

TOXICOLOGY OF PERSISTENT ORGANIC POLLUTANTS (POPs)

The following terms, used in discussing the toxicology of persistent organic pollutants, are commonly used in the toxicological literature

LD₅₀: LD₅₀ is a standardized measure for expressing and comparing the toxicity of chemicals. LD₅₀ is the dose that kills half (50%) of the animals tested (LD = "lethal dose"). The animals are usually rats or mice, although rabbits, guinea pigs, hamsters, and so on are sometimes used. In all these tests, the dose must be calculated relative to the size of the animal. The most common units are milligrams of chemical per kilogram of test animal (mg/kg or ppm).

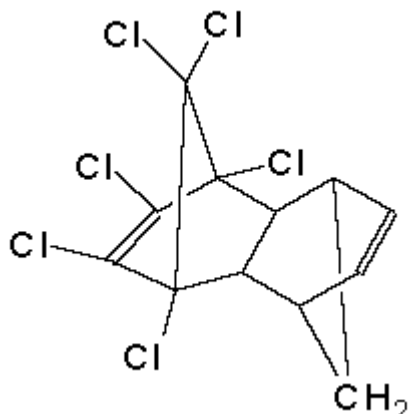
LC₅₀

LC stands for "Lethal Concentration". LC values usually refer to the concentration of a chemical in air but in environmental studies it can also mean the concentration of a chemical in water. For inhalation experiments, the concentration of the chemical in air that kills 50% of the test animals in a given time (usually four hours) is the LC50 value.

Note: Because a single test may kill as many as 100 animals, the United States and other members of the OECD agreed in December 2000 to phase out the LD₅₀ test in favour of alternatives that greatly reduce (or even eliminate) deaths of the test animals.

ALDRIN

Chemical properties



chemical name:

1,2,3,4,10,10-Hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalene.

Aldrin is a pesticide used to control soil insects such as termites, corn rootworm, wireworms, rice water weevil, and grasshoppers. It has been widely used to protect crops such as corn and potatoes, and has been effective to protect wooden structures from termites. Aldrin is readily metabolized to dieldrin by both plants and animals. As a result, aldrin residues are rarely found in foods and animals, and then only in small amounts. It binds strongly to soil particles and is very resistant to leaching into groundwater. Volatilization is an important mechanism of loss from the soil. Due to its persistent nature and hydrophobicity, aldrin is known to bioconcentrate, mainly as its conversion products.

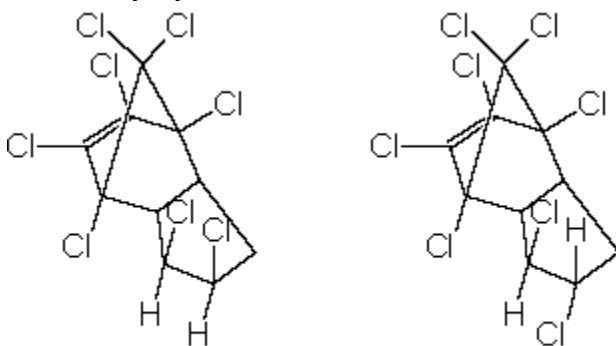
Aldrin is toxic to humans; the lethal dose of aldrin for an adult man has been estimated to be about 5g, equivalent to 83 mg/kg body weight. Signs and symptoms of aldrin intoxication may include headache, dizziness, nausea, general malaise, and vomiting, followed by muscle twitchings, myoclonic jerks, and convulsions. Occupational exposure to aldrin, in conjunction with dieldrin and endrin, was associated with a significant increase in liver and biliary cancer, although the study did have some limitations, including a lack of quantitative exposure information. There is limited information that cyclodienes, such as aldrin, may affect immune responses.

The acute oral LD₅₀ for aldrin in laboratory animals is in the range of 33 mg/kg body weight for guinea pigs to 320 mg/kg body weight for hamsters. Reproductive effects in rats were observed when pregnant females were dosed with 1.0 mg/kg aldrin subcutaneously. Offspring experienced a decrease in the median effective time for incisor teeth eruption and increase in the median effective time for testes descent. There is, as yet, no evidence of a teratogenic potential for aldrin. IARC has concluded that there is inadequate evidence for the carcinogenicity of aldrin in humans, and there is only limited evidence in experimental animals.

As aldrin is readily and rapidly converted to dieldrin in the environment its fate is closely linked to that of dieldrin. Aldrin is readily metabolised to dieldrin in both animals and plants, and therefore aldrin residues are rarely present in animals and then only in very small amounts. Residues of aldrin have been detected in fish in Egypt, the average concentration was 8.8 µg/kg, and a maximum concentration of 54.27 µg/kg.

The average daily intake of aldrin and dieldrin was calculated to be 19µg/person in India, and 0.55 µg/person in Vietnam. Dairy products, such as milk and butter, and animal meats are the primary sources of exposure.

CHLORDANE
Chemical properties



Cis

Trans

Chemical Name: 1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1H-indene

Chlordane is a broad spectrum contact insecticide that has been used on agricultural crops including vegetables, small grains, maize, other oilseeds, potatoes, sugarcane, sugar beets, fruits, nuts, cotton and jute. It has also been used extensively in the control of termites. Chlordane is highly insoluble in water, and is soluble in organic solvents. It is semi-volatile and can be expected to partition into the atmosphere as a result. It binds readily to aquatic sediments and bioconcentrates in the fat of organisms as a result of its high partition coefficient (log KOW = 6.00). Action to ban the use of chlordane has been taken in Austria, Belgium, Bolivia, Brazil, Chile, Columbia, Costa, Rica, Denmark, Dominican Republic, EU, Kenya, Korea, Lebanon, Liechtenstein, Mozambique, Netherlands, Norway, Panama, Paraguay, Philippines, Poland, Portugal, Santa Lucia, Singapore, Spain, Sweden, Switzerland, Tonga, Turkey, United Kingdom, Yemen and Yugoslavia. Its use is severely restricted or limited to non-agricultural uses in Argentina, Belize, Bulgaria, Canada, China, Cyprus, Dominica, Egypt, Honduras, Indonesia, Israel, Mexico, New Zealand, South Africa, Sri Lanka, USA and Venezuela.

Early studies on occupational exposure found no toxic effects in workers involved in the production of chlordane with up to 15 years of exposure. In a survey of 1105 workers associated with pest control, most of whom used chlordane, however, only three attributed illness to it (mild dizziness, headache, weakness). Chlordane exposure has not been associated with increased risk of mortality from cancer. Significant changes in the immune system were reported in individuals who complained of health effects which they associated with chlordane exposure.

Acute oral toxicity for chlordane in laboratory animals ranges from 83 mg/kg for pure cis-chlordane in rats to 1720 mg/kg for hamsters. Subchronic (90 day) inhalation exposure in rats and monkeys at doses up to 10 mg/m³ resulted in increases in the concentration of cytochrome P-450 and microsomal protein in rats. The results of this study provide a no-effect level in the rat of approximately 0.1 mg/m³ and in excess of in 10 mg/m³ the monkey.

