DIOXINS, FURANS AND POLYCHLORINATED BIPHENYLS ANIMAL AND HUMAN HEALTH RISK

PETRUȚA LAVINIA GALBENU

Faculty of Veterinary Medicine, Timisoara, Romania
Calea Aradului No 119, 300645

Summary

Dioxins, furans and polychlorinated biphenyls (PCBs) are three of the twelve United Nations Environment Programme (UNEP) internationally recognized Persistent Organic Pollutants (POPs). POPs are organic compounds of mainly anthropogenic origin which are characterized by their lipophilicity, semi-volatility and resistance to degradation. These characteristics pre-dispose these substances to long environmental persistence and to long-range transport. They are also known for their ability to bioconcentrate and biomagnify under typical environmental conditions, thereby potentially achieving toxicologically relevant concentrations. Because of their toxic characteristics they pose a threat to humans and to the environment. It is important to highlight that dioxins, furans and PCBs have similar chemical properties and hazardous characteristics but the sources of releases are different. Therefore an effective approach to controlling and reducing their release into the environment should address all of them, but taking into account the differences (3, 9).

The aim of this document is to provide a concise overview of the health hazards and sources of dietary exposure to dioxins, furans and PCBs. It also gives information on their chemical and physical characteristics, Toxic Equivalent Concentration (TEQ) and legislative limits.

Key words: dioxins, furans, polychlorinated biphenyls

Polychlorinated dibenzo-p-dioxins (PCDDs, dioxins), a group of 75 halogenated aromatic hydrocarbons (HAHs) and polychlorinated dibenzofurans (PCDFs, furans) a group of 135 HAHs are widely used under the term ‘dioxin’. Of the 210 different dioxin compounds, only 17 are of toxicological concern. The most widely studied and most toxic form of dioxin is 2,3,7,8-tetrachlorodibenzo-p-dioxin, abbreviated as 2,3,7,8-TCDD. It is measured in parts per trillion (ppt) the same as the individual chemicals within the group which are termed congeners (1,2,5,7,8). Structures and numbering of generic PCDD and PCDF molecules are shown in Fig. 1:

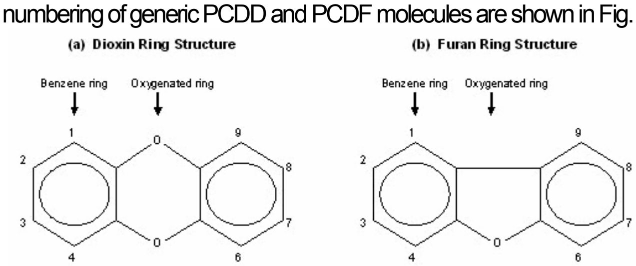

Fig.1.Double benzene ring structures of (a) dioxins and (b) furans.
http://www.nap.edu/catalog/11688.html (8)

Dioxins are colorless, odorless organic compounds containing carbon, hydrogen, oxygen and chlorine. Dioxins are not soluble in water and are highly soluble in fat. This means that they bind to sediment and other organic matter in the environment and are absorbed in animal and human fatty tissue. In addition they are not biodegradable so they are persistent and bio-accumulate in the food chain. This means that once released into the environment, via air or via water, they pile up in the fat tissue of animals and humans, they biomagnify (1, 4, 6).

Polychlorinated biphenyls or PCBs are structurally somewhat similar to the dioxins: they are chlorinated aromatic hydrocarbons synthesized by direct chlorinating of biphenyls. There are 209 PCB congeners, divided into two main groups: the “dioxin-like PCBs”, a group of 12 PCBs showing similar toxicological properties to the dioxins (the ones referred to in this document) and the non-dioxin-like PCBs, which are of lower toxicity, and which are normally the predominant congeners in environmental samples (1, 2, 5, 6, 8). The structure and numbering of generic PCB molecule is presented in Figure 2:

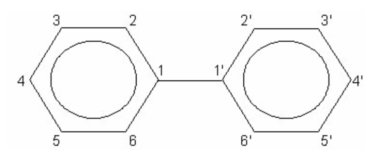

Figure 2.Biphenyl ring structure of PCBs.
http://www.nap.edu/catalog/11688.html (8)

PCBs are stable, unreactive, viscous liquids, commercial mixtures of related compounds (congeners), have very low solubility in water but high solubility in oils and organic solvents of low polarity (5, 8).

Sources

EPA classifies sources of dioxins, furans, and dioxin-like PCBs into five categories: (1) combustion; (2) metal smelting, refining, and processing; (3) chemical manufacturing and processing; (4) biological and photochemical processes; and (5) reservoir sources (8).

