**PESTICIDE RESIDUES IN FOOD - 1982**

Sponsored jointly by FAO and WHO

**EVALUATIONS 1982**

Data and recommendations of the joint meeting

of the FAO Panel of Experts on Pesticide Residues

in Food and the Environment and the

WHO Expert Group on Pesticide Residues

Rome, 23 November - 2 December 1982

Food and Agriculture Organization of the United Nations

Rome 1983

CHLORDANE

CHEMICAL STRUCTURE 1

Explanation

Chlordane was evaluated in the Joint Meetings of 1963, 1965,

1967, 1969, 1970, 1972, 1974 and 1977 (FAO/WHO, 1964, 1965, 1968,

1970, 1971, 1973, 1975 and 1978)1/. Several acute oral studies and a

90-day subchronic feeding study in rats, of Industrial Bio-Test

Laboratories (IBT) origin, have been identified, which have not been

validated. However, the no-effect level(s) (NEL) and ADI were not

taken from the results of these data.

Additional data pertaining to metabolism, absorption,

distribution and excretion have been made available and are reviewed

in this addendum.

EVALUATION FOR ACCEPTABLE DAILY INTAKE

BIOCHEMICAL ASPECTS

Absorption, Distribution and Excretion

More than 90% of single oral doses of high purity chlordane

(98% + of a 3:1 mixture of cis- and trans-chlordane), cis-chlordane

and trans-chlordane were eliminated from rats in the excreta within

7 days after treatment, with faeces being the major route of

elimination for both sexes. Single oral doses of oxychlordane resulted

in only 21% of the administered dose appearing in rat excreta after 7

days, demonstrating a greater potential for this metabolite of

chlordane to accumulate in animals than the cis- and trans-chlordane

isomers. Continuous feeding of cis- and trans-chlordane separately in

the diet of rats for 14 days demonstrated preferential elimination of

the cis-isomer. After 14 days of treatment, 75% of the total cis- and

65% for the trans-chlordane were eliminated which indicates that in

long-term exposures the trans-isomer would contribute a relatively

greater amount to the body burden of the exposed animal than would the

cis-isomer (Barnett and Dorough 1974).

1/ See Annex 2 for WHO and FAO documentation.

In a separate study, administration of cis-chlordane or trans-

chlordane in single oral doses to rats via stomach intubation resulted

in 86% of the total cis- and 66% of the total trans-chlordane being

eliminated within 7 days after treatment. Furthermore, the rate of

excretion of cis-chlordane (59% in 24 h) was more rapid than that of

trans-chlordane (27%) (Tashiro and Matsumura 1977). There were no

apparent sex differences with respect to the rate of dissipation, nor

did males and females differ in the nature and relative concentrations

of metabolites (Barnett and Dorough 1974).

Biotransformation

The metabolism of chlordane, per se, in rats resulted in the

formation of dichlorochlordene via dehydrogenation followed by

epoxidation to oxychlordane and subsequent hydroxylation. There was

also direct hydroxylation of both the cis and trans-isomers to

1-exo-hydroxydihydrochlordene with excretion in the faeces and urine

as the glucuronide (Tashiro and Matsumara 1977).

The level of residues in tissues of rats was generally low,

except in fat. Metabolism of trans-chlordane resulted in higher tissue

residues than cis-chlordane, primarily because of the formation of

1,2-dichlorochlordane, which was favoured for the trans-isomer, thus

leading to higher levels of oxychlordane. Feeding female rats high

purity chlordane at levels up to 25 ppm for 56 days resulted in

chlordane-14C equivalent in the fat at levels 3-4 times that in the

diet. These levels did not plateau at the end of the treatment period.

However, after 4 weeks removal from the diet, tissue levels were

reduced by 60%. The levels of residues in tissues (other than fat)

after 56 days of treatment were as follows (as the fraction of the

administered dose): liver (1/8) > kidney (1/10) > brain (1/25)

> muscle (1/50). Oxychlordane was the major component of all tissues

and, after removing chlordane from the diet, contributed most of the

14C residue in tissues (Barnett and Dorough 1974; Tashiro and

Matsumura 1977; Street and Blau 1972).

The metabolic intermediates of cis- and trans-chlordane, as well

as oxychlordane, were further converted to two major metabolites,

1-exo-hydroxy-2-chlorochlordene and 1-exo-hydroxy-2-chloro-2,3

epoxychlordene. These latter metabolites were not readily degraded

further in rats and may accumulate as terminal residues in the animal.

Neither appeared to be more toxic than the cis- or trans-isomers, but

this has not been verified in mammals (Tashiro and Matsumura 1977).

Rat and human in vitro liver preparations displayed almost

identical degradation abilities for trans-chlordane, but not for

trans-nonachlor, which accumulated in humans but not in rats. Trans-

nonachlor is a major constituent (7%) of technical chlordane. Both

single oral dosing (0.05 µ Ci) and four-week dietary administration

(100 ppm) of trans-nonachlor to rats have demonstrated the overall

metabolic pattern and rate of excretion to be the same as for trans-

chlordane. The fact that trans-nonachlor was not metabolized

efficiently by human liver cells may be due to the inability to form

trans-chlordane, which represents a significant difference from the

rat (Tashiro and Matsumura 1978).

