсектоакарицидное средство, субхроническая токсичность, D-цифенотрин, пиперонилбутоксид, пирипроксифен, цыплята, доклинические исследования

Для цитирования. Индюхова Е.Н. Субхроническая токсичность инсектоакарицидного средства на основе D-цифенотрина, пиперонилбутоксида и пирипроксифена при наружном применении у яичных цыплят. *Ветеринарная патология.* 2025;24(3):26–33. https://doi.org/10.23947/2949-4826-2025-24-3-26-33

Introduction. The development of safe and efficient insecticides-acaricides for simultaneous disacarization and desinsection of livestock and poultry facilities is an important objective of modern parasitology. For example, the red poultry mite is widespread in industrial poultry farming [1–3]. These temporary hematophagous ectoparasites inhabit hard-to-reach places of cage equipment, joints, cracks, etc. During a parasitological examination of poultry houses, approximately 100–500 mites are usually found per linear meter, alongside, in the organisms of laying chickens numerous negative changes in the central metabolic processes, the development of oxidative stress, severe anemia syndrome, mixed-type hypoxia [4], feather loss, emaciation, anxiety and reduction of egg production capacity [5] are reported.

In 2024, the All-Russian Research Institute of Fundamental and Applied Parasitology of Animals and Plants (Branch of the All-Russian Research Institute of Experimental Veterinary Medicine (VIEV) of the RAS, Moscow) had developed a medicinal product based on three components claimed low toxic to poultry by the scientists [6–8]. The first component is D-cyphenothrin — the synthetic pyrethroid, which is active against fluff lice, argasid ticks, ixodic ticks and red poultry mites [9–10]. The second component is piperonyl butoxide belonging to pyrethroid synergists. The third substance is pyriproxyfen, a suppressor of ectoparasite embryogenesis. This combination of three components is classified as hazard class 3 (moderately hazardous substances) for oral use and as hazard class 4 (low-hazardous substances) for external use [11]. It should be noted that pyrethroids are less toxic to birds than to mammals, due to the higher rate of pyrethroid biotransformation in birds compared to mammals [12–14].

The implementation of new medicinal products into veterinary practice is a complicated process that requires numerous and comprehensive preclinical studies to confirm their safety and efficacy. One of the most important studies is investigation of toxic effects resulting from multiple use of the product in target animal species. The article aims to investigate the subchronic toxicity of an insecticide-acaricide based on D-cyphenothrin, piperonyl butoxide and pyriproxyfen and its effect on egg-laying chickens in case of external application.

Materials and Methods. The experiment was conducted in 2024 at Podolsk Experimental and Production Base of the All-Russian Research Institute of Fundamental and Applied Parasitology of Animals and Plants (Branch of the All-Russian Research Institute of Experimental Veterinary Medicine (VIEV) of the RAS, Moscow). Fifteen 30-day-old Hisex White chickens were divided into three groups (two experimental and one control) of five birds each. The birds were fed a complete feed respective to their age group. Access to water was restricted for chickens from two experimental groups only during periods of treatment. The poultry were housed in two-tiered cages: the control group was housed on the upper tier, while the chickens from the first and second experimental groups were housed separately on the lower tier.

The experiment was conducted in compliance with the guidelines for medicinal product preclinical studies published in 2012 and edited by A.N. Mironov[1]. The dosage regimen and frequency of administration were chosen to identify potential toxic effects on birds during long-term use of a 0.005% aqueous emulsion of the tested product, as well as in the event of its overdosage. The aqueous emulsion of the tested product is intended for antiparasitic treatment of poultry houses in the presence of chickens. The product was sprayed twice, with an interval of 5 days or more, in a form of fine mist using various technical means. According to the instruction for use, the consumption of the product aqueous emulsion was 50 ml/m^2; 10.0 ml per 0.3 kg of bird body weight was conventionally considered a therapeutic dose.

Before each treatment, a 5.0% product was diluted in water at a ratio of 1:1000 to obtain a 0.005% aqueous emulsion. In the first experimental group, birds were treated at a dose of 33.3 ml/kg using a fine-mist spray pump. In the second experimental group, the therapeutic dose was tripled (100.0 ml/kg). Before each treatment, the chickens were individually weighed to calculate the required product dose. Birds from the control group were not treated.

