Appraisal of Tests to Predict the Environmental Behaviour of Chemicals
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4.3 *Modelling of Biotic Uptake*

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4.3.1 BASIC CONSIDERATIONS

The level of pollutant accumulated by an organism reflects the dynamic balance that exists between the rate of uptake and the rate at which the chemical is cleared by the organism. The uptake rate is a function of whether dermal, respiratory or dietary vectors are involved, and the concentration in the medium of exposure. The nature of the medium, as well as the nature of the chemical, are factors which significantly affect the efficiency of absorptive processes and hence the uptake rate (Wagner, 1971).

The uptake rate associated with the dietary and respiratory vectors are directly linked to the specific energy requirements of the organism, i.e. its requirements for food and oxygen (Norstrom *et al.*, 1976). Hence, there is a correlation between an organism's weight and the uptake rate. These fundamental relations are summarized in Table 4.3.1 for mammals, birds and fish. Because of the relatively low caloric content of a millilitre of air or a millilitre of water, an animal requires a greater volume of air or water than food to satisfy its metabolic requirements. Thus, the concentration of pollutant in the diet must generally be higher than the level in the water or air before the food vector can compete with respiratory vectors on a one-to-one basis, albeit in mammals and birds the vectors are more evenly matched than in the case of fish. For example, a fish will pass about 66 000 grams of water across its gills to balance the energy obtained from ingesting 1 gram of food. Hence, the concentration in a fish's food must be around 10^4–10^5 times the level in the water before the food vector can compete with the water vector.

Table 4.3.1 Relative magnitude of respiratory and dietary vectors to xenobiotic exposure in mammals, birds and fish (NRCC, 1981)

	Mammals[a]	Birds	Fish
Basal metabolic rate[b]			
($mg\ O_2 \cdot g\text{-}bw^{-0.8} \cdot d^{-1}$)	20	36	2
Caloric equivalent[c]			
($Cal \cdot g\text{-}bw^{-0.8} \cdot d^{-1}$)	70	125	10
Dietary vector			
Food required for basal maintenance[d]			
($mg \cdot g\text{-}bw^{-0.8} \cdot d^{-1}$)	70	125	10
Respiratory vector			
Respiratory volume (air or water) for basal maintenance	400[e]	714[e]	576f
($ml \cdot g\text{-}bw^{-0.8} \cdot d^{-1}$)			
Respiratory weight (air or water)	450[g]	800	576 000
($mg \cdot g\text{-}bw^{-0.8} \cdot d^{-1}$)			
Relative exposure			
(1) Between respiratory and food vectors within groups (mg(air or water) · mg^{-1} food)	6.4	6.4	57 600
(2) Respiration in fish as compared to other groups			
(a) respiration (mg water · mg^{-1} air)	1280	724	1
(b) food (mg water · mg^{-1} food)	8264	4608	57 600

[a] Basal metabolic rate for man = 43 $mg\ O_2 \cdot g\text{-}bw^{-0.8} \cdot d^{-1}$ (ICRP, 1975).
[b] After Hemmingsen (1960); Lasiewski and Dawson (1967); Boddington (1978); Rahn and Ar (1980); Boddington *et al.* (1979).
[c] 1 mg O_2 = 3.42 cal.
[d] 1 mg food = 1 cal.
[e] air = 20% O_2 and 20% O_2 extraction efficiency of lungs.
[f] 10 μg $O_2 \cdot ml\ H_2O^{-1}$ and 50% O_2 extraction efficiency.
[g] $mg_{air} = \frac{ml_{air} \cdot MW_{air}}{82 \cdot {}^{\circ}K}$ (Neely, 1979); molecular weight air approx. 28.

Complex pharmacokinetic models have been developed to describe the accumulation of chemicals in the various tissues of mammals through their diets or through inhalation (see Wagner, 1971). The same approaches have been applied to studies of the accumulation of chemicals by birds (e.g. de Freitas and Norstrom, 1974) and a detailed examination of these complex relations cannot be justified in this introductory chapter. Much simpler models have proven useful to describe the accumulation of chemicals in fish (Moriarty, 1975a, b).

