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 **EVALUATION OF THE TOXICITY OF PESTICIDE RESIDUES IN FOOD**

 The content of this document is the result of the deliberations of the

 Joint Meeting of the FAO Committee on Pesticides in Agriculture and

 the WHO Expert Committee on Pesticide Residues, which met in Rome,

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 Food and Agriculture Organization of the United Nations

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 Pesticides in Agriculture and the WHO Expert Committee on Pesticide

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 CHLORDANE

 Chemical name

 1,2,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetrahydro-4,7,

 methanoindane or

 1,2,4,5,6,7,10,10-octachloro-4-7-8-9-tetrahydro-4,7-methyleneindane or

 1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindane.

 Synonyms

 Toxichlor; Octachlorodihydro-dicyclopentadiene; Octachlor.

 Empirical formula

 C10H6Cl8

 Structural formula

 

 BIOLOGICAL DATA

 Biochemical aspects

 Chlordane is absorbed from the alimentary tract. It is stored in

 adipose tissue of sheep, goats, and cows and accumulates in the milk.

 Cows' milk contained 0.1 to 0.2 ppm of chlordane after the animals had

 been fed a diet containing a concentration equivalent to 0.36 to 0.42

 mg/kg body-weight for 150 days (Carter et al., 1953). Some

 water-soluble metabolites are excreted. Organically bound chlorine is

 excreted in the urine of rabbits (Stohlman & Smith, 1950).

 Both technical chlordane and one of its pure isomers

 (gamma-chlordane) have been shown to have stimulating effects on rat

 liver microsomes for the metabolism of certain drugs (Burns et al.,

 1965; Hart & Fouts, 1963; Hart et al., 1963; Kutzman et al., 1964).

 Acute toxicity

 Animal Route LD50 mg/kg References

 body-weight

 Rat Oral 200-590\* Ambrose et al., 1953

 Ingle, 1954

 Stohlman et al., 1950

 Oral 335-430 Gaines, 1960

 150-225 Ingle, 1954

 Mouse Oral 430 US Food & Drug Admin., 1947

 Rabbit Oral 100-300\* Stohlman et al., 1950

 20-40 Ingle, 1954

 Goat Oral 180 Welch, 1948

 Sheep Oral 500-1000 Welch, 1948

 Chicken Oral 220-230 Turner & Eden, 1952

 \* The differences are explained by the use of different solvents, and

 by the fact that the chlordane mentioned in the older literature

 contained a considerable amount of the very toxic hexachlorocyclo

 pentadiene (Ingle, 1954; Lehman, 1952).

 Man. In adults a dose of 104 mg/kg proved fatal (Derbes et al.,

 1955), An 18-year-old female showed convulsions but recovered after a

 dose of approximately 30 mg/kg (amount retained after vomiting

 estimated to be 10 mg/kg). In two infants respectively 15 months and 3

 years of age, 10 and 40 mg/kg gave severe poisoning (Stormont &

 Conley, 1955).

 Short-term studies

 Rat. When a diet containing 1000 ppm of chlordane was fed to 12

 male rats, all of them died within 10 days. At 500 ppm 12/12 died

 within 70 days, at 300 ppm 9/12 were alive after 100 days (Stohlman et

 al., 1950).

 Daily oral doses of 6.25-25 mg/kg given to 5 rats for 15 days

 produced no tremors or convulsions, but daily doses of 50 mg/kg

 produced toxic symptoms and 2 of the animals died. With 100 mg/kg all

 the animals died (Ambrose et al., 1953). Intracytoplasmic bodies in

 the liver-cells were found at all levels and their number was in

 proportion to the dose used (Ambrose et al., 1953).

 Rats in groups of 12 (6 females and 6 males) were fed for periods

 up to 9 months, 2.5 ppm or 25 ppm of a sample of technical chlordane

 containing 60-75% chlordane and 25-40% unrelated products.

 Centrolobular cell hypertrophy, peripheral migration of cytoplasmic

 granules and the presence of cytoplasmic bodies were observed in 1

 male at 2.5 ppm and in 5 males at 12.5 ppm (Ortega et al., 1957).

 Dog. Chlordane was given in varying oral doses to dogs for 7

 days; convulsions were seen in 1 dog at 200 mg/kg (lowest dose) but

 700 mg/kg (highest dose) did not produce any effect (Batte & Turk,

 1948).

 When 4 groups of 2 to 4 dogs were given chlordane orally in doses

 between 5 and 80 mg/kg body-weight daily they all died within periods

 of 25 days to 93 weeks (Lehman, 1952).