Treatments with an aqueous emulsion of the medicinal product were carried out six times at 48-hour intervals. Birds from three groups were weighed, their body temperature was measured, and blood samples were taken before treatment, the day after the sixth treatment, and 10 days after the sixth treatment. A range of hematological and biochemical parameters were determined in the blood samples according to generally accepted techniques [15]. The behaviour of the chickens, their motor activity, appearance, feed and water consumption were observed daily.

Statistical processing of digital data was performed using the Student's t-test in Microsoft Excel 2016. Results were considered statistically significant (reliable) if the significance level (P) was less than 0.05. The results of statistical data processing were presented in the following format: the mean value (M) is reported together with the standard error of the mean (± m).

Results. None of the chickens died during the entire experiment. During treatments, specimens from the first and second experimental groups bunched in a corner of the cage or moved actively around the cage with excessive vocalization. Feed and water intake by chickens from the experimental groups did not differ from that of the control group.

The dynamics of chicken body weight changes are presented in Table 1. There were no significant changes in body weight in birds from the two experimental groups. Furthermore, no statistically significant changes were detected when analysing the body temperature of chickens participating in the experiment compared to the ones from control group (Table 2).

[1] Guidelines for conducting preclinical studies of medicinal products. Part one. Moscow: Grif i K, 201. 944 p.. URL: https://rsmu.ru/fileadmin/templates/DOC/Zakon_RF/Mironov_Rukovodstvo_po_provedeniju_doklinicheskikh_issledovanii_lekarstvennykh_sredstv.pdf

Table 1

Dynamics of body weight changes in chickens (n=5), kg

Examination timeframes	Control group	First experimental group	Second experimental group
Before treatment	0.30 ± 0.00	0.29 ± 0.00	0.29 ± 0.01
After the 6th treatment	0.42 ± 0.01	0.41 ± 0.00	0.40 ± 0.01
10 days after the 6th treatment	0.52± 0.01	0.52± 0.01	0.51± 0.01

Note: P>0.05

Table 2

Temperature status of chickens (n=5), °C

Examination timeframes	Control group	First experimental group	Second experimental group
Before treatment	41.50± 0.15	41.70 ± 0.08	41.38± 0.24
After the 6th treatment	41.22 ± 0.17	41.58 ± 0.15	41.62 ± 0.17
10 days after the 6th treatment	41.54 ± 0.14	41.56 ± 0.14	41.44 ±0.17

Note: P>0.05

Upon analysis of some hematological and biochemical blood parameters, statistically significant changes were identified in chickens of the second experimental group compared to the control group. In egg-laying chickens, the number of erythrocytes, leukocytes and concentration of hemoglobin in the blood were assessed (Table 3).

Table 3

Some hematological parameters in the blood of chickens (n=5)

Indicator, unit of measurement	Examination timeframes	Control group	First experimental group	Second experimental group
Erythrocytes, $\times 10^{12}$/l	Before treatment	2.64 ± 0.14	2.59 ± 0.06	2.68 ± 0.12
	After the 6th treatment	2.94 ± 0.12	2.82 ± 0.11	2.73 ± 0.08
	10 days after the 6th treatment	2.86 ± 0.08	2.78 ± 0.06	2.92 ± 0.08
Hemoglobin, g/l	Before treatment	122.60 ± 2.99	121.60 ± 3.12	125.40 ± 2.73
	After the 6th treatment	126.40 ± 2.93	122.60 ± 2.38	113.80 ± 2.52*
	10 days after the 6th treatment	127.40 ± 2.66	128.60 ± 2.44	122.80 ± 2.75
Leukocytes, $\times 10^{9}$/L	Before treatment	7.34 ± 0.29	7.06 ± 0.58	6.88 ± 0.61
	After the 6th treatment	7.70 ± 0.26	7.66± 0.42	7.91 ± 0.39
	10 days after the 6th treatment	7.86 ± 0,29	8.30 ± 0.26	7.92 ± 0.29

Note: *P<0.05 compared to the control group

Cyanogen-containing pyrethroids, including D-cyphenothrin, are known to actively affect hematopoiesis [16]. Thus, a tendency towards a decrease in the number of erythrocytes by 7.1% was revealed in the specimens from the second experimental group after the 6th treatment compared to the control group. However, 10 days after the last treatment, the above mentioned tendency for this parameter was not observed. Also, in chickens from the second experimental group, a statistically significant decrease in concentration of the hemoglobin by 10.0% ($P < 0.05$) was found compared to the control group. After 10 days, no reliable changes of this parameter were found. Similar results have been presented in the publication studying changes of the hematological parameters in the blood of laboratory animals during use of a cyphenothrin-containing medicinal product [16].

