*MULTIVARIATE PHYSICO-CHEMICAL CHARACTERISATION OF POLYCHLORINATED NAPHTHALENES (PCNs)

Jerzy Falandysz[1], Tomasz Puzyn[1], Michal Markuszewski[2], Roman Kaliszan[2]

[1]Department of Environmental Chemistry & Ecotoxicology, University of Gdansk, 18 Sobieskiego Str., PL 80-952 Gdansk, Poland
[2]Department of Biopharmaceutics and Pharmacodynamics, Medical University of Gdansk, 107 Gen. J. Hallera Str., PL 80-416 Gdansk, Poland

Introduction

Polychlorinated naphthalenes (PCNs) contain one to eight chlorine atoms per naphthalene molecule and form a complex mixture of 75 congeners (Fig. 1). All 75 CN congeners are more or less planar compounds, structurally similar to highly toxic 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) (1). PCNs are industrial chemicals which were introduced into practice around 1910 and were further replaced mainly by polychlorinated biphenyls, which were introduced in 1929. Nevertheless, there are examples available that PCNs at least up to the late 1980s remained in service (2). The physical and chemical properties of PCNs and PCBs are largely similar and both groups found similar industrial applications (1). PCNs from many years are widespread environmental contaminants and very recently their isomer and congener composition has been elucidated in a range of biotic and abiotic environmental samples as well as in technical PCN formulations of the Halowax series (1, 3-7). Potential environmental exposure to PCNs may be cause for concern. The reconstruction of the historical inputs of PCNs in England using dated core from the profundal sediments did indicated that the PCNs peak in the late 1950s to mid-1960s predates the PCBs peak by around 20 years (8). 1972-92 time-trend study showed decrease in the load of PCNs in Swedish human milk (9).

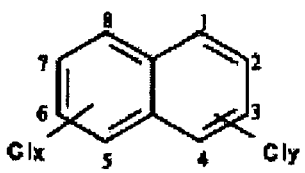

Fig. 1. Structure and ring numbering system of PCNs.

At some industrialised urban sites of the world such as the Detroit River (Michigan, USA) the concentrations of PCNs until 1996-97 remained high, and also their contribution to TCDD TEQs of dioxin-like compounds (10).

An elucidation of toxic properties of all theoretically possible constituents of the complex mixtures such as PCNs, PCBs, PCDDs, PCDFs or similar dioxin-like compounds using laboratory animals, bioassay and synthetic standards of high purity is usually economically nor experimentally feasible. Because of this, predictions of physicochemical properties and biological activity could give a significant insight into knowledge on those compounds, which have not been tested/synthesised yet or no any data are available. QASR methods are very useful in the predictions. The aim of this study is extraction from the battery of physicochemical descriptors an information describing in the best way differences existing between 75 congeners of CN.

Key words: polychlorinated naphthalenes, PCNs, principal component, PCA, multivariate study.

Materials and Methods

In the first step, 35 physico-chemical descriptors for all 75 congeners of chloronaphthalene were collected - taken from the literature (descriptors 1-18) or computed (descriptors 19-35) (Table 1).

Table 1
Physico-chemical data of all 75 congeners of chloronaphthalene used in this study

Descriptor	Parameter	Ref.
1-8	Substitution pattern	11
9	Symmetry of the molecule	12
10	Vicinal carbon atoms substitution pattern	13
11	Number of chlorine atoms at positions	14
12	Retention time	14
13	Vaporpressure	14
14	Standard entalphy of formation	12
15	Standard molar enthropy	12
16	Heatcapacity	12
17	Energy of HOMO	12
18	Energy of LUMO	12
19	X1 (a first-order molecular connectivity index)	15
20	Log K_{ow}	15
21	Wienl (the Wiener Index)	15
22	Specific polarizability of a molecule	15
23	Dipole moment of the molecule	15
24	Maxq+ (the largest positive charge over the atoms in a molecule)	15
25	Ka3 (Kappa Alpha 3; a third order shape index for molecules)	15
26	Absq (the sum of absolute values of the charges on each atom of the molecule, in electrons)	15
27	Maxq- (the largest negative charge over the atoms in a molecule)	15
28	Molecular weight of a molecule	15
29	Molecular polarizability	16
30	Molecularrefractivity	16
31	Log P (hydrophobicity)	16
32	SASsurf(solvent-accessiblesurfacearea)	16
33	VdWsurf(Van der Waals surface area)	16
34	SASvol (solvent-accessible volume)	16
35	VdWvol (Van der Waals volume)	16

