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Review Paper

Dioxins: a review of its environmental risk

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This review paper summarizes what is known about environmental risk following exposure to dioxins. It is meant primarily for health professionals, but was also written with the general public in mind. This work is reviews the available data about the properties, Sources and Toxicity of dioxins in environmental.

Keywords: Dioxins, DLCs, PCDDs, PCDFs.

INTRODUCTION

Since the middle of the 20th century there has been an increasing concern about the exposure of humans and wildlife to certain xenobiotic that were released into the environment due to diverse anthropogenic activities. One group of environmental toxicants that is of particular interest relative to potential environmental health effects are dioxin-like chemicals (DLCs).These ubiquitous compounds are hydrophobic, lipophilic and resistant to biological and chemical degradation, properties that impart persistency and a propensity to bio-accumulate and biomagnify to concentrations that can cause harmful effects. DLCs include polychlorinated dibenzo-p-dioxins and dibenzo furans (PCDD/Fs), dioxin-like polychlorinated biphenyls (DL-PCBs), polycyclic aromatic hydrocarbons (PAHs), as well as a multitude of other partially known and unknown compounds [1-6].The in vivo behavior of these compounds depends on their uptake, distribution and metabolism [7, 8] as well as modifying factors such as species, age and reproductive status [9]. Hence,the range of biological effects across different organisms is broad. Effects may include thymic atrophy, hepatotoxicity, certain types of cancer, immunotoxicity, wasting syndrome, reproductive toxicity and the induction of monooxygenase enzymes [10-15].

2. Dioxin

2.1. Chemical structures and properties

Dioxin is one of the most toxic chemicals known. A report released for public comment on September 1994 by the US Environmental Protection Agency [16, 17] clearly describes dioxin as a serious public health threat in the 1960s. According to the EPA report, not only does there appear to be no “safe” level of exposure to dioxin, but levels of dioxin and dioxin-like chemicals have been found in the general US population that is “at or near levels associated with adverse health effects”. The EPA report confirmed that dioxin is a cancer hazard to people, that exposure to dioxin can also cause severe reproductive and developmental problems (at levels 100 times lower than those associated with its cancer causing effects); and that dioxin can cause immune system damage and interfere with regulatory hormones.

Dioxins, as they are commonly called, are PCDDs and PCDFs are compounds with similar chemical properties. Each compound comprises two benzene rings interconnected by oxygen atoms. In the case of PCDDs, the benzene rings are joined by two oxygen bridges, and in the case of the PCDFs,

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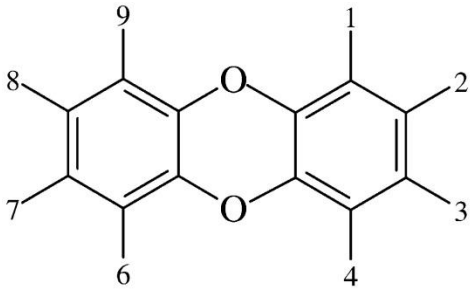
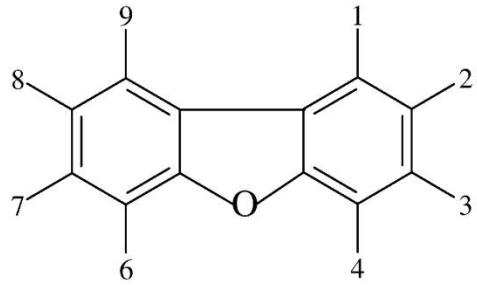
the benzene rings are connected by a carbon bond and an oxygen bridge. Figure 1 shows the generic structures of PCDDs and PCDFs, respectively. Much of the environmental behavior of polychlorinated biphenyls (PCBs) can be related to their physical characteristics. The non-polar nature of PCBs means that they are strongly hydrophobic and thus strongly lipophilic. They exhibit a high predilection for smooth surfaces, and combined with their lipophilic and hydrophobic properties, this explains their presence absorbed into soil and sediment particles. The high surface concentration of lipids and organic compounds tend to concentrate and stabilize PCBs on the surface of water bodies. All PCDDs and PCDFs are organic solids with high melting points and low vapor pressures. They are characterized by extremely low water solubility, and have a tendency for being strongly adsorbed on surfaces of particulate matter. The water solubility of dioxin and furans decreases and the solubility in organic solvents and fats increase with increasing chlorine content.



