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TOXIC EFFECT OF PYRETHROIDS ON THE TAIGA TICK *IXODES PERSULCATUS* SCHULZE: RELATIONSHIPS BETWEEN DOSE AND KNOCKDOWN TIME

ТОКСИЧЕСКОЕ ДЕЙСТВИЕ ПИРЕТРОИДОВ НА ТАЕЖНОГО КЛЕЩА *IXODES PERSULCATUS* SCHULZE (ACARINA: IXODIDAE): ЗАВИСИМОСТЬ <ДОЗА — ВРЕМЯ НОКДАУНА>

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ABSTRACT

The use of pyrethroids for personal protection against ticks is based on the knockdown effect, e.g. locomotor activity disorders and paralysis developing in a short period of time after contact with the toxicant. So the knockdown time (KT) is one of the critical characteristics of reliability of a pyrethroid as anti-tick clothing treatment agent. The present study is aimed to establish relationships between a dose and the KT for certain marketable pyrethroids (permethrin, α-cypermethrin, and flumethrin) which are used (or could be used) for protection against taiga ticks *Ixodes persulcatus* Schulze.

For all these pyrethroids the KT varied within a wide range at every dose used. We observed similar unimodal distributions of the KT in all experiments. The KT reduced with the increase of the dose, and this relationship was non-linear for all the compounds tested. Flumethrin at high doses caused knockdown developing in the shortest time, although its KT was longest at lower doses. In contrast, KT of permethrin and α-cypermethrin were less dependent to dosage.

РЕЗЮМЕ

Использование пиретроидов для индивидуальной защиты против нападения иксодовых клещей основано на нокдаун-эффекте (нарушения двигательной активности и параличи, которые быстро развиваются после контакта с токсикантом). Следовательно, время развития нокдауна (ВН) является одним из важнейших критериев надежности пиретроидных инсектицидов при их применении для противоклещевой обработки одежды. В настоящей работе исследованы зависимости между дозой и ВН для некоторых широко распространенных пиретроидов (перметрина, альфа-циперметрина и флуметрина), которые используются (или могут быть использованы) для защиты от нападения таежного клеща *Ixodes persulcatus* Schulze.

ВН для всех трех исследованных пиретроидов при каждой дозе варьировало в широких пределах. Во всех экспериментах мы наблюдали сходные унимодальные распределения ВН. С увеличением дозы среднее ВН уменьшалось, и связь между этими показателями была нелинейной. ВН флуметрина при высоких дозах было наименьшим, а при более низких — резко возрастало. В противоположность этому, ВН перметрина и альфа-циперметрина в значительно меньшей степени зависело от дозы акарицида.

INTRODUCTION

Pyrethroid insecticides (primarily permethrin and, in a lesser extent, cypermethrin) are used for personal protection against ixodid ticks [Lane, Anderson, 1984; Lane, 1989; Mount, Snoddy, 1983; Schreck et al., 1980; 1982a, b; Methodical..., 1997]. The protective effect of these preparations is based on the knockdown effect. The knockdown develops in a short period of time after the contact with a toxicant. The knockdown manifests itself in the tick locomotion disorders and the paralysis resulted from the loss of nervous conduction [Naumann, 1990; Dremova, Volkov, 1987]. The knockdown takes place in a rather short period of time after the beginning of contact with a pyrethroid and

results in loss of tick's ability to hold onto a surface treated with a pyrethroid. Therefore, the shorter is the knockdown time (KT) of a pyrethroid, the more reliable protection is provided. Nevertheless, pyrethroids are poorly studied in this regard. In a series of experiments simulating the contact of ticks with the surface of treated fabric, the KT has been estimated for a number of pyrethroids [Alekseev et al., 1994]. It has been found that this parameter varies in a great extent depending on a chemical structure of the compounds. To develop new preparations for anti-tick closing, one needs to answer the following questions: (1) how the KT depends on the dose and (2) which doses will be effective. We carried out a series of experiments with certain available pyrethroids, which differ in their chemical structure and toxic properties (permethrin, α-cypermethrin and flumethrin) using unfed female ticks *Ixodes persulcatus* Schulze.

MATERIAL AND METHODS

Ticks

We used ticks *I.persulcatus* from natural population. Unfed females were collected by flagging from vegetation near Novosibirsk in May and June, 1996. In our tests we used active non-damaged ticks, which were captured not more than 24 hrs before.

Pyrethroids

Permethrin {3-phenoxybenzyl 2,2-dimethyl-3(2,2-dichlorovinyl) cyclopropanecarboxylate} — racemic mixture (Z/E=2:3).

α-cypermethrin {α-cyano-3-phenoxibenzyl 2,2-dimethyl-3(2,2-dichlorovinyl) cyclopropanecarboxylate} — mixture of 1R-cis-αS and 1R-cis-αR isomers (1:1).

Flumethrin {pentafluorobenzyl 2,2-dimethyl-3(2,2-dichlorovinyl) cyclopropanecarboxylate} — racemic mixture (Z/E=2:3).

