Towards an improved understanding of processes controlling absorption efficiency and biomagnification of organic chemicals by fish

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HIGHLIGHTS

- We developed a fish bioaccumulation model to describe dietary uptake of chemicals.
- Including micelle-mediated diffusion in the model does not improve its performance.
- The model indicates that first-pass biotransformation reduces bioavailability of some PAHs.

ABSTRACT

Dietary exposure is considered the dominant pathway for fish exposed to persistent, hydrophobic chemicals in the environment. Here we present a dynamic, fugacity-based three-compartment bioaccumulation model that describes the fish body as one compartment and the gastrointestinal tract (GIT) as two compartments. The model simulates uptake from the GIT by passive diffusion and micelle-mediated diffusion, and chemical degradation in the fish and the GIT compartments. We applied the model to a consistent measured dietary uptake and depuration dataset for rainbow trout (n = 215) that is comprised of chlorinated benzenes, biphenyls, dioxins, diphenyl ethers, and polycyclic aromatic hydrocarbons (PAHs). Model performance relative to the measured data is statistically similar regardless of whether micelle-mediated diffusion is included; however, there are considerable uncertainties in modeling this process. When degradation in the GIT is assumed to be negligible, modeled chemical elimination rates are similar to measured rates; however, predicted concentrations of the PAHs are consistently higher than measurements by up to a factor of 20. Introducing a kinetic limit on chemical transport from the fish compartment to the GIT and increasing the rate constant for degradation of PAHs in tissues of the liver and/or GIT are required to achieve good agreement between the modelled and measured concentrations for PAHs. Our results indicate that the apparent low absorption efficiency of PAHs relative to the chemicals with similar hydrophobicity is attributable to biotransformation in the liver and/or the GIT. Our results provide process-level insights about controls on the extent of bioaccumulation of chemicals.

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1. Introduction

Bioaccumulation is the net result of competing rates of chemical uptake and elimination in an organism and bioaccumulation includes all possible routes of chemical exposure, such as transport across the respiratory surface, dermal absorption, and dietary absorption (Gobas and Morrison, 2000). Dietary absorption from the gastrointestinal tract (GIT) is recognized to be the dominant uptake pathway for persistent, hydrophobic chemicals by fish in the environment (Gobas and Morrison, 2000). The dietary absorption efficiency ($E_D$) quantifies the fraction of the ingested chemical that is transferred from the lumen of the GIT into the fish body. Niimi and colleagues used generally consistent methods to measure gross $E_D$, body burdens and depuration in a series of laboratory studies using rainbow trout (Oncorhynchus mykiss) for various organic chemicals (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986). We use the term gross $E_D$ to refer to the fraction of ingested chemical that is transferred from the GIT into the fish body. This definition of gross $E_D$ is used in many process-based models (Xiao et al., 2013). In contrast, net $E_D$ is the apparent absorption efficiency when chemical flow between the GIT and the fish body reaches steady state. Notably, the gross $E_D$ reported by Niimi et al. is low for certain polycyclic aromatic hydrocarbons (PAHs) (often less than 1%), and markedly lower than for other chemicals with comparable hydrophobicity (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986).

Many mass balance models have been developed and applied to quantify chemical flux in (by dietary and gill uptake) and out (by gill elimination, growth dilution, biotransformation, and fecal egestion) of fish (Gobas et al., 1988, 1993a; Barber et al., 1991; Arnot and Gobas, 2004; Kelly et al., 2004; Nichols et al., 2004; Bhavsar et al., 2008). For example, Clark et al. developed a one compartment, fugacity-based steady-state fish bioaccumulation model for chemical exposures from food using transport and transformation resistances (Clark et al., 1990). Barber et al. developed a model to describe uptake of organic chemicals from water and contaminated food, and they applied it to describe the bioaccumulation of polychlorinated biphenyls (PCBs) for different fish species (Barber et al., 1991). Gobas developed a one-compartment steady-state fish bioaccumulation model in rate constant format that agreed well with chemical concentrations measured in the field (Gobas, 1993). Nichols et al. developed a dynamic multi-compartment physiologically-based pharmacokinetic (PBPK) model for fish (Nichols et al., 2004). Some fish bioaccumulation models explicitly model micelle-mediated chemical transport in the GIT (Drouillard and Norstrom, 2000; Drouillard et al., 2012) and some do not (Gobas et al., 1993a,b; Arnot and Gobas, 2004).

