Efficacy of the pyrethroid compound possessing a new type of alcohol moiety

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Abstract: A new type of pyrethroid compounds which possessed a linear type chemical structure in the alcoholic moiety was synthesized, and the lethal and knock-down activities of the compounds were studied. As the result, SP-3243 (1-ethynyl-2-methyl-2-hexen-5-yn-1-yl 3-(2, 2-dichlorovinyl)-2, 2-dimethylcyclopropane-1-carboxylate) was found to possess the highest efficacy among these compounds against houseflies, mosquitoes and cockroaches.

The lethal activity of this compound against houseflies was more than 10 times higher than that of pyrethrins and allethrin. The knockdown activity of this compound against houseflies and mosquitoes was slightly inferior to that of pyrethrins, nevertheless, the efficacy of aerosol formulation was high enough. This compound also possessed insecticidal activity against cockroaches, but the efficacy was inferior to that of pyrethrins and permethrin.

Since the chemical structures of natural pyrethrins were elucidated by LaForge and Haller (1936), a number of studies on analogues of chrysanthemic acid esters have been conducted, and many insecticidal synthetic pyrethroids were discovered. These include allethrin (Schechter *et al.*, 1949), tetramethrin (Kato *et al.*, 1965), resmethrin (Elliot *et al.*, 1967), furamethrin (Katsuda *et al.*, 1969), proparthrin (Nakanishi *et al.*, 1970), phenothrin (Fujimoto *et al.*, 1973), butethrin (Sota *et al.*, 1973b) and permethrin (Elliot *et al.*, 1973). These pyrethroidal compounds possess the aromatics in the alcohol moieties.

On the other hand, Sota *et al.* (1973a) reported trans-2, 5-hexadien-1-yl chrysanthemate and related compounds as the pyrethroid compounds which possess no aromatics in the alcohol moieties. We synthesized, therefore, α -ethynyl allyl alcohol derivatives to study the lethal and knockdown activities.

As the result, it became clear that SP-3243 (1-ethynyl-2-methyl-2-hexen-5-yn-1-yl 3-(2, 2-dichlorovinyl)-2, 2-dimethylcyclopropane-1-carboxylate) was found to possess the highest efficacy among these derivatives.

This paper describes the efficacies of SP-3243 and the analogues against houseflies, mosquitoes, and cockroaches.

MATERIALS AND METHODS

1. Test insects

The following stock colonies of houseflies, mosquitoes and cockroaches were reared in this laboratory at $27 \pm 1^\circ\text{C}$ and at $60 \pm 5\%$ in relative humidity.

- (1) Houseflies *Musca domestica*. These susceptible strains of Lab-em-7-em, WHO and CSMA.
- (2) Mosquitoes *Culex pipiens pallens*. Two susceptible strains of Sumitomo and Gose.
- (3) German cockroach *Blattella germanica*. One susceptible strain of Sumitomo.

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2. Chemicals

The following synthetic chemicals were used in this study. SP-3243: The purity was higher than 95%. The physical and chemical properties were presented in Table 1.

Allethrin:	Technical grade (91.0%)
S-bioallethrin:	Technical grade (93.3%)
Bioallethrin:	Technical grade (90.9%)
Tetramethrin:	Technical grade (90.3%)
Permethrin:	Technical grade (92.9%)
Cypermethrin:	Technical grade (96.5%)
Phenothrin:	Technical grade (96.3%)
Resmethrin:	Technical grade (91.6%)
Pyrethrins:	20% pyrethrum extract supplied by Dainippon Jochugiku Co., Ltd.

3. Testing methods

(1) Topical application method (Okuno *et al.*, 1976) with CSMA strain of houseflies.

(2) Campbell's turntable method (Campbell and Sullivan, 1938) with Lab-em-7-em strain of houseflies.

