CYPERMETHRIN

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Cypermethrin was reviewed by the JMPR in 1979 and 1981-86, 1988 and 1990; MRLs have been recommended on a wide range of crops, meat and milk products and feed commodities.

Cypermethrin is active against a wide range of insects, which attack crops and can be used at a relatively low dose rate in the rage of 0.02-0.25 kg ai/ha. It is a moderately stable and water insoluble compound. The technical material contains not less than 90% w/w cypermethrin, which is a mixture of eight optical isomers, with a cis: trans isomer ratio of approximately 40:60. The maximum concentrations of residues in/on the treated crops are in the range of 0.05 – 2 mg/kg and decreases slowly (JMPR, 1979).

USE PATTERN

Animals

In Australia, three products containing cypermethrin are registered for ectoparasite control. "Barricade s" cattle dip and spray (25 g/l cypermethrin and 138 g/l chlorfenvinphos) is used at 19-21 day intervals to control cattle ticks *Boophilus microplus*. Dipping is used in *exiqua* infestation for up to 21 days. It controls other ticks (*Haematobia irritans* and *Ixodes holocyclus*), cattle lice *Linognathus vituli, Damalinia bovis* and *Hematopinus eaurysternus,* and buffalo fly on horses, deer, goats and sheep. It is diluted 1:250 with water giving a cypermethrin concentration of 100 mg/l. Outflank off-shears pour-on sheep lice treatment, contains 25 g/l cypermethrin. The application rate is 10 ml along the back line of shorn sheep weighing up to 50 kg, and 15 ml for sheep over 50 kg. One application controls sheep lice (*Damalinia ovis*) and ked (*Melophagus ovinus*). Control is achieved in 4-6 weeks. Outflank plunge and shower sheep dip, containing 47.5 g/l cypermethrin, diluted 1:2500, giving a cypermethrin concentration of 19 mg/l, is used for the control of lice and keds on sheep.

RESIDUES FROM SUPERVISED TRIALS

Plants

Wheat

Residue trials have been carried out on wheat in Canada and Brazil, with application rates up to 150 g/ha. In the grain residues did not exceed 0.1 mg/kg at harvest two weeks after application. Residues in the straw were higher, and the few data obtained suggest that under these conditions they may approach 10 mg/kg. The 1979 report from JMPR is not clear on the rate applied - 150 g ai/ha or 150 g formulation/ha.

Animals

Cow

Cattle were treated with 25 g/L cypermethrin formulation as an overspray treatment to control buffalo flies. Cattle were sprayed along the dorsal midline at concentrations of 0.1 and 0.2% ai (200 ml per animal). At 1, 3, 8 and 15 days post treatment, three animals were slaughtered and various samples collected. Residues in muscle, liver, and kidney at both dosage rates were all below the limit of determination (0.01 mg/kg) in animals treated once only. In animals treated twice, determinable residues ranged from 0.01 to 0.05 mg/kg (Shell, 1979). It is not clear if the residues are expressed on fat tissue or other tissue.

Other trials were conducted on dairy cows using a cypermethrin/chlorfenvinphos acaricidal mixture by plunge dipping in a bath containing 0.075 g/l of cypermethrin. Samples were taken from the bulked milk of a commercial herd at intervals up to 14 days and from six individual cows at intervals to seven days, after treatment. Three of the individual cows were dipped again on the eighth day with samples taken six days later. Residues of cypermethrin between <0.002 and 0.01 mg/kg were found in samples taken up to three days after treatment; declining to below the limit of determination (0.002 mg/kg) at the end of the first week. This report from 1986 is not clear on the expressions of cypermethrin residues- on a whole milk basis or a fat basis. However, concentrations expressed per kg (litre) suggest the whole milk.

Cattle were also dipped once or twice in a bath containing 0.075 g/l of cypermethrin using an interval of 7 days. Animals were slaughtered 1, 3, 4 or 7 days after the first dip and some animals at 7 days after a second dip. Residues in liver, kidney and muscle were all below the limit of determination (0.01 mg/kg) while residues in omental fat ranged from <0.01-0.02 mg/kg and in perirenal fat at 0.01-0.05 mg/kg.

Sheep

Animals (24 wethers) were manually dunked into a dip containing 0.01% cypermethrin. Residues were detected in omental fat, perirenal fat and muscle ranging for <0.01 (0 day) to a high of 0.17 mg/kg (in perirenal fat at 14 days after 3 dippings). Residues could not be detected in liver and kidney.