Here, we apply a fugacity-based multi-compartment fish bioaccumulation model to explore hypotheses about the roles of micelle-mediated uptake and chemical degradation processes in fish, especially for PAHs. The model is comprised of a single compartment for the fish body and two compartments for the GIT. We have parameterized the model to evaluate the role of micelle-mediated uptake and biotransformation of chemicals in fish by analyzing the measurements of chemical uptake and clearance from laboratory studies using rainbow trout (O. mykiss) that were conducted by Niimi and colleagues (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986). Their datasets include chlorinated benzenes and biphenyls, dioxins, chlorinated diphenyl ethers, and PAHs. The Niimi et al. studies of chemical uptake by rainbow trout provide a consistent set of measurements and cover a wide range of structural diversity, hydrophobicity, and potential for degradability in fish (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986). Our goal in this study is to use a mechanistic model to formalize two quantifiable hypotheses about processes that control dietary absorption of chemicals by fish (MacLeod et al., 2010). The two hypotheses are (1) micelle-mediated diffusion does not play a significant role in dietary uptake of certain organic chemicals in trout, and (2) chemical degradation in the liver and/or the GIT reduces dietary uptake of PAHs. We aim to evaluate the hypotheses against the experimental data produced by Niimi and colleagues.

2. Methods

2.1. Model description

The model describes chemical uptake and elimination from three compartments: fish (F), upper part of the GIT (GIT1), and lower part of the GIT (GIT2) (Fig. 1). The model is based on the Arnot and Gobas mass balance fish bioaccumulation model, which treats the fish as one compartment (Arnot and Gobas, 2004). Here, the Arnot and Gobas model is re-formulated using fugacity-based process equations rather than rate constants, the GIT is added as two compartments as described below, and a numerical solution to the dynamic (non-steady-state) mass balance equations is applied.

Fugacity ($f$, in Pa) reflects an equilibrium criterion and thus provides clear insight into the thermodynamic gradients driving chemical processes, especially passive diffusion. Chemicals diffuse from compartments with high fugacity to compartments with low fugacity. The fugacity capacity ($Z$, in mol/Pa m$^3$) of a compartment is a measure of storage capacity for a chemical, and is particularly useful for describing multimedia phases with variable compositions (e.g., digesta in the digestive tract). The $Z$ value depends on the nature of the chemical and the properties of the multimedia phase that contains it.

The division of the GIT and the parameterization used in our model is based on the elegant experiments conducted by Gobas and co-workers using PCBs that showed the fugacity capacity of digesta in the upper part of the GIT of fish is approximately four times higher than that in the lower part of the GIT (Gobas et al., 1999). The physicochemical properties of a chemical remain unchanged through the GIT. However, lipids are mainly absorbed in the upper part of the GIT. Lipids are a major component of the fugacity capacity of the digesta, therefore digesta in the lower part of the GIT has lower fugacity capacity, which in turn causes a stronger thermodynamic gradient for chemical transport from the GIT into the fish (Clark et al., 1990; Gobas et al., 1999). The transport parameter ($D$, in mol/Pa h) is the fugacity analogue to a first-order rate constant. Slow processes have small $D$-values, and vice versa (Mackay, 2001). Studies suggest micelle-mediated diffusion plays a role in the mass transport of chemical from the GIT into organisms, and this process can be characterized as a $D$-value (Drouillard and Norstrom, 2000; Kelly et al., 2004; Drouillard et al., 2012).

Fluxes of chemical uptake and elimination in fish ($N$, in mol/h) following dietary exposure are expressed as a product $df$ in our model (Fig. 1). The volume, temperature, and composition of each compartment in the model are assumed to be constant over time, so that for the fish (F), upper GIT (GIT1), and lower GIT (GIT2) compartments, the differential mass balance equations are:

$$\frac{df}{dt} = D_{GIT} \times f_{GIT1} + D_{GIT2} \times f_{GIT2} - (D_F + D_M + D_X + D_{GC1} + D_{GC2}) \times f_F$$

change of fugacity in GIT1:
change of fugacity in F:

\[ V \times Z \times \frac{df_f}{dt} = D_{GIF} \times f_{G1} + D_{GIF} \times f_{G1F} = (D_{AIF} + D_{AIF} + D_{G1F} + D_{G1F}) \times f_f \]

