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Studies on Insecticidal Aerosol Formulations[I]. Stability of Tetramethrin and Other Pyrethroids in Water-Based Aerosol Formulations. Takashi Yamaguchi, Isao Nishibe and Chuji Hirose (Research Department, Pesticides Division, Sumitomo Chemical Co., Ltd., Takarazuka, Hyogo, 665, Japan) Received Feb. 21, 1977. *Botyu-Kagaku*, 42, 104, 1977.

15. 殺虫エアゾール製剤に関する研究（第一報）水性エアゾール製剤におけるテトラメスリンおよびその他のピレスロイドの安定性

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水性エアゾール製剤に関し，(1)pH の異なる乳化剤を用いた製剤中のテトラメスリンの安定性と製剤のpH変化の関係，(2)保存された製剤と新しく調合された製剤間のイエバエに対する効力比較，(3)長期間保存された製剤中における各種ピレスロイドの安定性について調べ，次の点を明らかにした．

(1)製剤の pH は経時的に低下する傾向があり，使用された乳化剤によっては，たとえ着手時にアルカリ性であっても，ある時点で酸性に変化するものがあった．この変化は有効成分を含まない製剤中でも起こっており，乳化剤自身の変化によるものであると考えられた．(2)テトラメスリンは，アルカリ性製剤中で不安定であったが，pH が酸性に変化した後の分解は非常に少なかった．また，アルカリ性製剤を製造時に酸性に調節した場合には，テトラメスリンは，幾分安定化された．(3)酸性製剤では，35°C にて1年間保存された試料と新しく調合された試料との間には，効力面での有意差は認められなかったが，アルカリ性製剤では，両者間に差が認められ，製剤を酸性にすることは，効力的にも有効であった．(4)テトラメスリン，d-フェノトリン，レスメスリン，d-アレスリンは，酸性製剤において，室温で少なくとも2年間は極めて安定であった．

Water-based aerosol formulation has been studied since 1950s, mainly for the purpose of lowering cost of the conventional oil based aerosol. Water-based aerosols can be classified into two types, two-phase and three-phase aerosols. Two-phase type consists of two layers, namely, gaseous phase composed of vaporized propellant, and liquid phase composed of active ingredients, solvent, water, emulsifier, and liquefied propellant. Three-phase type consists of vaporized gas phase, water phase and another phase composed of active ingredients, solvent and liquefied gas. In the latter case, the containers have to be shaken before spraying for unification of the layers. Three-phase type has been widely used as a household insecticidal formulation owing to their better stability of active ingredients and generally less corrosion risk of container.

Compatibility of many active ingredients with water-based formulations has been studied. Glessner[1] has described that chlordane, heptachlor, and organo-phosphates such as DDVP and malathion are unsuitable for use in water-based formulation, because they are hydrolized in water solution producing trace amounts of acids. Therefore these organo-phosphates are used in oil-based aerosols. Brooke[2], Maciver[3], Johns *et al.*[4] and Moore *et al.*[5] reported that the synergised pyrethrins showed no significant decomposition in water-based formulations or certain emulsions. Several kinds of synthetic pyrethroids such as allethrin[6], tetramethrin[7], resmethrin[8] and phenothrin[9], developed after elucidation of the structures of natural pyrethrins, are very important as household insecticides because of their low mammalian toxicity and quick action against insects. Fujita *et al.*[10] studied stability of several representative pyrethroids in emulsion systems with buffer solution of different pHs, and the results showed that pyrethrins, allethrin, resmethrin and phenothrin were stable in the range of pH 5.8 to 9.2, whereas tetramethrin was unstable under alkaline coditions, though it was quite stable under acidic conditions. In the formulation containing tetramethrin, pH is one of the most important factors to keep the active ingredient stable.

The emulsifiers, which produce the water-in-oil type emulsion, are used in the three-phase type formulation. Individual water-in-oil type emulsifiers differ widely in their pH value, and may influence the pH of the formulations.

