Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/etap

Investigation on the relationship between bioconcentration factor and distribution coefficient based on class-based compounds: The factors that affect bioconcentration

*Yu Wang, Yang Wen, Jin J. Li, Jia He, Wei C. Qin, Li M. Su, Yuan H. Zhao**

State Environmental Protection Key Laboratory of Wetland Ecology and Vegetation Restoration, School of Environment, Northeast Normal University, Changchun, Jilin 130117, PR China

ARTICLE INFO

Article history:
Received 6 January 2014
Received in revised form 1 July 2014
Accepted 3 July 2014
Available online 11 July 2014

Keywords:
Bioconcentration
Nonlinear relationship
Influencing factor
Bioconcentration mechanism
Metabolism
Bioavailability

ABSTRACT

Bioconcentration factor (BCF) is one of the most important parameters in the assessment of the potential hazard of new compounds in aquatic ecosystems. However, the factors that influence the estimation of BCFs for a large variety of chemicals have not been systemically investigated in the literature. In this paper, a large BCF data set containing 1088 nonionic and ionic organic compounds was used to study the relationship between BCF and molecular descriptors and influencing factors. Step-by-step analysis on the class-based compounds showed that nonlinear Gaussian and Sigmoid equations could well describe relationships between log BCF and distribution coefficient for the compounds over a wide range of structures and chloro or/and bromo substituted aromatics, respectively. The quality of fit from the nonlinear models is better than the BCFBAF method from the Epi Suite program for the class-based compounds. Systemic prediction deviations have been observed for some types of compounds. The reasons for systemic deviations for these compounds can be attributed to the difference in bioconcentration mechanism for hydrophilic compounds, transformation for hydroxyphenols and three-membered rings, physical barrier for long chain and large polycyclic compounds, difference in determining methods of BCF (kinetic and steady-state), bioavailability for highly hydrophobic compounds and accuracy of BCF measurements for compounds with extremely high or low BCFs. These factors are important and should be considered in any reliable bioconcentration prediction.

1. Introduction

Bioconcentration is widely applied as a criterion to define the accumulative tendency of chemicals in an aquatic environment. It is the result of the uptake, distribution and elimination of water-borne chemicals by aquatic animals through nondietary routes (Van der Oost et al., 2003; Arnot and Gobas, 2006; Papa et al., 2007). The bioconcentration factor (BCF) is defined as the ratio of the chemical concentration in an organism to the concentration in water at steady-state (Mackay and Fraser, 2000; Schüürmann et al., 2007). Fish are

* *Corresponding author*. Tel.: +86 431 89165610; fax: +86 431 89165606.
E-mail address: zhaoyh@nenu.edu.cn (Y.H. Zhao).
http://dx.doi.org/10.1016/j.etap.2014.07.003
1382-6689/

the principal target organisms of BCF assessment due to their relevance as food for many species including humans. Since, however, experimental determination of BCF is expensive and time-consuming, the use of estimation methods able to correlate physical or structural properties of chemicals with the BCF has a crucial role in supplying the missing data (Papa et al., 2007; Nichols et al., 2009).

There have been numerous attempts to predict BCF values by using quantitative structure–activity relationships (QSARs) (Pavan et al., 2006, 2008; Schüürmann et al., 2007; Fernández et al., 2012). The most simple and common method for estimating bioconcentration potential consists of establishing correlations between the log BCF and the hydrophobicity ($\log K_{OW}$) of organic chemicals, where K_{OW} is the octanol/water partition coefficient. The majority of these relationships were obtained from linear regression models between log BCF and $\log K_{OW}$ (Pavan et al., 2006, 2008). There is a general agreement that the linear correlation gives a fair approximation of the BCF for nonionic and nonmetabolized substances with $\log K_{OW}$ in the range of 1–6, but the relationship breaks down for highly hydrophobic chemicals with $\log K_{OW}$ in the range of 6–8 (Meylan et al., 1999; Arnot and Gobas, 2006; Pavan et al., 2006). To develop an improved model based on a large data set, Meylan et al. (1999) proposed a model for 694 chemicals grouped as either nonionic or ionic compounds, and studied separately their relationships of log BCF with $\log K_{OW}$. Because of the deviation from rectilinearity, different models were developed for different $\log K_{OW}$ ranges. For the nonionic compounds, linear equations were derived for the compounds with $1 < \log K_{OW} < 7$ ($\log BCF = 0.77 \log K_{OW} - 0.70 + \Sigma F_i$) and $\log K_{OW} > 7$ ($\log BCF = -1.37 \log K_{OW} + 14.4 + \Sigma F_i$), respectively. A constant log BCF value of 0.5 was assigned for the chemicals with $\log K_{OW} < 1$ or >10.5. In order to improve the accuracy of BCF predictions, a set of correction factors (F_i) and rules were introduced. On average, the goodness of fit of the derived equations of Meylan et al. (1999) was within 0.5 log units for the compounds in the training set.

