Esfenvalerate: Its biological activity against German cockroach, *Blattella germanica* (Orthoptera: Blattellidae)

Kimitoshi UMEDA,* Toshihiko YANO* and Masachika HIRANO*

Agricultural Science Research Laboratory, Takarazuka Research Center,
Sumitomo Chemical Co., Ltd., Takarazuka 665, Japan

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Abstract: Insecticidal and knock-down activities of fenvalerate optical isomers against the German cockroach, *Blattella germanica*, were determined. [S, S]-isomer showed about 4 times higher insecticidal and knock-down activities than racemic fenvalerate. However, the insecticidal activity of [R, S]-isomer was only one-tenth that of racemic fenvalerate, and it showed no knock-down activity. [S, R]- and [R, R]-isomers did not show insecticidal activity. Electrophysiological study showed that only [S, S]-isomer was effective against the central nervous system of the insect. These results suggested that only [S, S]-isomer was the active component of fenvalerate. It was assumed that the insecticidal activity of [R, S]-isomer was due to [S, S]-isomer contained in the [R, S]-isomer sample as impurities or [S, S]-isomer isomerized from [R, S]-isomer in the body.

INTRODUCTION

Fenvalerate is a potent pyrethroid insecticide, which contains 4 optical isomers. It has been reported that the [S, S]-isomer, esfenvalerate, is largely responsible for insecticidal activity and that [R, S]-isomer also showed the activity though it was very low in comparison with that of [S, S]-isomer and racemic body (Nakayama *et al.*, 1979). It was biologically indicated that the insecticidal activity of [R, S]-isomer applied to *Spodoptera litura* resulted from conversion to a more toxic substance (Nakayama *et al.*, 1979).

The electrophysiological experiment was carried out to clarify that [S, S]-isomer was effective against the peripheral nervous sys-

tem of the locust which was the one of the target sites of pyrethroid compounds (Clements and May, 1977).

In this experiment, we investigated the relationship between the lethal, knock-down and electrophysiological activities of the optical isomers of fenvalerate, using the German cockroach.

MATERIALS AND METHODS

Insect. A susceptible strain of the German cockroach, *Blattella germanica*, which was introduced from Nagoya University in 1961 and reared in our laboratory without exposure to any insecticides, was used. It was reared at $28 \pm 1^\circ\text{C}$, 50–60% RH, 16L:8D, and given dry rat food and water.

Chemicals. The following esters were used in this study. They were synthesized at Sumitomo Chemical Co., Ltd.

* 梅田公利, 矢野俊彦, 平野雅親: 住友化学工業(株) 宝塚総合研究所 (〒665 宝塚市高司 4-2-1)

1. Racemic fenvalerate: (R, S)- α -cyano-3-phenoxybenzyl (R, S)-2-(4-chlorophenyl)-3-methylbutyrate. The purity was 94.2%.

2. [S, S]-isomer of fenvalerate, Esfenvalerate: (S)- α -cyano-3-phenoxybenzyl (S)-2-(4-chlorophenyl)-3-methylbutyrate.

3. [R, S]-isomer of fenvalerate: (R)- α -cyano-3-phenoxybenzyl (S)-2-(4-chlorophenyl)-3-methylbutyrate.

4. [S, R]-isomer of fenvalerate: (S)- α -cyano-3-phenoxybenzyl (R)-2-(4-chlorophenyl)-3-methylbutyrate.

5. [R, R]-isomer of fenvalerate: (R)- α -cyano-3-phenoxybenzyl (R)-2-(4-chlorophenyl)-3-methylbutyrate.

The components of isomers used in this experiment are shown in Table 1. Other impurities were not detected (<0.1%). The analytical method for optical isomers of fenvalerate was shown in Horiba *et al.* (1980).

Lethal activity. Insecticidal activity of each chemical was determined by the injection method. Adult males 7–14 days after emergence were used. One microliter of an acetone solution of each chemical was injected into the abdomen between the fourth and fifth sterna with a microapplicator (Burkard, England) under anesthesia with CO₂. After 48 hr, the mortality was determined and LD₅₀ value was obtained. The injection of 1 μ l of acetone had no lethality against cockroaches.

Knock-down activity. Ten adult cockroaches (5 males and 5 females) 7–14 days after emergence were released into a polyethylene cup covered with nylon net. After the cup was set on the bottom of a glass cylinder (38 cm in height, 10 cm in diameter), 0.6 ml of oil formulation (trichloroethane:kerosene=1:5) was discharged into

the cylinder with a spray gun. The number of knocked-down insects was counted at various time intervals for 20 min, and the KT₅₀ value was calculated.

Electrophysiological study. The saline solution, the preparation of nerve tissues and electrophysiological procedures were shown in a previous report (Umeda *et al.*, 1988). Adult males were used. In preparing the pyrethroid solution, dimethyl sulfoxide was used as a solvent of the stock solution. The stock solution was kept in a teflon bottle to prevent racemisation.

RESULTS AND DISCUSSION

The insecticidal activities of fenvalerate isomers are shown in Table 2. [S, S]-isomer was the most toxic to the German cockroach, and its activity was 4.5 and 50 times higher than that of racemate and [R, S]-isomer, respectively (Table 2). [S, S]-isomer contained in [R, S]-isomer sample as impurities might contribute to the insecticidal activity of [R, S]-isomer. [S, R]- and [R, R]-isomers showed no activity.

The knock-down activities of [S, S]-, [R, S]-isomers and racemic fenvalerate are shown in Table 3. The activity of 0.025% [S, S]-isomer was almost the same as that of 0.1% racemate. It was, therefore, assumed that knock-down activity of [S, S]-isomer was also about 4 times higher than that of racemic fenvalerate. On the other hand, [R, S]-isomer, which showed lethal activity against this species, possessed no knock-down activity even up to 20 min after treatment.

