CYHALOTHRIN

First draft prepared by
Denis Hamilton, Queensland, Australia
Susan Calumpang, Manila, Philippines

Cyhalothrin was first evaluated by the 1984 JMPR when an ADI of 0-0.02 mg/kg bw was estimated. Cyhalothrin is a mixture in equal parts of four Z-*cis*-isomers, which exist in two enantiomeric pairs:

(R)-α-cyano (R)-*cis*-Z-cyclopropanecarboxylate and (S)-α-cyano
(S)-*cis*-Z-cyclopropanecarboxylate, coded R157836

(S)-α-cyano (R)-*cis*-Z-cyclopropanecarboxylate and (R)-α-cyano
(S)-*cis*-Z-cyclopropanecarboxylate, coded R119321 and PP321

Cyhalothrin was last evaluated by the JMPR in 1988. Cyhalothrin was originally developed for the control of livestock ectoparasites. The development for crop uses in countries other than Japan was changed from cyhalothrin to the enantiomeric pair coded PP321 (see above) because PP321 is more insecticidally effective. The spectrum of insecticidal activity is unchanged. Products containing this material are now available commercially in some 30 countries (JMPR,1986). Cyhalothrin has not been classified as fat-soluble or not fat-soluble. As cyhalothrin has a log P_{ow} = 6.8 (Pesticide Manual, 11th Edition) and the data on distribution between meat and fat as determined in the goat metabolism study, JMPR would likely classify cyhalothrin as fat-soluble. No animal commodity MRLs were set.

A system for assigning common names to synthetic pyrethroids and related compounds was still under discussion within ISO in 1986. Subject to the outcome of the discussion, it is expected that lambda-cyhalothrin will be proposed as a common name for PP321. For convenience, this name was used in the evaluation (JMPR, 1986)

USE PATTERN

Cyhalothrin is a pyrethroid insecticide with a high level of activity against a wide range of *Lepidoptera, Hemiptera, Diptera* and *Coleoptera* spp. and has miticidal activity. The compound is a stomach, contact and residual insecticide. It shows adulticidal, ovicidal and, particularly, larvicidal activity. It is also extremely effective against a number of insects resistant to standard treatments such as organochlorines and organophosphates. Like other photostable synthetic pyrethroids, cyhalothrin is relatively stable to degradation in sunlight. Cyhalothrin is not plant systemic and has very little fumigant or translaminar activity (JMPR 1984).

RESIDUES FROM SUPERVISED TRIALS

Wheat

Two residue trials were carried out on wheat during 1985 in The Netherlands. One application of cyhalothrin, 5% EC at 7.5 g ai/ha, was made either during or two weeks after flowering. No measurable residues (less than 0.01 mg/kg) were found in the mature grain at harvest (after 28/29 days) and only low residues, 0.06-0.18 mg/kg, in the straw (Kinkaid and Sapiets, 1986).

Cotton

Supervised trials in Brazil, Israel and South Africa involving repeated spray applications of a 2.5% EC formulation at rates of 6-20 g ai/ha, yielded residues at or below the LOD (0.01 mg/kg) in cotton seeds sampled 11-33 days after the last application (Sapiets, 1984a, b; Tyldesley and Sapiets, 1985). A program of four applications at rates of 50-150 g ai/ha, with a 21-day pre-harvest interval (PHI) yielded lambda cyhalothrin residue levels in cotton seed up to 0.18 mg/kg (Sapiets, 1984b). Multiple applications of lambda-cyhalothrin were conducted in the USA using a 12% EC formulation at 33-44 g ai/ha through commercial type spray equipment and a total of 13 sites distributed among nine US states country-wide. Lambda cyhalothrin was applied by air (4 sites); up to 15 applications were made, with the cotton harvested 20-27 days after last application. A lambda cyhalothrin residue of 0.01 mg/kg was detected in only one cotton seed sample, all other samples had no residues (LOD; 0.01 mg/kg) (Fitzpatrick, 1984; Neal, 1985a).