All cyano-containing pyrethroids disrupt the transporting function of erythrocytes. Although, initially compensatory mechanisms maintain normal erythrocyte levels in the blood by stimulating erythropoietin synthesis, after some time, a decline in hematopoiesis is observed [16]. Furthermore, A. Khan et al. noted the inhibitory effect of synthetic pyrethroids on erythropoietin [17]. The above statement results in a decrease in the intensity of certain metabolic processes in chickens during multiple use of the combination product, as presented in Table 4.

Upon 6-fold application of the three-component product, a reliable decrease in the concentration of total protein by 9.1% ($P<0.05$) and globulins by 10.8% ($P<0.05$) was observed in the blood of chickens from the second experimental group, as well as a tendency towards a decrease in the albumin level by 7.4% compared to the control group. This indicates a disorder in the liver protein-synthesis function in chickens from the second experimental group and goes in line with other studies [17, 18]. However, 10 days after the application of the combination insecticide-acaricide, no statistically significant changes were observed, indicating the recovery of the protein-synthesizing function of liver in birds. Similar findings have been noted by peers in their publications [19]. It is known that the main target organ for piperonyl butoxide is the liver [20]. Studies conducted on laboratory animals have revealed an increase in the weight of this organ and increased activity of certain blood enzymes associated with liver pathologies [21]. However, many studies have confirmed the safety of piperonyl butoxide for birds, since even high doses of this drug did not cause death of animals [7, 21].

As a result of multiple external application of the medicinal product in chickens from the second experimental group, a decrease in the intensity of transamination processes was observed, which expressed in a reliable decrease in the activity of aspartate aminotransferase by 8.7% ($P < 0.05$), and a tendency towards a decrease in the activity of alanine aminotransferase by 15.5% compared to the control group. The current understanding of the diagnostic significance of these enzymes is presented in the work of A.S. Shidlovsky and A.I. Saltanov, in which a tendency towards a disruption of relationships within the carbohydrate, amino acid and energy metabolisms against the background of low activity of aminotransferases was noted [22]. Ten days after treatments were finished, no significant changes in the activity of these enzymes across the groups were detected.

During the experiment, no significant changes in creatinine concentrations in the blood of chickens from the two experimental groups were observed compared to the control group. It is known that one of the reasons underlying the decrease in creatine phosphokinase activity is the destabilisation of aerobic oxidation processes in the organism of animals. Thus, the day after the sixth treatment, chickens from the first experimental group showed a tendency towards a decrease in the activity of this enzyme by 7.9%, while birds from the second experimental group showed a significant decrease of its activity by 20.8% ($P<0.05$) compared to the control group. However, 10 days after the last treatment, these changes were not observed. This may be due to the normalization of energy metabolism in the birds' organisms against the background of stabilization of red blood cell parameters.

Analysis of some lipid metabolism parameters revealed no statistically significant changes in the concentration of triglycerides and cholesterol in the blood of chickens from the second experimental group compared to the control group.

No significant changes in blood glucose concentrations were detected in chickens, with levels within the physiological norm (11–15 mmol/l) in all experimental birds [23]. Furthermore, two tendencies were observed in the blood of chickens from the second experimental group after the sixth treatment: a 3.8% decrease in glucose concentration and a 3.3% decrease in α-amylase activity compared to the control group. After 10 days, no significant changes in carbohydrate and energy metabolism parameters were detected in chickens.

Thus, destabilization of red blood cell parameters and a decrease in protein metabolism were observed in chickens from the second experimental group after six external treatments of the medicinal product; however, these changes were reversible. Consequently, a dose of 100.0 ml/kg can be considered the threshold dose, and 33.3 ml/kg can be considered a dose of no observed effect, i.e. safe.