A 1982 Australian trial was conducted using a 2.5% cypermethrin pour-on sheep dip applied to merino ewes at 15 ml (normal maximum dosage rate) and 30 ml. The application was on a line 15-25 cm along the back line between shoulder and anterior pelvis. Sheep were slaughtered 1, 3, 7, 14 and 28 days after treatment and samples of muscle (neck), kidney, liver, omental fat and perirenal fat were analysed for residues of cypermethrin. For the recommended maximum dose rate of 15 ml of 2.5% cypermethrin, residues in both ometnal and perirenal fats reached peak values of 0.04 mg/kg after 7 days. Values for a double dose rate of 30 ml also peaked after 7 days at 0.07 mg/kg for omental fat and 0.08 for perirenal fat. The results for muscle, kidney and liver samples were all less than 0.02 mg/kg.

Goat

Four milking goats were dunked in a dipping vat containing 0.01% cypermethrin three times after the 0, 4 and 8-day morning milkings. Samples of homogenized goat milk were examined. Residues were detected in goat milk after 18 days (mean 0.002 mg/kg).

FATE OF RESIDUES

Plants

Residue trials have been carried out on wheat in Canada and Brazil, with application rates up to 150 g/ha. In the grain residues did not exceed 0.1 mg/kg at harvest two weeks after application. Residues in straw were higher and the few data obtained suggest that under these conditions they may approach 10 mg/kg.

Following applications to various crops cypermethrin may degrade to hydrolysis and oxidation products. The most likely degradation products present in crops at harvest following normal agricultural use of cypermethrin are the derived amide (compound B), 3-phenoxybenzoic acid and 2-(2′, 2′-dichloro vinyl)-3,3-dimethyl cyclopropane carboxylic acid (compound C). The latter two compounds are found in the free state as well as in conjugated forms. However, the evidence indicates that the major component of any residue present at harvest will be cypermethrin. Several crop samples obtained from supervised trials were analyzed also to determine residues of compounds B, C and phenoxybenzoic acid. The results of these examinations involving some 20 crops showed no residues of compound B, C or of 3-phenoxy benzoic acid in excess of 0.05 mg/kg.

Animals

Cattle

Two radiolabelled studies were undertaken to investigate cypermethrin residues in cattle and whether residues in meat or milk could arise from its use in feed containing products made from treated crops.

Low Dietary Intake (0.2 mg/kg)

Two lactating cows were given feed concentrate containing radiolabelled cypermethrin twice daily for a 3-week period at a feeding level equivalent to 0.2 mg/kg on total daily feed. The initial radioactivity in milk (time frames not noted) amounted to only 0.5% of radioactivity fed to animals. About 60-70% of the radioactivity in the milk was present in the cream fraction. The remainder was excreted in the urine (54%) and faeces (43%). At the end of the feeding period, cypermethrin residues were below 0.001 mg/kg in blood, muscle and brain. In subcutaneous and renal fats, liver and kidney samples, residue were at or below 0.012 mg/kg cypermethrin equivalents.

High Dietary Intake (5 mg/kg)

Radiolabelled cypermethrin was given in the feed concentrate twice daily at an amount equivalent to 4 mg/kg on total diet over a period of 7 days. It is not clear from the 1979 JMPR report what actual concentrations were used (5 mg/kg or 4 mg/kg).

The major excretory route was via the kidneys. The cream fraction contained 85-90% of the total radioactivity in the milk samples. These results indicate that cypermethrin does not accumulate in the animal tissues. Even at high intake levels, residues were mostly in the fat, liver and kidney. Cereals and components of feed (e.g. cotton seed) were treated with the highest recommended dose rates. The majority of residue in the feed is excreted in the urine and faeces. Therefore, measureable residues are unlikely to result in meat or milk of cattle. The residues in the milk are esters and contain both acidic and alcoholic moieties of the parent compound. The main metabolite in urine is 3- phenoxybenzoic acid as the glutamic and glycine derivatives. The faeces mainly contain the parent molecule.

Poultry and poultry products

Both radio- and non-labelled studies on the nature and level of residues in eggs and poultry meat were reviewed. Cypermethrin levels in whole eggs reached a plateau after approximately seven days of 0.05-0.09 mg/kg at the 40 ppm dietary level (the highest tested) with the residues being mainly in the yolk. Levels declined rapidly when dosing was stopped. The highest poultry flesh levels were 0.06 mg/kg at the 40 ppm dose level. It is unlikely that residues of parent compound or metabolites will reach significant levels in eggs or poultry meat, since dietary levels will seldom exceed 1 ppm in the poultry whole diet for any appreciable period. The JMPR proposed an MRL of 0.05 mg/kg for eggs and poultry meat.