create of fugacity in GIT1:

\[ V \times Z \times \frac{df_{G1}}{dt} = N_{inomerring} + D_{G1F} \times f_f - (D_{G1F} + D_{G1G2} + D_{G1M}) \times f_{G1} \]

create of fugacity in GIT2:

\[ V \times Z \times \frac{df_{G2}}{dt} = D_{G2F} \times f_{G1} + D_{G2F} \times f_f - (D_{G2F} + D_o + D_{G2M}) \times f_{G2} \]

where \( V \) is volume; \( N_{inomerring} \) is the chemical flux in the feed through dietary uptake; \( D_{G1F} \) and \( D_{G2F} \) denote the chemical transport from the GIT1 and GIT2 compartments to the fish compartment, and \( D_{G1G2} \) and \( D_{G2G1} \) denote transport from the fish to GIT1 and 2, respectively. Uptake of chemical from GIT1 and GIT2 to fish (\( D_{G1F} \) and \( D_{G2F} \)) is determined by parallel molecular diffusion of chemical in an unstirred water layer and micelle-mediated diffusion on the GIT side, and diffusion in octanol-equivalent lipid layer on the fish-side (Fig. S1 in the supplementary material). The reverse process of depuration from fish to GIT1 and GIT2 (\( D_{G1F} \) and \( D_{G2F} \)) is determined by parallel molecular diffusion of chemical in an unstirred water layer and micelle-mediated diffusion on the GIT side, and diffusion in octanol-equivalent lipid layer on the fish-side, and by diffusion in an unstirred water layer on the GIT1 and GIT2 side, because micelles are assumed to be absorbed at the gut wall (Drouillard and Norstrom, 2000; Drouillard et al., 2012). Therefore in model scenarios where micelle-mediated diffusion is included \( D_{G1F} > D_{G1G2} \) and \( D_{G2F} > D_{G2G1} \) (Table S1 in the supplementary material). As an alternative, we also examine the hypothesis that there is no micelle-mediated diffusion, and in these model scenarios \( D_{G1F} = D_{G1G2} \) and \( D_{G2F} = D_{G2G1} \). \( D_{G1F} \) describes chemical transport from GIT1 to GIT2 by advection of the gut contents. \( D_{G1A} \) and \( D_{G2A} \) are the chemical transport parameters describing ventilation, \textit{in-vivo} biotransformation after absorption from the GIT, and fecal egestion respectively. In addition, the decrease of concentration of chemicals in fish due to somatic growth during the depuration period (>48 days in the Niimi studies (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986)) was modeled using the study-specific empirical first-order fish growth rate data as \( D_{G1M} \) and \( D_{G2M} \), which describe transformation in tissues of the upper and lower GIT and/or liver, respectively, are assumed to be zero for all chemicals except in scenarios where we examine the hypothesis that PAHs are transformed in the GIT and/or liver (Dufier et al., 1998; Kleinow et al., 1998; Butt et al., 2010; Diggins et al., 2011).

In model scenarios that include biotransformation of PAHs in the GIT and/or the liver, a first-order rate constant for chemical transformation, \( k_{CM} \), was fitted using least-squares optimization so that discrepancies between the log-transformed model and empirical data are minimized. The relationships between \( k_{CM} \) and \( D_{G1M} \) and \( D_{G2M} \) are:

\[ D_{G1M} = k_{CM} \times V \times Z \times f_{G1} \]

\[ D_{G2M} = k_{CM} \times V \times Z \times f_{G2} \]

The equations to calculate all Z and D-values are tabulated and described in Table S1 in the supplementary material. In addition, octachlorodibenzo-p-dioxin (OCDD) data from Niimi and Oliver (1986) were used as an example (Table S2). The model includes 29 independent input parameters, and is programmed in Microsoft Excel using Visual Basic for Applications code. To describe the dynamic conditions of the laboratory dietary tests, the model is coded for dynamic simulations and we solved the model equations using Eulerian integration with a time step of 0.01 h.

2.2. Empirical and modeled data for model evaluation

Our dynamic multi-compartment model has many similarities to the model developed by Nichols et al. that was calibrated against feeding experiments for rainbow trout using \( ^{14}C \)-labeled PCB52 (Nichols et al., 2004). When parameterized to describe conditions in the Nichols et al. study, but without further calibration of kinetic parameters, our model qualitatively captures the time-course of measured concentrations of PCB52 in fish and the GIT and overestimates concentrations in fish by approximately a factor of 2 (Fig. S2 in the supplementary material).

