Environmental Toxicology and Chemistry, Vol. 6, pp. 495-504, 1987
Printed in the USA. Pergamon Journals Ltd.

0730-7268/87 $3.00 + .00

59

Environmental Chemistry

DYNAMICS OF HYDROPHOBIC ORGANIC CHEMICAL BIOCONCENTRATION IN FISH

FRANK A. P. C. GOBAS and DONALD MACKAY*
Department of Chemical Engineering and Applied Chemistry, University of Toronto, Toronto, Ontario, Canada M5S 1A4

(*Received* 11 *August* 1986; *Accepted* 15 *December* 1986)

Abstract—A model is presented describing the kinetics of uptake and release of nonmetabolizing organic chemicals by fish from water. The model contains three parameters: a bioconcentration factor which is specific to the chemical (and can be characterized by the octanol/water partition coefficient and fish lipid content), a water-phase resistance term and a lipid-phase resistance term which are specific to the fish. These parameters can be estimated from uptake–clearance experiments. Part of the water-phase resistance term can be attributed to gill ventilation rate as estimated from gill uptake efficiencies and part is an "internal" resistance. Procedures are suggested for scaling these parameters to different fish sizes. The dependence of these resistances, and uptake and clearance rate constants, on chemical hydrophobicity is discussed and quantified.

Keywords—Bioconcentration Fish Model Hydrophobicity Gill ventilation Octanol/water partition coefficient

INTRODUCTION

It is generally accepted that the bioconcentration process in which hydrophobic organic compounds are absorbed by fish from water and accumulated in fat tissue is basically one of physical–chemical partitioning controlled by the relative affinities of the compound for the water and fat tissue. If metabolic transformation of the absorbed compound is insignificant a simple two-compartment (water–fish) model with first-order rate constants usually gives a satisfactory description of the kinetics [1]. The ratio of the concentrations in the fish and the water under steady-state conditions (i.e., the bioconcentration factor K_B) reflects these relative affinities [2], and can be related to the 1-octanol/water partition coefficient, K_{ow} [3–5]. Elimination rate constants (k_2) generally decrease with increasing K_{ow} [3,6–11] and correlating equations have been proposed. Uptake rate constants (k_1), however, show a less clear dependence on K_{ow}. It has been reported that k_1 can either increase [3], remain constant [9], decrease, or show a parabolic relationship [6,8,12,13] with increasing K_{ow}.

To make reliable predictions about the kinetics of the bioconcentration process it is necessary to clarify how uptake and release kinetics are controlled and to elucidate which parameters are involved. For this purpose we develop a model which is an extension of one presented earlier by Mackay and Hughes [14] and is based on principles described by Yalkowsky [15,16]. The Mackay–Hughes model was derived entirely from elimination-rate data and no uptake-rate data were considered or tested. It has therefore not been demonstrated if or how the principles applicable to elimination apply to the uptake process.

Independently, Gobas et al. [17] derived similar equations relating bioconcentration kinetics to the process of passive diffusion of chemicals through biological barriers as described by Flynn and Yalkowsky [18]. It was shown that the behavior of both uptake and elimination rate constants with respect to hydrophobicity can be explained by diffusion through membranes and aqueous diffusion layers. A similar mechanism was proposed by McKim et al. [19] for gill uptake in rainbow trout.

The objective of this article is to determine and quantify the transport resistances controlling uptake and elimination of organic chemicals by fish from water and thus improve methods of predicting bioconcentration parameters. We do not consider uptake from food, nor do we treat metabolizing chemicals. This limits the scope of the model, but we believe that it is best to model the simplest situations first and then to introduce these complexities in later models which will then be more soundly based.

*To whom correspondence may be addressed.

MODEL DERIVATION

Accurate representation of chemical dynamics in a fish requires a pharmacokinetic model in which differential equations are written describing chemical uptake, release, reaction, and accumulation in all significant tissues. Since there are insufficient data to justify such models, only a simple model can be justified at present at which accumulation is primarily attributed to a lipid compartment which is accessed through a water compartment, the latter having a negligible capacity for the chemical.

Deriving such equations can be done in terms of fugacity [20] but the final equations can be written and even derived in conventional concentration form. We thus develop the equations using fugacity but use them in concentration form. We use the SI units of meters, moles, seconds and Pascals in the derivation, but the final equations can be used in more traditional units.

Briefly, fugacity f is the "escaping tendency" from a phase; it is linearly related to concentration C through a fugacity capacity term Z (i.e., $C = Zf$). Since two phases at equilibrium have equal fugacities, the partition coefficient K_{12} is C_1/C_2 or Z_1/Z_2. Transport is expressed by a transport parameter D, the rate of being $D(f_1 - f_2)$. D can reflect passive diffusion as expressed by diffusivities or mass transfer coefficients or fluid flow (e.g. in gill ventilation or blood flow) as GZ where G (m^3/s) is the volumetric fluid flow rate.

The simplest expression of fish-water exchange is given by Equation 1:

$$V_1 Z_1 \, df_1/dt = V_1 Z_1 \, dC_1/dt = D_F(f_W - f_1) \quad (1)$$

where V is volume (m^3), Z is fugacity capacity ($mol/m^3 \cdot Pa$), f is fugacity (Pa), t is time (s) and D is transport parameter (mol/Pa·s) including all resistances between the lipid compartment and the water. Subscripts W refer to water, F to fish, and L to lipid in which all the chemical is assumed to partition.

