ETHYLENETHIOUREA, ETU (108)

EXPLANATION

Ethylenethiourea (ETU) is a metabolite and decomposition product of the ethylenebis(dithiocarbamate) (EBDC) fungicides. It was first evaluated in 1974, and MRLs have been established to reflect maximum residue levels in raw agricultural commodities at harvest; they do not include ETU formed from ethylenebis(dithiocarbamate) residues during processing.

ETU was scheduled (ALINORM 93/24A, para 135) for toxicological and residue evaluation by the 1993 JMPR.

Extensive data on ETU residues in raw agricultural commodities and processed foods from supervised trials and in trade, and data on ETU occurrence from the plant and animal metabolism of mancozeb and maneb, were made available to the Meeting.

RESIDUES RESULTING FROM SUPERVISED TRIALS

Residues of ETU resulting from the uses of mancozeb and maneb are summarized in the monographs on those compounds. Mancozeb and maneb have a wide range of approved uses on agricultural and horticultural crops in many countries.

ETU residue data were available on citrus fruits, pome fruits, stone fruits, berry fruits, tropical and subtropical fruits, bulb vegetables, Brassica vegetables, fruiting vegetables, leafy vegetables, legume vegetables, root and tuber vegetables, stalk and stem vegetables, cereal grains, hops, oilseeds, tree nuts, cereal straws and fodders, legume animal feeds and miscellaneous fodder and forage crops.

In many situations ETU residues were low (0.1 mg/kg or less) or undetectable (LOD mostly 0.01-0.02 mg/kg). In those situations where mancozeb or maneb residues were 10 mg/kg or higher, such as in animal feeds, ETU residues were also sometimes higher. Some of these higher residues could be an artefact, because a small percentage of the ethylenebis(dithiocarbamate) residues can be converted to ETU during analysis (Onley *et al*., 1977).

Animal transfer studies on mancozeb with lactating dairy cows and laying hens are summarized in the mancozeb monograph.

In the dairy cow study ETU residues were not detected (<0.01 mg/kg) in milk from the highest feeding group (45 ppm mancozeb). ETU was detected in the thyroid of all animals (5, 15 and 45 ppm mancozeb in the feed), with the highest doses causing the highest levels. Levels in the thyroid decreased during 7 days on residue-free feed. ETU was not detected (<0.01 mg/kg) in the fat from the highest dose group; residues were present in other tissues of the highest feeding group on day 29 (28 days of dosing), but disappeared after 7 days on a residue-free diet. ETU levels in muscle tissue from the highest dose group on day 29 were <0.01-0.034 mg/kg.

In the laying hen study ETU levels in eggs from the highest feeding group (45 ppm mancozeb) were in the range <0.01-0.017 mg/kg. ETU residues were not detected (<0.02-<0.08 mg/kg) in the tissues.

FATE OF RESIDUES

In animals

Mancozeb and maneb metabolism studies on lactating goats and laying hens were made available to the Meeting. Summaries are included in the respective monographs. ETU was generally a minor metabolite, constituting few % or less of the total ^{14}C in tissues, milk and eggs.

In plants

Mancozeb metabolism studies on tomatoes, soya beans, sugar beet and wheat, and maneb metabolism studies on lettuce, potatoes and tomatoes are summarized in the respective monographs.

ETU was generally not detected in the mancozeb plant metabolism studies. In the maneb studies ETU levels expressed as a percentage of the total residue were lettuce 7%, potato peel 0.49%, tomato 7.9%. ETU was not detectable in the potato pulp. A major part of the detected ETU was present in the surface rinsings from the lettuce and tomatoes. Hoagland and Frear (1976) demonstrated that ^{14}C-labelled ETU was absorbed by the petioles and roots of maize, lettuce, peppers and tomatoes, and translocated principally in the xylem.

UV irradiation of ETU on silica gel yielded ethyleneurea as the major identified product (Cruickshank and Jarrow, 1973).

In soil treated with ^{14}C-labelled ETU the half-life of intact ETU was less than one week (Rhodes, 1977). The disappearance of residues from tomato and bean plants treated with radiolabelled ETU is shown in Table 1. The compounds identified by TLC in the extract from tomato plants one day after treatment and their percentages of the extractable ^{14}C were ETU 2%, ethyleneurea 21% and 1-(2-imidazolin-2-yl)-2-imidazolidinethione 75%.

Table 1. Disappearance of residues from tomato and bean plants treated with radiolabelled ETU (Rhodes, 1977).

Days after treatment	Tomato foliage and stems		Bean foliage and stems	
	Total ^{14}C, mg/kg as ETU	ETU, mg/kg	Total ^{14}C, mg/kg as ETU	ETU, mg/kg
0	2.2	0.08	5.5	0.66
1	2.1	0.06	6.2	0.21
3	0.95	0.01	3.9	0.05
7	0.75	0.03	3.0	0.03
14	0.25	<0.01	2.0	0.04
21	0.14	<0.01	1.9	0.01
35	0.06	<0.01	1.5	<0.01

Rhodes (1977) identified by TLC the products of the aqueous UV photodecomposition of ETU by a mercury-vapour lamp (Table 2). ETU was completely degraded (>99%) after 6 hours irradiation with no photosensitiser, and after 3 hours in the presence of acetone.

