Is there any Connection between the Toxicity of Polychlorinated Polyaromatic Compounds with their Solubility in Water?

Sergei S. Yufit
N.D. Zelinsky Institute of Organic Chemistry of Russian Academy of Sciences. Russia, Moscow, 117913, GSP-1, 47 Leninsky pr. Fax: +7 095 135 5328; e-mail: yufit@ioc.ac.ru

Abstract

For comparing the toxicity of various mixtures of polichlorinated dibenzo-p-dioxins, -furans and biphenyls there exists the system of the toxic equivalency factors (TEF) where the toxicity of the most dangerous ones is expressed in terms of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin that is assumed to be one. Although the controversies around the methods of determination of dioxin toxicity have not abated, the direct determination of the toxicity in the experiments with a biological objects is still the main procedure. The quest for new approaches to understanding of the dioxin's movement in living organisms and in trophic chains and causes of their toxicity seems to be quite useful. We have found that the composition of human milk pollutants (i.e. dioxins/furans) sampled in different regions of Russia and in different countries are surprisingly close, although the sources of pollution and population diets are quite different. This work is aimed at attracting the attention of investigators to possible connection between the water solubility of dioxins/furans (and other substances having similar activity) and their toxicity expressed in the terms of TEF.

Introduction

Polychlorinated polyaromatic compounds, first of all polychlorinated dibenzo-p-dioxins, -furans and biphenyls (all this group is commonly christened "dioxins") are substances that are the most toxic and dangerous for humans and their environment. For comparing the toxicity of various mixtures of these compounds for humans there exists the system of the equivalent toxicity factors (TEF) where the toxicity of the most dangerous ones is expressed in terms of toxicity of 2,3,7,8-tetrachlorodibenzodioxin (2378-TCDD or D4) that is assumed to be one.

Toxic Equivalency Factor (TEF) are widely used for determination of the toxicity of dioxin-polluted breast milk and for the comparison of the toxicity of different breast milk samples. The comparison of the congener profiles is used for making far-reaching conclusions concerning the sources of pollution and the pollution levels in the region.

We have studied the congeners profiles of different breast milk samples and found that there are only slight differences between them. This samples strongly differ in their toxicity but not in congener profile. This fact indicates a presence of a some leveling factor of unknown nature. We suppose that differences in the water solubility of dioxin and furans can be an important, although not the single, contribution to this leveling.

Results and Discussion

The results are shown on transformed hypsograms based on the toxicity table (Table) where are listed some physic-chemical properties of toxic polychlorinated dioxins/furans arranged in order approved by the international agreement (USEPA, 1989). The independent variable is the ordinal number of the dioxin/furan (the X-axis). The functions are shown on Y-axis. The points are connected with lines. These transformed hypsograms are very useful and easy to analyze.

The comparison of composition of dioxin/furan pollutants in the human milk sampled in Salavat and Suzdal (urban and rural city in Russia), Honolulu (state Hawaii USA) and West German and Vietnamese cities[3, 4] revealed that the profiles of pollution for all the human milk samples are quite similar (Fig. 1). This striking uniformity of pollutant composition can not be caused by similarity of population diet in sampling sites[5, 6]. We suggest that the actual reason of this phenomenon may be the different solubility of these dioxins/furans in water. In any way of getting of the dioxin molecule into the living organism they comes into the aqueous phase. The transfer of this molecule to the lipid membrane is described by the partial coefficient $K_{o/w} = C_o/C_w$, where C_o is the equilibrium concentration of this dioxin in octanole, and C_w is its concentration in water. If the permeation of dioxin into cell was an equilibrium process than the concentrations of each dioxin outside of cell $Cw_{(out)}$ and inside it $Cw_{(in)}$ would be equal. It is evident that it is not so. The achievement of the equilibrium in a case of poorly soluble dioxins/furans of the D8, F5 and F6 type demands a long time. At the same time solutions of fairly soluble dioxins/furans of the D4, D5, F4 and F5 type may be unsaturated. As the equilibrium concentrations of all dioxins in octanole are 6-11 orders of magnitude bigger than their concentrations in water, the former ones can be assumed to be very big and constant comparing to the concentrations in the aqueous phase. For poorly soluble compounds we assume that all equilibrium concentrations of dioxins are equal to their solubility limits. In this way the concentration of toxicants inside the sell can be connected with their concentration outside it. Also the concentrations of poorly soluble dioxins/furans inside and outside of the cell would correspond to their solubility limits, and for fairly soluble dioxins the inside concentration would depend on the outside one.

