A Generic QSAR for Assessing the Bioaccumulation Potential of Organic Chemicals in Aquatic Food Webs

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Abstract

This study presents the development of a quantitative-structure activity relationship (QSAR) for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. The QSAR is derived by parameterization and calibration of a mechanistic food web bioaccumulation model. Calibration of the QSAR is based on the derivation of a large database of bioconcentration and bioaccumulation factors, which is evaluated for data quality. The QSAR provides estimates of the bioaccumulation potential of organic chemicals in higher trophic level fish species of aquatic food webs. The QSAR can be adapted to include the effect of metabolic transformation and trophic dilution on the BAF. The BAF-QSAR can be applied to categorize organic chemical substances on their bioaccumulation potential. It identifies chemicals with a log K_{OW} between 4.0 and 12.2 to exhibit BAFs greater than 5000 in the absence of significant metabolic transformation rates. The BAF-QSAR can also be used in the derivation of water quality guidelines and total maximum daily loadings by relating internal concentrations of organic chemicals in upper trophic fish species to corresponding concentrations in the water.

1 Introduction

In recent years, several countries and international organizations have worked towards the development of methods and criteria for assessing the impacts of anthropogenic chemicals on both ecosystem and human health [1–5]. A general approach of these methods is to determine the potential of substances to be persistent (P), bioaccumulative (B) and toxic (T) in the environment. The difficulties of these initiatives include: the large numbers of chemicals that require appraisal, the general absence of reliable empirical data, the costs and scientific challenges in obtaining the required information and the relative urgency of these efforts [2, 6, 7]. Therefore, there is a need to develop expeditious and cost-effective methods to identify potentially hazardous substances in an effective and conservative manner. In Canada, the Canadian Environmental Protection Act 1999 (CEPA 1999) defines a set of criteria to assess whether a substance is persistent, bioaccumulative and toxic [2, 8]. The criteria for the bioaccumulative properties of substances identify the chemical's bioaccumulation factor (BAF) to be the preferred measure of the chemical's bioaccumulation potential and chemicals with a BAF equal to or greater than 5000 are considered to be bioaccumulative [8]. In absence of information on the BAF, the bioconcentration factor (BCF) can be used to assess the bioaccumulation potential and substances with a BCF equal to or greater than 5000 are considered to be bioaccumulative [8]. In absence of both BAF and BCF data, the logarithm_{10} of the octanol-water partition coefficient (log K_{OW}) has been identified as a surrogate measure of a chemical's bioaccumulation potential and chemicals with a log K_{OW} greater than 5 are considered to have bioaccumulative potential [8].

Quantitative Structure Activity Relationships (QSARs) and Quantitative Structure Property Relationships (QSPRs) are a few tools that are available to screen large number of chemicals on their behavior in the environment. Several QSARs have been proposed for the BCF [6, 9–12]. QSARs for the BAF are as of yet unavailable. This is due to the fact that BAFs are subject to a large number of site-specific environmental variables in addition to chemical properties. A number of models have been developed to estimate BAFs [13–18]. These models are parameter and computationally intensive and thus remain cumbersome for their application to a large number of chemicals. To address this problem we present in this paper the application of a food web bioaccumulation model to derive a simple QSAR for bioaccumulation factors. The approach that we follow consists of (i) the development of a bioaccumulation model,

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(ii) the parameterization of the model to reflect Canadian conditions and (iii) the calibration of the model to a large BCF and BAF database. The resulting QSAR presents a simple functional relationship that has the advantages of being well based on mechanistic considerations and consistent with many laboratory and field observations.

2 Theory

Definitions: Bioaccumulation is the process where the chemical concentration in an aquatic organism achieves a level that exceeds that in the water as a result of chemical uptake through all routes of chemical exposure (e.g. dietary absorption, transport across the respiratory surface, dermal absorption). Bioaccumulation typically takes place under field conditions and is a combination of chemical bioconcentration and biomagnification. The extent of chemical bioaccumulation is usually expressed in the form of a bioaccumulation factor (BAF), which is the ratio of the chemical concentration in the organism (C_B) and the water (C_W) [7]:

$$BAF = C_B/C_W \quad (1)$$

Bioconcentration is the process where the chemical concentration in an aquatic organism achieves a level that exceeds that in the water as a result of the exposure of an organism to a chemical in the water but does not include exposure via the diet. Bioconcentration refers to a situation, typically derived under controlled laboratory conditions, wherein the chemical is absorbed from the water via the respiratory surface (e.g. gills) and/or the skin only. Standard protocols for conducting bioconcentration tests have been developed [19, 20]. The extent of chemical bioconcentration is usually expressed in the form of a bioconcentration factor (BCF), which is the ratio of the chemical concentration in the organism (C_B) and the water (C_W) [7]:

$$BCF = C_B/C_W \quad (2)$$

Biomagnification is the process by which lipid normalized chemical concentrations (i.e. C_B/lipid content) increase with trophic level in a food-chain. Trophic dilution is the opposite process causing lipid normalized concentrations to decrease with increasing trophic level as a result of metabolic transformation. The process of bioaccumulation is described in more detail in recent reviews [7, 21].