Mice were fed diets containing chlordane for 6 generations. At 100 mg/kg, viability was decreased in the first and second generation, and no offspring were produced in the third generation. At 50 mg/kg, viability was decreased in the third and fourth generation, and at 25 mg/kg no statistically significant effects were observed after 6 generations. Offspring of rabbits administered chlordane orally on the 5th - 18th days of gestation did not exhibit changes in behaviour, appearance or body weight were observed, and no teratogenic effects were reported. IARC has concluded that, while there is inadequate evidence for the carcinogenicity of chlordane in humans, there is sufficient evidence in experimental animals. IARC has classified chlordane as a possible human carcinogen (Group 2B).

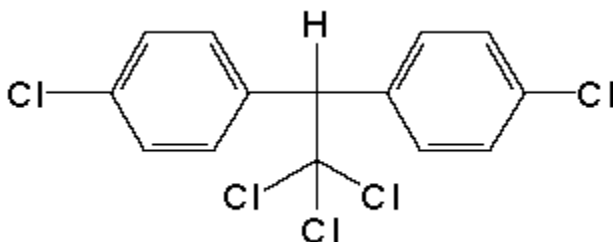
The acute toxicity of chlordane to aquatic organisms is quite variable, with 96-hour LC₅₀ values as low as 0.4 µg/L for pink shrimp. The acute oral LD₅₀ to 4-5 month old mallard ducklings was

1200 mg/kg body weight. The LC50 for bobwhite quail fed chlordane in their diet for 10 weeks was 10 mg/kg diet. The half-life of chlordane in soil has been reported to be approximately one year. This persistence, combined with a high partition coefficient, provides the necessary conditions for chlordane to bioconcentrate in organisms. Bioconcentration factors of 37,800 for fathead minnows and 16,000 for sheepshead minnow have been reported. Data suggest that chlordane is bioconcentrated (taken up directly from the water) as opposed to being bioaccumulated (taken up by water and in food). The chemical properties of chlordane (low water solubility, high stability, and semi-volatility) favour its long range transport, and chlordane has been detected in arctic air, water and organisms.

Chlordane exposure may occur through food but, due to its highly restricted uses, this route does not appear to be a major pathway of exposure. The isomer gamma-chlordane was detected in only 2 (8.00 and 36.17 µg/kg wet weight) of 92 samples of Egyptian fish and in 2 of 9 samples (2.70 and 0.48 ppb) of food products imported into Hawaii from western Pacific rim countries. Chlordane has been detected in indoor air of residences of both Japan and the US. Exposure to chlordane in the air may be an important source of exposure to the US population. Mean levels detected in the living areas of 12 homes in New Jersey prior to and after treatment for termites ranged from 0.14 to 0.22 µg/m³, respectively. Mean levels in non-living areas (crawl spaces and unfinished basements) were higher; 0.97 µg/m³ before treatment and 0.91 µg/m³ after treatment. Levels detected in New Jersey homes before and after regulations restricting chlordane use fell from 2.6 to 0.9 µg/m³.

DDT

Chemical properties



Chemical Name: 1,1'-(2,2,2-Trichloroethylidene)bis(4-chlorobenzene)

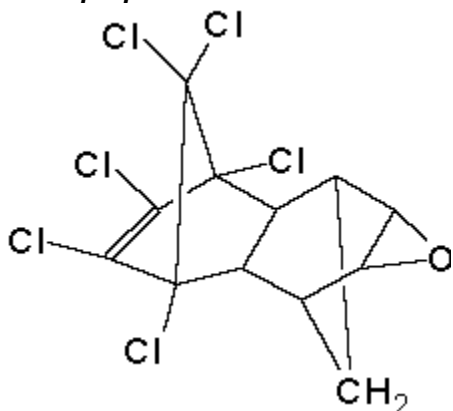
DDT was widely used during the Second World War to protect the troops and civilians from the spread of malaria, typhus and other vector borne diseases. After the war, DDT was widely used on a variety of agricultural crops and for the control of disease vectors as well. It is still being produced and used for vector control. Growing concern about adverse environmental effects, especially on wild birds, led to severe restrictions and bans in many developed countries in the early 1970s. The largest agricultural use of DDT has been on cotton, which accounted for more than 80% of the US use before its ban there in 1972. DDT is still used to control mosquito vectors of malaria in numerous countries.

DDT is highly insoluble in water and is soluble in most organic solvents. It is semi-volatile and can be expected to partition into the atmosphere as a result. Its presence is ubiquitous in the environment and residues have even been detected in the arctic. It is lipophilic and partitions readily into the fat of all living organisms and has been demonstrated to bioconcentrate and biomagnify. The breakdown products of DDT, 1,1-dichloro-2,2-bis(4-chlorophenyl)ethane (DDD or TDE) and 1,1-dichloro-2,2-bis(4-chlorophenyl)ethylene (DDE), are also present virtually everywhere in the environment and are more persistent than the parent compound.

The use of DDT has been banned in 34 countries and severely restricted in 34 other countries.

DIELDRIN

Chemical properties



CAS Chemical Name: 3,4,5,6,9,9-Hexachloro-1a,2,2a,3,6,6a,7,7a-octahydro-2,7:3,6-dimetanonaph[2,3-*b*]oxirene.

Dieldrin has been used in agriculture for the control of soil insects and several insect vectors of disease but this latter use has been banned in a number of countries due to environmental and human health concerns. Principle contemporary uses are restricted to control termites and wood borers and against textile pests (WHO, 1989). Dieldrin binds strongly to soil particles and hence is very resistant to leaching into groundwater. Volatilization is an important mechanism of loss from the soil and, because of its persistent nature and hydrophobicity, dieldrin is known to bioconcentrate.

Action to ban dieldrin has been taken in many countries, including Bulgaria, Ecuador, the EU, Hungary, Israel, Portugal, Singapore, Sweden, and Turkey. Its use is severely restricted in numerous countries, including Argentina, Austria, Canada, Colombia, Cyprus, India, Japan, New Zealand, Pakistan, USA and Venezuela.

In a study using human volunteers, the subjects received dieldrin daily for 2 years. All the volunteers continued in excellent health, and clinical, physiological and laboratory findings remained essentially unchanged through the exposure period and an 8 month follow up. In a study of workers from a plant involved in the manufacture of aldrin, dieldrin and endrin, a statistically significant increase in liver and biliary tract cancers was observed, although the study did have some limitations, including lack of quantitative exposure information.

In laboratory studies, acute oral LD₅₀ values in the range of 37 mg/kg body weight in rats to 330 mg/kg in hamsters have been found for dieldrin. As with other organochlorine compounds, the liver is the major target organ in rats, with effects that included increased liver/body weight ratio, hypertrophy and histopathological changes. The no observed adverse effect level (NOAEL) in rats is 0.5 mg/kg diet, equal to 0.025 mg/kg body weight/day. When rats were fed dieldrin in their diet over three generations, no changes in reproductive capacity were observed at any dose level tested. A NOAEL of 2 mg dieldrin /kg diet has been set for reproduction in rats. There was no evidence for teratogenic potential in studies in rats, mice or rabbits using oral doses of up to 6 mg/kg body weight. Abnormal development and fetotoxicity were observed in hamsters and mice, however, these results are unlikely to be of significance in view of the maternal toxicity noted at the high dose levels. There is limited evidence that cyclodienes such as dieldrin may affect immune responses. IARC has concluded that there is inadequate evidence for the carcinogenicity of dieldrin in humans, and limited evidence in experimental animals and has been classified by IARC in Group 3.