We sought to evaluate our hypotheses about the potential roles of micelle-mediated transport and biotransformation of PAHs by modeling four Niimi studies that were conducted under generally consistent experimental conditions (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986). In all four of the Niimi studies, rainbow trout (O. mykiss) were exposed to chemical using a single gavage dose. The trout were anesthetized and then exposed by directly inserting a gelatin capsule containing the test chemicals into the stomach with a glass tube. The exposure method minimizes inter-fish variability in the administered dose of chemical. After exposure, the trout were fed commercial dry diet at 0.5–1% of body weight every day. The body weights of the trout at the time of exposure in the four studies were 300 (Niimi and Oliver, 1988), 325 (Niimi, 1986), 700 (Niimi and Palazzo, 1986), 910 (Dulfer et al., 1998; Kleinow et al., 1998; Butt et al., 2010; Diggins et al., 2011).
and 970 g (Niimi and Oliver, 1986), respectively. The depuration period in the studies ranged from 48 to 85 days (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986). The temperatures of the water in the fish tanks were maintained at 10 (Niimi and Oliver, 1986), 11 (Niimi and Palazzo, 1986), and 13 °C (Niimi, 1986; Niimi and Oliver, 1988), respectively. The measured concentrations were reported as mean ± standard deviation of six fish at each sample interval. Taken together, the Niimi studies report 215 individual measurements of chemical concentration in fish for 46 chemicals (seventeen halogenated benzenes and biphenyls, seven dioxins, sixteen diphényl ethers, and six PAHs), covering a wide range of structural diversity, hydrophobicity, and degradability in the fish compartment (Table S3 in the supplementary material) (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986).

For all the chemicals in this study, k_{SB} values for the fish compartment are estimated from the Niimi et al., dietary exposure data (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986), as documented in the Arnot et al. (2008) database. In the model, the chemical flux entering the GIT1 compartment through feeding is calculated as the product of feeding rate and chemical concentration in the feed. We parameterized the model with the same feeding rates used in the Niimi studies, and adjusted the incoming chemical flux in the first hour of our model scenarios to deliver the same amount of chemical to the GIT1 compartment as was reported in the experiments.

Average absolute model bias (AMB), coefficient of determination (R^2) and root mean-square error (RMSE) were used to assess model performance for the dataset (Arnot and Gobas, 2004; Armitage et al., 2013).

### 3. Results

The whole-body concentrations of the test chemicals from the Niimi et al. studies were compared to modeled concentrations in the fish compartment to evaluate model performance under different scenarios designed to test our two hypotheses (Niimi, 1986; Niimi and Oliver, 1986, 1988; Niimi and Palazzo, 1986). Fig. 2 shows modeled concentrations of four selected chemicals in a scenario that models the rate of biotransformation in the fish compartment as f_DGM where D_M = k_M/M_2, no degradation in the GIT compartments (i.e., k_{GM} = 0), and including micelle transport. The results selected for Fig. 2 are representative of results under this scenario for each of the four Niimi et al. studies. Fig. 2a compares measured and modeled concentrations for OCDD; Fig. 2b decachloro-diphenylether (decachloro-DPE); Fig. 2c 1,3,5-tribromobenzene; and Fig. 2d fluorene. The model is clearly biased for the PAH fluorene where modeled concentrations range from 5.1 to 9.4 times higher than the measured concentrations.

#### 3.1. Model scenarios to analyze the role of micelle transport

We compared two model scenarios to evaluate the role of micelle transport. The first scenario includes biotransformation in the fish compartment (k_{SB}), no degradation in the GIT compartments (k_{GM} = 0), and no micelle transport (Fig. 3a). The second scenario includes biotransformation in the fish compartment (k_{SB}) and no degradation in the GIT compartments (k_{GM} = 0), but with micelle transport (Fig. 3b and Table S4).

Ignoring the data for the PAHs (coded in blue\(^1\) in Fig. 3) which are discussed in detail below, the model scenario without micelle transport explains 75% of the variability in measured data for the test chemicals (Fig. 3a, R^2 = 0.75, RMSE = 2.37 \times 10^{-4} \text{ mol/m}^3).