Model Development: Bioaccumulation is the result of competing processes of chemical uptake into and chemical elimination from the organism (Figure 1). The major routes of uptake include absorption directly from the water via the respiratory surface (e.g. gills) of the organism and absorption from the diet. The major routes of chemical elimination include elimination via the respiratory surface, by fecal egestion, metabolic transformation of the parent compound, and growth dilution. In addition, the degree of bioaccumulation that occurs in an organism is a function of the degree of biomagnification or trophic dilution that occurs in organisms of lower trophic levels in the food web, thus regulating the concentration of the chemical in the diet of upper trophic level organisms.

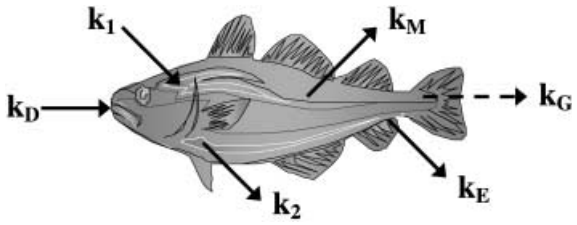

Figure 1. A conceptual diagram representing the major routes of chemical uptake and elimination in an aquatic organism. k_1 – gill uptake rate constant, k_2 – gill elimination rate constant, k_D – dietary uptake rate constant, k_E – fecal egestion rate constant, k_M – metabolic rate constant, k_G – growth rate constant.

To obtain a generic expression for the BAF in organisms of aquatic food webs that is not specific to any particular species in the food web, we modified the bioaccumulation model derived in Gobas [15] for an upper trophic level aquatic organism to:

$$BAF = C_B/C_W = (1 - L_B) + ((k_1 \cdot \phi + (k_D \cdot \beta \cdot \tau \cdot \phi \cdot L_D \cdot K_{OW}))/(k_2 + k_E + k_G + k_M)) \quad (3)$$

which is further documented in Table 1. This model derives the BAF as the ratio of the chemical concentration in an upper trophic level organism (C_B) and the total chemical concentration in unfiltered water (C_W). ϕ is the fraction of the total chemical concentration in the water that is freely dissolved and which can permeate through the membranes of the respiratory surface area [7, 21]. It reflects the "bioavailable" chemical concentration in the water (C_{WD}), which is $\phi \cdot C_W$. The model accounts for the rates of chemical uptake and elimination. k_1, k_D, k_2, k_E, k_G and k_M are rate constants describing respectively the rates of chemical uptake via the respiratory area and the diet and chemical elimination via the respiratory surface, fecal egestion, growth dilution and metabolic transformation. The model includes the overall biomagnification that occurs in the food web in terms of an overall biomagnification factor β (unitless). β is an empirical value derived by calibrating the model to empirical data. It provides a conservative upper trophic level BAF that incorporates a number of trophic interactions and sediment-water disequilibrium. τ (unitless) represents the degree of trophic dilution that occurs for substances that are metabolized at a significant rate in organisms of a food web. The term $1 - L_B$ accounts for chemical partitioning into non-lipid (i.e. aqueous) components of the organism. The inherent bioaccumulation factor, based on the freely dissolved concentration in the water (BAF_{fd}), is equivalent to BAF/ϕ. It represents the bioaccumulation potential of the chemical substance itself

Table 1. Parameters used to derive the BAF-QSAR. The parameter values were selected to represent Canadian environmental conditions.