Integration of this equation with a constant f_W and an initial f_1 of zero gives

$$f_1 = f_W[1 - \exp(-D_1 t/V_1 Z_1)] \quad (2)$$

Since f_1 is C_1/Z_1 and f_W is C_W/Z_W, Equation 2 can be rewritten as

$$C_1 = C_W(Z_1/Z_W)(1 - \exp[-D_1 t/V_1 Z_1]) \quad (3)$$

Equation 3 is equivalent to the solution of the traditional differential equation describing the uptake and release in fish

$$dC_F/dt = k_1 C_W - k_2 C_F \quad (4)$$

where k_1 is the uptake and k_2 the elimination rate constant. Integration of this equation gives

$$C_F(t) = C_W k_1/k_2(1 - \exp(-k_2 t)) = C_W K_B(1 - \exp(-k_2 t)) \quad (5)$$

Fish concentrations and bioconcentration factors can be expressed on a whole-fish wet-weight basis (i.e., C_F and C_F/C_W or K_B) or on a lipid basis (i.e., C_1 and C_1/C_W or K_L). If all accumulation is assumed to be in the lipid and the volumes are V_1 and V_F then the lipid volume fraction L is V_1/V_F and C_1 is C_F/L, K_1 is K_B/L or Z_1/Z_W. K_B is Z_1/Z_W and Z_1 is Z_F/L. Comparison of Equations 3 and 5 shows that k_1/k_2 is equivalent to K_B or Z_1/Z_W or LZ_1/Z_W. The elimination rate constant k_2 is equivalent to $D_F/V_F Z_F$ or $D_F/V_1 Z_1$. Thus in summary

$$k_2 = D_F/V_1 Z_1 = D_F/V_F Z_F \quad (6)$$

$$k_1 = k_2 Z_F/Z_W = D_F/V_F Z_W = D_F L/V_L Z_W \quad (7)$$

Equilibrium is thus controlled entirely by Z_W, Z_F, or Z_1 but the kinetics are also controlled by the relative volumes of lipid and water in the fish and D_F.

To gain insight into the processes controlling the exchange of solute chemical between the water and the fish it is assumed that solute transport to, and within the fish takes place in a series of aqueous and lipid phases. Therefore all D values applying to transport processes in aqueous phases are grouped together in one term D_W describing the net transport of the solute in these phases. Similarly, D_L expresses the net transport of the solute in all lipid phases.

The D_W and D_L terms can be designated respectively $Q_W Z_W$ and $Q_L Z_L$. Each transport parameter Q (m^3/s) combines all diffusion processes characterized by diffusion transfer terms (such as mass transfer coefficients (m/s) times area (m^2) or diffusivity (m^2/s) divided by path length (m) times area (m^2) and real flow rates (m^3/s) involved in solute transport in the respective phases. The net transport of solute between the water and the fish can now be expressed in terms of D_W and D_L as

$$1/D_F = 1/D_W + 1/D_L = 1/Q_W Z_W + 1/Q_L Z_L \quad (8)$$

This assumes that water and lipid transport processes apply in series and that transport resistances across lipid/water interfaces are negligible. Substituting Equation 8 into Equation 6 and Equation 7 results in the following equations expressing the elimination and uptake rate constants in terms of D_W and D_L:

$$1/k_2 = V_1(Z_L/Q_W Z_W + 1/Q_L) \quad (9)$$

and

$$1/k_1 = (V_L/L)(1/Q_W + Z_W/Q_L Z_L) \quad (10)$$

Since there are few data for lipid/water partitioning (i.e., Z_L values) octanol is used as a surrogate organic phase for fish lipids. We can thus rewrite Equations 9 and 10 for correlating purposes in terms of octanol, replacing Z_L by Z_O in which K_{OW} is Z_O/Z_W (and essentially redefine Q_L and Q_W) to give

$$1/k_2 = V_L(K_{OW}/Q_W + 1/Q_L) \quad (11)$$

$$1/k_1 = V_L(1/Q_W + 1/Q_L K_{OW})/L \quad (12)$$

The significance of the terms in Equations 11 and 12 is worthy of emphasis. The ratios V_L/Q_W and V_L/Q_L have dimensions of time. They can be viewed as the times of chemical transport to or from V_L m^3 of water or lipid. Since the water and lipid transport processes occur in series, these times are additive and the longer time controls. But, if clearing a given quantity of chemical requires clearance or transport of V m^3 of lipid, it will require the clearance or transport of a much larger volume, $K_{OW}V$ m^3 of water, because the chemical concentration in the water is a factor of K_{OW} lower. The clearance time for water must thus be multiplied by K_{OW}, prior to addition to that of the lipid clearance time. The times or "resistances" in the water phase and in the lipid phase are thus respectively $K_{OW}V_L/Q_W$ and V_L/Q_L, or V_F/Q_W and $V_F/Q_W K_{OW}$.

As K_{OW} increases, the water concentration drops relative to the lipid phase; thus the total resistance or clearance time increases and the overall process rate becomes dominated by water-phase processes. We amplify this point later in the discussion.

In the conventional uptake Equation 4, the uptake constant k_1 is often viewed as being related to the water flow rate being brought into contact with the fish. Indeed, in the absence of a lipid resistance k_1 equals Q_W/V_F and can be viewed as a water flow rate Q_W divided by the fish volume. This occurs for large K_{OW}, water-phase-resistant chemicals.