Pyrethroid compounds applied to the abdominal nerve cord of the German cockroach increased and then extinguished the spon-

Table 1 Components of 4 isomers of fenvalerate used in this experiment.

Isomers	Components (%)			
	[S, S]	[R, S]	[S, R]	[R, R]
[S, S]	99.6	0.4	ND	ND
[R, S]	1.6	96.3	2.1	ND
[S, R]	ND	0.8	99.0	0.2
[R, R]	ND	ND	0.3	99.7

ND: not detected (<0.1%).

Table 2 Insecticidal activities of 4 isomers and racemic fenvalerate against *B. germanica* by injection.

Chemicals	LD ₅₀ (μ g/♂)
[S, S]	0.0060
[R, S]	0.30
[S, R]	>5
[R, R]	>5
Racemate	0.027

Table 3 Knock-down activities of optical isomers and racemic fenvalerate against *B. germanica*.

Chemicals	Conc. (%) [*]	KT ₅₀ (min)
[S, S]	0.025	6.6
[R, S]	0.1	>20
Racemate	0.1	7.7

^{*} Concentration is expressed as w/v.

taneous discharge (Umeda *et al.*, 1988). The time taken for the disappearance of spontaneous discharge after applying the compounds was measured as an indication of electrophysiological activity. The time depended on the concentration of the chemicals. It took about 9 and 15 min for the spontaneous discharge to disappear after applying 2.5×10^{-5} M [S, S]-isomer and racemic fenvalerate, respectively (Fig. 1). In the case of [R, S]-

Fig. 1 Time course of the firing frequency of the central nervous system treated with 2.5×10^{-5} M racemate, [S, S]-isomer and [R, S]-isomer.

Arrow indicates the application of compound solution.

Table 4 The time for the disappearance of spontaneous discharge of abdominal nerve cord after applying the compounds.

Conc. (M)	Time (min)				
	[S,S]	[R,S]	[S,R]	[R,R]	Racemate
2.5×10^{-5}	$8.9 \pm 2.4^*$	>60	>60	>60	$15.2 \pm 3.6^*$
10^{-5}	14.6 ± 1.0				25.7 ± 5.4
5×10^{-6}	23.3 ± 4.6				28.7 ± 4.8
2.5×10^{-6}	26.0 ± 4.1				36.1 ± 6.7
10^{-6}	36.2 ± 3.8				46.3 ± 3.5
5×10^{-7}	38.1 ± 7.2				>60
2.5×10^{-7}	>60				

* Mean $\pm$ standard deviation ($n=5$).

Fig. 2 Correlation between the concentration of [S, S]-isomer and racemic fenvalerate and the time required until the spontaneous discharge disappeared.

○, racemate; ●, [S, S]-isomer.

isomer, although the frequency of spontaneous discharge increased after application, no disappearance was observed even up to 60 min (Fig. 1). Moreover, [S, R]- and [R, R]-isomers did not have any activity against the abdominal nerve cord at a concentration of 2.5×10^{-5} M during 60 min (Table 4). In the case of racemic and [S, S]-isomer of fenvalerate, the time taken for the disappearance of spontaneous discharge depended on the concentration (Table 4). The relationship between the concentration and the time is shown in Fig. 2. Two regression lines obtained from [S, S]-isomer and racemate were essentially straight, and almost parallel. The activity of [S, S]-isomer against the

nervous system is about 3 times higher than that of racemate. From these results, only [S, S]-isomer seemed to be active against the nervous system among the 4 isomers.

Nakayama *et al.* (1979) have reported that the insecticidal activity of [S, S]-isomer was the highest among 4 isomers and [R, S]-isomer possessed insecticidal activity though the activity was very low in comparison with that of [S, S]-isomer. [S, S]- and [R, S]-isomers also showed insecticidal activity against the German cockroach (Table 2). However, [R, S]-isomer showed no knock-down activity against this species (Table 2). Nakayama *et al.* (1979) suggested that [R, S]-isomer was biologically converted to a more toxic substance, which was assumed to be [S, S]-isomer. In this study, [S, S]-isomer showed high knock-down activity, but [R, S]-isomer did not. Furthermore, although [R, S]-isomer increased the frequency of spontaneous discharge, no disappearance was observed on the nervous system, which was a target of fenvalerate. It was suggested that only [S, S]-isomer seriously affected the nervous system to show knock-down and insecticidal activity among the 4 isomers of fenvalerate against the German cockroach. It was also assumed that the insecticidal activity of [R, S]-isomer shown in Table 2 was due to [S, S]-isomer contained in the [R, S]-isomer sample as impurities or [S, S]-isomer isomerized from [R, S]-isomer in the body.

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摘 要

エスフェンバレレート：チャバネゴキブリに対する生物活性

チャバネゴキブリに対する、フェンバレレート光学異性体の殺虫活性およびノックダウン活性を調べた。[S,S]-isomer (エスフェンバレレート) は、ラセミ体 (フェンバレレート) に比較し、約4倍の殺虫活性およびノックダウン活性を示した。また [R,S]-isomer の殺虫活性はラセミ体の約1/10であったが、ノックダウン活性は認められなかった。[S,R]- および [R,R]-isomer は殺虫活性を示さなかった。

さらに電気生理学的実験により、チャバネゴキブリの中枢神経系に対しては [S,S]-isomer のみがその自発性スパイクを抑制した。

これらの結果より、[S,S]-isomer のみがフェンバレレートの活性成分であることが示唆された。また [R,S]-isomer の殺虫活性は、[R,S]-isomer のサンプル中に不純物として含まれる [S,S]-isomer, または、チャバネゴキブリ体内で異性化により生じた [S,S]-isomer によるものと推定された。