This paper discusses the stability of tetramethrin at various pHs as measured chemically and biologically in the presence of various kinds of emulsifiers, and also presents the results of the chemical stability of tetramethrin in combination with other pyrethroids in practical water-based aerosol formulations.

Materials and Methods

Materials

The active ingredients and emulsifiers used are listed in Table 1. In some experiments, the pH values of the formulations containing Span 80, Emcol 14 and Emcol 511 were adjusted using phosphoric acid as follows; four grams of an emulsifier and 196m*l* of deionized water were mixed with vigorus stirring, and insoluble materials were removed by filtration. Span 80 solution and Emcol 14 solution were titrated with 0.06N phosphoric acid solution, and Emcol 511 solution with 0.3N phosphoric acid solution to pH 3 to 4. Titration curves obtained using a potentiometric titration apparatus (Potentiograph, E 436, Metrohm Herisan, Switzerland) are shown in Figure 1. From the figure, the amount of phosphoric acid solution necessary to adjust the pH to about 5, which is equivalent to pH of Atmos 300 formulation, was obtained.

Formulation

The composition of water-based aerosols is

Table 1. Materials used in this experiments.

Tetramethrin	Technical grade (93. 5% pure) of N-(3, 4, 5, 6-tetrahydrophthalimido)-methyl-*dl-cis, trans* chrysanthemate (Neo-pynamin®, Sumitomo Chemical Co., Ltd.)
d-Allethrin	Technical grade (93. 2% pure) of allethronyl-*d-cis, trans*-chrysanthemate (Pynamin-forte®, Sumitomo Chemical Co., Ltd.)
d-Phenothrin	Technical grade (94. 6%pure) of 3-phenoxybenzyl-*d-cis, trans*-chrysanthemate (Sumithrin®, Sumtomo Chemical Co., Ltd.)
Resmethrin	Technical grade (94.1% pure) of 5-benzyl-3-furylmethyl-*dl-cis, trans*-chrysanthemate (Chrysron®, Sumitomo Chemical Co., Ltd.)
Piperonyl butoxide	Technical grade of butyl-6-(propyl piperonyl) ether (Takasago Perfumery Co., Ltd.)
Atmos 300®	Glycerol monooleate (Atlas Chem. Ind.)
Span 80®	Sorbitan monooleate (Atlas Chem. Ind.)
Emcol 14®	Polyglycerol oleate (Witco Chemical)
Emeol 511®	Alkanol amide (Witco Chemical)

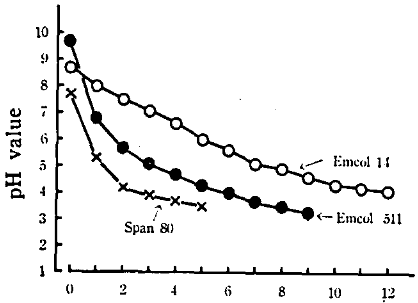

Fig. 1. Titration curves. Two hundred ml of 2% Span 80 solution and Emcol 14 solution we retitrated with 0.06N phosphoric acid solution, Emcol 511 solution with 0.3 N phosphoric acid solution to pH 3 to 4.

shown in Table 2. Seventy grams of aerosol was filled in 120ml of an aluminum container according to the conventional procedure.

Analysis of active ingredients

Aerosol samples were analysed by gas-chromatography according to the method of Horiba *et al.*[11]. Namely, aerosol samples were chilled in a dry-ice-methanol bath for about one hour. A small hole was made at the top of the can in order to remove propellant. The can was kept standing until the propellant had discharged completely. Thereafter, the top of the can was cut off, the residue (emulsion) was transferred into a separatory funnel. Active ingredients were extracted three times with 30ml of chloroform. The chloroform solution was concentrated with a rotary evaporater and the residual materials were transferred into a 20ml of volumetric flask,

Table 2. Composition of water based aerosol formulations.

Active ingredients	a given dosage
Emulsifier	1.0g
Deodorized kerosene	varied up to 10.0g
Deionized water	50.0g
Liquefied petroleum gas (LPG)	40.0g
Total	100.0g

which was then filled up to the mark with additional chloroform. This solution was subjected to gas-chromatographic analysis. Gas-chromatographic conditions are shown in Table 3.

pH measurment

The pH of the emulsion or water after extraction of active ingredients was measured using a pH meter (M-7, Horiba seisakusho).