Processing

Cypermethrin is a moderately stable and water insoluble compound. Data relating to the effect on residue levels of various treatments given to harvested crops are as follows:

Crop peelings

Numerous data show that the residue in a crop is largely on the surface. Analyses of pulp and peel after peeling apples, pears, peaches and citrus fruits show that levels in the pulp were below 30% of the applied dose, and in most instances below 10%, of those in whole fruit.

Oil seeds

Cottonseed was deliberately treated at the high rate of 300 g/ha and harvested one day after treatment. Cottonseed contained 0.12 mg/kg cypermethrin on a whole seed basis, with adhering linters. The sample was processed by simulating commercial practices in a laboratory specializing in the technique. Residues were transferred to kernels that originally did not contain any detectable residue in the seed during the commercial mechanical separation process. The cypermethrin residues in the extracted oil at various stages are: crude oil 0.10 mg/kg, neutralized oil 0.07 mg/kg, bleached oil 0.08 mg/kg and deodorized oil 0.05 mg/kg. Both the alkali wash and deodorization steps contribute to some losses. The results from this experiment suggest that the two processes together may be expected to remove about half of the residue. Hence, it is possible that residues may occasionally occur in oil obtained from seed treated under practical conditions at levels approaching those in whole seed. The report from JMPR (1979) is not clear on the rate applied on the cotton seed sample - 300 g ai/ha or 300 g formulation/ha.

METHODS OF ANALYSIS

Several methods have been developed for residue analysis of agricultural commodities. The methods are all based on gas-liquid chromatography procedures using equipment commonly found in modern analytical laboratories. Limits of determination of 0.01–0.02 mg/kg are usually attainable.

Experiments have shown that most samples may be stored for long periods in the deep freeze without appreciable loss of residues. Residue levels were determined in crop and soil samples at intervals following addition of known quantities of cypermethrin at 0.2-1 mg/kg. The samples were stored at –18°C from treatment to analysis, for 1-54 weeks for crops and 4-49 weeks for soil. Recoveries of cypermethrin added to crops (21 samples) were 85-110%, apart from one sample of tobacco that reported yields of 45% after 6 months storage. In the case of soils (5 samples) recoveries were all 90-110% (Shell R. 152).

Studies have also been carried out on the stability of residues of 3-phenoxybenzoic acid and Compounds B and C in storage at –18°C. Over three months there was no evidence of loss of 3-phenoxybenzoic acid, since the total amounts recovered from the 6 crops used (lettuce, potatoes, cabbage, apples, pears and maize grain) were 75-100% and comparable to recovery values of the method itself. With Compound B experiments were carried over three months with sweet corn and over five months with apples and cabbage. Recoveries were 70%, 75% and 75%, respectively. Cabbage and apples treated with Compound C were also stored at –180°C for five months. Recoveries were 90-95%, respectively. These data indicate that loss of any of the three degradation compounds mentioned were negligible over periods of 3-5 months at –18°C.

APPRAISAL

Degradation in crops occurs mainly by hydrolysis of the ester bond followed by further hydrolytic and oxidative processes to give a variety of products. Less rapid processes observed were hydrolysis of the nitrile group to amide and hydroxylation of the phenoxy-ring. The compounds formed were, in turn, also hydrolyzed at the ester link. However, metabolites have not been detected in crop commodities from supervised trials. At least 90% of the total residue present in plant material is extractable with acetone. Processing of treated crops after harvest usually reduces the residue significantly (JMPR 1979).

Cypermethrin is readily absorbed, distributed and metabolized in mammals. Because of the chemical and especially the isomeric complexity of the molecule, the metabolic profile with respect to all of its isomers is extremely complex. Cypermethrin is readily cleaved at the ester linkage and subjected to oxidative degradation and conjugation of the metabolic products. Elimination following acute and subacute administration is rapid. However, the clearance rate from adipose tissue is slow and a half-life in rats and mice may range from 10-30 days. The data suggest a potential for bioaccumulation following continuous exposure (JMPR 1979).

Cattle consuming feed items treated with cypermethrin eliminate the residue rapidly. Equilibrium between intake and excretion is reached in 3-4 days. The total radioactivity found in milk was only 0.5% of the radioactivity fed to the animals; 60-90% of this residue is present in the cream fraction. The residues in the milk are esters and contain both acidic and alcoholic moieties of the parent compound. The majority of the residue in feed is excreted in the urine and faeces in similar proportions. The main metabolite in urine is 3-phenoxybenzoic acid present as glutamic acid conjugate and glycine derivatives. The faeces mainly contain the intact molecule.

