STUDY OF THE ACUTE TOXICITY AND COMBINED ACTION OF THE PESTICIDES ACREX AND ACTELIC

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Material and methods

Acrex (isopropyl-2-1 methyl'n-propyl-4,6-dinitrophenyl-carbonate) is a contact acaracide and fungicide from the group of the nitroderivatives of phenol. The base mechanism of action upon the insects and vertebrates is connected directly with disorders in the processes of oxidative phosphorilation.

Actelic (2-diethylamino-6-methylpyrimidine-4-il-dimethyl-phosphate) is an insecticide and acaracide with a broad spectrum of action. The main mechanism of its toxic activity is the inhibition of some esterases.

The experiments were carried out with 220 white rats, weighing 150—200 g, female and male, divided into two groups (experimental and control). The studied agents were given per os by means of a stomach drill. We applied a technical acrex (30 % active reagent) and technical actelic (50 % active reagent).

The actual experiment itself with the combined acrex and actelic was held on 150 white rats, divided into groups of 6 animals each. The average lethal dose (LD_{50}) of the acrex was determined by treating of the experimental animals with 25, 50, 100, 200, 250 mg/kg, whereas the actelic was respectively 500, 700, 1000, 1250, 1500, 1750, 2000 mg/kg; the rats were examined after that for a period of 14 days. As for the determination of the LD_{50} of the combination of acrex and actelic we used equitoxic doses of both compounds: 0.2, 0.3, 0.7, 1.0, 1.5 LD_{50} which all were applied consequently following an internal of maximum several seconds.

The acute oral, mean lethal doses of the active substances and the combination of them were estimated after Leenfield Willcoxon (9). The type of the combined action was determined by using the method of Finney and the method of Kagan (2,9).

The histological changes in parenchyma organs as a result of the application of the combination acrex and actelic were studied over a total of 70 rats, divided into 3 experimental groups and another one control. The experimental animals were treated as follows: I group — 1/2 LD_{50} acrex (71 mg/kg), II group — 1/2 LD_{50} actelic (625 mg/kg), III group — 1/2 LD_{50} mixture (400 mg/kg).

The experimental animals were decapitated on the first, fourth and fifteenth day after a single-dose-application. After that histological preparations from their internal organs were prepared (liver, heart, spleen, kidney, stomach).

Results and discussion

The development of the acute intoxication and the results of lethality were investigated in dynamics — 14 days after a single-dose-application. Table 1 shows the results of the experiment: the preparation acrex (nitrophenol) is one of the

Table 1

Levels of oral doses LD_{50} in mg/kg for white rats

Preparation	LD_{16}	LD'_{50}	Confidential interval	LD_{84}
Acrex	53,0	142,0	71—284,0	380,0
Actelic	720,0	1250,0	1087—1437	2400,0
Double mixture (acrex and actelic)	280,0	800 0	615—1040,0	2300,0

highly toxic compounds with LD_{50} 142 mg/kg, whereas actelic is one of the slightly toxic ones with LD_{50} 1250 mg/kg; their mixture is an averagely toxic preparation with LD_{50} 800 mg/kg.

The quantitative evaluation of the combined effect of the pesticides acrex and actelic, held after Finney and Kagan was 115 % (88—145 %) and 1.18 ± 0.32. The ratio between the expected LD_{50} and the experimental LD_{50}, specially after the combined treatment and additive effect, according to the methods of Finney and Kagan was equal to 1.0. Having in mind the individual variability the authors suggested all ratios under 0.57 to be directed as antagonism and above 1.75 as synergism (1, 2, 8).

According to our data the expected LD_{50} is 696 mg/kg and the experimental one — 800 mg/kg. Ratio 0.87 shows already a tendency of antagonism after additive action. It is known that pesticides from the group of dinitrophenols and POC can be metabolised in the liver, which is the first barrier after a stomach application. There are enough bibliographical data that the acrex is an inducer of oxidases with combined functions (7). The simultaneous application of acrex and actelic decreases the inhibiting cholinesterase action of the actelic as a result of the activated liver metabolism of the latter (9). This is a direct result of the acute intoxicative effect of the combination, as well as it can be established by studying the histological disorders in the parenchyma organs.

