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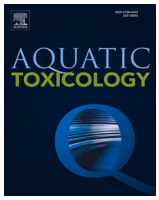

Do DOM quality and origin affect the uptake and accumulation of lipid-soluble contaminants in coastal filter feeders? An experimental simulation of teflubenzuron exposure to blue mussels

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ABSTRACT

The increased export of terrestrial dissolved organic matter (terrDOM) to coastal marine ecosystems may affect local filter feeders and the local food web via the altered uptake of organic material and associated contaminants. To compare terrDOM to marine DOM (marDOM) as contaminant vectors to coastal biota, we exposed blue mussels (*Mytilus* sp.) to the different DOM types in combination with teflubenzuron, a widely applied lipophilic aquaculture medicine targeting salmon lice (*Lepeophtheirus salmonis*). A 16-day exposure of the blue mussels to DOM and teflubenzuron was followed by a depuration phase of 20 days without teflubenzuron. We calculated teflubenzuron adsorption rates and bioaccumulation factors (BAF) using a Bayesian model, expecting teflubenzuron uptake to be greater with terrDOM than marDOM due to the higher prevalence of large amphipathic humic acids in terrDOM. Humic acids have strong absorption properties and are able to envelope lipophilic molecules. Thus, humic acids can function as an efficient contaminant vector when taken up by filter feeders. Although there were varying degrees of overlap, the mussels tended to accumulate higher amounts of teflubenzuron in the DOM treatments than in the seawater control (bioaccumulation factor [BAF] in seawater: median 106 L/kg; 2.5 %–97.5 % percentile: 69–160 L/kg). Contrary to expectations, mussels exposed to marDOM showed a trend toward more bioaccumulation of teflubenzuron than those exposed to terrDOM (BAF marine 144 L/kg; 102–221 L/kg versus BAF terrestrial: 121 L/kg; 82–186 L/kg). The highest teflubenzuron accumulation was observed with the 50:50 mixture of marDOM and terrDOM (BAF mix: 165 L/kg; 117–244 L/kg). The slight difference in DOM-type accumulation rates observed in this experiment—especially the accumulation rate of terrDOM compared to that of the seawater-only treatment type—was not considered environmentally relevant. Further studies are necessary to see if the observed trends transfer to complex environmental systems.

1. Introduction

Ongoing increases in the export of terrestrially derived dissolved organic matter (terrDOM) from land to aquatic systems cause the "browning" of lakes and rivers. Freshwater browning ultimately affects coastal waters, where a corresponding darkening is observed (Creed et al., 2018; Dupont and Aksnes, 2013; Opdal et al., 2019). The browning and subsequent coastal darkening stem from a multitude of issues: anthropogenic land use changes, temperature shifts, terrestrial productivity increases, climate change-related precipitation and runoff, and soil acidity reduction from decreasing acid rain (de Wit et al., 2021; Evans et al., 2005; Finstad et al., 2016; Larsen et al., 2011). Along with the drivers of increased terrDOM export, factors such as coastal eutrophication, suspended particulate matter from land, and increased turbulence from wind pattern changes can further hinder marine light penetration (Capuzzo et al., 2015; Krause-Jensen et al., 2008; McGovern et al., 2020; Wilson and Heath, 2019).

The size of dissolved organic matter (DOM) is usually defined as less than 0.2–0.7 μm (Xu and Guo, 2017). The size classifications of DOM and particulate organic matter (POM), which is the size class above

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DOM, are only operational due to dynamic interchanges via aggregation and dissolution mechanisms. However, the molecular structure and size of the organic matter can have substantial effects on processes such as sedimentation and remineralization and, subsequently, CO_2 production due to respiration by associated organisms (He et al., 2016). Compared to POM, DOM represents a considerably higher fraction of the natural organic matter in the oceans (approximately 22 times higher) and is essential for many biological processes (Hansell et al., 2009; He et al., 2016). DOM is a mixture of various organic breakdown products, with some fractions that are labile and reactive and others that are more refractory. The labile fraction includes organic breakdown products such as carboxylic acids, free amino acids, peptides, proteins, sugars, and nucleic acids. The more refractory fractions contain humic and fulvic acids (Thomas, 1997; Thurman, 1985), which are macromolecules. Humic acids have hydrophobic side chains or segments, and compared to fulvic acids, they contain more total and aromatic carbon. Fulvic acids contain more aliphatic carboxylates (Worsfold et al., 2019). Thus, the chemical properties of humic and fulvic acids differ due to molecular size, configuration, and polarity (Chiou et al., 1986). Compared to marDOM, terrDOM contains a greater quantity of the larger humic acids (Creed et al., 2018). Thus, terrDOM has a different surface charge, different spectral properties, and different binding properties for other compounds, including toxic substances (Chiou et al., 1986; Ravichandran, 2004; Weishaar et al., 2003).