 Sheep. Chlordane administered by stomach-tube to sheep in a

 dose of 0.5 g/kg body-weight produced toxic symptom (incoordination,

 partial blindness) in 5 to 6 days. A dose of 1 g/kg body-weight

 produced severe respiratory and nervous symptoms at 16 hours and death

 after 48 hours (Welch, 1948).

 Long-term studies

 Rat. In one experiment published in 1952, 24 rats (12 of each

 sex) were given 2.5, 25 and 75 ppm of chlordane in the diet for 2

 years. The sample of chlordane used had an LD50 of 450 mg/kg (Lehman,

 1951). It was found that 25 and 75 ppm gave moderate to severe signs

 of intoxication; 2.5 ppm still caused liver histological damage, the

 nature of which has not been reported (Lehman, 1952).

 In another experiment, groups of 40 rats (20 males and 20

 females) were fed concentrations of 5, 10, 30, 150 and 300 ppm of

 "technical chlordane" in the diet over a 2-year period. Throughout the

 experiment tremors and convulsions appeared or could be induced at 30

 or more ppm. Following fasting, no neurological symptoms appeared at 5

 or 10 ppm. Growth rate was affected at 150 or 300 ppm. Liver

 histological damage was observed in the form of hypertrophy of

 centrolobular cells, cytoplasmic oxyphilia and hyalinization, nuclear

 karyorhexis or cellular pyknosis, presence of fat in the cytoplasm and

 some bile-duct proliferation. These changes were obvious at 150-300

 ppm slight at 30 ppm, minimal at 10 ppm and absent at 5 ppm (Ingle,

 1952).

 In a subsequent experiment from the same laboratory, which was

 carried on between late 1953 and late 1955, "technical chlordane of

 recent manufacture" was used. Groups of 40 rats were given chlordane

 at 2.5, 5, 10, 25, 50, 75, 150 or 300 ppm. A control group was given

 no chlordane. Changes concerning food consumption, growth and

 mortality were seen only in the 300 ppm group. Liver cell changes were

 not present in the animals given 2.5-25 ppm. At 50 ppm only

 "cytoplasmic peripheralization" was present. At higher doses the

 changes were as those previously described (Ingle, 1955).

 In a study published in 1953 a sample of chlordane exhibiting an

 oral LD50 for the rat of 590 mg/kg was used. Groups of 5 rats of each

 sex were given 0, 10, 20, 40, 80, 160, 320, 640 or 1280 ppm of

 chlordane in their diets for approximately 407 days. The animals at

 640 and 1280 ppm died early. At lower dosages, survival was

 unaffected. Increased liver-weight (in comparison with the control

 group) was observed over 320 ppm. In a sample of liver of a male at

 320 ppm the average nuclear volume was 377µ3 compared to 268µ3 in a

 control rat. Cytoplasmic vacuoles containing fat and clusters of

 granules at the periphery of the cytoplasm were often seen. In the

 males they were equivocal at 10 ppm, absent at 20 ppm and infrequent

 at 40 ppm. In the females these lesions were common and were seen only

 at 80 ppm and over (Ambrose et al., 1953).

 Comments on experimental studies reported

 It appears that at least in two reports concerning the rat a dose

 level was found at which no histopathological changes occurred

 (Ambrose et al., 1953; Ingle, 1955). Such dose levels appear to be in

 the order of 20-25 ppm in the diet (1-1.25 mg/kg/day). This figure

 applies to samples of "late" chlordane and would require clear

 specifications concerning the formulations of chlordane falling into

 this category. This cannot be done at the present time because of

 incomplete information about chemical structure and toxicity of

 impurities occurring in technical chlordane.

 EVALUATION

 Estimate of acceptable daily intake for man

 Because:

 (i) there is still some doubt about the composition of the chlordane

 entering into commerce;

 (ii) some metabolic problems, e.g. the effects of chlordane on the

 hydroxylation of steroids, are not resolved (Burns et al., 1965;

 Kutzman et al., 1964);

 (iii) of the fact that, with one or two small exceptions, the animal

 experiments have been limited to only one species, viz. the rat;

 (iv) of the possible persistence of this compound in the environment,

 the Committee considers that caution should still be exercised, and

 that every effort should be made to see that the intake of chlordane

 for man should be kept at the lowest possible level.

 Further work required

 Standardization of the technical product. Investigation on the

 nature and toxicity of the residue occurring in the plant.

 Determination of a maximum no-effect level in other species than the

 rat. Long-term toxicity in other species than the rat. Reproduction

 studies.

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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/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: 1982 evaluations)](http://www.inchem.org/documents/jmpr/jmpmono/v82pr08.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)