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Use of Polynomial Expressions to Describe the Bioconcentration of Hydrophobic Chemicals by Fish

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For the bioconcentration of hydrophobic chemicals by fish, relationships have been previously established between uptake rate constants (k_1) and the octanol/water partition coefficient (K_{OW}), and also between the clearance rate constant (k_2) and K_{OW}. These have been refined and extended on the basis of data for chlorinated hydrocarbons, and closely related compounds including polychlorinated dibenzodioxins, that covered a wider range of hydrophobicity ($2.5 < \log K_{OW} < 9.5$). This has allowed the development of new relationships between log K_{OW} and various factors, including the bioconcentration factor (as log K_B), equilibrium time (as log t_{eq}), and maximum biotic concentration (as log C_B), which include extremely hydrophobic compounds previously not taken into account. The shape of the curves generated by these equations are in qualitative agreement with theoretical prediction and are described by polynomial expressions which are generally approximately linear over the more limited range of log K_{OW} values used to develop previous relationships. The influences of factors such as hydrophobicity, aqueous solubility, molecular weight, lipid solubility, and also exposure time were considered. Decreasing lipid solubilities of extremely hydrophobic chemicals were found to result in increasing clearance rate constants, as well decreasing equilibrium times and bioconcentration factors.

INTRODUCTION

The bioconcentration factor (K_B) of lipophilic compounds is defined as the ratio of the concentration in the body of an aquatic organism to that in the surrounding water. It is a measure of the tendency of lipophilic organic pollutants to accumulate in aquatic organisms. Predicting the K_B values of chemicals, particularly new ones, is an important aspect of hazard evaluation and management.

Bioconcentration can be considered to be the partitioning of compounds between the lipid phase of an organism and water. As a consequence, bioconcentration factors have been correlated with various partition coefficients, most notably the 1-octanol/water partition coefficient (K_{OW}). Mackay (1982) found the following relationship for a wide range of compounds,

$$\log K_B = 1.00 \log K_{OW} - 1.32. \tag{1}$$

Accordingly, similar linear relationships have been found by other workers (e.g., Zaroogian *et al.*, 1985; Davies and Dobbs, 1984). In general, however, these compounds possess log $K_{OW} < 6$ to 6.5. In considering this relationship over a wider range of log K_{OW}, including those >6.5, curvilinear relationships between log K_B and log K_{OW} have been observed (Konemann and van Leeuwen, 1980; Sugiura *et al.*, 1978) while sigmoidal (Spacie and Hamelink, 1982) and parabolic (Tulp and Hutzinger, 1978) ones have also been proposed.

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Thus, while simple partitioning provides an adequate model at log $K_{OW} < 6.5$, over a wider range it is apparent that bioconcentration factors are not solely explicable on the basis of a partitioning process and that other factors are involved. We have previously identified the time period required for attainment of equilibrium as an important factor (Hawker and Connell, 1985a,b; 1986). Since those investigations, additional data, particularly for extremely hydrophobic compounds (i.e., log $K_{OW} > 6.5$) such as polychlorinated dibenzodioxins (PCDD), have become available (Muir *et al.*, 1985; Opperhuizen *et al.*, 1985, 1986). These substances are of considerable environmental interest since they are toxic and, because they are often the product of urban waste incineration, may become more widespread in the environment. One aim of the present work then was to investigate the relationship between log K_B and log K_{OW} for such compounds and thus extend existing relationships. It was also of interest to determine the influence of molecular size and weight on the magnitude of bioconcentration factors since Zitko *et al.* (1974) have previously postulated an upper limit at molecular weight about 600 for the accumulation of chlorinated paraffins.

In addition, in previous work utilizing first-order uptake and clearance rate constants (k_1 and k_2, respectively), linear relationships between log k_1 and log K_{OW}, as well as log$(1/k_2)$ and log K_{OW} over a limited range of K_{OW} values were found (Hawker and Connell, 1985a). As with the log K_B to log K_{OW} relationship described above, such simple relationships may not be applicable over a wider K_{OW} range. Some authors have suggested that overall, the relationships may in fact be curvilinear (Konemann and van Leeuwen, 1980; Gobas *et al.*, 1986; Kubinyi, 1978), in agreement with theoretical prediction (Mackay and Hughes, 1984). The availability of rate constant data for PCDDs may, therefore, help determine the influence of factors such as molecular size and weight, and thus another aim of the present work was the development of such relationships for a wide range of K_{OW} values and compounds.

THEORY

Assuming a single-compartment model, the bioconcentration factor for nondegradable hydrophobic compounds may be described in terms of first-order uptake (k_1) and clearance (k_2) rate constants by

$$K_B = k_1/k_2(1 - e^{-k_2 t}) \tag{2}$$

and at equilibrium

$$K_B = k_1/k_2. \tag{3}$$

On the basis of fugacity considerations, Mackay and Hughes (1984) proposed that a direct linear relationship exists between $1/k_2$ and K_{OW} of the form

$$\frac{1}{k_2} = \frac{V_L}{Q_W} K_{OW} + \frac{V_L}{Q_O}, \tag{4}$$

where V_L is the volume of the lipid phase in the organism, and Q_W and Q_O are hypothetical effective flow rates of water and organic matter or octanol between the surrounding aqueous medium and the lipid phase. When plotted on logarithmic scales, such a relationship is curvilinear. Gobas *et al.* (1986) have developed a model for bioconcentration that assumes uptake and clearance kinetics for compounds of low lipophilicity are controlled by membrane permeation, while for compounds of higher