Increasing terrDOM input in the coastal zone can affect interconnected ecosystems via several mechanisms, ultimately impacting food webs. For example, terrDOM can influence factors such as shading and reduced light availability, nutrient patterns, and carbon availability and cycling. This, in turn, can alter the abundance, diversity, and stoichiometry of heterotrophic bacteria and primary producers, and higher trophic levels as well as the structure and function of the food web (Bartels et al., 2016; Creed et al., 2018; Demars et al., 2020; Leroux and Loreau, 2008).

Increases in terrDOM, which has chelating properties for certain metals, can lower metal contaminant concentrations (e.g., Cu and Hg) in the open water column (Arnold et al., 2009; Playle, 1998). However, due to its chemical structure, DOM can also enhance the solubility of some compounds with otherwise low water solubility (Chiou et al., 1986), facilitating the aqueous transport of organic contaminants (Ravichandran et al., 1998). Compared to marDOM, terrDOM more strongly enhances the solubility of certain compounds due to the larger size and more pronounced amphipathic properties (i.e., combined lipophilic and hydrophilic properties) of the humic acids. Indeed, terrDOM may even act like a micelle (pseudo-micelle) and envelope lipophilic substances (Chiou et al., 1986; He et al., 2016; von Wandruszka, 1999). The bioconcentration of contaminants—which reflects their direct partitioning between water and biota—is reduced when the contaminants are bound to organic matter (Akkanen and Kukkonen, 2003; Lu et al., 2018). However, the digestive tract is more permeable than gills or skin to most contaminants and is often a critical uptake route for lipophilic contaminants (Arnot et al., 2010). In pharmacology, humic substances can even serve as drug vectors for orally administered lipophilic drugs (Mirza et al., 2011a, 2011b).

For organisms whose feeding activities expose them to high DOM loads, the extent to which terrDOM acts as a lipophilic contaminant vector is currently unknown. While microbes are dominant consumers or mineralizers of DOM (Creed et al., 2018), other species—especially filter feeders—may take up or feed on DOM with varying levels of efficiency (Ciborowski et al., 1997; De Goeij et al., 2013; He et al., 2016; Kach and Ward, 2008; Rosa et al., 2018). Filter-feeding blue mussels (*Mytilus* spp.) are geographically widespread in coastal zones and are important components of local food webs. They occur naturally in estuarine conditions with fluctuating DOM levels and compositions and can be exposed to high concentrations of terrDOM (Beyer et al., 2017).

In coastal regions, mussels are exposed to contaminants from both land and sea due to terrestrial runoff, river transport, and coastal activities such as aquaculture. But due to their sessile nature, mussels have a limited capacity to escape contaminant exposure or other negative environmental conditions once they are attached to a substrate (Riisgård et al., 2011). Mussel beds have declined over recent decades in many parts of the Atlantic coast as a result of interactions of several anthropogenic factors (Baden et al., 2021). Because mussels are ubiquitous and robust, have the propensity to concentrate contaminants, and have high filtration rates, they are commonly used in biomonitoring (Beyer et al., 2017). Blue mussels can filter approximately 3 L per individual per hour (Famme et al., 1986), and they actively feed on particle sizes down to about 0.5 μm (Kach and Ward, 2008). Similar to other filter feeders, they may also passively uptake even smaller particles through agglomeration mechanisms, electrical attraction, or passive encounters between particles and the filtration apparatus (Flood and Fiala-Medioni, 1981; Riisgård et al., 2011).

Although smaller than typical food particles, DOM (especially its amino acids and sugars) contributes to fulfilling the energy needs of some species of mussels, including the blue mussel (Hawkins and Bayne, 1992 and references therein; Roditi et al., 2000), making it an ideal organism for the present study. In addition, mussels are an essential food for various seabirds, fish, and decapods and thus, may represent a pathway to the bioaccumulation—which is the accumulation of contaminants via both food and bioconcentration processes—of toxic compounds at higher trophic levels, with potential relevance for human consumption (Baden et al., 2021; Haukås et al., 2010; Parolini et al., 2020).

