INSECTICIDAL ACTIVITY OF MACROTETROLIDE ANTIBIOTICS

Sir :

Residual toxicity of synthetic insecticides such as DDT and BHC is a serious problem for the welfare of humans, since these chemicals decompose slowly. They therefore remain in nature for extended times and are accumulated in animals and plants. Easily decomposable pesticides with low toxicity would be very advantageous.

In our screening for insecticidal antibiotics, it was found that macrotetrolide antibiotics showed remarkable mitecidal activity. A streptomyces, which was later identified as *Streptomyces aureus*, was isolated from a soil sample collected from the Saitama Prefecture in Japan. The acetone extract of this organism exerted significant activity against a test insect, *Callosofruchus chinensis* (Azukibean weevil). The active principle was isolated from the filter cake of the fermented broth by extracting with acetone followed by silica gel column chromatography. The principle thus obtained was crystallized from *n*-hexane as large prisms, m.p. 70~71°C. However, when the principle was subjected to thin-layer chromatography with silica gel using the solvent system of ethyl acetate - chloroform (2 : 1), it showed 3 components. Each component was separated by silica gel column chromatography. Infrared absorption spectra of these components closely resembled each other, and indicated that they belonged in the macrotetrolide group[1,2,3]. It was concluded from nmr and mass spectra that the active principle consisted of 3 macrotetrolide antibiotics, dinactin, $C_{42}H_{68}O_{12}$, trinactin, $C_{43}H_{70}O_{12}$, and a new antibiotic named tetranactin $C_{44}H_{72}O_{12}$.

Table 1. Effect of the macrotetrolide complex on the female adult of *Callosofruchus chinensis* by the topical application method.

	Dose (mcg/insect)				
	0.25	0.50	1.00	1.50	3.00
Mortality (%)	0	10.3	84.8	100	100

An acetone solution of the macrotetrolide antibiotics was topically applied to the insect. The amount applied was 0.02 ml/insect. Fifty to 100 female adults of *Callosofruchus chinensis* were used in each dose. Insecticidal activity was determined 3 hours after application.

Table 2. Mitecidal activity of the macrotetrolide antibiotics against *Tetranychus kanzawa* in field test.

Agents	Concentrations (mcg/ml)	Numbers of mites after spray			
		0 day	2 days	6 days	10 days
Macrotetrolide complex	200	156	0	2	11
	133	815	0	4	5
Kelthane	200	86	0	3	6
	200	54	0	3	7
Control		133	244	578	413

The macrotetrolide antibiotic was dissolved in a small amount of cyclohexane. After addition of Nonipol for dispersion, the solution was diluted with distilled water to the given concentrations. The suspensions were sprayed and the number of mites on the leaves of the host plant were determined.

The structure of tetranactin was confirmed by $LiAlH_4$ reduction and acid hydrolysis. However, nonactin, which is the first macrotetrolide isolated from some streptomyces cultures, was absent in our complex.

Table 1 shows the insecticidal activity of our macrotetrolide complex against *Callosofruchus chinensis*, an insect used in our screening. The antibiotic complex is very effective when it is directly applied to the insect, although it is completely ineffective in the film contact method.

Mitecidal activity in a field test of the complex is shown in Table 2. Kelthane was selected as a positive control, because this hydroxylated derivative of DDT is most widely used for the control of mites. The activity in the field test was approximately comparable to that of kelthane at the two concentrations tested. The antibiotic complex is also effective against other mites such as those of apple, mandarin orange, and peach.

Acute toxicity of the antibiotic complex is low to mammals ; mice could tolerate oral administration of 3,250 mg/kg and intraperitoneal administration of 500 mg/kg. The LD_{50} in rats is over 320 mg/kg orally. Quail could also tolerate a dose of 2,000 mg/kg administered orally.

Thus, our macrotetrolide antibiotic complex shows promising insecticidal activity especially in view of the low toxicity and

easy decomposition.

Studies on the biological properties and chemistry of the complex are now under way and the results will be presented elsewhere.

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