(3) Glass chamber method by oil or emulsifiable concentrate spray. After 10 female mosquitoes (oil with Sumitomo, EC with Gose) and 10 houseflies (WHO) were released in a glass chamber (0.34 m³), 0.6 ml of each formulation was sprayed into the glass chamber through an atomizer at a pressure of 0.9 kg/cm². The number of knocked down insects was counted at various time intervals for 10 min. KT₅₀ value was calculated by Finney's graphic method. After 10 min, the knocked down insects were collected and transferred into a recovery container to observe the mortality after 24 hrs.

(4) Mosquito coil test. After 10 female mosquitoes (Sumitomo) and 10 houseflies (WHO) were released in a glass chamber (0.34 m³), 1 gram of test coil was fixed on a stand at the center of the chamber bottom and ignited at the both ends. The number of knocked down insects was counted at various time intervals for 24 min to calculate KT₅₀ value. Mortality was recorded as same as (3).

(5) Film contact. One ml of acetone solution of each chemical was applied to 55 cm² of an aluminium plate. After acetone was evaporated off, 10 adult cockroaches were released. After 24 hrs, the exposed

cockroaches were transferred to a plastic cup, and the mortality was recorded at 48 hrs after treatment.

(6) Direct spray against cockroaches (Okuno *et al.*, 1976).

(7) Aerosol test method against cockroaches. Test method was as in (6). Instead of oil formulation, each aerosol was used.

(8) Aerosol test method against the flying insects (Aerosol test method, 1965), the Gose strain of mosquitoes and the WHO strain of houseflies.

RESULTS AND DISCUSSION

1. Screening the pyrethroid compounds possessing the new alcohol moiety

Eight compounds shown in Table 1 were synthesized and the efficacies were examined. Among these compounds, those whose R₁ was alkynyl or alkenyl showed high lethal and knockdown activities against houseflies and mosquitoes.

Compound 5 (R₁: allyl, R₂: methyl, R₃: hydrogen) was reported by Sota *et al.* (1973 a). However, the lethal activity of α -ethynyl derivative of compound 5 (R₁: allyl, R₂: methyl, R₃: ethynyl, namely compound 6) was 5 times higher than that of compound 5, and the knockdown activity was also higher than that of compound 5.

The lethal activity of compound 4 (R₁: propargyl, R₂: methyl, R₃: ethynyl) was equal to that of compound 6, nevertheless, the knockdown activity of compound 4 was much higher than that of compound 6.

As the influence of R₂ on the efficacy was examined among the propargyl compounds, the efficacy of the methyl moiety was more effective than the hydrogen moiety. It showed the same tendency as the result reported by Sota *et al.* (1973a).

Moreover, compounds 7 and 8 were synthesized to compare with compounds 5 and 6, but these were less effective than compounds 5 and 6.

In conclusion, α -ethynyl allyl alcohol esters possessed high lethal and knockdown activities against houseflies and mosquitoes. And, among these compounds, compound 4 (hereafter designated as SP-3243) showed the highest efficacy.

Table 1 Chemical structures and efficacies of candidate compounds

Compound No.	Chemical structures			Turntable <i>M. domestica</i> LC ₅₀ (mg/100ml)	Oil spray (0.1%) KT ₅₀ (sec)	
	R ₁	R ₂	R ₃		<i>C. p.</i> *	<i>M. d.</i> **
1	HC≡C—CH ₂ —	H—	H—	500	>600	>600
2	HC≡C—CH ₂ —	H—	HC≡C—	72	204	252
3	HC≡C—CH ₂ —	CH ₃ —	H—	96	255	312
4***	HC≡C—CH ₂ —	CH ₃ —	HC≡C—	25	232	275
5	H ₂ C=C—CH ₂ —	CH ₃ —	H—	120	>600	>600
6	H ₂ C=C—CH ₂ —	CH ₃ —	HC≡C—	25	540	420
7	HC≡C—CH ₂ CH ₂ —	CH ₃ —	HC≡C—	40	252	285
8	H ₂ C=CHCH ₂ CH ₂ —	CH ₃	HC≡C—	33	>600	>600
Phenothrin				40		
Pyrethrins				320	180	178

* *Culex pipiens pallens*** *Musca domestica*

*** SP-3243

Table 2 Physical and chemical properties of SP-3243

Item	Outlines of properties
Empirical formula	C ₁₇ H ₁₈ O ₂ Cl ₂
Molecular weight	325
Appearance	Yellowish oily liquid
Refractive index	<i>n</i> _D ^{24.0} 1.5175
Vapor pressure*	2.0×10 ⁻⁴ mm Hg at 25°C
Solubility	Miscible with almost all of aromatic or aliphatic hydrocarbons and other organic solvents

* By gas-chromatographic determination

2. Efficacy of SP-3243

The physical and chemical properties of SP-3243 is shown in Table 2.