Gill uptake efficiency

The rate at which a chemical is absorbed from the water depends on the water solution flow rate through the gill compartment and the efficiency with which the chemical is extracted. The efficiency for uptake of chemicals from water, E, can be defined as the ratio of the flux of chemical into the fish (i.e., $D_F(f_W - f_1)$) to the flux of chemical into the gill compartment (i.e., $D_V f_W$), namely

$$E = [D_F/D_V]((f_W - f_1)/f_W) \quad (13)$$

where D_F is the net transport parameter into the fish and D_V is the transport parameter into the gill compartment and is $G_V Z_W$, where G_V (m^3/s) is the ventilation rate. Equation 13 suggests that at the beginning of the exposure period, when no compound is present in the fish and f_1 is zero, the uptake efficiency is maximal and is D_F/D_V. Substitution of Equation 2 into Equation 13 shows that the efficiency should decrease with time and will eventually reach zero as the fish reaches equilibrium:

$$E = (D_1/D_V)\exp(-D_1 t/V_1 Z_1) \quad (14)$$

As a result we can write the following equation for the initial or maximum gill uptake efficiency E_0 in fish:

$$1/E_0 = D_V/D_F = G_V(1/Q_W + 1/Q_L K_{OW}) \quad (15)$$

Equation 15 shows that the gill uptake efficiency is related to Q_W and Q_L in a similar fashion to that of the uptake rate constants. Using Equation 12 it can be shown that k_1 and E_0 are related by

$$k_1 = E_0 G_V L/V_1 \quad (16)$$

Interestingly, when K_{OW} is large, Equations 15 and 16 suggest that E_0 and k_1 become constant, E_0 approaching Q_W/G_V and k_1 approaching $Q_W L/V_1$.

of V_l, K_{ow}, Q_w and Q_l. Generally V_l and K_{ow} can be obtained from either simple measurements or calculations. However, no general procedures exist to predict the parameters Q_w and Q_l, which are presumably specific to a particular fish species, its size, and its physiological condition.

Since relationships exist between the oxygen uptake capacity and body weight, similar relationships may exist between Q_w or Q_L and body weight (M). In order to investigate how Q_w and Q_l are related to body weight, elimination rate constants for several fish species were gathered from the literature [8,10,11,19,22]. For illustrative purposes, $1/k_2$ data for all fish species are plotted versus K_{ow} in Figure 2, showing that $1/k_2$ and thus V_l/Q_w vary with size and species, and tend to increase with increasing fish size. Figure 3 demonstrates that $1/V_l k_2$ and hence Q_w varies from fish to fish. Apparently as fish weight M increases, Q_w increases but not in proportion. Examination of the data suggests that Q_w is proportional to M raised to a power of 0.6 ± 0.20, namely

$$Q_w = 1.4M^{0.6\pm0.2}$$

where the confidence interval has a 95% probability.

Unfortunately Q_l cannot be calculated accurately from these data because the elimination rate constants are primarily dependent on Q_w rather than on Q_l. It can be speculated from Figure 2 that for McKim's data set at low K_{ow} values, k_2 may approach a value of approximately 10 d^{-1} corresponding to a half-time of 100 min. If this is the case Q_l would be approximately 10 V_l L/d. More experimental data for low K_{ow} substances are needed before any reliable relationship between Q_l and fish body weight can be established.

Further justification for derived values of Q_w and information about the relationship between Q_w and body weight can be obtained by using a correlation for gill ventilation rate as it affects oxygen uptake. Norstrom et al. [21] and later Neely [3] and Bruggeman [8] expressed the ventilation volumetric rate as a function of the oxygen concentration in the water C_{ox} (ml of O_2/ml of water), the total energy metabolism of the fish T (ml $O_2 \cdot h^{-1}$), and the efficiency of oxygen transfer across the gills E_{ox} according to

$$G_v = T/(E_{ox} C_{ox}) \quad (22)$$

T has been shown to be related to the fish's body weight, M, according to

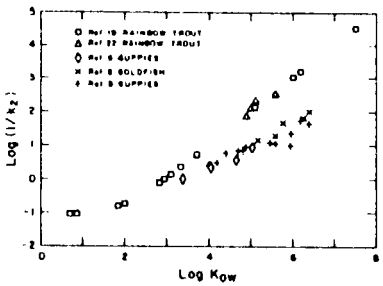

Fig. 2. Observed elimination rate constants in various fish species.

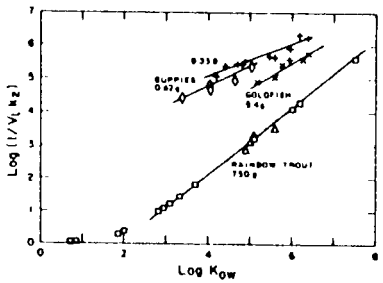

Fig. 3. Observed elimination rate constants corrected for lipid volume in various fish species.

$$T = AM^{0.8} \quad (23)$$

where A is the metabolic rate coefficient (ml of $O_2 \cdot h^{-1} \cdot g^{-0.8}$). G_v can be estimated by Equation 24, which is a combination of Equations 22 and 23:

$$G_v = AM^{0.8}/(E_{ox} C_{ox}) \quad (24)$$

Neely [3] reported values for A for the rainbow trout and goldfish of 0.14 and 0.24 ml $O_2 \cdot g^{-0.8} \cdot d^{-1}$, respectively. For guppies we determined A to be 0.16 ± 0.02 ml $O_2 \cdot g^{-0.8} \cdot d^{-1}$ by measuring the decrease in oxygen concentration in closed bottles containing 1-yr-old male guppies. M and C_{ox} were reported in the respective articles or could be estimated and E_{ox} and was estimated to be 0.62 [19] for all fish species. Values for G_v could thus be calculated as listed in Table 2, and

