DIMETHIPIN (151)

EXPLANATION

Dimethipin was evaluated in 1985, 1987 and in 1988. It was identified for re-evaluation at the 1997 CCPR (ALINORM 97/24 A) and scheduled for consideration by the 2001 JMPR.

Data to support the existing CXLs for cotton, linseed, potatoes, rape seed, sunflower seed and animal commodities and other critical data required for the recommendation of MRLs have been reported by the manufacturer. The governments of Australia and Germany have reported information on GAP and/or residue data.

IDENTITY

ISO Common name: dimethipin

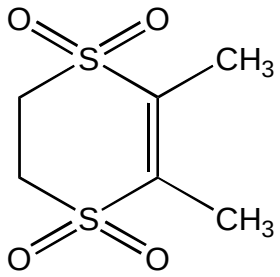
Chemical name:
IUPAC: 2,3-dihydro-5,6-dimethyl-1,4-dithiine 1,1,4,4-tetraoxide
CA: 2,3-dihydro-5,6-dimethyl-1,4-dithiin 1,1,4,4-tetraoxide

CAS No.: 55290-64-7

CIPAC No.: 151

Synonyms/trade names: Harvade, UBI-N252, oxidimethiin, tetrathiin.

Structural formula:



Molecular formula: $C_6H_{10}O_4S_2$

Molecular weight: 210.3

Physical and chemical properties

Technical material

Appearance: white crystalline (Riggs, 1990a)
Odour: sweet molasses-like (Riggs, 1990b)
Density: 1.5935 g/cm^3 at 23°C (Thomson, 1989)
Melting point: 162-172°C

Solubility (Spare, 1987a, Young 1991)

Solvent	Solubility at 25°C (g/100 ml solvent)
Water	0.46

Solvent	Solubility at 25°C (g/100 ml solvent)
Aqueous buffer pH 4	0.21
Aqueous buffer pH 7	0.18
Aqueous buffer pH 10	0.17
Acetone	9.7
Acetonitrile	18
1-Butanol	0.16
Methanol	1.07
1-Octanol	7.9×10^{-2}
Propylene glycol	0.76
Toluene	0.90
Hexane	$1.2\text{-}1.7\times10^{-3}$

pH of 1% solution in 50% (v/v) aqueous dioxane = 4.52 at 30.2°C (Thomson, 1990a)
Dissociation constant: $pK_a = 10.88 \pm 0.39$ at 25°C (Thomson, 1990b)
Vapour pressure: less than 3.81×10^{-7} Torr at 24°C (Spare 1987b)
Partition coefficient (*n*-octanol/water): $\log P_{ow} = -0.174$ (Steeves 1986)
Stability in presence of transition metals: the technical material is stable when mixed with stainless steel particles or sodium tungstate dihydrate and stored at 25°C for sixteen weeks (Riggs 1990c).
Technical dimethipin is stable when stored at 20°C and 50% RH in polyethylene containers for 12 months (Thomson 1991).

Hydrolysis (Fitzpatrick 1981, Lengen 1982)

25°C	stable at pH 3
	stable at pH 6
	estimated half-life 0.9-2 years based on data from 57 days storage at pH 9
45°C	stable at pH 3
	stable at pH 6
	half-life 330 days based on data from 57 days storage at pH 9

At 70°C and pH 9, [^{14}C]dimethipin accounted for 24% of the radioactivity giving a half-life of about 4 months. Major hydrolysis products were 2-hydroxymethyl-3-methyl-1,4-dithiane 1,1,4,4-tetraoxide and 1,4-dithiane 1,1,4,4-tetraoxide (Fitzpatrick and Wong, 1981).

Photolysis:
Stability in sunlight: the technical material is stable on exposure to continuous simulated sunlight for 7 days (Riggs, 1990d).

UV absorption: $\lambda_{max} = 219$ nm, $\varepsilon = 5.16\times10^{-2}$ (Pierce, 1996)

Formulations

The following formulation types are available: flowable powder (DF), suspension concentrate (SC)

METABOLISM AND ENVIRONMENTAL FATE

Animal metabolism

In metabolism studies on rats, goats and hens [^{14}C]dimethipin and [$^{13/14}$C]dimethipin were used to trace the fate of different parts of the dimethipin molecule.

The following abbreviations are used for the metabolites:

red-DMP = 2,3-dimethyl-1,4-dithiane 1,1,4,4-tetraoxide

acetyl dithiane = 2-acetyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-S-cys = *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian 2-yl)-L-cysteine
glu-cys-S-DMP = *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-cysteinyl-γ-glutamic acid
DMP-S-acetate = 2-[(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)thio]acetic acid
DMP-GSH = *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-glutathione
DMP-SH = 2-mercapto-2,3-dimethyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-S-methyl = 2,3-dimethyl-2-methylthio-1,4-dithiane 1,1,4,4-tetraoxide
DMP-tert-OH = 2-hydroxy-2,3-dimethyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-prim-OH = 2-hydroxymethyl-3-methyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-SO-methyl = 2,3-dimethyl-2-(methylsulfinyl)-1,4-dithiane 1,1,4,4-tetraoxide
hydroxy-DMP = 2,3-dihydro-5-hydroxymethyl-6-methyl-1,4-dithiine 1,1,4,4-tetraoxide
demethyl-hydroxy-DMP = 2,3-dihydro-5-hydroxymethyl-1,4-dithiine 1,1,4,4-tetraoxide
methylene-DMP = 2-methyl-3-methylene-1,4-dithiane 1,1,4,4-tetraoxide
demethyl-DMP = 1,4-dithiane 1,1,4,4-tetraoxide
N-acetyl-cys-DMP = *N*-acetylcysteinyl conjugate
Cys-gly-DMP = cysteinyglycine conjugate
HESB = 3-(2-hydroxyethylsulfonyl)butan-2-one

Rats. Charles River rats were dosed orally with 1 mg of [^{14}C]dimethipin labelled at the 2 and 3 positions of the dithi-ine ring and killed after 96 hours (Caplan and Merricks, 1978). 93% of the dose was excreted in the urine and faeces, 89% being excreted within 48 hours. Less than 0.1% was recovered as volatiles or expired carbon dioxide. Radioactivity was highest in blood and low levels were detected in tissues and the gastrointestinal tract. In both the pooled urine and faecal samples (Smilo *et al.*, 1978) less than 5% of the radioactivity was extractable with organic solvents, and 80-90% was polar. Comparisons of retention times indicated that approximately 5% of the radioactivity was associated with unchanged dimethipin.

In another study Byrd and Billings (1989) compared the absorption, distribution and excretion of [^{14}C]dimethipin in groups of Sprague-Dawley rats dosed orally with [^{14}C]dimethipin at 50 mg/kg bw and 1.2 mg/kg bw as well as intravenously at 2 mg/kg bw. Another group was pre-dosed at 1000 mg/kg in the diet with unlabelled dimethipin before being given single oral doses of 50 mg/kg [^{14}C]dimethipin. 27-57% of the dose after oral dosing was recovered in the urine and 27-62% in the faeces within 96 hours of the last dose. Residues in the tissues accounted for 0.2-4% of the administered radioactivity at 96 hours. Total radioactive residues (TRR) were highest in the liver with lower levels in the fat, kidney and muscle.

Five products were detected in all samples of the urine from all dose groups: unchanged dimethipin, the *N*-acetylcysteine conjugate, red-DMP, a cysteinylglycine conjugate and a polar fraction supporting the involvement of glutathione conjugation in the metabolic pathway (Mcmanus, 1987a).

In a separate study, rats were dosed orally at 800 mg/kg bw with [2,3-^{14}C]dimethipin and urine was collected for 72 hours after dosing (Mcmanus, 1987b). 29% of the radioactive dose was excreted in the urine with most recovered in the first 24 hours. Almost no unchanged dimethipin was detected. Seven metabolites were detected by HPLC. Of these three were identified and accounted for 77% of the radioactivity in the urine: a cysteinylglycine conjugate (54%), an *N*-acetylcysteine conjugate (12%) and red-DMP (11%). It was considered that metabolism involves conjugation with glutathione and degradation to cysteinylglycine and cysteine conjugates and the formation of mecapturic acid conjugates.

To study dermal absorption of [^{14}C]dimethipin by rats it was applied to their backs at a rate of 682 μg ai/cm^2. Approximately 0.6 and 0.9% of the dose had been absorbed through the skin in both male and female rates after 12 hours (Frederick, 1983). Most of the absorbed dose was excreted with minor residues detected in the blood, with lower levels in the tissues when the rats were killed 72 hours after application.

Goats. Singh (1982) dosed a lactating and a non-lactating goat weighing 46 and 50 kg bw with gelatine capsules containing 500 mg [2,3-^{14}C]dimethipin twice daily for three consecutive days. The bile duct of the non-lactating goat was cannulated and the daily dose was about 20 mg/kg bw equivalent to a nominal feeding rate of about 700 ppm in the feed. Milk and excreta were collected throughout and the goats were slaughtered 18 hours after the last dose. Samples of blood, liver and kidneys were collected and residues characterized by a variety of techniques including chromatography, mass spectrometry, NMR and acid and enzymatic hydrolysis.

The TRRs were highest in urine. Approximately 25% of the radioactivity was extracted from urine with ethyl acetate after acidification with dilute HCl. Five compounds were isolated from the ethyl acetate extract by HPLC and TLC. Three of the compounds accounting for less than 3% of the TRR in the urine were identified as dimethipin, and 2-ethyl-2-methyl-1,3-dithiolane 1,1,4,4-tetraoxide and 2-ethyl-1,3-dithiolane 1,1,4,4-tetraoxide, thought to be impurities. The other two compounds were identified by MS and ^{1}H NMR as the alcohols DMP-prim-OH and DMP-tert-OH, accounting for 24 and 16% of the TRR in the urine respectively. At least four polar metabolites were detected in the HPLC profile of the aqueous urine extract, three of which were isolated by repetitive HPLC and analysed by NMR and MS. Structures consistent with the data were hydroxy-DMP, demethyl-hydroxy-DMP and DMP-prim-OH. Most of the residues in the aqueous extract were not identified but were thought to be polar conjugates. Alcohols hydroxy-DMP, demethyl-hydroxy-DMP, DMP-tert-OH and DMP-prim-OH would be expected ultimately to be conjugated to endogenous materials in the goat.

Acidification of the bile and extraction with ethyl acetate recovered 41% of the TRR with 59% remaining in the aqueous phase. Dimethipin and seven metabolites were detected in the ethyl acetate extract. A comparison of the ethyl acetate and aqueous extracts indicated incomplete partitioning of the polar metabolites. A major metabolite representing approximately 40% of the TRR in the bile was identified as the ring-opened product HESB (M+1 181 m/e). Additional polar metabolites were identified by acid and β-glucuronidase hydrolysis by which 18 and 26% respectively of the ^{14}C in the aqueous fraction was made extractable with ethyl acetate. Comparison of TLC of the extracts before and after hydrolysis indicated the formation of less polar compounds on hydrolysis, suggesting that some of the polar metabolites in the bile were glucuronides. Comparison of the chromatographic properties of dimethipin reaction mixtures with L-cysteine and *N*-acetylcysteine confirmed the presence of their conjugates in the bile.

The TRR in livers were 14 and 19 mg/kg for the lactating and dry goat respectively and in the kidneys were 17 and 24 mg/kg (all expressed as dimethipin). Acetone/water extraction of liver and kidney homogenates removed 58 and 81% of the TRR respectively. For liver, hydrolysis with acid and base did not release any more radioactivity. Partitioning of the acetone/water extracts with ethyl acetate and analysis by TLC resulted in chromatograms qualitatively the same for liver, kidney and urine, with HESB and DMP-tert-OH identified in liver and kidney samples. Analysis of the liver and kidney extracts by gel permeation chromatography and β-glucuronidase hydrolysis indicated a glucuronide conjugate. The high levels of polar and bound residues also indicated extensive conjugation.

Bile and urine samples collected 12 hours after the first dose were further studied by McManus (1989). Samples were centrifuged and filtered through LID-X 0.2 μm nylon before analysis by HPLC. The profiles for urine and bile samples showed essentially the same metabolic pattern with most of the metabolites classed as polar. At least 6 metabolites more polar than dimethipin were detected. Four metabolites common to urine and bile were identified: a reduced product, a carboxylic acid, a demethylated product related to an impurity present in dimethipin (2-ethyl-1,3-dithiolane 1,1,4,4-tetraoxide) and an *N*-acetylcysteine conjugate. However, it was not possible to identify the two dominant metabolites, though reduction with Raney nickel or dithiothreitol resulted in an increase of the reduced product suggesting the presence of a sulfur conjugate.

Table 1. Identity of metabolites and their distribution in the milk and tissues of goats dosed with [^{14}C]dimethipin equivalent to 500 ppm in the diet for 3 days (Singh, 1982; Mcmanus, 1984).

	Liver	Bile	Kidney	Urine
TRR (mg/kg as dimethipin)	19	500	24	1800
Compound	% of TRR			
Dimethipin	2	8	2	2
Hydroxy-DMP				6
demethyl-hydroxy-DMP				10
HESB	9	30	8	20
DMP-tert-OH	6		5	16
DMP-prim-OH				24
N-acetyl-cys-DMP		12		
2-ethyl-2-methyl-1,3-dithiolane-1,1,3,3-tetraoxide				0.5
2-(1-hydroxyethyl)-2-methyl-1,3-dithiolane-1,1,3,3-tetraoxide	1			
2-ethyl-1,3-dithiolane-1,1,3,3-tetraoxide				0.5
Polar metabolites[1]	40	50	65	21
Bound[2]	42		19	

[1]acid hydrolysis showed numerous ethyl acetate-extractable products
[2]mainly high molecular weight residues (>500)

Lactating goats were dosed orally with 0.15 and 50 mg/kg bw 2,3-ring-labelled [^{14}C] or 50 mg/kg bw 2,3-ring-labelled [^{14}C] and 5,6-ring- and methyl-labelled [^{13}C]dimethipin once daily for five days (Byrd, 1992; Lau and Gay, 1996), equivalent to 3, 1010 and 1290 ppm in the feed based on mean daily feed consumptions. Milk was collected twice daily, and urine and faeces daily. The goats were slaughtered 22-24 hours after the last dose. The radioactive residues in the tissues were characterized by HPLC, GC-MS, LC-MS and ^{13}C-NMR.

Radioactivity in faeces and urine collected up to 22 hours after the last dose accounted for 95% of the administered dose for both ^{14}C-animals with 39% and 54% excreted in faeces and urine for the low-dose group and 51% and 42% in faeces and urine respectively for the high. Approximately 0.1% and 0.2% was eliminated in milk of the low- and high-dose animals and approximately 97% and 96% of the total dosed radioactivity was recovered from the low- and high-^{14}C-dose animals respectively.

Table 2. Distribution of radioactivity in the blood, milk and tissues of lactating goats dosed orally with [^{14}C] or [$^{13/14}$C]dimethipin for 5 days (Byrd, 1992; Lau and Gay, 1996).

Sample	TRR (mg/kg calculated as dimethipin)		
	^{14}C-Low dose goat (3 ppm)	^{14}C-High dose goat (1010 ppm)	$^{13/14}$C-High dose goat (1290 ppm)
Whole blood	0.006	2.75	
Milk	0.005-0.006	0.68-1.2	3.1-4.3
Muscle	0.002	0.64	2.04
Fat	0.001	0.32	0.99
Kidney	0.15	28	55
Liver	0.27	79	45
Gastrointestinal tract	0.05	11	

In centrifuged milk samples the aqueous layer accounted for 69-86% of the radioactivity in the milk, and the only significant metabolite was DMP-S-cys, confirmed by co-chromatography with an authentic standard.

Less than 13% of the TRR from the high-dose liver was extracted with organic solvents, but about 50% with water or phosphate buffers (pH 7.5). Most of the extracted radioactivity was

associated with protein precipitates. The radioactive residues would not pass through a 50 kDa molecular weight cut-off filter. Enzymatic digestion released all the radioactivity which HPLC revealed to be associated with ethane-1,2-disulfonic acid and peptide conjugates. Reduction of the liver homogenate gave red-DMP as the major product while HCl-butanol hydrolysis resulted in a single product, acetyl dithiane. It is proposed that metabolites in liver are covalently bound to proteins.

It appears that the double bond of dimethipin forms a thioether bond with protein sulfhydryl groups, which upon digestion with proteases give multiple peptide fragments conjugated to red-DMP. Scission of the thioether bonds gives reduced dimethipin. Acid hydrolysis cleaves the peptide and thioether bonds to form an intermediate that rearranges to acetyl dithiane. The protease digestion also required addition of acid, yielding an intermediate that can fragment to give ethane-1,2-disulfonic acid.

All of the radioactivity from the kidney samples was extracted with water. Ethane-1,2-disulfonic acid was the only metabolite observed in the low-dose (3 ppm) goat, and in the high-dose (1010 ppm) goat ethane-1,2-disulfonic acid was the only free metabolite together with conjugated products released on acid hydrolysis to give acetyl dithiane.

The main metabolite in muscle was red-DMP present at approximately 30% of the TRR: no other metabolite accounted for more than 8% of the TRR.

The levels of ^{14}C in fat were too low to allow further characterization.

Table 3. Distribution of ^{14}C and identities of metabolites in the milk and tissues of lactating goats dosed with [^{14}C]dimethipin for 5 days (Byrd, 1992; Lau and Gay, 1996).

	^{14}C-low-dose goat (3 ppm)			^{14}C-high-dose goat (1010 ppm)			
	Milk	Liver	Kidney	Milk	Liver	Kidney	Muscle
TRR (mg/kg as dimethipin)	0.005	0.27	0.15	1.01	79	28	0.64
Aqueous extract recovery (%)	70	<50	99.7	>85	<50	104	50
HCl-BuOH recovery (%)	-	106	-	-	91	92	95
acetyl dithiane[1]	-	0.12 (44%)	-	-	46 (59%)	9.2 (32%)	-
ethane-1,2-disulfonic acid[1]	-	0.035 (15%)	0.11 (76%)	-	20 (45%)[2]	7.8 (28%)	-
red-DMP[1]	-	-	-	-	-	-	0.19 (30%)
DMP-S-cys[1]	0.001 (20%)	-	-	0.37 (37%)	-	-	-

[1] mg/kg as dimethipin (% of TRR)
[2] Metabolites were not determined for the liver of the ^{14}C-high dose goat (1010 ppm). The value reported is for the trypsin-pepsin digest of liver from $^{13/14}C$-high dose goat (1290 ppm) for which the liver TRR was 45 mg/kg calculated as dimethipin.

Liver homogenates from the three goats were hydrolysed and stored frozen for 1 (1290 ppm), 31 (3 ppm) and 26-30 (1010 ppm) months resulting in the same single ^{14}C product, acetyl dithiane. The aqueous extracts from kidneys were analysed after 25 (3 ppm), 25 (1010 ppm) and 4 (1290 ppm) months' storage and showed the same metabolite, ethane-1,2-disulfonic acid.

The main metabolic pathway for dimethipin is via a Michael addition of sulfhydryl to the double bond. Glutathione addition yields DMP-S-cys, via the mercapturic acid pathway, which is eliminated in urine and milk. This conjugate was not observed in edible tissues. Protein addition yields protein-bound reduced dimethipin which is the only residue observed in liver and muscle, and approximately half the residue observed in kidney. Hydrolysis of the bound residue and subsequent rearrangement yielded three products: red-DMP, acetyl dithiane and ethane-1,2-disulfonic acid. The

last was the only metabolite observed in the kidney of the ^{14}C low-dose goat and accounted for about one third of the ^{14}C in the high-dose.

Hens. Of seven groups of five single-comb White Leghorn pullets (1.3-2.4 kg bw) (Bodden *et al*., 1982), two groups were dosed with [^{14}C]dimethipin at nominal levels equivalent to 1 (0.06 mg/kg bw), 6 (0.34 mg/kg bw) and 30 (1.7 mg/kg bw) ppm in the feed. The remaining group was an untreated control. The hens were dosed by capsule with doses calculated on average consumption figures of 110 g feed per day for 30 days. One group at each dose level was then slaughtered. The remaining 5 birds at each dose level were slaughtered 11 days later. Egg and excreta samples were collected daily, and muscle (1:1 white and dark), liver and kidney after slaughter. Radioactive residues were determined by LSC.

The total recovery of radioactivity in the excreta was 90, 92 and 92% of the administered dose for the 1, 6 and 30 ppm dose groups respectively. Samples from days 30-34 and 36-40 were not analysed, so the true recovery figures are likely to be higher. Approximately 0.3% of the dose was found in tissues after the last dose with about 0.1% remaining in the withdrawal group after 11 days. Residues in eggs accounted for 0.2% of the dose at the end of feeding decreasing to below the limit of detection of 6 μg/kg after 5 days in the 1 ppm dose group and 11 days in the 5 ppm group. It was near the limit of detection after 11 days at 30 ppm. ^{14}C residues in eggs reached a plateau 10 days after the start of dosing reaching maximum levels of 11, 41 and 198 μg/kg for the 1, 6 and 30 ppm dose groups respectively. The TRR was highest in liver and lowest in fat. Residues were roughly proportional to dosage rates.

Table 4. Distribution of ^{14}C in tissues of hens dosed with [^{14}C]dimethipin for 30 days (Bodden *et al*., 1982).

Nominal dose (ppm)	TRR (μg/kg as dimethipin)				
	Kidney	Liver	Muscle	Fat	Blood
30 days feeding					
1	23 ± 4.4	74 ± 22	<8	<19	56 ± 20
6	114 ± 25	365 ± 90	30 ± 4.7	<18	303 ± 58
30	490 ± 23	1430 ± 158	129 ± 22	29 ± 5.9	1450 ± 114
11 days withdrawal					
1	<7	<7	<7	<18	14 ± 3.9
6	10 ± 2	28 ± 5.0	12 ± 2.0	<18	79 ± 15
30	72 ± 11	137 ± 30	53 ± 7.2	19 ± 2.4	363 ± 55

Residues of dimethipin were <0.01 mg/kg in liver at all doses (Abdel-Kader and Blaszczynski, 1984).