\(^1\) For interpretation of color in Fig. 3, the reader is referred to the web version of this article.

AMB = 0.32, and n = 189). The model scenario with micelle transport explains 68% of the variability in the same set of measured data, and has similar error and bias (Fig. 3b, R^2 = 0.68, RMSE = 2.43 \times 10^{-4} \text{ mol/m}^3, AMB = 0.32, and n = 189). The statistically similar model performance in these two scenarios demonstrates that including micelle-mediated diffusion in the model does not significantly improve its description of the bioaccumulation of these chemicals as observed in the Niimi experiments for trout exposed by gavage.

The parameterization of D_{micelle} in this study is based on the assumption that the micelle flow rate perpendicular to the intestinal wall is the same as that of lipid moving through the GIT. Our assumption implies that the gut contents are randomly mixed at small spatial and temporal scales. In order to evaluate our D_{micelle} parameterization, we tested the model performance using two alternative values for D_{micelle}; one from a mechanistic calculation for the human GIT (Cahill et al., 2003) and an empirical value derived by Drouillard et al. in a study of Japanese koi (Drouillard et al., 2012). We investigated the uptake and depuration kinetics of hydrophobic OCDD (logK_{OW} = 8.20) and less hydrophobic 1,3,5-tribromobenzene (logK_{OW} = 4.51). Different parameterizations of D_{micelle} affect the modeled concentration in fish for the more hydrophobic OCDD but not for the less hydrophobic 1,3,5-tribromobenzene (Fig. S3 in the supplementary material). For OCDD, the parameterization of D_{micelle} using the mechanistic calculation for the human GIT significantly overestimates OCDD concentrations observed in the Niimi study. The modeled OCDD concentrations without D_{micelle} and with D_{micelle} parameterized using either lipid equivalent flow rate in this study or empirically determined values from Drouillard et al. are close to the reported concentrations (Drouillard et al., 2012). The model simulation assuming no micelle-mediated transport is also in reasonable agreement with the measured data. Mass transport parameters describing chemical flux from the GIT compartment to fish and fish to the GIT compartment for OCDD and 1,3,5-tribromobenzene are tabulated in Table S5.

In addition, we examined assumptions about feeding rates (C_{food}) and gut volumes (V_{GIT}) in the model that result in uncertainty in the advective residence times of food in the GIT, i.e. t_{food} = V_{GIT}/C_{food}. We model the mass transport parameter for micelle-mediated diffusion as being proportional to the daily feeding rate (Table S1), which is consistent with a high feeding rate inducing a high degree of formation of bile salt and micelles (Holfmann, 1999; Bhown and Stroeve, 2007), thus higher transport of micelles to the intestinal wall. The parameterization of D_{micelle} in this study depends on hydrophobicity of the chemical in the GIT and reflects intestinal physiology since micelle diffusion is higher at higher feeding rates. Reducing the food flow rate through the GIT increases the residence time of the chemical in the GIT, which increases the absorption of chemicals from the GIT. Similarly, decreasing the residence time decreases the absorption rate. To illustrate the sensitivity of the model to t_{food}, we investigated the uptake and depuration kinetics of OCDD using four different daily feeding rates (i.e., 0.1%, 0.5%, 1%, and 5% of the fish body weight). The corresponding t_{food} values are 348.9, 69.8, 34.8, and 6.9 h, respectively. The nominal feeding rate reported in the test is 1% body weight per day (Niimi and Oliver, 1986). The modeled concentrations corresponding with the feeding rates of 0.5% and 1% of body weight are generally in good agreement with reported values (Fig. S4 in the supplementary material). Fig. S4 also illustrates that without micelle-mediated diffusion, decreasing the food flow rate through the GIT (thus increasing the chemical residence time in the GIT) increases absorption of the chemical. Interestingly, with micelle-mediated diffusion, decreasing the food flow rate through the GIT results in absorption occurring sooner than the simulations without micelle-mediated transport, thus increasing the time lag for the depuration phase.
Concentrations of PAHs are not well described in either of our modeling scenarios that consider only biotransformation in the fish compartment (blue data points in Fig. 3a and b). We compared three scenarios to test the hypothesis that degradation in the gut and/or the liver could account for the poor model performance for PAHs. The three scenarios are, (1) only degradation in fish compartment, (2) degradation in both fish and GIT compartments, and (3) degradation in the liver/GIT modeled by introducing a kinetic limit on transport from the fish compartment to the GIT compartments. All the quantitative model results for the PAHs are detailed in the supplementary material. In summary, the model does not fit the data for the PAHs in a satisfactory way when only biotransformation in the fish compartment is considered (Figs. S5 and S6 black dotted lines). Model fits to the data could not be significantly improved by adjusting the $k_b$ in the fish body. Although the predicted and measured rates of chemical elimination (i.e., slopes) are similar, the predicted concentrations are greater than the measured concentrations indicating an initial loss of chemical into the organism that is not captured by the model. Inclusion of degradation in the GIT compartments leads to a poor compromise between fitting the slope and intercept of the depuration data for the PAHs (Figs. S5 and S6 black solid lines). A plausible explanation for the poor fits for PAHs is that there is first-pass biotransformation of the PAHs in the liver and/or the lumen of the GIT and/or at the gut wall that significantly reduces the dose of PAH that enters systemic circulation in the fish. For PAHs that enter systemic circulation, the empirical data imply that all PAHs are depurated from the fish with approximately the same whole-body removal rate constant. That observation would be consistent with mobilization from storage lipids in the fish’s body and transport to the liver being the rate-limiting process, followed by rapid degradation in the liver. Another possible explanation for the similar removal rates is that elimination is rate-limited in all four cases by the rate of blood flow to the liver. Describing these processes in a mechanistic manner would require a more resolved model that includes the liver as a discrete compartment and flow rate information for internal compartments. However, our model scenario where we include a kinetic limit on transport of PAHs from the fish compartment to the GIT provides satisfactory fits to the data without explicitly modeling the liver as a discrete compartment (Figs. S5 and S6 red solid lines).