Table 2. Observed and calculated transport parameters for hydrophobic organic chemicals in different fish species showing relationship of Q_w and Q_l to body weight

Fish species	$\bar{M}$ (g)	V_l (L)	Q_w (L/d)	Q_l (L/d)	G_v (calc)
Rainbow trout [19]	750	82×10^{-3}	94	1.2	143
Rainbow trout [22]	900	98×10^{-3}	89	0.98	165
Goldfish [8]	4.5	0.18×10^{-3}	5.4		2.4
Guppy [6]	0.62	0.037×10^{-3}	0.51		0.49
Guppy [9]	0.35	0.026×10^{-3}	1.0		0.31

shown to be similar in magnitude to Q_w. In principle it is impossible for Q_w to exceed G_v since this would imply that the total resistance ($1/Q_w$) is less than the gill ventilation resistance ($1/G_v$). The large experimental error made in these calculations is believed to cause the somewhat higher values of Q_w compared to G_v for the guppy and goldfish. It seems that Q_w and G_v are similar for these species, thus demonstrating that gill ventilation has a major influence on uptake kinetics in small fish. For larger fish, however, like the rainbow trout, ventilation rate seems to have less effect on uptake and elimination kinetics. Other water-phase resistances thus become more important.

DISCUSSION

The model presented gives a good correlation of the experimental kinetic data and provides an insight into the parameters controlling the transfer of chemicals between the water and the fish. An increase in the lipid content of the fish leads to a proportional decrease in both k_1 and k_2, which has been observed experimentally by Bruggeman et al. [8].

We believe that it is worthwhile discussing the significance of the model equations in some detail, especially to explain the relative roles of the various resistances.

Figure 4 is a schematic diagram of the bioconcentration system in which chemical is transported from water through the gills, through a second internal water resistance, and finally through a lipid resistance to a lipid storage. Each resistance is characterized by a Q or G term which could be an actual fluid flow (G) or a diffusion process characterized by a mass transfer coefficient or a diffusivity. In reality these resistances may be in a different order and may be split into several components. The two water resistances (gill ventilation and internal) may be combined as shown in one resistance characterized by Q_w. In each case the resistance is proportional to $1/Q$; thus Q is a conductivity.

Numerical examples with K_{ow} values of 100 and 1,000 illustrate the roles of the resistances. In the uptake cases transfer is from water to lipid and at the conditions described has reached 1% of the final equilibrium value, the lipid concentrations (in arbitrary units) being 100 in both cases. The water concentrations for K_{ow} of 100 is thus 100, and for K_{ow} of 1,000 is 10, the equilibrium lipid concentrations thus being 10,000 in both cases. The values of Q_w, Q_l, G_v, V_l and L which are common to both systems and independent of the chemical are given, as are the values of k_1, k_2, E_0 and E, which are chemical-specific. Furthermore, if Z of 1,000 is arbitrarily assigned to both chemicals in the lipid phase, then Z in water is 10 for K_{ow} of 100 and 1.0 for K_{ow} of 1,000. The corresponding fugacities and D values can then be calculated as shown.

The fluxes and concentration and fugacity profiles through the system can be calculated using the equations presented earlier. At the interfaces between the resistances where equilibrium is assumed to be achieved, fugacities are equal, and the lipid/water concentration ratios are the K_{ow} values.

In the case of K_{ow} of 100, the fugacity drops from 10 in water to 7.525 at the gill surface A, to 5.05 at the water/lipid interface B, and to 0.1 in the lipid. Half of the total resistance thus lies in the water phases, the relative resistance values being K_{ow}/G_v of 0.5, K_{ow}/Q_l of 0.5, and $1/Q_l$ of 1.0, totalling 2.0. The total water resistance K_{ow}/Q_w is 1.0. The flux is 4,950 units/d.

When K_{ow} is increased to 1,000, more resistance is added to the water phase because the water concentrations are lower and the water can only transport a smaller amount of chemical at these fixed flow rates. The flux is reduced to 900 units/d, the resistances being respectively 5, 5 and 1, totalling 11 (i.e., an increase by a factor of 5.5). The fugacities drop from 10 to 5.5 to 1.0 to 0.1.

For K_{ow} of 100, k_2 is 5.0 and k_1 is 50, whereas for K_{ow} of 1,000, k_2 is reduced to 0.909 and k_1

A similar equation was proposed by Norstrom et al. [21] to describe uptake of chemicals from water in fish. However, in Norstrom's model E was considered to describe permeation across the gill membrane and thus to be independent of the ventilation rate of the fish. Equations 13 and 15 show that efficiency varies with G_V.

By experimental measurement of K_B, k_1, k_2 and E for a series of chemicals of varying K_{ow} it is possible to "probe" the fish and determine the fundamental kinetic terms Q_W, Q_L and G_V. Assuming that the ventilation resistance $1/G_V$ applies in series with another "internal" water resistance, which we designate as $1/Q_L$, we can quantify the contributions of each to the total water resistance $1/Q_W$, namely

$$1/Q_W = 1/G_V + 1/Q_L \quad (17)$$

For those who prefer to avoid using the fugacity approach, a conventional derivation can also be undertaken. Starting with the well-established Equation 5, one can postulate that k_2 can be correlated by Equation 11 (following Flynn and Yalkowsky [18]), and since K_B is k_1/k_2 or LK_{ow}, Equation 12 can be derived. Finally, if Equation 17 is postulated the uptake efficiency can be expressed as Equations 15 and 16. Although SI units have been used in this derivation it is more convenient to use traditional units in the comparison with experimental data. For example, all Q and G terms are expressed in L/d.