FATE OF RESIDUES

Plants

Cotton

^{14}C-cyclopropyl-labelled and ^{14}C-benzyl-labelled lambda-cyhalothrin (98% pure radio-chemically) were formulated as a 2.5% emulsifiable concentrate formulation, diluted with water and sprayed on cotton plants at a rate equivalent to 66 g ai/ha at flowering. These applications were repeated 3 and 7 weeks after flowering. The plants were grown to maturity. A residue of 0.010 mg cyhalothrin equivalents /kg was found in the cotton seeds from plants treated with ^{14}C-benzyl-labelled lambda-cyhalothrin. A residue of 0.020-0.027 mg cyhalothrin equivalents/kg was found in cotton seeds from plants treated with the cyclopropyl-labelled material. Although some characterization of the latter residue was possible, the levels of radioactivity present were too small to allow identification of any of the radioactive products present in these mature seeds (Leahey and French, 1985).

These data indicate that lambda-cyhalothrin and its metabolites are not readily translocated into cotton seeds following foliar application of lambda-cyhalothrin. The largest single source of residues on cotton seeds is likely to be from direct contamination of the seeds, by spraying after the bolls have begun to split.

To study the fate in the latter situation, ^{14}C-cyclopropyl-labelled and ^{14}C-benzyl-labelled lambda-cyhalothrin were formulated as a 2.5% emulsifiable concentrate formulation in water and spotted on to cotton seeds, in freshly ripened bolls, on plants maintained in a greenhouse for a further 14 days. 96% of the radioactivity present after 14 days was extractable with hexane; virtually all of it was present as lambda-cyhalothrin, with no significant change in isomeric composition (Leahey and French, 1985).

Growing cotton leaves were treated with the separated *cis* and *trans* isomers of ^{14}C-cyclopropyl-labelled [(RS)-α-cyano-3-phenoxy-benzyl-(1 RS)-*cis, trans*-3-(EZ-2-chloro-3, 3, 3-trifluoroprop-1-enyl)-2,2-dimethylclopropanecarboxylate] and were exposed to sunlight. After 28 days exposure, 68% (cis treatment) and 65% (trans treatment) of the radioactivity recovered from the leaves was due to unchanged pyrethroid. After 48 days, about 65% of the radioactivity on the *cis* compound treated leaves was polar, water-soluble compounds. On acid hydrolysis 66% was converted to organic soluble compounds, containing (1 RS)-*cis* and *trans*-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclo-propanecarboxylic acid and two unknown compounds. Some photoisomerisation (less than 10%) at the 1, 3 bond of the cyclopropane ring of the pyrethroid occurred on the leaf surface after 28 days (Curl and Leahey, 1979).

Animals

Goat

A goat was dosed orally for seven days with ^{14}C-cyclopropyl-labelled lambda-cyhalothrin. The dose rate was equivalent to approximately 11 ppm. During dosing, the maximum residue level in the milk was 0.27 mg cyhalothrin equivalents/kg (mean value during days 3-7 of 0.21 mg/kg), virtually all of which was characterized as lambda-cyhalothrin. The update from JMPR 1986 is not clear on the expression of cyhalothrin residues – on a whole milk basis or a fat basis. The goat was slaughtered 16 hours after receiving the final dose, when residues in the tissues, expressed in cyhalothrin equivalents, were 0.024-0.028 mg/kg in meat; 0.13 -0.44 mg/kg in fat; 0.34-0.35 mg/kg in liver; and 0.20 mg/kg in kidney.

The residues in meat and fat were due mainly to lambda-cyhalothrin. However, in the liver and kidney, intact pyrethroid accounted for only a small part of the residue. (1RS)-*cis*-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane-carboxylic acid and 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclo-propanecarboxylic acid were the major components of the residue identified in liver and kidney (Leahey, French and Heath, 1985).

Cow

In the above-mentioned study with the goat, lambda-cyhalothrin was labelled in the acid portion of the molecule. This gave information on the fate of the whole molecule as well as of metabolites derived from the acid part. Information on metabolites derived from the alcohol portion of lambda-cyhalothrin was already available from previous studies conducted with cypermethrin, since the alcohol part of cypermethrin is identical to the alcohol part of cyhalothrin.