Lau and Gay (1993) dosed White Leghorn laying hens with [^{14}C]dimethipin for five days at 15.8 or 152 mg/bird, equivalent to 203 or 2770 ppm in the diet. Egg and excreta samples were collected daily and the birds killed within 24 hours of the last dose. Samples of liver, kidney, gizzard, muscle and fat were collected for characterization by HPLC and co-chromatography with authentic standards, LC-MS and ^{1}H NMR.

The recovery of radioactivity from excreta, expired-air traps and carcases was >95% with 90-91% excreted within 24 hours of the last dose. Only 5.1-5.6% of the dose was recovered in edible tissues and eggs. Radioactive residues in eggs did not reach a plateau during the 5 days of the study.

Table 5. Radioactive residues in eggs and tissues of laying hens dosed orally with [^{14}C]dimethipin for 5 days (Lau and Gay, 1993).

	TRR (mg/kg as dimethipin)	
Sample	Low-dose hens (203 ppm)	High-dose hens (2770 ppm)
Liver	9.7	65

Sample	TRR (mg/kg as dimethipin)	
	Low-dose hens (203 ppm)	High-dose hens (2770 ppm)
Kidney	4.5	39
Gizzard	1.4	20
Muscle (breast)	0.63	10
Muscle (thigh)	0.72	10
Egg yolk	1.1	6.9
Egg white	0.68	6.6
Fat	0.20	2.4

20-50% of the TRR was extracted from the egg and tissue samples with organic solvents and water. A further 25-50% was released by acid and base extraction, and proteolytic digestion of the post-extraction solids released nearly all the remainder. Significant bound radioactivity was only found in egg white (20% of the TRR) and fat (24% of the TRR).

Table 6. Distribution of radioactivity in extracts of eggs and tissues of laying hens dosed orally with [^{14}C]dimethipin for 5 days (Lau and Gay, 1993).

Sample	% of TRR			
	Solvent extracted[1]	Enzyme hydrolysate of post extraction solids[2]	Bound[3]	Total recovery
Liver	75	23	1.3	99
Kidney	49	27	2.3	78
Gizzard	63	33	1.3	97
Muscle (breast)	58	29	0.1	87
Muscle (thigh)	59	18	0.2	77
Egg yolk	85	16	0.1	100
Egg white	80	4.3	20	100
Fat	54	-	24	78

[1] sum of solvent extracts, hexane, ethyl acetate, methanol, water, acid/base
[2] based on the most effective enzyme of proteases, sulfatases, β-glucuronidase, β-glucosidase, pepsin, trypsin and esterases, all incubated at 37°C.
[3] based on combustion of post-hydrolysis solids.

To further characterize the metabolites present the various extracts were purified on C-18 solid-phase extraction and silica gel columns and by HPLC. Individual metabolites were identified in the excreta by co-chromatography with authentic standards, mass spectrometry and ^{1}H NMR.

The main metabolite was DMP-S-cys in hen livers and glu-cys-S-DMP in other tissues. It is proposed that the addition of glutathione to dimethipin (glutathione S-transferase-catalysed or spontaneous) gives DMP-GSH which can be transported out of the cells in which it is formed and the glutathione moiety degraded by endogenous peptidases to produce glu-cys-S-DMP and DMP-S-cys. Oxidative transamination and loss of pyruvic acid or decarboxylation can give DMP-SH and DMP-S acetate. Methylation of DMP-SH in the presence of S-adenosine-methionine (SAM) would produce DMP-S-methyl which could be further oxidised to DMP-SO-methyl. Another product could be the *N*-acetylcysteinyl conjugate, a compound expected to be retained by the strong anion exchange columns used. An unidentified metabolite found in several of the extracts had similar chromatographic behaviour to products obtained by reacting dimethipin with *N*-acetylcysteine. Reduction and hydroxylation reactions are also possible as evidenced by the presence of red-DMP and the hydroxylated metabolites DMP-tert-OH and DMP-prim-OH.

Samples of excreta were extracted successively with methanol/methylene chloride (1:1), methanol, methanol/water (1:1) and water. The methanol/methylene chloride and methanol extracts were combined to form an organic extract, and the methanol/water and water to form an aqueous extract. Following extensive chromatography on C-18 solid-phase extraction and silica gel columns and HPLC, DMP-prim-OH, DMP-SO-methyl, DMP-tert-OH and glu-cys-S-DMP, DMP-S-cys, DMP-S-acetate and DMP-SH metabolites were identified in the excreta by co-chromatography with authentic standards, mass spectrometry and ^{1}H NMR.

Table 7. Identity and distribution of metabolites in the edible tissues and eggs of hens dosed with [^{14}C]dimethipin for 5 days (Lau and Gay, 1993).

Compound or fraction	% of TRR							
	Liver	Kidney	Muscle (breast)	Muscle (thigh)	Fat	Gizzard	Egg yolk	Egg white
Unknown #1	1.3	-	0.13	1.7	3.1	0.3	-	0.25
Unknown #2	3.1	17	28	16	-	15	7.6	1.1
Unknown #3	0.45	-	-	-	-	-	-	-
Unknown #4	2.4	2.8	2.2	-	-	-	-	-
Unknown #5	0.58	1.6	-	-	-	-	-	-
DMP-S-methyl	7.3	-	-	-	-	-	0.62	-
DMP-prim-OH	3.1	-	-	-	-	0.8	2.9	2.3
DMP-tert-OH	2.9	4.4	-	-	-		-	1.2
DMP-SO-methyl	0.95	1.2	0.18	-	-		0.95	6.0
DMP-S-cys	22	7.0	2.3	5.0	-	11	3.9	0.01
red-DMP	7.6	0.98	2.1	-	-	2.5	4.7	7.8
DMP-GSH	5.9	3.5	1.0	-	-	4.1	8.1	3.4
Unknown #6	0.36	-	-	-	-		5.0	-
glu-cys-S-DMP	7.4	19	32	28	20	21	36	25
DMP-SH	0.92	-	-	-	-	0.7	0.22	3.8
DMP-S-acetate	-	-	-	-	-		6.8	2.1
Unknown #7	-	-	-	-	-		-	3.8
Unknown #8	0.91	4.0	3.4	3.6	-	8.8	4.1	12
Unknown #9	0.25	-	-	0.51	-	0.86	-	-
Baseline	26	12	14	13	16	31	15	20
Bound	1.3	2.3	0.96	2.1	5	1.3	1.9	20
Total	95	76	87	74	74[1]	97	98	110

[1] includes 11% not analysed and 19% combustion loss

The results in rats, goats and hens show that dimethipin is extensively metabolized with almost no residual parent compound retained. The main residues in animals form as the result of glutathione, amino acid and protein conjugation and subsequent degradation. Minor metabolites are formed as a result of hydrolytic hydroxylation and/or oxidation to form hydroxy-DMP, DMP-tert-OH and DMP-prim-OH. The proposed metabolic pathway for dimethipin in domestic animals and birds is shown in Figure 1.

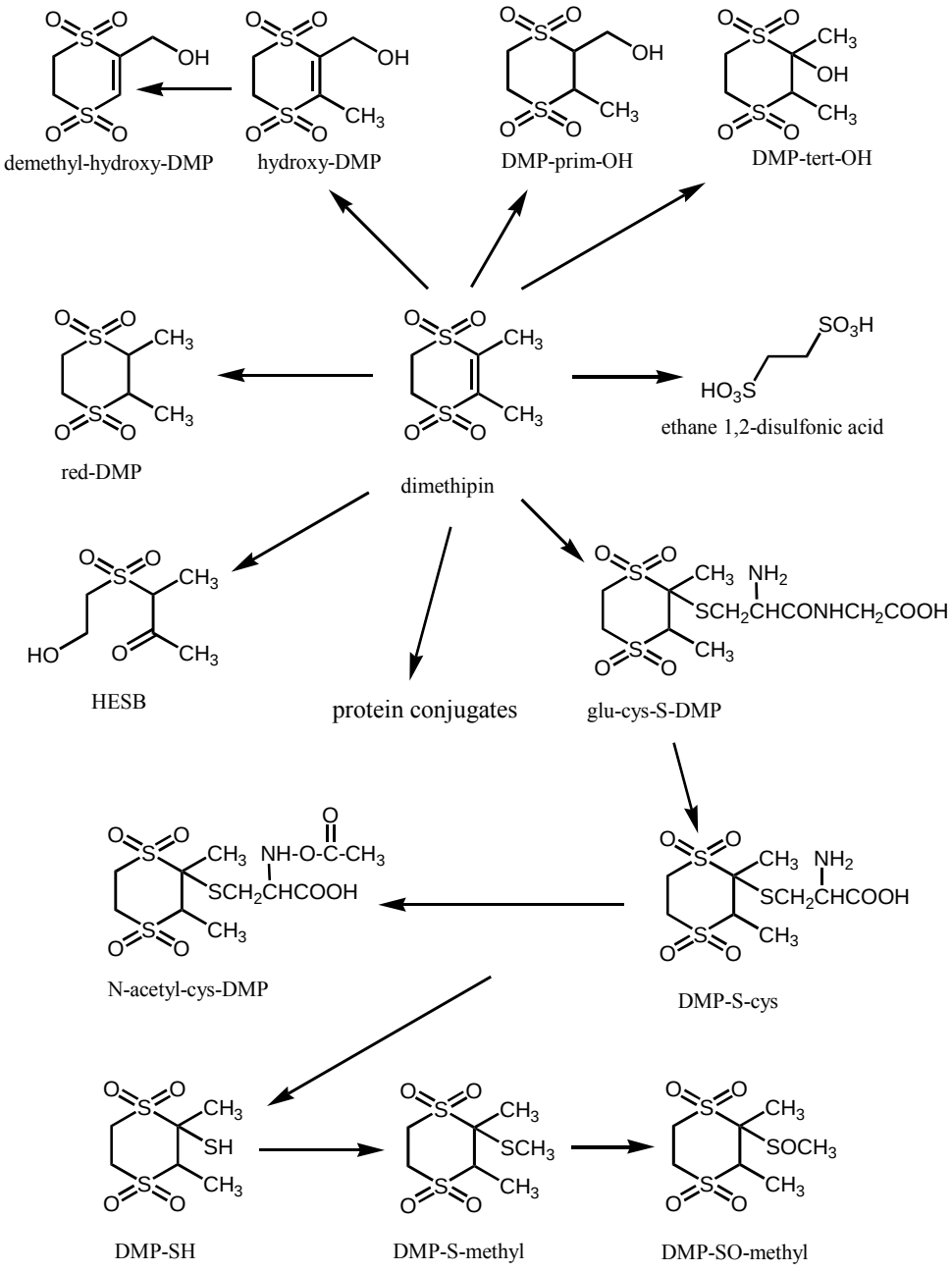


Figure 1. Proposed metabolic pathway of dimethipin in goats and hens.

Plant metabolism

Studies on cotton, potatoes, sunflowers, rice and grapes were reported to the Meeting.

Cotton and potatoes. In a study by Lengen (1987) cotton seedlings entering the second trifoliate stage were removed from their potting soil, their roots were rinsed and the seedlings grown hydroponically for 3 days in half-strength nutrient solution (Murashige Skoog) containing 75 mg/kg [^{14}C]dimethipin. Samples of the desiccated leaves (wilting, dry and brittle) were collected. Cotton callus was initiated from roots of asceptically germinated Stoneville seeds maintained on the nutrient medium. At 4-week intervals the medium was changed and the callus injected with [^{14}C]dimethipin. Potato callus was initiated in a similar fashion and also injected with [^{14}C]dimethipin.

The cotton leaves were extracted with $CHCl_3$/methanol/water and the combined extracts partitioned with $CHCl_3$ to produce a two-phase system; $CHCl_3$ and aqueous. Approximately 98% of the radioactivity was extracted, 20% in the $CHCl_3$ phase and 78% in the aqueous phase. HPLC analysis of the $CHCl_3$ phase revealed a single peak that co-chromatographed with dimethipin, and the identity was confirmed by mass spectrometry. The aqueous phase contained five metabolites of which dimethipin accounted for 51% of the radioactivity. Two of the metabolites, at 1.2 and 3.6% of the TRR, co-chromatographed with reaction products from a mixture of [^{14}C]dimethipin and L-cysteine, although their identity could not be established. Comparison of the plant extract HPLC profile with that from urine in a rat feeding study (Mcmanus, 1987a) indicated that one of the metabolites was cys-gly-DMP. An additional two metabolites which co-chromatographed with reaction products from a mixture of [^{14}C]dimethipin and glutathione represented 11 and 8.8% of the TRR. The former also co-chromatographed with the rat metabolite *N*-acetylcysteinyl-dimethipin while the latter was identified as red-DMP. Reduction of an aliquot of the aqueous phase to confirm the presence of intact dimethipin or red-DMP in the unidentified metabolites proved inconclusive. Enzymatic hydrolysis of an aliquot of the aqueous phase with glucosidase and cellulase resulted in no significant changes indicating that the metabolites were neither sugar- nor cellulose-based conjugates.

The cotton callus cultures gave extracts with similar metabolite profiles to the hydroponically treated plants except the dimethipin/L-cysteine reaction products increased and red-DMP decreased. The potato callus culture produced extracts with an additional polar peak over and above the other five peaks in the HPLC chromatogram, which had an identical retention time to an unidentified polar rat metabolite.

As dimethipin is applied to plants close to natural senescence at or about harvest, biochemical activity is very limited resulting in minimal metabolism, and the main residue is the parent compound. In a study of the fate of dimethipin in cotton seedlings and callus cell cultures of cotton and potatoes most of the plant metabolites resulted from the conjugation of dimethipin with glutathione and/or cysteine and subsequent degradation to yield cyclic and acyclic dimethipin derivatives.

Cotton. Four mature indoor-grown plants, each with 1-4 bolls open, were treated with a single application of a flowable formulation of [^{14}C]dimethipin at 1.12 kg ai/ha (Curtiss, 1980). The bolls were harvested 7 days after spraying and seeds and linters removed. Approximately 94% of the TRR in seeds with linters (0.81 mg/kg as dimethipin) was removed by Soxhlet extraction with methanol of which 94% or 0.76 mg/kg was identified as unchanged parent compound by TLC with LSC using an SiO_2 IBF TLC plate developed with acetone/$CHCl_3$. In seeds delinted by acid (H_2SO_4), rinsed with water, air-dried and homogenized, 18% of the TRR was extractable with methanol (0.18 mg/kg calculated as dimethipin) of which 38% was identified by TLC as unchanged dimethipin. The methanol extract was partitioned with hexane with the oil fraction accounting for 1.1% of the total extractable residue.

Burke and Johnson (1994) treated mature indoor-grown Stoneville 215 cotton plants with [^{13,14}C]dimethipin at 0.34 and 1.6 kg ai/ha two weeks before harvest. Samples of bolls and foliage were separated into foliage, carpel walls, fibre and seed and ^{14}C determined by combustion LSC. Samples were extracted and profiled by reverse-phase and anion-exchange chromatography, NMR and mass spectrometry. Approximately 98% of the ^{14}C in foliage was extracted with acetone and methanol/water. The main residue was unchanged dimethipin (72%) with no other individual compound accounting for more than 5% of the TRR. Approximately 85% of the radioactivity in mature seeds harvested from plants treated at 0.34 kg ai/ha was removed by rinsing with acetone. The major compound in the surface rinse was unchanged dimethipin. Extraction of ground seeds with acetone, hexane and methanol/water recovered 77-80% of the TRR. 80-90% of the residue in seeds was identified as dimethipin: no other component accounted for more than 5.2%. The minor metabolites were a group of closely-related highly polar anionic compounds that could be extracted into polar solvents but were not associated with cellular components of cotton seeds.

Table 8. Distribution of radioactivity in cotton plants treated with [^{14}C]dimethipin (Burke and Johnson, 1994).

Sample	TRR (mg/kg as dimethipin)	
	0.34 kg ai/ha	1.55 kg ai/ha
Cotton fibre	12 ± 9.3	97 ± 95
Carpel walls	8.7 ± 1.1	37 ± 4
Foliage	97 ± 6	341 ± 18
Immature seed	0.084 ± 0.036	-
Mature seed	0.29 ± 0.18	1.4 ± 1.1
Homogenized seed	0.20 ± 0.02	1.1 ± 0.07

Potatoes. A field-grown Kennebec plant was sprayed with a flowable formulation of [^{14}C]dimethipin at 2.24 g ai/ha (Lengen and Harned, 1981a), and the potatoes harvested after 14 days. The unwashed, unpeeled potatoes were analysed by LSC after dry combustion. Residues in soil and potatoes were characterized by TLC (Whatman silica gel LK_6 glass-backed plates) or GLC with an ECD. The TRR in the tubers was 0.059 mg/kg calculated as dimethipin. Unchanged dimethipin, determined by methanol extraction and the standard GLC analytical method, accounted for 20-25% of the TRR (0.012-0.015 mg/kg). The low levels of radioactivity precluded analysis of the unextracted material. Untreated control samples contained low levels of radioactive residue (0.005 mg/kg as dimethipin). The TRRs in the soil at depths of 0-15 cm and 15-30 cm were 1.1 and 0.04 mg/kg respectively, as dimethipin. Residues of unchanged dimethipin in soil from the 0-15 cm profile measured using TLC with LSC were 0.8 mg/kg.

Sunflowers. The backs of the seed heads of six mature plants grown outdoors in plastic-lined wooden bins were sprayed with flowable [^{13,14}C]dimethipin at 1.4 kg ai/ha (Curtiss and Harned, 1980). Seeds were harvested after a two-week senescence period (outdoors) and a two week drying period (indoors), and homogenized and Soxhlet-extracted with acetonitrile. Hexane was used to partition the oil from the acetonitrile. Extracts were analysed by TLC with LSC and GLC with an ECD. Samples of seed were also sequentially extracted with methanol and methanol/water/HCl to ensure that all the extractable material had been removed.

The TRRs in seeds at harvest (calculated as dimethipin) were 19 mg/kg of which 14 mg/kg was extractable with a variety of solvents. 61% of the extractable residue was dimethipin. No other single component exceeded 5.7% of the TRR.

Table 9. Distribution of radioactivity in sunflower seed from plants treated with [^{14}C]dimethipin (Curtiss and Harned, 1980).

	TRR (mg/kg as dimethipin)	% dimethipin
CH_3CN extract	10	89
Hexane partition of CH_3CN extract (oil)	0.14	11
Methanol extract	3.5	-
Methanol/water/HCl (Soxhlet)	0.34	-
Methanol/water/HCl (room temperature)	0.23	-
Unextractable	4.5	-
Total	19	

Rice. Balba and Dzialo (1983) treated indoor-grown plants with [^{14}C]dimethipin at 2.24 g ai/ha. The plants were harvested 17 days later and separated into straw, hulls and seed. Radioactivity was determined by combustion and LSC. Residues in the straw, hulls and seed were extracted with $CHCl_3$/water with further extraction of the seed using methanol/water. Analysis was by TLC and GLC. TRRs in straw, hulls and seed were 162, 325 and 8 mg/kg respectively, calculated as dimethipin. Solvent-extractable residues represented 89, 90 and 78% of the TRR in straw, hulls and seed respectively with unchanged dimethipin representing 67 (108 mg/kg), 80 (261 mg/kg) and 50%

(4.1 mg/kg) respectively of the extractable TRR. Three metabolites were separated by TLC or GLC but were not identified.

Grapes. Six field-grown Mueller-Thurgau vines were sprayed with an EC formulation at 115 mg [^{14}C]dimethipin/vine (Ellgehausen and Fisher, 1982). Samples of leaves and grapes were collected 2 hours, 6 days and (at harvest) 24 days after application. Grapes were separated from the stems and crushed. The resulting juice was separated from skins and seed by filtration, and also processed into wine. The total radioactive residues were determined by LSC. The TRRs in leaves were 16, 7.8 and 3.6 mg/kg as dimethipin 2 hours and 6 and 24 days after application respectively.

Table 10. Distribution of radioactivity in grapes treated with [^{14}C]dimethipin at 115 mg/vine (Ellgehausen and Fisher, 1982).

Sample	TRR (mg/kg as dimethipin)		
	2 hours	6 days	24 days
Juice	0.70 (44%)	0.44 (33%)	0.26 (33%)
Skins & seed	0.78 (32%)	0.72 (44%)	0.43 (47%)
Stems	4.1 (24%)	3.1 (24%)	1.4 (20%)

Figures in parentheses are % of TRR in whole grapes.

Table 11. Characterisation of ^{14}C radioactivity in grapes and processed products (Ellgehausen and Fisher, 1982).

	Compound or fraction	% of TRR						
		2 hours		6 days		24 days		
		Juice	Seeds + skins	Juice	Seeds + skins	Juice	Seeds + skins	Wine
$CHCl_3$ extract								
	Polar			11	21	0.6		5.9
	M1		4.3			1.0	0.4	
	M2		2.1			0.2		
	M3				2.3	0.8	0.6	11
	M4			8.0		4.4		29
	Dimethipin	97	77	50	14	14	1.0	54
	M6				0.7		1.9	
	M7, other						<0.01, 8.1	
Sub-total		97	84	68	38	21	12	99.9
MeOH			7.6		-			
MeOH/water			4.7		52		48	
Unextractable			4.0		9.8		40	
Water- soluble		3.0		32		79		

Owing to the low levels of radioactivity in the aqueous extracts of juice they were first fractionated by ultrafiltration. Samples of the filtrate were passed down a Bio-Bead column or treated with pectinase. Nine metabolites were resolved by TLC of the Bio-Bead fraction with no single metabolite accounting for more than 3.2% of the juice TRR. No conjugates were released by HCl- or β-glucosidase hydrolysis.

Approximately 96, 90 and 60% of the radioactivity in skins and seed was extractable with $CHCl_3$, methanol, methanol/water at 2 hours, 6 days and 24 days respectively after treatment. At least seven metabolites were determined by TLC of the $CHCl_3$ extract, and no single metabolite accounted for more than 10% of the TRR.