Table 2. Products identified from the photodecomposition of radiolabelled ETU (Rhodes 1977).

Compound	% of total ^{14}C	
	No photosensitiser	0.1M acetone
Hydantoin	9.3	24
Ethyleneurea	14	7.3
1-(2-imidazolin-2-yl)-2-imidazolidinethione	11	17
Glycine	63	50

Ross and Crosby (1973) showed that ETU in aqueous solution was stable to sunlight, but in the presence of dissolved oxygen and sensitisers such as acetone or riboflavin it was rapidly converted to ethyleneurea and glycine sulphate.

In storage and processing

Processing studies for mancozeb on apples, grapes, sweet corn, tomatoes, potatoes, sugar beet, barley, wheat, maize and peanuts and for maneb on apples, beans, grapes, sugar beet, sweet corn and tomatoes were made available to the Meeting and are summarized in the respective monographs. The studies included data on ETU residues.

Mancozeb and maneb residues, which are on the surface, can be substantially diminished by vigorous washing. The remaining ethylenebis(dithiocarbamate) residues will be converted in part to ETU residues if processing includes a heating step. Levels of ETU in the processed product bear no relationship to the ETU levels in the raw commodity.

Table 3 presents a selection of data from the supervised processing trials. It should be noted that the trials were conducted with exaggerated rates of application to achieve high residues in the raw commodity. The chances of measuring residues in the processed commodity are then improved. The data suggest that the degree of conversion to ETU depends very much on the process.

Table 3. ETU residues in processed commodities in processing trials. Data were selected from more detailed tables in the mancozeb and maneb monographs.

Raw commodity	EBDC residues (as CS_2), mg/kg	Processed commodity	ETU residues, mg/kg
Mancozeb			
Washed apples	2.8	Unclarified canned juice	0.04
		Clarified canned juice	<0.03
Apples	4.7	Apple juice	<0.01
Grapes, de-stemmed and heated	19	Clear juice	2.5
Grapes	9.0	Unfiltered juice	0.025
		Red wine	0.64
		White wine	0.79
Washed tomatoes	0.2	Canned tomato juice	0.09
Potatoes, washed and brushed	<0.06	Baked potato flesh	0.013
Maneb			

Apple	9.7	Fresh juice	0.018
Raw bean pods	3.5	Canned beans	0.49
Raw grapes	6.6	Thick grape juice	5.0
Sugar beet roots	0.069	White sugar	<0.01
Tomatoes, unwashed	0.087	Tomato juice, from paste	0.02

Marshall (1977) showed that conversion of ethylenebis(dithiocarbamates) to ETU during cooking depended on pH. The yields of ETU from two hours refluxing of mancozeb were: pH 2.2 11%, pH 4.0 19%, pH 5.6 70%, pH 8.0 79%.

Studies in the open literature on the fate of EBDC residues during food processing were included in a recent review of the effects of processing on pesticide residues (Holland *et al., in press*).

The effects of typical consumer practices during food preparation on residues of dithiocarbamates were reported by Johnson (1991), and are summarized in the mancozeb monograph. Very little, if any, ETU is produced during the removal of dithiocarbamate residues by washing, scrubbing and drying.

Stability of pesticide residues in stored analytical samples

Studies of the freezer storage stability of ETU in apples, tomatoes, wheat, dry beans, frozen corn, lettuce, raw potatoes, raw tomatoes, meat and milk are included in the mancozeb monograph.

More than 70% of the ETU remained in tomato and wheat matrices after 12 months storage at -20°C, but not after two years. ETU residues in the apple matrix had declined to less than 70% after 6 months storage and to less than 50% after 12 months. ETU residues were shown to be stable in 3-6 month tests at -20 ± 5°C in stored analytical samples of dry beans, corn, lettuce (marginal stability), meat, milk, raw potato (marginal stability), and tomato.

Residues in the edible portion of food commodities

Information on ETU residues is discussed in conjunction with mancozeb and maneb residues in the respective monographs.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

A number of studies were made available to the Meeting and are summarized in the mancozeb monograph.

Under a US Food and Drug Administration monitoring programme 864 samples of baby foods were monitored for pesticide residues (Yess *et al.*, 1993). ETU residues were detected in 65 samples; the highest levels detected were 0.06 mg/kg.

In 1989-90 in the USA a large survey of food items (approximately 300 samples each of 19 different raw and processed commodities) was conducted for dithiocarbamate and ETU residues (Slesinski, 1990). No measurable residues of ETU (LOD 0.001 mg/kg) were found in 82% of the samples. All ETU residue levels were less than 0.1 mg/kg. A summary of the results is included in the mancozeb monograph.