COMPARISON WITH EXPERIMENTAL DATA

Uptake efficiency (E) data reported by McKim et al. [19] for a number of organic substances in rainbow trout (fish weight: 660-840 g) were fitted to Equation 15 as summarized in Table 1. Linear regression of the data (i.e., $1/E$ vs. $1/K_{ow}$) is not desirable because $1/K_{ow}$ varies over several orders of magnitude and would thus weigh heavily in favor of the data points with low K_{ow}. In addition, errors in K_{ow} generally involve similar factors rather than similar absolute amounts. The most appropriate regression is believed to be on a semilogarithmic basis of $1/E$ versus log K_{ow}, but using the linear equation. A trial-and-error selection of the parameters Q_W and Q_L, using the reported G_V of 170 L/d with repeated plotting of $1/E$ versus log K_{ow}, was used to fit the data. Assuming a fish density of 1.0 kg/L and a lipid density of 0.90 kg/L, values for Q_W of 94 L/d and Q_L of 1.2 L/d gave the best fit of the experimental data. Q_L is thus 210 L/d.

To test if the parameters Q_W, Q_L, and Q_L also give a reasonable description of the elimination kinetics of rainbow trout, we used data on biological half-lives of PCBs reported by Niimi and Oliver [22] for rainbow trout of approximately the same weight and kept under similar conditions to those used by McKim et al. [19]. Unfortunately, only 4 of 31 reported half-lives of the PCBs were considered to reflect accurately the elimination process. For the other PCBs decreasing lipid levels in the fish or metabolic transformation contributed more to the depuration of the chemicals than pure elimination itself. The biological half-lives of the four PCBs, summarized in Table 1, were corrected for decreasing lipid levels in the fishes as indicated by the authors and then converted into elimination rate constants by equating k_2 to 0.693/(half-life). Values for Q_W and Q_L of 89.1 L/d and 0.98 L/d respectively resulted in the best fit of these elimination data. Since the Q_W and Q_L values are similar as deduced from both studies it appears that the same transport processes apply to uptake and elimination.

Table 1. Experimental (exp) and calculated (cal) kinetic parameters for a series of 18 hydrophobic organic chemicals in rainbow trout*

Compound	log K_{ow}	E_{exp}	E_{cal}	k_1 (cal)*	k_2 (exp)	k_2 (cal)†
Ethylacetate	0.73	0.07	0.03	7	—	13
n-Butanol	0.85	0.08	0.04	9	—	12
Nitrobenzene	1.85	0.26	0.25	56	—	7.2
p-Cresol	2.00	0.24	0.29	66	—	6.1
Monochlorobenzene	2.84	0.56	0.48	109	—	1.4
2,4-Dichlorophenol	2.93	0.52	0.49	111	—	1.2
Decanol	3.09	0.59	0.51	134	—	0.85
Pentachlorophenol	3.32	0.52	0.52	118	—	0.51
2,4,5-Tetrachlorophenol	3.70	0.50	0.54	120	—	0.22
Dodecanol	5.10	0.55	0.54	122	—	0.0089
2,5,2',5'-Tetrachlorobiphenyl	6.00	0.50	0.54	122	—	0.0011
Hexachlorobenzene	6.18	0.60	0.54	122	—	0.00074
Fenvalerate	7.2	0.30	0.54	122	—	0.000071
Mirex	7.5	0.20	0.54	122	—	0.000036
2,2'-Dichlorobiphenyl	4.9	—	0.54	122	0.014	0.014
2,3-Dichlorobiphenyl	5.0	—	0.54	122	0.0079	0.011
2,5-Dichlorobiphenyl	5.1	—	0.54	122	0.0047	0.0089
2,3,2',3'-Tetrachlorobiphenyl	5.6	—	0.54	122	0.0030	0.0028

*1 to 14 from ref. 19, 15 to 18 from ref. 22.
*Calculated from E_{exp}, G_V (170 L/d) and V_F (750 g) with ρ_F = 1.0 kg L^{-1}.
†Calculated from Equation 19 with ρ_L = 0.90 kg·L^{-1}.

In summary, for rainbow trout investigated in these studies, the following parameters apply in units of L and days:

$$V_F = 0.750 \text{ (L)}$$
$$V_L = 0.082 \text{ (L)}$$
$$L = 0.109 \text{ (L/L)}$$
$$Q_W = 92 \pm 3 \text{ (L/d)}$$
$$Q_L = 200 \pm 10 \text{ (L/d)}$$
$$G_V = 170 \pm 40 \text{ (L/d)}$$
$$Q_L = 1.1 \pm 0.2 \text{ (L/d)}$$

The following equations thus describe the uptake and elimination kinetics, representing the substitution of these values into Equations 11, 12 and 15 and equating the bioconcentration factor K_B to k_1/k_2.

$$K_B = 0.082K_{ow} \quad (18)$$

$$1/k_2 = 8.9 \times 10^{-4}K_{ow} + 7.5 \times 10^{-2} \text{ (d)} \quad (19)$$

$$1/k_1 = 8.2 \times 10^{-3} + 0.68/K_{ow} \text{ (d)} \quad (20)$$

$$1/E_0 = 1.85 \pm 155/K_{ow} \quad (21)$$

The fraction of the total resistance in the water phase is $8.9 \times 10^{-4}K_{ow}/(8.9 \times 10^{-4}K_{ow} + 7.5 \times 10^{-2})$.