Dieldrin has low phytotoxicity. Plants are affected only by application rates much higher than suggested use rates. The acute toxicity of dieldrin is quite variable for aquatic invertebrates, with insects being the most sensitive group (values range from 0.2-40 µg/L). It is highly toxic to most species of fish tested in the laboratory (values range from 1.1-41 µg/L). Acute toxicity of dieldrin in frogs (96-h LC₅₀) ranged from 8.7 µg/L for *Rana catesbeiana* tadpoles to 71.3µg/L for the tadpoles of *Rana pipiens*. Spinal deformities in embryo-larval tests were observed at concentrations as low as 1.3 µg/L for *Xenopus laevis* after a 10 day exposure.

The acute toxicity of dieldrin to avian species varies widely, with acute oral LD50 values in the range of 26.6 in pigeons to 381 mg/kg in mallard ducks. Mallard ducklings were exposed to dieldrin in the diet for 24 days. A 24 d NOAEL of 0.3µg dieldrin/g diet, based on growth impairment, was determined. Reproduction success in birds has not been consistently affected in the absence of maternal toxicity.

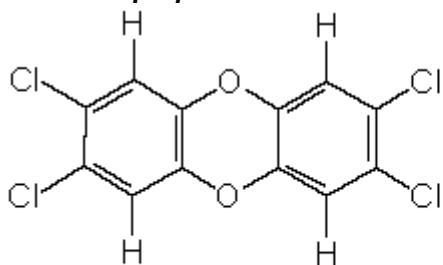
The acute LD50 of dieldrin to four species of voles range from 100 to 210 mg/kg body weight, suggesting that these microtine rodents are less susceptible than laboratory rodents to dieldrin. In another study, white tailed deer (*Odocoileus virginianus*) were fed diet containing dieldrin for up to 3 years. Adult survival was not affected, and fertility and *in utero* mortality was comparable for all groups. Fawns from treated does were smaller at birth, experienced greater postpartum mortality and weight gain was reduced. Blesbuck (*Damaliscus dorcas phillipsi*) were fed diets containing dieldrin for 90 days. None of the animals fed 5 or 15 mg/kg diet died during the study period, but all animals at the higher dose levels died within 24 days.

The half life of dieldrin in temperate soils is approximately 5 years. This persistence, combined with high lipid solubility, provides the necessary conditions for dieldrin to bioconcentrate and biomagnify in organisms. Bioconcentration factors of 12,500 and 13,300 have been reported for guppies and sculpins, respectively. It is likely that dieldrin is bioconcentrated by aquatic organisms rather than bioaccumulated. Dieldrin's chemical properties (low water solubility, high stability, and semi-volatility) favour its long range transport, and dieldrin has been detected in arctic air, water and organisms.

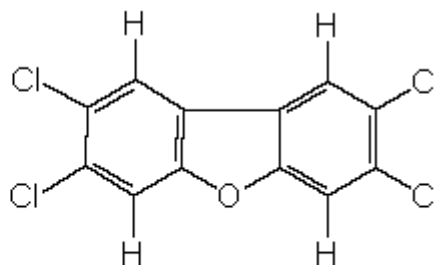
Dieldrin residues have been detected in air, water, soil, fish, birds and mammals, including humans and human breast milk. As aldrin is readily and rapidly converted to dieldrin in the environment and in organisms, the levels of dieldrin detected likely reflect the total concentrations of both compounds. In Egypt, the estimated dietary intake of dieldrin by breast fed infants of 1.22 µg/kg body weight/ day. Diet is the main source of exposure to the general public. Dieldrin was the second most common pesticide detected in a survey of US pasteurized milk, detected in 172 of the 806 composite samples tested, with a maximum level of 0.003 ppm. Dieldrin residues were detected in 9 of 602 (1.5%) samples of domestic animal fats and eggs in Canada, with a maximum of 0.050 mg/kg. Dieldrin was also detected in Spanish meat, residues of 20 to 40 ppb were detected in the fat of 8 to 15% of pork products (meat, cured sausage, pork bologna) and in 28% fresh poultry sausage. Dieldrin residues were detected in Oriental party beans at 3.45 ppb. The average daily intake of aldrin and dieldrin in India was calculated to be 19 µg/person, exceeding the acceptable daily intake of 6.0 µg/60 kg of body weight recommended by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Dairy products, such as milk and butter, and animal meats were the primary sources of exposure. Exposure through food intake has been estimated at 0.55 µg/person in Vietnam.

POLYCHLORINATED DIBENZO - *p* - DIOXINS AND FURANS

Chemical properties



2,3,7,8-TCDD



2,3,7,8-TCDF

Dioxins

Congener Group	Molecular weight (g/molecular) (Pa X 10 ⁻³)	Vapour Pressure	Water Solubility (mg/m ³)	Log KOW
M1CDD	218.5	73-75	295-417	4.75-5.00
D2CDD	253.0	2.47-9.24	3.75-16.7	5.60-5.75
T3CDD	287.5	1.07	8.41	6.35
T4CDD	322.0	0.00284-0.275	0.0193-0.55	6.60-7.10
P5CDD	356.4	0.00423	0.118	7.40
H6CDD	391.0	0.00145	0.00442	7.80
H7CDD	425.2	0.000177	0.0024	8.00
O8CDD	460.0	0.000953	0.000074	8.20

Polychlorinated dibenzo-*para*-dioxins (dioxins) and polychlorinated dibenzofurans (furans) are two groups of planar tricyclic compounds that have very similar chemical structures and properties. They may contain between 1 and 8 chlorine atoms; dioxins have 75 possible positional isomers and furans have 135 positional isomers. They are generally very insoluble in water, are lipophilic and are very persistent. The chemical properties of each of the isomers has not been elucidated, further complicating a discussion of their properties which vary with the number of chlorine atoms present. Neither dioxins nor furans are produced commercially, and they have no known use. They are by-products resulting from the production of other chemicals. Dioxins may be released into the environment through the production of pesticides and other chlorinated substances. Furans are a major contaminant of PCBs. Both dioxins and furans are related to a variety of incineration reactions, and the synthesis and use of a variety of chemical products. Dioxins and furans have been detected in emissions from the incineration of hospital waste, municipal waste, hazardous waste, car emissions, and the incineration of coal, peat and wood. Of the 210 dioxins and furans, 17 contribute most significantly to the toxicity of complex of mixtures. In order to facilitate a comparison mixtures, International Toxicity Equivalency Factors (TEFs) have been assigned to individual dioxins and furans based on a comparison of toxicity to 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD). For example, 2,3,7,8-TCDF has been shown to be approximately one-tenth as toxic as 2,3,7,8-TCDD in animal tests, and its toxic equivalent value is 0.1. TEFs are regarded as risk management tools and they do not necessarily represent

actual toxicity with respect to all endpoints. Rather, they tend to overestimate the toxicity of mixtures.