Table 4

Some biochemical parameters of chicken blood (n=5)

Indicator, unit of measurement	Examination timeframes	Control group	First experimental group	Second experimental group
Total protein, g/l	Before treatment	37.80 ± 0.92	37.40 ± 1.17	37.00 ± 1.10
	After the 6th treatment	39.40 ± 0,40	38.20 ± 0.58	35.80 ± 1.02*
	10 days after the 6th treatment	39.80 ± 0.37	39.60 ± 0.51	39.00 ± 0.71
Albumins, g/l	Before treatment	18.80 ± 0.49	18.60 ±0.40	18.20 ± 0.37
	After the 6th treatment	19.00 ± 0.63	18.60 ± 0.24	17.60 ± 0.60
	10 days after the 6th treatment	20.20 ± 0.20	19.40 ± 0.24	18.80 ± 0.49
Globulins, g/l	Before treatment	19.00 ± 0.45	18.80 ± 0.86	18.80 ± 0.86
	After the 6th treatment	20.40 ± 0.51	19.60 ± 0.40	18.20 ± 0.49*
	10 days after the 6th treatment	19.60 ± 0.40	20.20 ± 0.37	20.20 ± 0.37
Alanine aminotransferase, U/l	Before treatment	30.40 ± 1.89	32.20 ± 1.85	30.60 ± 2.18
	After the 6th treatment	25.80 ± 2.82	26.00 ± 2.45	21.80 ± 2.87
	10 days after the 6th treatment	14.20 ± 1.07	15.40 ± 0.68	15.00 ± 0.94
Aspartate aminotransferase, U/l	Before treatment	271.80 ± 7.81	273.00 ± 8.70	277.80 ± 9.01
	After the 6th treatment	269.00 ± 3.69	257.00 ± 5.16	245.60 ± 6.68*
	10 days after the 6th treatment	205.20 ± 7.77	210.00 ± 9.02	209.40 ± 9.21
Creatinine, μmol/l	Before treatment	27.60 ± 0.81	28.20 ± 0.97	27.80 ± 0.58
	After the 6th treatment	29.20 ± 0.80	27.80 ± 0.73	29.00 ± 0.71
	10 days after the 6th treatment	28.80 ± 0.80	29.20 ±1.16	29.00 ± 1.26
Creatine phosphokinase, U/l	Before treatment	1979.40 ± 70.89	2001.60 ± 80.69	2013.20 ± 88.46
	After the 6th treatment	2001.40 ± 60.58	1843.60 ± 26.02	1585.00 ± 67.44*
	10 days after the 6th treatment	1947.00 ± 44.47	2051.40 ± 47.98	1895.60 ± 68.71
Cholesterol, mmol/l	Before treatment	3.56 ± 0.12	3.60 ± 0.14	3.58 ± 0.14
	After the 6th treatment	3.92 ± 0.10	3.70 ± 0.15	3.88± 0.12
	10 days after the 6th treatment	3.98 ± 0.16	3.78 ± 0.11	3.70 ± 0.10
Triglycerides, mmol/l	Before treatment	0.57 ± 0.04	0.53 ± 0.05	0.59 ± 0.04
	After the 6th treatment	0.56 ± 0.04	0.52 ±0.04	0.55± 0.03
	10 days after the 6th treatment	0.66 ± 0.04	0.62 ± 0.04	0.59 ± 0.01
Glucose, mmol/l	Before treatment	12.46 ± 0.42	13.42 ± 0.21	13.06 ± 0.39
	After the 6th treatment	12.72 ± 0.30	12.58 ± 0.35	12.24 ± 0.27
	10 days after the 6th treatment	13.02 ± 0.26	13.18 ± 0.32	12.34 ± 0.29
Lactate dehydrogenase, U/l	Before treatment	1351.80 ± 35.03	1322.80 ± 42.71	1286.40 ± 31.20
	After the 6th treatment	1413.20 ± 52.41	1343.40 ± 79.28	1335.00 ± 26.61
	10 days after the 6th treatment	1395.00 ± 33.86	1361.20 ± 30.69	1439.40 ± 48.55
α-Amylase, U/L	Before treatment	326.80 ± 12.17	357.40 ± 24.02	320.20 ± 10.86
	After the 6th treatment	311.60 ± 11.99	318.00 ± 11.73	301.40 ± 21.85
	10 days after the 6th treatment	337.00 ± 13.67	349.00 ± 17.56	351.80 ± 10.68

Note: *P<0.05 compared to the control group

Discussion and Conclusion. The study results indicate

that the new combination product based on D-cyphenothrin, piperonyl butoxide, and pyriproxyfen is safe for laying chickens across a wide range of doses when applied externally. Statistically significant changes in some blood parameters were detected only in chickens from the second experimental group, which received the product at a dose of 100.0 ml/kg, and even these changes were reversible. Therefore, there is reason to believe that the use of a 0.005% aqueous emulsion of the combination product at a dose of 33.3 ml/kg for disacarization of premises (twice with an interval of 5 days or more) in the presence of poultry can be considered safe.