Efficacy test

The CSMA aerosol test method for flying insects[12] was adopted. Adult houseflies (*Musca domestica*, each of 50 males and females) were confined in a Peet Grady chamber of 6 feet cube and the test aerosol was sprayed into the chamber. The spray amount of aerosol was in the range of 650±100mg. The knocked down houseflies were counted at 3, 5, 7, 10 and 15 minutes after spraying, and then the knocked and unknocked down houseflies were collected into a recovery container within 5 minutes to observe the mortality after 24 hrs. Five replications were made. The KT_{50} was calculated by the Finney's graphic method.

Table 3. Conditions for gas-chromatography.

Apparatus	Shimazu GC-3BF equipped with FID.
Column	Stainless steel, 1m in length and 3mm in diameter
Liquid phase	2% Diethyleneglycol succinate (DEGS)
Support	Chromosorb w (AW, DMCS, 60-80 mesh)
Temperatuer	Column and detector; 200°C Injection port; 220°C
Carrier gas	N_2; 1kg/cm^2
Hydrogen gas	0.5kg/cm^2
Air	1kg/cm^2
Internal standard	Diphenyl phthalate

Results and Discussion

Change in pH values with time

Water-based aerosol formulations with several kinds of emulsifiers without any active ingredients were stored at 35°C for 2 months in order to ascertain the change of pH values (Table 4). The emulsifiers used were ester or amide compounds which are essentially neutral materials, but seemed to possess different pH values owing to some acidic or alkaline material used in the rinsing process during their manufacture. The pH value of Atmos 300 formulation, which was initially weakly acidic stayed relatively constant for 2 months. The pH values of Span 80 and Emcol 14 formulations, which were initially weakly alkaline, changed weakly acidic. The change of pH value of the former proceeded more easily than that of the latter. This tendency was similar to the cases of solutions of these emulsifiers shown in Figure 1. On the other hand, the pH of Emcol 511 formulation, which was also initially alkaline, remained alkaline during the storage period. In the practical formulations, distilled or deionized water is commonly used as in the present experiments. As described above, the pH values of the formulations changed acidic, which is favorable for tetramethrin, so that tetramethrin in the practical formulations with Span 80 or Emcol 14 may be more stable thant that in the formulation using a buffer solution.

Table 4. Change in pH of water based aerosols containing several kind of emulsifiers.

Emulsifier	pH after indicated time (months)				
	0	2	4	6	8
Atmos 300	5.1	5.4	4.8	5.1	4.9
Span 80	7.7	6.5	6.6	6.2	6.1
Emcol 14	8.1	7.0	7.0	6.6	6.3
Emcol 511	9.4	8.5	8.3	8.0	8.0

Stability of tetramethrin in the water-based aerosol formulations with different emulsifiers.

The formulations containing 0.2% of tetramethrin and 1.0% of piperonyl butoxide with several kinds of emulsifiers were stored at 35°C for one year to examine stability of tetramethrin

Table 5. Stability of tetramethrin and change in pH of water based aerosol stored at 35°C for indicated months.
All aerosols contained 0.2% tetramethrin and 1.0% piperonyl butoxide.

Emulsifier	% of remaining tetramethrin after indicated time (months)				
	0	1	3	6	12
Atmos 300	100	99.0	97.9	98.3	97.0
	(5.3)	(5.4)	(—)	(4.3)	(4.4)
Span 80	100	97.7	96.6	96.6	96.5
	(7.7)	(6.7)	(—)	(6.5)	(5.6)
Emcol 14	100	93.4	91.7	88.1	87.9
	(8.9)	(7.0)	(—)	(6.4)	(6.2)
Emcol 14AC	100	95.2	93.2	92.9	91.9
	(4.8)	(5.8)	(—)	(6.1)	(5.8)
Emcol 511	100	92.8	87.7	77.8	—
	(9.6)	(8.3)	(8.3)	(8.2)	(—)
Emcol 511AC	100	96.8	91.0	90.4	88.5
	(4.5)	(5.3)	(5.8)	(7.2)	(8.2)

The numbers in brackets denote pH values.