When the acute intoxicatin of the preparations is with high doses of the reagents (absolute lethal dose LD_{100}), we register a decreased mobility of the treated with acrex animals, higher frequency of breathing and pulse, ataxia, released evacuation of reservoirs, febrility. The acute intoxication with actelic can be demonstrated 65 minutes after the oral application and is characterized by increased irritation, ataxia, strong atonia, even paresis of the rear extremities, salivation, frequent breathing, tremor and pulsations. The animals die in tetanic spasm. The acute intoxication after the combined action of both reagents is manifested about 75—80 minutes after the oral application and the syndrome here is slightly weaker (muscarin-like), also there are no tetanic spasms.

After decapitation of the treated rats with LD_{50} of both reagents and their mixture in the parenchyma organs of the animals can be seen macroscopic haemor-

rhages and oedema. The histological analysis of the organs after treatment with acrex shows cyanosis and slight parenchyma distrophy. After actelic treatment the tissue changes are quite heavier: parenchyma, even vacuolar distrophy prevailing in the hepatocytes. In the parenchyma of the lungs can be registered larger haemorrhages than those after acrex treatment. Most weakly expressed changes are established after a combined treatment with both reagents together. More demonstrative are those disorders in the organs of the animals after 4 days. In the liver, for example, for all three types of intoxication we found a vacuolar-spotted distrophy of the hepatocytes, vessels' dilatation, erythrostasis, somewhere with plasmorrhagia. In the myocard can be seen erythrostasis, vessels' dilatation, parenchyma microhaemorrhages, distrophic changes and zones fragmentation of cardiomyocytes. In the kidneys we registered vessels' di atation and erythrostasis.

Most serious are the lung disorders: large parenchyma haemorrhages, vessels' dilatation and actelectasis with stightly expressed oedema (in the rats treated separately with the reagents). Weaker were the changes in the animals treated with the combined mixture: only parenchyma microhaemorrhages.

Conclusions

1. The combined effect of the preparations acrex and actelic is demonstrated by the type of additive action with a tendency towards antagonism.

2. The weaker toxic activity of the combination upon experimental animals and its relatively well expressed insecticidic and acaracidic properties allows the simultaneous application of acrex and actelic in the agriculture.

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ИССЛЕДОВАНИЕ ОСТРОЙ ТОКСИЧНОСТИ И КОМБИНИРОВАННОГО ДЕЙСТВИЯ ПЕСТИЦИДНЫХ АКРЕКС И АКТЕЛИК

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РЕЗЮМЕ

Авторы изучают острую токсичность, симптомы отравления и морфологические изменения внутренних органов белых крыс, которым вводились пестицидные препараты — акрекс (30 %), актелик (50 %) и двойная смесь обоих веществ.

Устанавливается, что препарат акрекс принадлежит у высокотоксичным веществам, соответственно с $ЛД_{50}$-142 мг/кг, а препарат актелик относится к слабо токсичным пестицидам — с $ЛД_{50}$-800 мг/кг.

Комбинированный эффект обоих веществ проявляется по типу адитивного действия, установленого методом Фини — 115 % (88 %—145 %) и методом Ю. С. Каган — 1,18—0,32 с тенденцией к антагонизму. При анализе морфологических изменений паренхиматозных органов животных, которым вводились препараты, устанавливаются значительные дистрофические, некротические и воспалительные увреждания, что отмечалось преимущественно при введении препаратов в дозах 1/2 $ЛД_{50}$.

В результате проведенного исследования авторами рекомендуется применение двойной смеси препаратов акрекс и актелик в оранжерийных условиях.