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Development of a New Acaricide, Fenpyroximate

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INTRODUCTION

Since 1980, insecticides of synthetic pyrethroids, herbicides of sulfonylurea and fungicides of azole compounds attracted much attention due to their novel efficacy. On the other hand in the area of acaricides, new compounds with such a novel activity were not developed, because of the difficulty of development such as, rather small market, and the risk of resistance problem. But the spider mite is one of the most serious arthropod pests in agriculture not only because it causes severe damage on crops. And the intensive use of synthetic pyrethroids has recently caused another problem, the resurgence of mites.

In order to solve these problems, we focused our research on the development of a new acaricide and discovered fenpyroximate among phenoxypyrazol compounds in 1985.

DISCOVERY OF FENPYROXIMATE

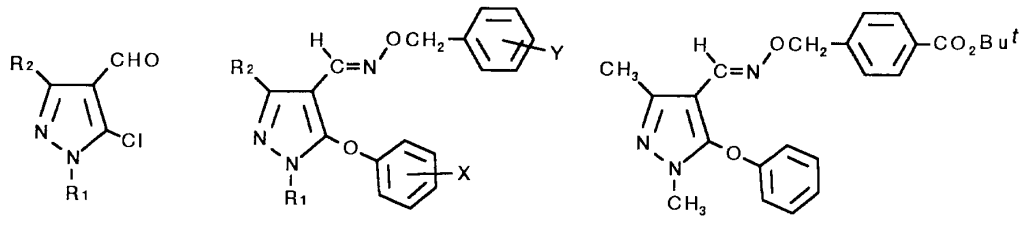
We aimed at chroloformylpyrazol as the starting compound for a new acaricide. Because the compound is easily synthesized and is substituted by various substituent groups at 1-, 3-, 4- and 5-positions of pyrazol ring. We have synthesized about 2000 compounds related to chroloformylpyrazol and evaluated acaricidal activities of them. Among them pyrazoloxime ether was worthy of attention by its relative high activity. Then we have synthesized derivatives of pyrazoloxime ether, and found the compound substituted by methyl group at 1- and 3-positions of pyrazol ring, by bulky alkyl ester such as *tert*-butyl ester at 4-position of benzyl ring, and by phenoxy group at 5-position of pyrazol ring showed most high activity. As a result, we selected fenpyroximate.

CHARACTERISTIC OF ACARICIDAL ACTIVITY OF FENPYROXIMATE

Fenpyroximate shows high activity on important phytophagous mites such as Tetranychidae, Eriophyidae, Tarsonemidae and Tenuipalpidae. Its activity on predacious mites such as Phytosaiidae is relatively low, and that on animal-parasitic and soil-living mites is almost no active.

Fenpyroximate shows effect on all stage of mites of *Tetranychus urticae* and *Panonychus citri* and is the most effective on larvae followed by nymphs, adults and eggs, indicating fenpyroximate is available for any stage of mites.

Fenpyroximate shows quick knock-down effect on adult mites. Prior to knock-down, mites treated with fenpyroximate represent



Chloroformylpyrazol Pyrazoloxime ether Fenpyroximate

spin down from leaves but not walk off observed characteristically in mites treated with synthetic pyrethroids.

Fenpyroximate shows another characteristic effects, suppression of oviposition, on adult mites. Fenpyroximate kills adult mites in one day after treatment through knock-down activity. Once mites knocked down, they do not recover, which result in the stopping feeding and the suppression of oviposition.

The LC_{50} value of fenpyroximate on larva is 0.98 mg/*l*, while cumulative mortality through successive developmental stage was 0.071 mg/*l* at protochrysalis and 0.041 mg/*l* at duetochrysalis, and the difference between these values is 14–24 times. Quick knock down type compounds such as dicofol or cyhexatin do not show the different LC_{50} value of either on larvae or successive stage.

Larvicidal type ones do not show quick efficacy on larvae and show only molting-inhibitory activity through successive development stage like insect growth regulators. Fenpyroximate seems to have both type of properties and is a unique acaricide compared to conventionals.