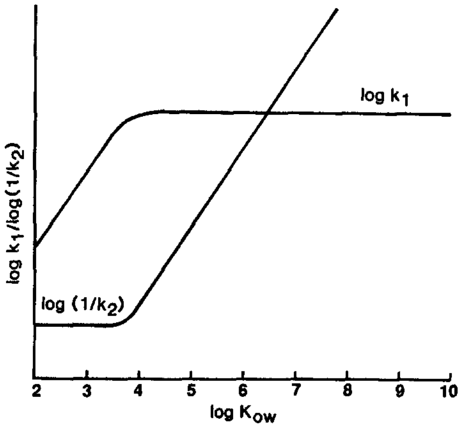

FIG. 1. Theoretical relationship between log k_1 and log K_{OW}, and log(1/k_2) and log K_{OW} from Gobas *et al.* (1986).

lipophilicity (log $K_{OW} > 3$ to 4), the controlling factor is diffusion. This also results in curvilinear relationships between log k_1 and log K_{OW} as well as log(1/k_2) and log K_{OW}, such as those depicted in Fig. 1. The authors have suggested (Hawker and Connell, 1987) that qualitatively similar relationships may also arise on the basis of diffusion through aqueous and lipid or membrane boundary layers within aquatic organisms according to equations of the form

$$k_1 = \frac{lK_{OW}A}{V_L(\Delta x_W K_{OW}/d_W) + \Delta x_L/d_L} \tag{5}$$

and

$$\frac{1}{k_2} = \frac{V_L}{A}\left(\frac{\Delta x_W K_{OW}}{d_W} + \frac{\Delta x_L}{d_L}\right), \tag{6}$$

where l is the lipid fraction, V_L is the lipid phase volume, A is the interfacial area between lipid and aqueous phases, Δx_W and Δx_L are the boundary layer thicknesses for aqueous and lipid phases, respectively, and d_W and d_L are the diffusion coefficients for aqueous and lipid phases.

Additionally, deviations from the curves in Fig. 1 (i.e., decreased k_1 and increased $1/k_2$) may occur for more hydrophobic (high K_{OW}) compounds due to their generally larger size and consequent decreased diffusion coefficient (Hawker and Connell, 1987).

Relationships such as those described by Eqs. (5) and (6) and depicted in Fig. 1 theoretically afford a direct linear relationship between log K_B and log K_{OW}. This is because at equilibrium, $K_B = k_1/k_2$, and for compounds with low lipophilicity, k_1 increases while $1/k_2$ is approximately constant. For compounds with high lipophilicity k_1 is now approximately constant while $1/k_2$ increases.

Several authors (e.g., Konemann and van Leeuwen, 1980; Sugiura *et al.*, 1978; Muir *et al.*, 1985; Opperhuizen *et al.*, 1985; Bruggeman *et al.*, 1984; Anliker and Moser, 1987) have observed that chemicals which have large molecules and are extremely hydrophobic (log $K_{OW} > 6$) do not bioconcentrate as much as predicted on the basis of linear equations such as Eq. (1).

On a lipid basis, if octanol is a perfect surrogate for lipid, $C_B/C_W = K_B = K_{OW} = C_O/C_W$ where C_B, C_O, and C_W are maximum biotic, octanol, and aqueous solubilities, respectively (Gobas *et al.,* 1986; Geyer *et al.,* 1985). Since for some chemicals at equilibrium, $K_B < K_{OW}$, then it follows that $C_B < C_O$. The most apparent difference between octanol and lipid is molecular size. The solubility of hydrophobic solutes, taking into account solvent size, may be treated by an adaptation of the Flory–Huggins theory (Chiou, 1985) and hence approximated by equations of the general form

$$\log C_X = -\log \nu_{SOL} - (1 - \nu_{SOL}/\nu_X^*)/2.303 - \chi/2.303, \tag{7}$$

where C_X is the solubility in either octanol or lipid, ν_{SOL} is the molar volume of the solute, ν_X^* is the molar volume of water-saturated solvent, and χ is the Flory–Huggins interaction parameter, which is a measure of solute–solvent compatibility. The molar volume for water-saturated 1-octanol is approximately 127 $cm^3\ mol^{-1}$ (Miller *et al.,* 1985), while that for lipid (as represented by glyceryl triolate) is some seven times larger (Chiou, 1985). It could be expected that solute molar volume and molecular size would roughly increase with hydrophobicity for related chemicals. The second term of Eq. (7), i.e., $(1 - \nu_{SOL}/\nu_X^*)/2.303$, is larger for lipid than for octanol as a solvent, and this therefore tends to make lipid an increasingly poor solvent relative to octanol, with increasing solute size. For solute molecules whose molar volume is roughly that of octanol, within a factor of 2 or 3, however, octanol and lipid solubilities are equal because this tendency is apparently roughly balanced by increasing solute incompatibility ($\chi_O/2.303$) in octanol. The incompatibility term is negligible for lipid since $\nu_{SOL} \ll \nu_L$. Only for relatively large solutes will the solute incompatibility term ($\chi_L/2.303$ from Eq. (7)) have an effect for lipid. With such compounds, an increasing ($\chi_L/2.303$) term means that lipid concentration (C_L) and hence C_B may become less than C_O.