When ^{14}C-benzyl-labelled cypermethrin was administered orally to cows, the radioactive residues in the milk, fat and meat were identified as the parent compound. The only residues arising from ester cleavage and the alcohol half of cypermethrin were found in the liver and kidney, the major residue being N-(3-phenoxybenzoyl) glutamic acid.

Hydrolysis of the liver and kidney metabolites yielded 3-phenoxybenzoic acid and 3-(4-hydroxyphenoxy)benzoic acid (FAO/WHO, 1982).

Friesian cows were fed for up to 30 consecutive days on diets containing lambda-cyhalothrin at 1, 5 and 25 mg/kg. No effects were seen on milk yields or upon the general health of the animals. Lambda-cyhalothrin residues in milk correlated well with dietary inclusion rates, with mean plateau residue levels of 0.02 mg/kg, 0.09 mg/kg and 0.52 mg/kg, respectively for the 1, 5 and 25 mg/kg dietary inclusion rates. Lambda-cyhalothrin residue levels in milk did not accumulate and they declined when the feeding of the treated diet ceased. At the end of the 30 days, three cows from each group were slaughtered. The remaining two cows from the 25 mg/kg group were fed an untreated diet for a further 14 days before they were slaughtered. Lambda-cyhalothrin residue levels in the tissues were detected in the kidney, peritoneal and subcutaneous fat. Residues could not be detected in the liver while residues in the adduetes and pertoramuscle ranged from <0.01 to 0.05 mg/kg. (Sapiets, 1985). The update from JMPR 1986 is not clear on the expression of cyhalothrin residues – on a whole milk basis or a fat basis.

Processing Studies

Cotton

A study was conducted in the USA to determine the residues of PP321 (lambda-cyhalothrin) and its opposite enantiomer pair (R157836) in the processed fractions of cotton seed relative to the concentration in the whole ginned cotton seed. Cotton seed samples taken from a field trial in Goldsboro, North Carolina were processed to yield delinted cotton seed, hulls, linter motes, linters, lint, solvent extracted crude oil, refined oil and soapstock. In the field trial the cotton crop had received twelve applications of lambda-cyhalothrin at 33 g ai/ha. This was followed by three applications of an exaggerated rate of 100 g ai/ha, to ensure measurable residues. The insecticide was sprayed with ground equipment in spray volumes of 180 l/ha. The results showed that lambda-cyhalothrin was present in the ginned cotton seed as surface residues, most of which were removed in the delinting process. Concentrations of lambda-cyhalothrin in the delinted cotton seed, and in the process food fractions of the delinted cotton seed, were lower that those on the ginned cotton seed (Neal, 1985b).

METHODS OF ANALYSIS

The method of crop residue analysis for cyhalothrin is also applicable to lambda-cyhalothrin. It was reviewed by the 1984 meeting. The crop samples were prepared for analysis by mincing or chopping until homogenous. For small fruits the whole sample was prepared; large vegetables, e.g. cabbages, were quartered and opposite quarters taken. Samples were extracted using 50% acetone in hexane and the extracts washed with water. Co-extractives were removed by liquid-liquid partition chromatography where necessary (crops requiring this clean-up include cabbages). All crop extracts were cleaned up using Florisil adsorption chromatography. Final quantitative determination of cyhalothrin residues was by gas-liquid chromatography using electron-capture detection. The limit of determination for total cyhalothrin isomers is 0.01 mg/kg.

The analytical procedure used an internal standard, (SR)-α-cyano-3-phenoxybenzyl-(1RS)-*cis*-3-(Z-2-bromo-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate, for the quantitative measurement of residues. The internal standard was added to each sample prior to extraction. The response ratio of cyhalothrin to internal standard in the final extract of each sample was used for quantitative measurement of residues. Using the internal standard allows the size of the sample aliquot processed through the method to be reduced without loss of accuracy. Since the recovery of the pyrethroid is effectively monitored for each sample, the precision of the assay is significantly improved. Calibration curves plotted for cyhalothrin versus response ratio of cyhalothrin to the internal standard gave a linear regression (correlation coefficient r >0.99) with an intercept passing through the origin (Sapiets and Swaine, 1985).