Dibenzo-*para*-dioxin



dibenzofuran

Figure 1: Generic structures of PCDDs and PCDFs

Some of the key properties of the dioxins are presented in Table 1 and full physico-chemical properties have been reviewed [16,18]. There are 75 PCDDs and 135 PCDFs, each differing in the number and position of the chlorine atoms. Each individual PCDD or PCDF is termed a congener (giving 210 in total), while groups of congeners with the same number of chlorine atoms are called homologues.

Table 1: Typical physico-chemical properties of PCDD/Fs

Homologue group									
TCDD	PeCDD	HxCDD	HpCDD	OCDD	TCDF	PeCDF	HxCDF	HpCDF	OCDF
Vapor pressure									
8.1×10^{-7}	7.3×10^{-10}	5.9×10^{-11}	3.2×10^{-11}	8.3×10^{-13}	2.5×10^{-8}	2.7×10^{-9}	2.8×10^{-10}	9.9×10^{-11}	3.8×10^{-12}
Log K_{ow}									
6.4	6.6	7.3	8.0	8.2	6.2	6.4	7.0	7.9	8.8
Solubility (mg l^{-1} at 25℃)									
3.5×10^{-4}	1.2×10^{-4}	4.4×10^{-6}	2.4×10^{-6}	7.4×10^{-8}	4.2×10^{-4}	2.4×10^{-4}	1.3×10^{-5}	1.4×10^{-6}	1.4×10^{-6}
Henry's constants									
1.35×10^{-3}	1.07×10^{-4}	1.83×10^{-3}	5.14×10^{-4}	2.76×10^{-4}	6.06×10^{-4}	2.04×10^{-4}	5.87×10^{-4}	5.76×10^{-4}	4.04×10^{-5}

The number of congeners in each homologue group is shown in Table 2. The homologue groups are often abbreviated for convenience; for example, tetrachloro CDDs and CDFs (PCDD/Fs with four substituted chlorine atoms) are abbreviated to TCDDs and TCDFs, respectively, while the fully chlorinated octachloro congeners (eight substituted chlorine atoms) are abbreviated to OCDD and OCDF, respectively.

Table 2: Homologues and congeners of PCDDs, PCDFs and PCBs

Homologue (abbreviation)	Number of congeners		
	PCBs	PCDDs	PCDFs
Monochloro (M)	3	2	4
Dichloro (D)	12	10	16
Trichloro (Tr)	24	14	28
Tetrachloro (T)	42	22	38
Pentachloro (Pe)	46	14	28
Hexachloro (Hx)	42	10	16
Heptachloro (Hp)	24	2	4
Octachloro (O)	12	1	1
Nonachloro	3	-	-
Decachloro	1	-	-
Total	209	75	135

2.2. Sources

Earlier human tissue samples show very lower levels of dioxins than found today [19]. Studies of the sediments near industrial areas of the United States have shown that dioxins were very low until about 1920 [20, 21]. These studies show increases in dioxin concentrations from 1920s and continuing until about 1970. Some decline in concentrations has been observed this time. These findings can be explained by the corresponding trends of chlorophenol production [22].

Therefore, it appears that the presence of dioxin-like compounds in the environment occurs principally as a result of anthropogenic sources. These compounds are released to the environment in a variety of ways and in varying quantities depending upon the source. This ubiquitous nature of dioxin compounds suggests that multiple sources exist and that long range transport can occur. The major identified sources of environmental release have been grouped into four major categories as shown in Figure 2.