If this is the case, then the bioconcentration factor on a lipid basis for relative large solutes with high log K_{OW} values may be expressed as

$$K_B = \frac{C_L}{C_W} = \frac{Z_L}{Z_W} < \frac{Z_O}{Z_W} = \frac{C_O}{C_W} = K_{OW} \tag{8}$$

and, therefore, $Z_L < Z_O$ where Z_L and Z_O are fugacity capacity constants ($mol\ m^{-3}\ Pa^{-1}$) for lipid and octanol. In the derivation of Eq. (4),

$$\frac{1}{k_2} = \frac{V_L Z_L}{Q_W Z_W} + \frac{V_L Z_L}{Q_O Z_O}$$

and because Z_L is usually assumed to be equal to Z_O, then

$$\frac{1}{k_2} = \frac{V_L}{Q_W} K_{OW} + \frac{V_L}{Q_O}$$

and a plot of $\log(1/k_2)$ versus log K_{OW} will result in a curve such as that shown in Fig. 1, with the inverse clearance rate constant for relatively hydrophobic molecules (log $K_{OW} > 4$) described by

$$\frac{1}{k_2} = \frac{V_L Z_O}{Q_W Z_W} = \frac{V_L}{Q_W} K_{OW}. \tag{9}$$

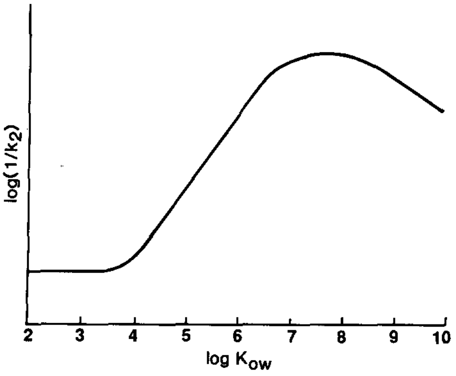

FIG. 2. Theoretical relationship between $\log(1/k_2)$ and $\log K_{OW}$ taking into account decreasing lipid solubility for very hydrophobic compounds.

If however $Z_L = fZ_O$ where $O < f < 1$, then

$$\frac{1}{k_2} = \frac{V_L f K_{OW}}{Q_W} \tag{10}$$

and $1/k_2$ is in fact smaller than would be the case if $Z_L = Z_O$ and $C_L = C_O$. Therefore, for those compounds where K_B (on a lipid basis) $< K_{OW}$, due to decreased lipid solubility, then $1/k_2$ increases more slowly with increasing K_{OW} than predicted by Eq. (9) and depicted in Fig. 1 and may even decrease such as shown in Fig. 2. The uptake rate constant remains unaffected by this factor, however, since k_1 is independent of K_{OW} for these chemicals, and expressions such as Eq. (5) are still applicable.

The k_2 values are related to the time period required to establish equilibrium between organism and water (t_{eq}). As has been demonstrated previously (Hawker and Connell, 1985a),

$$t_{eq} = 4.605/k_2. \tag{11}$$

From Eq. (11), smaller $1/k_2$ values result in correspondingly smaller equilibrium times. This means that for a related series of chemicals, sections of both plots of $\log(1/k_2)$ versus $\log K_{OW}$ and $\log t_{eq}$ versus $\log K_{OW}$ may be approximately parabolic in shape (see Fig. 2).

EXPERIMENTAL DATA AND RESULTS

Using data from guppies (*Poecilia reticulata*), goldfish (*Carassius auratus*), and trout (*Salmo gairdneri*) with mainly chlorinated hydrocarbons whose $\log K_{OW}$ values ranged 3 to 6, we have previously investigated the relationships between $\log k_1$ and $\log K_{OW}$ and also $\log(1/k_2)$ and $\log K_{OW}$ (Hawker and Connell, 1985a). This, together with more recent additional k_1 and $1/k_2$ data (Muir *et al.*, 1985; Opperhuizen *et al.*, 1985, 1986) for chlorinated naphthalenes, dibenzodioxins, and biphenyls, is presented in Table 1. In addition, $\log K_B$ values determined either by direct observation (i.e., C_B/C_W) or from the ratio of k_1 and k_2 for these compounds are also found in Table 1. The $\log K_{OW}$ values employed are those that we considered the most reliable