The lethal activity of SP-3243 against houseflies by topical application method was almost equal to that of permethrin and resmethrin and more than 10 times higher than that of pyrethrins and allethrin (Table 3). The lethal activity of SP-3243 against houseflies by Campbell's turntable method was superior to that of phenothrin and pyre-

Table 3 Insecticidal activity against *Musca domestica* by topical application method

Insecticide	LD ₅₀ (μg/fly)	
SP-3243	0.029	(0.025–0.034)*
Permethrin	0.022	(0.019–0.026)
Resmethrin	0.034	(0.027–0.042)
Cypermethrin	0.012	(0.007–0.026)
Allethrin	0.53	(0.46–0.61)
Pyrethrins	1.01	(0.89–1.14)

* Figures in parentheses indicate 95% confidence limit.

thrins as shown in Table 1.

SP-3243 possessed high knockdown activity against houseflies and mosquitoes also. Knockdown activity of the EC formulation was higher than that of tetramethrin and bioallethrin against houseflies, and was higher than that of tetramethrin but almost equal to that of bioallethrin against mosquitoes as shown in Table 5. Knockdown activity of the oil formulation was almost equal to that of pyrethrins against mosquitoes, but less than that of pyrethrins and S-bioallethrin

Table 4 Knockdown activity of oil formulations against *Culex pipiens pallens* and *Musca domestica*

Insecticide	Conc. (%)	<i>C. pipiens</i>		<i>M. domestica</i>	
		KT ₅₀ (min)	Kill (%)	KT ₅₀ (min)	Kill (%)
SP-3243	0.05	7.2	(5.9-10.6)*	5.8	(5.0-6.6)
	0.1	3.9	(3.4- 4.3)	4.6	(3.7-5.8)
Pyrethrins	0.1	3.0	(2.4- 3.7)	3.0	(2.4-3.6)
S-bioallethrin	0.05	3.0	(2.5- 3.5)	3.0	(2.6-3.5)

* Figures in parentheses indicate 95% confidence limit.

Table 5 Efficacy of the emulsifiable concentrates and the oil-based aerosol formulations against *Musca domestica* and *Culex pipiens pallens*

Insecticide	Conc. (%)	Emulsifiable concentrate				Oil-based aerosol			
		<i>C. pipiens</i>		<i>M. domestica</i>		<i>C. pipiens</i>		<i>M. domestica</i>	
		KT ₅₀ (min)	Kill (%)	KT ₅₀ (min)	Kill (%)	KT ₅₀ (min)	Kill (%)	KT ₅₀ (min)	Kill (%)
SP-3243	0.1	3.2	50	5.2	45	6.6	30	15.3	31
	0.2	3.2	100	2.7	85	3.7	91	9.5	64
	0.4					2.5	86	6.1	70
Tetramethrin	0.1	>10	20	9.2	0				
	0.2	>10	25	4.2	30				
Bioallethrin	0.1	3.7	11	9.6	15				
Pyrethrins	0.15					12.0	70	>20	—
	0.3					7.0	86	>20	11
OTA*						14.2	100	10.9	66

* OAT means official test aerosol, and contains 0.2% of pyrethrins and 1.6% of piperonyl butoxide.

Table 6 Efficacy of the mosquito coil formulations against *Culex pipiens pallens* and *Musca domestica*

Insecticide	Conc. (%)	<i>C. pipiens</i>		<i>M. domestica</i>	
		KT ₅₀ (min)	Kill (%)	KT ₅₀ (min)	Kill (%)
SP-3243	0.3	8.5	60	17.0	0
	0.6	7.2	65	11.5	10
Allethrin	0.3	4.4	15	13.0	0
	0.6	4.3	82	10.5	10

against houseflies as shown in Table 4.