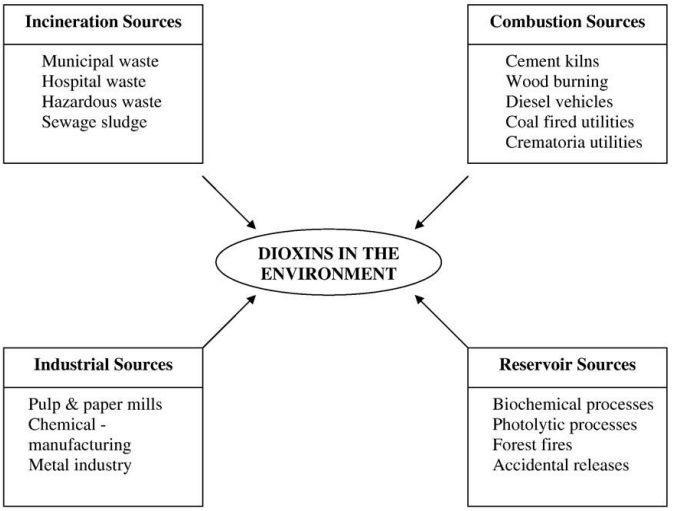


Figure 2: Dioxins release in the environment [23].

2.2.1. Incineration sources

It is the largest source of dioxin release into the environment. Dioxins can be generated and released to the environment from following incineration processes.

Municipal solid waste incinerators: Dioxins are predominantly produced by municipal solid waste incineration processes. Several researchers have described their mechanism of formation. Overall, it is observed that the emission of dioxins and furans into the environment can be explained mainly by two principal surface catalytic processes:

i) Formation from precursors and ii) formation by de novo synthesis [24]. An informative review of the formation and mechanism of dioxins from municipal solid waste incineration was presented [25]. It was observed that several past studies demonstrated the presence of significant quantities of dioxins and dioxin precursors in municipal solid waste around 50 ng I-TEQ/kg [26].

Hospital waste incinerators: Hospital waste includes human organs, bandages, blood tubes, test tubes, needles, syringes, tissue cell culture, and other plastic materials. Incineration has been the most widely used treatment of hospital waste in every country. However, these incinerators do not rely on advanced technologies, are high in number, burn high chlorine content waste and hence are an important source of dioxin emissions [27].

Hazardous waste incinerator: The harmful products of chemical processes produced from industries are called hazardous waste. Depending on the waste type, hazardous waste can be explosive, oxidizing, highly flammable, corrosive, infectious, mutagenic, irritant, toxic, or carcinogenic. A practice of separate incineration for hazardous waste has also started several years ago. Hazardous organic compounds such as chlorinated phenols can be incinerated under this method [28].
Sewage sludge incinerator: Wastewater treatment generates a solid residue with high organic and toxic metal contents called sewage sludge. The limitations facing land filling and recycling and the planned ban on sea disposal has led to the use of incineration processes for the disposal of sewage sludge. A few studies were reported on the sewage sludge incineration [29].

2.2.2. Combustion sources

Cement kilns: The switch to burning hazardous waste as fuels for cement kilns has created problem for individuals and organizations. About 16% of the facilities burns hazardous waste as an auxiliary fuel; limited data suggest that PCDD/PCDF levels in clinker dust and stack emissions of these kilns may be significantly higher than the kilns which do not burn hazardous waste [30, 31].

Wood burning: A number of studies have found dioxins in the emissions and ash/soot from wood fires in non-industrial situations [32]. According to the European Emission Inventory, wood combustion is at present one of the most important air emission sources of dioxins [33]. In an appealing review paper, it is reported that the dioxin emission from wood burning is about 945 g I-TEQ/year [34].

Diesel vehicles: A very scant literature available on emission of dioxin from diesel vehicles. Researchers from Sweden and Norway have studied dioxin emission from diesel vehicles [35, 36]. As these studies depend on the fuel used in a particular country more studies are required in order to reach a conclusive estimate.

Crematoria: Crematoria procedures can be a ready source of organic material and chlorine, and hence are possible source of dioxin emission [37]. Inventory estimates rate this source as 0.3% of European output [38] and 0.24% of US output [39].
Coal-fired utilities: Although emission of dioxins compared to the wood burning are very less, they are numerous, large in size and their high stacks indicate that they could impact very large areas [40, 41]. Considering the large scale usage the importance of these facilities is very much unknown.