The radioactivity in the methanol extract from the skin and seed samples collected 6 hours after treatment was too low for further analysis. Methanol extracts from 6- and 24-day samples were partitioned with $CHCl_3$ and first incubated with pectinase and then partitioned with $CHCl_3$, then incubated with β-glucosidase and partitioned with ethyl acetate. Most of the radioactivity was in the

$CHCl_3$ extract as the two metabolites D6 and D8. Only 1.7% of the skin and seed radioactivity was extractable with $CHCl_3$ after pectinase incubation with metabolites D5, D6 and D8 observed.

Residues of dimethipin were 0.036, 0.004 and 0.033 mg/kg in juice, stems/seeds and wine respectively of the combined 6- and 24-day samples. Numerous metabolites were detected although none were identified. The major metabolite, M4, accounted for 0.06 and 0.02 mg/kg in juice and wine respectively, calculated as dimethipin.

Samples of juice were processed into wine by alcoholic fermentation, then filtered. No radioactive CO_2 was evolved during fermentation. 11% of the radioactivity was in the yeast and solids and 89% in the clear wine.

Environmental fate in soil

Degradation

Aerobic degradation. The aerobic degradation of [^{14}C]dimethipin in a silt loam (sand 24%, silt 56%, clay 16%; pH 5.6; organic matter 4.4%; CEC 34 meq/100 g) and a sand (sand 96%, silt 3.6%, clay 0%; pH 6.1; organic matter 1.8%; CEC 7.3 meq/100 g) kept at 25°C in the dark was studied by Fitzpatrick (1982). Dimethipin was applied to the soils at a rate of 1 mg/kg, equivalent to 1.12 kg ai/ha, and incubated for up to a year. Extractable dimethipin accounted for 50% of the applied radioactivity in the silt loam after a year while bound residue and $^{14}CO_2$ accounted for 23 and 1.4% respectively. In the sand, 76-84% of the applied radioactivity was recovered of which 51-66% was identified as dimethipin. Bound residues and $^{14}CO_2$ accounted for 2.6 and 0.26% of the applied radioactivity after a year of aerobic ageing.

The aerobic metabolism of [^{14}C]dimethipin was studied in two standard German soils (standard 1: loamy sand high; sand 86%, silt 7.1%, clay 4.9%; pH 6.0; organic matter 2.6%; CEC 7.5 meq/100 g; standard 2: loamy sand low; sand 76%, silt 13%, clay 11%; pH 6.6; organic matter 0.7%; CEC 4.5 meq/100 g) and a field loam (sandy loam: sand 69%, silt 13%, clay 19%; pH 6.3; organic matter 1.9%; CEC 18 meq/100 g) for 168 days (Ellgehausen, 1985). Sieved samples were mixed with [^{14}C]dimethipin at 0.99 mg/100 g soil and the mixture adjusted with water to 40% maximum holding capacity. Dimethipin was the only compound detected in the extractable radioactivity from the German standard soil 2 and the field loam. It accounted for 33, 38 and 40% of the applied radioactivity in German standard soils 1 and 2 and the field loam respectively after 168 days. In standard soil 1 three metabolites were detected in addition to parent dimethipin in the extractable ^{14}C. Two were tentatively identified as methylene-DMP (up to 5.3%) and demethyl-DMP (up to 6.8%) by co-chromatography with authentic standards, and the third tentatively identified in a separate study by mass spectrometry as the carboxylic acid DMP-COOH (M + 1 243 m/e) (Mcmanus, 1985). Approximately 30% of the radioactivity applied to the field loam was converted to $^{14}CO_2$. Unextractable radioactivity increased with time in all soils reaching 25, 19 and 25% of the applied radioactivity respectively for standard soils 1 and 2 and the field loam. Recoveries of radioactivity were 94-101%.

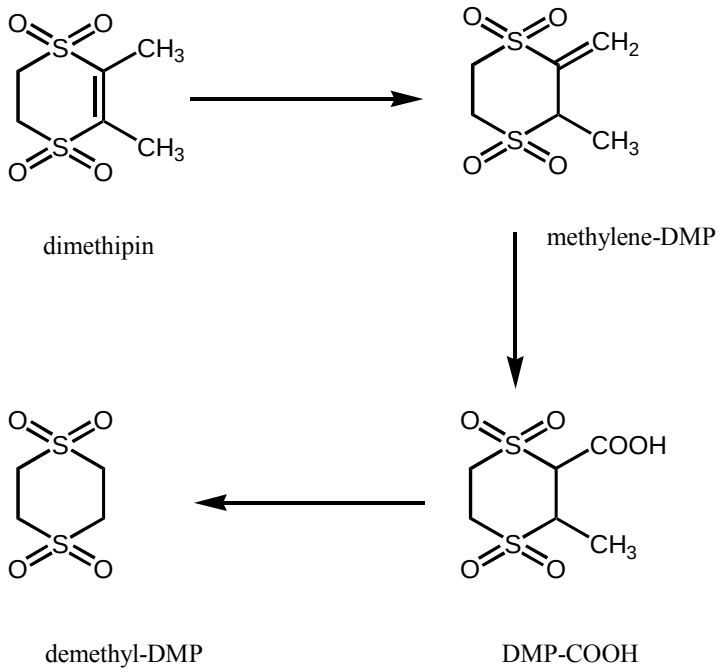


Figure 2. Proposed aerobic degradation pathway of dimethipin in soil

Anaerobic degradation. The same types of soil were again used by Fitzpatrick (1982) to study the anaerobic degradation of [^{14}C]dimethipin stored at 25°C in the dark. Dimethipin was applied at 1 mg/kg and the soils were incubated under aerobic conditions for one month before flooding with oxygen-free sterile water. ^{14}C desorbed from the soils into the water from 0 to 30 days: 76% desorbed from sand at day 0 and 87% after 30 days. Approximately 13% of the applied radioactivity was extractable from the silt loam soil with acetone with bound residues accounting for 5.2% of the ^{14}C. Dimethipin accounted for 70% of the radioactivity in the aqueous extracts. After 60 days 60-69% of the applied radioactivity was dimethipin. Recovery of ^{14}C was 88%.

In the sand, negligible ^{14}C was extracted with acetone (<2% at 60 days). Most of the radioactivity was desorbed into the aqueous phase (85% of the ^{14}C of which 80% was dimethipin). Bound residues accounted for 2% of the ^{14}C at 60 days. The recovery of ^{14}C at 60 days was greater than 90%.

Aqueous photolysis. Lengen and Harned (1981b) found the degradation of [^{14}C]dimethipin in a 2900 mg/kg aqueous solution to be slow with 92 and 89% of the radioactivity in control and photolyzed solutions respectively shown to be dimethipin after 28 days. The degradation was much more rapid when air was continuously bubbled through the solutions, when after 14 days only 51-52% of the radioactivity was present as dimethipin in both control and photolysed solutions. In a parallel study with argon-saturated solutions, degradation products in both solutions accounted for less than 15%. Degradation products were not amenable to analysis by chromatography or mass spectrometry, possibly owing to low molecular weights.

Fackler (1991) studied the photolytic stability of aqueous solutions of dimethipin at pH 5, 7 and 9 under natural sunlight. The temperature of the solutions varied diurnally and with weather conditions. Significant hydrolysis was not observed in control solutions maintained in the dark. Estimated half-lives at pH 5 and 9 were 35 and 47 days respectively. No significant degradation occurred at pH 7.

Soil photolysis. Lengen and Harned (1981b) applied dimethipin to thin films of sandy loam soil at a rate equivalent to 1.68 kg ai/ha exposing the films to ultraviolet light for 28 days. Dimethipin accounted for 89-99% and 47-51% of the ^{14}C in control and irradiated films respectively.

Fackler (1992) determined the half-life of [^{14}C]dimethipin in Paxton sandy loam soil exposed to sunlight for 30 days at 25°C. After 30 days dimethipin accounted for 81-87% and 58-65% of the ^{14}C in control and irradiated samples respectively. Volatile components accounted for less than 1% of the applied radioactivity. Recoveries of ^{14}C at each sampling interval were 92 ± 7% for exposed samples and 94 ± 9% for dark samples.

Field studies. In a study of the field dissipation of dimethipin by Harned (1981a) Kats potatoes were treated with a flowable formulation at 1.12 kg ai/ha (748 l/ha). Samples of gravely silt loam soil (pH 5.3, organic matter content 3.5%) were taken at 0-15 and 15-30 cm depths before and after treatment. The pre-treatment soil samples had the highest levels of dimethipin at 13.2 mg/kg in the 0-15 cm core, with 0.048 mg/kg in the 15-30 cm core, and the next highest were 2.1 mg/kg in the 0-15 cm core collected 4 days after spraying. The study cannot be used to determine the degradation of dimethipin under field conditions owing to the pre-treatment results.

Dimethipin was applied as one or two sprays at 0.56 kg ai/ha to cotton in Mississippi, Georgia and Arizona, USA (Harned, 1981b) grown in silt loam in Mississippi (sand 26%, silt 58%, clay 16%; pH 4.3; organic matter 1.1%; CEC 24 meq/100 g), loamy sand in Georgia (sand 85%, silt 11%, clay 3%; pH 4.9; organic matter 1.6%; CEC 14 meq/100 g) and clay loam in Arizona (sand 28%, silt 36%, clay 35%; pH 7.9; organic matter 1.4%; CEC 42 meq/100 g). Soils were sampled at 0-15 cm and 15-30 cm (Wong, 1976). Residues of dimethipin in Mississippi at the 0-15 cm depth were 0.086 mg/kg on the day of application decreasing to 0.083 mg/kg at 30 days and <0.025 mg/kg at 164 days after spraying. Maximum residues in the 15-30 cm cores were 0.033 mg/kg at 7 days. In Georgia, the highest residue of 0.36 mg/kg was determined immediately after the first of two applications. 164 days after the second application residues had decreased to 0.043 and 0.039 mg/kg at 0-15 and 15-30 cm respectively. At the Arizona site there was no clear decline pattern with the highest residues observed at 164 and 14 days at 0.59 mg/kg for the 0-15 cm core and 0.56 mg/kg for the 15-30 cm core respectively. The Arizona field was disced and deep-ploughed between days 30 and 164 resulting in some mixing of sampling depths. At 249 days residues were 0.26 and 0.028 mg/kg for the 0-15 and 15-30 cm sampling depths respectively. Residues in soil decreased at the Mississippi and Georgia sites where rainfall was significantly greater (117 and 31 cm respectively for 6 months after application) than in Arizona (7.3 cm) which has a year-round dry, warm to hot climate.

Table 15. Field studies on the dissipation of dimethipin in soil in the USA (Harned, 1981b).

Crop/variety/location/ year	Soil	Application rate (kg ai/ha)	DALA	Accumulated rainfall (cm)	Residue (mg/kg)	
					0-15 cm	15-30 cm
Cotton/Stoneville-213/Mississippi/1981	Silt loam	0.56	-0	-	<0.025	<0.025
			0	-	0.086	<0.025
			7	0.0	0.11	0.033
			14	2.8	0.10	<0.025
			30	2.8	0.083	<0.025
			164	117	<0.025	<0.025
Cotton/DPL-41/Georgia/1981	Loamy sand	2×0.56	-0	-	0.031	0.043
			0 1st spray	-	0.36	0.075
			3 1st spray	0.05	0.082	0.064
			7 1st spray	0.15	0.10	0.030
			0 2nd spray	0.15	0.21	0.066
			3	0.79	0.21	<0.025
			7	2.0	0.19	<0.025
			14	2.0	0.15	<0.025
			30	4.0	0.18	<0.025
			170	31	0.043	0.039

Crop/variety/location/ year	Soil	Application rate (kg ai/ha)	DALA	Accumulated rainfall (cm)	Residue (mg/kg)	
					0-15 cm	15-30 cm
Cotton/DPL-61/Arizona/1981	Clay loam	2×0.56	-0	-	<0.025	<0.025
			0 1st spray	-	0.084	0.059
			7 1st spray	0.00	0.12	0.029
			0 2nd spray	0.00	0.18	0.037
			3	0.00	0.26	0.46
			7	0.05	0.48	0.25
			14	0.05	0.43	0.56
			30	0.05	0.43	0.031
			164	7.3	0.59	0.23
			249	[1]	0.26	0.028

DALA: days after last application
[1]plot received 61 cm of irrigation water

Residues of dimethipin were also determined in two Californian field plots planted with cotton and rotational crops of lettuce, carrots and beets for four years. The cotton crops were defoliated with dimethipin at 0.28 or 2 × 0.28 kg ai/ha. The soil was adobe clay with 4% organic matter, the crops were irrigated with about 76-91 cm/year by furrows and the rainfall was 52, 30, 29 and 26 cm. Residues in core samples at depths of 0-15 and 15-30 cm were <0.02 mg/kg 337-347 days after the last application.

Dzialo *et al*. (1994a) studied the field dissipation of dimethipin on bare ground and a cotton crop in Georgia. Both plots were harrowed and roto-tilled twice to a depth of 8 cm before planting. The cotton plot was planted with the variety Coker 315 and the bare-ground plot was roto-tilled once more before treatment. Dimethipin was applied as two sprays at 0.34 kg ai/ha and 0.26 kg ai/ha seven days apart with the first application at about the 50% boll-open stage, and the soil was sampled at various intervals up to 547 days later. The samples sectioned into increments of 0-15, 15-30, 30-46, 46-61, 61-76, 76-91, 91-107 and 107-122 cm were analysed for dimethipin by GLC with an ECD with residues in selected samples confirmed by GC-MS. The soil at the 0-15 cm depth was sandy clay loam (sand 76%, silt 0.0%, clay 24%, pH 6.2, organic matter 1.1%, CEC 2.9 meq/100 g) for both the cotton crop and bare ground plots. The average monthly minimum and maximum temperatures were 7 and 23°C while the total irrigation and rainfall for the two plots was 239-241 cm.

In the cropped plot residues peaked at 0.10 mg/kg 14 days after the second application, probably a result of treated foliage transferring residues to the soil. Residues decreased to <0.01 mg/kg at 547 days after the first spray.

Table 16. Residues of dimethipin in cores of soil treated with two sprays of a flowable formulation on a cotton crop in Georgia (average of three replicates).

Sample interval (days)	Dimethipin (mg/kg)							
	0-15 cm	15-30 cm	30-46 cm	46-61 cm	61-76 cm	76-91 cm	91-107 cm	Total
-1	ND	ND	ND	ND	ND	ND	ND	ND
0	0.042	ND	ND	ND	NA	NA	NA	0.042
1	0.059	ND	ND	ND	NA	NA	NA	0.059
2	0.063	ND	ND	ND	NA	NA	NA	0.063
6	0.066	ND	ND	ND	NA	NA	NA	0.066
7[1]	0.084	ND	ND	ND	NA	NA	NA	0.084
10	0.090	ND	ND	ND	NA	NA	NA	0.090
14	0.084	ND	ND	ND	NA	NA	NA	0.084
21	0.10	ND	ND	ND	NA	NA	NA	0.10
35	0.098	ND	ND	ND	NA	NA	NA	0.098
67	0.065	0.01	ND	ND	NA	NA	NA	0.075
97	0.047	0.018	ND	ND	NA	NA	NA	0.065
127	0.051	0.020	ND	ND	NA	NA	NA	0.071
157	0.044	0.021	ND	ND	NA	NA	NA	0.065
187	0.037	0.018	0.015	0.012	ND	ND	NA	0.082

Sample interval (days)	Dimethipin (mg/kg)							
	0-15 cm	15-30 cm	30-46 cm	46-61 cm	61-76 cm	76-91 cm	91-107 cm	Total
247	0.014	0.012	0.010	ND	ND	0.011	ND	0.047
367	ND	ND	ND	ND	ND	ND	NA	ND
490	ND	0.011	ND	ND	ND	ND	NA	0.011
547	ND	ND	ND	ND	ND	ND	NA	ND

ND: not detected
NA: not analysed
[1] second application

Residues in the bare-ground plot peaked on the day of the second application at 0.209 mg/kg decreasing to below the limit of detection by day 490.

Table 17. Residues of dimethipin in cores of soil from a bare-ground plot in Georgia treated with two sprays of a flowable formulation. Average of three replicates.

Sample interval (days)	Dimethipin (mg/kg)							
	0-15 cm	15-30 cm	30-46 cm	46-61 cm	61-76 cm	76-91 cm	91-107 cm	Total
-1	ND	ND	ND	ND	ND	ND	ND	ND
0	0.081	ND	ND	ND	NA	NA	NA	0.081
1	0.075	ND	ND	ND	NA	NA	NA	0.075
2	0.090	ND	ND	0.011	ND	ND	NA	0.090
6	0.073	ND	ND	ND	NA	NA	NA	0.073
7[1]	0.209	ND	ND	ND	NA	NA	NA	0.209
10	0.193	ND	ND	ND	NA	NA	NA	0.193
14	0.134	ND	ND	ND	NA	NA	NA	0.134
21	0.131	ND	ND	ND	NA	NA	NA	0.131
35	0.126	ND	ND	ND	NA	NA	NA	0.126
67	0.078	ND	ND	ND	NA	NA	NA	0.078
97	0.072	0.018	0.013	ND	0.010	ND	ND	0.113
127	0.040	0.035	0.011	0.012	ND	ND	NA	0.098
157	0.064	0.029	0.016	0.015	ND	ND	NA	0.124
187	0.053	0.026	0.014	0.010	ND	ND	NA	0.103
247	0.034	0.028	0.016	0.014	ND	ND	NA	0.092
367	0.013	0.019	0.014	0.015	ND	ND	NA	0.061
490	ND	ND	ND	ND	ND	ND	NA	ND
547	ND	ND	ND	ND	ND	ND	NA	ND

ND: not detected
NA: not analysed
[1] second application

The half-lives of dimethipin, calculated from the first-order constants using linear regression analysis, in the cropped and bare-ground plots were 168 and 177 days respectively.

Dzialo *et al*. (1994b) studied the dissipation of dimethipin on a cotton field crop in Mississippi tilled to a depth of 5-8 cm three times during the study to remove weeds and stubble. The plot was planted with variety DES 119 and dimethipin was sprayed twice seven days apart at 0.34 kg ai/ha and 0.26 kg ai/ha, with the first application when the crop was at about the 75% boll-open stage and the second at the 90% stage. Soil samples sectioned into increments of 0-15, 15-30, 30-46, 46-61, 61-76, 76-91, 91-107 and 107-122 cm were collected at various intervals up to 548 days after the first application. The soil for the 0-15 cm depth samples was sandy loam (sand 33%, silt 58%, clay 9.2%, pH 6.8, organic matter 0.8%, CEC 5.5 meq/100 g). Average monthly minimum and maximum temperatures were 5 and 17°C while the total rainfall was 171 cm. Analysis for dimethipin in the soil samples was by GLC with an ECD with residues in selected samples confirmed by GC-MS.

Residues peaked at 0.16 mg/kg on the day of the second application and decreased to 0.019 mg/kg 548 days after the first spraying.

Table 18. Residues of dimethipin in cores of soil from a cotton plot in Mississippi treated with two sprays of a flowable formulation. Average of three replicates.

Interval (days)	Dimethipin (mg/kg)							
	0-15 cm	15-30 cm	30-46 cm	46-61 cm	61-76 cm	76-91 cm	91-107 cm	Total
-1	ND	ND	ND	ND	ND	ND	ND	ND
0	0.031	ND	ND	ND	NA	NA	NA	0.031
1	0.080	ND	ND	ND	NA	NA	NA	0.080
2	0.017	ND	ND	ND	NA	NA	NA	0.017
6	0.078	0.012	ND	ND	NA	NA	NA	0.090
7[1]	0.147	0.011	ND	ND	NA	NA	NA	0.158
10	0.061	0.011	ND	ND	NA	NA	NA	0.072
14	0.123	0.016	ND	ND	NA	NA	NA	0.139
21	0.096	0.017	ND	ND	NA	NA	NA	0.113
35	0.088	0.018	ND	ND	NA	NA	NA	0.106
65	0.016	0.031	0.057	0.014	ND	ND	NA	0.118
97	0.012	0.032	0.042	0.022	ND	ND	NA	0.108
126	ND	0.021	0.047	0.050	0.015	ND	ND	0.133
159	ND	0.014	0.019	0.045	0.026	ND	ND	0.104
187	ND	0.008	0.017	0.024	0.025	ND	ND	0.074
247	ND	0.007	0.011	0.033	0.030	ND	ND	0.081
367	ND	ND	0.009	0.024	0.024	ND	ND	0.057
489	ND	ND	ND	ND	0.015	ND	ND	0.015
548	ND	ND	ND	ND	0.019	ND	NA	0.019

[1] second application

The half-life of dimethipin in the 0-122 cm depth calculated from first-order constants using linear regression analysis was 196 days.

Dimethipin was applied as a single spray at 2.24 kg ai/ha to sunflowers 14 days before harvest in North Dakota, USA (Harned, 1982). The soil was clay loam (sand 40%, silt 40%, clay 19%; pH 7.0; organic matter 16%; CEC 54 meq/100 g). 21 days after spraying the plot was disced to a depth of 10-13 cm. Soils were sampled to a depth of 30 cm as two cores, 0-15 cm and 15-30 cm and analysed for dimethipin (Wong, 1976). Under the climate conditions typical of North Dakota severe cold and low precipitation occurred for the seven months after application that autumn. The delayed dissipation of dimethipin appears to be related to the onset of warm weather. A possible reason for the variability in results is the incorporation of sunflower stubble/organic matter in the soil, discing at 21 days

In another trial a single spray of dimethipin was applied at 1.12 kg ai/ha to sunflowers 14 days before harvest in North Dakota (Fitzpatrick, 1983). The soil was silt loam (sand 36%, silt 51%, clay 13%; pH 7.0; organic matter 5.2%; CEC 52 meq/100 g). The crop was harvested so that no part of the normal harvested portion remained on the plot and the plot was not disced or ploughed. Soils were sampled to a depth of 30 cm as two cores, 0-15 cm and 15-30 cm and analysed for dimethipin. The initial residue at 0-15 cm was 0.10 mg/kg and decreased to <0.02 mg/kg after 18 months. The highest residue of 0.18 mg/kg correlated with an increase in precipitation and the seasonal thaw with subsequent stubble run-off.

Table 19. Field studies on the dissipation of dimethipin in soil in the USA (Harned, 1982, Fitzpatrick, 1983).