Dioxins and furans are formed essentially as **unintentional by-products** in a number of chemical processes as well as in almost every combustion process. These range from natural events such as volcano eruptions and forest fires to manmade processes such as manufacturing of chemicals, pesticides, steel and paints, pulp and paper bleaching, exhaust emissions and incineration. For example, when chlorinated waste is burned in an uncontrolled way in an incinerator, the emissions to the air contain dioxins (5, 6, 8).

Soils and sediments are important reservoir sources given the persistence of these pollutants in the environment. The most important route for human exposure to dioxins is food consumption, contributing for more than 90 % of total exposure, of which products of fish and other animal origin account for approximately 80 % of the overall exposure (1, 3, 9).

Polychlorinated biphenyls or PCBs are **intentionally produced** chemicals (the main difference with dioxins) , which were manufactured for decades (e.g. Aroclor 1254, Aroclor 1260, Clophen A60) before the ban in marketing and use was adopted in 1985 due to their reproductive toxicity and bio-accumulative effects (5, 6, 9).

The main part of these products, which are very persistent and bioaccumulate in fat of biota, is now spread in soils, sediments and in the whole aquatic environment ("historical pollution"). There are two types of uses of PCBs: 1) Closed uses: dielectric fluids in electrical equipment. From these uses, the main sources of releases are: leakage, fires, accidents, illegal dumping and inadequate disposal. 2) Open uses: as pesticide extender, flame retardants, sealants, paints, etc. From these uses the main sources of releases are: landfilling, migration, air emissions from evaporation. Other less significant sources are waste incineration, sewage sludge application to land, combustion of waste oils, as well as PCB reservoirs, such as marine and river sediments and harbour sludges (1, 9).

The fact that dioxins are more toxic than PCBs, but that the quantities of PCBs released to the environment are several times higher has to be taken into account (9).

Toxicity

On a global scale, exposure to dioxins, furans, PCBs resulting from accidental, occupational or incidental exposure through dermal contact, inhalation, or ingestion has been associated with different adverse effects on animal and human health (4, 8).

As mentioned before, PCDDs, PCDFs and PCBs are fat-soluble compounds which accumulate in the tissues of animals and humans, in addition to binding to soil and other organic matter in the environment. Their ability to accumulate in the body, together with their chlorinated structure, in part explains their toxicity. The various dioxin congeners contain between 1 and 8 atoms of chlorine, and those that are of concern in terms of their effects on health contain chlorine in each of the 2-, 3-, 7- and 8-positions of the molecule (2, 5, 7).

The majority of the toxic effects of the 17 PCDD+PCDF and 12 PCB congeners of toxicological concern are mediated through the initial binding to the Aryl hydrocarbon Receptor (AhR). The AhR is a ligand-actvated transcription factor that is involved in the regulation of a number of genes, including those for enzymes that play a role in the metabolism of xenobiotics as well as genes involved in cell growth regulation and differentiation. It plays an important role in the altered gene expression and species- and tissue-specific toxicity resulting from exposure to specific PCDD, PCDF and PCBs congeners (2, 4).

The toxic responses are dependent on several factors including the chlorine content, the purity of the commercial mixture, the route and duration of exposure, as well as on the dose, age, sex, species and strain of animal (2).

Early life stages (eggs, embryos, larval stages), young animals and babies are more sensitive than adults; females are more sensitive than males, hamsters and amphibians are more resistant. Humans, sea birds and aquatic mammals are priority targets and victims, as they are at the end of the aquatic trophic chain of these products which bioaccumulate in fat tissue (2, 9). The oral LD50 values for TCDD are 0,6-0,2 µg/kg body weight for the guinea pig, 114-284 µg/kg body weight for the mouse and 1157-5000 µg/kg body weight for the hamster (Safe, 1990 quoted by Brusian) (2).

Exposure to dioxins can result in a wide range of health effects including acute lethality, wasting syndrome, thymic and splenic atrophy, impairment of immune responses, hepatotoxicity and porphiria, chloracne and related dermal lesions, tissue-specific hypo- and hyperplastic responses, disruption of multiple endocrine pathways, carcinogenesis, teratogenicity, and reproductive toxicity. Although dioxin is known as a human carcinogen, cancer is not considered to be the critical effect for the derivation of the Tolerable Intake. The critical effects are neurobehavioral changes, endometriosis and immunosuppression (2, 4, 7, 9).