In the second step, this data were analysed using Principal Component Analysis (PCA) method. PCA is a multivariate projection method summarising the systematic information in the data matrix. Mathematically, it is the matrix decomposition into means x_k^{mean}, scores t_{in}, loading p_{ak} and residuals e_{ik} according to the equation:

$$x_{ik} = x_k^{mean} + \sum_{a=1}^{A} t_{ia} p_{ak} + e_{ik} \qquad (1)$$

x_{ik} are the physicochemical descriptors compiled in the multivariate characterisation. The index i is used for the compounds (i = 1,2,3,...,75), index k for the descriptors (k = 1,2,3,...,35). Each score t_{ia} describes the location of the i-th compound along a-th principal component (PC) at the score plot. The absolute value of a loading p_{ak} informs how much the descriptor (variable k) contributes to a-th PC. The sign of a loading shows if the variable is positively or negatively correlated to the PC.The first calculated principal component explains the main variation in the data, the second represents the next largest variance, and so on (17-20).

Results and Discussion

The PCA of the physicochemical data matrix gave four-dimensional model that explained 76% (58% + 9% + 5% + 4.5%) of the total variance. The loading plot (Fig. 2) shows that the first PC is influenced by variables describing degree of chlorination, molecular weight, polarizability and lipophilicity. The best positively correlated descriptors are: retention time, standard molar entropy, heat capacity, a first-order molecular connectivity index, Log K_{ow}, the Wiener Index,

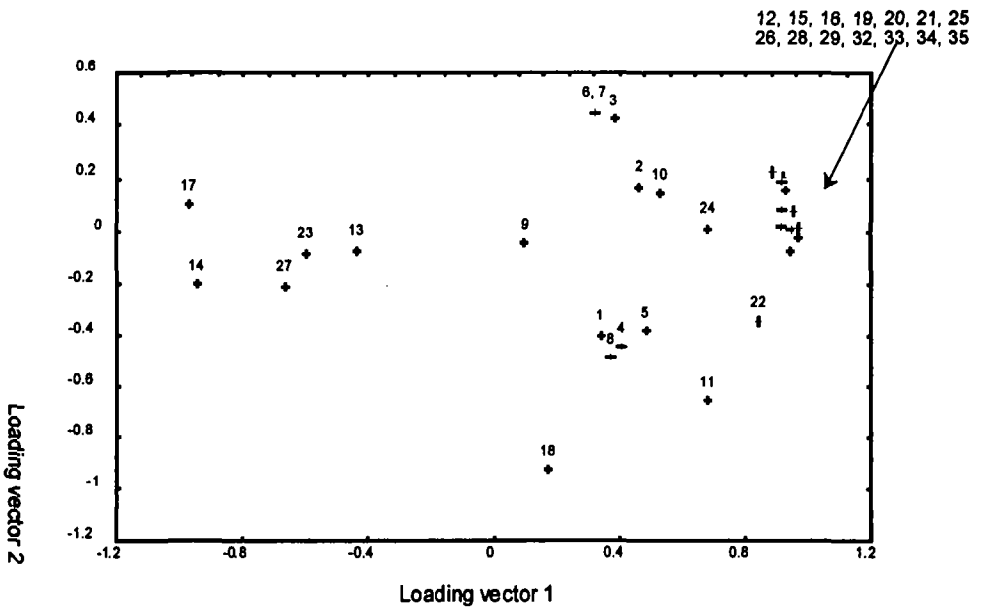

Fig. 2. Loading plot. Loading vector 2 versus Loading vector 1 (description of variables is explained in Table 1).

