2002 BELTWIDE COTTON CONFERENCES, ATLANTA, GA – JANUARY 8-12

KOROMITE™: A NEW MITICIDE FOR USE IN COTTON

R.L. Kepner
Gowan Company
Madera, CA

Abstract

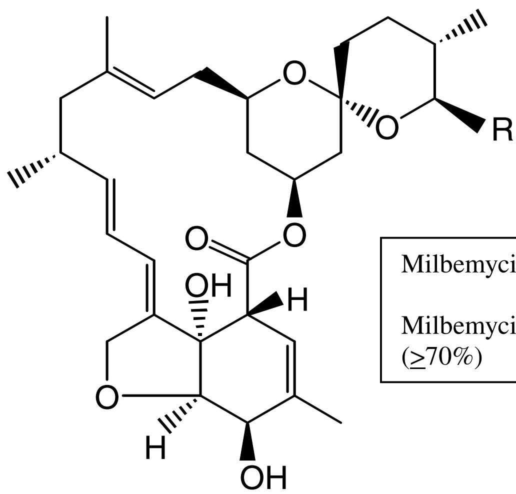
Koromite™ is a new selective acaricide for mite control in cotton. The active ingredient milbemectin is a mixture of natural compounds derived from the soil microorganism *Streptomyces hygroscopicus* subsp. *aureolacrimosus*. Milbemectin is highly effective against a wide range of pest mite species including the strawberry spider mite (*Tetranychus turkestani)*, two-spotted spider mite (*T. urticae)*, and pacific spider mite (*T. pacificus)* in cotton. Milbemectin acts through both contact and ingestion. It is active on all life stages of mites including eggs and at sub lethal levels significantly reduces the egg-laying capacity of treated adult females. Milbemectin has a good toxicological and environmental profile and has recently been classified by the US-EPA as a reduced risk compound. Milbemectin has excellent crop safety, minimal impact on beneficial arthropods and is not cross-resistant to existing acaricides thus making it an excellent choice for use in integrated pest management and resistance management programs.

Introduction

Milbemectin is the common name for the active ingredient in Koromite™ miticide. Milbemectin is a mixture of naturally derived compounds (milbemycins) derived from the soil microorganism, *Streptomyces hygroscopicus* subsp. *aureolacrimosus* first isolated in Hokkaido, Japan. This compound was originally discovered and developed by Sankyo Company of Japan and is now marketed in nine countries outside the US. Milbemectin is currently being developed in North America by Gowan Company with federal registration on cotton expected in 2003. This compound has recently been granted reduced risk status by the US-EPA.

Chemical and Physical Properties

Structural formula:



Milbemycin A_3: R=CH_3 ($\leq$30%)

Milbemycin A_4: R=CH_2CH_3 ($\geq$70%)

Common name:	Milbemectin [CAS No. 51596-10-2(M.A_3) and 51596-11-3 (M.A_4)]
Chemical family:	milbemycin fermentation products of *Streptomyces spp*.
Formulation:	1% EC (1% w/w EC) containing 0.0775 lbs. milbemectin per U.S. gallon
Appearance:	white crystal
Odor:	Odorless
Molecular weight:	A_3=528.7; A_4=542.7
Melting point:	212-215°C

Solubility in water (20°C):	A_3=0.88ppm; A_4=7.23ppm
Stability:	Heat: stable (50° C for 14 days) Acid: slightly unstable Neutral and Alkali: stable Light: slightly unstable
Hydrolysis:	A_4: t½ =11.6, 259.9 and 226.3 @ 25°C (pH 5, 7, 9)
Vapor pressure:	<1 X 10^{-7} mm Hg
Octanol/water partition coefficient:	K_{ow} A_3 = 6.54; K_{ow} A_4 = 7.00

Toxicological Profile

Study Type	Organism	Milbemectin 1%EC
Oral LD_{50}	Rat	>5,000 mg/kg
Dermal LD_{50}	Rat	>2,000 mg/kg
Inhalation LC_{50}	Rat	>6.75 mg/l (4hr)
Eye irritation	Rabbit	Mild, reversible
Dermal irritation	Rabbit	Mild, non-sensitizing

Ecological Profile

Study Type	Organism	Milbemectin 1%EC
Acute LC_{50}	Rainbow Trout	450 ppb
Acute LC_{50}	Daphnia	420 ppb
Dietary LC_{50}	Mallard Duck	>2,250 mg/kg
Acute LD_{50}	Honeybee	4.23 µg/bee (topical) >100 µg/bee (oral)

Environmental Fate

Milbemectin is not persistent or mobile in the soil due to high soil binding characteristics and rapid degradation in the environment. This compound is not expected to bioaccumulate and does not pose any significant environmental fate effects.