2.2.3. Industrial sources

Pulp and paper mills: The manufacture of bleached pulp and paper has in the past resulted in dioxin releases to water, land and paper products. These compounds can be formed through the chlorination of naturally occurring phenolic compounds such as those present in wood pulp [42]. It is reported that the waste generated from a pulp mill of China produces dioxin concentration of 300 pg/l I-TEQ [43].

Metals industry: The metallurgical processes such as high temperature steel production, smelting operations, and scrap metal recovery furnaces are found to be typical sources of dioxins [44]. Processes in the primary metals industry, such as sintering of iron ore, have also been identified as potential sources [45, 46]. In several countries the annual release of dioxins is estimated to be 500–4000 g I-TEQ [44].

Chemical manufacturing: PCDDs and PCDFs can be formed as by-products from the manufacture of chlorinated compounds such as chlorinated phenols, PCBs, phenoxy herbicides, chlorinated benzenes, chlorinated aliphatic compounds, chlorinated catalysts and halogenated diphenyl ethers [47-49]. Although the manufacture of many chlorinated phenolic intermediates and products, as well as PCBs, was terminated in the late 1970s in the United States, production continued around the world until 1990, and continued, limited use and disposal of these compounds can result in release of dioxins into the environment.

2.2.4. Reservoir sources

The persistent and hydrophobic nature of these compounds causes them to accumulate in soils, sediments, landfill sites, vegetation and organic matter. They have potential for redistribution and circulation of dioxins in the environment. The dioxin compounds in the “reservoirs” can be redistributed and circulated in the environment by dust or sediment suspension and transport [50, 51]. The major reservoir sources include:

Biological processes: The action of microorganisms on chlorinated phenolic compounds results in the formation of dioxins under certain environmental conditions [52].
Photochemical processes: Dioxins like OCDD (1,2,3,4,5,6, 7,8,9-octachlorodibenzodioxin), HPCD (1,2,3,4,5,6,7,8-heptachlorodibenzodioxin) formation occurs by photolytic radical reactions of pentachlorophenol [53,54].

Accidental sources: The incidents of dioxin release at Seveso, Italy and Yusho Japan can be considered as an accidental release of dioxins into the atmosphere. Further, forest fires and volcanoes also come under this category [55, 56].

Miscellaneous sources: Miscellaneous sources include formation of dioxins in FBC (Fluidized Bed Combustion) boilers, thermal oxygen cutting of scrap metal at demolition sites, power generation, PVC in house fires, Kraft liquor boilers, laboratory waste, drum and barrel reclaimers, tire combustors, carbon reactivation furnaces and scrap electric wire recovery facilities, etc. [57-59].

2.3. Toxicity

Acute exposure to dioxins in animals induces gastrointestinal hemorrhage, liver toxicity, weight loss and death [60, 62]. In rodents and rabbits the liver is the first target organ, whereas in guinea pigs, the most sensitive species, thymus and lymphatic tissue atrophy is the most sensitive biomarker [60]. There is a great variety of sensitivities to TCDD among species, the guinea pig being 10,000 most sensitive that the Syrian hamster (Table 3).

The bioavailability of TCDD, its metabolism, which determines its biological half-life, the possible crosstalk’s of AhR with other signaling pathways are just some examples of the diversity of the biological effects of TCDD observed among many species including humans. Geyerand colleagues found a relationship between the TCDD sensitivity and the body fat, and concluded that accumulation of dioxins and related persistent organic pollutants in fat is a detoxification mechanism that removes biologically active xenobiotic from their target [63, 64] (Table 3, Figure3).