On fig. 1 it is clearly seen the existence of a distinct link between the toxicant solubility in water and the toxicant concentration in the human milk. This link is even more clear if one would use toxicants concentration expressed in terms of TEQ ($TEQ = TEF \times P_i$), where P_i is the weight concentration of the component. The dioxin solubility compared with their international toxicity factors (I-TEF) are shown on fig. 2. It is evident that these values are somewhat correlated. The presence of characteristic plateaus for the three D6 and four F6, the change of the slope for (D4, D5, D6), (D6(3), D7, D8, F4) and the minimal for D8 on the both curves are not purely incidental. Also it can be supposed that for F8 the values of either I-TEF, or solubility are not valid.

The link between the dioxin water solubility and its concentration in the human milk can explain the uniformity of human milk pollution in samples taken from different regions. Also the similarity of dioxin solubility and I-TEF curves indicates the deep connection between these two parameters and expresses the role of the aqueous phase in explaining the dioxin toxic action. And if such link exists, than it does mean that the aqueous phase plays the deciding role in the mechanism of the dioxin action on the living organisms.

I thank the J. and K. MacArthur Foundation and WHO/EURO for financial support and Dr. A.K.D. Liem and Dr. W. Traag from the Netherlands for analysis of milk samples from Russian.

Literature Cited

(1) Liem, A.K.D.; Berg, R.v.d.; Bremmer, H.J.; Hesse, J.M.; Slooff, W. (eds.). *Integrated criteria document dioxins.* National Institute of Public Health and Environmental Protection. Report no 710401032. The Netherlands. 1993.

(2) United States Environmental Protection Agency. *Estimating Exposure to Dioxin-Like Compounds.* 1994. EPA/600/6-88/005Cb, June 1994.

(3) Dai, L.C.; Minh, D.Q.; Quynh, H.T.; Thom, L.H.; Thuy, L.B. (with the cooperation of Dr. A.Schecter). *Dioxin'93, ANA.* 1993, 7-10.

(4) Schecter, A.; Furst, P.; Furst, Ch.; Groebel, Ch.; Kolesnikov, S.; Savchenkov, M.; Beim, A.; Boldonov, A.; Trubitsun, E.; Vlasov, B. *Chemosphere* **1990**, 20, 927.

(5) Brodsky, E.S.; Klyuev, N.A.; Sojfer, V.S.; Karimova, L.K.; Maksimov, G.G. *Thesis of the Conference "Dioxins: environmental problems and analytical methods".* Ufa, **1995**, p. 39. (in Russian).

(6) Takizava, Y.; Muto, H. *Chemosphere*, **1987**,. 16, no 8/9, 1971.