Crop/variety/location/year	Soil	Application rate (kg ai/ha)	DALA	Accumulated rainfall (cm)	Residue (mg/kg)	
					0-15 cm	15-30 cm
Sunflower/894-oil type /North Dakota /1982	Clay loam	2.24	-0	-	0.025	<0.025
			+0	-	0.43	0.035
			3	0.064	0.37	<0.025
			7	0.064	0.28	<0.025
			14	0.064	0.54	<0.025
			30[1]	3.7	0.38	<0.025

Crop/variety/location/year	Soil	Application rate (kg ai/ha)	DALA	Accumulated rainfall (cm)	Residue (mg/kg)	
					0-15 cm	15-30 cm
			180	10	0.49	<0.025
			270	24	0.54	<0.025
			365	52	0.087	<0.025
			545	70	0.055	0.055[2]
Sunflower/894-oil type/ North Dakota /1982	Silt loam	1.12	-0	-	<0.02	<0.02
			+0	-	0.10	<0.02
			14	4.0	0.10	<0.02
			30	4.4	0.07	<0.02
			90	12	0.06	<0.02
			180	30	0.18	<0.02
			270	44	0.04	<0.02
			365	61	0.04	<0.02
			540	81	<0.02	<0.02

DALA: days after last application
[1] plot disced to a depth of 10-13 cm 21 days after application
[2] residues in 0-30 and 30-58 cm cores were 0.065 and <0.025 mg/kg indicating the absence of significant deep soil leaching

Residues in rotational crops. In a confined rotational crop study (Perhach and Jalal, 1993) a small outdoor plot of Hanford sandy loam soil 0.61 m × 2.44 m was sprayed with [^{14}C]dimethipin at 0.6 kg ai/ha and subplots planted with Waldmann lettuce, var. 425 barley and Imperator carrots after 30 days. Samples of lettuce, barley (heads and straw) and carrots (tops and roots) were collected at half-mature growth and at maturity together with soil samples to a depth of 30 cm. The ^{14}C was determined by combustion and LSC. Crop samples were extracted twice with acetone followed by methanol/water. The acetone extracts were pooled as were the aqueous methanol extracts. The extracts were analysed by HPLC in a C-18 reverse-phase column with UV detection. Radio-chromatograms were constructed from LSC analysis of column fractions. Identification of compounds was by TLC on silica gel 60 F254 plates and co-chromatography with authentic standards. Further characterization was by column chromatography (Sephadex A-25 anion exchanger, Sephadex LH 20 and Biogel P2) combined with mass spectrometry in electron impact, chemical ionisation and fast atom bombardment modes.

Radioactive residues in 0-15 cm soil cores were 0.19, 0.06 and 0.39 mg/kg as dimethipin respectively in the lettuce, carrot and barley subplots immediately after application. At planting 30 days after treatment the levels were 0.25, 0.15 and 0.14 mg/kg respectively, and at harvest were 0.03 (100 DAT), 0.02 (238 DAT) and 0.03 (296 DAT) mg/kg. The variation in observed TRR is probably due to inhomogeniety in the application (stated to be made uniformly) and reflects the small number of core samples collected.

Most of the radioactivity in the soil at application and planting was extracted with acetonitrile (85-100% of the TRR), dimethipin being the only compound extracted. The percentage of bound, unextractable residue increased with time after application reaching 60-93% of the TRR at harvest.

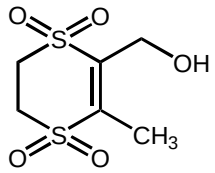
The concentrations of radioactivity were highest in barley forage, carrot tops and lettuce leaves. Only low levels of dimethipin were detected in the crops at harvest with residues ranging from undetectable in barley grain to 0.05 mg/kg in carrot roots.

Table 20. Radioactive residues in rotational crops after application of [^{14}C]dimethipin (Perhach and Jalal, 1993).

		Lettuce		Carrot				Barley		
		Immature	Mature leaf	Immature		Mature		Immature	Mature	
				Tops	Root	Tops	Root	Forage	Straw	Grain
TRR (mg/kg[1])		1.4	0.42	1.8	0.10	0.69	0.10	2.5	0.34	0.02
Fraction		% of TRR								
Organic	dimethipin	7.3	13	-	46	3.7	14	1.8	4.3	-
	hydroxy-DMP								3.3	
	U1						36			
	U2	10	22	32	4.3	29		14		
	U3		0.02					5.6	4.7	
	Other	7.3				2.5				
	Total	29	36	37	50	37	50	22	12	21
Aqueous/ MeOH	U1	5.7	8.9	5.9	27	7.2	26	48	30	
	U2	1.1	-	2.2		6.4				
	U3		0.4	-		-				
	Other	4.5	1.1	2.9		7.0				
	Total	11	10	13	27	21	26	48	30	18
Bound		60	54	50	23	42	24	31	58	61
Total		92	115	70	83	83	107	53	82	101

[1]calculated as dimethipin

In addition to dimethipin and hydroxy-DMP, three compounds, U1, U2 and U3 were detected in plant extracts. They did not co-chromatograph with the prepared standards but appeared to be related. When U2 and U3 were exposed to aqueous methanol they were converted into U1, and U2 and U3 formed at different stages of U1's purification. Mass spectra (EI, CI and FAB modes) of the compounds revealed fragments of hydroxy-DMP so the products are probably derivatives of hydroxy-DMP conjugated to the hydroxyl oxygen through ester or ether linkages. The FAB mass spectra of a mixture of U2 and a related compound, U4, showed a large number of ion peaks in the range m/z 450-650, though none corresponded to glucose, glucuronic acid or glutathione, the most likely candidates for conjugation to hydroxy-DMP. Hydrolysis of U1 in acid resulted in hydroxy-DMP, U2 and U3.



hydroxy-DMP

Korpalski (1996a) determined dimethipin in rotational crops after spraying it on cotton. In two field trials in Mississippi and Texas in sandy loam soil (Mississippi: sand 66%, silt 30%, clay 4%; pH 5.8; organic matter 1.2%; CEC 5.1 meq/100 g; Texas: sand 68%, silt 16%, clay 16%; pH 8.3; organic matter 0.9%; CEC 25 meq/100 g) dimethipin was sprayed twice on maturing cotton at 0.34-0.35 and 0.25-0.26 kg ai/ha. Approximately 30 days after the second application (after harvest) lettuce, carrots and wheat were planted. A sample of wheat forage was collected before harvest. Residues in lettuce at harvest were 0.02 to 0.03 mg/kg in Mississippi but quantifiable residues were not detected in Texas, nor in carrot roots or wheat grain at either site.

Table 21. Residues of dimethipin in rotational crops after application of dimethipin to mature cotton, 1 month plant back period (Korpalski, 1996a).

Crop	Location	Variety	Plant back interval (days)	Days from planting to harvest	Residue (mg/kg)
Lettuce	Mississippi	Black-seeded Simpson	28	217	0.02, 0.03, 0.03
	Texas	Golden State D	30	96	<0.02 (3)
Carrot (roots)	Mississippi	Early Coreless	28	232	<0.02 (3)
	Texas	Imperator 58	30	96	<0.02 (3)
Carrot (tops)	Mississippi	Early Coreless	28	232	0.04, 0.06, 0.07
	Texas	Imperator 58	30	96	0.03, 0.05, 0.04
Wheat (forage)	Mississippi	Mixed (mostly Cardinal)	28	157	0.03, 0.04, 0.04
	Texas	MIT	30	157	0.04, 0.04, 0.03
Wheat straw	Mississippi	Mixed (mostly Cardinal)	28	234	0.02, 0.02, 0.03
	Texas	MIT	30	230	<0.02 (3)
Wheat grain	Mississippi	Mixed (mostly Cardinal)	28	234	<0.02 (3)
	Texas	MIT	30	230	<0.02 (3)

Recoveries at fortifications of 0.1 and 0.5 mg/kg 83-109%.
Residues corrected for analytical recoveries when below 100%

Korpalski (1995a) also studied residues in rotational crops of lettuce, carrots and oats after dimethipin was sprayed twice on growing cotton in two field trials in Mississippi and Texas at 0.35-0.36 and 0.26 kg ai/ha. The soils were sandy loam at both sites (Mississippi: pH 6.3; organic matter 0.7%; Texas: pH 5.0; organic matter 0.5%). Approximately 6 months after the second application, after the cotton crop was harvested, lettuce, carrots and oats were planted. A sample of oat forage was collected before harvest of the grain.

The residues in the rotational crops were all <0.02 mg/kg, except in carrot tops and oat straw at the Texas site. A plant back interval of 6 months results in lower residues in rotational crops than an interval of 3 months.

Table 22. Residues of dimethipin in rotational crops after spray applications of dimethipin to cotton, 6 month plant back period (Korpalski, 1995a).

Crop	Location	Variety	Plant back interval (days)	Days from planting to harvest	Residue (mg/kg)
Lettuce	Mississippi	Black-seeded Simpson	184	55	<0.02 (3)
	Texas	Salad Bowl	179	52	<0.02 (3)
Carrot (roots)	Mississippi	Coreless	184	82	<0.02 (3)
	Texas	Imperator 58	179	95	<0.02, 0.02 (2)
Carrot (tops)	Mississippi	Coreless	184	82	<0.02 (3)
	Texas	Imperator 58	179	95	0.06, 0.13, 0.18
Oat (forage)	Mississippi	Bob	184	52	<0.02 (3)
	Texas	Troy	179	52	<0.02 (3)
Oat straw	Mississippi	Bob	184	92	<0.02 (3)
	Texas	Troy	179	80	0.03 (3)
Oat grain	Mississippi	Bob	184	92	<0.02 (3)
	Texas	Troy	179	80	<0.02 (3)

Recoveries at fortifications of 0.1 and 0.5 mg/kg 74-106%.
Residues corrected for analytical recoveries when below 100%

The results showed that dimethipin is extensively metabolized with the parent compound accounting for ≤14% of the TRR in crops. Residues in rotational crops after application at the USA label rate for cotton were <0.02-0.07 mg/kg at a plant-back interval of 1 month and <0.02 mg/kg in

crops planted 6 months after spraying, but in carrot tops the residues were up to 0.18 mg/kg at harvest in crops planted 6 months after the last application.

Adsorption/desorption. The adsorption/desorption of [^{14}C]dimethipin was studied in the USA and Canada (Curry, 1980). The soil in the US trial was Bethany sandy loam (sand 61%, silt 24%, clay 15%; pH 5.5; organic matter 1.9%; CEC 8.5 meq/100 g), and in Ontario the five soils were Haldimand silty clay loam (sand 9.3%, silt 60%, clay 31%; pH 6.1; organic matter 3.8%; CEC 36 meq/100 g), Berrin sand (sand 82%, silt 13%, clay 5.8%; pH 6.6; organic matter 2.8%; CEC 19 meq/100 g), Fox sandy loam (sand 69%, silt 22%, clay 9.1%; pH 7.0; organic matter 3.0%; CEC 21 meq/100 g), Huron silt loam (sand 24%, silt 54%, clay 22%; pH 6.9; organic matter 4.5%; CEC 38 meq/100 g) and Bradford muck (pH 5.3; organic matter 89%; CEC 204 meq/100 g). All were treated at four application rates of [^{14}C]dimethipin, 1, 2, 4 and 8 µg/ml. The adsorption isotherms were modelled using the Freundlich[1] adsorption equation.

Dimethipin was weakly adsorbed by all the soils and there was a close relationship between adsorbtion and percentage of organic matter. Average adsorption partition coefficients (K_a) were 0.04 for Bethany sandy loam, 0.20 Haldimand silty clay loam, 0.20 Berrien sand, 0.27 Fox sandy loam, 0.36 Huron silt loam and 13.6 Bradford muck. Correlation coefficients were 0.94, 0.97, 0.98, 1.00, 0.99 and 0.99 respectively. The corresponding K_{oc} values were 4, 9, 12, 15, 14 and 26. Adsorption was essentially completely reversible with almost all dimethipin desorbed after 6 extractions with water from all the soils except Bethany muck which required more than 8 extractions.

Spare (1990) studied the adsorption/desorption of [^{14}C]dimethipin in four US Department of Agriculture soils; Sharkey clay (sand 25%, silt 33%, clay 42%; pH 6.5; organic matter 4.8%; CEC 24 meq/100 g), Sassafras sand (sand 96%, silt 2%, clay 2%; pH 6.5; organic matter 0.9%; CEC 1.8 meq/100 g), Paxton sandy loam (sand 64%, silt 29%, clay 7%; pH 6.3; organic matter 3.1%; CEC 8.5 meq/100 g) and Hesperia loam (sand 44%, silt 47%, clay 9%; pH 6.7; organic matter 0.8%; CEC 4.3 meq/100 g) by batch equilibrium at concentrations of 0, 0.2, 0.5, 1.0, 5.0 and 10 µg/ml. Sharkey clay was the only soil for which the Freundlich isotherm was applicable, with an adsorption partition coefficient of 0.092 (K_{oc} 3.3), because adsorption by the other soils was too weak. Desorption constants could not be determined. The recovery of ^{14}C from the soils and solutions ranged from 100 to 105%.

From the adsorption K_a values the mobility of dimethipin was very high in all soils studied.

Mobility. The mobility of dimethipin was studied in four soils, sand (sand 99%, silt 0.2%, clay 1.3%; pH 7.2; organic matter 1.0%; CEC - meq/100 g), loamy sand (sand 87%, silt 4.6%, clay 8.0%; pH 7.7; organic matter 0.9%; CEC 5.8 meq/100 g), sandy loam (sand 61%, silt 24%, clay 15%; pH 5.5; organic matter 1.9%; CEC 8.5 meq/100 g) and silt (sand 10%, silt 78%, clay 12%; pH 4.4; organic matter 2.1%; CEC 12 meq/100 g) (Erdmann *et al*., 1981). ^{14}C-labelled dimethipin was applied to the tops of 30 cm soil columns, moistened to field capacity, at the equivalent of 1.68 kg ai/ha. The columns were leached with 51 cm of distilled water. An aged soil column was prepared by treating 7.6 column cm of sandy loam with [^{14}C]dimethipin which was then aerobically aged in the dark at ambient temperature for 30 days, poured onto a 23 cm column of sandy loam and leached with 1.25 column cm of distilled water daily for 45 days. The eluate and 7.6 cm soil sections were analysed by

[1] The Freundlich equation was used to interpret the adsorption data

$$\frac{x}{m} = KC_e^{\frac{1}{n}}$$

x/m: soil equilibrium concentration in µg/g
C_e: aqueous phase equilibrium concentration in µg/ml
K_a: Freundlich adsorption constant or coefficient
n is a constant
K_{oc}: adsorption coefficient based on soil organic carbon content = $K \times 100$ / %OC
%OC: organic carbon content = % organic matter divided by 1.7

LSC and TLC with LSC. 77 to 102% of the applied radioactivity was eluted, with dimethipin accounting for 71-96% of the eluted radioactivity. The ^{14}C retained in the soil, as a percentage of the applied radioactivity, was 23, 1.0, 4.8, 0.8 and 8.3% respectively for sand, loamy sand, sandy loam, silt loam and aged sandy loam. Elution of the radioactivity was faster from the loamy sand, silt loam and aged sandy loam than from the sand and sandy loam soils.

Dimethipin is highly mobile and is not degraded significantly under simulated leaching conditions.

Environmental fate in water/sediment systems

Dzalio (1993) studied the anaerobic aquatic degradation of dimethipin in a water/sediment mixture from a pond in a cotton-producing region of Seminole County, Georgia, USA. The sediment (#90877) was a loamy sand (sand 86%, silt 6%, clay 8%; pH 6.4; organic matter 1.2%; CEC 2.6 meq/100 g). The sediment/water system was maintained under a nitrogen atmosphere for 31 days before treating with [^{14}C]dimethipin at 5.2 mg/kg. Samples were analysed at intervals after treatment and degradation and product formation were monitored by HPLC and LSC. At the start of the experiment 97% of the applied ^{14}C was present in the aqueous filtrate, and after 365 days 56% was associated with the water filtrate with dimethipin accounting for 65% of the ^{14}C in water or 37% of the applied radioactivity. Extractable residues from the soil accounted for 5% of the applied ^{14}C, with dimethipin accounting for 89%. Bound residues accounted for 17 and $^{14}CO_2$ for 7% of the applied ^{14}C. The half-life of dimethipin under anaerobic aquatic conditions was 277 days calculated by linear regression.

The bound residues were sonicated and extracted with methanol/acetone/$CHCl_3$/distilled water, then treated by Soxhlet extraction with 0.1 M formic acid and room-temperature extraction with 0.1 M ammonium hydroxide. 3% of the applied radioactivity was liberated from the sample aged for 9 months with thirteen peaks observed in the HPLC profile of the combined extracts. To aid the identification of degradation products an accelerated ageing study was conducted at 35°C using 15 mg/kg [^{14}C]dimethipin, but no significant degradation was observed even after over a year. To investigate whether some of the degradation products had been formed by anaerobic oxidation, activated sludge from a municipal waste treatment plant was treated with [^{14}C]dimethipin and incubated under aerobic conditions in an attempt to generate substantial quantities of oxidation products for comparison with the anaerobic products. This produced a variety of metabolites, but comparing retention times on a variety of chromatography columns proved inconclusive.

In summary, dimethipin is degraded only slowly under aerobic aquatic conditions, and in or on soil under aerobic and anaerobic conditions. It is relatively persistent in the environment and considered highly mobile in all the soils studied.

Bioconcentration. Kuc (1980) studied the bioconcentration of dimethipin in bluegill sunfish over a 30-day exposure with a mean [^{14}C]dimethipin concentration in the water of 2.7 mg/kg and a 14-day depuration period. The maximum bioconcentration factor (BCF) in the whole fish was 3.4 with a maximum residue level of 8.4 mg/kg during uptake. The BCF for edible tissues was 2.8 with a maximum residue of 7.1 mg/kg. After 14 days depuration, the ^{14}C concentration was 3.8 mg/kg in the whole fish and 4.1 mg/kg in the edible parts, as dimethipin.

Residues in channel catfish were also studied after 30 days exposure to an aerobically aged sandy loam soil which was then aged for 14 days under flooded conditions and treated with [^{14}C]dimethipin at 1.12 kg ai/ha (Harned *et al.*, 1981). Bioconcentration factors were 3.6 for edible tissues and 4.0 for whole fish. After 15 days depuration, residues in edible tissues and whole fish had decreased to 70 and 57% of the maximum levels respectively. Parent dimethipin was the only ^{14}C compound detected in the water after the 30-day uptake period.

METHODS OF RESIDUE ANALYSIS

Cotton seed (Womer and Sisken, 1974). Ground seed was extracted with acetone/water and the combined filtered extracts washed with petroleum ether (5% NaCl solution was added to aid separation) and the petroleum ether was back-washed with acetone/water. The residue was partitioned with $CHCl_3$, and the organic layer concentrated by rotary evaporation (40°C) and cleaned up on a column of Florisil and alumina. Further clean-up was by partitioning with octanol-nitromethane. The sample was then concentrated by rotary evaporation at 40°C and analysed by GLC with a sulfur-specific detector. Recoveries through the extraction procedure determined using samples fortified with radiolabelled dimethipin (levels not specified) were 88-99% (average 94%, n=6), and for the corresponding GLC analyses were 85-105% (average 93%).

In the US FDA Pesticide Analytical Method Volume II, §180.406 (1975), cotton seed is extracted with methanol/water (9:1) and the oil removed by a hexane wash with aqueous NaCl to prevent emulsion formation. The methanol/water layer is partitioned with $CHCl_3$, and the $CHCl_3$ concentrated and cleaned up on a Florisil and alumina column. Dimethipin is eluted with $CHCl_3$/acetone (23:2) and the eluate evaporated to dryness. The residue is dissolved in acetone for analysis by GLC with an FPD (sulfur mode). Recoveries from samples fortified at 0.5 mg/kg were 77-97%.

Koch and Cooper (1994) and Korpalski (1992a, 1993a) validated a revision of this method by Wormer and Sisken (1975), described by Brookey *et al*. (1993), for cotton seed and cotton seed processed products. The initial extraction procedure was different for the different samples. Ground ginned cotton seed or cotton seed hulls were extracted twice with methanol/water (9:1) and the combined extracts partitioned with hexane. The hexane layer was discarded and the aqueous phase was extracted three times with $CHCl_3$. The $CHCl_3$ was dried over anhydrous sodium sulfate and 10% decanol in acetone was added before concentration to a volume of 2 ml by rotary evaporation at 40°C. The decanol-acetone keeper solution was added at each of the solvent concentration steps. The remaining liquid was evaporated to dryness under a stream of nitrogen before redissolving in dichloromethane. Soapstock samples were blended with Celite and acetonitrile and the extracts dried with anhydrous sodium sulfate before partitioning with hexane. The acetonitile phase was evaporated to dryness and the residue dissolved in dichloromethane. Oil samples were mixed with hexane and the residue partitioned with acetonitrile. The hexane layer was discarded and the acetonitrile layer evaporated to dryness and the residue dissolved in dichloromethane.

The dichloromethane solutions were cleaned up on a gel permeation column. The cotton seed solution was passed through a 0.45 µm disposable cartridge filter before loading on the column. The eluate was concentrated by rotary evaporation followed by evaporation under nitrogen and the remaining residue dissolved in toluene/$CHCl_3$ (4:1). The solution was cleaned up on an alumina/Florisil column eluted with 8% acetone in $CHCl_3$. The solution was evaporated to dryness as previously and the residue dissolved in ethyl acetate for analysis by GLC with an FPD (sulfur mode). Recoveries determined by fortification with dimethipin at 0.5-2.0 mg/kg were 70-90%. It was noted that successful application of the method required proper calibration of the alumina-Florisil clean-up column owing to the variable performance of commercially purchased alumina. In addition, low recoveries were observed if on concentration of the solutions by rotary evaporation, they were allowed to go dry.

Table 23. Validation data for the analysis of cotton seed and processed commodities (Koch and Cooper, 1994, Korpalski, 1992a, 1993a).