* Emcol 14AC and emcol 511AC denote acidified emcol 14 and emcol 511, respectively.

and the change of pH values of the formulations (Table 5). Tetramethrin was the most stable in the formulation containing Atmos 300 among the formulations tested, namely only 3% broke down in a year. In the formulations containing Span 80, Emcol 14, and Emcol 511, 2.3, 6.6, and 7.7% of tetramethrin was decomposed in the first one month, and 3.5, 12.1, and 22.2% in one year, respectively. The initial pH values were alkaline with Emcol 511, Emcol 14, and Span 80 in these orders and Atmos 300 formulation was acidic as shown in the Table 4. Tetramethrin was more stable in the formulation at lower pH than that at higher pH, which agrees with the results obtained by Fujita *et al.*[10]. Noticeable decomposition of tetramethrin occurred in Span 80 and Emcol 14 formulations in the first one month and 3 months, respectively. This may be closely related to the change in pH of the formulations. Namely, the pH values of Span 80 formulation and Emcol 14 formulation became acidic within one month and 3 months, respectively. This change may be due to decomposition products of the emulsifiers themselves. The pH value of the Atmos 300 formulation was kept acidic and that of the Emcol 511 formulation alkaline for the testing periods. This may account for the findings that tetramethrin is stable in Atmos 300 formulation, but unstable in Emcol 511 formulation.

The Emcol 14 and the Emcol 511 formulations were made acidic with phosphoric acid in order to ascertain how pH affects the stability of tetramethrin. Tetramethrin decomposed at a rate of 4.8% and 3.2% in one month and 8.1% and 11.5% in one year in Emcol 14AC and Emcol 511AC formulations, respectively. To acidify alkaline formulations is an effective way to improve stability of tetramethrin to a certain extent, but the stability of these formulations is inferior to that in Atmos 300 or Span 80 formulations. The pH value of the Emcol 14AC tended to become constant at around 6 after a sufficient length of time, whereas that of the Emcol 511AC formulation tended to rise over a long period of time. The reason has not yet been clarified but it can be supposed that tetramethrin in the Emcol 511AC formulation will decompose to a considerable degree after storage of one year, as in the case of Emcol 511 formulation.

Insecticidal efficacy of the formulations with different emulsifiers.

Water-based aerosols with Atmos 300, Emcol 14 and Emcol 14AC were tested after storage at 35°C for 12 months to ascertain relationship between the stability of active ingredients and insecticidal efficacy against houseflies. Table 6 presents relationship between the concentration of active ingredients and insecticidal efficacy with stored samples. In Atmos 300 formulation, both

Table 6. Relationship between concentration of active ingredients and insecticidal efficacy against houseflies.

Emulsifier	period of storage at 35°C (months)	Concentration(%) of active ingredients		Insecticidal efficacy	
		Tetramethrin	PBO*1	KT_{50}*2 (min.)	% Mortality (at 24 hrs.)
Atmos 300	0	0.201	1.04	6.2 (5.9-6.5)*3	84
	12	0.195	1.02	6.5 (6.2-6.9)	82
Emcol 14	0	0.210	1.02	5.8 (5.4-6.1)	84
	12	0.185	0.96	7.9 (7.5-8.3)	80
Emcol 14AC	0	0.205	1.02	6.0 (5.6-6.4)	82
	12	0.188	0.97	6.5 (6.2-7.0)	78

*1. Piperonyl butoxide

*2. Time required for 50% knockdown of houseflies.