Teflubenzuron (CAS registry no. 83121-18-0) is a veterinary medicine commonly used in Norwegian salmon aquaculture to reduce infestation with the sea lice *Lepeophtheirus salmonis* (Norwegian Institute for Public Health, 2023). Teflubenzuron is lipophilic, with a log octanol-water partition coefficient (log K_{OW}) of 5.4 and an octanol-water distribution coefficient (log D) of 4.1 at pH 8. It is expected to interact more with terrDOM than with marDOM (Marsella et al., 2000) due to the larger molecules in the constituents of terrDOM along with terrDOM's more complex molecular structure, which enables lipophilic contaminants to more readily mix with water (e.g., via pseudo-micelle formation). When measured near fish farms, teflubenzuron is typically found at higher concentrations in sediment, POM, and biota (including blue mussels) and at much lower concentrations in the water (Langford et al., 2011; Samuelsen et al., 2015). As a chitin synthesis inhibitor that disrupts the molting process, teflubenzuron is highly toxic to a wide range of arthropods (Eisler, 1992; El Saidy et al., 1989; Haya et al., 2005; Langford et al., 2011 and references therein). Similar benzyl-urea insecticides (e.g., diflubenzuron) have a low acute toxicity on mollusks with a no observable adverse effect concentration of (NOEC) < 45 μg /L (Eisler, 1992)). Therefore, no direct toxic effects of teflubenzuron on blue mussels were expected in our exposure range (nominal concentration 20 μg/l).

The main aim of the present study is to assess how terrestrial DOM influences the bioaccumulation of teflubenzuron in blue mussels compared to marine derived DOM or seawater with low overall DOM content. We hypothesize that DOM acts as a vector for the uptake of lipophilic contaminants in organisms that are efficient filter feeders on low particle size classes and that terrDOM is a better vector than marDOM. To test our hypothesis, we exposed blue mussels (*Mytilus* spp.) to different types of DOM (marDOM; terrDOM; a 50:50 mix comprised of 50 % terrDOM and 50 % marDOM; and seawater only without any DOM addition) and teflubenzuron in a semi-static system. We expected the highest bioaccumulation of teflubenzuron in mussels exposed to terrDOM, followed by the mixDOM treatment, the marDOM treatment, and the seawater-only treatment.

2. Material and methods

Mussels 4–6.5 cm long were collected in the intertidal area of the outer Oslofjord (Norway) in August 2018. They were kept for

approximately one week in a flow-through seawater system at the Norwegian Institute for Water Research (NIVA) facility at Solbergstrand (near Oslo) and then transferred into a large plastic tank containing seawater and transported to the University of Oslo, a trip that took 45 min. The tank was aerated upon arrival. After three days, the mussels were mechanically cleaned to remove epibionts and transferred to 24 small stainless-steel baskets (13 mussels per basket, including 10 mussels that were analyzed and 3 spare mussels per aquarium in case of mortality). The baskets were individually placed in glass aquaria (Fig. 1) containing 2 L of seawater, which was obtained from NIVA's Solbergstrand facility at the outer Oslofjord from a depth of 50 m, pre-filtered to 0.22 μm, and stored in food-safe plastic containers. The mussels and water were maintained using a 24 h light regime in a temperature-controlled room at 14–16.9 ℃, which is a typical temperature in shallow fjord waters during summertime. The mussels were acclimatized for 14 days, including eight days with DOM exposure.

2.1. Experimental design

The exposure duration to teflubenzuron was 16 days, while the depuration phase, which included continued DOM treatment but no addition of teflubenzuron, lasted 20 days (Fig. 1, Table S1). The experiment employed a factorial design of three replicates of four DOM treatments with and without teflubenzuron. The four DOM treatments included terrDOM, marDOM, mixDOM, and seawater without any additions. Teflubenzuron (teflubenzuron pestanal, analytical standard, Sigmal-Aldrich; target concentration 20 μl/L teflubenzuron in the ready-mixed solution), was added to half of each treatment while the other half was used as control.

The set-up consisted of 24 distinct experimental units (glass aquaria) (Fig. 1). The aquaria were placed according to a randomized design with four aquaria connected to one air pump (pressure $>$ 0.25 bar) via separate silicone tubes terminating in a glass tube for aeration and water movement. Each time the water was exchanged, the pumps were exchanged with each other to reduce bias. The DOM and the teflubenzuron-containing water were prepared in eight glass mixing containers that were aerated using stronger pumps to induce water movement and teflubenzuron dissolution.