The toxicity of PCDD, PCDF and PCB congeners are expressed using Toxic Equivalency Factors (TEFs), representing the toxicity of a particular congener relative to the most toxic congener, TCDD. Several different TEF schemes have been proposed. The most common scheme currently used is that of WHO-TEFs, developed by the WHO-ECEH (World Health Organization - European Centre for Environment and Health). These have recently been updated by WHO-ECEH, but the new scheme is not yet widely in use (7). The currently used WHO-TEFs for the dioxin and dioxin-like PCB congeners of main concern are shown in Table 1:

Table 1*

WHO-TEFs for dioxin and dioxin-like PCBs

Congener	TEF value	Congener	TEF value
Dibenzo-p-dioxins (PCDDs)		**'Dioxin-like' PCBs Non-ortho PCBs + Mono-ortho PCBs**	
2,3,7,8-TCDD	1	*Non-orto PCBs*	
1,2,3,7,8-PeCDD	1	PCB 77	0,0001
1,2,3,4,7,8-HxCDD	0,1	PCB 81	0,0001
1,2,3,6,7,8-HxCDD	0,1	PCB 126	0,1
1,2,3,7,8,9-HxCDD	0,1	PCB 169	0,01
1,2,3,4,6,7,8-HpCDD	0,01		
OCDD	0,0001		

Dibenzofurans (PCDFs)		*Mono-orto PCBs*	
2,3,7,8-TCDF	0,1	PCB 105	0,0001
1,2,3,7,8-PeCDF	0,05	PCB 114	0,0005
2,3,4,7,8-PeCDF	0,5	PCB 118	0,0001
1,2,3,4,7,8-HxCDF	0,1	PCB 123	0,0001
1,2,3,6,7,8-HxCDF	0,1	PCB 156	0,0005
1,2,3,7,8,9-HxCDF	0,1	PCB 157	0,0005
2,3,4,6,7,8-HxCDF	0,1	PCB 167	0,00001
1,2,3,4,6,7,8-HpCDF	0,01	PCB 189	0,0001
1,2,3,4,7,8,9-HpCDF	0,01		
OCDF	0,0001		
Abbreviations used: 'T' = tetra; 'Pe' = penta; 'Hx' = hexa; 'Hp' = hepta; 'O' = octa; 'CDD' = chlorodibenzodioxin; 'CDF' = chlorodibenzofuran; 'CB' = chlorobiphenyl.			

* Table 1 is reproduced from *Commission Regulation (EC) No. 1883/2006* of 19 December 2006 laying down methods of sampling and analysis for the official control of levels of dioxins and dioxin-like PCBs in certain foodstuffs, *Appendix to Annex II (*13).

Toxic Equivalent Concentration (TEQ)

Each congener of dioxins or dioxin-like PCBs exhibits a different level of toxicity. In order to be able to sum up the toxicity of these different congeners, the concept of toxic equivalency factors (TEFs) has been introduced to facilitate risk assessment and regulatory control. This means that the analytical results relating to all the individual congeners or compounds of toxicological relevance (17 dioxin and 12 dioxin-like PCB congeners) are converted into one result which summarizes all and is expressed as TCDD toxic equivalent concentration" or "TEQ" (6, 12).

The Scientific Committee for Food (SCF) has established a tolerable weekly intake (TWI) of 14 picogram toxic equivalents (TEQ) per kilogram body weight for dioxins and dioxin-like PCBs. This TWI is in accordance with the Provisional Tolerable Monthly Intake (PTMI) of 70 pg/kg bodyweight/month established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at its fifty-seventh meeting (Rome, 5-14 June 2001) and concurs with the lower end of the range Tolerable Daily Intake (TDI) of 1-4 pg WHO-TEQ/kg body weight, established by the World Health Organisation (WHO) Consultation in 1998. The SCF (May 2001) established a maximum intake of 2 pg/kg bodyweight/ day, JECFA (June 2001) 2.3 pg/kg bodyweight/ day and the WHO Consultation (May 1998) a range of 1 to 4 pg/kg bodyweight/ day (6, 8).

Legislative limits

In 2001, the European Commission published a *Community strategy for reduction of dioxins, furans and polychlorinated biphenyls* in food and in the environment, which established the principle of a proactive approach to reducing levels in combination with measures to limit emissions (9). Since then it has underpinned this with two Commission Recommendations: *Recommendation 2006/88/EC* of 6 February 2006 concerning the reduction of the presence of dioxins, furans and PCBs in feedingstuffs and foodstuffs and *Recommendation 2006/794/EC* of 16 November 2006 on the monitoring of background levels of dioxins, dioxin-like PCBs and non-dioxin-like PCBs in foodstuffs. Romania is also included in this latter Reccomandation (2006/794/EC, Annex I), with a minimum recommended number of food samples to analyse every year (7, 11).

Commission Regulation (EC) No 1883/2006 of 19 December 2006 lays down methods of sampling and analysis for the official control of levels of dioxins and dioxin-like PCBs in certain foodstuffs. This regulation also lays down requirements for laboratories carrying out dioxin analysis. Laboratories shall be accredited by a recognized body following the EN ISO/IEC 17025 standard, in accordance with ISO guide 58, to ensure that they are applying analytical quality assurance (7, 13). The determination procedure is described in *EPA Method 1613 Revision B,* by Isotope Dilution HRGC/HRMS (High Resolution Gas Chromatography/High Resolution Mass Spectometry) (14).