Symbol	Parameter	Value
T	Mean water temperature	10 °C
W	Weight of organism	1 kg
L_B	Lipid content of organism	20%
L_D	Lipid content of lowest trophic level organisms	1%
χ_{POC}	Concentration of particulate organic carbon	$5 \cdot 10^{-7}$ g/ml
χ_{DOC}	Concentration of dissolved organic carbon	$5 \cdot 10^{-7}$ g/ml
ϕ	Fraction of freely dissolved chemical in water	$1/(1 + \chi_{POC} \cdot 0.35 \cdot K_{OW} + \chi_{DOC} \cdot 0.1 \cdot 0.35 \cdot K_{OW})$
β	Overall food web biomagnification factor	130
τ	Maximum trophic dilution factor	1 (default)
k_M	Metabolic transformation rate constant	0 day^{-1} (default)
n	Number of trophic interactions in the food web	3 (default)
K_{OW}	Octanol-water partition coefficient	Chemical dependent
k_1	Uptake rate constant	$1/((0.01 + 1/K_{OW}) \cdot W^{0.4})$
k_D	Dietary uptake rate constant	$0.02 \cdot W^{-0.15} \cdot e^{(0.06 \cdot T)}/(5.1 \cdot 10^{-}8 \cdot K_{OW} + 2)$
k_2	Elimination rate constant	$k_1/L_B \cdot K_{OW}$
k_E	Fecal egestion rate constant	$0.125 \cdot k_D$
k_G	Growth rate constant	$0.0005 \cdot W^{-0.2}$

and is independent on the concentration of particulate and dissolved matter that can bind the chemical and make it unavailable for uptake and bioaccumulation via the respiratory surface.

A number of simple relationships have been developed to estimate the rate constants for organic chemicals in fish [15]. This allows us to apply the model to fish, which is often a biological entity of interest because of the high trophic status of many fish species and the role of fish as a major food item for the human population. These relationships are:

k_1: The rate at which chemicals are absorbed from the water via the gills is expressed by the gill uptake rate constant k_1 ($L/kg \cdot d$), which is a function of the K_{OW} of the chemical and the weight of the organism W (kg) as:

$$k_1 = 1/((0.01 + 1/K_{OW}) \cdot W^{0.4}) \quad (4)$$

k_D: The rate at which chemicals are absorbed from the diet via the gastrointestinal tract is expressed by the dietary uptake rate constant k_D ($kg/kg \cdot d$). This can be viewed as a result of the combined process of the feeding rate, which is based on the bioenergetics of organism weight W (kg) and temperature T (°C), and of the diffusion rate of the chemical across the intestinal wall, which is a function of K_{OW}, such that:

$$k_D = 0.02 \cdot W^{-0.15} \cdot e^{(0.06 \cdot T)}/(5.1 \cdot 10^{-8} \cdot K_{OW} + 2) \quad (5)$$

k_2: The rate at which organic chemicals are eliminated via the respiratory surface can be expressed as the gill elimination rate constant k_2 (d^{-1}), which can be approximated as a function of the lipid content of the organism (L_B) and the K_{OW} of the chemical as:

$$k_2 = k_1/L_B \cdot K_{OW} \quad (6)$$

k_E: The rate at which chemicals are eliminated by the egestion of fecal matter can be expressed as the fecal elimination rate constant k_E (d^{-1}). As with the dietary uptake rate constant, this parameter is dependant on the K_{OW} of the chemical and the feeding rate. The fecal egestion rate constant can be determined based on the composition and digestions of the organism's diet [22] but for this purpose it can be generalized to be up to eight times lower than the ingestion rate constant [23] as:

$$k_E = 0.125 \cdot k_D \quad (7)$$

k_G: A generalized growth equation that provides a reasonable approximation for the growth rate constant of aquatic organisms k_G (d^{-1}) is dependent on the weight of the organism W (kg) and the temperature of its environment (assumed here to be 10 °C) and can be expressed as:

$$k_G = 0.0005 \cdot W^{-0.2} \quad (8)$$

k_M: The rate at which a parent compound can be eliminated via metabolic transformation is represented by the metabolic transformation rate constant k_M (d^{-1}). There is significant uncertainty for applying this parameter towards a wide range of species since this process is chemical and species dependent and there is a paucity of empirical metabolic transformation data.

ϕ: For non-ionizing hydrophobic organic substances, the fraction of freely dissolved chemical in the water can be estimated from the concentrations of particulate and dissolved organic carbon as:

$$\phi = C_{WD}/C_W = 1/(1 + \chi_{POC} \cdot 0.35 \cdot K_{OW} + \chi_{DOC} \cdot 0.1 \cdot 0.35 \cdot K_{OW}) \quad (9)$$

where χ_{POC} is the concentration of particulate organic carbon in the water (g/ml) and χ_{DOC} is the concentration of dissolved organic carbon in the water (g/ml) [21], 0.35 is a proportionality constant reflecting the degree to which organic carbon mimics the partitioning property of octanol [24] and 0.1 reflects the partitioning properties of dissolved organic carbon relative to particulate organic carbon [25].