TABLE 1

KINETIC DATA FOR BIOCONCENTRATION OF CHLORINATED HYDROCARBONS BY FISH

Compound	log K_{OW}	log($1/k_2$) (days)	log k_1 (days^{-1})	log K_B	Reference[a]
1,4-Dichlorobenzene	3.37	—	1.99	1.98	1
1,2,3-Trichlorobenzene	4.11	0.34	2.65	2.85	1
1,3,5-Trichlorobenzene	4.15	0.40	2.63	2.88	1
1,2,3,5-Tetrachlorobenzene	4.48	−0.42	2.91	3.59	1
Pentachlorobenzene	4.94	0.96	3.08	4.14	1
Hexachlorobenzene	5.50	—	2.73	4.19	1
2,5-Dichlorobiphenyl	5.06	1.18	2.96	4.15	2
2,2′,5-Trichlorobiphenyl	5.24	1.32	2.98	4.30	2
2,4′,5-Trichlorobiphenyl	5.67	1.68	2.95	4.62	2
2,2′,5,5′-Tetrachlorobiphenyl	5.84	1.82	2.87	4.69	2
2,3′,4′,5-Tetrachlorobiphenyl	6.20	2.00	2.62	4.62	2
Tetrachloroethene	2.60	−0.30	1.90	1.60	3
Carbon tetrachloride	2.64	−0.77	1.99	1.24	3
1,4-Dichlorobenzene	3.37	0.20	2.14	2.33	3
Diphenyl ether	4.21	0.18	2.12	2.29	3
Biphenyl	4.09	0.43	2.21	2.64	3
2-Biphenylyl phenyl ether	4.55	0.45	2.29	2.74	3
Hexachlorobenzene	5.50	1.24	2.65	3.90	3
Pentachlorobenzene	4.94	0.83	2.11	2.96	4
2,2′,5,5′-Tetrachlorobiphenyl	5.84	1.82	3.08	4.26	4
2,5-Dichlorobiphenyl	5.06	0.96	3.07	4.92	4
2,2′,4,4′,5,5′-Hexachlorobiphenyl	6.92	2.39	2.90	5.32	4
2,2′,3,3′,4,4′,5,5′-Octachlorobiphenyl	7.80	2.15	2.18	4.35	4
Decachlorobiphenyl	8.18	2.39	1.60	4.02	4
1,3,6,8-Tetrachlorodibenzodioxin	8.10	1.0	2.26	3.32	5
	8.10	1.0	2.75	3.76	5
1,2,3,4,7,8-Hexachlorodibenzodioxin	9.05	1.34	2.01	3.36	5
	9.05	1.52	2.05	3.63	5
1,2,3,4,6,7,8-Heptachlorodibenzodioxin	9.55	1.38	1.74	3.15	5
	9.55	1.40	1.26	2.71	5
Octachlorodibenzodioxin	9.84	0.92	1.04	1.92	5
	9.84	1.30	2.15	3.35	5
2,3,7,8-Tetrachlorodibenzodioxin	6.64	1.34	2.78	4.11	6
p,p′-DDT	6.19	2.05	2.91	4.97	5
2,2′,4,4′,5,5′-Hexachlorobiphenyl	6.92	2.10	2.66	4.84	5
2-Chloronaphthalene	4.19	0.51	2.86	3.63	7
1,4-Dichloronaphthalene	4.88	0.96	3.08	3.36	7
1,8-Dichloronaphthalene	4.41	0.80	2.99	3.79	7
2,3-Dichloronaphthalene	4.71	0.85	3.20	4.04	7
2,7-Dichloronaphthalene	4.81	0.85	3.20	4.04	7
1,3,7-Trichloronaphthalene	5.59	1.08	3.36	4.43	7
1,2,3,4-Tetrachloronaphthalene	5.94	1.04	3.52	4.52	7
1,3,5,7-Tetrachloronaphthalene	6.38	1.66	2.88	4.53	7
1,3,5,8-Tetrachloronaphthalene	5.96	1.35	3.08	4.40	7
Pentachlorobenzene	5.46	1.11	3.15	4.23	7
2,3′,4′,5-Tetrachlorobiphenyl	6.20	1.74	2.58	4.32	7

[a] References: (1) Konemann and van Leeuwen, 1980; (2) Bruggeman *et al.*, 1981; (3) Neely *et al.*, 1974; (4) Bruggeman *et al.*, 1984; (5) Muir *et al.*, 1985; (6) Opperhuizen *et al.*, 1986; (7) Opperhuizen *et al.*, 1985.

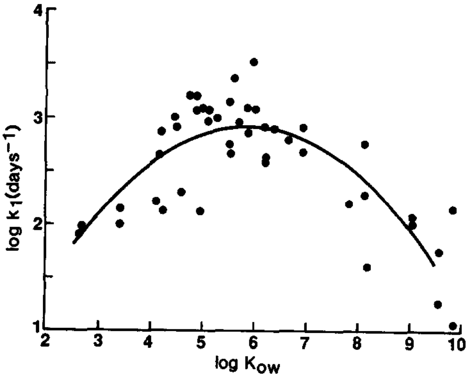

FIG. 3. Plot of log k_1 versus log K_{OW} for uptake of chlorinated hydrocarbons and closely related compounds by fish, showing experimental data points, together with the curve of best fit.

available. Data from all chemicals for which reliable partition coefficients could be found were used.