At the present time, the only persistent effect associated with dioxin exposure in humans is chloracne. Other health effects that have been reported include peripheral neuropathies, fatigue, depression, personality changes, hepatitis, enlarged liver, abnormal enzyme levels and porphyria cutanea tarda though no causal relationships were established in every case. Results of a study on 1,520 workers known to have been exposed to 2,3,7,8-TCDD for a period of at least one year, and with a latency of at least twenty years between exposure and diagnosis of disease, revealed a slightly, but significantly elevated mortality from soft tissue sarcoma and cancers of the respiratory system. As with other studies, interpretation of results was limited by the small number of deaths and by possible confounders including smoking and other occupational exposures. Two recent studies followed a young population from the area of the Seveso, Italy industrial accident. The first, a cancer study, examined a cohort of people aged 0-19 years living in the accident area at the time of the accident, for the period 1977-1986. While a consistent tendency toward increased risk was apparent, none of the relative risks were significantly elevated. Non-significant increases in thyroid cancer and myeloid leukemia were also observed. The study is limited, however, by the relatively short latency periods, the definition of exposure based on place of residence and the limited number of events. The second study examined the mortality of the same cohort of people for the same time period. Among the exposed, mortality owing to all causes did not deviate from expectations, however, as noted above, this study provides only limited evidence. Direct exposure of humans to furans has been reported in two incidents of rice oil contamination by PCBs contaminated with PCDFs, in Japan (Yusho) and Taiwan (Yucheng). While it is possible that the effects observed in these incidents may be due to the presence of furans, the similarity of structure, effects and mode of action of PCBs and PCDFs precludes a definite conclusion on the causative agent.

The acute oral toxicity in laboratory animals is highly variable, with LD50 values ranging from 0.6 µg/kg body weight in guinea pigs to 1,157 µg/kg in hamsters. Effects of dioxin exposure that are common to most, and sometimes all, species include wasting, lymphoid involution, hepatotoxicity, chloracne and epidermal changes, and gastric lesions. Other characteristic responses include edema, ascites and hypopericardium in chickens; fetal death and resorption in rats and fetal wastage, embryotoxicity and malformations in mice. A three-generation study was conducted in which rats were fed diets containing 2,3,7,8-TCDD. Significant decreases in fertility and neonatal survival were observed in the f0 group receiving 0.1 µg TCDD/kg/day. At 0.01 µg TCDD/kg/day, fertility was significantly reduced in the f1 and f2 generations. Decreases in litter size, gestation survival and neonatal survival and growth were also observed at this dose level. No effect on fertility, litter size at birth or post natal body weight was observed in any generation of the 0.001 µg TCDD/kg/day group. Some teratogenic effects have been observed in mice in association with dioxin and furan exposure, including hydronephrosis and cleft palate. The most teratogenic isomer was 2,3,4,7,8-pentachlorodibenzofuran, with an ED50 of 36 µg/kg for cleft palate and 7 µg/kg for hydronephrosis. Teratogenic responses observed are similar to those seen with TCDD, but these compounds are only 1/10 to 1/100 as potent.

Dioxins, specifically 2,3,7,8-TCDD, are associated with a variety of adverse effects on the reproductive systems of both male and female rats. Male reproductive toxicity has included altered regulation of luteinizing hormone secretion, reduced testicular steroidogenesis, reduced plasma androgen concentrations, reduced testis and accessory sex organ weights, abnormal testis morphology, decreased spermatogenesis, and reduced fertility. Signs of female reproductive toxicity included hormonal irregularities in the oestrous cycle, reduced litter size and reduced fertility. A review of recent literature concerning 2,3,7,8-TCDD effects on immunocompetence suggests that 2,3,7,8-TCDD either indirectly (in the case of T-cells) or directly (in the case of B-cells) affects the maturational or differentiative processes of immunocompetent cells. Studies in exposed human populations and in non-human primates have shown that halogenated aromatic hydrocarbons produce measurable alterations in both innate and acquired immunity, although significant deficits in immunocompetence have not been conclusively associated with these changes. IARC has concluded that while there is inadequate

evidence for the carcinogenicity of 2,3,7,8-TCDD in humans, there is sufficient evidence in experimental animals. IARC has classified 2,3,7,8-TCDD as a possible human carcinogen (Group 2B). Other chlorinated dibenzodioxins (other than 2,3,7,8-TCDD) are deemed not classifiable as to their carcinogenicity in humans.

Exposure of fish to dioxins and furans results in a delayed mortality that can continue many days post-exposure. Rainbow trout exposed to 2,3,7,8-TCDD and to 2,3,7,8-TCDF for 28 days, followed by a 28 day depuration period had a 56-day LC50 of 46 pg/L for TCDD, and a NOEC for TCDD based on growth and mortality below the lowest exposure concentration of 38 pg/L. The 56-day NOEC for TCDF was calculated to be 1.79 ng/L for mortality and 0.41 ng/L for growth. Mortality and behavioural changes such as lethargic swimming, feeding inhibition and lack of response to external stimuli continued after the 28 day exposure period ended. Early life stages of fish are very sensitive to the effects of dioxins, furans, and PCBs. Parts per trillion concentrations of these structurally related chemicals in lake trout and rainbow trout eggs exhibit toxicity through sac fry mortality associated with yolk sac edema and hemorrhages.

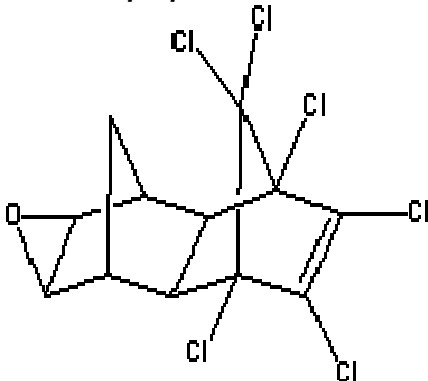
Great blue heron eggs collected from sites of low, intermediate and high contamination had levels of 2,3,7,8-TCDD in eggs of 10 ng/kg (wet weight), 135 ng/kg and 211 ng/kg, respectively. Although there was no effect on mortality of chicks, effects of contamination included decreased growth with increased TCDD level, depression of skeletal growth with increased TCDD levels and subcutaneous edema which increased with increasing PCDD and PCDF contamination. Also observed were shortened beaks and a scarcity of down follicles in the chicks from the more contaminated sites. Mink administered TCDD experienced the wasting syndrome associated with TCDD intoxication and gastric lesions at higher dosages. A 28 day oral LD50 was calculated to be 4.2 µg TCDD/kg body weight.

Dioxins and furans are considered to be very stable and persistent, as illustrated by the half life of TCDD in soil of 10-12 years. This persistence, combined with high partition coefficients (up to 8.20 for OCDD) provides the necessary conditions for these compounds to bioconcentrate in organisms. Bioconcentration factors of 26 707 has been reported in rainbow trout (*Salmo gairdneri*) exposed to 2,3,7,8-TCDD. The chemical properties of dioxins and furans (low water solubility, high stability and semi-volatility) favour their long range transport and these compounds have been detected in arctic organisms.

As with most other organochlorines, food is a major source of dioxins and furans in the general population, with food of animal origin contributing the most to human body burdens. In a survey of dioxins in US food, total PCDD/Fs ranged from 0.42 ppt to 61.8 ppt (wet weight) (total TEQ range: 0.02 to 1.5 ppt). The estimated daily intake for adults ranged from 0.3 to 3.0 pg TEQs/kg body weight, and for breast fed infants the range was 35.3 to 52.6 pg TEQs/kg body weight. Recent estimates of adult average daily intake for Canada, Germany and the Netherlands are 1.52, 2 and 1 pg TEQ/kg bodyweight, respectively. These are below the TDI of 10 pg/kg body weight for lifetime exposure estimated by WHO.

ENDRIN

Chemical properties



Chemical Name: 3,4,5,6,9,9,-Hexachloro-1a,2,2a,3,6,6a,7,7a-octahydro-2,7:3,6-dimethanonaphth[2,3-*b*]oxirene.