β: The degree of food web accumulation, represented by β, is highly dependent on the species of interest, food web structure, environmental conditions and ecosystem characteristics. We therefore suggest that for the derivation of a generic QSAR for the BAF, β is determined by calibration to an appropriate data set. In this paper, we present a large BAF database that can be used for this purpose. It is further interesting to note that if β is set to zero (i.e. there is no dietary uptake), the BAF model (i.e. Equation 3) converts to a BCF model:

$$BCF = (1 - L_B) + (k_1 \cdot \phi/(k_2 + k_E + k_G + k_M)) \quad (10)$$

τ: The trophic dilution factor τ represents the ability of organisms in the food web to metabolize absorbed parent compounds. If metabolic transformation is significant it can counteract the effects of biomagnification in the food web and actually cause the chemical concentration to decrease with increasing trophic level. The trophic dilution factor can be approximated as:

$$\tau = (0.0065/(k_M + 0.0065))^{n-1} \quad (11)$$

where k_M is the metabolic transformation rate applied to the entire food web and n is the number of trophic interactions in the food web. The constant 0.0065 reflects the rate at which metabolic transformation becomes greater than the other routes of chemical elimination (i.e. k_2, k_E and k_G) for a lower trophic level aquatic species (250 g, 5% lipid content). For substances that are not significantly metabolized (i.e. $k_M = 0$), the trophic dilution factor is 1 (indicating no trophic dilution). A significant rate of metabolic transformation will cause τ to drop below 1, counteracting the effect of β. Metabolic transformation rate constants can be measured in controlled laboratory studies and then used in equations 11 and 3 to assess the effect of the metabolic rate on the food web bioaccumulation and the BAF in higher trophic levels. In absence of empirical metabolic transformation rates, τ can be determined by calibrating k_M using high quality empirical BCF or BAF data for individual compounds or groups of compounds that can be assumed to undergo similar metabolic pathways. This can be accomplished by calibrating the BCF-QSAR to reliable BCF data and/or the BAF-QSAR to reliable BAF data assuming that the discrepancy between the model predictions for non-metabolizing substances and empirical data are due to metabolic transformation.

3 Methods

Model Parameterization: A small number of input parameters are required to characterize environmental conditions. Table 1 depicts the model parameter values used in this study that were chosen to represent food-chain bioaccumulation in a higher trophic level fish species under Canadian conditions. These values can be altered to reflect specific conditions. The Canadian conditions are probably applicable for aquatic food webs in temperate climates, but caution should be exercised when applying the same parameters to tropical or arctic food webs.

Model calibration: To calibrate the model, a database was compiled of empirical BCF and BAF data for organic chemicals in fish and aquatic invertebrates. The data were derived from an in-house database, the United States Environmental Protection Agency's ECOTOX AQUIRE database [26]; the Syracuse Research Corporation's BCFWIN data set [27]; Japan's Chemical Evaluation Research Institute [28]; the Physical-Chemical Properties and Environmental Fate Handbook [29]; the National Library of Medicine's Hazardous Substances Data Bank [30]; and the review "Comparative QSAR: A Comparison of Fish Bioconcentration Models" [31]. When possible, details of the experimental or field conditions were documented to determine the quality and reliability of the reported BCF and BAF values. Parameters that were considered relevant for this purpose for both BCF and BAF values are (i) chemical characteristics (CAS #, chemical name, molecular weight and empirical or estimated K_{OW}); (ii) organism characteristics (species, weight, lipid content, tissue analyzed, gender, age, chemical concentration in organism); (iii) environmental conditions (water temperature, pH, organic carbon content, water type); (iv) exposure conditions (exposure duration, total chemical concentration, method of water analysis, exposure route); (v) experimental design (flow through, static, renewal, methodology in deriving BCF/BAF) and (vi) the primary literature reference. Repetitive and discrepant values were removed from the data set. In cases where conflicting BCF or BAF values were reported in the different databases, the primary literature was consulted. If the BCF or BAF was reported on a lipid normalized basis (i.e. L/kg lipid) and no lipid content for the sampled tissue or organism was reported, the BCF or BAF was expressed on a wet weight basis assuming a lipid content of 5% [4, 32].