Sample	Fortification level (mg/kg)	Recovery (%)
Cotton seed	0.1	100, 88, 105, 95
	0.2	88, 85, 92, 90
	0.5	86, 78, 100, 110, 70, 73
	2.0	89, 90

Sample	Fortification level (mg/kg)	Recovery (%)
Cotton seed hulls	0.1	88, 88, 105, 105
	0.2	82, 78, 96, 100
	0.5	78, 72, 102, 96
Cotton seed oil	0.1	97, 92, 100,100
	0.2	71, 91, 75, 95
	0.5	85, 85, 88, 78
Cotton soapstock	0.1	69, 69
	0.2	68, 82
	0.1	66, 90

In an independent laboratory validation of the method of Womer and Sisken (1975) to determine residues of dimethipin in cotton seed, essentially as described above, average recoveries were 92% from samples fortified at 0.1, 0.2 and 0.5 mg/kg (range 83-100%).

In another independent laboratory validation (PTRL-West Inc Method No. P671W/RP97009 for cereal substrates) residues of dimethipin were extracted from grain forage and straw by being homogenized twice with acetone/water (9:1) and the extract filtered, diluted with water and partitioned twice with hexane. The aqueous phase was partitioned twice with dichloromethane and the combined dichloromethane extracts dried and concentrated after adding 10% decanol in acetone as a keeper [taken from yellow note]. Hexane was added and the solution cleaned up on a silica "BondElut" cartridge sequentially washed with toluene and hexane/acetone (95:5). The dimethipin was eluted with hexane/acetone (75:25) and the eluate concentrated by rotary evaporation after adding 1% decanol in acetone as a keeper. The extracts were analysed by GLC with an FPD (sulfur mode). Minor modifications included adding saturated NaCl solution before hexane partition to minimise emulsion formation. Recoveries were 74-113% at 0.02-0.05 mg/kg from fortified samples of wheat grain, 71-88% at 0.02-0.5 mg/kg from wheat forage and 104-110% at 0.02-0.5 mg/kg from barley straw. The results confirmed an LOQ of 0.02 mg/kg.

Korpalski (1995b) described the validation of a method based on the "Determination of dimethipin (Harvade®) residues in various wet and dry crops", Morse Laboratories SOP#Meth-74, 10/94 for rotational crops (lettuce, carrot roots, carrot tops, oat straw, oat forage, oat grain and wheat grain). All samples were ground to a fine consistency with dry ice and extracted twice with acetone/water (9:1), partitioned with $CHCl_3$, the $CHCl_3$ dried with sodium sulfate and concentrated at less than 40°C using a rotary evaporator after adding 10% decanol in acetone. The remaining solvent was removed under a stream of nitrogen and the residue dissolved in dichloromethane for clean-up on a gel permeation column followed by a Florisil column. Residues of dimethipin were determined by GLC with an FPD (sulfur mode). Recoveries from fortified samples of lettuce at 0.02-0.3 mg/kg were 90-108%, carrot roots at 0.02-0.29 mg/kg 87-115%, carrot tops at 0.02-0.34 mg/kg 85-113%, oat forage at 0.02-0.29 mg/kg 83-100%, oat straw at 0.02-0.28 mg/kg 87-112%, oat grain at 0.02-0.3 mg/kg 81-92% and wheat grain at 0.02-0.3 mg/kg 92-110%. The results confirm a limit of quantification of 0.02 mg/kg.

In the US FDA Pesticide Analytical Method Volume II, §180.406 (1975), beef liver is extracted with acetonitrile, the filtrate dried over anhydrous sodium sulfate and washed with petroleum ether. The acetonitrile layer is concentrated and the residue dissolved in benzene-$CHCl_3$ (1:1) and cleaned up on a Florisil and alumina column. Dimethipin is eluted with $CHCl_3$/acetone (23:2) and the eluate evaporated to dryness. The residue is dissolved in ethyl acetate for analysis by GLC with an ECD or GC-MS with selected ion monitoring at m/z 118. Recoveries from samples fortified at 0.02-0.04 mg/kg were 85-102% and 71-99% for GLC with an ECD and GC-MS analysis respectively.

A method for the determination of dimethipin in animal tissues was described by Singh and Eckhert (1996) (SOP EBT #270, 10/11/95). Animal tissues (muscle, kidney and liver) were homogenized with acetonitrile, anhydrous sodium sulfate and Celite®. The filtered acetonitrile extract was washed with petroleum ether and evaporated to dryness on a rotary evaporator at 40-50°C. The

residue was dissolved in 50% $CHCl_3$/benzene, cleaned up on an alumina/Florisil column and eluted with 8% acetone in $CHCl_3$. The eluate was reduced by rotary evaporation followed by evaporation under a stream of nitrogen. The residue was dissolved in acetone for analysis by GLC with an ECD. Average recoveries (n=18) for samples fortified at 0.01, 0.05 and 1.0 mg/kg were 95 ± 4.2% for muscle, 95 ± 5.8% for liver and 98 ± 9.5% for kidney.

A method for the determination of dimethipin in chicken liver was described by Abdel-Kader and Blaszczynski (1984). Samples were extracted by blending with acetonitrile, filtered and cleaned by partitioning twice with petroleum ether. The acetonitrile layer was dried over anhydrous sodium sulfate, evaporated to dryness and redissolved in 50% $CHCl_3$ in toluene, cleaned up on a mixed alumina/Florisil column and eluted with 8% acetone in $CHCl_3$. The solution was evaporated to dryness and the residue redissolved in ethyl acetate for analysis by GLC with an ECD. Recoveries from samples fortified at 0.01, 0.02, 0.04 and 0.1 mg/kg were 109, 95, 97 and 99% respectively.

In a method for the determination of the dimethipin metabolite ethane-1,2-disulfonic acid in beef kidney reported by Batorewicz (1993) the kidney is diced, homogenized and water is added. Proteins are precipitated with aqueous potassium ferrocyanide and zinc acetate. The suspension is centrifuged and the supernatant filtered. An aliquot of the filtrate is cleaned up on a solid-phase extraction strong anion-exchange column. The column is washed with 1% trifluoroacetic acid (TFA) with the analyte eluted with 3% TFA, the solution evaporated to dryness and the residue reconstituted in water for analysis by ion-exchange chromatography with conductivity detection. Recoveries from samples fortified with ethane-1,2-disulfonic acid at 0.2 and 0.5 mg/kg ranged from 70 to 108% (mean 95%, n=6). The performance of the method was re-examined by Batorewicz and Long (1996). Three kidney samples from an animal feeding study were analysed together with samples fortified at 0.2 and 0.5 mg/kg. The fortified samples gave recoveries of 90 and 78% respectively, with average incurred residues in the three kidney samples of 0.47 ± 0.05 mg/kg in the original feeding study and 0.34 ± 0.05 mg/kg in the performance study.

In a method described by Henderson (1981) residues of dimethipin in milk are extracted by blending samples with ethyl acetate. The filtered ethyl acetate is concentrated by evaporation and the solution partitioned with acetonitrile and petroleum ether. The acetonitrile layer is evaporated to near dryness, and the sample dissolved in dichloromethane and purified by passage through a silica column. The eluted dichloromethane is concentrated by rotary evaporation to near dryness, followed by evaporation under a stream of nitrogen. The residue is dissolved in acetone for analysis by GLC with an ECD. Recoveries from samples fortified at 0.01 mg/kg were 70, 80 and 98% and from a sample fortified at 0.05 mg/kg 76%. The limit of quantification is 0.01 mg/kg. Validation was carried out without any modification (Milad, 1981). Recoveries from milk samples fortified at 0.5-3.0 mg/kg were 70-100%. Analytical verification recoveries in a dairy cow feeding study were 98 ± 9.4% for milk (Singh and Ekert, 1996).

In the determination of dimethipin in soil, samples were extracted by Soxhlet with acetone (Wong, 1976). The extract was evaporated to dryness and the residue dissolved in 20% chloroform in toluene, dried over anhydrous sodium sulfate and cleaned up on a mixed alumina/Florisil column eluted with 8% ethyl acetate in chloroform. The eluate was evaporated to dryness, and the residue dissolved in acetone for analysis by GLC with an FPD (sulfur mode). Recoveries from five different soils (Agawam sandy loam, Foster fine sandy loam, Tifton sandy loam, slit loam and Bethany sandy loam) fortified at 0.2 mg/kg with [^{14}C]dimethipin were 99-110%. In a study reported by Vithala and DeMatteo (1999) recoveries of dimethipin from soil ranged from 66 to 96% but fortification levels were not specified. The reported limit of detection was 0.04 mg/kg.

Dimethipin was determined in fresh water after filtering through a 0.45 µm disposable cartridge by HPLC with UV detection at 210 nm (Stauffer, 1990). The limit of detection was stated to be 0.1 mg/kg. Recoveries from samples fortified at 1 and 100 mg/kg were 87-93% and 90-99% respectively.

Stability of pesticide residues in stored analytical samples

The freezer storage stability of dimethipin in a variety of crops and processed commodities was studied by Korpalski (1998). Ground samples of lettuce, carrot roots, wheat grain and oat straw fortified with dimethipin at 0.2 mg/kg and stored at -20 ± 5°C were analysed at regular intervals for 12 months. The analytical method used was the "Determination of dimethipin (Harvade®) residue in various wet and dry crops" (Morse Laboratories Ltd. SOP #Meth-74, Rev 2, 01/95, LOQ 0.02 mg/kg). Residues were uncorrected for procedural recoveries.

Table 24. The stability of dimethipin in fortified samples stored at -20°C (Korpalski, 1998).

Storage period (days)	% remaining after storage			
	Lettuce	Carrot roots	Wheat grain	Oat straw
0	95, 105	105, 100	83, 83	95, 88
37	108, 93	100, 110	100, 93	88, 90
92	94, 97	103, 103	94, 94	94, 91
180	97, 97	97, 100	88, 94	113, 100
280	103, 106	100, 91	97, 103	97, 97
366	106, 110	100, 103	100, 100	98, 95

Procedural recoveries from samples fortified at 0.05 and 0.3 mg/kg were 87-107% for lettuce, 82-105% for carrot root, 73-105% for wheat grain and 82-116% for oat straw.

Korpalski (1993b, 1996b) studied the freezer storage stability of dimethipin in cotton seed and processed products using the Morse Laboratories Ltd. MLSOP #Meth-60 method (LOQ 0.02 mg/kg). Samples of ground cotton seed, meal, hulls and crude oil were fortified with dimethipin at 0.2 or 0.5 mg/kg and stored at -20 ± 5°C. The seed was stored for 12 months and all the other samples for 7 months.

Table 25. The stability of dimethipin in fortified samples stored at -20°C (Korpalski, 1993b, 1996b).

Storage period (months)	% remaining after storage			
	Seed (0.5 mg/kg)	Meal (0.2 mg/kg)	Hulls (0.5 mg/kg)	Crude oil (0.2 mg/kg)
0	81, 82	75, 73	78, 90	98, 100
1	82, 84	73, 78	86, 84	100, 115
2 + 23 days	80, 83	60, 80	82, 78	100, 105
3		75, 39	68, 72	63, 83
4	87, 81			
5		78, 78	72, 68	83, 83
7		85, 78	79, 73	90, 96
8	82, 84			
12	89, 81			

Procedural recoveries from cotton seed fortified at 0.5 mg/kg were 85-105%, and from meal, hulls and crude oil fortified at 0.1 or 0.5 mg/kg 74-94%, 62-89% and 74-120% respectively

Hughes and Halverson (1996) studied the freezer storage stability of ethane-1,2-disulfonic acid in beef kidney. Samples containing incurred residues of ethane-1,2-disulfonic acid were analysed after 0, 93 and 178 days of freezer storage. Mean residues were 0.41, 0.44 and 0.45 mg/kg after 0, 93 and 178 days respectively.

The frozen storage stability of dimethipin in milk and tissues of dairy cows was studied by Singh and Eckert (1996). Samples of milk and homogenized muscle, liver and kidney were fortified with dimethipin at 0.05 mg/kg and analysed after 0, 1 and 2 months frozen storage.

Table 26. The stability of dimethipin in fortified samples stored at -20°C (Singh and Eckert, 1996).

Storage period (months)	% remaining			
	Milk	Muscle	Liver	Kidney
0	103, 106	82, 84	90, 92	79, 79
1	94, 95	83, 78	81, 78	80, 83
2	97, 98	91, 91	95, 86	89, 94

Definition of the residue

Dimethipin is not significantly metabolized by plants when applied close to harvest. The main component of the extractable residue in plants is dimethipin, accounting for 38-72, 61, 20-25, 50 and 14-50% of the extractable residue in cotton, sunflower seeds, potatoes, rice grain and grape juice respectively. In animals dimethipin is extensively metabolized with the main pathways involving conjugation to glutathione, amino acids and peptides and subsequent degradation. Minor routes of metabolism include hydrolytic hydroxylation and oxidation.

The definition of the residue for commodities derived from plants and animals should be dimethipin for compliance with MRLs and the estimation of dietary intake.

USE PATTERN

Dimethipin is registered as a flowable formulation in many countries. It is a plant growth regulator and is used as a defoliant, to enhance maturation and reduce seed moisture in grain and oil seed crops.

The information available to the Meeting on registered uses is shown in Table 19.

Table 27. Registered uses of dimethipin. All foliar applications.

Crop	Country	Form.	Application			PHI (days)
			Rate (kg ai/ha)	Spray conc., (kg ai/hl)	No.	
Barley (malt)	Poland	25F	0.38-0.5			
Bean	Poland	25F	0.38-0.5			14-21
Bean (broad)	Poland	25F	0.38-0.5			14-21
Bean (horse)	Poland	25F	0.38-0.5			14-21
Buckwheat	Poland	25F	0.38-0.5			
Cabbage	Czech Republic	25F	0.63-1.0			10-14
Cabbage	Poland	25F	0.5			
Cabbage	Slovakia	25F	0.63			
Carrot	Poland	25F	0.5-0.75			
Cauliflower	Poland	25F	0.5			
Cauliflower	Slovakia	25F	0.63-1.0			
Clover (red)	Poland	25F	0.75			
Cotton	Bulgaria	25F 25% FS	0.4			apply to cotton at 10-150 open bolls per 100 plants stage
Cotton	Egypt	25F	0.5-0.63			
Cotton	France	25F	0.31	6.9		14-21
Cotton	Greece	25F	0.31	0.039-0.063		None
Cotton	Greece	5F, 60%FL		0.05-0.1		
Cotton (medium fibre)	Kazakhstan	25F	0.38-0.55			10-14
Cotton (fine fibre)	Kazakhstan	25F	0.5-0.63			10-14
Cotton	South Africa	25F	0.31-0.63			
Cotton	Spain	25F	0.31			
Cotton	Turkey	25F	0.31			
Cotton	Turkmenistan	25F				

Crop	Country	Form.	Application			PHI (days)
			Rate (kg ai/ha)	Spray conc., (kg ai/hl)	No.	
Cotton	USA	5F (48%)	0.23-0.28	0.12-0.30 grd 0.49-1.5 air	2	7-21
Cotton	USA	25F (22%)	0.26-0.32		2	7-21
Cotton	Uzbekistan	25F	0.38-0.63			
Facelia	Poland	25F	0.75			
Fodder beet	Poland	25F	0.75-1.0			
Fruit trees	Czech Republic	25F		1%		14
Fruit (nursery)	Slovakia	25F		0.3-1%		
Grass (seed)	Poland	25F	0.38-0.5			
Kohlrabi	Poland	25F	0.5			
Kohlrabi	Slovakia	25F	0.63			
Lettuce	Czech Republic	25F	0.63-1.0			10-14
Lettuce	Poland	25F	0.5-0.75			14-21
Lettuce	Slovakia	25F	0.63-1.0			
Linseed (flax seed crop)	Belarus	25F, 25% FS	0.38-0.55			
Linseed (flax)	Bulgaria	25F, 25% FS	0.5			14
Linseed (flax)	Czech Republic	25F	0.5			10-15
Linseed (flax)	Eire	25F	0.5	0.13-0.2		21-28 after full flowering
Linseed (flax)	Kazakhstan	25F	0.38-0.5			10-14
Linseed (flax floret seed)	Poland	25F	0.5			
Linseed	Slovakia	25F	0.5			
Lupin	Poland	25F	0.38-0.5			14-21
Maize	Czech Republic	25F	0.5-0.63			21
Maize	Hungary	25F	0.45-0.63			14
Maize	Slovakia	25F	0.5-0.63			
Onion	Czech Republic	25F	0.63			10-14
Onion (sets)	Poland	25F	0.38-0.5			
Onion	Slovakia	25F	0.63			
Parsnip	Poland	25F	0.5-0.75			14-21
Pea	Czech Republic	25F	0.5-0.63			14
Pea	Hungary	25F	0.3-0.5			14
Pea	Poland	25F	0.38-0.5			14-21
Pea	Slovakia	25F	0.5-0.63			
Pepper (red)	Bulgaria	25F, 25% FS	0.3			
Pisum sativum convar speciosum	Slovakia	25F	0.5-0.63			
Potato (seed)	Belarus	25F, 25% FS	0.75			
Potato	Belarus	25F, 25% FS	0.75			
Potato	Bulgaria	25F, 25% FS	0.63			14
Potato	Czech Republic	25F	0.5-0.75			14
Potato	Eire	25F	0.63	0.13-0.31		21
Potato	Hungary	25F	0.5-0.63			14
Potato	Kazakhstan	25F	0.75			18-21
Potato (seed)	Kazakhstan	25F	0.75			18-21
Potato	Poland	25F	0.5-0.75			14-21
Potato	Romania	25F	0.63			7
Potato	Slovakia	25F	0.5-0.75			
Radish	Czech Republic	25F	0.63-1.0			10-14
Radish	Poland	25F	0.5			
Radish	Slovakia	25F	0.63-1.0			
Rape seed	Czech Republic	25F	0.38-0.5			10-14
Rape seed	Croatia	25F	0.38-0.5			
Rape seed	Eire	25F	0.5	0.1-0.25		10-14
Rape seed	Hungary	25F	0.3-0.5			14
Rape seed	Kazakhstan	25F	0.38			10-14
Rape seed	Kyrgyzstan	25F	0.38-0.5			10-14

Crop	Country	Form.	Application			PHI (days)
			Rate (kg ai/ha)	Spray conc., (kg ai/hl)	No.	
Rape seed	Poland	25F	0.38-0.5			
Rape seed	Slovakia	25F	0.38-0.5			
Red beet	Poland	25F	0.75-1.0			
Rice	Bulgaria	25F, 25% FS	0.38-0.5			14
Rice	Hungary	25F	0.25-0.3			14
Rice	Romania	25F	0.5			7
Soya bean	Czech Republic	25F	0.5-0.63			21
Soya bean	Croatia	25F	0.38-0.5			
Soya bean	Hungary	25F	0.38-0.5			14
Soya bean	Poland	25F	0.38-0.5			14-21
Soya bean	Slovakia	25F	0.5-0.63			
Sugar beet	Poland	25F	0.75-1.0			
Sunflower	Belarus	25F, 25% FS	0.3			
Sunflower	Bulgaria	25F, 25% FS	0.38-0.5			14
Sunflower	Czech Republic	25F	0.5			10-14
Sunflower	Croatia	25F	0.38-0.5			
Sunflower	Hungary	25F	0.38-0.5			14
Sunflower	Kazakhstan	25F	0.3			10-14
Sunflower	Poland	25F	0.5			
Sunflower	Romania	25F	0.38			7
Sunflower	Slovakia	25F	0.5			
Sunflower	Spain	25F	0.5			
Sunflower	Turkey	25F	0.5			
Tomato	Bulgaria	25F, 25% FS	0.31			14
Tomato (processing)	Czech Republic	25F	0.38			21
Tomato	Slovakia	25F	0.38			
Tomato	Turkey	25F	0.31			

RESIDUES RESULTING FROM SUPERVISED TRIALS

The results of the residue trials are shown in Tables 28-32 and are reviewed in order of the Codex Alimentarius Classification of Foods and Feeds.

Table 28 *Potato.* France, Germany, Netherlands, Norway, Sweden, UK.
Table 29 *Cotton seed.* Spain, USA.
Table 30 *Linseed.* Czech Republic.
Table 31 *Rape seed.* Czech Republic, Germany, Hungary, Norway, UK.
Table 32 *Sunflower seed.* Hungary.

Where residues were not detected the results are reported as below the limit of quantification (LOQ), e.g. <0.05 mg/kg. Residues, application rates and spray concentrations have generally been rounded to 2 significant figures. Although trials included results for untreated controls these are not reported in the Tables unless they were greater than the LOQ. The prefix "c" indicates samples from control plots. Where possible residues are reported uncorrected for analytical recoveries. It should be noted that unless stated otherwise concurrent recoveries were acceptable and any corrections were small.

Except for the trials on flax and linseed in Hungary and Czechoslovakia, trials were fully reported.

In supervised trials on potatoes in France, Germany, Norway, The Netherlands, Sweden and the UK the plots were 10 - 3240 m^2. Dimethipin was sprayed on the leaves using knapsack sprayers, hand-held boom sprayers and tractor-mounted boom sprayers. The period of frozen storage before analysis was 247-381 days for the trials in Germany and Norway.

Table 28. Residues of dimethipin in potatoes after foliar applications of various dimethipin formulations. Analyses of replicate field samples from one plot or from duplicate plots in one trial are shown separately. Double-underlined residues are from treatments according to GAP and were used for the estimation of maximum residue levels.