Endrin is a foliar insecticide used mainly on field crops such as cotton and grains. It has also been used as a rodenticide to control mice and voles. It is rapidly metabolised by animals and does not accumulate in fat to the same extent as other compounds with similar structures. It can enter the atmosphere by volatilization, and can contaminate surface water from soil run-off. Endrin is banned in many countries, including Belgium, Cyprus, Ecuador, Finland, Israel, Philippines, Singapore, Thailand and Togo. Its use is severely restricted in many countries, including Argentina, Canada, Chile, Colombia, the EU, India, Japan, New Zealand, Pakistan, USA, and Venezuela.

A study of workers involved in the production of aldrin, dieldrin and endrin did not find endrin in the blood of workers, except in cases of accidental, acute over-exposure. These findings are in agreement with results of a study of 71 workers in an endrin plant in the USA. Data on absenteeism, results of liver function tests, blood chemistry, blood morphology, urine analysis, occurrence of sensitization, the incidence and pattern of diseases including the occurrence of malignant growth showed no difference between workers exposed to endrin and other chemical plant operators. A study of workers involved in the manufacture of aldrin, dieldrin and endrin found a statistically significant increase in liver and biliary tract cancers, although the study did have some limitations such as lack of quantitative exposure information. There is limited evidence that cyclodienes such as endrin may also depress immune responses.

The acute oral LD50 of endrin is in the range of 3 mg/kg body weight in monkeys to 36 mg/kg in guinea pigs. Male and female Long-Evans rats were fed endrin in the diet over three generations. No difference in appearance, behaviour, body weight, or number or size of litters was observed. The weights of liver, kidneys and brain were normal, and no histopathological abnormalities were observed in third generation weanlings. Significant increased mortality of pups in the second and third generations of rats fed 3 mg/kg was noted. Endrin was not teratogenic at levels that did not cause maternal toxicity. Endrin is metabolised rapidly by animals, and very little is accumulated in fat compared to compounds of similar structure (including its stereoisomer dieldrin). The formation of *anti*-12-hydroxyendrin is considered to be the major route of metabolism of endrin. IARC has concluded that there is inadequate evidence for the carcinogenicity of endrin in humans, and there is only limited evidence in experimental animals. Endrin is therefore not classifiable as to its carcinogenicity in humans (Group 3).

Endrin is highly toxic to fish, with most LC50 values below 1.0 µg/L. Sheepshead minnows embryos exposed for 23 weeks to 0.31 and 0.72 µg/L hatched early, and all those exposed to 0.72 µg/L died by the ninth day of their exposure, while those exposed at 0.31 µg/L were initially stunted and some died. The reproductive ability of the survivors of the 0.31 µg/L was impaired. No significant effects were observed at an exposure concentration of 0.12 µg/L. The lowest observed adverse effect level (LOAEL) for aquatic organisms was 30 ng/L over 20 days for

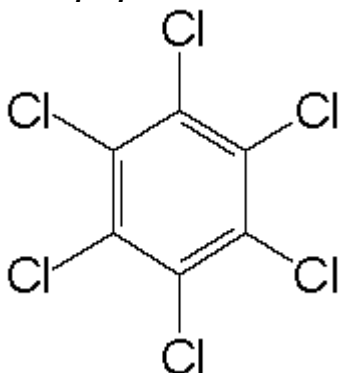
reproduction in mysid shrimp. Reproduction in male and female mallard ducks was not impaired by diets containing 0, 0.5 or 3.0 mg/kg.

The half life of endrin in soil may be up to 12 years, depending on local conditions. This persistence, combined with a high partition coefficient (log KOW = 3.21-5.340), provides the necessary conditions for endrin to bioconcentrate in organisms. A bioconcentration factor of 6,400 was recorded for sheepshead minnows exposed to endrin from embryonic stage through adulthood. Bluegill sunfish exposed to water containing ¹⁴C-labelled endrin took up 91% of the radiolabelled endrin within 48 hours, with a half life of loss from the tissues of approximately four weeks. *Leiostomus xanthurus* exposed to 0.05 µg/L for 5 months had a tissue residue level of 78 µg/kg tissue. After 18 days in uncontaminated water, no residues were detected, suggesting that endrin disappears rapidly from this organism.

The chemical properties of endrin (low water solubility, high stability in the environment, and semi-volatility) favour its long range transport, and it has been detected in arctic freshwater. The main source of endrin exposure to the general population is residues in food however, contemporary intake is generally below the acceptable daily intake of 0.0002 mg/kg body weight recommended by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Recent food surveys have generally not included endrin, and hence recent monitoring data are not available.

HEXACHLOROENZENE

Chemical properties



Chemical Name: hexachlorobenzene

The most notable episode involving the effects of HCB on humans involves the ingestion of HCB treated seed grain in eastern Turkey between 1954 and 1959. The patients who ingested the treated seed experienced a range of symptoms including photosensitive skin lesions, hyperpigmentation, hirsutism, colic, severe weakness, porphyrinuria, and debilitation. Approximately 3,000-4,000 people developed porphyria turcica, a disorder of haem biosynthesis. Mortality was up to 14%. Mothers who ingested the seeds passed the HCB to their children by placental transfer and through maternal milk. Children born to these women developed "pembe yara" or pink sore, with a reported mortality rate of approximately 95%. A study of 32 individuals twenty years after the outbreak showed that porphyria can persist years after the ingestion of HCB. A small cross-sectional study of workers exposed to HCB did not find any evidence of cutaneous porphyria or any other adverse effects associated with exposure of 1 to 4 years.

The acute toxicity of HCB to laboratory animals is quite low, with acute oral LD50 values in the range of more than 2,600 mg/kg body weight in rabbits and 4,000 mg/kg in mice. Porphyria, skin lesions, hyperexcitability and changes in weight, enzyme activities and morphology of the liver have been reported in association with subchronic toxicity of HCB. HCB has also been reported to stimulate the immune system in rats, and suppress the immune system of mice. HCB has also been reported to produce adverse effects on reproduction and reproductive tissue. Female rats fed HCB in the diet experienced offspring mortality, with a 21 day LD50 of 100 ppm. A four-generation reproduction study in rats fed HCB in the diet was conducted. HCB affected reproduction by reducing the number of litters whelped, litter size and the number of pups

surviving to weaning. In a separate study, HCB at a concentration of 100 mg/kg body weight/day was associated with cleft palate and some kidney malformations in CD-1 mice. HCB exposure in several studies in cynomolgous monkeys has resulted in degenerative changes in the ovarian surface epithelium, suppression of serum progesterone, atrophy of thymic cortex, a reduction in the number of lymphocytes, degenerative changes in the ovaries and kidney and degenerative changes in the liver compatible with porphyria tarda. IARC has concluded that while there is inadequate evidence for the carcinogenicity of HCB in humans, there is sufficient evidence in experimental animals. IARC has classified HCB as a possible human carcinogen (Group 2B).