The accumulated empirical data were assessed to determine their general quality and reliability by applying a set of guidelines. These guidelines were based on currently accepted protocols for conducting bioconcentration tests [19, 20] and on the common difficulties in the reporting of these experiments [6, 21, 31, 33, 34]. Similar approaches have been suggested [4]. We used a semi-quantitative scoring system based on the following criteria:

1. Was the identity of the chemical and biological species in the reported study well defined and was the analytical methodology appropriate?

2. Was the exposure duration sufficient to achieve steady-state? If not, were appropriate methods employed to account for this in the calculation of the BCF or BAF?
3. Was the BCF derived based on measured chemical concentration in the water determined throughout the bioconcentration experiment?
4. Was the chemical concentration in the water below the chemical's water solubility?
5. If the BCF or BAF was derived from a tissue sample rather than the whole organism, was the lipid content of the tissue reported such that the concentration could be lipid normalized?

For each criterion above, if the answer was "no" one point was subtracted from a value of 5 to arrive at an overall score between 0 and 5. Reported BCF values that were scored to have a quality value of 4 or greater were considered to be 'acceptable', whereas empirical data with quality values equal to or less than 3 were deemed 'unacceptable'. This methodology reduces the number of erroneous BCF data from the database. It removes BCF and BAF data that are seriously flawed but it does not fully eliminate experimental errors from the database.

Our database includes 1398 unique BCF and 997 BAF observations for 233 organic chemical substances in 176 different fish and aquatic invertebrate species. Of the combined data set, 916 BCF and 61 BAF observations were considered to be of poor quality and were not used for model calibration. The poor quality BAFs were the result of experiments involving microcosm studies that did not provide sufficient exposure duration to achieve steady-state in the test organisms or from the use of radioisotopes.

The model calibration for β included the good quality BAF data only ($n = 936$). The value of β was selected to ensure that 97.5% of the empirical BAF data were equal or less than the model-predicted values. This ensures that the BAF-QSAR will be conservative and minimizes the probability that BAFs will be underestimated. The reason for using the upper 97.5 % probability interval of the empirical data rather than the more conventional 95% is that the majority of the BAF data in the BAF data represent BAFs in lower trophic organisms. For biomagnifying chemicals, the BAFs in lower trophic level organisms are lower than those in the higher trophic levels to which the QSAR is meant to apply.

To illustrate the model calibration for metabolizing substances, once β was established the calibration of τ was carried out for polycyclic aromatic hydrocarbons (PAHs). For this class of chemical substances a reasonable database exists that can be used for calibration. Also, similar mechanisms for metabolic transformation may apply to this class of chemical substances. The model calibration involved high quality BCF and BAF observations and was conducted by deriving a value for τ which produced the best agreement between observed and model predicted BCF and BAF values.

4 Results and Discussion

BCF-QSAR: Figure 2a depicts the combined data set of BCF and BAF data and Figure 2b shows the data that were considered to be of good quality. Figure 2 illustrates that the poor quality data predominantly include BCF observations for relatively high K_{OW} substances (i.e. log $K_{OW} > 4$). For these substances, experimental artifacts (e.g. water concentration exceeding the solubility, an insufficient exposure duration, and difficulties in measuring water concentrations throughout the experiment) are the most pronounced. These experimental artifacts have a tendency to underestimate the BCF. Hence, the removal of these flawed or unreliable data affects lower BCF observations for higher K_{OW} substances the most. Figure 2b shows that the BCF-QSAR (i.e. equation 10, where $\beta = 0$ and $\tau = 1$), which was not calibrated to the empirical data, tends to fit the upper bound BCF observations. 79.7% of the good quality BCF observations fall below, while 20.3% of the BCF observations are above the BCF-QSAR predictions. There are