Location, year, variety	Form	Application			PHI (days)	Dimethipin (mg/kg)	Reference
		kg ai/ha	kg ai/hl	No.			
Lillers, France (1984) Bintje	25F	0.75	0.15	1	34	Peel 0.03, 0.04, 0.02, <0.01	N6.2.3.13
						Peeled tuber <0.01 (4)	
						Whole tuber <0.01 (4)	
St Remy, France (1984) Bintje	25F	0.75	0.13	1	21	≤0.1 (different analytical laboratory, LOQ 0.1, whole tubers analysed)	N6.2.3.13
Dom Loup, France (1984) Sirtema	25F	0.75	0.15	2	25	Peel 0.02 (3), 0.01	N6.2.3.13
						Peeled tuber <0.01 (4)	
						Whole tuber <0.01 (4)	
					18	Peel 0.015, 0.01, 0.02, <0.01	
						Peeled tuber <0.01 (4)	
						Whole tuber ≤0.01 (4)	
					14	Peel 0.03	
						Peeled tuber <0.01	
						Whole tuber <0.01	
					10	Peel <0.01	
						Peeled tuber <0.01	
						Whole tuber <0.01	
Pocany, France (1984) Bintje	25F	0.75	0.15	2	32	Peel <0.01 (6), 0.01 (2)	N6.2.3.13
						Peeled tuber <0.01 (8)	
						Whole tuber <0.01 (8)	
Brillit, Germany (1986) Roxy	25F	0.75	0.19	1	14	≤0.02	N6.2.3.24
Kalen Born, Germany (1986) Grata	25F	0.75	0.19	1	14	≤0.02	N6.2.3.24
Nordheim, Germany (1986) Ulla	25F	0.75	0.19	1	14	≤0.02	N6.2.3.24
Winzerhavsen, Germany (1986) Granola	25F	0.75	0.19	1	14	≤0.02	N6.2.3.24
Otter Weier, Germany (1986) Sieglinde	25F	0.75	0.19	1	15	≤0.02	N6.2.3.24
Mattenkofen, Germany (1986) Juliver	25F	0.75	0.19	1	14	≤0.02	N6.2.3.24
Dinteloord, Netherlands (1983) Bintje	25F	0.5	0.08	1	9-40[1]	≤0.05	N6.2.3.14
Luttelgeest, Netherlands (1983) Bintje	25F	0.5	0.08	1	9-40[1]	≤0.05	N6.2.3.14
Ottersum, Netherlands (1983) Bintje	25F	0.5	0.08	1	9-40[1]	≤0.05	N6.2.3.14
Ottersum, Netherlands (1984) Bintje	25F	0.63	0.1	1	[4]	≤0.05 (4)	N6.2.3.23
Rilland, Netherlands (1984) Bintje	25F	0.63	0.1	1	[4]	≤0.05 (4)	N6.2.3.23
Tollebeek, Netherlands (1984) Bintje	25F	0.63	0.1	1	[4]	≤0.05 (4)	N6.2.3.23
Mohn Kirkenaer, Norway (1985) Beate	25F	0.5	0.1	1	23	<0.05	N6.2.1.21
Mohn Kirkenaer, Norway (1985) Beate	25F	0.75	0.15	1	23	<0.05	N6.2.1.21
Mohn Kirkenaer, Norway (1985) Beate	25F	1.0	0.2	1	23	<0.05	N6.2.1.21
Gjesasen, Norway (1985) Ostara	25F	0.5	0.1	1	34	<0.05	N6.2.1.21
Gjesasen, Norway (1985) Ostara	25F	0.75	0.15	1	34	<0.05	N6.2.1.21

Location, year, variety	Form	Application			PHI	Dimethipin	Reference
		kg ai/ha	kg ai/hl	No.	(days)	(mg/kg)	
Gjesasen, Norway (1985) Ostara	25F	1.0	0.2	1	34	<0.05	N6.2.1.21
Skännige, Sweden (1983) Magnum bonum	25F	1.5	0.3	1	22-52[2]	<0.003	N6.2.3.15
Skepparslöv, Sweden (1983) Dianella	25F	1.5		1	22-52[2]	0.009	N6.2.3.15
Ugerup, Sweden (1983) Dianella	25F	1.5	0.38	1	22-52[2]	<0.003	N6.2.3.15
Ultuna, Sweden (1983) Bintje	25F	1.5	0.3	1	22-52[2]	<0.003[3]	N6.2.3.15
Röbäcksdalen, Sweden (1983) Sabina	25F	1.5	0.38	1	22-52[2]	0.010	N6.2.3.15
Skännige, Sweden (1983)	25F	1.5		1	22-52[2]	<0.003	N6.2.3.15
Pershore, UK (1982) Desiree	25F	0.5		1	21-28[4]	<u>≤0.005</u> (5)	N6.2.3.12
Cutsdean, UK (1982) Maris piper	25F	0.5		1	21-28[4]	<u>≤0.005</u> (5)	N6.2.3.12
Northleach, UK (1982) Desiree	25F	0.5		1	21-28[4]	<u>≤0.005</u> (5)	N6.2.3.12
Northleach, UK (1982) Desiree	25F	1.0		1	21-28[4]	<u>≤0.005</u> (5)	N6.2.3.12

[1]when potato haulm had dried off, 9-40 days after application
[2]when potato haulm had dried off, 22-52 days after application
[3]residues in soil were 0.16 mg/kg
[4]when the potato haulm had died down.
Peel constituted 8-19% of total weight for the Dom Loup trial, 14-19% for the Lillers trial and 14-18% for the Pocany trial
Recoveries: 98, 91 and 80% at 0.0198, 0.0988 and 0.988 mg/kg respectively N6.2.3.24; 80, 93 and 85% at 0.051, 0.25 and 1.01 mg/kg respectively N6.2.3.21; 82, 76 and 84% at 0.051, 0.51 and 1.03 mg/kg respectively N6.2.3.14; 82, 87 and 86% at 0.050, 0.50 and 1.01 mg/kg respectively N6.2.3.23; 112, 91, 82, 81 and 79% at 0.0052, 0.010, 0.103, 0.52 and 1.03 mg/kg respectively N6.2.3.12

Supervised trials were reported on cotton in Spain and the USA. In the USA trials dimethipin was sprayed using CO_2 (or compressed air) backpack or tractor-mounted boom sprayers and from aircraft. The first application was made with at least 70% bolls open and the second 5 days later. Plot sizes for the ground applications ranged from 8 rows × 15 m to 4 rows × 91 m and for aerial application were 0.25 and 0.8 ha. Samples were stored frozen for 49-191 days. The plot sizes for the Spanish trials ranged from 4-50 ha and were sprayed from the air; samples were stored frozen for 125-134 days.

Table 29. Residues of dimethipin in cotton seed after foliar applications of various dimethipin formulations. Analyses of replicate field samples from one plot or from duplicate plots in one trial are shown separately. Double-underlined residues are from treatments according to GAP used to estimate maximum residue levels.

Location, year, variety	Form	Application			PHI	Dimethipin	Reference
		kg ai/ha	kg ai/hl	No.	(days)	(mg/kg)	
Diaz Martinez, Spain (1986) Coker 304	25F ✈	0.31	0.31	1	14	<u>0.03</u>, 0.02	N6.2.1.3
Las Baracas, Spain (1986)	25F ✈	0.31	0.31	1	7	<u>0.07</u>, 0.04	N6.2.1.3
Laura Abad El Ruidero, Spain (1986) Copa	25F ✈	0.31	0.31	1	5	<u>0.07</u>, 0.04, <0.02	N6.2.1.3
Sotillo Gallego, Spain (1986)	25F ✈	0.31	0.31	1	14	<u>0.02</u>, 0.02, <0.02	N6.2.1.3
Helm, California (1993) GC 510	5F	0.35 0.26	0.34 0.25	2	7	0.2, <u>0.2</u>	RP-92026
Donna, Texas (1993) Delta Pine 50	5F	0.35 0.26	0.37 0.28	2	7	<u>0.2</u>, 0.1	RP-92026
Hawkinsville, Georgia (1993) Stoneville 825	5F	0.35 0.26	0.38 0.28	2	7	<0.1, <u>0.1</u>	RP-92026

Location, year, variety	Form	Application			PHI	Dimethipin	Reference
		kg ai/ha	kg ai/hl	No.	(days)	(mg/kg)	
Senatobia, Mississippi (1993) DPL-50	5F	0.35 0.26	0.37 0.28	2	7	0.2, 0.3	RP-92026
Proctor, Arizona (1992) Stoneville 453	5F	0.35 0.26	0.19 0.14	2	7	<0.1, ≤0.1	RP-91034
Proctor, Arizona (1992) Stoneville 453	5F	0.35 0.26	0.19 0.14	2	7	≤0.1, <0.1	RP-91034
Senatobia, Mississippi (1992) DPL-50	5F	0.35 0.26	0.19 0.14	2	7	0.2, 0.12	RP-91034
Senatobia, Mississippi (1992) DPL-50	5F ✈	0.35 0.26	0.75 0.56	2	7	0.1, 0.1	RP-91034
Charleston, Mississippi (1992) DPL-50	5F	0.35 0.26	0.19 0.14	2	7	0.1, 0.2	RP-91034
Toone, Tennesse (1992) DPL-50	5F	0.35 0.26	0.19 0.14	2	7	0.7, 0.6, 0.7, 0.7	RP-91034
Raymondville, Texas (1992) DPL-5690	5F	0.35 0.26		2	7	0.1, 0.2	RP-91034
Raymondville, Texas (1992) DPL-5690	5F ✈	0.35 0.26		2	7	<0.1, ≤0.1	RP-91034
Donna, Texas (1992) Stoneville 453	5F	0.35 0.26	0.25 0.19	2	7	<0.1, ≤0.1	RP-91034
Meigs, Georgia (1992) DPL-90	5F	0.35 0.26	0.19 0.14	2	7	<0.1, 0.1	RP-91034
Opelousas, Louisiana (1992) DPL-50	5F	0.35 0.26	0.38 0.28	2	7	0.2, 0.2	RP-91034

Loamy sand (pH 8.7), sandy loam (pH 7.9), sand (pH 7.3-7.9), silt loam (pH 6.1), loam (pH 6.0), loam (pH 5.9), silt loam (pH 6.9), silt loam (pH 5.3), silt loam (pH 6.6), silt loam (pH 7.6), silt loam (pH 8.3), sandy loam (pH 8.4), loamy sand (pH 6.6), loam (pH 4.4)
Recoveries: 80, 95% at 0.1 mg/kg, 90, 76% at 0.5 mg/kg, LOQ 0.1 mg/kg RP-92026; 95, 77, 79, 77, 84, 78% at 0.1 mg/kg, 92, 80, 78, 75, 90, 78% at 0.5 mg/kg, LOQ 0.1 mg/kg RP-91034; 118 and 80% at 0.071 mg/kg, LOQ 0.02 mg/kg N6.2.1.3
✈ aerial application

Table 30. Residues of dimethipin in linseed after foliar applications of various dimethipin formulations. Analyses of replicate field samples from one plot or from duplicate plots in one trial are shown separately. Double-underlined residues are from treatments according to GAP and were used to estimate maximum residue levels.

Location, year, variety	Form	Application			PHI	Dimethipin (mg/kg)		Reference
		kg ai/ha	kg ai/hl	No.	(days)	Seed	Straw	
Czech Republic	-	-		-	-	<0.1	7.0	N6.2.7.3/4
Czech Republic	-	-		-	-	0.1	10	N6.2.7.3/4
Czech Republic	-	-		-	-	<0.1	6.3	N6.2.7.3/4
Czech Republic	-	-		-	-	<0.1	8.2	N6.2.7.3/4
Czech Republic	-	-		-	-	<0.1	0.4	N6.2.7.3/4
Czech Republic	-	-		-	-	<0.1	<0.1, <0.1	N6.2.7.3/4
Czech Republic	-	-		-	-	<0.1	<0.1, <0.1	N6.2.7.3/4
Czech Republic	-	-		-	-	<0.1		N6.2.7.3
Rýmařov, Czech Republic (1982)	WP	1.3			8	<0.1	25	N6.2.7.1/2
Kežmarok, Czech Republic (1982)	WP	1.0			11	<0.1	13	N6.2.7.1/2
Kežmarok, Czech Republic (1982)	WP	1.5			11	<0.1	<0.1	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			11	<0.1	4.8	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			14	<0.1	8.9	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			17	<0.1	11	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			20	<0.1	9.1	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			7	0.9	10 c0.3	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			10	0.2	7.3	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	0.5			14	≤0.1	4.5	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	0.5			14	≤0.1	4.0	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.0			14	0.1	12	N6.2.7.1/2

Location, year, variety	Form	Application			PHI (days)	Dimethipin (mg/kg)		Reference
		kg ai/ha	kg ai/hl	No.		Seed	Straw	
Všúptl, Czech Republic (1982)	WP	1.0			14	<0.1	18	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.5			14	0.1	20	N6.2.7.1/2
Všúptl, Czech Republic (1982)	WP	1.5			14	0.1	18	N6.2.7.1/2

Recoveries: 80, 75 and 78% at 0.52, 2.6 and 5.2 mg/kg respectively N6.2.7.1, LOQ 0.1 mg/kg; 110, 94 and 95% at 0.10, 0.52 and 1.04 mg/kg respectively N6.2.7.2, LOQ 0.1 mg/kg; 85, 83 and 88% at 0.098, 0.492 and 0.985 mg/kg respectively N6.2.7.3, LOQ 0.1 mg/kg; 86, 104 and 85% at 0.197, 0.985 and 9.85 mg/kg respectively N6.2.7.4, LOQ 0.4 mg/kg.

Supervised trials were reported on rape seed from the Czech Republic, Germany, Hungary, Norway and the UK. Dimethipin was applied using knapsack sprayers and tractor-mounted boom sprayers. Plot sizes ranged from 7.5 m^2 to 5 ha. Samples were stored frozen for 14 to 405 days.

Table 31. Residues of dimethipin in rape seed after foliar applications of various dimethipin formulations. Analyses of replicate field samples from one plot or from duplicate plots in one trial are shown separately. Double-underlined residues are from treatments according to GAP and were used to estimate maximum residue levels.

Location (year) variety	Form	Application			PHI (days)	Dimethipin (mg/kg)	Reference
		kg ai/ha	kg ai/hl	N			
Moravia, Czech Republic (1983)	50W	0.25	0.063	1	7	<0.1	N6.2.13.2
					11	<0.1	N6.2.13.2
					14	<0.1	N6.2.13.2
Moravia, Czech Republic (1983)	50W	0.5	0.13	1	7	<0.1	N6.2.13.2
					11	<u><0.1</u>	N6.2.13.2
					14	<0.1	N6.2.13.2
Moravia, Czech Republic (1983)	50W	0.75	0.19	1	7	<0.1	N6.2.13.2
					11	<0.1	N6.2.13.2
					14	<0.1	N6.2.13.2
Moravia, Czech Republic (1983) Jet neuf	5F	0.6	0.15	1	7	<u><0.1</u>	N6.2.13.2
Moravia, Czech Republic (1983) Jet neuf	25F	0.38	0.094	1	7	<u><0.1</u>	N6.2.13.2
Straubing, Germany (1985) Jet neuf	25F	0.25	0.063	1	16	<0.05, <0.05	N6.2.13.4
Straubing, Germany (1985) Jet neuf	25F	0.5	0.13	1	16	<0.05, <u><0.05</u>	N6.2.13.4
Matting, Germany (1986) Belinda	25F	0.5	0.13	1	0 3 6 10	1.2 0.2 <0.1 <u><0.1</u>	N6.2.13.7
Gutrohlstorp, Germany (1986) Jet neuf	25F	0.5		1	0 pod 3 pod 7 pod 10 pod 11 seed	4.6 c0.3 0.5 0.3 0.3 <u><0.1</u>	N6.2.13.7
Gutrohlstorp, Germany (1986) Miranda	25F	0.5		1	0 pod 3 pod 7 pod 10 pod 11 seed	4.8 0.5 0.3 0.3 <u><0.1</u>	N6.2.13.7
Lichtenau, Germany (1986) Loras	25F	0.5		1	3 7 10	0.3 <0.1 <0.1, <u>0.1</u>	N6.2.13.7

Location (year) variety	Form	Application			PHI (days)	Dimethipin (mg/kg)	Reference
		kg ai/ha	kg ai/hl	N			
Ausserhienthal, Germany (1986) Jet neuf	25F	0.5		1	0 pod 0 3 6 10	12 0.9 0.3 <0.1 ≤0.1	N6.2.13.7
Fejer County, Hungary (1998)	25EC	0.45	0.19	1	23	≤0.05 (3)	98 UNI AB 01 02
Østfold, Norway (1985)	25F	0.25	0.05	1	13	<0.05	N6.2.13.6
Østfold, Norway (1985)	25F	0.5	0.1	1	13	<0.05	N6.2.13.6
Cirencester, UK (1983) Jet neuf	25F	0.25	0.071	1	8	0.033[1]	N6.0.3
Pershore, UK (1983) Jet neuf	25F	0.25	0.071	1	7		N6.0.3
Stow, UK (1983) Jet neuf	25F	0.25	0.071	1	15		N6.0.3
Stow, UK (1983) Jet neuf	25F	0.25	0.071	1	15		N6.0.3
Pershore, UK (1983) Jet neuf	25F	0.5	0.14	1	7	0.025[2]	N6.0.3
Stow, UK (1983) Jet neuf	25F	0.5	0.14	1	15		N6.0.3
Stow, UK (1983) Jet neuf	25F	0.5	0.14	1	15		N6.0.3
Pershore, UK (1984) Jet neuf	25F	0.5	0.31	1	21	0.04[3] c0.015	N6.0.3
Pershore, UK (1985) Bien venu	25F	0.63	0.23	1	20	<0.05[4] (4)	N6.2.13.4
Tenbury, UK (1985) Bien venu	25F	0.63	0.23	1	25		N6.2.13.4
Essex, UK (1986) Mikado	25F	0.5	0.13	1	22	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Mikado	25F	1.0	0.25	1	22	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Bienvenu	25F	0.5	0.13	1	19	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Bienvenu	25F	1.0	0.25	1	19	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Mikado	25F	0.5	0.13	1	11	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Mikado	25F	1.0	0.25	1	11	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Rafal	25F	0.5	0.13	1	16	<0.05 (oil)	N6.2.13.5
Essex, UK (1986) Rafal	25F	1.0	0.25	1	16	0.06 (oil) (<0.05)	N6.2.13.5

[1]average of the 4 trials carried out at 0.25 kg ai/ha in UK in 1983
[2]average of the 3 trials carried out at 0.5 kg ai/ha in UK in 1983
[3]average of 2 replicates
[4] average of 2 trials, 8 replicates, carried out at 0.625 kg ai/ha in UK in 1985
Recoveries: 93, 94, 72 and 78% at 0.05, 0.1, 0.2 and 0.5 mg/kg respectively 98 UNI AB 01 02; 87, 97 and 97% at 0.051, 0.25 and 1.01 mg/kg respectively N6.2.13.5; 106, 88 and 98% at 0.0988, 0.25 and 0.988 mg/kg respectively N6.2.13.7; 82, 70 and 93% at 0.051, 0.26 and 1.01 mg/kg respectively N6.2.13.6; 85, 84, 101 and 108% at 0.975, 0.244, 0.098 and 0.049 mg/kg respectively for oilseed, 83, 95 and 80% at 0.982, 0.246 and 0.049 mg/kg respectively for oil, 94, 104 and 76% at 0.975, 0.244 and 0.049 mg/kg respectively for cake N6.2.13.4; 105, 99 and 105% at 0.098, 0.492 and 0.985 mg/kg respectively N6.2.13.2

Supervised trials were reported on sunflowers from Hungary. Foliar application of dimethipin was by aircraft to plots that ranged in size from 5 to 249 ha.

Table 32. Residues of dimethipin in sunflowers after foliar applications of various dimethipin formulations. Analyses of replicate field samples from one plot or from duplicate plots in one trial are shown separately. Double-underlined residues are from treatments according to GAP and were used to estimate maximum residue levels.

Location, year, variety	Form	Application			PHI	Dimethipin	Recoveries	Ref.
		kg ai/ha	kg ai/hl	No.	(days)	(mg/kg) [1]		
Hunyadi, Hungary (1984)	25F ✈	0.38	0.75	1	20	0.4, 0.55, 0.35, 0.4, 0.7, 0.35, 0.2	71 ± 11%	N6.2.5.5
Dunaföldvár, Hungary (1984)	25F ✈	0.38	0.75	1	22	≤0.1 (7)	75 ± 8%	N6.2.5.5
Hajdu, Hungary (1986) Iregi	25F ✈	0.38	0.63	1	10	0.11, 0.08, 0.30, 0.25, 0.21, 0.11, 0.14	88%	N6.2.5.8
Hajdu, Hungary (1986) Iregi	25F ✈	0.38	0.63	1	10	0.02, 0.03, 0.03, 0.09, 0.04, 0.03, 0.01	0.01-0.2 mg/kg, 80-95%	N6.2.5.8
Baranya, Hungary (1986) Ihnk-81	25F ✈	0.38	0.75	1	10	≤0.01 (5)	64 ± 6% at 0.3 mg/kg, 78 ± 5% at 0.5 mg/kg	N6.2.5.8
Baranya, Hungary (1986) Nsh-26	25F ✈	0.38	0.75	1	10	≤0.01 (5)	64 ± 6% at 0.3 mg/kg, 78 ± 5% at 0.5 mg/kg	N6.2.5.8
Jászalsózentgyörgy, Hungary (1986) Iregi	25F ✈	0.38	0.75	1	32	0.18, <0.05, 0.26, 0.11, 0.17	94 ± 4% at 0.1 mg/kg	N6.2.5.8
Jászalsózentgyörgy, Hungary (1986) Nsh-26	25F ✈	0.38	0.75	1	32	0.77, 0.25, 0.71, 0.43, 0.58	94 ± 4% at 0.1 mg/kg	N6.2.5.8
Balatonfökajár, Hungary (1986) Nsh-26	25F ✈	0.38	0.75	1	13	≤0.01 (7)	68 ± 3% at 0.1 mg/kg	N6.2.5.8
Balatonfökajár, Hungary (1986) Nsh-26	25F ✈	0.38	0.75	1	13	≤0.01 (7)	68 ± 3% at 0.1 mg/kg	N6.2.5.8
Tolna, Hungary (1986) Topflor	25F ✈	0.25	0.42	1	9	0.06, 0.15, 0.05, 0.22, 0.08	78 ± 8%	N6.2.5.8
Tolna, Hungary (1986) Topflor	25F ✈	0.38	0.63	1	9	0.10, 0.08, 0.25, 0.38, 0.35	78 ± 8%	N6.2.5.8

✈ aerial application
[1] corrected for average analytical recovery

Animal feeding studies

Lactating cows. Groups of 3 lactating Holstein dairy cattle (487-737 kg bw) were dosed with dimethipin in the diet for 28 days (Singh and Eckert, 1996). The average feed consumption before commencement of dosing was 14.5 kg per day. Doses, calculated using the average consumption figure and administered in gelatine capsules by balling gun after the morning milking, were nominally equivalent to 5, 15 or 50 ppm in the feed (72.5, 217.5 or 725 mg ai per capsule). Daily composite milk samples were collected for each cow, with proportionate quantities of morning and evening milk mixed. Cows from each group were slaughtered twenty-four hours after receiving the final dose. Samples of muscle, liver and kidney collected at slaughter and milk were analysed for dimethipin. Kidney samples were also analysed for the metabolite ethane-1,2-disulfonic acid (Hughes and Patzer, 1996).