Complete water exchange occurred every four days and involved temporarily removing the mussels in their baskets from the aquaria. One day before the water exchange, the mussels were fed with 0.04 g untreated *Isochrysis galbana*, Tahitian strain (Proviron: IsoPrime) per aquarium to encourage filtration. Samples were taken on the water exchange day, immediately before the exchange: Samples included the following: one mussel per aquarium (24 in total) per time point; a teflubenzuron water sample per treatment type from the mixing containers; absorption spectra samples (for $SUVA_{254}$ calculations) from the mixing containers; and water for pH samples from all aquaria (Table S1). The pH was measured before water exchange in all aquaria and was found to be similar between treatment types, remaining stable throughout the experiment (Fig. S5). The total mortality during the experiment was six individuals. Except for one aquarium in which two deaths occurred, deaths were not clustered in a single aquarium but did occur exclusively in the terrDOM and mixDOM aquaria, with and without teflubenzuron treatment.

2.2. DOM preparation

MarDOM was produced using commonly occurring haptophytes (freeze-dried), while terrDOM was produced using tree leaves from local vegetation. An equal mixture of the two DOM types produced the mixDOM treatment. In greater detail, marDOM was based on a solution of freeze-dried *Isochrysis galbana*, Tahitian strain (Proviron: IsoPrime), and pre-filtered (0.22 μm) seawater. The *I. galbana* was sonicated in filtered seawater for 10 min to fragment the cell walls and then centrifuged at 3000 rpm (or 1741 g-force) for 10 min to separate the large fragments and ease the subsequent filtration process. The filtration was conducted with a sterile PES 0.22 μm filter (Corning life sciences, vacuum top, product no. 525-3409). Dissolved organic carbon (DOC) concentrations in both the DOM stock solutions and diluted samples were determined with a Shimazu ASI-V in combination with TOC V CPH total organic carbon analyzer (non-purgeable organic carbon method) at the University of Oslo. The concentrated marDOM was stored in a refrigerator at 4 ± 2 °C. During all steps, the DOM stock solution was kept in the dark.

To produce terrDOM, a mixture of dried oak (*Quercus* spp.) and birch leaves (*Betula* spp.) was cold infused in filtered seawater and subsequent filtered to 0.22 μm to exclude bacteria. The mixture consisted of roughly 90 % oak, 9 % birch, and 1 % other fresh autumnal leaves and plant materials (by volume) from the forests around Oslo, sampled either directly from trees or the ground beneath them. Leaves were dried at

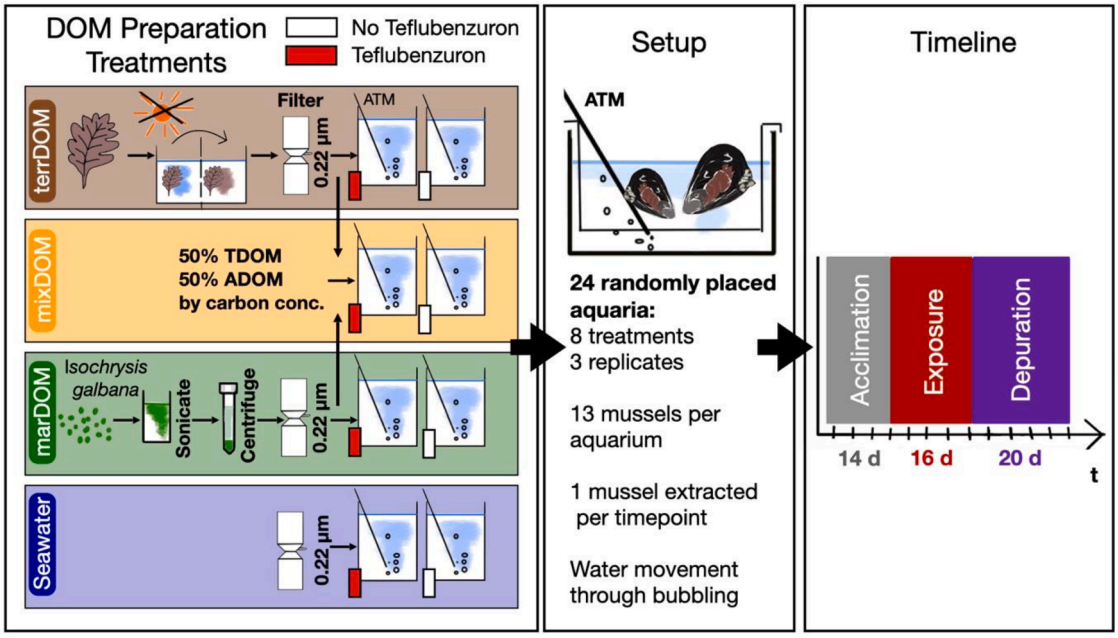

Fig. 1. Experimental treatments, setup, and timescales.

approximately 50 °C overnight, shredded into fragments by hand, and then transferred to a large glass aquarium that was filled with pre-filtered seawater and protected from light. The mixture was left to cold infuse for 48 h at room temperature, and then larger leaf fragments were removed by a sieve. The filtration was conducted in the same way as for the marDOM solution, with the terrDOM stored in the dark at 4 ± 2 °C until use (see also Lush and Hynes 1973, Mcmeans et al. 2015).