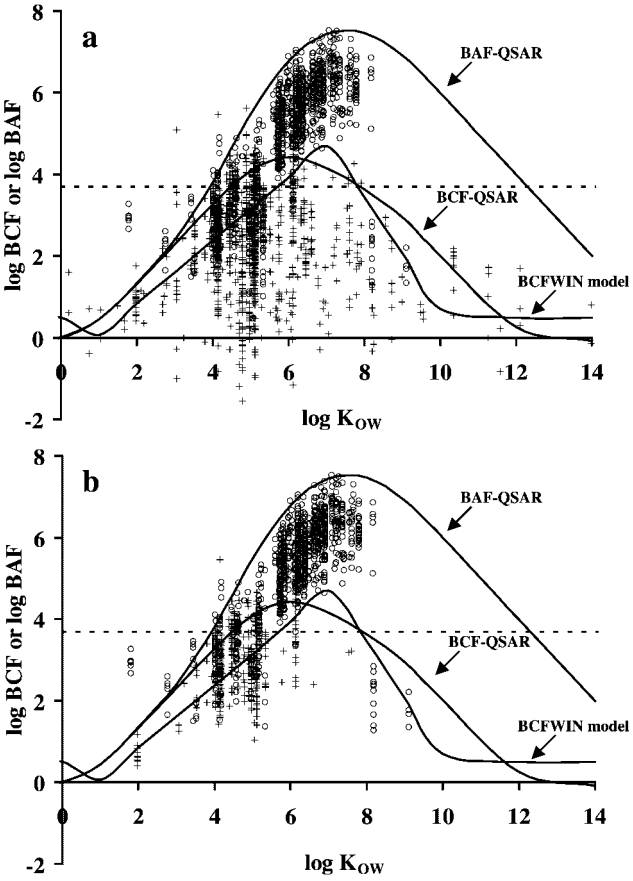

Figure 2. The BAF-QSAR ($\beta = 130$, $\tau = 1$), BCF-QSAR ($\beta = 0$, $\tau = 1$) and BCFWIN model (presented in the graphs without correction factors) in relation to the combined database of good and poor quality empirical BCFs (+; $n = 1398$) and BAFs (circles; $n = 997$) (a) and good quality BCF (+; $n = 482$) and BAF (circles; $n = 936$) data (b). The dashed line represents the CEPA 1999 BCF and BAF bioaccumulation criterion of 5000 [8].

several reasons why a large fraction of the empirical BCFs are below the model derived BCF-QSAR. They include (i) the fact that many laboratory BCF experiments are carried out with organisms of lower lipid content (i.e. less than the 20% used to derive the BCF-QSAR); (ii) experimental artifacts, which are not totally ruled out by our data quality assessment methodology, show in most cases a tendency to underestimate the actual BCFs; and (iii) metabolic transformation reduces the BCF of the parent compound below the QSAR predicted value. The QSAR, which is unaffected by experimental error; assumes no metabolic transformation and applies a reasonable 20% lipid content for an upper trophic level fish species, tends to reduce the probability of underestimating the BCF. We believe that this is a good attribute for a model that is to be used for assessing the BCFs of chemical compounds in absence of data on their metabolic transformation rates.

Our methodology is different from that used in regression models such as the BCFWIN model [6]. Regression based models have a tendency to arrive at an "average" BCF value, allowing for a relatively large number of occurrences where the actual BCF is greater than the BCF predicted values. For example, 67.6% of the good quality BCF data are greater than the BCFWIN model predictions (which included the model correction factors) and are therefore underestimated by the regression model. In Figure 2 the BCFWIN model is graphed without including correction factors so that it retains a single relationship since the correction factors are dependent on chemical class not K_{OW}. It is further important to stress that regression based BCF estimation models are dependent on the empirical database used for the regression. If the database is subject to a large number of observations of poor quality or subject to experimental error, or includes data for organisms of low lipid content, or for substances that are metabolized regression, models will underestimate BCFs of substances that are not affected by these factors.

BAF-QSAR: Figure 2 illustrates the large discrepancy between BCF and BAF data. BAFs of chemicals with a log K_{OW} above approximately 4 are substantially larger than their BCFs due to the effect of dietary accumulation and biomagnification in the food web. This illustrates the preference of using BAF based bioaccumulation models over bioconcentration based models to assess the bioaccumulation potential of chemicals [8]. The calibration of the model to the empirical BAF data resulted in a value for β of 130. The resulting QSAR produces BAF estimates that are exceeded by only 2.5% of the available empirical data. The calibration of the model to the data is designed to produce a QSAR for the BAF in higher trophic levels of a Canadian aquatic food web. The QSAR BAFs can therefore be expected to exceed BAFs in organisms which are (i) of lower trophic level and/or (ii) of lower lipid content and/or (iii) rapidly growing and/or (iv) metabolize the substance at a significant rate.

