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TOXICOKINETICS OF CONFODOR 200 SL IN RAT ORGANISM AFTER SINGELE PER ORAL ADMINISTRATION

У статті наведені результати з вивчення токсикокінетичних властивостей інсектициду Конфідор 200 SL (імідаклоприд) після одноразового введення щурам у дозі 260 мг/кг маси тіла. Встановлено, що біотрансформація імідаклоприду в органах і тканинах щурів відбувається протягом перших трьох діб експериментального дослідження. Максимальна концентрація імідаклоприду виявлена у шлунково-кишковому тракті, печінці та нирках.

Ключові слова: токсикокінетика, інсектицид, білі щури, залишкові кількості.

Statement of the problem. In a wide variety of biological substances and chemicals that can significantly reduce labor costs, increase productivity and efficiency, reduce the cost of agricultural products, a large arsenal of different means [1] is used. A relatively new class of substances used for this purpose is neonicotinoide class – synthetic analogues of natural nicotine. One of the members of this group is insecticide Confidor 200 SL with an active ingredient – imidacloprid. Emergance on the pesticides market of a large number of different formulations with an active ingredient imidacloprid requires more in-depth study of their toxicological characteristics concerning biological objects.

Analysis of recent research and publications. According to the literature data [2] the metabolism of imidacloprid was studied on corn, potatoes, tomatoes using labeled [14C] in pyridine moiety imidacloprid. 21 days after the application the most part of the radioactivity was associated with the starting substance – 80%. In most cultures studied the major metabolites were cyclic huanidin, 4- and 5-hydroxy-derivatives of imidacloprid and 6-chloro nicotinic acid.

Also, it is known from the literature data that imidacloprid in the organism is 92% absorbed from the gastrointestinal tract and within 48 hours is completely cleared from the body without forming metabolites and it is not accumulated in animal body [3]. With the introduction of labeled [14C] in pyridine moiety imidacloprid maximum concentration of research material was observed after 2.5 hours, and the concentration in body tissues after 48 hours was extremely low [4]. In experiments on mice, rats and dogs after oral administration of imidacloprid there was found that the liver and kidneys are the main target organs for the accumulation of imidacloprid [5,6].

Thus, information on the accumulation and transformation of imidacloprid in animals is insufficient and sometimes it has contradictions. Foreign scientists have studied the biotransformation of imidacloprid only in liver, kidneys and in blood.

The purpose of research – to study toxicokinetics of Confidor 200 SL (imidacloprid) in rats after a single oral administration.

Materials and methods. The **s**tudies have been carried out on the basis of the vivarium of the Department of toxicology, safety and quality of agricultural products NSC "IECVM". As the object of research there were used 40 sexually mature male rats, weighing 170 – 220 g. By the analogues principle there were formed 2 groups of animals – the control and experimental, 20 rats in each. Before the experiment, the rats were kept in adaptation period during one week. Pesticide was given once intragastrically as aqueous emulsions using the probe. Before the introduction of pesticide each animal was weighed and each animal was given a pilot solution individually, according to body weight. To determine toxicokinetic properties of Confidor 200 SL animals from the research group were given insecticide in a dose 260 mg/kg (1/3 LD_{50}) and rats from the control group were given distilled water.

Experimental animals were observed for 14 days. There were taken into account the following indicators: appearance, animal behavior, response to external stimuli, a condition of hair and visible mucous membranes, eating of food, rhythm and respiration rate, time of occurrence and the character of intoxication, its severity after 4 h., 1, 3, 7 and 14 days. Euthanasia was performed by decapitation during light chloroform anesthesia, 4 rats from each group. Samples of internal organs (brain, heart, lungs, kidneys, liver, muscles, fat, blood, stomach contents and the contents of the large intestine) were selected for determination of residual amounts of experimental drug by the developed by us method of thin layer chromatography [7].

Experimental studies on animals were carried out with the main principles of bioethics: the maintenance, care for animals and their feed were carried out in accordance with the norms and rations recommended for this type of laboratory animals. During the experiment the animals of all groups had free access to water [8, 9].

Results and discussions. At a single oral administration of insecticide at a dose 260 mg/kg body weight (1/3LD50) the clinical picture of rats' poisoning was characterized by mild depression and refusal of feed only during the first day. On the third day after the drug administration the mentioned clinical signs of poisoning were not observed and the behavior of animals in the experimental group was not significantly different from the control. During the autopsy, the changes in the internal organs were not found. The results of studies of internal organs and tissues of rats concerning the content of residual quantities of imidacloprid are given in Table 1. As can be seen from the table, the greatest levels of accumulation of residual quantities of imidacloprid were detected in 4 hours and one day after the introduction of insecticide.