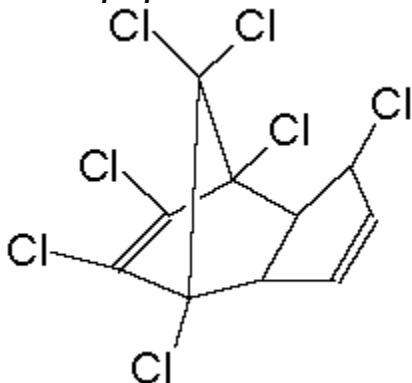
HCB is unlikely to cause direct toxicological effects in aquatic animals at or below saturation concentrations (approximately 5 µg/L) in water. At an exposure concentration of 4.8 µg HCB/L for 32 days, there was no observed effect on embryonic through juvenile stages in developing fathead minnows (*Pimephales promelas*) giving a NOEC of 4.8 µg/L. The caldoceran *Daphnia magna*, the amphipods *Hylella azeteca*, and *Gammarus lacustris*, the annelid worm *Lumbricus variegatus*, and the fathead minnow *Pimephales promelas* were exposed to HCB at saturation concentration (5 µg/L) for 68 days. No effects on survival, growth or reproduction were observed. Adult Japanese quail (*Coturnix japonica*) were fed diets containing HCB for 90 days, resulting in increased mortality at 100 µg/g diet and significantly reduced hatchability at 20 µg/g. At 5 µg/g increased liver weight, slight liver damage and increased faecal excretion of coproporphyrin were observed. Experiments conducted in mink (*Mustela vison*) and European ferrets (*Mustela putorius furo*) with dietary HCB resulted in adult mortality at higher doses (125 and 625 mg HCB/kg diet) and decreased litter size, increased percentage of stillbirths, increased kit mortality and decreased kit growth. Mink were generally more susceptible than ferrets to the effects of HCB. Results from another study indicate that *in utero* exposure to HCB resulted in higher kit mortality than exposure via the mothers milk.

HCB is very persistent. Estimated half lives in soil from aerobic and anaerobic degradation range from 2.7 to 22.9 years. This persistence, combined with a high partition coefficient (log KOW = 3.03-6.42), provides the necessary conditions for HCB to bioconcentrate in organisms. Bioconcentration factors of 22,000 and 106,840 have been reported in fathead minnows and *Lumbricus variegatus* respectively. The chemical properties of HCB (low water solubility, high stability, and semi-volatility) favour its long range transport, and HCB has been detected in arctic air, water and organisms.

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CB is ubiquitous in the environment, and has been measured in foods of all types. HCB was one of two organochlorines detected in all samples of Spanish meat and meat products surveyed with mean levels ranging from 8 ppb (fat weight) in pork products (cured ham) to 49 ppb in lamb, with a maximum level of 178 ppb in lamb. HCB was detected in 13 of 241 serum samples from Colorado beef cattle in a monitoring program, with an average concentration of 3.1 ppb. A survey of US pasteurized milk detected HCB in 8 of 806 composite milk samples. A survey of foods from India found average concentrations of HCB ranging from 1.5 ng/g (fat weight) in both oils and milk to 9.1 ng/g in fish and prawns, with a maximum concentration of 28 ng/g in fish and prawns and an estimated daily intake of 0.13 µg/person. Average HCB residues in foods from Vietnam ranged from 0.28 ng/g (fat weight) in pulses to 27 ng/g in caviar, with an estimated daily intake of 0.10 µg/person.

HEPTACHLOR
Chemical properties



Chemical Name: 1,4,5,6,7,8,8-Heptachloro-3a,4,7,7a-tetrahydro-4,7-methanol-1H-indene.

Heptachlor is a non-systemic stomach and contact insecticide, used primarily against soil insects and termites. It has also been used against cotton insects, grasshoppers, some crop pests and to combat malaria. Heptachlor is highly insoluble in water, and is soluble in organic solvents. It is quite volatile and can be expected to partition into the atmosphere as a result. It binds readily to aquatic sediments and bioconcentrates in the fat of living organisms. Heptachlor is metabolised in animals to heptachlor epoxide, whose toxicity is similar to that of heptachlor, and which may also be stored in animal fat. The use of heptachlor has been banned in Cyprus, Ecuador, the EU, Portugal, Singapore, Sweden, Switzerland and Turkey. Its use is severely restricted in Argentina, Israel, Austria, Canada, Czechoslovakia, Denmark, Finland, Japan, New Zealand, Philippines, USA and USSR.

There is no information on accidental or suicidal intoxication by heptachlor in humans. Symptoms in animals include tremors and convulsions. A study of workers from a plant involved in the production of heptachlor and endrin found a significant increase in bladder cancer. This result was unexpected as no known bladder carcinogens were used at the plant, however, the small number of deaths (3) makes interpretation of these findings difficult. No deaths from liver or biliary tract cancer were observed, although mortality from cerebrovascular disease was higher than expected. There is limited evidence that cyclodienes such as heptachlor may affect immune responses.

The acute oral LD₅₀ of heptachlor to laboratory animals is in the range of 40 mg/kg body weight in rats to 116 mg/kg in rabbits. Groups of male and female rats were administered daily doses of heptachlor orally beginning at 4 months of age, and continuing for 200 days. All the animals in the 50 and 100 mg/kg groups died by the 10th day of exposure. Three animals in the 5 mg/kg group and 1 in the control died before the end of the study. Beginning on the 50th day to the study, hyper-reflexia, dyspnoea and convulsions were observed in the rats exposed to 5 mg/kg. Histological examination revealed fatty degeneration of the liver cells and moderate fatty infiltration of the epithelium of the renal tubules in the 5 mg/kg exposed group.

In a reproduction study, rats were fed diets containing heptachlor in their diet throughout three generations. Mortality of pups in the 10 mg/kg group was slightly increased during the second and third weeks after birth in the second generation only. No adverse effects were observed in the lower dose levels. WHO has reported no evidence of teratogenicity of heptachlor in rats and rabbits. IARC has concluded that, while there is inadequate evidence for the carcinogenicity of heptachlor in humans, there is sufficient evidence in experimental animals. IARC has classified heptachlor as a possible human carcinogen (Group 2B).

Heptachlor has been strongly implicated in the decline of several wild bird populations including Canada geese and the American Kestrel in the Columbia Basin in the US. A population of Canada geese at the Umatilla National Wildlife Refuge in Oregon experienced lowered reproductive success, and adult mortality. Heptachlor epoxide residues were detected in the brains of dead birds and in the eggs of nests with low success. The reproductive success of

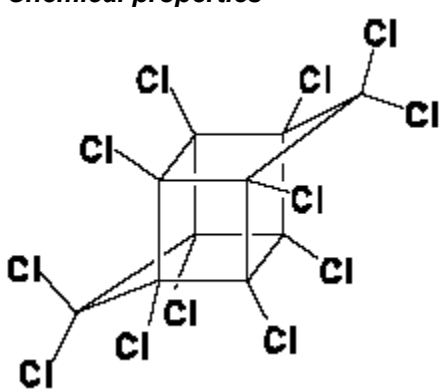
American Kestrels in the same area was also reduced. Heptachlor epoxide residues in the eggs were associated with reduced productivity. The presence of residues in the eggs indicates that heptachlor is transferred through the food chain, as Kestrels are not seed eaters, which was the presumed route of exposure for the geese. Concentrations on the treated seeds were lower than the recommended usage level indicating that effects on wildlife may occur, even if heptachlor is used responsibly.