The BAF-QSAR exhibits a "parabolic" shape. At low K_{OW}, the BAF increases with increasing K_{OW} in a linear fashion, as partitioning of the chemical between the water and the organism controls bioaccumulation. If log K_{OW} exceeds 4, the BAF increases at a rate greater than linearity due to biomagnification in the food web. The model's decline in the BAF with increasing K_{OW} for the very high K_{OW} chemicals (i.e. log $K_{OW} > 7.5$) is due to a reduction in ϕ with increasing K_{OW}. ϕ represents the bioavailable fraction of the chemical concentration in the water, which decreases with increasing K_{OW} because of the increase in the chemical's sorption coefficient to particulate and dissolved organic carbon. The BAF-QSAR therefore identifies sorption in the water phase as the main reason why the BAF decreases with increasing K_{OW} for these high K_{OW} chemicals. The decline is not due to a lack of biomagnification or steric factors affecting membrane permeation. The overriding influence of sorption in the water can therefore cause the BAF to fall to low numbers (e.g. less than 5000) while the substance may still have a significant potential to biomagnify in the food web. If the BAF would be presented as the ratio of the concentration in the organisms divided by the freely dissolved chemical concentration in the water as $C_B/(C_W \cdot \phi)$, the bioaccumulation factor of very high K_{OW} chemicals would exhibit values of approximately 10^7 and would not vary with increasing K_{OW}.

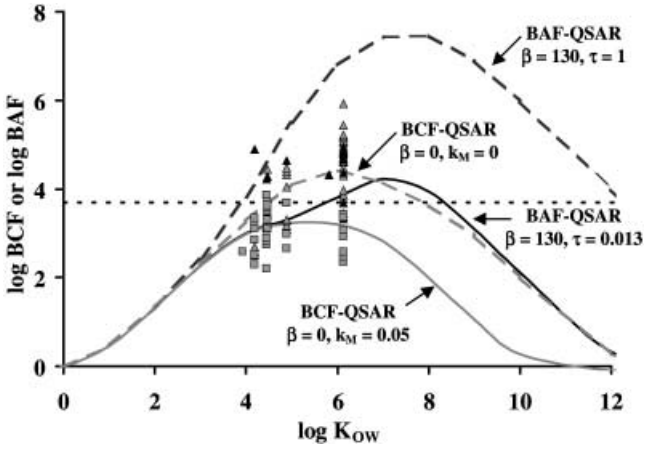

Figure 3. Calibration of the trophic dilution factor ($\beta = 130$, $\tau = 0.013$) to good quality empirical vertebrate BCFs (grey squares, $n = 29$), invertebrate BCFs (grey triangles, $n = 48$) and invertebrate BAFs (black triangles, $n = 13$) for various PAHs. The black line represents the BAF-QSAR with trophic dilution (solid) and without trophic dilution (dashed). The grey line represents the BCF-QSAR with metabolic transformation (solid) and without metabolic transformation (dashed). The horizontal dashed line represents the CEPA 1999 BCF and BAF bioaccumulation criterion of 5000 [8].

Metabolism: While the BAF-QSAR recognizes many of the bioaccumulation mechanisms that generally apply to organic chemicals, it is unable to predict metabolic transformation rates of chemical substances in aquatic biota. However, if information on metabolic transformation rates are available from laboratory bioconcentration experiments or can be derived from field BAFs, the QSAR can be adapted to include the effect of metabolic transformation on the BAF. The latter is illustrated in Figure 3. It illustrates the

derivation of a trophic dilution factor for a group of PAHs. In this example, the model is fitted to available BCF and BAF data, resulting in a k_M of 0.05 d^{-1} and a τ of 0.013. τ counteracts β and essentially reduces the influence of food web magnification of these substances. Further, a k_M of 0.05 d^{-1} results in a half-life of approximately 13.2 days which is in agreement with the range of empirical half-lives observed for PAHs in Rainbow trout (*Oncorhynchus mykiss*) (1 – 25 days) [35]. In addition, Figure 3 illustrates that based on the BCF data metabolic transformation of PAHs is greater in higher trophic level species. While this example illustrates the fitting of the model to BCF and BAF data, it is preferable to use metabolic transformation rates that have been measured in controlled studies as, in addition to metabolic transformation, field derived BAF data are subject to several other environmental and analytical factors that could produce low BAFs.