PREPERATION OF SUSPENDED CONCENTRATE OF FENPYROXIMATE

The residual activity of a emulsifiable concentrate of fenpyroximate is lower than a suspended concentrate in field study, because fenpyroximate is unstable to light. We needed a suspended concentrate of fenpyroximate to obtain the stable and residual effect on mites. Acaricides are usually used by mixing with another formulations, in particular with Bordeaux mixture for apple tree. Most suspended concentrates prepared in those days contained xanthan gum as a thickner and coagulated with Bordeaux mixture. The preliminary suspended concentrates of fenpyroximate coagulated with Bordeaux mixture also. We prepared various formulations and tested them, and we could make the formulation containing 5% of fenpyroximate using smectite minerals as a thickner. This formulation can be mixed homogeneously with Bordeaux mixture. We obtained a patent on this. This formulation is free of organic solvents and low toxicity.

TOXICITY OF FENPYROXIMATE

The toxicities of fenpyroximate are summarized in Table 1. Acute toxicity of technicals is relatively strong but that of the 5% suspended concentrates is weak (LD_{50}: >8000 mg/kg).

METABOLISM OF FENPYROXIMATE

After a single oral administration of [Pyrazol-3-^{14}C], [Phenyl-^{14}C(U)] or [Benzyl-^{14}C(U)] fenpyroximate to rats, the radiocarbons are almost completely excreted into feces and urine within 72 hr. Fenpyroximate degrades

Table 1 Toxicity of fenpyroximate in animals.

Items	Animals	Results (LD_{50}, NOEL)
Acute oral toxicity	Rats	M: 480, F: 245 mg/kg
	(5% SC)	M: 9000, F: 8000 mg/kg
Acute dermal toxicity	Rats	M and F: >2000 mg/kg
Acute inhalation toxicity	Rats	M: 0.33, F: 0.36 mg/*l*
Skin irritation	Rabbits	Slightly irritant
Eye irritation	Rabbits	No irritant
Skin sensitization	Guinea pigs	Negative
Subacute oral toxicity	Dogs	M and F: 2 mg/kg/day
	Rats	M: 1.30, F: 1.65 mg/kg/day
Chronic oral toxicity	Dogs	M and F: 1.5 mg/kg/day
	Rats	M: 0.93, F: 1.21 mg/kg/day
Carcinogenicity	Rats · mice	No carcinogenic
Reproduction, taratology	Rats · rabbits	Negative
Mutagenicity	*In vivo, in vitro*	Negative

M: male, F: female.

with half-lives of 26.3–49.7 days in diluvial and valcanic ash soils under upland laboratory conditions, and finally is mineralized to CO_2 and/or bound to soil organic matter.

In animals, crops and soils, fenpyroximate seems to be metabolized *via* oxidation of the methyl group at 3-position in the pyrazol ring, *p*-hydroxylation in the phenyl moiety, *N*-demethylation, hydrolysis of the *tert*-butyl ester, cleavage of the oxime ether bond and/or *E*/*Z* isomerization. In rats, the *tert*-butyl group of benzyl ring is also oxidized.

EFFECT OF FENPYROXIMATE ON NATURAL ENEMIES AND OTHER ANIMALS

Fenpyroximate shows almost no effect on Misumenops, Licosa, Apis and Osmia, and little effect on Amblyserius, Chrysopa, Oligota and Orius. And it moderately effects on Phytoseiulus and Harmonia. *Bombyx mori* is delayed growth rate.

Fenpyroximate shows strong toxicities for carp (TLm=0.0061mg/*l*, 48 hr), rainbow trout (TLm=0.00057 mg/*l*, 48 hr) and daphnia (TLm=0.085 mg/*l*, 3 hr).

REGISTRATION OF FENPYROXIMATE IN THE WORLD

In 1991, fenpyroximate was registered and marketed for the control of mites in Japan, China and Swiss. And now it is registered in 27 countries among Asian, European, the Middle East, Africa, South America, and Oceania.