A single nonlinear empirical model between log BCF and $\log K_{OW}$ derived by Dimitrov et al. (2002a) from 443 chemicals successfully represented the complex relationship between hydrophobicity and bioconcentration. Analysis of the fitted BCF data for 443 chemicals revealed that hydrophobicity could be used to explain more than 70% of the variation of the bioconcentration potential. Despite the relatively good results, a significant scatter was obtained around the maximum of the log BCF–$\log K_{OW}$ curve indicating that other factors were important and should be considered for reliable bioconcentration prediction. In addition to the $\log K_{OW}$-based models, other traditional approaches were based on experimentally derived and theoretical molecular descriptors for the prediction of BCFs in fish. These descriptors included molecular connectivity indices, solubility, soil adsorption coefficient, fragment constants, quantum chemical descriptors and linear solvation energy relationship (LSER) descriptors (Lu et al., 2000; Fatemi et al., 2003; Gramatica and Papa, 2003; Papa et al., 2007; Toropov et al., 2009). Reviews of quantitative structure–activity relationship (QSAR) models for bioconcentration prediction have been given by Pavan et al. (2006, 2008) and Schüürmann et al. (2007), respectively. Models of bioconcentration based on physicochemical parameters other than hydrophobicity had similar predictive power, but did not provide a method for estimating bioconcentration in other species, body sizes and under different environmental conditions. The quality of fit of models derived from nonlinear log BCF–$\log K_{OW}$ relationship and theoretical molecular descriptors were approximately the same as that obtained by Meylan et al. (1999) for nonionic compounds (Lu et al., 2000; Dimitrov et al., 2002a).

It is generally accepted that organic chemical hydrophobicity is the principal driving force of bioconcentration. The hydrophobicity model considers bioconcentration as compound partitioning from water into the lipid compartment of the organism (Schüürmann et al., 2007). However, the relationship between $\log K_{OW}$ and log BCF appears to be relatively complex (Wen et al., 2012). A number of factors, such as bioavailability, molecular size, methods of BCF determination, dissolved organic matter, metabolism, interspecies variation, ionization of ionizable compounds and environmental conditions, can contribute to the variability of BCF. Experimental measurements above the water solubility result in too low BCF values if these are based on nominal concentrations (Schüürmann et al., 2007). A bioavailable fraction is often equated to the true dissolved fraction. Low solubility for chemicals with $\log K_{OW} > 5$ can cause the dissolved fraction to be reduced (Mackay and Fraser, 2000). Many studies have shown decreases in bioconcentration in the presence of dissolved organic matter (Haitzer et al., 1998). For highly hydrophobic compounds, sorption to dissolved or particulate organic matter may compete with bioconcentration to a significant degree, which in turn depends on the amount of sorbent matrices present in aqueous solution (OECD guideline, 1996; Schüürmann et al., 2007). Molecular size is associated with bioavailability. Three-dimensional molecular structure and conformational flexibility were accounted for when assessing the contribution of the size effect by making use of the maximum diameter of the molecule (Dimitrov et al., 2002b; Sakuratani et al., 2008). One of the most significant factors defining the bioavailability of chemicals investigated is ionization. The bioavailability decreases with increase in the ionization of ionic compounds, resulting in a significant decrease of BCF (Meylan et al., 1999; Escher and Hermens, 2004; Erickson et al., 2006; Pavan et al., 2006; Arnot et al., 2008; Armitage et al., 2013). Metabolism is another important factor in addition to respiratory (and diffusive) elimination, and typically reduces the BCF of metabolically active compounds (Mackay and Fraser, 2000; Schüürmann et al., 2007).

Currently available BCF models are useful for screening a large number of chemicals, but they have some limitations and the physical or chemical interpretations of the theoretical descriptors are usually not straightforward (Dimitrov et al., 2002a; Schüürmann et al., 2007). In order to improve the accuracy of BCF predictions, a set of correction factors and rules had to be introduced into these models (Meylan et al., 1999; Lu et al., 2000). It is obvious that more studies are required in order to develop a satisfactory model and investigate the influencing factors for estimating the BCFs of a wide range of compounds. In the present paper, a BCF data set in fish for 1088 compounds reported in literature and database was investigated. The aims of the present work are to develop class-based models between log BCF and molecular descriptors basing on class-by-class analysis. Basing on