In one of the simplest useful schemes, a three-compartment model and assumed first-order kinetics are used to describe the uptake and accumulation

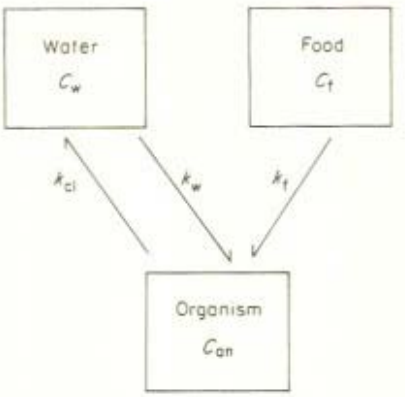

Figure 4.3.1 Simple three-compartment model describing uptake, loss and retention of chemicals in organisms from water and food vectors

of the organic chemical (Figure 4.3.1). Here k_f and k_w are the rate constants associated with the uptake of the pollutant via the food and water vectors and k_{cl} is the first-order rate constant describing the clearance of the pollutant from the organism. The terms C_w, C_{an} and C_f are the concentrations of chemical in the water, organism and food, respectively. This simplified approach has been used with a reasonable measure of success to describe bioaccumulation in fish (e.g. Neely *et al.*, 1974; Branson *et al.*, 1975; Norstrom *et al.*, 1976; Roberts *et al.*, 1977).

For preliminary screening purposes, the bioaccumulation potential of an organic pollutant can be assessed solely in terms of the water vector because the concentration of pollutant in the food vector would need to be exceedingly high for the food vector to be completely dominant (Johnson, 1973; Streit, 1979; Roberts *et al.*, 1979, 1981). An expression describing the accumulation of a chemical in this case is the differential equation

$$\frac{dC_{an}}{dt} = \frac{k_w C_w}{W} - k_{cl} C_{an} \qquad (1)$$

where W (g) is the weight.

This relation predicts that if the concentration of the pollutant in the water remains relatively constant, accumulation in the tissues of the organism will follow the pattern depicted in Figure 4.3.2. Subsequently, the rate of accumulation decreases (Part B) until a steady state plateau is reached (Part C). Here, the rate of accumulation is zero. At this point, the rate of uptake equals the rate of clearance.

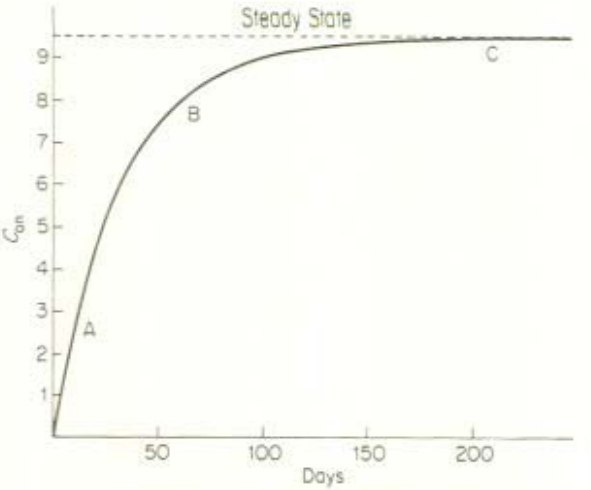

Figure 4.3.2 Theoretical accumulation curve assuming that the concentration in the water phase is constant (Roberts *et al.*, 1981)

Until steady state is reached, the measured ratio, C_{an}/C_w is a function of time elapsed from the beginning of the exposure.