The uptake rate constant data were fitted to a parabola as shown in Fig. 3. The maximum log k_1 value of 2.92 corresponds to a log K_{OW} of 5.87 with the curve of best fit described by the following second-order polynomial in log K_{OW}:

$$\log k_1 = 2.92 - 9.86 \times 10^{-2}(\log K_{OW} - 5.87)^2 \qquad (r = 0.81, n = 46). \qquad (12)$$

The logarithms of the reciprocal first-order clearance rate constants were best fitted to a polynomial of fourth order in log K_{OW}. Figure 4 shows a plot of log$(1/k_2)$ versus log K_{OW} containing experimental data points and the regression line described by

$$\log\left(\frac{1}{k_2}\right) = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.65(\log K_{OW})^2 - 5.34 \log K_{OW} + 5.27 \qquad (r = 0.89, n = 45). \qquad (13)$$

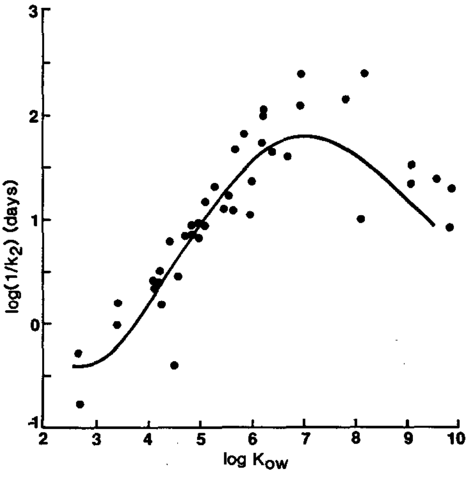

FIG. 4. Plot of log$(1/k_2)$ versus log K_{OW} for clearance of chlorinated hydrocarbons and closely related compounds by fish, showing the experimental data points, together with the curve of best fit.

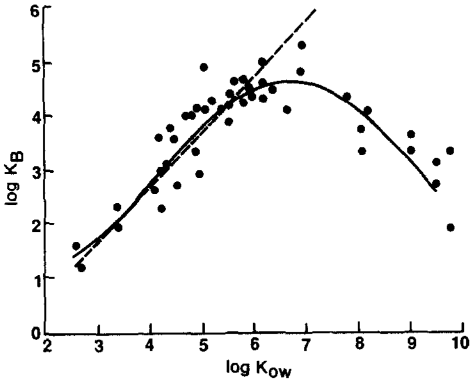

FIG. 5. The relationship of log K_B to log K_{OW} for fish as described by Eq. (14) together with experimental log K_B values and the line described by Eq. (1).

An expression relating equilibrium log K_B to log K_{OW} is obtained by addition of Eqs. (12) and (13). This eliminates any influence of varying equilibrium time requirements and ensures that calculated K_B values are equilibrium values. Thus

$$\log K_B = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.55(\log K_{OW})^2 - 4.18 \log K_{OW} + 4.79. \quad (14)$$

The line described by this equation is depicted in Fig. 5, in which the experimental log K_B values from Table 1 and line described by Eq. (1) are also added for comparison.

DISCUSSION

Rate Constants (k_1 and k_2) to Partition Coefficient (K_{OW}) Relationships

For the log K_{OW} range from about 3 to 6, a direct linear relationship has been previously found (e.g., Spacie and Hamelink, 1982; Hawker and Connell, 1985a) between log k_1 and log K_{OW}, but over a more extended log K_{OW} range, particularly log $K_{OW} > 6$, extrapolation of these linear relationships may be inappropriate. In fact, using recently published data, together with previous data for compounds with log K_{OW} values from 2.60 to 9.84, a significant empirical parabolic relationship (Eq. (12)) has been found between log k_1 and log K_{OW} (see Fig. 3). The maximum k_1 of 832 day^{-1} corresponds to a log K_{OW} value of 5.87. This pattern of behavior has also been observed experimentally in a number of other investigations (Sugiura *et al.*, 1978; Muir *et al.*, 1985; Bruggeman *et al.*, 1981; Dearden and Williams, 1978). In addition, a plot very similar to Fig. 3, with a maximum for chemicals with log K_{OW} of about 5 to 6, has been found for the gill uptake rate of 14 organic compounds by trout (McKim *et al.*, 1985).

Various theoretical models based on fugacity or diffusion behavior (Gobas *et al.*, 1986; Mackay, 1984) suggest that for extremely hydrophobic compounds (log $K_{OW} > 6$), log k_1 is independent of hydrophobicity as measured by log K_{OW}. Thus, a curvilinear relationship as shown in Fig. 1 would be expected. However, this current investigation indicates that for extremely hydrophobic molecules increasing log K_{OW}, and therefore generally increasing molecular size, leads to a decrease in diffusion coefficient and hence log k_1 decreases. Overall then, log k_1 increases with log K_{OW} for compounds with log $K_{OW} < 6$, and is under membrane permeation control. After passing through a maximal or optimal log k_1, log k_1 may decrease with increasing log K_{OW} for compounds of high hydrophobicity, with uptake controlled by diffusion through the aqueous phases of the fish (Gobas *et al.*, 1986). The slopes of the log k_1 versus log K_{OW} relationship on either side of the maximum would not necessarily be equal, but, in general, the shape of the log k_1 versus log K_{OW} plot may be expected to resemble a parabola.

For elimination or clearance rate constants of nonmetabolizable lipophilic compounds, direct linear relationships between log($1/k_2$) and log K_{OW} have been found for compounds whose log K_{OW} values were mainly between 3 and 6 (Konemann and van Leeuwen, 1980; Spacie and Hamelink, 1982; Hawker and Connell, 1985a). In this current investigation, over a wider range of log K_{OW} values, the empirical regression curve (Eq. (13)) depicted in Fig. 4 was obtained. This is qualitatively similar to the curve in Fig. 2 for compounds with log $K_{OW} \geqslant 2.5$ which was derived from theoretical considerations.