4. Discussion

The dynamic multi-compartment bioaccumulation model that we describe here has a focus on modeling the kinetics of dietary chemical absorption by fish. Agreement between the model and measurements for the PAHs was improved considerably by modifying the model to include a kinetic limit on transport from the body of the fish to the GIT and fitting rapid rates of degradation assumed to occur in the liver/GIT. This highlights the importance of degradation of PAHs in the liver/GIT as a process that mitigates uptake of PAHs by fish.

Our model and the model scenarios we describe here provide valuable guidance for future research to reduce uncertainties in process-oriented descriptions of biomagnification of organic chemicals. In its current form, our model only fits the empirical data for PAHs when we introduce a kinetic limit on transport from the fish compartment to the GIT, and in this scenario the model cannot distinguish between degradation of chemicals in the GIT and degradation in the liver. It seems likely that degradation in the liver is the important controlling process, but enzymatic and microbial transformation of PAHs in the GIT is also possible (Scheline, 1973; Vanveld et al., 1988; Kleinow et al., 1998; Arnot et al., 2008; Sousa et al., 2008; Cai et al., 2010). A model that considers the liver as a separate compartment would be appropriate to model the PAHs in more detail (Nichols et al., 2004, 2007). Also for the non-PAH chemicals, degradation in the liver/GIT analogous to that for PAHs may also occur. Fig. 3 indicates that the model fits to empirical data for the dioxins and furans could be improved.

In the present study, we used a dynamic multi-compartment fish model to examine the hypotheses that micelle-mediated diffusion...
plays a role in chemical uptake processes, and that degradation in the liver and/or the GIT reduces uptake of PAHs after ingestion. We found that including micelle-mediated transport did not have a strong effect on model performance, root mean squared error or bias relative to measured concentrations of chemicals in fish. However, the role of micelle-mediated transport may be more significant than our scenarios imply due to uncertainty in the model assumptions. Our modeling also provides preliminary estimates of the time-scale for biotransformation of PAHs in liver or gut tissues and can be used to refine the model to include other compartments in the fish's body, application to other empirical PAH dietary absorption datasets, and comparison to other empirical PAH uptake studies in fish. Further refinements to the model to include other compartments in the fish's body, application to other empirical PAH dietary absorption datasets, and comparison to other empirical studies are needed to corroborate and possibly improve the rate constants estimated in this study. For example, a model that considers the liver as a separate compartment and that includes an explicit description of blood flow through the fish's body would be appropriate to model the PAHs in more detail (Nichols et al., 2004, 2007).

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.chemosphere.2015.05.053.

References


