PREDICTING THE BIOCONCENTRATION POTENTIAL OF ORGANIC CHEMICALS IN FISH

by

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ABSTRACT

A regression equation was developed to predict the bioconcentration potential of chemicals in fish with the partition coefficient as the independent variable, using chemicals with a wide range in partition coefficient (carbon tetrachloride to hexachlorobenzene). The regression equation was then used to predict the bioconcentration factor of Chlorpyrifos and Endrin in fish. The predicted values agreed with the experimental values reported in the literature. The equation may be used to estimate the potential of new chemicals to bioconcentrate in fish.

INTRODUCTION

The recent concern (1-3) over the wide spread residue levels in our environment of DDT and PCB (polychlorinated biphenyls) has raised questions regarding the distribution of other chlorinated hydrocarbons. There has been and still is a tendency in both the lay press and in some scientific circles to generalize that other carbon-chlorine containing materials will have environmental characteristics similar to DDT. It is the purpose of this article to relate bioconcentration to the chemical and physical properties and to suggest a method for estimating the potential of a chemical to concentrate in fish. Knowledge of this potential is useful in making the business decision regarding the possible development of new chemicals.

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Kenega[4] pointed out the difficulties of defining the general term of bioconcentration. It is our belief that by confining our attention to fish in an aquatic environment we can circumvent these difficulties. Hence we shall define bioconcentration factor as the ratio of the concentration of the chemical in the fish at steady state with the concentration of the chemical in the exposure water under laboratory conditions[5]. When dealing with bioconcentration under these conditions and with relatively stable molecules the equilibrium situation of the chemical between the fish and water should be related to a simple partitioning. In other words, the fish to a first approximation may be considered as a non polar solvent mixed with the polar solvent, water. If this is true, then the partition coefficient of the chemical should be correlated in a linear manner with the ratio of the steady state concentration of the chemical in the fish and water.

This is the thesis that we will attempt to support by the experimental evidence to be presented.

MATERIALS AND METHODS

Chemicals - The following chemicals were evaluated: 1) 1,1,2,2-tetrachloro ethylene, 2) hexachlorobenzene, 3) 2,2',4,4'-tetrachlorobiphenyl, 4) 2-biphenylyl phenyl ether, 5) diphenyl ether, 6) carbon tetrachloride, and 7) p-dichlorobenzene.

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Bioconcentration factor in fish - The method described by Branson et al.[5] was used to determine the bioconcentration factor in rainbow trout (Salmo gairdneri Richardson). This method is based on determining the steady state concentration of the chemical in the muscle of 4-5" trout. Essentially there are three parts to the procedure; a) the rate of uptake of the chemical by fish is measured, b) the remaining fish are transferred to fresh water and the clearance rate is determined, c) a computer based technique is used to calculate the bioconcentration at steady state.

Partition coefficient - The partition coefficient of the chemical between n-octanol and water was either taken from the tabulation of Hansch et al.[6] or calculated using the additivity principles[7] as illustrated below. A partition coefficient between n-octanol and water for a chemical may be calculated using equation 1.

$$\log P_X = \Sigma \text{ substituent constants} + \log P_H \qquad (1)$$

where P_X = Partition coefficient of chemical

P_H = Partition coefficient of parent structure

the substituent constants were obtained from the listing of Hansch[6].

The various substituent constants used in this paper are shown in Table 1. The following is a typical example using 1,1,2,2-tetrachloro ethylene as the chemical.

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$$\log P_x = +(4 \times .39) \text{ (four aliphatic Cl atoms)}$$
$$-(1 \times .3) \text{ (double bond)}$$
$$+(2 \times .5) \text{ (2, } -CH^2- \text{ groups)}$$
$$= 2.26 \text{ (Sum of substituent constants)}$$

RESULTS

The results of measuring the bioconcentration factor in rainbow trout and the partition coefficient of the various chemicals are shown in Table II. Using standard regression analysis[8] the line of best fit was drawn through the points of partition coefficient vs. bioconcentration factor and is shown in Figure 1 with the equation for the line being given in Equation 2.

$$\log (\text{Bioconc. factor}) = 0.56 \log (\text{Part. coeff.}) + 0.124 \quad (2)$$

A multiple correlation coefficient of 0.951 and a standard error of 0.369 was obtained for the regression. The 95% confidence level for these values are shown in Figure 1. The lines were calculated from the statistical equation given in Draper & Smith[8].