Biological Properties

Pest Spectrum

Milbemectin is highly effective against a wide range of economically important mite species including tetranychid, eriophyid and tarsonemid mites. This compound is active against all stages of mite development including eggs (Table 1). In addition to its broad spectrum acaricidal activity, milbemectin has also demonstrated limited activity against a variety of insect pests.

Mode of Action

Milbemectin inhibits the gamma-amino butyric acid (GABA) mediated nervous system in mites and insects causing loss of cell function and disruption of nerve impulses to the muscles. This action causes a quick and irreversible paralysis in arthropod pests that ultimately results in cessation of feeding and eventual death. Although maximum mortality may not be observed for several days, target pests cease movement and feeding activity soon after treatment. Therefore caution must be taken when evaluating initial control following milbemectin applications.

Milbemectin is active through both contact and ingestion. It is unique in that it acts not only as a fast acting acaricide on all mite life stages but, at sub lethal levels, also significantly reduces subsequent oviposition in exposed adult females (Table 2). Milbemectin rapidly degrades in the environment and quickly disappears from treated surfaces making contact activity short-lived. However, milbemectin provides outstanding residual control of target pests through feeding on treated foliage and subsequent reduction in oviposition rate.

Influence of Temperature

Milbemectin demonstrates excellent acaricidal activity over a wide temperature range (Table 3). Acaricidal activity is not significantly affected by either high or low temperatures, as is characteristic of several other commercial products. This allows for greater flexibility in the use of milbemectin as an effective acaricide under a wide range of conditions.

Translaminar Activity

Milbemectin shows excellent translaminar activity on treated foliage by controlling mite pests on the upper-leaf surfaces as well as the under side of leaves where mites predominately feed (Figure 1). In addition to milbemcetin's short environmental persistence, this translaminar activity also provides for an added margin of safety to beneficial predators and parasites.

Field Performance

Koromite™ has proven to be highly effective against the major mite pests infesting cotton including *Tetranychus turkestani, T. urticae,* and *T. pacificus* in numerous California field studies. Koromite™ has been efficacious at rates of 0.005-0.007 lb. ai/a in seedling cotton and 0.01-0.02 lb. ai/a in mid-season/layby cotton.

In two California trials conducted in 2000, Koromite™ applied at 0.005-0.01 lb. ai/a provided 28-38 days control of building spider mite populations in seedling cotton (Figure 2-3). Overall control was comparable to Zephyr (avermectin) with no phytotoxicity observed in either trial.

In two mid-season trials conducted in California in 1998 and 2000, Koromite™ applied at 0.01-0.02 lb. ai/a provided 30-42 days control of building spider mite populations (Figure 4-5). Overall control was comparable to Zephyr (avermectin) with no phytotoxicity observed in either trial.

Non-Target Impact

Milbemectin has little or no impact on beneficial arthropods based on numerous laboratory and field studies. The western flower thrips, *Frankliniella occidentalis* , occasionally an early season pest in cotton, is considered an important predator of mite eggs throughout the cotton-growing season. In a 1998 California trial, milbemectin treatments resulted in only a short-term reduction in thrips levels with populations increasing in proportion to those in the untreated check after a few weeks (Figure 6). The overall impact was comparable to the standard Zephyr (avermectin) which has long been used successfully in cotton IPM programs in California.

In addition to thrips, hemipteran predators are also important mite predators in cotton. In a laboratory study conducted in Europe in 1999, milbemectin treatments at rates as high as 0.025 lb. ai/a did not show any significant impact on mortality, reproduction or egg viability in the hemipteran predator, *Orius laevigatus* (Table 4). These studies represent only a small sample but do demonstrate the safety of milbemectin to important beneficial arthropods in cotton.