Table

PROPERTIES OF TOXIC POLYCHLORODIBENZO-p-DIOXINS AND DIBENZOFURANS

Nos.	CODES	CONGENERS	SOLUBILITY ng/l	Log(Kow)	I-TEF
1	D4	2378-TCDD	200	6.8	1
2	D5	12378-PeCDD	120	(6.64)	0.5
3	D6(1)	123478-HxCDD	4.4	7.8	0.1
4	D6(2)	123678-HxCDD	(4.4)	(7.3)	0.1
5	D6(3)	123679-HxCDD	(4.4)	(7.3)	0.1
6	D7	1234678-HpCDD	2.4	8.0	0.01
7	D8	OCDD	0.4	8.1 (7.59)	0.001
8	F4	2378-TCDF	419	5.8 (6.53)	0.1
9	F5(1)	12378-PeCDF	(240)	6.79 (6.4)	0.05
10	F5(2)	23478-PeCDF	236	(6.92)	0.5
11	F6(1)	123478-HxCDF	8.2	[7.5]	0.1
12	F6(2)	123678-HxCDF	18	[7.5]	0.1
13	F6(3)	123789-HxCDF	(13)	[7.5]	0.1
14	F6(4)	234678-HxCDF	(13)	[7.5]	0.1
15	F7(1)	1234678-HpCDF	1.4	(7.92)	0.01
16	F7(2)	1234789-HpCDF	1.4	(7.9)	0.01
17	F8	OCDF	1.2	11 (8.78)	0.001

Comments:

1. Solubility and (Log($K_{o/w}$) from review[1]. The figures in the parenthesis are an average values or was taken from[2].

2. Toxicity equivalency factors (I-TEF) and Nos. congeners was taken from the International convention list.

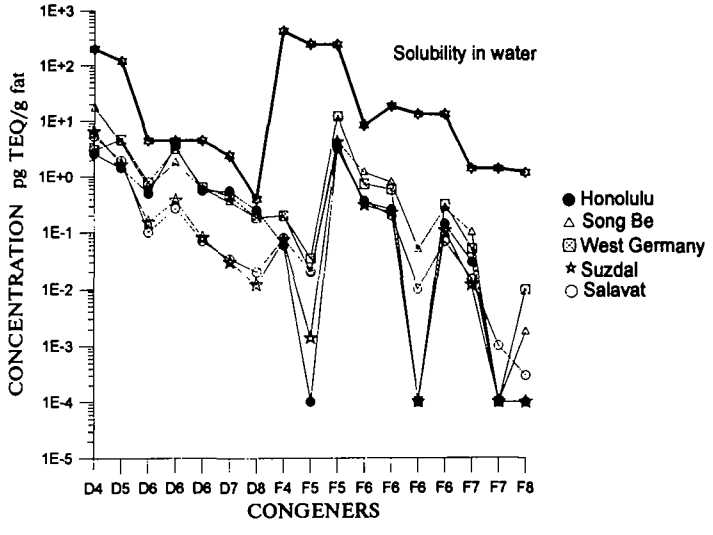

Fig. 1. Comparison of toxicity of breast milk samples from various world regions: Salavat (Russia), Dr. Djien Liem data (RIVM, the Netherlands); Suzdal (Russia) and Honolulu (Hawaii, USA), Dr. Wim Traag (RIKILT-DLO, the Netherlands); Song Be (Vietnam) and West Germany, see [3,4]. Solubility in water see Table in text.

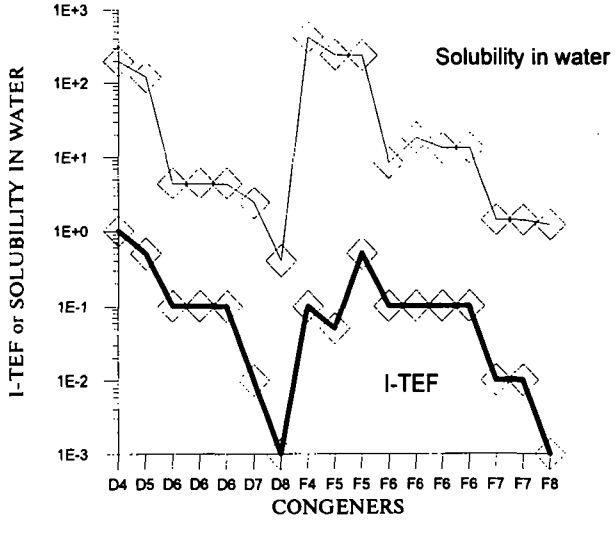

Fig.2 Comparison of water solubility of 17 dioxins/furans congeners and their toxicity (I-TEF).