Figure 1 and Table 1 present the experimental and correlated values of these quantities using these equations applied to the data from McKim et al. [19] and Niimi and Oliver [23]. The agreement is clearly satisfactory.

These plots illustrate the relative contributions of the water- and the lipid-phase transport to uptake by the fish. For compounds of low hydrophobicity (i.e., $K_{ow} \leq 10$) uptake is primarily controlled by transport processes in the lipid phases of the fish (i.e., $1/Q_L \geq K_{ow}/Q_W$). For these compounds uptake rate constants and gill uptake efficiencies increase with increasing hydrophobicity. For compounds of higher hydrophobicity (i.e., $K_{ow} \geq$ 1,000) uptake kinetics are primarily controlled by transport in aqueous phases of the fish (i.e., $K_{ow}/Q_W \geq 1/Q_L$) and uptake rate constants and gill uptake efficiencies are independent of the compound's hydrophobicity. Equal water and lipid resistances are encountered when K_{ow} is 84.

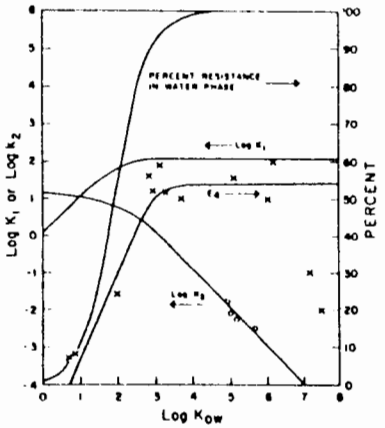

Fig. 1. Experimental and correlated uptake and elimination rate constants, initial gill uptake efficiency and percent resistance in the water phase for rainbow trout. The dots are k_1 and the crosses E_0 data.

The ventilation volumetric rate contributes 55% of the total resistance to solute transfer in the water phase. The other 45% of the water-phase resistance phase is presumably due to other water-phase transport processes between the gill compartment and the final storage sites in the fish. These processes may involve diffusion through aqueous diffusion layers (in the gills or elsewhere in the fish) or flow-controlled transport, for example in blood.

TRANSPORT PARAMETERS AND FISH BODY WEIGHT

To predict the bioconcentration rate constants for organic chemicals in a fish requires estimates

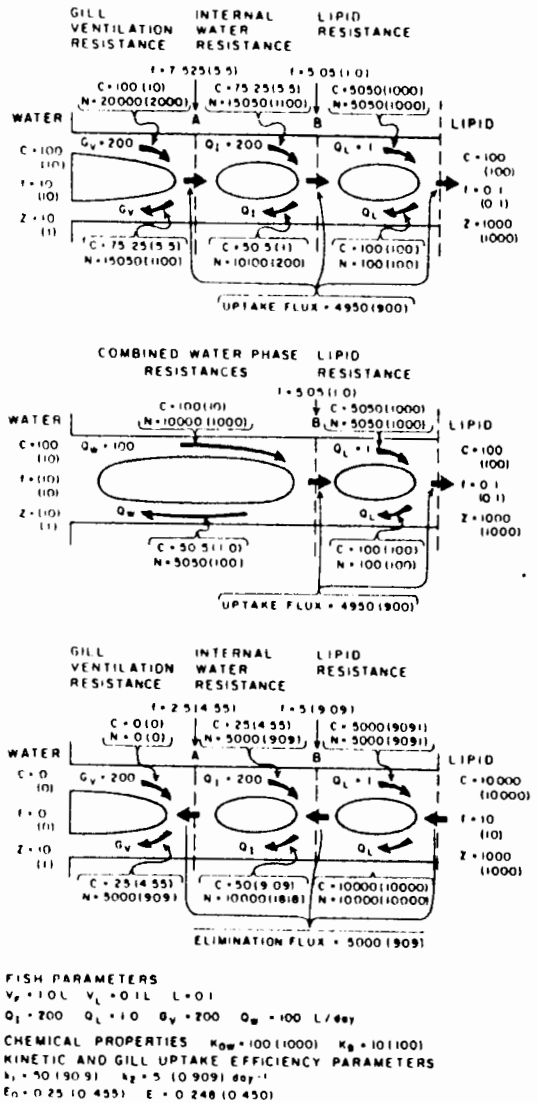

Fig. 4. Schematic diagram showing (top) uptake through two water resistances and a lipid resistance, (middle) identical uptake but with combined water resistance, and (bottom) elimination. The first values are for K_{ow} of 100 and the second in parentheses are for K_{ow} of 1,000.

increases to 90.9. The decrease in k_2 is due to the increase in the water resistance, which slows transfer. The increase in k_1 reflects the increase in gill uptake efficiency, resulting in a relative decrease in lipid-phase resistance. Also shown in Figure 4 is the condition for elimination of these chemicals from a fugacity of 10 into clean water. Again for the higher K_{ow} compounds most of the fugacity drop, and resistance, lies in the water phase. The changes in k_1, k_2, E_0 and the percentage resistance in the water phase are shown in Figure 1. The most important feature is that at low K_{ow} values (≤ 10) the lipid resistance controls; k_1 increases with increasing K_{ow}, while k_2 is constant. At intermediate K_{ow} (10–1,000) both resistances are important, k_2 falls and k_1 rises. At high K_{ow} values the water resistance controls, k_1 and E_0 are constant, and k_2 falls. The transfer from aqueous- to lipid-controlled bioconcentration kinetics in rainbow trout occurs at a log K_{ow} of approximately 2.