Resistance

Milbemectin is a naturally derived acaricide characterized by a novel mode of action. Based on laboratory and field studies conducted to date, no cross-resistance has been documented with milbemectin to acaricides from different classes of chemistry as well as avermectin (Tables 5-6 and Figure 7). Additionally, there have been no reports of resistance to milbemectin in the field since it was first launched commercially in Japan in 1990.

Summary

Milbemectin is an excellent new tool for mite control in cotton. It is highly effective against major pest mites at low use rates and has limited impact on beneficial predators and parasites. Milbemectin is active against all mite life stages including eggs and at sub lethal levels significantly reduces oviposition in treated adult females. Milbemectin has a good toxicological and environmental profile and has recently been classified by the US-EPA as a reduced risk compound. Milbemectin has excellent crop safety, is not temperature sensitive, and is not cross-resistant to existing acaricides thus making it an excellent choice for use in integrated pest management and resistance management programs.

Table 1. Toxicity of milbemectin against various life stages of *Tetranyuchus urticae*.

Egg	Larvae	LC_{50} (ppm) Protonymph	Deutonymph	Adult
3.3	1.0	1.3	1.8	4.7

Table 2. Effect of milbemectin on reproduction in adult female, *Tetranychus kanazawa* (Sapporo-strain) confined on field treated bean leaves collected at periodic intervals.

Treatment	Response	Day leaves sampled			
		0	**4**	**7**	**10**
Milbemectin	% Mortality	100	34.1	13.6	7.9
(10 ppm)	Eggs/Survivor	-	-	0.21	**0.4**
Dicofol	% Mortality	100	91.4	80.4	56.8
(267 ppm)	Eggs/Survivor	-	-	3.04	**4.35**
Control	% Mortality	0	5.6	3.6	0
	Eggs/Survivor	-	-	6.64	**7.53**

Table 3. Influence of temperature on milbemectin performance against *Tetranychus urticae* under laboratory conditions.

Milbemectin (ppm)	% Mortality		
	20°C	**25°C**	**30°C**
2.0	98	97	95
0.6	97	95	76
0.2	6	8	9

Table 4. Impact of milbemectin on adult *Orius laevigatus* in the laboratory (Agrochemical Evaluation Unit, University of Southhampton, UK, 1999).

Treatment	% Mortality	# Eggs/Female/Day	# Viable Eggs/Female/Day
Milbemectin (0.008 lb. ai/a)	0	8.1	7.0
Milbemectin (0.025 lb. ai/a)	3	9.9	7.6
Dimethoate (0.31 lb. ai/a)	100	-	-
Control	-	7.7	6.9

Table 5. Efficacy of milbemectin against resistant strains of *Tetranychus urticae* collected from four locations in Japan to various acaricides.

Treatment	AI (ppm)	% Mortality			
		Shimizu	**Shimada**	**Kakegawa**	**Sapporo**
Milbemectin	10	100	100	100	100
Pyridaben	100	0	0	100	80
Fenproximate	25	57	100	100	100
Clofentezine	133	0	0	0	0
Fenpropathrin	50	0	0	80	90
Kelthane	400	0	100	100	100
Amitraz	250	0	57	0	30
Fenbutatin oxide	167	0	0	100	100

Table 6. Toxicity of milbemectin against avermectin resistant adult female *Tetranychus urticae* in laboratory bioassays.

Treatment	LC_{50} (ppm)		
	Resistant*	**Susceptible**	**RR**
Avermectin[1]	7.1	0.1	71
Milbemectin	**11.1**	**2.2**	**5.1**
Avermectin[2]	12.6	0.09	140
Milbemectin	**2.0**	**6.0**	**1**

* Wild mite strains collected from greenhouses in Holland[1] and Watsonville, California[2].