This hypothesis is supported by our observations when analyzing the adipose tissue from a patient highly exposed to TCDD [65] and a study on 3T3-L1 adipocyte-like cells [66].According to the relationship between oral TCDD LD50and the body fat content reported by Geyer and colleagues [63] (Figure3), humans, with an average body fat around 24%, should be one of the most resistant species with a LD50 of ≈12.5 mg/kg! How-ever, the patient we examined in the years 2005 to 2009 developed life-threatening conditions such as toxic pancreatitis and hepatitis shortly after receiving an estimated TCDD dose of 20 µg/kg [67], indicating that the human LD50 for TCDD might be significantly lower than

previously estimated. Following acute TCDD intoxication, the target organs develop pathology and recover with very different kinetics: the GI tract, the liver and the pancreas are the first organs to be affected and recover within 6 to 10 weeks, whereas the clinical manifestations of the skin start to develop only after several weeks, reach a peak at18 months and decrease slowly over a period of 3 to 5 years [65].

Table 3: Relation between TCDD LD50 and body fat and percentage.

Species (strain)	Body fat [%]	LD_{50} [µg/kg]
Guinea pig (Hartley)	4.5	1
American dark mink	-	4
Hare	7.5	10
Chicken	-	35
Macaque	10	50
Rat (Sprague-Dawley)	10	50
Dog	-	100
Rabbit	10	120
Mouse (C57BL)	8	150
Rat (Fischer)	10	300
Mouse (BALB/c)	-	400
Dog (Beagle)	14	1000
Frog		1000
Mouse (DBA)	20	2500
Hamster (golden Syrian)	15	10,000

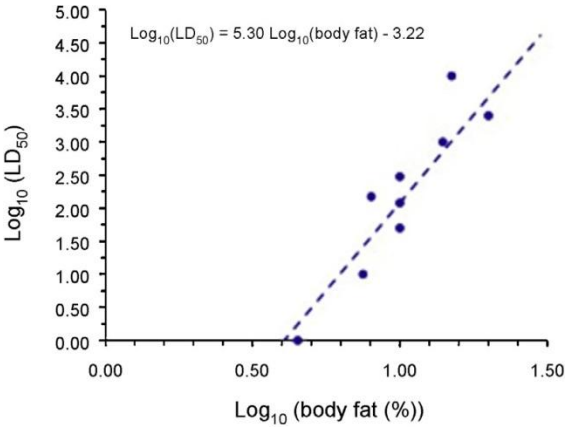


Figure 3: TCDD oral LD50vs. Body fat percentage. See text for details (toxicity) [63]

3. Conclusions

Dioxin compounds are environmentally and biologically stable and, as a result, human exposure is chronic and widespread. An exposure to such type of chemicals can damage the immune system, leading to increased susceptibility and it can disrupt the functions of several hormones.

Over the past several years, there has been a shift in the major sources of dioxins, in large part due to the stringent regulations and focused voluntary efforts. Production of pesticides used to be associated with relatively high levels of contamination with dioxins. Many of these products have been banned. Bleaching of paper and pulp products using free chlorine in Kraft mills led to the production of dioxins. But the use of alternative processes, reduced dioxin formation. Therefore, the chemical industries are taking proper measures to avoid the generation of dioxins. Although the incineration process of municipal solid waste once used to be the major source, its contribution to the current emission inventories is now decreasing. However, medical waste incineration is still a major source of dioxins. Polyvinyl chloride (PVC) plastic, as the dominant source of organically bound chlorine in the medical waste stream, is the main cause of dioxin formation by the incineration of medical wastes. Therefore, health professionals have a responsibility to work to reduce dioxin exposure from medical sources. Health care institutions should implement policies to reduce the use of PVC plastics as much as possible, thus achieving major reductions in medically related dioxin formation. Emissions of these toxic contaminants are believed to have reduced in some industrial countries and there are suggestive data indicating that background levels in human blood and milk in Germany, the Netherlands, and the United States have declined, recently. The other important sources of dioxin family compounds today involve combustion processes and reservoir sources. Uncontrolled burning and collection of small sources are the significant sources of new dioxin emissions today. Attempts should be made in order to tap these sources.In our opinion, need for more research for the development of sustainable methods of treatment.

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