From Eq. (4), for clearance under aqueous diffusion control (i.e., log $K_{OW} > 3$ to 4)

$$\frac{1}{k_2} = \frac{V_L}{Q_W} K_{OW}$$

or

$$\log\left(\frac{1}{k_2}\right) = 1.00 \log K_{OW} + \log\left(\frac{V_L}{Q_W}\right). \tag{15}$$

This is comparable with the equation for the linear portion of Eq. (13) in Fig. 4 between log K_{OW} values of and 3.5 and 5.5, i.e.,

$$\log\left(\frac{1}{k_2}\right) = 0.72 \log K_{OW} - 2.67. \tag{16}$$

Equation (15) is also comparable to the equation previously obtained for fish (Hawker and Connell, 1985a) over a similar range of log K_{OW} values, i.e., log($1/k_2$) = 0.663 log K_{OW} − 0.947.

Theoretical reasoning similar to that developed for k_1 suggests a curvilinear relationship (see Fig. 1) between log($1/k_2$) and log K_{OW} over a relatively wide partition coefficient range (Gobas *et al.*, 1986; Mackay and Hughes, 1984). However, for extremely hydrophobic compounds (log $K_{OW} >$ about 6.5), any increase in $1/k_2$ due to diffusion effects may be outweighed by the rapid decrease in lipid solubility of these large chemicals (Anliker and Moser, 1987) compared to their octanol solubility. The theoretical principles involved in this effect are outlined under Theory. As a consequence, such compounds are likely to be depurated at an increased rate, and therefore $1/k_2$ becomes smaller with increasing K_{OW} (Eq. (10)). A plot of log($1/k_2$) versus log K_{OW}, over a sufficiently wide log K_{OW} range, should resemble that in Fig. 2 and has been observed as shown in Fig. 4. Thus, it is suggested that the clearance rate constant is independent of K_{OW} and under membrane permeation control, for compounds with log K_{OW} values less than about 3.5. Aqueous phase diffusion operates with com-

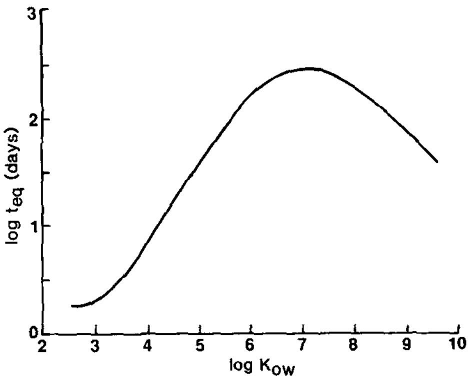

FIG. 6. Relationship of log t_{eq} to log K_{OW} as described by Eq. (17) for bioconcentration of chlorinated hydrocarbons and closely related compounds by fish.

pounds having log K_{OW} values from about 3.5 to about 6.5 but for chemicals of greater hydrophobicity decreased lipid solubility is the major controlling factor.

Time Periods to Establish Equilibrium

The time period required to attain the equilibrium bioconcentration factor (t_{eq}) is related to $1/k_2$ by Eq. (11). Therefore, from Eq. (13), log t_{eq} (days) with fish for chlorinated hydrocarbons and related compounds having log K_{OW} values between approximately 2.5 and 9.5 is given by

$$\log t_{eq} = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.65(\log K_{OW})^2 - 5.34 \log K_{OW} + 5.93. \quad (17)$$

The curve described by this equation is shown in Fig. 6 and has a shape similar to that in Fig. 4 resulting from the correlation between $\log(1/k_2)$ and log K_{OW}. Gobas *et al.* (1986) has predicted that for compounds of relatively low lipophilicity (log K_{OW} $<$ 3 to 4), $\log(1/k_2)$ is independent of log K_{OW}. For such compounds, t_{eq} will be approximately 1.8 days as shown in Fig. 6. With compounds of greater lipophilicity, t_{eq} rises with log K_{OW} until the maximum equilibrium time requirement of 325 days or 0.89 years is attained for compounds having a log K_{OW} value of approximately 7. Thereafter, t_{eq} becomes shorter with extremely hydrophobic molecules such as those possessing log K_{OW} values of 8 and 9 requiring 225 days (0.62 years) and 84 days (0.23 years), respectively, to reach equilibrium.

The Bioconcentration Factor (K_B) to Partition Coefficient (K_{OW}) Relationship

Bioconcentration factors at equilibrium can be obtained from Eq. (14), which is represented by the curve shown in Fig. 5. The approximately linear portion of this curve between log K_{OW} values of 3 and 6 can be described by

$$\log K_B = 0.94 \log K_{OW} - 1.00. \quad (18)$$

This is very similar to previous equations developed relating log K_B to log K_{OW} such as Eq. (1), and

$$\log K_B = 1.16 \log K_{OW} - 0.75$$

(Spacie and Hamelink, 1982). Theoretically, if octanol perfectly represents the fish lipids, then for compounds of relatively modest molecular size, the maximum lipid and octanol solubilities are roughly equal. Therefore

$$K_B = lK_{OW}$$

and

$$\log K_B = 1.00 \log K_{OW} + \log l,$$

where l is the fraction of lipid in the fish. With an average lipid content for the fish species in Table 1 of 5%, $l = 0.05$, and

$$\log K_B = 1.00 \log K_{OW} - 1.30. \tag{19}$$

This theoretical equation also is in close agreement with that derived above from the experimental data.