Residues in milk from the highest dose group were <0.01 mg/kg in all samples analysed, from days 0, 7, 14, 21 and 28 of dosing. Residues in muscle, liver and kidney in the highest group were also <0.01 mg/kg. It was therefore decided not to analyse milk and tissues from the other dose groups.

Residues of ethane-1,2-disulfonic acid were <0.01, <0.01 and <0.01 mg/kg in the 5 ppm, 0.22, 0.27 and 0.38 mg/kg in the 15 ppm and 0.32, 0.66 and 0.44 mg/kg in the 50 ppm dose groups.

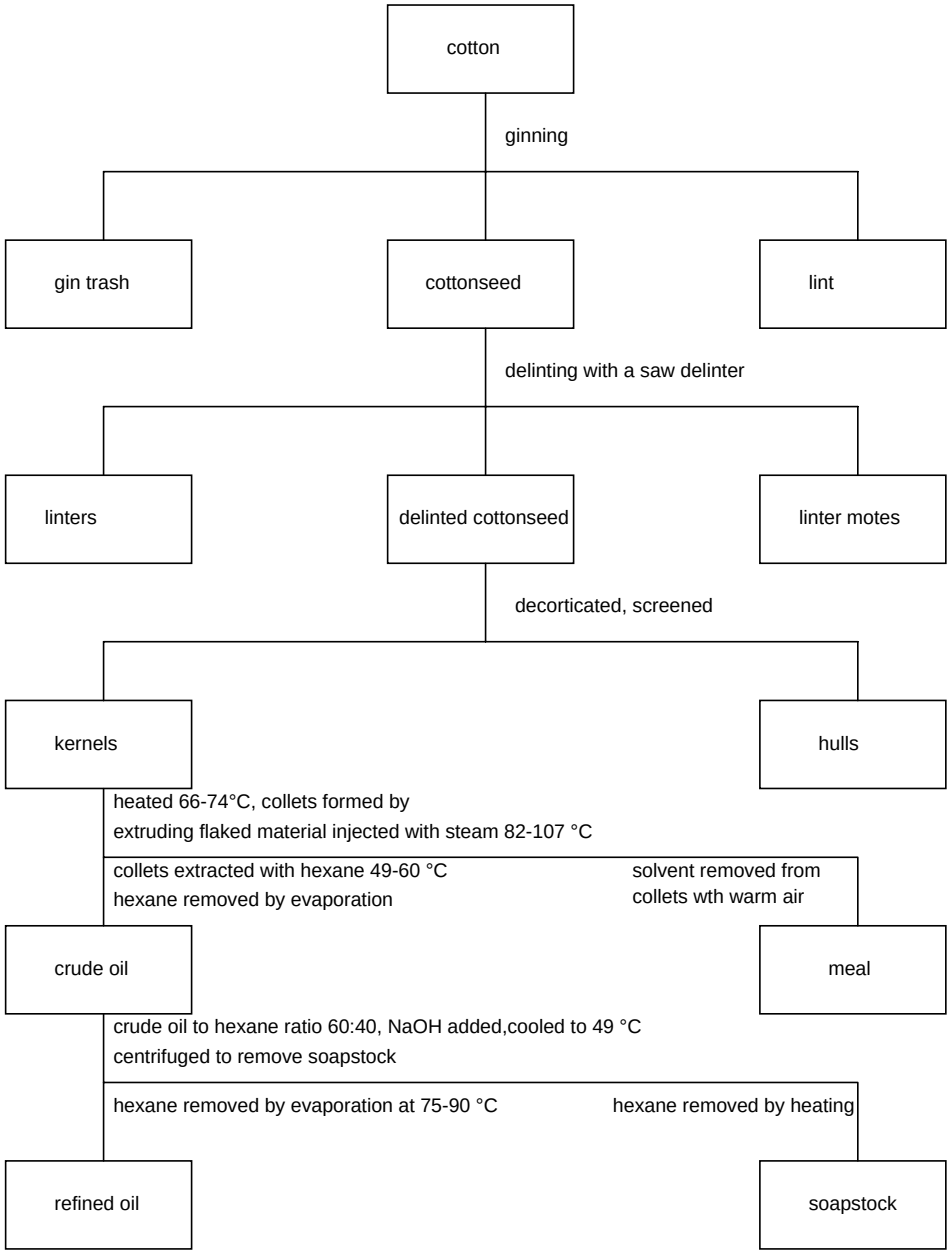
FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

Processing studies on cotton (Korpalski, 1993d) were provided to the Meeting.

Dimethipin was applied to cotton as two sprays 5 days apart at 0.68 and 0.51 kg ai/ha with harvest 7 days after the last application. The trials were in Texas and Mississippi with replicate samples taken from the two sites. The cotton seed was ginned to separate the seed cotton into seed and lint as well as ginning trash. Ginned seed was passed through a saw delinter to remove excess lint before hulling. The delinted seed was mechanically decorticated and screened to separate the majority of the hull material from the kernel and samples of hulls were collected. The kernel material was heated (66-74°C), flaked, and expanded into collets by extruding flaked material injected with steam (82-107°C). The collets were then extracted three times with hexane at 49-60°C. Solvent was removed from the spent collets with warm forced air. Meal samples were collected from the spent collets. Crude oil samples were obtained by evaporation of the hexane. Refined oil was obtained after adjusting the crude oil and hexane mixture to the proper ratio, and the miscella refined by distillation. The hexane was evaporated from the original miscella to bring the crude oil to hexane ratio to 60:40. NaOH was added with vigorous mixing and the mixture cooled to 49°C without stirring. Refined oil was separated from the soapstock by centrifugation and recovered from the miscella by evaporation of the hexane at 75-90°C. The soapstock was heated to remove residual hexane.

Figure 3. Cotton processing (Korpalski, 1993d).



Processing factors were all less than one, indicating that dimethipin is not concentrated in processed cotton commodities.

Table 33. Residues of dimethipin in cotton seed and processing fractions (Korpalski, 1993d).

Sample	Ginned seed	Meal	Hulls	Soapstock	Crude oil	Refined oil
1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
2	0.50	0.12	0.54	<0.1	<0.1	<0.1
3	0.46	0.11	0.44	<0.1	<0.1	<0.1
4	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
5	0.61	<0.1	0.42	<0.1	<0.1	<0.1
6	0.68	<0.1	0.40	<0.1	<0.1	<0.1
Average	0.56	0.11	0.45	<0.1	<0.1	<0.1

Sample	Ginned seed	Meal	Hulls	Soapstock	Crude oil	Refined oil
Processing factor	-	0.2	0.8	<0.2	<0.2	<0.2

Recoveries from samples fortified with dimethipin at 0.1 and 0.5 mg/kg were 82-86, 88-94, 94-100, 100, 106-115 and 88-120% for seed, meal, hulls, soapstock, crude oil and refined oil respectively.
Residues were corrected for analytical recoveries where recoveries were less than 100%

Residues in the edible portions of food commodities

No additional information.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

Dimethipin was determined in foods prepared for consumption in the 1997, 1998 and 1999 USA Food and Drug Administration Pesticide Program Residue Monitoring Total Diet Studies. It was reported that the incidence of detections was less than 2%.

NATIONAL MAXIMUM RESIDUE LIMITS

The residue is defined as dimethipin in Australia, the countries of the EU and the USA, the only countries for which information was provided. The Meeting was made aware that the following national MRLs had been established.

COUNTRY	COMMODITY	MRL (mg/kg)
Australia	Cotton seed	0.5
	Cotton seed oil, crude ; Cotton seed oil, refined	*0.1
	Milks, meat (mammalian), edible offal (mammalian), poultry meat, poultry edible offal	*0.01
	Eggs	*0.02
Japan	Sunflower seed	0.5
	Cotton seed	0.5
	Rape seed	0.1
	Other oil seeds	0.2
	Potato	0.05
Taiwan	Rice	0.5
USA	Cotton, undelinted seed	0.5
	Cotton, hulls	0.7
	Cattle meat by-products including offal, cattle fat, cattle meat, goat meat by-products including offal, goat fat, goat meat, horse meat by-products including offal, horse fat, horse meat, sheep meat by-products including offal, sheep fat, sheep meat, hog meat by-products including offal, hog fat, hog meat	0.02

APPRAISAL

Dimethipin is a plant growth regulator used mainly as a defoliant and harvest aid to accelerate desiccation of plant material. Dimethipin was first evaluated in 1985. It was listed by the 1997 CCPR (ALINORM 95/24 A) for periodic re-evaluation and was scheduled for consideration by the FAO Panel of the 2001 JMPR. The Meeting received information on its physicochemical properties, metabolism, environmental fate, analytical methods, stability in storage, registered uses, and residues in supervised trials and processing studies.

The Meeting was provided with studies in which dimethipin radiolabelled at the 2 and 3 positions of the dithiin ring was used in order to follow its distribution and metabolism in animals and plants. The following abbreviations are used for the metabolites discussed below:

red-DMP = 2,3-dimethyl-1,4-dithiane 1,1,4,4-tetraoxide
acetyl dithiane = 2-acetyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-S-cys = *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian 2-yl)-L-cysteine

glu-cys-S-DMP = *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-cysteinyl-γ-glutamic acid
DMP-S-acetate = 2-[(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)thio]acetic acid
DMP-GSH = *S*-(2,3-dimethyl-1,1,4,4-tetraoxo-1,4-dithian-2-yl)-L-glutathione
DMP-SH = 2-mercapto-2,3-dimethyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-S-methyl = 2,3-dimethyl-2-methylthio-1,4-dithiane 1,1,4,4-tetraoxide
DMP-tert-OH = 2-hydroxy-2,3-dimethyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-prim-OH = 2-hydroxymethyl-3-methyl-1,4-dithiane 1,1,4,4-tetraoxide
DMP-SO-methyl = 2,3-dimethyl-2-(methylsulfinyl)-1,4-dithiane 1,1,4,4-tetraoxide
hydroxy-DMP = 2,3-dihydro-5-hydroxymethyl-6-methyl-1,4-dithiine 1,1,4,4-tetraoxide
demethyl-hydroxy-DMP = 2,3-dihydro-5-hydroxymethyl-1,4-dithiine 1,1,4,4-tetraoxide
methylene-DMP = 2-methyl-3-methylene-1,4-dithiane 1,1,4,4-tetraoxide
demethyl-DMP = 1,4-dithiane 1,1,4,4-tetraoxide
N-acetyl-cys-DMP = *N*-acetylcysteinyl conjugate
Cys-gly-DMP = cysteinyglycine conjugate
HESB = 3-(2-hydroxyethylsulfonyl)butan-2-one

Metabolism

Animals

After oral administration of [^{14}C]dimethipin to rats, unchanged dimethipin, *N*-acetylcysteine conjugate, red-DMP, a cysteinylglycine conjugate and a polar fraction were identified in urine.

Two female goats (one lactating) were given [^{14}C]dimethipin orally at a dose of 20 mg/kg bw, equivalent to a nominal feeding rate of 500 ppm, for 3 consecutive days. The metabolites identified in urine were DMP-*prim*-OH, DMP-*tert*-OH, hydroxy-DMP and 2,3-dihydro-5-hydroxymethyl-1,4-dithiine-1,1,4,4-tetraoxide. Most of the residue in urine was not characterized, but was thought to consist of polar conjugates. Bile extracts contained dimethipin and seven metabolites, including the ring-opened product 3-(2-hydroxyethylsulfonyl)butan-2-one and dimethipin L-cysteine and *N*-acetyl cysteine conjugates. The concentrations of radiolabelled residues in edible tissues were highest in liver and kidney and much lower in muscle and fat. Intact dimethipin accounted for 2% of the TRR in liver and kidney. The metabolites 3-(2-hydroxyethylsulfonyl)butan-2-one and DMP-*tert*-OH were identified in liver and kidney, while β-glucuronidase hydrolysis indicated the presence of a glucuronide conjugate. The high concentrations of polar and bound residues in liver and kidney indicated extensive conjugation.

Lactating goats were dosed orally with radiolabelled dimethipin once daily for 5 consecutive days, at doses of 0.15 and 50 mg/kg bw [^{14}C]dimethipin and 50 mg/kg bw [$^{13/14}$C]dimethipin, equivalent to feeding at 3, 1010 and 1290 ppm in the diet. Radiolabel in excreta collected up to 22 h after the last dose (slaughter) accounted for 95% of the administered dose, while 0.1–0.2% of the dose was eliminated in milk. The only metabolite detected in milk in significant quantities was DMP-S-cys. The association of most of the ^{14}C in liver with protein suggests that the metabolites in liver were protein conjugates. In kidney, 1,2-ethane disulfonic acid was the only metabolite found in the goat given the low dose, while 1,2-ethane disulfonic acid was the only free metabolite in the goat given the high dose, with conjugated products that were released on acid hydrolysis. The main metabolite in muscle was red-DMP, which was present at approximately 30% of the TRR; no other metabolite accounted for more than 8% of the TRR. The concentrations of radiolabel in fat were too low to permit characterization of metabolites.

The main route of transformation of dimethipin is a Michael addition of a sulfhydryl to the double bond. Addition of glutathione yields DMP-S-cys, via the mercapturic acid pathway, which is eliminated in urine and milk. This conjugate was not observed in edible tissues. If the addition is made to a protein sulfhydryl, the result is protein-bound reduced dimethipin, which was the only residue observed in liver and muscle and approximately half that observed in kidney. Hydrolysis of the bound residue and subsequent rearrangement gave three products: red-DMP, acetyl dithiane and

1,2-ethane disulfonic acid. The latter was the only metabolite observed in kidney in the goat given the lower radiolabelled dose but represented about one-third of the radiolabelled residues in kidney in the goat given the higher dose.

White Leghorn pullets (1.3–2.4 kg bw) were given [^{14}C]dimethipin at nominal levels equivalent to 1 (0.06 mg/kg bw), 6 (0.34 mg/kg bw) and 30 (1.7 mg/kg bw) ppm in the feed. The concentration of radiolabelled residues in eggs plateaued 10 days after the start of dosing and reached maxima of 11, 41 and 198 μg/kg at the three doses, respectively. The TRR in eggs decreased to below the limit of detection of 6 μg/kg after 5 days' withdrawal from dosing at 1 ppm. After 11 days' withdrawal, the concentration of radiolabel in eggs was below the limit of detection for the group given 5 ppm and near the limit of detection for that given 30 ppm. Of the edible tissues, liver and kidney had the highest TRR and fat had the lowest. The concentration of dimethipin residues in liver was < 0.01 mg/kg at all doses.

The material balance after oral dosing of white Leghorn laying hens with [^{14}C]dimethipin for 5 days at 15.8 or 152 mg/bird (equivalent to feeding at 203 or 2770 ppm in the diet) was > 95%. Most of the radiolabel was eliminated in excreta (90–91%) within 24 h of the last treatment, and 5.1–5.6% of the amount given was recovered in edible tissues and eggs. The concentrations of radiolabelled residues were greatest in liver followed by kidney, muscle, eggs and fat. The main metabolite identified in hen liver was DMP-S-cys, and glu-cys-*S*-DMP was the main metabolite detected in other tissues. Other metabolites identified in liver included DMP-*prim*-OH, DMP-*tert*-OH, hydroxy-DMP, DMP-SH, DMP-*S*-methyl, DMP-SO-methyl and DMP-*S*-acetate.

It has been proposed that addition of glutathione to dimethipin (catalysed by glutathione *S*-transferase or spontaneous) gives DMP-GSH, which can be transported out of the cells in which it is formed and the glutathione moiety degraded by endogenous peptidases to produce glu-cys-*S*-DMP and DMP-*S*-cys. Oxidative transamination and loss of pyruvic acid or decarboxylation can give DMP-SH and DMP-*S*-acetate. Methylation of DMP-SH in the presence of *S*-adenosine-methionine would produce DMP-*S*-methyl, which could be further oxidized to DMP-SO-methyl. Another product that could be formed is the *N*-acetylcysteinyl conjugate, which would be expected to be retained by the strong anion-exchange columns used. An unidentified metabolite found in several extracts had chromatographic behaviour similar to that of products obtained by reacting dimethipin with *N*-acetylcysteine. Reduction and hydroxylation reactions are also possible, as evidenced by the presence of red-DMP and the hydroxylated metabolites DMP-*tert*-OH and DMP-*prim*-OH.

The data on metabolism in rats, goats and hens show that dimethipin is extensively metabolized, almost no residual parent compound being retained in any of these species. The main residues in animals form as the result of glutathione, amino acid and protein conjugation and subsequent degradation. Minor metabolites are formed as a result of hydrolytic hydroxylation and/or oxidation.

Plants

Studies on metabolism in cotton, sunflower, potato, grape and rice were made available to the Meeting.

When mature indoor-grown cotton plants, each with one to four bolls open, were treated with a single application of [^{14}C]dimethipin at 1.12 kg ai/ha, the extractable residue in seeds with linters accounted for 94% of the TRR, of which 94% was identified as dimethipin. In acid-delinted seeds, 18% of the TRR was extractable with methanol, of which 38% was dimethipin.

Dimethipin was the major component (72%) of the residue in foliage of cotton plants treated with [^{13}C/^{14}C]dimethipin at 0.34 and 1.6 kg ai/ha 2 weeks before harvest. No other individual compound accounted for more than 5% of the TRR. Most of the radiolabelled residue (80–90%) in

seeds was identified as dimethipin, no other component accounting for more than 5.2% of the extracted residue.

When the backs of the seed heads of mature sunflower plants were sprayed with [^{13}C/^{14}C]-dimethipin at 1.4 kg ai/ha and harvested 4 weeks later, dimethipin accounted for 61% of the extractable residue, with no other single component exceeding 5.7% of the TRR.

A field-grown potato plant (*cv.* Kennebec) was sprayed with a flowable formulation of [^{14}C]dimethipin at 2.24 g ai/ha and harvested 14 days later. Unchanged dimethipin accounted for 20–25% of the TRR (0.012–0.015 mg/kg) in unwashed potato tubers.

Indoor-grown rice plants were treated with [^{14}C]dimethipin at 2.24 g ai/ha, and the plants were harvested 17 days later. The TRRs in straw, hulls and seed were 162, 325 and 8 mg/kg, respectively, calculated as dimethipin. More than 78% of the radiolabelled residues in straw, hulls and grain were extractable in solvents, dimethipin representing 50–80% of the extractable TRR.

When Mueller-Thurgau grape vines were sprayed with [^{14}C]dimethipin at 115 mg/vine, the TRRs in leaves were 16, 7.8 and 3.6 mg/kg (calculated as dimethipin) 2 h and 6 and 24 days after application, respectively. The concentrations of dimethipin residues were 0.036 mg/kg in juice, 0.004 mg/kg in stems and seeds and 0.033 mg/kg in wine in combined 6- and 24-day samples. Numerous metabolites were detected, although none was identified. When samples of juice were processed into wine by alcoholic fermentation, no $^{14}CO_2$ evolved. In wine filtered after fermentation, 11% of the radiolabel was in yeast and solids and 89% in the clear wine.

Most of the radiolabel in the leaves of cotton seedlings grown hydroponically with [^{14}C]-dimethipin in the nutrient medium for 3 days were dimethipin (79%). Metabolites identified as minor constituents were cysteine and glutathione conjugates of dimethipin. Extracts of cotton callus cultures treated with [^{14}C]dimethipin had metabolite profiles similar to that of hydroponically treated cotton plants, but with more dimethipin–L-cysteine reaction product. An additional polar metabolite with an identical HPLC retention time to an unidentified rat metabolite was observed in [^{14}C]dimethipin-treated potato callus cultures

As dimethipin is applied to plants close to harvesting, when the plants are close to natural senescence, the biochemical activity is very limited, resulting in minimal metabolism. As a result, the main plant residue is the parent compound. In a study of the fate of dimethipin in cotton seedlings and callus cell cultures of cotton and potato, most of the plant metabolites resulted from conjugation of dimethipin with glutathione and/or cysteine.

Environmental fate

Studies were reported on degradation, dissipation and mobility in soil, adsorption and desorption, photodegradation on soil, confined rotational crops and aquatic dissipation.

Soil

The aerobic metabolism of [^{14}C]dimethipin was studied on a silt loam, a sand, two loamy sands and a field loam at 25 °C. Under aerobic conditions, bound residues and $^{14}CO_2$ accounted for < 25 and 30% of the radiolabel, respectively. After 168 days of incubation, 50–66% of the radiolabel was recovered as dimethipin. The main metabolites identified were 2-methyl-3-methylene-1,4-dithiane-1,1,4,4-tetraoxide, 1,4-dithiane-1,1,4,4-tetraoxide and a carboxylic acid derivative of dimethipin. The mass balances for the radiolabel were 94–101%.

The anaerobic metabolism of [^{14}C]dimethipin was studied on a silt loam and a sand. Desorption of radiolabel from the soils to the water used to maintain anaerobic conditions was noted.

On silt loam and sand, 60–80% of the radiolabel was present as dimethipin after incubation for 60 days at 25 °C. The mass balances for the radiolabel were 88–90% after 60 days' incubation.

Dimethipin is not susceptible to anaerobic photolytic degradation. In aerated solutions, the photolytic half-time was reduced to 14 days. The rate of photolysis was observed to be pH-dependent, with no significant degradation at pH 7 but half-times at pH 5 and 9 of 35 and 47 days, respectively.

Significant photolytic losses were seen after irradiation of [^{14}C]dimethipin on sandy loam soils when compared with degradation by hydrolysis and soil metabolism. After 30 days, dimethipin accounted for 47–65% and 81–99% of the radiolabel in irradiated and dark control samples, respectively. Volatile components accounted for < 1% of the applied radiolabel. The mass balances were 92 ± 7% for exposed samples and 94 ± 9% for dark samples.