BAF-QSAR application: Areas of application of the BAF-QSAR include the categorization of bioaccumulative substances, the derivation of water quality criteria and the estimation of total maximum daily loadings for aquatic ecosystems. The BAF-QSAR identifies chemicals with a log K_{OW} greater than approximately 4.0 and less than approximately 12.2 that are not being metabolized at a significant rate to exhibit BAFs larger than 5000 in upper trophic level fish species and to have a bioaccumulation potential in aquatic food webs. For substances with a log $K_{OW} > 4.0$, BAFs are substantially greater than BCFs and BCF models are not appropriate estimators of the bioaccumulation behavior. BCF models that do not include dietary uptake or food web biomagnification identify a much smaller range of chemicals to be bioaccumulative in the sense that the BCF exceeds the criterion value of 5000. For example, the BCF-QSAR predicts chemicals with a log K_{OW} range between approximately 4.5 and 8 to exhibit a BCF greater than 5000. The regression model BCFWIN estimates chemicals with a log K_{OW} between approximately 5.8 and 8 to have the potential to exhibit BCFs exceeding 5000. The large discrepancy between BAF and BCF data and their relationship with K_{OW}, especially for chemicals with a log K_{OW} exceeding 4.0, implies that BCF based QSARs, models and empirical data should preferably not be used to categorize the bioaccumulation potential of organic chemicals in aquatic systems. A useful application of BCF data is in the measurement of metabolic transformation rates. If metabolic transformation rates can be reliably determined, these rates can be used to assess their potential to cause trophic dilution in the food web using the BAF model. We believe that in the absence of good quality empirical BAF data the BAF-QSAR presented in this study is the preferred tool for the assessment of the bioaccumulation potential of organic chemicals in aquatic food webs. It is based on current mechanistic understanding of the bioaccumulation process and is consistent with currently available empirical BAF data. The BAF-QSAR produces realistic estimates of the BAF in higher trophic fish species in Canadian waters for chemicals that are not readily metabolized. For chemicals that are metabolized, it can be used to assess the rate of metabolic transformation that is required to cause trophic dilution. For example, a chemical with a log K_{OW} of 7 requires a rate of metabolic transformation greater than approximately 0.09 d^{-1} to produce a BAF for the parent compound of less than 5000 in upper trophic level fish species. If this rate can be confirmed in laboratory bioconcentration tests with fish and benthic invertebrates, there is reasonable evidence to assume that the substance will not exhibit BAFs greater than 5000 in aquatic food webs.

While the BAF-QSAR can be applied to many organic substances caution is required when it is applied to charged or ionic compounds and surface-active chemicals. For chemical substances that exhibit a considerable degree of dissociation, there is currently a lack of information regarding the uptake and bioaccumulation via the respiratory surface or the diet of aquatic organisms. Also, there is a lack of reliable K_{OW} values that could be used. Another key limitation of the BAF-QSAR is that it only applies to bioaccumulation in aquatic food webs. There is empirical and theoretical evidence indicating that certain chemicals which do not biomagnify in aquatic food webs have the potential to biomagnify in terrestrial food webs and that the octanol-air partition coefficient (K_{OA}) should be included in QSARs for assessing the bioaccumulation behavior of organic chemicals in terrestrial food webs [36, 37].

A second application of the BAF-QSAR is in the derivation of water quality guidelines (WQG). In essence, the BAF represents the relationship between the concentration in the water and that in the organism of a higher trophic level fish species. If critical body residues (CBR) are available from toxicological tests, the water quality guideline can be derived as the CBR/BAF multiplied by an uncertainty factor. This methodology is advantageous over methods based on statistical treatments of LC_{50}s because (as Figure 2 illustrates) the relationship between the internal concentration in the organism and the water in the field are in many cases much greater than those found in laboratory tests [38]. Water quality guidelines that recognize food web bioaccumulation are more likely to provide an appropriate level of ecosystem health protection than water quality guidelines that ignore food web bioaccumulation.

A third application is in the development of Total Maximum Daily Loadings (TMDLs) for impacted systems. The objective of the development of TMDLs is to assess whole ecosystem loadings that meet certain environmental quality criteria such as the safe consumption of fish and sport fish. The methodology for the derivation of the TMDL typically involves the development of a mass balance model relating the loading to water and sediment concentrations and a food web model to relate the water and sediment concentrations to concentrations in fish and other aquatic organisms. In absence of resources or data to characterize the food web in aquatic systems, the BAF-QSAR can be a reasonable substitute for a food web model. If necessary, the input parameters for the QSAR can be adjusted to better reflect local conditions.

5 Conclusion

In summary, the generic BAF-QSAR model described here provides a method to assess the potential of organic chemical substances to bioaccumulate in a hazard-based intensive property approach. The model requires very few input parameters and is presented as a simple, single equation that is based on the current underlying theories and mechanisms of bioaccumulation in aquatic organisms and is verified with a large set of empirical data. Furthermore, this tool provides reasonable confidence by which chemicals that are not considered to be bioaccumulative hazards in the environment can avoid further scrutiny while those that are can be more closely investigated in subsequent evaluations. Moreover, this approach provides an existing framework that can be modified by contributing empirical metabolic and bioaccumulation data as it becomes available while meeting the time constraints imposed by legislation in an effective and affordable, yet conservative manner.

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