DISCUSSION

As can be seen from Fig. 1 there is a high correlation between the partition coefficient of the chemical and its propensity

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to bioconcentrate in fish. It would appear, in these examples, that chlorine is no more significant than any other group in making a contribution to lipophilicity. As more lipophilic groups are added the tendency to bioconcentrate is enhanced.

The explanation for 2-biphenylyl-phenyl ether falling outside the 95% confidence region in Figure 1 may be due to metabolism with the subsequent formation a more polar compound. Such a situation would yield a structure(s) with a partition coefficient lower than the parent compound.

In using equation 2 for predicting the bioconcentration factor in fish for a specific chemical it must be remembered that the confidence intervals about the regression line have to be expanded[8]. Only as the number of observations for a chemical are increased will the confidence level be as pictured in Figure 1.

With this in mind, it is instructive to see how good a predictor equation 2 is for determining the bioconcentration factor in fish. The data presented in Table III was taken from unpublished work at The Dow Chemical Company[15-16] as well as from the literature[17]. In both cases the experimental procedure was slightly different and the fish species was mosquito fish (Gambusia affinia). It is rather striking, in view of these differences that such a close agreement between the experimental and calculated bioconcentration factor was observed.

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In interpreting the bioconcentration factor for chlorpyrifos or any chemical it must be remembered that metabolism is an active process[18]. Consequently the absolute amount of insecticide is constantly being reduced while the ratio will remain relatively fixed. The amount of fat deposits in the fish will also be an important factor in dictating the absolute amount of chemical found.

It will be noted that as you move away from the middle of the regression line (Figure 1) the confidence level increases. This is illustrated with the large standard deviation that is associated with the calculated value for pyridinol in Table III. Consequently, less confidence must be placed on any predictions that fall outside the range of the line in Figure 2. Since the experimental bioconcentration factor value for DDT of 5.23[19] was outside the region established by this regression, no attempt was made to make a prediction.

As more data is generated it will be important to verify and extend the confidence regions of this type of correlation. However, the present study does allow an investigator to begin rating the potential of new materials to concentrate. By matching this potential with the intended end use an early judgment decision can be made as to the possible long term environmental problems that may be faced.

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Finally, it should be stressed that in assessing the potential environmental hazard created by the presence of a foreign chemical the following considerations in addition to the partition coefficient are important.

1. Biological reactivity. If a molecule has a high metabolic rate the chances of accumulation are decreased. This is especially so since materials are usually converted to more polar chemicals and hence the affinity for lipids is decreased.

2. How used. If the chemical is used in an open ended system i.e. has direct access to the environment the chances for having an environmental stress are improved.

3. Volume. If the annual production of the chemical is high (i.e. DDT production was in excess of 60 million lbs.) and all the other factors such as high partition coefficient, unreactive and wide distribution are present an environmental hazard will probably be present.

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Relationship Between Partition Coefficient
&
The Potential Of Chemicals To Accumulate In Trout Muscle