$$\frac{C_{an}}{C_w} = \frac{k_w}{k_{cl}w}(1 - e^{-k_{cl}t}) \qquad (2)$$

If C_w is relatively constant, C_{an}/C_w at time t is described by equation (2). At steady state (when $e - k_{cl}t = 0$), C_{an}/C_w is constant and equals the ratio $k_w/k_{cl}w$. This is usually referred to as the bioconcentration factor (BCF) and it is the accepted indicator of the tendency for a chemical to accumulate. While bioconcentration is a function of time in real-life situations (e.g. equation (2)), when comparing bioconcentration factors, they should refer to concentration factors determined under steady state conditions. It is important that any reference to bioconcentration factors clearly documents how they were determined to avoid incorrect conclusions. This is a particularly important point and is often overlooked by those unfamiliar with the principles behind the phenomenon. If the 'bioconcentration factor' was determined from the linear part (A) of the accumulation curve (Figure 4.3.2), the result could reflect only the uptake rate and not necessarily the overall tendency for the pollutant to accumulate in the tissues of the organism. Only bioaccumulation factors for steady state or plateau conditions (Part C) accurately reflect the competing processes of uptake and clearance.

The steady state bioconcentration factors of a large number of organic chemicals in fish have been correlated with various indicators of lipophilicity

Table 4.3.2 Regression equations currently in use for estimation of bioconcentration factors from indicators of lipophilicity

Indicator	Relationship	Correlation coefficient	Range (Indicator)	Animal	Number of chemicals	References
K_{OW}	$\log BCF^b = -0.973 + 0.767 \log K_{OW}$	0.76	2.0×10^{-2}–2.0×10^{6}	Fish species[a]	36	Kenaga and Goring, 1978
K_{OW}	$\log BCF^b = 0.7504 + 1.1587 \log K_{OW}$	0.98	7.0×10^{0} –1.6×10^{4}	Mosquito fish	9	Metcalf *et al.*, 1975
K_{OW}	$\log BCF^b = 0.7285 + 0.6335 \log K_{OW}$	0.79	1.6×10^{0} –1.4×10^{4}	Mosquito fish	11	Lu and Metcalf, 1975
K_{OW}	$\log BCF^c = 0.124 + 0.542 \log K_{OW}$	0.95	4.4×10^{2} –4.2×10^{7}	Trout	8	Neely *et al.*, 1974
K_{OW}	$\log BCF^c = -1.495 + 0.935 \log K_{OW}$	0.87	1.6×10^{2} –3.7×10^{6}	Fish species[a]	26	Kenaga and Goring, 1978
K_{OW}	$\log BCF^c = -0.70 + 0.85 \log K_{OW}$	0.95	1.0×10^{0} –1.0×10^{7}	Fathead minnow, bluegill, mosquito fish, rainbow trout, green sunfish	59	Veith *et al.*, 1979
K_{OC}	$\log BCF^b = -2.024 + 1.225 \log K_{OC}$	0.91	0.4×10^{0} –4.3×10^{4}	Fish species[a]	22	Kenaga and Goring, 1978
K_{OC}	$\log BCF^c = -1.579 + 1.119 \log K_{OC}$	0.87	3.2×10^{0} –1.2×10^{6}	Fish species[a]	13	Kenaga and Goring, 1978
S (mg l^{-1})	$\log BCF^b = 2.183 - 0.629 \log S$	−0.66	1.7×10^{-3}–6.5×10^{5}	Fish species[a]	50	Kenaga and Goring, 1978
S (μg l^{-1})	$\log BCF^b = 3.9950 - 0.3891 \log S$	−0.92	1.2×10^{0} –3.7×10^{7}	Mosquito fish	11	Lu and Metcalf, 1975
S (μg l^{-1})	$\log BCF^b = 4.4806 - 0.4732 \log S$	−0.97	1.3×10^{0} –4.0×10^{7}	Mosquito fish	9	Metcalf *et al.*, 1975
S (mg l^{-1})	$\log BCF^c = 2.791 - 0.564 \log S$	−0.72	1.7×10^{-3}–6.5×10^{5}	Fish species[a]	36	Kenaga and Goring, 1978
S (μmol/l)	$\log BCF^c = 3.41 - 0.508 \log S$	−0.96	2.0×10^{-2}–5.0×10^{5}	Trout	7	Chiou *et al.*, 1977
P_c	$\log BCF^c = 0.034 + 0.0058 P_c$	0.80	2.2×10^{2} –5.8×10^{2}	Trout	8	Tulp and Hutzinger, 1978
BCF^b	$\log BCF^c = 0.024 + 1.074 \log BCF^b$	0.87	1.1×10 –8.5×10^{4}	Fish species[a]	20	Kenaga and Goring, 1978
BCF^c	$\log BCF^b = 0.717 + 0.703 \log BCF^c$	0.87	0×10 –7.3×10^{4}	Fish species[a]	20	Kenaga and Goring, 1978