The model indicates that approximately half the resistance to solute transfer in the aqueous phase of the rainbow trout is due to gill ventilation and the other half is provided by other water-phase transport processes such as diffusion or flow. As a result, an increase in the ventilation rate of the fish leads to a less-than-proportional increase in uptake rate.

Only when the lipid-phase resistance ($1/Q_l K_{ow}$) is insignificant with respect to the water-phase resistance ($1/Q_w$) and the ventilation volumetric rate controls the water-phase resistance (i.e., $G_V \leq Q_l$) does an increase in G_V lead to a proportional increase in k_1 and k_2. This has been demonstrated for the brook trout [23], where the gill ventilation can be calculated to provide 80% of the total water-phase resistance and the endrin uptake rate constant increases by a factor of 2.2 as a result of 4.3-fold increase in gill ventilation rate.

The observed phenomenon [8,9,12,13,19] that uptake rates in fish decrease with respect to K_{ow} for superhydrophobic compounds (log $K_{ow} \geq 6$) shown by two data points in Figure 1 cannot be explained by this model. We are unable to identify the cause of this phenomenon, but the model does provide some insight into possible causes. The model shows that uptake and release of these compounds is almost fully controlled by solute transport in a water phase of the fish. If this effect is due to a resistance increase, it seems likely that it will be reduced solute transport in an aqueous phase rather than a lipid phase that causes the relatively low uptake rates.

To illustrate this point, we can explore the effect of variation in K_{ow} on the resistances for a situation in which $Q_w = 100$ L/d, Q_L is 1.0 L/d, $V_F = 1.0$, V_l is 0.1 and L is 0.1. In all cases K_B is LK_{ow}.

The resistances for K_{ow} of 10^4 are respectively water ($V_l K_{ow}/Q_w$) = 1,000 and lipid (V_L/Q_L) = 0.1, to give a total of 1,000.1.

Now if increasing K_{ow} from 10^6 to 10^7 (i.e., by a factor of 10) causes k_1 to decrease by a factor of 2 (to say 50 d^{-1}) instead of remaining constant at 100 d^{-1}, and this was due to a doubling of the total resistance, it could be caused by a decrease in Q_W by a factor of 2, or a decrease of Q_l by a factor of 10^4, or a decrease in Z_l/Z_W by a factor of 10^4, or to a combination of these changes.

It is difficult, but not impossible, to conceive that Q_l or Z_l/Z_W change by this magnitude for a relatively small change in K_{ow}. It does not seem likely that Q_W changes, because it is a basic property of the fish. We suggest that the most likely explanation is sorption of the chemical on particulate matter, rather than on an increased resistance reflected by a decreased D_F. If this reduced uptake rate is viewed as being characterized by a reduced $D_F f_W$ product in Equation 1, we suggest that the reason lies in a decreased f_W or bioavailability in the water.

Indeed, several studies have shown that reduced bioavailability causes both low uptake rates and bioconcentration factors [24,25]. Although a reduced membrane permeation of superhydrophobic compounds seems less likely to cause these low uptake rates – since it involves a transport process in a lipid phase – no definite conclusion can be reached at present. For example, it has been suggested by Opperhuizen et al. [9,26] that the observed lack of uptake of several superhydrophobic compounds in guppies may be due to molecular dimensions interfering with diffusion through the membrane-water interface. Molecules with relatively large cross sections may therefore experience an unusually high resistance for membrane permeation, causing low uptake rates. Obviously this is a topic requiring further investigation before the factor or combination of factors causing this phenomenon can be identified.

CONCLUSIONS

We have developed and discussed a model describing the uptake and clearance of conservative chemicals by fish from water. The key quantities are the fish weight and lipid content, the chemical's K_{ow}, and transport parameters Q_W, Q_l

(which can be obtained from uptake/clearance experiments), and if desired G_V, the gill ventilation rate. From these data the bioconcentration factor, the uptake and clearance rate constants, and the uptake efficiency can be deduced. The model clearly shows the roles of water- and lipid-phase resistances in controlling exchange kinetics, lipid-phase resistance controlling at low K_{ow}, and water-phase resistance at high K_{ow}. It is suggested that Q_W, Q_L and G_V are related to fish size and tentative relationships are proposed, but more experimental data are needed before a validated relationship can be established. We believe, however, that the general form of the relationships is correct.

Acknowledgements—The authors gratefully acknowledge the financial support of NSERC, the Ontario Ministry of Environment and the Wildlife Toxicology Fund.