The pyrethroids were purified by column chromatography and subsequent crystallization to ≥95% purity.

Evaluation of the knockdown time

We applied topically 0.5 μL of an acetone solution of pyrethroid on back shield of the tick using 10 μL Hamilton Chromatographic Syringe. After evaporation of the solvent the tick was placed on the lover edge of cotton fabric ribbon (70×10 cm), fixed at 70° angle to horizontal.

The tick was stimulated to move along the ribbon by placing a finger at a short distance (1–2 cm) from the tick. If the tick reached the upper edge of the ribbon, we put it on the lower edge again. The KT was estimated as the period of time from the moment of a toxicant application to the moment when the tick lost its ability to hold onto the fabric and fell down.

Pyrethroids were applied in doses 0.5, 5, 50, and 500 μg/g. The test was performed not less than in 30 replicates for each dose. We used parametric criteria for statistical comparisons [Plokhinskii, 1970].

RESULTS AND DISCUSSION

The distribution patterns of KT were similar for all three pyrethroids, the distributions for each dose being symmetric and close to normal.

Parameters of variability of KT at the same doses were also similar for different pyrethroids. In particular, the coefficient of variation was approximately 50–60% for the dose 5 μg/g (see the Table). Thus, in spite of the fact that in each series of tests we recorded extremes with the difference in KT of 10–30 times, this parameter was close to mean value for overwhelming majority of ticks.

The mean KT of all three pyrethroids reduced with increase of dose. The relationship between these parameters was nonlinear: when the dose increased ten times, the KT reduces not more than three times (Fig.2). For permethrin and α-cypermethrin the relationship between the mean KT and *log* of the dose approximated by similar *log* equations ($Y = 26.2 + 2.4\ln X$; $R^2 = 0.92$ and $Y = 22.4 + 2.6\ln X$; $R^2 = 0.96$, respectively). In contrast, the relationship for flumethrin within the studied dose range described by hyperbolic function $Y = 3.9 + 121.8/X$ ($R^2 = 0.99$).

At the dose of 0.5 μg/g the mean KT for permethrin and α-cypermethrin was approximately three times less than for flumethrin ($P<0.001$). At the doses of 5 and 50 μg/g the mean KT was

Table. Mean values and parameters of the variability of KT for pyrethroids (the dose of 5 μg/g).
Таблица. Средние значения и параметры изменчивости времени нокдауна при дозе пиретроидов 5 мкг/г.

Pyrethroid	n	M±SE, min	Coefficient of variation, %
Permethrin	36	19.0±1.8	57
α-cypermethrin	40	16.4±1.4	53
Flumethrin	30	22.9±3.8	53

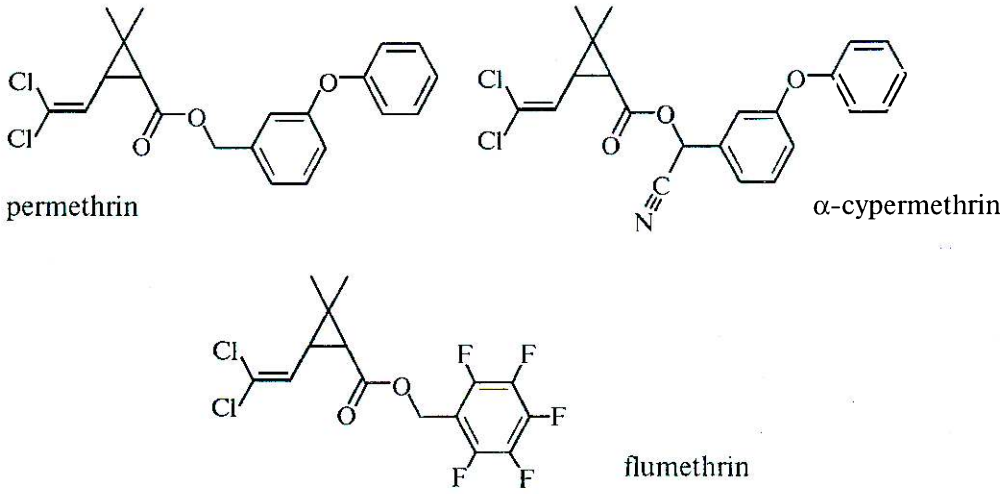

Fig 1. Chemical structure of the pyrethroids tested.
Рис. 1. Химическая структура исследованных пиретроидов.