ETU was not detected (<0.005 mg/kg) in any of 100 commercial grape juice samples in the USA taken from producers using grapes from areas where dithiocarbamate fungicides were used (Honeycutt, 1991).

METHODS OF RESIDUE ANALYSIS

The methods for ETU are reviewed in association with the dithiocarbamate methods in the mancozeb monograph.

APPRAISAL

Ethylenethiourea (ETU) is a metabolite and decomposition product of the ethylenebis(dithiocarbamate) (EBDC) fungicides. MRLs have been established to reflect maximum residue levels in raw agricultural commodities at harvest. ETU was scheduled (ALINORM 93/24A, Appendix IV, Annex I) for periodic (toxicological and residue) re-evaluation by the 1993 JMPR.

Extensive data were made available to the Meeting on ETU residues in raw agricultural commodities from supervised trials, in processed foods from supervised trials, and in raw and processed commodities in trade, and on the production of ETU in the plant and animal metabolism of mancozeb and maneb.

ETU residues in raw agricultural commodities were generally low (0.1 mg/kg or less) or undetectable (LOD mostly 0.01-0.02 mg/kg). Some reported ETU residues could be an artefact of the analysis, because a small percentage of the ethylenebis(dithiocarbamate) residues can be converted to ETU during the determination.

Animal metabolism and animal transfer studies with mancozeb and maneb on lactating dairy cows, lactating goats and laying hens showed that ETU was a minor metabolite and that ETU residues in milk, eggs and tissues arising from ethylenebis(dithiocarbamate) (EBDC) feed residues would normally be very low or undetectable.

ETU was either undetectable or a minor residue in plant metabolism studies with applied mancozeb or maneb. Where ETU was detected, it was mostly in surface rinsings.

ETU was generally short-lived when applied to plant leaves or soil. It was rapidly degraded by UV light.

Ethylenebis(dithiocarbamate) residues are readily converted in part to ETU if processing includes a heating step. Levels of ETU in processed products bear no relationship to the ETU levels in the raw commodities. ETU levels in processed commodities depend on the levels of EBDC which are present at crucial stages where heating takes place and the duration and temperature of that heating.

Under a US Food and Drug Administration monitoring programme (1990-1991) a variety of baby foods (864 samples) were monitored for pesticide residues. ETU residues were detected in 65 samples; the highest levels detected were 0.06 mg/kg. In 1989-90 in the USA a large survey of food items (approximately 300 samples each of 19 different raw and processed commodities) was conducted for dithiocarbamate and ETU residues. No measurable residues of ETU (LOD 0.001 mg/kg) were found in 82% of the samples. All ETU residue levels were less than 0.1 mg/kg. ETU was not detected (LOD 0.005 mg/kg) in any of 100 commercial grape juice samples in the USA taken from producers using grapes from areas where dithiocarbamate fungicides were used.

The Meeting agreed that MRLs for ETU did not assist in deciding whether GAP in the use of EBDCs was being followed. The Meeting agreed to recommend the withdrawal of all MRLs for ETU.

Normally the regulation of a residue in the raw agricultural commodity sets a limit

on the levels in processed food because some or all of the residue is lost during the process. The levels of ETU in the processed commodity bear no relation to the levels in the raw agricultural commodity. ETU is more likely to occur in processed food where it can be generated by the heating of EBDC residues during the process.

Processing trials demonstrate that under some conditions considerable conversion of EBDCs to ETU can occur. Processing studies available to the Meeting showed that an initial commercial washing and cleaning of the raw agricultural commodity removes much of the EBDC, which is a surface residue, and reduces the potential for ETU formation.

The extensive food surveys in the USA, which have included many processed foods, have generally found only low levels of ETU (less than 0.1 mg/kg) and only in a minority of samples (fewer than 20%). The data suggest that, if good processing practices are followed, ETU residues in processed food would rarely exceed 0.1 mg/kg.

The 1990 JMPR reported results of the monitoring of food in commerce or at consumption for ETU in Canada for 1975-1985. Residues in a number of processed products were all below the limit of detection (0.05 mg/kg). Limited 1989-1990 data from Canada on a variety of fruit juices and drinks showed residues to be below 1 µg/kg.

RECOMMENDATIONS

On the basis that ETU residues in raw agricultural commodities are not a useful indicator of good agricultural practice and bear no relationship to potential ETU residues in processed commodities the Meeting recommended the withdrawal of previous recommendations for ETU maximum residue levels.

Definition of residue: ethylenethiourea.

Commodity		Recommended MRL, mg/kg	
CCN	Name	New[1]	Previous TMRL
VR 0577	Carrot	W	0.01*
VS 0624	Celery	W	0.01*
VL 0482	Lettuce, Head	W	0.01*
VR 0589	Potato	W	0.01*

[1] W: the previous recommendation is withdrawn.

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