References

1. Küntüz T, Güneş Y, Sarı AB, Keleş OÜ. Navigating the Resistance: Current Perspectives on Ectoparasite Control in Veterinary Medicine. *Journal of Istanbul Veterinary Sciences*. 2023;7(2):56–67. https://doi.org/10.30704/http-www-jivs-net.1328872

2. Pavlićević A, Ratajac R, Stojanov I, Pavlovic I. The Control Program of Red Poultry Mite (*Dermanyssus Gallinae*), Today. *Arhiv Veterinarske Medicine (Archives of Veterinary Medicine)*. 2018;11(2):71–88. https://doi.org/10.46784/e-avm.v11i2.27

3. Sparagano OAE, Ho J. Parasitic Mite Fauna in Asian Poultry Farming Systems. *Frontiers in Veterinary Science.* 2020;7:400. https://doi.org/10.3389/fvets.2020.00400

4. Indyuhova EN, Arisov MV, Azarnova TO, Maximov VI. *Sanogenetic Basis for Correction of Physiological and Biochemical Status in Hens with Dermanyssosis.* Moscow: Publishing House Nauka, 2024. 242 p. (In Russ.) https://doi.org/10.31016/978-5-6050437-5-1-2024-242

5. Katsavou E, Vlogiannitis S, Karp-Tatham E, Blake DP, Ilias A, Strube C, et al. Identification and Geographical Distribution of Pyrethroid Resistance Mutations in the Poultry Red Mite *Dermanyssus Gallinae*. *Pest Management Science*. 2020;76(1):125–133. https://doi.org/10.1002/ps.5582

6. Gajendiran A, Abraham J. An Overview of Pyrethroid Insecticides. *Frontiers in Biology*. 2018;(13):79–90. https://doi.org/10.1007/s11515-018-1489-z

7. Toca C, Nica D, Panchiosu A., Gheorghe A. Determination of Piperonyl Butoxide in Honey Bees by Gas Chromatography Coupled With Mass Spectrometry. *Revista Română de Medicină Veterinară*. 2017;27(3):45–48. URL: https://agmv.ro/wp-content/uploads/2019/10/DETERMINAREA-PIPERONIL-BUTOXIDULUI.pdf (accessed: 01.09.2025).

8. Unlu I, Faraji A, Williams GM, Marcombe S, Fonseca DM, Gaugler R. Truck-Mounted Area-Wide Applications of Larvicides and Adulticides for Extended Suppression of Adult *Aedes Albopictus*. *Pest management science*. 2019;75(4):1115–1122. https://doi.org/10.1002/ps.5227

9. Arisov MV, Magomedshapiev GM, Kurochkina KG, Uspensky AV, Malakhova EI., Novik TS, et al. New Remedies for Preventive and Treatment Measures against Ixodidosis in Cattle in Livestock Farms of Dagestan. *Russian Journal of Parasitology*. 2015;(1):35–40. (In Russ.) URL: https://vniigis.elpub.ru/jour/article/view/130/133 (accessed: 01.09.2025)

10. Indyuhova EN, Arisov MV. Insectoacaricide Activity of 5% D-Cyphenothrin Emulsion against Argasid Ticks and Biting Lice. *Russian Journal of Parasitology*. 2024;18(2):211–218. (In Russ.) https://doi.org/10.31016/1998 8435-2024-18-2-211-218

11. Arisov MV, Indyuhova EN, Arisova GB, Poselov DS, Stepanov AA, Poselova EV. Acute Oral and Dermal Toxicity Parameters of a Drug Based on D-Cyphenothrin, Pyriproxyfen and Piperonyl Butoxide in Laboratory Animals. *Russian Journal of Parasitology*. 2024;18(4):410–418. (In Russ.) https://doi.org/10.31016/1998-8435-2024-18-4-410-418