From Eq. (14), a maximum bioconcentration factor of $10^{4.61}$ or 41,000 is achieved for compounds in this group with a log K_{OW} value of 6.7, and from Eq. (17), it takes 305 days to attain this value. For larger, more hydrophobic hydrocarbons, log K_B values are lower due to decreasing lipid solubility, relative to octanol solubility. Therefore, these values are difficult to measure experimentally because of the low lipid solubility and extremely low aqueous solubility of the compounds. The overall shape of the log K_B versus log K_{OW} plot is in qualitative agreement with predictions of a parabolic relationship (Tulp and Hutzinger, 1978) and is described by Eq. (14). For smaller less hydrophobic compounds log K_B increases with log K_{OW} until decreasing lipid solubility causes log K_B to become increasingly smaller than $\log(lK_{OW})$.

Miller *et al.* (1985) have developed the following relationship between log C_W, the maximum aqueous solubility (mol m^{-3}), and log K_{OW} for chlorinated benzenes and polychlorinated biphenyls:

$$\log C_W = -1.24 \log K_{OW} + 4.01. \tag{20}$$

This equation enables the bioconcentration factor to be related to the maximum aqueous solubility by substituting into Eq. (14). Thus,

$$\log K_B = 2.91 \times 10^{-3}(\log C_W)^4 + 5.02 \times 10^{-2}(\log C_W)^3 + 1.23 \times 10^{-1}(\log C_W)^2 - 4.15 \log C_W + 1.98. \tag{21}$$

Biotic Concentrations Attained by Fish

From Fig. 5, it can be seen that the same bioconcentration factor (6300) is reached for compounds with log K_{OW} values of 5.0 and 8.3. However, this does not mean that the maximum biotic concentration C_B is the same in both cases. Due to decreasing maximum aqueous solubility C_W with log K_{OW}, the C_B value for the more hydrophobic chemical (log K_{OW} of 8.3) is less than that for the one with log $K_{OW} = 5.0$.

The precise nature of the relationship between C_B and K_{OW} has been established as follows. Since

$$K_B = C_B/C_W$$

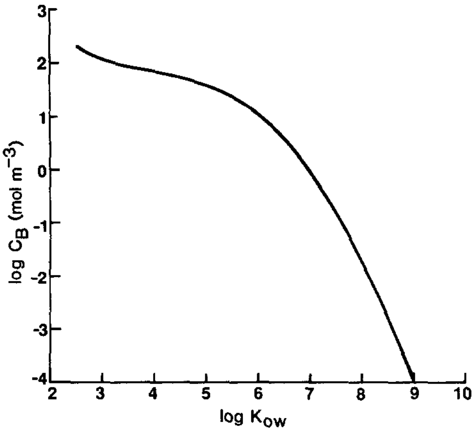

FIG. 7. A plot of log C_B versus log K_{OW} for bioconcentration of chlorinated hydrocarbons and closely related compounds by fish.

then

$$\log C_B - \log C_W = \log K_B$$

and from Eq. (14)

$$\log C_B = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.55(\log K_{OW})^2 - 4.18 \log K_{OW} + 4.79 + \log C_W. \quad (22)$$

Combining Eqs. (20) and (22),

$$\log C_B = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.55(\log K_{OW})^2 - 5.42 \log K_{OW} + 8.80. \quad (23)$$

The curve described by Eq. (23) is presented in Fig. 7. This demonstrates that value log C_B decreases slowly with increasing log K_{OW} until a log K_{OW} value of 5.5 is reached. For more hydrophobic molecules log C_B decreases more rapidly, with C_B for a compound with log K_{OW} of 9 reaching only 10^{-4} mol m^{-3}. The major repository of chlorinated hydrocarbons in fish is in the lipid tissues, and therefore the maximum biotic concentration is closely related to the maximum lipid solubility. Both Anliker and Moser (1987) and Dobbs and Williams (1983) have observed decreasing fat solubilities with increasing K_{OW}. Figure 7 is also in qualitative agreement with theoretical prediction based on Eq. (7).

The decreasing biotic concentrations and bioconcentration factors for extremely hydrophobic compounds from Eqs. (23) and (14) may in part account for observations (Zitko *et al.*, 1974) of an apparent molecular weight cut-off of approximately 600 in accumulation of chlorinated hydrocarbons by fish. For chlorinated benzenes and biphenyls, log K_{OW} is related to the molecular weight (MW) (Miller *et al.*, 1985) by

$$\log K_{OW} = 1.55 + 1.42 \times 10^{-2}\,\text{MW} \qquad (r = 0.98, n = 29). \quad (24)$$

For a compound with a molecular weight of 560, for example, from Eq. (24), its log

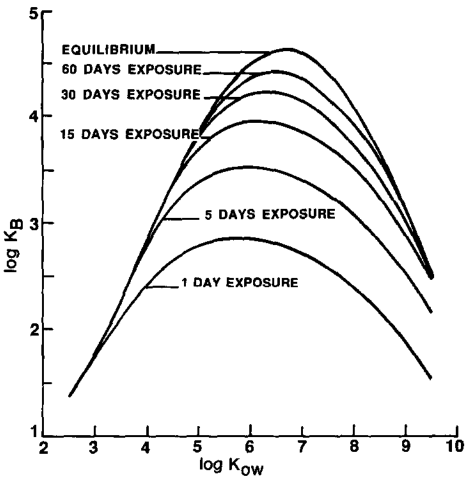

FIG. 8. A plot of log K_B versus log K_{OW} for fish following varying exposure times.