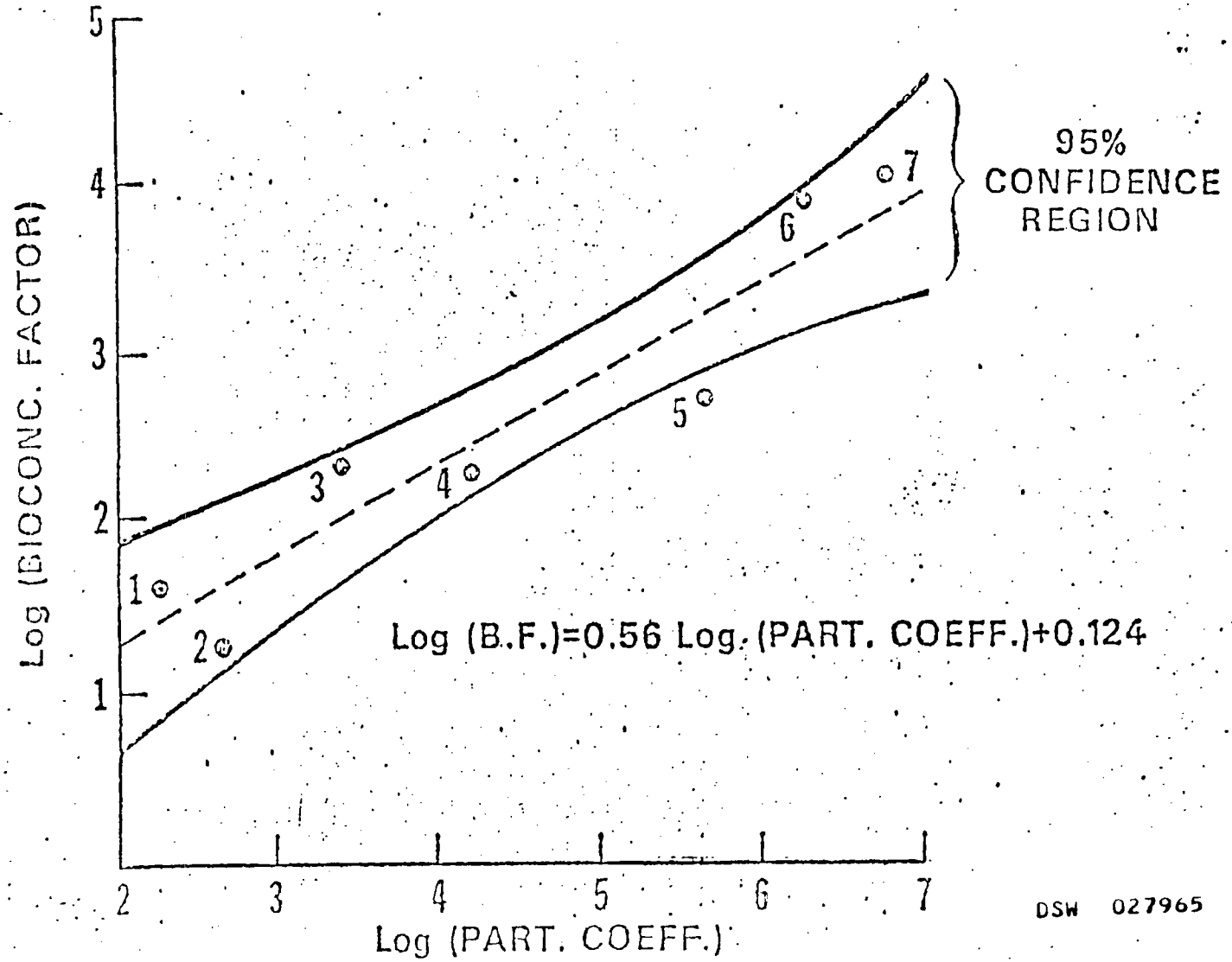

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TABLE I

List of Substituent Constants Used for Calculating Partition Coefficients (see Ref. 6 for complete listing.)

Group	Substitutent Constant
Aromatic	
Cl on benzene	0.7
Cl on phenol	
o	0.73
m	1.04
p	0.98
Benzene	2.13
Phenol	1.46
Aliphatic	
Cl	0.39
double bond	-0.30
$-CH_2-$	0.50
$CHCl_3$	1.97

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TABLE II

Bioconcentration factor in fish and the partition coefficients of the chemicals studied.

Chemical	Partition Coeff.[1]	Bioconc. Factor[1]	Ref.
1. 1,1,2,2-tetrachlor ethylene	2.26[2]	1.59(1.4-1.74)[4]	9
2. CCl_4	2.36[2]	1.28(1.16-1.30) ~~1.59(1.49-2.05)~~	10
3. p-dichlorobenzene	3.38[3]	2.36(2.32-2.39)	11
4. diphenyl ether	4.20[3]	2.30(2.23-2.34)	12
5. 2-biphenylyl phenyl ether	5.66[2]	2.74(2.64-2.81)	13
6. hexachlorobenzene	6.22[2]	3.93(3.80-4.07)	14
7. 2,2',4,4'-tetrachloro diphenyl ether	6.72[2]	4.09(4.00-4.16)	5.

[1] All values are logarithms to the base 10.
[2] Calculated value.
[3] Experimental value (Ref. 6).
[4] Figures in parenthesis are the nonsymmetrical 95% confidence limits calculated by a Bayesian estimation procedure (Ref. 20).

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TABLE III

The use of regression equation 2 for predicting the bioconcentration factor.

Chemical	log (Part. coeff.)	log (Bioconc. factor)	
		Calculated	Experimental
Endrin	5.6[b]	3.47 ± .989[d]	3.17[17]
Chlorpyrifos[a]	4.82[c]	2.87 ± 0.963[d]	2.67[15]
3,5,6-trichloro pyridinol	1.35[b]	0.88 ± 1.139[d]	0.49[16]

[a]0,0-diethyl 0-(3,5,6-trichloro-2-pyridyl) phosphorothioate

[b]Calculated

[c]Experimental

[d]Standard deviation calculated from Draper & Smith (Ref. 20).

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