Mink were fed diets containing heptachlor for 28 days, followed by a 7 day recovery period to determine the subacute toxicity of heptachlor to mink. The NOEL for mortality was 50 mg/kg (5.67 mg/kg body weight/day). Signs of toxicity including reduced food consumption and loss of body weight were observed in mink fed the 25 mg/kg diet. In another study, adult male and female mink were fed diets containing heptachlor for 181 days (before and during the reproductive period) to determine effects on reproduction. All the mink fed diets containing 25 µg/g (male and female) died, within 88 and 55 days respectively. The LOAEL, based on reduced kit growth, was 6.25 µg/g.

The half life of heptachlor in temperate soil is up to 2 years. This persistence, combined with a high partition coefficient (KOW = 4.4-5.5), provides the necessary conditions for heptachlor to bioconcentrate in organisms. Bioconcentration factors of heptachlor and heptachlor epoxide in fathead minnows (*Pimephales promelas*) were 9,500 and 14,400, respectively. The chemical properties of heptachlor (low water solubility, high stability, and semi-volatility) favour its long range transport, and heptachlor and its epoxide have been detected in arctic air, water and organisms.

WHO suggests that food is the major source of exposure of heptachlor to the general population. Heptachlor has been detected in the blood of cattle from both the US and Australia. Heptachlor was detected in 30 of 241 samples in American cattle, and violations of the MRL for heptachlor were detected in 0.02 % of Australian cattle. In both instances, heptachlor was among the most frequently detected organochlorine. A daily intake of 0.25 µg/person/day (for heptachlor and heptachlor epoxide combined, based on a 60 kg person) was estimated for Vietnam, and of 0.07 µg/person/day (for heptachlor alone) for India.

MIREX
Chemical properties



Chemical name: 1,1a,2,2,3,3a,4,5,5a,5b,6-dodecachloroacta-hydro-1,3,4-metheno-1H-cyclobuta[cd]pentalene

Mirex is a stomach insecticide with little contact activity. It's main use was against fire ants in the southeastern United States, but it has also been used to combat leaf cutters in South America, harvester termites in South Africa, Western harvester ants in the US, mealybug of pineapple in Hawaii and has been investigated for possible use against yellow jacket wasps in the US. It has also been used as a fire retardant in plastics, rubber, paint paper and electrical goods. Mirex is very resistant to breakdown, is very insoluble in water and has been shown to bioaccumulate and biomagnify. Due to its insolubility, mirex binds strongly to aquatic sediments.

There are no reports of injuries to humans resulting from exposure to mirex. Mirex residues in human adipose have been reported. A range of 0.16 - 5.94 ppm was reported in 6 of 1,400 samples collected in 1971-1972 in the southern US. Samples from 8 southeastern US states were collected, and residues detected in 10.2 percent of those tested, with a geometric mean of 0.286 ppm in lipid.

In acute studies, the oral LD50 of mirex to rats ranges from 600 to >3,000 mg/kg, depending on sex of the test animal and nature of the formulation tested. Short term effects included decreased body weight, hepatomegaly, induction of mixed function oxidases, and morphological changes in liver cells. Rats which were fed 5 ppm mirex in their diets for 30 days prior to mating and for 90 days after, showed reduced litter size and increased parental mortality. Reduced litter sizes, and viability of neonates, along with formation of cataracts were observed in rats fed 25 ppm mirex in the diet. IARC has concluded that while there is inadequate evidence for the carcinogenicity of mirex in humans, there is sufficient evidence in experimental animals. IARC has classified mirex as a possible human carcinogen (Group 2B).

A reduction in germination and emergence in several plant species was observed, which increased as the concentrations of mirex increased. Uptake, accumulation and translocation of mirex by a variety of plant species has also been seen. These results are questionable, however, as lipophilic compounds such as mirex are generally not known to be taken up and translocated by plants. Contamination of plants is primarily a surface phenomenon resulting from aerial deposition of emissions or deposition of compound that has volatilized from the surface of the soil.

Crustaceans are the most sensitive aquatic organisms, with larval and juvenile stages being the most sensitive. Delayed mortality is typical of mirex poisoning in crustaceans. Larval crabs exposed to 0.1 and 10 µg/L did not exhibit any adverse effects on survival for 5 days after hatching. Delayed mortality then occurred at the 1 and 10 µg/L exposure levels. Mirex is also toxic to fish and can affect fish behaviour. Mirex has a low short term toxicity to birds with acute oral LD50 values in the range of 1,400 mg/kg body weight in pheasant to 10,000 mg/kg in quail. Mirex is considered to be one of the most stable and persistent pesticides, with a half life of up to 10 years. This persistence, combined with lipophilicity, provides the conditions necessary for mirex to bioconcentrate in organisms. Bioconcentration factors of 2,600 and 51,400 have been observed in pink shrimp and fathead minnows, respectively. The chemical properties of mirex (low water solubility, high lipid solubility, high stability, and semi-volatility) favour its long range transport, and mirex has been detected in arctic freshwater and terrestrial organisms. The main route of exposure of mirex to the general population is through food, especially meat, fish and wild game, and intake is generally below established residue tolerances. Mirex residues were found in only one of 806 milk sample composites collected in a survey of US pasteurized milk. No residues of mirex were detected in any samples of fish in Egypt nor in any samples from the fat of domestic farm animals in Ontario, Canada.

POLYCHLORINATED BIPHENYLS

Chemical properties



Congener Group	Molecular weight (g/molecular)	Vapour Pressure (Pa)	Water Solubility (g/m ³)	log KOW
Monochlorobiphenyl	188.7	0.9-2.5	1.21-5.5	4.3-4.6
Dichlorobiphenyl	223.1	0.008-0.60	0.06-2.0	4.9-5.3
Trichlorobiphenyl	257.5	0.003-0.22	0.015-0.4	5.5-5.9
Tetrachlorobiphenyl	292.0	0.002	0.0043-0.010	5.6-6.5
Pentachlorobiphenyl	326.4	0.0023-0.051	0.004-0.02	6.2-6.5
Hexachlorobiphenyl	360.9	0.0007-0.012	0.0004-0.0007	6.7-7.3
Heptachlorobiphenyl	395.3	0.00025	0.000045-0.000	6.7-7
Octachlorobiphenyl	429.8	0.0006	0.0002-0.0003	7.1
Nonachlorobiphenyl	464.2	-	0.00018-0.0012	7.2-8.16
Decachlorobiphenyl	498.7	0.00003	0.000001-0.000	8.26

Polychlorinated biphenyls (PCBs) are mixtures of chlorinated hydrocarbons that have been used extensively since 1930 in a variety of industrial uses, including as dielectrics in transformers and large capacitors, as heat exchange fluids, as paint additives, in carbonless copy paper and in plastics. The value of PCBs for industrial applications is related to their chemical inertness, resistance to heat, non-flammability, low vapour pressure and high dielectric constant. There are 209 possible PCBs, from three monochlorinated isomers to the fully chlorinated decachlorobiphenyl isomer. Generally, the water solubility and vapour pressure decrease as the degree of substitution increases, and the lipid solubility increases with increasing chlorine substitution. PCBs in the environment may be expected to associate with the organic components of soils, sediments, and biological tissues, or with dissolved organic carbon in aquatic systems, rather than being in solution in water. PCBs volatilize from water surfaces in spite of their low vapour pressure, and partly as a result of their hydrophobicity; atmospheric transport may therefore be a significant pathway for the distribution of PCBs in the environment.