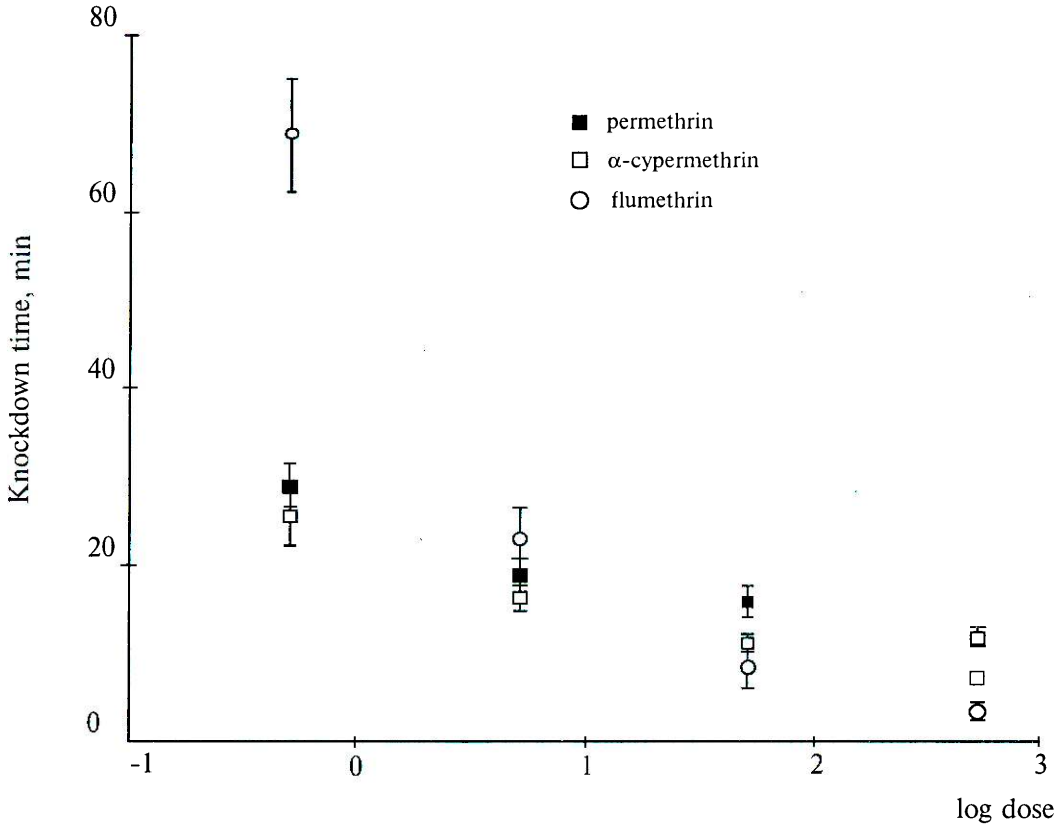

Fig 2. Mean values of KT at different doses of the pyrethroids. The standard errors of mean are indicated by error bars.
Рис. 2 Средние значения времени нокдауна при разных дозах пиретроидов. Ошибки средних показаны отрезками.

approximately equal for all three pyrethroids. At 500 μg/g the KT was the greatest for permethrin and the least for flumethrin ($P<0.05$). At all the doses used the mean KT for α-cypermethrin was a little lower than for respective doses of permethrin, but the difference was insignificant.

Paralysis in an arthropod caused by action of pyrethroid was found to be a result of a complex process including diffusion of toxicant through cuticle and internal tissues, saturation of detoxication systems, and binding target structures, the rates of the processes being determined ultimately by physico-chemical properties of pyrethroids [Naumann, 1990; Dremova, Volkov, 1987]. The molecules of the pyrethroids studied are similar in the structure of the acidic moiety (derivatives of permethric acid) but differ significantly in alcoholic fragment that determines the difference in physical and chemical properties of the compounds and their mechanism of action.

The molecules of permethrin and α-cypermethrin, having the same 3-phenoxybenzyl moiety, are more similar in size, space structure and lipophylic properties as compared to that of flumethrin. In spite of the fact that permethrin and α-cypermethrin affect the nervous system of arthropods differently (so-called I type and II type pyrethroids), practically identical relations between the dose and KT for them can be explained, probably by the similarity of their physico-chemical properties. The molecule of flumethrin with pentafluorobenzyl moiety is noticeably more lipophylic as compared to permethrin and α-cypermethrin, so the relative rates of the prossesses determined by physical and chemical properties are not the same, that may cause in another dose-KT relationship.

Thus, the nonlinear decrease of KT with the growth of the dose of toxicant is a characteristic for all the pyrethroid insecticides studied. Judging from the dose-KT relationships, within the range of doses exceeding LD_{50} hundreds times, KT tends to a minimum extreme value which is limited by the rate of intoxication processes. Although flumethrin at high doses produced the shortest KT, the KT grown dramatically when the dose was reduced. Therefore flumethrin cannot be considered as an agent for personal protection against ticks. Contrary to this, permethrin and α-cypermethrin produced satisfactory KT within the whole range of investigated doses. It was found previously that sublethal doses of permethrin speeded up the attachment of ticks [Alekseev et al., 1994; Fryauff et al., 1994]. In contrast, the same doses of α-cypermethrin prevented the attachment completely [Alekseev et al., 1994]. Taking into consideration these facts, one can suppose that α-cypermethrin (or other pyrethroids with similar properties, probably, like deltamethrin or cygalothrin) is the most reliable active compound for anti-tick formulations and clothing treatment.

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