*3. Confidence limit.

the concentration of the active ingredients and the efficacy did not deteriorate. In the Emcol 14 formulation, tetramethrin and piperonyl butoxide in the stored sample decomposed by about 10% and 5%, respectively, and there was a significant difference in knockdown effect, but not in mortality between the stored sample and the freshly prepared one. However, in the Emcol 14AC formulation, there was no significant difference in both knockdown and killing effect between the stored sample and the fresh sample, though the active ingredients decomposed to the same extent as in the Emcol 14 formulation. This indicates that the adjustment of pH of the formulation was effective to hold the insecticidal efficacy, especially knockdown effect, and suggests that the insecticidal efficacy of water based aerosols may be influenced not only by the stability of active ingredients, but also by other factors, for example, the stability of emulsifier. Therefore, it seems to be very important to select an appropriate emulsifier.

Stability of tetramethrin and other pyrethroids.

Water-based aerosols containing tetramethrin in combination with other pyrethroids such as d-phenothrin, resmethrin and d-allethrin were stored at room temperature and their stability was examined during two years period (Table 7). The results show that all pyrethroids were stable in the formulation with Atmos 300 or Span 80 as an emulsifier. These emulsifiers may be suitable for a wide range of pyrethroids. Sometimes, a small amount of an oil-in-water type emulsifier such as Sorbon T-81 was mixed with water-in-oil type emulsifier in order to obtain sufficient emulsion stability. Tetramethrin and resmethrin were also stable in the formulations with this mixture of emulsifiers. However, both tetramethrin and resmethrin in the formulation with Emcol 511 were definitely unstable, especially tetramethrin decomposed at a rate of 20% in 2 years. d-Phenothrin and d-allethrin in the formulation with Emcol 511 have not yet been tested, but the results of resmethrin suggest that this emulsifier may be unsuitable for these pyrethroids.

Summary

The water-based aerosol formulations were tested as to the followings;

Table 7. Stability of tetramethrin and other pyrethroids in water based aerosols stored at room temperature.

Active ingredients	Concentration (%, w/w)	Emulsifier	% of remaining pyrethroids			
			Initial	6months	12months	24months
Tetramethrin	0.2	Atmos 300	100	—	102	99
d-Phenothrin	0.1		100	—	100	99
Tetarmethrin	0.2	Atmos 300	100	100	97	98
Resmethrin	0.1	+Sorbon T-81*	100	100	103	101
Tetramethrin	0.2	Emcol 511	100	92	85	81
Resmethrin	0.1		100	97	90	90
Tetramethrin	0.2	Atmos 300	100	—	102	100
(Piperonyl butoxide	1.0)					
Tetramethrin	0.2	Span 80	100	—	98	100
(Piperonyl butoxide	1.0)					
Tetramethrin	0.1	Atmos 300	100	—	99	96
d-Allethrin	0.1		100	—	98	98
d-Phenothrin	0.1		100	—	101	100
Tetramethrin	0.12	Span 80	100	—	99	96
d-Allethrin	0.1		100	—	102	98
(Piperonyl butoxide	1.0)					

* Polyoxyethylene sorbitan monooleate (Toho Chemical Co., Ltd.)

(1) the relationship between the stability of tetramethrin in the formulations containing various emulsifiers and their pH values, (2) comparison in insecticidal efficacy between the stored samples and freshly prepared ones, and (3) stability of several pyrethroids stored for a long period of time. The results obtained may be summarized as follows;

(1) The pH values of the aerosol formulations had a tendency to become lower with time, the rate of which depended on the emulsifier used. The change in pH occurred in the formulations without any active ingredient, suggesting dependency upon the decomposition of emulsifier itself.

(2) Tetramethrin was more stable in acidic formulations than in alkaline formulations. However, even if the formulation was alkaline at initial pH, tetramethrin did not decompose once the pH changed acidic. To acidify alkaline formulation is effective way to keep tetramethrin stable.

(3) There was no significant difference in insecticidal efficacy of acidic formulations between the samples stored at 35°C for one year and those freshly prepared, but in alkaline formulation, there was significant difference between them. The acidic pH was also an effective way to stabilize the insecticidal efficacy.

(4) Tetramethrin, d-phenothrin, resmethrin and d-allethrin in the formulations with suitable emulsifier were quite stable for at least 2 years at room temperature.

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