MAXIMUM RESIDUE LIMITS

Codex MRLs have been established for cabbages, head, cotton seeds, cotton seed oil, crude, cotton seed oil, edible, pome fruits and potato. These are summarised in Table 1.

Table 1. Cyhalothrin MRLs as a pesticide

Main uses	8 INSECTICIDE
JMPR	84, 86R, 88R
ADI	0.02 mg/kg body weight (1984)
RESIDUE	Cyhalothrin (sum of all isomers)

Commodity Code	Name	MRL (mg/kg)	Step	JMPR	CCPR
VB 0041	Cabbages, head	0.2	CXL		
SO 0691	Cotton seed	0.02	CXL		
OC 0691	Cotton seed oil, Crude	0.02	CXL		
OR 0691	Cotton seed oil, Edible	0.02	CXL		
FP 0009	Pome fruits	0.2	CXL		
VR 0589	Potato	0.02	CXL		

The only crops in the Codex MRL table that could lead to residues in animals are cotton seed and pome fruits. The MRL for cotton seed is 0.02 mg/kg, so residues are very low or undetectable. The MRL for pome fruits is 0.2 mg/kg. No further information was provided on residues in crops leading to residues in animals even though the 1986 JMPR recognized the possibility (Desirable Further Information).

FURTHER WORK OR INFORMATION

The following information was requested by JMPR in 1986.

1. Further information on residues of cyhalothrin in foods of animal origin arising from feeding with treated crops or from direct treatments.

REFERENCES

Curl, E.A. and Leahey, J.P. (1979). "PP564: Degradation in Cotton Leaves", ICI Plant Prot. Div. Report. No. TMJ 1762B.

FAO/WHO, (1982). 1981 Evaluations: Pesticide Residues in Food.

Fitzpatrick, R.D. (1984). "PP321 Residues in cottonseed", ICI Americas Inc. Ag. Chem. Div. Report No. TMU 1518/B (unpublished).

Kimkaid, A. and Sapeits, A. (1986). Residue levels on wheat for 1985 trials in The Netherlands, ICI Report Series M 4198B.

Leahey, J.P. and French, D.A. (1985). "PP321: Characterization of radioactive residues found in cotton seeds from plants treated with ^{14}C-PP321 and degradation of ^{14}C-PP321 applied directly to cotton seeds". ICI Plant Prot. Div. Report No. RJ0393B

Leahey, J.P., French, D.A.and Heath, J. (1985). PP321: Metabolism in a goat, ICI Plant Prot. Div. Report. No. RJ0435B

Neal, J. (1985a). "PP321 residues in cottonseed", ICI Americas Inc. Ag. Chems Div. Report No. TMU 1778/B (unpublished).

Neal, J. (1985b). "PP321 residues in the process fractions of cottonseed", ICI Americas Inc. Ag. Chem. Div. Report. No. TMU 1805 (unpublished).

Sapiets, A. (1984a). Residue levels in cottonseed from a 1984 trial in Brazil, ICI Plant Prot. Div. Report No. M3826B

Sapiets, A. (1984b). Residue levels on cottonseed from a 1984 trial in Israel, ICI Plant Prot. Div. Report No. M3949B

Sapiets, A. (1985). PP321: Residue transfer study with dairy cows fed on a diet containing the insecticides, ICI Plant Prot. Div. Report. No. M3936B.

Sapiets, A and Swaine, H. (1985). The determination of residues of cyhalothrin in crops- a gas liquid chromatographic technology using an internal standard, ICI Plant Prot. Div. Residue Analytical Method (PPRAM) No. 70.

Tyldesley, D.J. and Sapiets, A. (1985). PP321: residue levels in cottonseed from a 1985 trial in South Africa, ICI Plant Prot. Div. Report No M4093B.