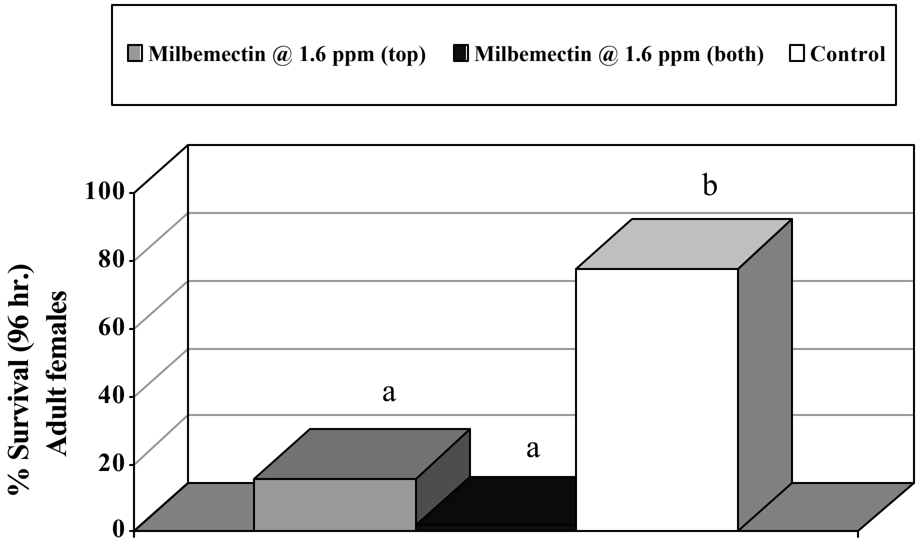


Figure 1. Translaminar activity of milbemectin against adult female *Tetranychus urticae* confined on the underside of strawberry leaves treated either on upper surface only or on both upper and lower leaf surfaces (Zalom and Walsh, 1995).

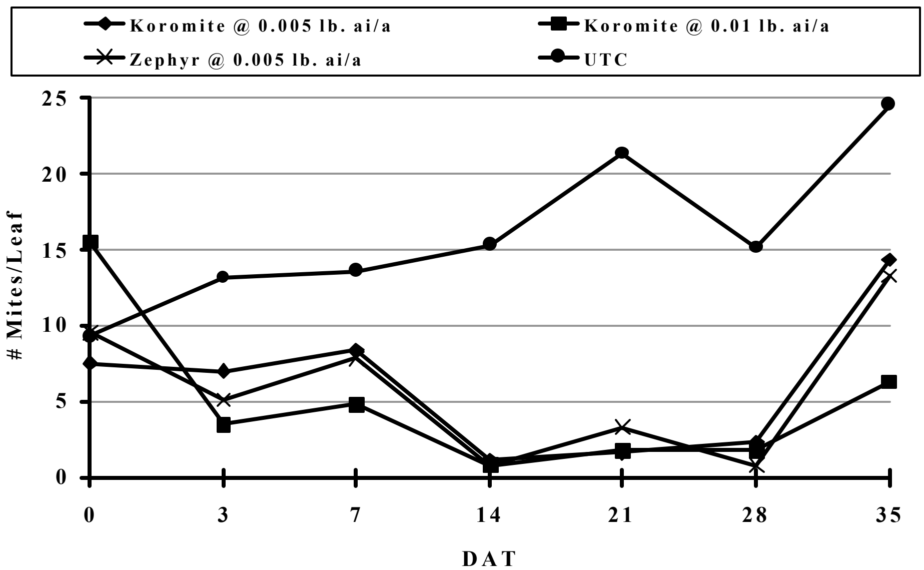


Figure 2. Control of spider mites (*Tetranychus spp*.) with milbemectin in seedling cotton near Visalia, CA (2000).