specific polarizability, a third order shape index for molecules, the sum of absolute of the charges on each atom of the molecule, molecular weight, polarizability, refraction, sa surface, van der Waals surface, sa volume, van der Waals volume. Negatively correlated are: standard enthalpy of formation and energy of HOMO. The second PC is strongly influenced by energy of LUMO, while substitution pattern parameters, number of chlorine atoms at _- positions and vicinal (adjacent) carbon atoms substitution pattern are less important. The third PC (data not shown) is depended on dipole moment and the largest negative charge, and on substitution at

position 2 of naphthalene nuclei, while symmetry group parameter is determined by PC4. Based on the PC analysis CN congeners substituted with chlorine at positions 1, 2, 3, 6 and 7, and next those substituted at the positions 1, 2, 3 and 6 or 7 are considered to be most potent in terms of dioxin-like toxicity. It seems to be possible using mathematical modelling to estimate TCDD TEFs (or REPs; relative potencies) of the CN congeners till now not tested experimentally or for which no standards are available.

References

1. Falandysz J. (1998) Environ. Pollut. 101, 77.
2. Popp W., Norpoth K., Vahrenholz C., Hamm S., Balfanz E. and Theisen J. (1997) American J. Ind. Med. 32, 413.
3. Järnberg U., Asplund L., de Wit C., Egeback A-I., Widequist U. and Jakobsson E. (1997) Arch. Environ. Contam. Toxicol. 32, 232.
4. Falandysz J., Strandberg L., Strandberg B. and Rappe C. (1998) Chemosphere 37, 2473.
5. Helm P.A., Jantuinen L.M.M., Bidleman T.F. and Dorman F.L. (1999) J. High. Resol. Chrom. 22, 639.
6. Falandysz J., Kawano M., Ueda M., Matsuda M., Kannan K., Giesy J.P. and Wakimoto T. (2000) J. Environ. Sci. Health. 35A, 281.
7. Espadaler I., Eljarrat E., Caixach J., Rivera J., Marti I. and Ventura F. (1997) Rapid Comm. Mass Spectrom. 11, 410.
8. Gevao R., Harner T. and Jones K.C (2000). Environ. Sci. Technol. 34, 33.
9. Lundén Å. and Norén K (1998) Arch. Environ. Contam. Toxicol. 34, 414.
10. Kannan K., Yamashita N., Imagawa T., Decoen W., Kim J.S., Day R.M., Summer C.L. and Giesy J. (2000) Environ. Sci. Technol. 34, 566.
11. Tysklind M., Tillitt D., Eriksson L., Lundgren K., Rappe C. (1994) Fundam. Appl. Toxicol. 22, 277.
12. Falandysz J., Raciniewska M., Blazejowski J., Golaszewska I. and Skurski P. (1998) Organohalogen Compd.. 36, 471.
13. Falandysz J. (1997) Organohalogen Compd. 32, 374.
14. Lei Y.D., Wania F. and Shiu W.Y. (1999) J. Chem. Eng. Data. 44, 577.
15. Sci QASR™ 3.0 User Guide.
16. Chem Plus, Hypercube.
17. Tysklind M., Lundgren K., Rappe C., Eriksson L., Jonsson J., Sjostrom M. and Ahlborg U.G. (1992) Environ. Sci. Technol. 26, 1023.
18. Jackson J.E. (1991) A user's guide to principal components. J. Wiley & Sons, N.Y., USA.
19. Jolliffe T. (1986) Principal component analysis. Springer-Verlag, N. Y., USA.
20. Wold S., Esbensen K. and Geladi P. (1987) Chemom. Intell. Lab. Syst. 2, 37.