Table 1 – **Dynamics of the of residual content of imidacloprid (Confidor 200 SL) in the internal organs and tissues of rats under a single oral administration at a dose of 260 mg/kg**

Studied objects	Content of imidacloprid mg/kg after introduction			
	4 hours	1 day	3 days	7 – 14 days
Blood	< l.o.d.	0,06±0,02	< l.o.d.	< l.o.d.
Brain	< l.o.d.	< l.o.d.	< l.o.d.	< l.o.d.
Heart	< l.o.d.	0,08±0,01	< l.o.d.	< l.o.d.
Lungs	< l.o.d.	0,18±0,07	< l.o.d.	< l.o.d.
Kidneys	< l.o.d.	1,16±0,01	< l.o.d.	< l.o.d.
Liver	< l.o.d.	1,28±0,11	0,07*	< l.o.d.
Muscle	< l.o.d.	0,08*	< l.o.d.	< l.o.d.
Fat	< l.o.d.	0,06*	< l.o.d.	< l.o.d.
Stomach content	12,64±2,1	1,09±0,06	0,05*	< l.o.d.
Colon content	8,20±1,80	0,97±0,28	< l.o.d.	< l.o.d.

Notes: 1. < l.o.d. – less than limit of detection (0,02 mg/kg); 2. * – was detected in one sample from four studied.

After 4 hours the maximum quantity of imidacloprid residue was found only in the stomach content – 12,64 ± 2,1 mg/kg and the content of colon – 8,20 ± 1,80 mg/kg. In other studied organs and tissues the quantity of residues was less than the limit of detection.

In one day after the introduction of insecticide residual quantities of imidacloprid were detected in almost all studied organs and tissues. The highest concentrations were in the liver – 1,28 ± 0,11 mg/kg, kidney – 1,16 ± 0.01 mg/kg, in the contents of stomach – 1,09 ± 0,06 mg/kg and colon – 0,97 ± 0,02 mg/kg, lungs – 0,18 ± 0,21 mg/kg, heart – 0,08 ± 0,01 mg/kg and blood – 0,06 ± 0,02 mg/kg. It should be noted that in brain of rats the drug residues were not found throughout the experiment. In muscle tissue imidacloprid residues were found only in one animal (0.08 mg/kg), in the fat the residue quantities were also found only in one animal (0.06 mg/kg).

On the third day of the experimental study the residual quantities of imidacloprid in organs and tissues of rats were less than the limit of detection, but in one animal there were detected the substance residues in the liver (0.07 mg/kg), and in the other one in the stomach contents – 0.05 mg/kg. Within 7 – 14 days the residual quantities of imidacloprid were not detected.

Thus, imidacloprid after a single oral administration to rats at a dose of 260 mg/kg after 4 hours was detected in the gastrointestinal tract. After one day insecticide was found in almost all organs and tissues, indicating its maximum concentration values. However, on the 3rd day after the introduction of insecticide the residue was recorded only in some rats. On the 7th and 14th day from the beginning of the experiment the content of imidacloprid residues was less than the limit of detection.

Conclusions and prospects for further research. 1. After a single oral administration of Confodor 200 SL (imidacloprid) to rats at a dose of 260 mg/kg maximum residue quantities of experimental drug were detected in 4 hours in stomach contents – 12,64 ± 2,1 mg/kg and in the contents of the colon – 8,20 ± 1,80 mg/kg.

2. On the first day of the experiment there was recorded maximum accumulation of residual imidacloprid, an insecticide was found in almost all organs and tissues, and, the highest concentration was found in the liver – 1,28 ± 0,11 mg/kg and in the kidney -1,16 ± 0,01 mg/kg.

These results are part of comprehensive studies on toxicokinetics and toxicodynamics of insecticide Confidor 200 SL. The next stage of research is to study the toxicokinetics of the drug in the poultry body.

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Токсикокинетика Конфидора 200 SL в организме крыс после его однократного перорального введения

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В статье приведены результаты по изучению токсикокинетических свойств инсектицида Конфидор 200 SL (имидаклоприд) после его однократного введения крысам в дозе 260 мг/кг массы тела. Установлено, что биотрансформация имидаклоприда в органах и тканях крыс происходит в течение первых трех суток экспериментального исследования. Максимальная концентрация имидаклоприда обнаружена в желудочно-кишечном тракте, печени и почках.

Ключевые слова: токсикокинетика, инсектицид, белые крысы, остаточные количества.

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