Cypermethrin does not accumulate in muscle tissue. Even when fed at high dose rate, residues are mostly in the fat, liver and kidney. The data indicate that the feeding of crops treated with cypermethrin following the recommended use patterns does not result in measurable residues in meat or milk of cattle. Since the compound may be used for direct treatments of animals, and data deriving from the latter use are not available, recommendations of MRLs for animal products were not made at the 1979 JMPR meeting.

From the information on residues resulting from the use of cypermethrin for ectoparasite control and feeding studies, it was concluded that residues of cypermethrin are not likely to exceed 0.2 mg/kg for meat (in the fat) and 0.05 mg/kg for muscle, liver, kidney and milk.

MAXIMUM RESIDUE LIMITS

Codex MRLs have been established for a variety of fruits and vegetables. MRLs for animal products include: edible offal (mammalian), eggs, meat (from mammals other than marine mammals), milks and poultry meat. Feed commodities with MRLs include barley, maize, maize fodder, sorghum straw and fodder, dry, soya bean (dry), wheat and wheat straw and fodder, dry. MRLs are summarized in Table 1.

Table 1. Cypermethrin residues in crops and meat products

Main uses	8 INSECTICIDE
JMPR	79, 81, 82R, 83R, 84R, 85 R, 86 R, 88R, 90R (00R')
ADI	0.05 mg/kg body weight (1981; confirmed in 1996 by JECFA)
RESIDUE	Cypermethrin (sum of isomers) (fat-soluble)

Code	Commodity	MRL (mg/g)	Step	JMPR	CCPR
AL 1021	Alfalfa forage (green)	5 dry wt	CXL		
GC 0640	Barley	0.5	CXL		
VP 0062	Beans, shelled	0.05	CXL		
FB 0018	Berries & other small fruits	0.5	CXL		(1991)
VB 0040	Brassica vegetables	1	CXL		
FS 0013	Cherries	1	CXL		
FC 0001	Citrus fruits	2	CXL		
SB 0716	Coffee beans	0.05	CXL		
VP 0526	Common bean (pods and/or Immature seeds)	0.5	CXL		
VC 0424	Cucumber	0.2	CXL		
MO 0105	Edible offal (mammalian)	0.05 V	CXL		
VO 0440	Egg plant	0.2	CXL		
PE 0112	Eggs	0.05	CXL		
VL 0480	Kale	1	CXL		
VA 0384	Leek	0.5	CXL		
VL 0482	Lettuce, Head	2	CXL		
GC 0645	Maize	0.05	CXL		
AS 1645	Maize fodder	5 dry wt	CXL		
MM 0095	Meat (from mammals other than marine mammals	0.2 (fat) V	CXL		
ML 0106	Milks	0.05 (fat) V	CXL		
VO 0450	Mushrooms	0.05	CXL		
FS 0245	Nectarine	2	CXL		
SO 0089	Oilseed, except peanut	0.2	CXL		
VA 0385	Onion, bulb	0.1	CXL		
FS 0247	Peach	2	CXL		
SO 0697	Peanut	0.05	CXL		
VP 0063	Peas (pods and succulent-immature seeds)	0.05	CXL		
VO 0051	Peppers	0.5	CXL		
FS 0014	Plums (including prunes)	1	CXL		
FP 0009	Pome fruits	2	CXL		
PM 0110	Poultry meat	0.05	CXL		
VR 0075	Root and tuber vegetables	0.05	CXL		
AS 0651	Sorghum straw and fodder, Dry	5	CXL		
VD 0541	Soya bean (dry)	0.05	CXL		
VL 0502	Spinach	2	CXL		
VO 0447	Sweet corn (corn-on-the-cob)	0.05	CXL		
DT 114	Tea, Green, Black	20	CXL		
VO 0448	Tomato	0.5	CXL		
OR 0172	Vegetable oils, Edible	0.5	CXL		
GC 0654	Wheat	0.2	CXL		
AS 0654	Wheat straw and fodder, Dry				

FURTHER WORK OR INFORMATION

Desirable

1. Use pattern for animal health use and residues in animal products deriving from the recommended application (JMPR 1979)

REFERENCES

Australia, (1980), Cypermethrin residues in animal tissues and milk. Submission to the 1986 JMPR.

Shell Chemical (Australia) Pty. Ltd. (1979). Cypermethrin residue data in animal tissues and milk. Project S/AU/D 2-78 (unpublished).