The efficacy of SP-3243 in mosquito coil agent was less than that of allethrin (Table 6).

The oil-based aerosol formulation of SP-3243 was more effective than that of pyrethrins and official test aerosol against mosquitoes, and than that of pyrethrins against houseflies as shown in Table 5. The efficacy of 0.2% aerosol formulation of SP-3243

against houseflies was almost equal to that of official test aerosol. SP-3243 showed not only high knockdown activity but also high lethal activity in case of the oil-based aerosol formulation.

The lethal activity of SP-3243 against cockroaches was less than that of permethrin, resmethrin and pyrethrins by each test method as shown in Table 7. And, the knockdown acti-

Table 7 Insecticidal activities against *Blattella germanica*

Insecticide	Film contact LD ₅₀ (mg/m ²)	Topical application LD ₅₀ (μg/insect)
SP-3243	5.2	0.70
Permethrin	2.0	0.34
Resmethrin	4.0	—
Pyrethrins	2.5	0.62

Table 8 Knockdown activity of oil formulation against *Blattella germanica*

Insecticide	Conc. (%)	KT ₅₀ (min)	Mortality (%)
SP-3243	0.025	>20	70
	0.05	6.2(4.5-8.8)*	100
Pyrethrins	0.025	2.6(1.8-3.5)	100
	0.05	2.4(1.9-3.1)	90

* 95% confidence limit

Table 9 Efficacy of the oil-based aerosol formulations against *Blattella germanica*

Composition		Dosage (mg/2,900cm ³)	% Knockdown at elapsed time (min)					Kill (%) in 72 hrs
			1.3	2.5	5.0	10.0	20.0	
SP-3243	0.1%	90	20	20	40	30	60	10
	0.2%	70	10	30	40	70	90	0
Pyrethrins	0.15%	85	25	50	55	60	60	5
	0.3%	100	25	40	40	65	80	30
Untreated			0	0	0	0	0	0

vity of this compound against cockroaches was inferior to that of pyrethrins as shown in Table 8. Besides, the efficacy of oil-based aerosol formulation of this compound was slightly less than that of pyrethrins (Table 9).

In conclusion, SP-3243 possessed not only high lethal activity but also knockdown activity against houseflies and mosquitoes. Especially, the oil-based aerosol formulation of this compound was excellent. Nevertheless, the efficacy against cockroaches was slightly lower than that of pyrethrins, permethrin and resmethrin.

REFERENCES

- Aerosol test method (1915): Aerosol and pressurized space spray insecticide test method for flying insects. Soap and Chemical Specialties Blue Book, pp. 236-238.
- Campbell, F. L. and W. N. Sullivan (1938): Testing fly sprays, a metal turntable method for comparative tests of liquid spray contact insecticides. *Soap Sanit. Chem.* **14**(6): 119-149.
- Elliot, M., A. W. Farnham, N. F. Janes, P. H. Needham and B. C. Pearson (1967): 5-Benzyl-3-furylmethyl chrysanthemate, a new potent insecticide. *Nature*, **213**: 493-494.
- Elliot, M., A. W. Farnham, N. F. Janes, P. H. Needham, D. A. Pulman and J. H. Stevenson (1973): A photostable pyrethroid. *Nature*, **246**: 169-170.
- Fujimoto, K., N. Itaya, Y. Okuno, T. Kadota and T. Yamaguchi (1973): A new insecticidal pyrethroid ester. *Agric. Biol. Chem.*, **37**(11): 2681-2682.
- Kato, T., K. Ueda and K. Fujimoto (1965): New insecticidally active chrysanthemates. *Agric. Biol. Chem.*, **28**(12): 914-915.
- Katsuda, Y., T. Chikamoto, H. Ogami, H. Hirobe and T. Kunishige (1969): Novel insecticidal chrysanthemic esters. *Agric. Biol. Chem.*, **33**(9): 1361-1362.
- LaForge, F. B. and H. L. Haller (1936): Constituents of pyrethrum flowers VI. The structure of pyrethrolone. *J. Am. Chem. Soc.*, **58**: 1777-1780.
- Nakanishi, M., A. Tsuda, K. Abe, S. Inamasu and T. Mukai (1970): Insecticidal activity of a new pyrethroid kikuthrin, studies on insecticide III. *Botyu-Kagaku*, **35**(3): 91-96.
- Okuno, Y., T. Yamaguchi and Y. Fujita (1976): Insecticidal activity of a new synthetic pyrethroidal compound, 3-phenoxy benzyl-(+)*cis*, *trans* chrysanthemate (*d*-phenothrin). *Botyu-Kagaku*, **41**(1): 42-55.
- Schechter, M. S., N. Green and F. B. LaForge (1949): Constituents of pyrethrum flowers. XXIII. Cinerolone and the synthesis of related cyclopentenolones. *J. Am. Chem. Soc.*, **71**:

3165-3173.

Sota, K., T. Amano, A. Hayashi and I. Tanaka (1973a): *Trans*-2, 5-hexadien-1-yl chrysanthemates and related esters. *Agric. Biol. Chem.*, **37**: 1019-1025.

Sota, K., T. Amano, A. Hayashi and I. Tanaka (1973b): New insecticidal cyclopropanecarboxylic esters. Part IV. 4-Aryl-2-buten-1-yl chrysanthemates and related esters. *Botyu-Kagaku*, **38**(4): 181-190.

摘 要

新しいアルコールを有するピレスロイド 化合物の殺虫効果

アルコール側に環状基を含まない新しいタイプのピレスロイド化合物を多数合成し、イエバエ、アカイエカおよびチャバネゴキブリに対する致死効果とノックダウン効果について検討した。

その結果、SP-3243 (1-エチニル-2-メチル-2-ヘキセン-5-イン-1-イル 3-(2, 2-ジクロロビニル)-2, 2-ジメチルシクロプロパン-1-カルボキシレート) がもっとも高い活性を示した。SP-3243 のイエバエに対する致死効果は、ピレトリンやアレスリンの約10倍であり、ノックダウン効果も認められた。とくにエアゾールの効果が優れていた。一方、チャバネゴキブリに対する効果はピレトリンやレスメスリンには及ばなかった。

新著紹介

Venoms: Chemistry and Molecular Biology

T. Tu, Anthony (コロラド州立大学生化学教室)

Wiley, New York, 1977, 560 pp.

動物毒はなにかしら魅力がある。動物毒作用の生物学的活性は多様で、複雑で、興味深く、また、それに含まれる物質から未知の有益な物質が発見される可能性がある。

このたび動物毒の莫大な資料をもとに、著者の研究成果を含めた *Venoms* が出版されたことは、医動物をはじめ生化学、薬理学、生理学、生物学の領域にたずさわる者の大きな喜びである。従来の動物毒関係の出版物とちがって、動物毒の化学、分子生物学の立場から論じられている点が大きな特徴である。

この本の大部分は、著者の専門であるへび毒にさかれているが、クモ、サソリ、ハチ、アリなどの節足動物毒や短いながらトカゲ毒も含まれている。4章からなり第1章から第3章で、へび毒の非タンパク成分、酵素、タンパク成分の特性と作用が論じられている。とくに第3章には毒へびの大系や薬理作用、病理所見、純毒の構成成分が含まれ、世界の毒へびおよびへび毒の概要が要約されている。へび毒の生物活性として示されている神経毒、心臓毒、細胞毒、出血毒、溶血毒などの活性は、その他の動物毒の活性を代表するものであり、その作用機序も詳細に論じられていてわかりやすい。第4章に節足動物毒とトカゲ毒が含まれている。短いながら従来の研究成果と今後の研究課題が示唆されている。

多くの研究成果を正しく評価し、わかりやすい項目に整理し、重要な文献をほとんどもれなく含んだ大著はめずらしく、多くの研究者の参考になる本である。

(大利昌久)