Commission Directive 2006/13/EC, sets the limits for PCDDs, PCDFs and dioxin-like PCBs for animal feedstuffs, amending Annexes I and II to Directive 2002/32/EC of the European Parliament and of the Council on undesirable substances in animal feed, recognizing the importance of establishing limits for both food and feed (10).

Commission Regulation (EC) No 1881/2006 of 19 December 2006 sets maximum levels (MLs) for certain contaminants in foodstuffs, e.g. meat and meat products, milk, oils and fats. The maximum levels for PCDDs/PCDFs in food are shown in column 3 of Table 2, while column 4 shows the maximum levels for the sum of dioxins, furans and dioxin-like PCBs. This Commission Regulation replaces Council Regulation 2375/2001 of 29 November 2001 amending Commission Regulation (EC) No 466/2001 (7, 12).

Table 2*

Maximum levels for dioxins and for dioxin and dioxin-like PCBs in certain foodstuffs

Maximum levels for dioxins and for dioxin and dioxin-like PCBs in certain foodstuffs		**Maximum levels**	
Foodstuffs		Sum of dioxins (WHO-PCDD/ F-TEQ) (32)	Sum of dioxins and dioxin-like PCBs (WHO-PCDD/ F-PCB-TEQ) (32)
5.1	Meat and meat products (excluding edible offal) of the following animals (6) - bovine animals and sheep - poultry - pigs	3,0 pg/g fat (33) 2,0 pg/g fat (33) 1,0 pg/g fat (33)	4,5 pg/g fat (33) 4,0 pg/g fat (33) 1,5 pg/g fat (33)

5.2	Liver of terrestrial animals referred to in 5.1 (6), and derived products thereof	6,0 pg/g fat ([33])	12,0 pg/g fat ([33])
5.3	Muscle meat of fish and fishery products and products thereof, excluding eel ([25]) ([34]). The maximum level applies to crustaceans, excluding the brown meat of crab and excluding head and thorax meat of lobster and similar large crustaceans (Nephropidae and Palinuridae)	4,0 pg/g fresh weight	8,0 pg/g fresh weight
5.4	Muscle meat of eel (*Anguilla anguilla*) and products thereof	4,0 pg/g fresh weight	12,0 pg/g fresh weight
5.5	Raw milk ([6]) and dairy products ([6]), including butterfat	3,0 pg/g fat ([33])	6,0 pg/g fat ([33])
5.6	Hen eggs and egg products ([6])	3,0 pg/g fat ([33])	6,0 pg/g fat ([33])
5.7	Fat of the following animals: - bovine animals and sheep - poultry - pigs	 3,0 pg/g fat 2,0 pg/g fat 1,0 pg/g fat	 4,5 pg/g fat 4,0 pg/g fat 1,5 pg/g fat
5.8	Mixed animal fats	2,0 pg/g fat	3,0 pg/g fat
5.9	Vegetable oils and fats	0,75 pg/g fat	1,5 pg/g fat
5.10	Marine oils (fish body oil, fish liver oil and oils of other marine organisms intended for human consumption)	2,0 pg/g fat	10,0 pg/g fat

* Table 2 is reproduced from Commission Regulation (EC) No. 1881/2006. The references ( ) in the table refer to footnotes in this Regulation and people intending to use the MLs should refer to the Regulation for details.

Conclusions

Dioxins, furans and PCBs are highly resistant to breakdown processes, and consequently persist in the environment, followed by uptake into the food chain. Up to 90% of human exposure to dioxins results from the consumption of food containing dioxins, mainly foodstuffs of animal origin with a high fat content, since these contaminants accumulate in fatty tissues. Foodstuffs in which dioxins can occur include meat, fish, eggs and milk.

These toxic chemicals can provoke serious health effects such as cancer, hormone disruption, reduced ability to reproduce, skin toxicity and immune system disorders.

Because of their serious health effects and their persistence in the environment, it is essential to minimize their release into the environment, including the establishment of emission limits for dioxins to air, prohibition of the use of

PCBs, and safe collection, storage and environmentally compatible disposal or destruction of dioxin and PCB-contaminated devices and products.

In order to ensure that MLs are not exceeded, routine surveillance of food and feed must be carried out, involving the taking of samples of potentially contaminated product followed by laboratory analysis to determine the levels of dioxins and PCBs in the sample.

Also, Food Business Operators (FBOs) must ensure that their products comply with the legislative limits for dioxins and PCBs as laid down in Commission Regulation (EC) No 1881/2006. It is important that FBOs identify critical control points (CCPs) in their processes that may result in dioxin and PCB contamination. The identification of appropriate CCPs along their process chain will enable them to develop and apply proper HACCP systems which will ensure that there are no unforeseen sources of dioxin in their products.

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