The Meeting concluded that dimethipin is relatively persistent in soils.

Dimethipin was weakly adsorbed onto each of the soils, and a strong relationship was observed between adsorbed dimethipin and percentage of organic matter. The desorption was essentially completely reversible. The adsorption K_a values (< 15) and ease of desorption indicate that the mobility of dimethipin was high in all soils studied.

Studies of leaching were reported for four soil types, sand, loamy sand, sandy loam and silt, treated with dimethipin at 1.7 kg ai/ha. Dimethipin was readily leached from 30-cm soil columns with 51 column cm of water. Between 77 and 102% of the applied radiolabel eluted, of which 71–96% was dimethipin. The rate of elution of the radiolabel was fastest in loamy sand, silt loam and aged sandy loam soil columns, with a more gradual rate in sand and sandy loam soils. Dimethipin is considered to be highly mobile and does not degrade significantly under conditions simulating leaching.

Field studies were conducted under natural conditions of rainfall and irrigation in several states of the USA at sites with loamy sand, clay loam and silt loam soils. The soils were treated according to GAP in the USA for cotton (two sprays, 0.35 and 0.25 kg ai/ha) and sunflowers (2.24 kg ai/ha). Dimethipin migrated below the top 30 cm of soil, and low concentrations of residue were detected at depths down to 91 cm (0.01 mg/kg). The half-time for degradation of dimethipin in the 0–122-cm depth was 168–196 days.

In a study of confined rotational crops, lettuce, barley and carrots were planted in soil treated with [^{14}C]dimethipin at 0.6 kg ai/ha after a fallow period of 30 days and grown to maturity. Dimethipin accounted for most of the radiolabel in soil at application and planting (85–100% of TRR). The percentage of bound, unextractable residue increased with time after application, reaching 60–93% of the TRR in soil samples at harvest. The concentrations of residues of dimethipin in immature and mature crops were 0.01–0.10 mg/kg. No residues of dimethipin were detected in wheat grain. Three crop metabolites were isolated, one of which was identified as hydroxy-DMP.

Lettuce, carrot and wheat or oats were planted in soil treated with two sprays of dimethipin at 0.35 and 0.26 kg ai/ha (GAP for cotton in the USA) after fallow periods of 1 and 6 months. The concentrations of residues of dimethipin in these rotational crops were significant (< 0.02–0.07 mg/kg) at a plant-back interval of 1 month and mostly negligible (< 0.02 mg/kg) in crops planted 6 months after application. The notable exception was carrot tops, which had concentrations ≤ 0.18 mg/kg at harvest in crops planted 6 months after the last application.

The Meeting concluded that the concentrations of inadvertent residues of dimethipin in rotational crops would not be significant after a 6-month plant-back period and that the carryover of dimethipin under field conditions should be < 0.02 mg/kg. Dimethipin is degraded only slowly under aerobic aquatic conditions or on soil under aerobic and anaerobic conditions. It is relatively persistent in the environment and considered to be highly mobile in all the soil types studied.

Water–sediment systems

The half-time of dimethipin in an anaerobic water–sediment system was 277 days. At the start of the experiment, 97% of the applied ^{14}C was present in the aqueous filtrate. By the end of the experiment (365 days), 56% of the applied radiolabel was associated with the water filtrate, dimethipin accounting for 65% of the radiolabel in water or 37% of that applied. Extractable residues from the soil accounted for 5% of the applied radiolabel, dimethipin comprising 89%. Bound residues and $^{14}CO_2$ accounted for 17 and 7% of the applied radiolabel, respectively.

Methods of analysis

Adequate methods have been developed for the analysis of residues of dimethipin on crops and of dimethipin and 1,2-ethane disulfonic acid in animal commodities. Dimethipin is extracted from the matrix with a polar solvent (methanol, aqueous methanol or acetonitrile). The extract is cleaned up with a hexane wash, GPC and a Florisil column. Dimethipin is quantified by GC with a sulfur-specific flame photometric detector, ECD or mass-selective detector. The LOQ and LOD depended on the detector used. The LOQs for most matrices were generally 0.01–0.05 mg/kg.

The Meeting concluded that adequate analytical methods are available for enforcement of MRLs and monitoring purposes.

Stability of residues in stored analytical samples

The stability of dimethipin during frozen storage of fortified samples of cotton seed, meal, hulls and crude oil, lettuce, carrot and wheat grain as well as bovine milk, muscle, kidney and liver was reported. The stability of the metabolite 1,2-ethane disulfonic acid in samples of bovine kidney with incurred residues was also reported.

The periods for which the concentrations of residues of dimethipin remained > 70% of the initial concentration were at least 12 months for lettuce, carrot root, wheat grain and cotton seed; 7 months for cotton seed meal, hulls and crude oil; and 2 months for bovine milk, muscle, kidney and liver. Residues of 1,2-ethane disulfonic acid in bovine kidney were stable for at least 6 months.

The Meeting concluded that dimethipin is stable in crop matrices stored frozen for periods of up to 12 months.

Definition of the residue

Dimethipin is not significantly metabolized by plants when applied close to harvest. The main component of the extractable residue in plants is dimethipin, comprising 38–72, 61, 20–25, 50 and 14–50% of the extractable residue in cotton, sunflower seeds, potatoes, rice grain and grape juice, respectively. In animals, dimethipin is extensively metabolized, the main pathways involving conjugation to glutathione, amino acids and peptides and subsequent degradation. Minor routes of metabolism include hydrolytic hydroxylation and oxidation. There is no reasonable expectation that feeding of dimethipin-treated commodities to animals would result in residues of dimethipin or metabolites in animal commodities that are above typical LOQs.

On the basis of the metabolism of dimethipin in plants, the conclusions of the 1999 JMPR on the toxicology of the compound and the available analytical methods, the Meeting concluded that the residue for compliance with MRLs and for estimation of dietary intake should continue to be defined as dimethipin.

Results of supervised trials

Dimethipin is registered as a plant growth regulator for use as a crop defoliant and harvest aid to accelerate desiccation of plant material. It is applied at the end of plant maturity and close to its natural senescence. At this time, the biochemical activity in plants is very limited, and the penetration, translocation and metabolism of dimethipin in plants are slow. As dimethipin is used as a growth regulator in crops, it is usually best to harvest crops at the appropriate stage of desiccation or defoliation rather than to set minimum pre-harvest intervals. Considerable latitude with respect to the PHI has been allowed in assessing compliance with GAP. Supervised trials were reported on potato, cotton, rape, linseed and sunflowers.

Data were available from supervised trials on potato in France, Germany, The Netherlands, Norway, Sweden and the United Kingdom, but with no corresponding GAP. The Meeting decided to evaluate the trials from France, Germany, The Netherlands and the United Kingdom according to the GAP of Ireland.

In Ireland, dimethipin is registered for application to potatoes at a rate of 0.63 kg ai/ha with a 21-day PHI. The concentrations of residues of dimethipin in four trials in France with application of 0.75 kg ai/ha and PHIs of 18–34 days were < 0.01 (3) and < 0.1 mg/kg. In six trials in Germany at 0.75 g ai/ha with PHIs of 13–14 days, the concentrations of residues of dimethipin were < 0.02 mg/kg (6). Six trials in The Netherlands conducted at 0.5–0.63 kg ai/ha with PHIs of 9–40 days showed concentrations < 0.05 (6) mg/kg. The concentrations in three trials in the United Kingdom at 0.5 kg ai/ha and PHIs of 21–28 days were < 0.005 mg/kg (3).

The concentrations of residues of dimethipin in potatoes in 19 trials, in ranked order (median underlined), were < 0.005 (3), < 0.01 (3), < 0.02 (6), < 0.05 (6) and < 0.1 mg/kg. All the values in potato tubers were below the LOD. The Meeting considered that an appropriate LOQ for a regulatory analytical method is 0.05 mg/kg. The observation of detectable residues of dimethipin in a trial of metabolism in potatoes after application at an exaggerated rate led to the conclusion that the concentration could not be considered zero. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in potatoes of 0.05(*), 0.02 and 0.02 mg/kg respectively. The results of a number of trials conducted in countries without corresponding GAP but with PHIs and similar or excessive application rates in comparison with GAP in Ireland support the conclusion that the concentrations of residues are < 0.05 mg/kg. The estimated maximum residue level confirms the current recommendation (0.05(*) mg/kg) for potato.

Supervised field trials on cotton were reported from Spain and the USA.

The registered use pattern in Spain is 0.31 kg ai/ha with no specified PHI. The concentrations of residues in cotton seed in four trials at an application rate of 0.31 kg ai/ha were 0.02, 0.03 and 0.07 (2) mg/kg 5–14 days after application.

Fifteen trials in the USA followed GAP in that country, which is two sprays at 0.23–0.32 kg ai/ha with a minimum re-treatment interval of 5 days and a PHI of 7 days. The concentrations of residues of dimethipin were < 0.1 (4), 0.1 (3), 0.2 (6), 0.3 and 0.7 mg/kg.

The concentrations of dimethipin in cotton seed in the 19 trials, in ranked order, were 0.02, 0.03, 0.07 (2), < 0.1 (4), 0.1 (3), 0.2 (6), 0.3 and 0.7 mg/kg. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in cotton seed of 1, 0.1 and 0.7 mg/kg respectively. The estimated maximum residue level replaces the current recommendation (0.05(*) mg/kg) for cotton seed.

Supervised trials on linseed were provided from the Czech Republic. In two trials approximating GAP in that country (0.5 kg ai/ha; PHI, 10–15 days), the concentrations of residues of dimethipin were < 0.1 (2) mg/kg.

The number of trials with linseed is insufficient for setting a maximum residue level. The Meeting recommended withdrawal of the current maximum residue level of 0.2 mg/kg for linseed.

Supervised field trials on rape seed were reported from the Czech Republic, Germany, Hungary, Norway and the United Kingdom. Details of GAP in Norway were not provided. The trials in the United Kingdom did not approximate the relevant GAP and/or were not adequately described.

The registered use pattern in the Czech Republic is 0.38–0.5 kg ai/ha with a PHI of 10–14 days. The concentrations of residues in rape seed in three trials with application rates of 0.38–0.6 kg ai/ha were < 0.1 mg/kg 7–14 days after application.

Six trials in Germany approximated GAP in Hungary, which is application at 0.3–0.5 kg ai/ha with a PHI of 14 days. The concentrations of residues of dimethipin were < 0.1 (5) and 0.1 mg/kg.

In one trial in Hungary conducted according to GAP, the concentration in rape seed was < 0.05 mg/kg.

The concentrations of residues of dimethipin in rape seed in the 10 trials were < 0.05, ≤ 0.1 (8) and 0.1 mg/kg. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in rape seed of 0.2, 0.1 and 0.1 mg/kg, respectively.

Data were available on a supervised trials on sunflowers conducted according to GAP in Hungary, which is application at 0.38–0.5 kg ai/ha with harvesting 14 days after the final spray. In 11 trials approximating GAP, the concentrations of residues of dimethipin were < 0.01 (4), < 0.1, 0.09, 0.26, 0.30, 0.38, 0.70 and 0.77 mg/kg.

The concentrations of residues of dimethipin in sunflower seed in the 11 trials in ranked order were < 0.01 (4), 0.09, ≤ 0.1, 0.26, 0.30, 0.38, 0.70 and 0.77 mg/kg. The Meeting estimated a maximum residue level, an STMR value and a highest residue for dimethipin in sunflower seed of 1, 0.1 and 0.77 mg/kg respectively. The estimated maximum residue level replaces the current recommendation (0.5 mg/kg) for sunflower seed.

Fate of residues during processing

Information was provided to the Meeting on the fate of dimethipin residues during processing of cotton seed. Processing factors were calculated for dimethipin residues in processed commodities derived from this raw agricultural commodity only when dimethipin was the residue of concern for surveillance and estimation of dietary intake. When the concentrations of residues in a processed commodity did not exceed the LOQ, the processing factor was calculated from the LOQ and is prefixed with a 'less than' symbol (<).

The average factor for processing of cotton seed to meal was 0.2, that for cotton seed to hulls was 0.8, that for cotton seed to soapstock was < 0.2, that for cotton seed to crude oil was < 0.2 and that for cotton seed to refined oil was < 0.2. Application of a processing factor of 0.2 to the STMR of 0.1 mg/kg for cotton seed gives an STMR-P value for crude and refined oil of 0.02 mg/kg. The Meeting estimated maximum residue levels of 0.1 mg/kg for crude cotton seed oil and edible cotton seed oil. The estimated maximum residue level for crude cotton seed oil confirms the current recommendation (0.1 mg/kg), while that for edible cotton seed oil replaces the current recommendation (0.02 * mg/kg).

Residues in animal commodities

The studies of animal transfer indicate that feeding dimethipin at concentrations up to 50 ppm in the diet will not result in residues in milk and tissues that exceed 0.01 mg/kg, the LOQ for dimethipin in milk and tissues with the analytical method provided.

The dietary burden of dimethipin residues in farm animals was estimated by the Meeting on the basis of the diets listed in Appendix IX of the *FAO Manual*. Potential feed items for which information on residues was available were cotton seed, cotton seed meal and hulls, rape seed and sunflower seed. The estimated intakes of dimethipin by beef and dairy cattle are shown in the table below.

Commodity	Group	Residue (mg/kg)	Basis	Dry matter (%)	Residue, dry weight (mg/kg)	Choose diets (%)			Residue contribution (mg/kg)		
						Beef cattle	Dairy cows	Poul-try	Beef cattle	Dairy cows	Poul-try
Cotton seed	SO	1	MRL	90	1.1	10	10		0.11	0.11	
Cotton seed meal	SO	0.02	STMR-P	88	0.02						
Cotton seed hulls	SO	0.08	STMR-P	90	0.09						
Potato culls		0.02	STMR	20	0.1						
Rape seed	SO	0.2	MRL	88	0.23						
Sunflower seed	SO	1	MRL	92	1.08	15	15	30	0.16	0.16	0.32
Total						25[a]	25[a]	30[b]	0.27	0.27	0.32

[a] Assuming that total oilseed products will not be fed at more than 25% of the diet to beef cattle and dairy cows
[b] Assuming that total oilseed products will not be fed at more than 30% of the diet to poultry

The dietary burden of dimethipin for beef and dairy cattle is 0.27 mg/kg. No residues of dimethipin were detected in milk or tissues of dairy cows fed at 50 ppm in the diet for 28 days, a level that is 185 times the estimated dietary burden for cattle. The Meeting estimated maximum residue levels, STMR values and highest residues for dimethipin in edible offal (mammalian) and meat (mammalian) of 0.01*, 0 and 0 mg/kg respectively. The Meeting also estimated a maximum residue level and STMR of *0.01 mg/kg and 0 mg/kg for milk. The estimated maximum residue levels replace the current recommendations (0.02* mg/kg) for edible offal (mammalian), meat (mammalian) and milk.

The dietary burden of dimethipin for poultry is 0.32 mg/kg. No residues of dimethipin were detected in eggs or tissues of hens dosed orally for 5 days at a rate equivalent to feeding at 2770 ppm, a level that is > 8000 times the estimated dietary burden for poultry. The concentrations of TRRs in tissues and eggs of hens dosed at up to 30 ppm in the diet for 30 days were < 1.4 mg/kg (calculated as dimethipin). The studies with radiolabelled compound indicate that there is no reasonable expectation that detectable residues of dimethipin will be found in eggs or tissues of hens fed at the estimated dietary burden of 0.32 mg/kg. The Meeting estimated maximum residue levels, STMR values and highest residues for dimethipin in eggs, edible offal of poultry and poultry meat of 0.01*, 0 and 0 mg/kg, respectively. The estimated maximum residue levels replace the current recommendations (0.02* mg/kg) for eggs, poultry, edible offal and poultry meat.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the concentrations of residue listed below are suitable for establishing maximum residue limits and for assessing IEDIs and IESTIs.

Definition of the residue (for compliance with MRL and estimation of dietary intake): agricultural commodities: Dimethipin.

Commodity		Recommended MRL (mg/kg)		STMR or STMR-P	HR or HR-P
CCN	Name	New	Previous	(mg/kg)	(mg/kg)
SO 0691	Cotton seed	1	0.5	0.1	0.7
OC 0691	Cotton seed oil, crude	0.1	0.1	0.02	
OR 0691	Cotton seed oil, edible	0.1	0.02 (*)	0.02	
MO 0105	Edible offal (mammalian)	0.01 (*)	0.02 (*)	0	0
PE 0112	Eggs	0.01 (*)	0.02 (*)	0	0
SO 0693	Linseed	W	0.2		
MM 0095	Meat (from mammals other than marine mammals)	0.01 (*)	0.02 (*)	0	0
ML 0106	Milks	0.01 (*)	0.02 (*)	0	
VR 0589	Potato	0.05 (*)	0.05 (*)	0.02	0.02
PM 0110	Poultry meat	0.01 (*)	0.02 (*)	0	0
PO 0111	Poultry, edible offal	0.01 (*)	0.02 (*)	0	0
SO 0495	Rape seed	0.2	-	0.1	0.1
SO 0702	Sunflower seed	1	0.5	0.1	0.77
OC 0702	Sunflower seed oil, crude	W	0.1		
OR 0702	Sunflower seed oil, edible	W	0.02 (*)		

W: the previous recommendation is withdrawn

Dietary risk assessment

Long-term intake

The periodic review of dimethipin resulted in recommendations for new and revised MRLs and new STMRs for raw and processed commodities. Data on consumption were available for 12 food commodities and were used in the dietary intake calculation. The results are shown in Annex 3 (Report 2001).

The IEDIs for the five GEMS/Food regional diets, based on estimated STMRs, were 3-20% of the ADI of 0–0.02 mg/kg bw. The Meeting concluded that long-term intake of residues of dimethipin from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The IESTI for dimethipin was calculated for processed cotton seed products, potatoes, rape seed and sunflower seed as well as animal products for which maximum residue levels and STMRs were estimated and for which data on consumption were available. The results are shown in Annex 4 (Report 2001). The IESTI represented 0–10% of the acute RfD (0.02 mg/kg bw) for the general population and 0–10% of the acute RfD for children.

The Meeting concluded that short-term intake of dimethipin residues is unlikely to present a public health concern.

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Cross-index of report numbers and references

HARV 3 Womer and Sisken 1974
HARV 62 Bodden *et al*. 1982
HARV.155 Hughes and Patzer 1996
HARV.162 Hughes and Halverson 1996
HARV-103 Spare *et al*. 1990
HARV-109 Young 1991
HARV-11 Wong 1976
HARV-110 Thomson 1991
HARV-114 Fackler 1991
HARV-115 Fackler 1992
HARV-117 Perhach and Jalal 1993
HARV-118 Dzialo 1993
HARV-119 Lau and Gay 1993
HARV-121 Byrd 1992
HARV-127 Dzialo *et al*. 1994a
HARV-128 Dzialo *et al*. 1994b
HARV-129 Burke and Johnson 1994
HARV-130 Caplan and Merricks 1978
HARV-132 Pierce 1996
HARV-132 Riggs 1990
HARV-135 Singh and Eckert 1996
HARV-15 Smilo *et al*. 1978
HARV-154 Batorewicz and Long 1996
HARV-157 Batorewicz 1993
HARV-159 Stauffer 1990
HARV-16 Erdmann *et al*. 1981
HARV-174 Vithala 1999
HARV-21 Curtiss 1980
HARV-29 Curtiss and Harned 1980

HARV-34 Harned 1981
HARV-34 Kuc 1980
HARV-40 Henderson 1981
HARV-41 Lengen and Harned 1981
HARV-48 Milad 1981
HARV-49 Harned and Lengen 1981
HARV-51 Fitzpatrick 1982
HARV-53 Fitzpatrick 1981
HARV-54 Fitzpatrick and Wong 1981
HARV-55 Harned *et al*. 1981
HARV-56 Harned 1982
HARV-56 Kuc 1981
HARV-65 Lengen 1982
HARV-66 Lau and Gay 1996
HARV-70 Frederick 1983
HARV-71 Balba and Dzialo 1983
HARV-73 Fitzpatrick 1983
HARV-74 Mcmanus 1984
HARV-76 Abdel-Kader and Blaszczynski 1984
HARV-78 Singh 1982
HARV-81 Spare 1987
HARV-83 Mcmanus 1987
HARV-84 Byrd and Billings 1989
HARV-85 Lengen 1987
HARV-86 Mcmanus 1987
HARV-88 Spare 1987
HARV-89 Ellgehausen 1985
HARV-90 Mcmanus 1985
HARV-91 Steeves 1986
HARV-92 Mcmanus 1989
HARV-94 Thomson 1989
HARV-97 Riggs 1990
HARV-98 Thomson 1990
HARV-99 Thomson 1990
N.6.0.3 Tomkins 1985c
N.6.2.1.21 Tomkins 1985a
N.6.2.1.3 Tomkins 1986b
N.6.2.13.10 Laszlo 1998
N.6.2.13.2 Tomkins 1983
N.6.2.13.5 Tomkins 1986c
N.6.2.13.6 Tomkins 1985b
N.6.2.13.6 Tomkins 1985b
N.6.2.13.7 Tomkins 1986e
N.6.2.3.12 Tomkins 1982
N.6.2.3.13 Tomkins 1984d
N.6.2.3.14 Tomkins 1984c
N.6.2.3.15 Tomkins 1984b
N.6.2.3.23 Tomkins 1984a
N.6.2.3.24 Tomkins 1986a
N.6.2.5.5 Tomkins 1984e
N.6.2.5.8 Tomkins 1986f
N.6.2.7.1 G.C. Laboratories 1983a
N.6.2.7.2 G.C. Laboratories 1982
N.6.2.7.3 G.C. Laboratories 1983b
N.6.2.7.4 G.C. Laboratories 1983c
N6.2.13.4 Tomkins 1985d
Project No.: 7524 Womer and Sisken 1974
Project No.: 7603 Fitzpatrick 1981
Project No.: 7603 Fitzpatrick and Wong 1981
Project No.: 7603 Lengen 1982
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