K_{OW} value is 9.5. From previous log K_B versus log K_{OW} correlations for fish, such as that by Mackay (1982) (Eq. (1)), the calculated bioconcentration factor is 1.5×10^8. However, on the basis of Eq. (14), the bioconcentration factor is only 360, and it takes 50 days to attain this level. In addition, the biotic concentration (Eq. (23)) is 3.4×10^{-3} g m^{-3} or 3.4 ppb assuming a biotic density of 1 g cm^{-3}.

The Relationship between Bioconcentration Factors (K_B) and Exposure Times

For exposure times less than the required time period to establish equilibrium the observed bioconcentration factors will be less than those predicted for equilibrium. Nonequilibrium bioconcentration factors can be calculated from Eq. (2), where $(1 - e^{-k_2 t})$ represents the fraction that the nonequilibrium K_B value is of the equilibrium value. The effect of exposure time on the observed bioconcentration factor is illustrated in Fig. 8 where log K_B is plotted against log K_{OW} assuming varying exposure times. Depending on the exposure time, directly determined bioconcentration factors may be only small fractions of the maximum potential bioconcentration factors. As an example, for a compound with a log K_{OW} of 7, and an exposure time of 15 days, the observed K_B value of 7000 is only one-fifth of the equilibrium bioconcentration factor, which requires 325 days to attain. Figure 8 also indicates that because of decreasing lipid solubility for extremely hydrophobic compounds, the times required to attain equilibrium also decrease which means that their maximum bioconcentration factors could eventually be reached. However, the equilibrium biotic concentrations are very low and may be difficult to measure experimentally.

CONCLUSIONS

For chlorinated hydrocarbons and closely related compounds, with $2.5 < \log K_{OW} < 9.5$, uptake rate constants (k_1) for fish are related to log K_{OW} by the polynomial equation, which represents a parabola,

$$\log k_1 = 2.92 - 9.86 \times 10^{-2}(\log K_{OW} - 5.87)^2.$$

The k_1 values are controlled by membrane permeation or lipid diffusion control for compounds of low lipophilicity and are aqueous-phase diffusion-layer controlled for more hydrophobic compounds. Clearance rate constants (k_2) are related to log K_{OW} by the polynomial expression

$$\log\left(\frac{1}{k_2}\right) = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.65(\log K_{OW})^2 - 5.34 \log K_{OW} + 5.27.$$

The k_2 values are controlled by factors similar to those for k_1, but are additionally affected by decreasing lipid solubility for extremely hydrophobic compounds. The shape of curves generated by these empirical equations are in accordance with theoretical prediction.

Equilibrium times (days) for these compounds are given by the polynomial expression

$$\log t_{eq} = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.65(\log K_{OW})^2 - 5.34 \log K_{OW} + 5.93.$$

This means that compounds having a log K_{OW} value of approximately 7.0 take the maximum time to reach equilibrium (0.89 years).

Equilibrium bioconcentration factors are related to log K_{OW} by the equation

$$\log K_B = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.55(\log K_{OW})^2 - 4.18 \log K_{OW} + 4.79.$$

The curve described by this equation resembles a parabola with a maximum log K_B value at log K_{OW} of 6.7, and decreasing log K_B values for chemicals with log $K_{OW} > 6.7$. However, the section of this curve between log K_{OW} values of 3 and 6 is approximately linear and closely related to linear equations previously obtained for this range of log K_{OW} values. Since K_{OW} can be related to maximum aqueous solubility (C_W) and MW, K_B can also be described in terms of these variables. Nonequilibrium bioconcentration factors can be calculated and generally, for a given exposure time, compounds show increasing deviations from the equilibrium value with increasing log K_{OW} up to approximately log K_{OW} values of 7.0.

The maximum solubility of hydrophobic compounds in natural fish lipid, and hence maximum biotic concentration, is an important factor and can be related to log K_{OW} by

$$\log C_B = 6.9 \times 10^{-3}(\log K_{OW})^4 - 1.85 \times 10^{-1}(\log K_{OW})^3 + 1.55(\log K_{OW})^2 - 5.42 \log K_{OW} + 8.80.$$

Maximum lipid solubilities of extremely hydrophobic molecules decrease sharply at log K_{OW} values > 5.5 and may in part account for observations of negligible bioconcentration of these compounds. It is therefore a misnomer to call these compounds superlipophilic, since while they are very hydrophobic, they exhibit decreasing lipophilicity with increasing log K_{OW}.

Overall, bioconcentration of a wide range of chlorinated hydrocarbons and closely related compounds may be successfully described by a single-compartment model for fish. The process is influenced by a variety of factors including lipophilicity, aqueous diffusion, membrane permeability or lipid diffusion, exposure time, and lipid solubility.

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