The toxicology of PCBs is affected by the number and position of the chlorine atoms, as substitution in the *ortho* position hinders the rotation of the rings. PCBs without *ortho* substitution are generally referred to as coplanar and all others as noncoplanar. Coplanar PCBs, like dioxins and furans, bind to the AL-receptor and may exert, thus, dioxin-like effects, in addition to AL-receptor independent effects which they share with non-coplanar PCBs (e.g. tumor promoter).

Association between elevated exposure to PCB mixtures and alterations in liver enzymes, hepatomegaly, and dermatological effects such as rashes and acne has been reported. Adverse effects are predominantly associated with higher blood concentrations.

Contamination of rice oil by PCBs in Japan (1968) and Taiwan (1979) has resulted in the exposure of a large number of people to PCBs and their contaminants PCDFs. Signs and symptoms of exposure from these incidents include enlargement and hyper secretion of the Meibomian glands of the eyes, swelling of the eyelids, and pigmentation of the nails and mucous membranes, occasionally associated with fatigue, nausea and vomiting. This was followed by hyperkeratosis and darkening of the skin with follicular enlargement and acneform eruptions, often with a secondary staphylococcal infection. Children born up to 7 years after maternal exposure in the Taiwan incident had hyperpigmentation, deformed nails and natal teeth, intrauterine growth delay, poorer cognitive development up to 7 years of age, behavioural problems and higher activity levels. The affected children appeared to "catch up" to controls at 12 years of age. Children born seven to twelve years after maternal exposure experienced mildly delayed development, but no differences in behaviour. Effects observed in these children is likely a result of the persistence of PCBs in the human body, resulting in prenatal exposure long after the exposure took place. These effects are consistent with the observations of poorer short term memory functioning in early childhood, in children exposed prenatally by mothers who had high consumption of Lake Michigan sports fish containing PCBs, amongst other POPs.

People exposed in the Yucheng incident had low resistance, and suffered from a variety of infections. Examination during the first year revealed decreased concentrations of IgM and IgA, decreased percentages of total T-cells, active T-cells and helper T-cells, but normal percentages of B-cells and suppressor T-cells; suppression of delayed type response to recalling antigens; enhancement of lymphocyte spontaneous proliferation and an enhancement in lymphoproliferation to certain mitogens. After three years, some, although not all, of the effects had disappeared. Cancer deaths in both male and female workers involved in the manufacture of electrical capacitors were significantly increased. A significant increase in haematological neoplasms and gastrointestinal cancers was observed in male workers. A non-significant increase in lung cancer was observed. The study was, however, limited by the small numbers of deaths.

PCBs have a low acute toxicity to laboratory animals, with acute oral LD50 values in rats in the range of 2 to 10 g/kg body weight. Effects are manifested primarily through chronic exposure. Effects on the liver, skin, immune system, reproductive system, gastrointestinal tract and thyroid gland have been observed associated with exposure to PCB mixtures or individual congeners. Adverse reproductive effects observed in several studies on monkeys exposed to PCBs include low birth weights, skin hyperpigmentation, behavioural disturbances, atrophy of the thymus and lymph nodes, bone marrow hypoplasia and hyperplasia of the gastric mucosa. Female rhesus monkeys fed diets containing Aroclor 1016 in the diet were bred after 7 months of dietary exposure. Neonatal weights in the 1.0 ppm group were significantly decreased. PCBs have not been observed to be teratogenic in studies involving rats and non-human primates when tested orally, during critical periods of organogenesis. A moderate but statistically significant inhibitory effect on the immune system of rhesus monkeys has been observed, resulting from chronic, low level exposure to Aroclor 1254 and that these effects may be due to altered T-cell and/or macrophage function. IARC has concluded that there is limited evidence for the carcinogenicity of PCBs in humans, and there is sufficient evidence in experimental animals. PCBs are therefore classified as probable human carcinogens (Group 2A).

PCBs are toxic to aquatic organisms, with 96-hour LC50 values in the range of 0.015 mg/L in fathead minnows to 2.74 mg/L in bluegills. Fathead minnows were exposed to Aroclor 1242, 1248 or 1254 in a continuous flow bioassay for 9 months. Reproduction occurred at and below 5.4 µg Aroclor 1242/L, however, results were highly variable. A significant reduction in spawning was observed in fish exposed to 1.8 µg Aroclor 1254/L. Early life stages of fish are more sensitive to the effects of dioxins, furans, and PCBs. Parts per trillion concentrations of these structurally related chemicals in lake trout and rainbow trout eggs produce toxicity through sac fry mortality associated with yolk sac edema and haemorrhages.

PCBs have a low acute toxicity to birds, with 5-day dietary LC50 values in the range of 747 mg/kg diet in quail to >5,000 mg/kg in several species. Broiler breeder and leghorn hens who were fed diets Aroclor 1242 for one week experienced reduced hatchability and the effects continued after exposure was terminated.

There is growing evidence linking persistent halogenated aromatic hydrocarbons such as PCBs to reproductive and immunotoxic effects in wildlife. Two groups of 12 female seals (*Phoca vitulina*) were fed diets of fish from the western part of the Wadden Sea, or from the north-east Atlantic. Residue analysis showed statistically significant differences between the two diets for PCBs and DDE. The average daily intake for group 1 was 1.5 mg PCBs and 0.4 mg DDE, and 0.22 mg and 0.13 mg for group 2. Females were mated with undosed males and reproductive success was significantly lower in group 1. Mink fed Lake Michigan Coho salmon containing between 10 and 15 ppm PCBs as 30% of their diet for five months failed to whelp as did those fed a diet containing 5 ppm Aroclor 1254. The clinical signs and lesions observed in mink fed a diet containing Lake Michigan coho salmon included anorexia, bloody stools, fatty liver, kidney degeneration and gastric ulcers, and were similar to those fed a diet supplemented with PCBs.

The degradation of PCBs in the environment depends largely on the degree of chlorination of the biphenyl, with persistence increasing as the degree of chlorination increases. Half-lives for PCBs undergoing photodegradation range from approximately 10 days for a monochlorobiphenyl to 1.5 years for a heptachlorobiphenyl. The persistence of PCBs, combined with the high partition coefficients of various isomers (log KOW ranging from 4.3 to 8.26) provide the necessary conditions for PCBs to bioaccumulate in organisms. Bioconcentration factors of 120,000 and 270,000 have been reported in fathead minnows. Concentration factors in fish exposed to PCBs in their diet were lower than those for fish exposed to PCBs in water, suggesting that PCBs are bioconcentrated (taken up directly from the water) as opposed to being bioaccumulated (taken up by water and in food). The chemical properties of PCBs (low water solubility, high stability, and semi-volatility) favour their long range transport, and PCBs have been detected in arctic air, water and organisms.

The main source of PCB exposure to the general population is through food, especially fish. PCB residues were detected in 8.5% of samples, with a maximum of 0.30 mg/kg fat, taken during a survey of the fat of domestic farm animals in Ontario, Canada between 1986 and 1988. In a survey of foods in Vietnam, the highest levels of PCBs were detected in fish and shellfish, with levels of 760 and 1,400 ng/g fat. The main sources of PCBs in the Vietnamese diets is cereals (including rice) and vegetables, and the daily intake of 3.7 µg/person/day is comparable to those of some industrialized countries. A survey of foods in India also found that the highest levels of PCBs were in fish, with an average of 330 ng/g fat. Again, the main source of PCB dietary intake (0.86 µg/person/day) was cereal and vegetable oil.