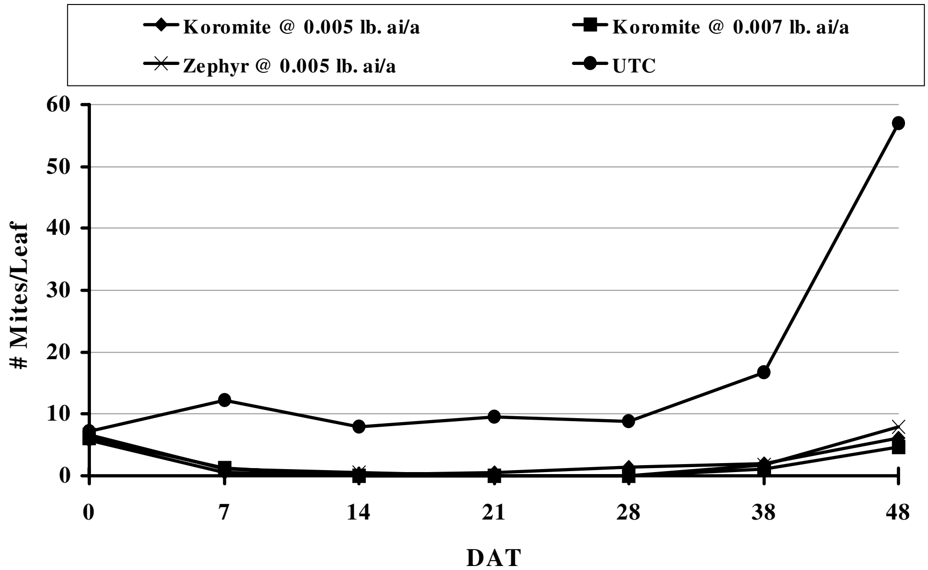


Figure 3. Control of spider mites (*Tetranychus spp*.) with milbemectin in seedling cotton near Bakersfield, CA (2000).

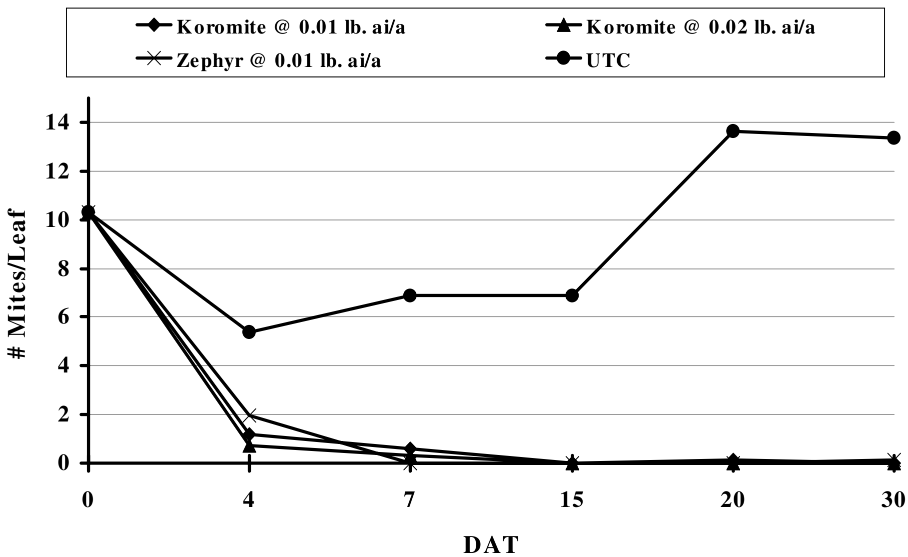


Figure 4. Control of spider mites (*Tetranychus spp*.) with milbemectin in mid-season cotton near Bakersfield, CA (1998).

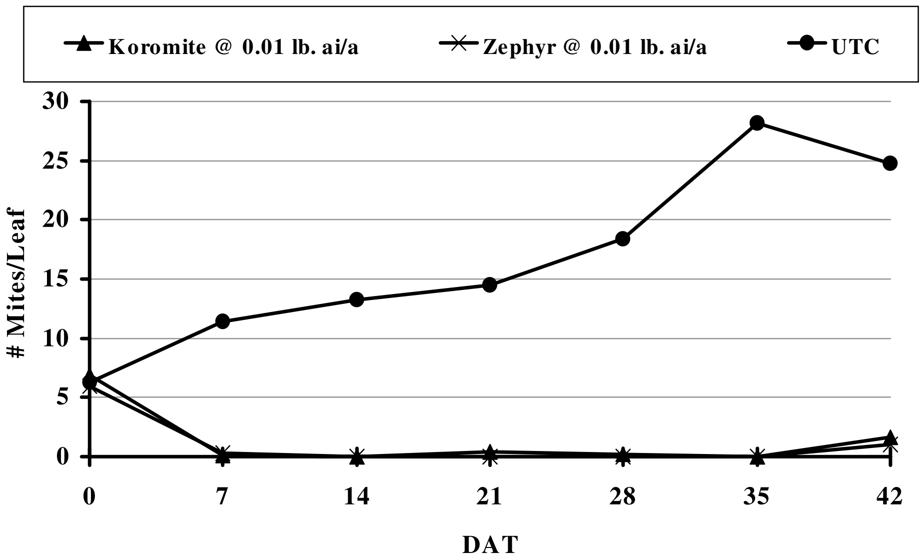


Figure 5. Control of spider mites (*Tetranychus spp.*) with milbemectin in mid-season cotton near Kerman, CA (2000).