12. Maund SJ, Campbell PJ, Giddings JM, Hamer MJ, Henry K, Pilling ED, et al. Ecotoxicology of Synthetic Pyrethroids. In book: *Matsuo N, Mori T (Eds.). Pyrethroids. Topics in Current Chemistry, Vol 314.* Berlin, Heidelberg: Springer; 2011. P. 137–165. https://doi.org/10.1007/128_2011_260

13. Ahamad A, Kumar J. Pyrethroid Pesticides: An Overview on Classification, Toxicological Assessment and Monitoring. *Journal of Hazardous Materials Advances*. 2023;10:100284. https://doi.org/10.1016/j.hazadv.2023.100284

14. Ruberti M. One Hundred Years of Pyrethroid Chemistry: A Still-Open Research Effort to Combine Efficacy, Cost-Effectiveness and Environmental Sustainability. *Sustainability*. 2024;16(19):8322. https://doi.org/10.3390/su16198322

15. Kondrakhin IP. *Methods of Veterinary Clinical Laboratory Diagnostics*. Moscow: Kolos Publishing House; 2004. 520 p. (In Russ.) URL: https://bioenc.ru/diagnostika-laboratornaya-klinicheskaya/metodyi-veterinarnoy-klinicheskoy-laboratornoy.html (accessed: 01.09.2025).

16. Srinivas BN, Muniswamy D. Effect Of Cyphenothrin-Induced Splenic Damage and Hematological Alterations in Male Wistar Rats (*Rattus Norvegicus*). *International Journal of Pharmacy and Pharmaceutical Sciences*. 2023;15(11):26–30. https://doi.org/10.22159/ijpps.2023v15i11.48970

17. Khan A, Ahmad L, Khan MZ. Hemato-Biochemical Changes Induced by Pyrethroid Insecticides in Avian, Fish and Mammalian Species. *International Journal of Agriculture and Biology*. 2012;14(5):834–842. URL: https://www.researchgate.net/profile/Ahrar-Khan/publication/235997317_IJAB-834-842-2012/links/0046351563b0282368000000/IJAB-834-842-2012.pdf (accessed: 01.09.2025).

18. Verma R, Pathak SK. Haemato-Biochemical Alteration in Chicks (*Gallus Domesticus*) Following Short Term Exposure of Synthetic Pyrethroid Type II Fenvalerate. *Environment Conservation Journal*. 2015;16(1&2):139–142. https://doi.org/10.36953/ECJ.2015.161221

19. Addy-Orduna LM, Zaccagnini ME, Canavelli SB, Mineau P. Formulated Beta-Cyfluthrin Shows Wide Divergence In Toxicity among Bird Species. *Journal of Toxicology*. 2011;(1):803451. https://doi.org/10.1155/2011/803451

20. Isshiki K, Tsumura S, Watanabe T. Residual Piperonyl Butoxide in Agricultural Products. *Bulletin of Environmental Contamination and Toxicology*. 1978;(19):518–523. https://doi.org/10.1007/BF01685835

21. *Reregistration Eligibility Decision for Piperonyl Butoxide (PBO) List B, Case No. 2525*. United States, Environmental Protection Agency. Prevention. Pesticides and Toxic Substances. (7508C). EPA 738-R-06-005. CiteSeer; 2006. 111 p. URL: https://www3.epa.gov/pesticides//chem_search/reg_actions/reregistration/red_PC-067501_14-Jun-06.pdf (accessed: 01.09.2025).

22. Shidlovsky AS, Saltanov AI. Variants of Mechanisms to Change the Transaminase Activity: Clinical Interpretation. *Annals of Critical Care.* 2015;(1):22–32. (In Russ.)

23. Buyko NV, Lizun RP, Nasonov IV, Zakharik NV. Biochemical and Hematological Parameters in Hysex White and Hysex Brown Laying Hens. *Ecology and Animal World*. 2014;(1):31–35. URL: https://bievm.by/gallery/Экология%20и%20животный%20мир%20№%201%202014.pdf#page=31 (accessed: 02.09.2025). (In Russ.)

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Conflict of Interest Statement: **the author declares no conflict of interest.**

The author has read and approved the final manuscript.

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Конфликт интересов: **автор заявляет об отсутствии конфликта интересов.**

Автор прочитал и одобрил окончательный вариант рукописи.

Received / Поступила в редакцию 28.07.2025
Reviewed / Поступила после рецензирования 25.08.2025
Accepted / Принята к публикации 28.08.2025