[a] BCF data compiled from studies on the fathead minnow, bluegill, rainbow trout, brook trout and mosquito fish.
[b] Terrestrial aquatic static bioconcentration test.
[c] Flowing water bioconcentration test.

(Table 4.3.2). Using these relations, it is possible to estimate bioconcentration factors from the physical properties of a chemical. Some of the chemical parameters that have been used in these relations include solubility in water (S), the n-octanol–water partition coefficient (K_{OW}), the soil organic carbon–water sorption coefficient (K_{OC}), and the parachor (molecular volume indicator) (P_c) (Table 4.3.2). While similar correlations are expected in the case of birds and mammals, they are not well established. Kenaga (1980a,b) has developed a relation between a chemical's K_{OW} and its tendency to accumulate in beef fat, i.e. BCF–beef-fat/diet = 0.50 log K_{OW}.

Estimates of bioconcentration factors made using the more extensive correlations (Table 4.3.2) generally lie within one order of magnitude of the experimentally measured values (Kenaga and Goring, 1978). Important exceptions arise in the case of compounds which, due to structure or size, do not readily pass through membranes. For example, the data of Zitko (1974), on the uptake of chlorinated paraffins by salmon, indicated an upper molecular weight for the linear relations of about 600. In general, the correlating relations are not established for compounds with K_{OW} in excess of 10^6 and their validity for the super lipophilic compounds must still be proven. It has been suggested that overestimates of bioconcentration factors may be obtained using these relations for chemicals which are easily metabolized, such as 2-bis-(*p*-methylthiophenyl)-1,1,1-trichloroethane, a structural analog of DDT (Kapoor *et al.*, 1973).

The correlation of bioaccumulation to lipophilicity in turn means that adiposity will be of particular concern because of its profound effect on the clearance rate of organochlorines. This is found in endotherms (Pocock and Vost, 1974; de Freitas and Norstrom, 1974), while Roberts *et al.* (1977) have found that the clearance of *trans*- and *cis*-chlordane is inversely related to the adiposity of the individual fish. This latter observation, together with recent reports (Addison and Zinck, 1977; Bruggeman *et al.*, 1981), support the suggestion of Hamelink *et al.* (1971) and Harvey *et al.* (1971) that field residue patterns of chlorinated hydrocarbons may be as much a function of lipid content of the fish as of its specific position in the food web. At the present time, corrections for adiposity have not been included in any of the correlating relations.

4.3.2 CONCLUSIONS

Two levels of model resolution are available today to the environmental scientist. One may use either the empirical correlating relations to develop first estimates of a chemicals accumulation potential or one may use simple pharmacokinetic models based on exposure situations amenable to laboratory study. Neither approach can mimic the more complex exposure scenarios encountered in the environment, albeit the information on the kinetics of the

processes obtained in the laboratory do provide a basis for the analysis of less complex exposure patterns such as those encountered in the case of the more ubiquitous persistent pollutants.

The models do allow one to predict the relative importance of the various vectors of exposure operative in a given situation. Hence, they provide information on the relevance of specific toxicological studies, for example dermal or inhalation studies, to a specific situation. Additionally, the correlating relations are useful in screening for gross accumulation patterns, but they do not provide sufficient resolution where the exposure vectors are nearly competitive. The correlating relations cannot reflect subtle shifts in structure that are known to alter significantly accumulation patterns in the case of homeotherms and presumably other animals. This is a particularly important consideration when extrapolations are developed from the residues found in a specific indicator species to ambient exposure levels in other compartments. Except as gross screens the correlating relations are inadequate for this purpose.

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