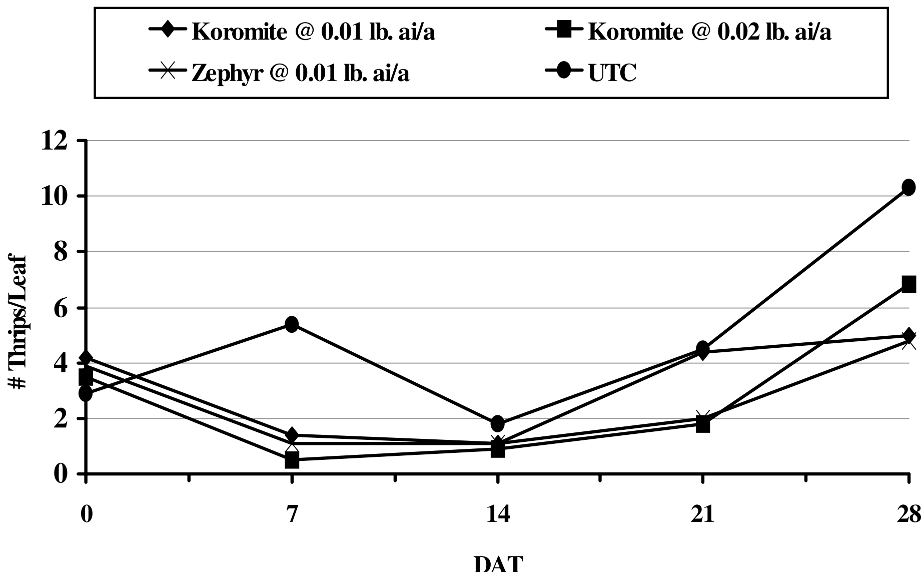


Figure 6. Impact of milbemectin on western flower trips, *Frankliniella occidentalis* in cotton near Tulare, CA (1998)

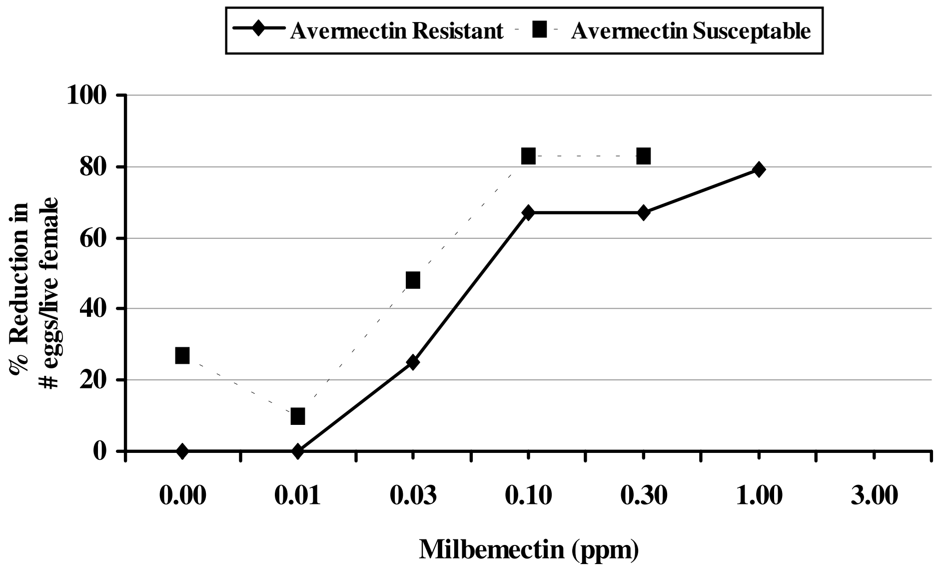


Figure 7. Sub lethal impact of milbemectin on an avermectin susceptible lab strain and a resistant population of *Tetranychus urticae* collected from a greenhouse in Watsonville, California.