A proposed metabolic pathway for chlordane in mammalian species

is shown in Figure 1.

TOXICOLOGICAL STUDIES

Long-Term Study

Rat

The data submitted to the 1982 Meeting for evaluation of long-

term effects were not sufficient in many critical areas of data

content and were, therefore, inadequate for inclusion in this

monograph.

COMMENTS

The ADI and long-term studies considered in support of the ADI

were evaluated by the JMPR in 1967 and 1977 (FAO/WHO 1968 and 1978).

Additional data on metabolism have been received.

Significant differences in the metabolism of chlordane between

rats and humans have been identified. Specifically, trans-nonachlor, a

major constituent of technical chlordane, is poorly metabolized in

humans. The Meeting was concerned about the accumulation of trans-

nonachlor in humans. However, this concern was partly alleviated by

the information that only very low levels (0.1 ppm on milk fat basis)

appear to have been found in human milk samples.

The Meeting was informed that studies pertaining to chlordane

toxicology were in progress at the Research Institute for Animal

Science in Biochemistry and Toxicology in Japan. The Meeting hopes

that this data will eventually be made available to it.

Pending receipt of a study on oxychlordane of at least 90 days

duration in the rat, the Meeting assigned a temporary ADI to

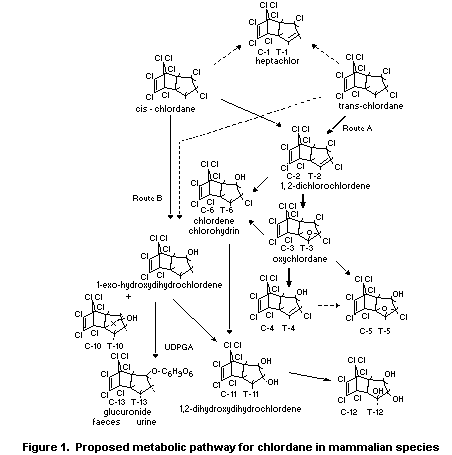
chlordane.

TOXICOLOGICAL EVALUATION

Level Causing no Toxicological Effect

Rat: 5 mg/kg in the diet, equivalent to 0.25 mg/kg bw

Dog: 3 mg/kg in the diet, equivalent to 0.075 mg/kg bw



Estimate of Temporary Acceptable Daily Intake in Man

0 - 0.001 mg/kg bw

FURTHER WORK OR INFORMATION

Required (by 1984)

A study of at least 90 days' duration in rats using oxychlordane.

Desirable

1. Submission of the ongoing studies in Japan.

2. Submission of monitoring data pertinent to the oxychlordane and

trans-nonachlor levels found in humans.

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1974 Agric. Food Chem. 22:612-619.

Street, J.C. and Blau, S.E. Oxychlordane: accumulation in rat

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chlordane. J. Agric. Food Chem. 20:395-397.

Tashiro, S. and Matsumura, F. Metabolic routes of cis- and trans-

1977 chlordane in rats. J. Agric. Food Chem. 25:872-880.

1978 Metabolic routes of trans-nonachlor and related chlordane

components in rat and man. Arch. Environm. Contam. Toxicol.

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See Also:

[Toxicological Abbreviations](http://www.inchem.org/documents/eintro/eintro/abreviat.htm)

[Chlordane (EHC 34, 1984)](http://www.inchem.org/documents/ehc/ehc/ehc34.htm)

[Chlordane (HSG 13, 1988)](http://www.inchem.org/documents/hsg/hsg/hsg013.htm)

[Chlordane (PDS)](http://www.inchem.org/documents/pds/pds/pest36_e.htm)

[Chlordane (PIM 574)](http://www.inchem.org/documents/pims/chemical/pim574.htm)

[Chlordane (FAO Meeting Report PL/1965/10/1)](http://www.inchem.org/documents/jmpr/jmpmono/v065pr09.htm)

[Chlordane (FAO/PL:1967/M/11/1)](http://www.inchem.org/documents/jmpr/jmpmono/v067pr06.htm)

[Chlordane (FAO/PL:1969/M/17/1)](http://www.inchem.org/documents/jmpr/jmpmono/v069pr07.htm)

[Chlordane (AGP:1970/M/12/1)](http://www.inchem.org/documents/jmpr/jmpmono/v070pr03.htm)

[Chlordane (WHO Pesticide Residues Series 2)](http://www.inchem.org/documents/jmpr/jmpmono/v072pr06.htm)

[Chlordane (WHO Pesticide Residues Series 4)](http://www.inchem.org/documents/jmpr/jmpmono/v074pr09.htm)

[Chlordane (Pesticide residues in food: 1977 evaluations)](http://www.inchem.org/documents/jmpr/jmpmono/v077pr13.htm)

[Chlordane (Pesticide residues in food: 1984 evaluations)](http://www.inchem.org/documents/jmpr/jmpmono/v84pr12.htm)

[Chlordane (Pesticide residues in food: 1986 evaluations Part II Toxicology)](http://www.inchem.org/documents/jmpr/jmpmono/v86pr03.htm)