REFERENCES

1. **Branson, D.R., G.E. Blau, H.C. Alexander and W.B. Neely.** 1975. Bioconcentration of 2,2′,4,4′-tetrachlorobiphenyl in rainbow trout as measured by an accelerated test. *Trans. Am. Fish Soc.* **104**:785–792.
2. **Mackay, D.** 1982. Correlation of bioconcentration factors. *Environ. Sci. Technol.* **16**:274–278.
3. **Neely, W.B.** 1979. Estimating rate constants for the uptake and clearance of chemicals by fish. *Environ. Sci. Technol.* **13**:1506–1510.
4. **Veith, G.D., D.L. DeFoe and B.V. Bergstedt.** 1979. Measuring and estimating the bioconcentration factor of chemicals in fish. *J. Fish Res. Board Can.* **36**:1040–1048.
5. **Tulp, M. and O. Hutzinger.** 1978. Some thoughts on aqueous solubility and partition coefficients of PCB, and the mathematical correlation between bioaccumulation and physico-chemical properties. *Chemosphere* **10**:849–860.
6. **Könemann, H. and K. Van Leeuwen.** 1980. Toxicokinetics in fish: Accumulation and elimination of six chlorobenzenes by guppies. *Chemosphere* **9**:3–19.
7. **Elgehausen, H., J.A. Garth and H.O. Esser.** 1980. Factors determining the bioaccumulation potential of pesticides in the individual compartments of aquatic food chains. *Ecotox. Environ. Safety* **4**:134–157.
8. **Bruggeman, W.A., L.B.J.M. Matron, D. Kooiman and O. Hutzinger.** 1981. Accumulation and elimination kinetics of di-, tri- and tetra-chlorobiphenyls by goldfish after dietary and aqueous exposure. *Chemosphere* **10**:811–832.
9. **Opperhuizen, A., E.W. van den Velde, F.A.P.C. Gobas, D.A.K. Liem, J.M.D. van den Steen and O. Hutzinger.** 1985. Relationship between bioconcentration in fish and steric factors of hydrophobic chemicals. *Chemosphere* **14**:1871–1896.
10. **Spacie, A. and J.L. Hamelink.** 1982. Alternative models for describing the bioconcentration of organics in fish. *Environ. Toxicol. Chem.* **1**:309–320.
11. **Hawker, D.W. and D.W. Conell.** 1985. Relationships between partition coefficient, uptake rate constant, clearance rate constant and time to equilibrium for bioaccumulation. *Chemosphere* **14**:1205–12
12. **Muir, D.C.G., W.K. Marshall and G.R.B. Web** 1985. Bioconcentration of PCDD's by fish: Effects of molecular structure and water chemistry. *Chemosphere* **14**:829–833.
13. **Bruggeman, W.A., A. Opperhuizen, A. Wybenga and O. Hutzinger.** 1984. Bioaccumulation of super-lipophilic chemicals in fish. *Toxicol. Environ. Chem.* **7**:173–189..
14. **Mackay, D. and A.I. Hughes.** 1984. Three-parameter equation describing the uptake of organic compounds by fish. *Environ. Sci. Technol.* **18**:439–444.
15. **Yalkowsky, S.H., O.S. Carpenter and G.L. Flynn.** 1973. Drug absorption kinetics in goldfish. *J. Pharm. Sci.* **62**:1949–1954.
16. **Yalkowsky, S.H., T.G. Slunick and G.L. Flynn.** 1974. Effects of alkyl chain length on biological activity: Alkyl *p*-aminobenzoate-induced narcosis in goldfish. *J. Pharm. Sci.* **63**:691–695.
17. **Gobas, F.A.P.C., A. Opperhuizen and O. Hutzinger.** 1986. Bioconcentration in fish related to membrane permeation of hydrophobic chemicals. *Environ. Toxicol. Chem.* **5**:637–646.
18. **Flynn, G.L. and S.H. Yalkowsky.** 1972. Correlation and prediction of mass transport across membranes. I. Influence of alkyl chain length on flux-determining properties of barrier and diffusant. *J. Pharm. Sci.* **61**:838–851.
19. **McKim, J., P. Schnieder and G. Veith.** 1985. Absorption dynamics of organic chemical transport across trout gills as related to octanol/water partition coefficient. *Toxicol. Appl. Pharmacol.* **77**:1–10.
20. **Mackay, D. and S. Paterson.** 1982. Fugacity revisited. *Environ. Sci. Technol.* **16**:654A–660A
21. **Norstrom, R.J., A.E. McKinnon and A.S deFreitas.** 1976. A bioenergetics based model .. pollutant accumulation by fish. Simulation of PCB and methyl mercury residue level in Ottawa River yellow perch (*Perca flavescens*). *J. Fish Res. Board Can.* **28**:815–819.
22. **Niimi, A.J. and B.G. Oliver.** 1983. Biological half-lives of polychlorinated biphenyl (PCB) congeners in whole fish and muscle of rainbow trout (*Salmo gairdneri*). *Can. J. Fish Aquat. Sci.* **40**:1388–1394.
23. **McKim, J.M. and H.M. Goeden.** 1982. A direct measure of a xenobiotic chemical across the gills of brook trout (*Saluetinus fontinalis*) under normoxic and hypoxic conditions. *Comp. Biochem. Physiol.* **72C**:65–74.
24. **McCarthy, J.F.** 1983. Role of particulate organic matter in decreasing accumulation of polynuclear aromatic hydrocarbons by *Daphnia magna*. *Arch. Environ. Contam. Toxicol.* **12**:559–568.
25. **Landrum, P.F., M.D. Reinhold, S.R. Nihart and B.J. Eadie.** 1985. Predicting the bioavailability of organic xenobiotics to *Pontoporeia hoyi* in the presence of humic and fulvic materials and natural dissolved organic matter. *Environ. Toxicol. Chem.* **4**:459–467.
26. **Opperhuizen, A., F.A.P.C. Gobas and O. Hutzinger.** 1984. Unmetabolized compounds; their properties and implications. In J. Caldwell and G.D. Paulson, eds., *Foreign Compound Metabolism*. Taylor and Francis, London, pp. 109–117.