The day before each water exchange, the concentrated DOM was diluted to the target nominal concentration of 20 mg C/L and added to the appropriate aquaria. Actual concentrations (mean ± SD) were 18.4 ± 2.0 mg C/L for terrDOM; 19.0 ± 1.6 mg C/L for marDOM; 19.1 ± 1.8 mg C/L for mixDOM; and 1.5 mg ± 0.8 mg C/L for seawater) and added to the appropriate aquaria. The seawater treatment with no additional DOM maintained its natural background value of DOM (see above). The mixDOM treatment was obtained using 50 % carbon from marDOM and 50 % from terrDOM (Fig. S1).

$SUVA_{254}$ (carbon-specific UV absorbance at 254 nm) is positively correlated with the aromaticity and molecular weight of DOM (Weishaar et al., 2003) and is widely used as an indicator of terrDOM. Specific absorption of the DOM treatments was measured in 1 nm intervals within a 200–900 nm spectrum using a Perkin-Elmer Lambda 40P UV/VIS spectrophotometer and a quartz cuvette with a 5 cm path length. Absorbance values were blank-corrected based on Milli-Q blanks and corrected for potential absorption offset by subtracting the mean absorbance between 700 and 900 nm for each sample run (Blough and Del Vecchio, 2002; Jaffé et al., 2008). The UV absorbance was then divided by the DOC concentration and multiplied by the factor 20 (due to the 5 cm path length) resulting in the absorbance per meter. The $SUVA_{254}$ was calculated via dividing the absorbance at 254 nm by the DOC concentration in L mg $C^{-1}m^{-1}$ after blank and offset correction according to Weishaar et al. (2003).

The measured $SUVA_{254}$ values (Fig. 2) of the mixDOM were between those recorded for marDOM and terrDOM and thus, were distributed according to expectations. The preparation method proved efficient for large quantities of marDOM and terrDOM. However, within the natural environment, DOM occurs as a mixture of different sources and types, which our experiment could not accurately reflect. While the $SUVA_{254}$ of the marDOM is at the lower end of the spectrum, terrDOM can reach considerably higher values, for example when derived from peat systems (Freixa et al., 2016; Weishaar et al., 2003). Overall, however, the measured $SUVA_{254}$ values of our experimental marDOM and terrDOM types are representative of the contrasts found in natural freshwater versus open ocean systems (Helms et al., 2013; Schultze et al., 2022; Weishaar et al., 2003).

2.3. Teflubenzuron treatment

The teflubenzuron was dissolved in 650 µl acetone and pipetted into the mixing containers (nominally 20 µg/L) one day before the water change, with aeration employed to encourage mixing. The same amount of acetone was added to the mixing containers of the controls (Fig. S1). While the teflubenzuron-acetone stock solution used for spiking was measured and showed the expected concentration of teflubenzuron in the liquid, the median measured concentration in the containers was 33.8 µg/L. This was very likely due to the inefficient mixing of the large water volumes via air bubbles, which was the mixing method employed before taking the samples. However, before the water was transferred to the aquaria, thorough mixing was performed again by sloshing the containers by hand. Thus, the waterbody was assumed to be better mixed at this crucial point just before the transfer, as reflected in the teflubenzuron concentrations in the blue mussels, which did not diverge between replicate aquaria, with one exception (see Fig. 3). During the three-week depuration phase, the same regime was used as in the exposure phase but without adding teflubenzuron or acetone to the mixing containers.

2.4. Sample preparation

After sampling, the mussels were immediately frozen in liquid nitrogen and transferred to a freezer at −28 °C. The water samples for teflubenzuron analysis were frozen in glass vials at −28 °C until needed, while the water samples for absorption spectra were refiltered to 0.22 µm using a PES 0.22 µm filter (Corning life sciences, vacuum top, product no. 525-3409) and stored in the dark at 4 ± 2 °C until needed. To prepare the mussels for chemical analysis, individual mussels were thawed carefully to remove moisture from the shell before the valves split open. The entire mussel with its shell was then weighed and measured before the shell was removed and weighed separately. All byssus threads were removed and discarded before the soft tissues—including all liquids from inside the mussel—were extracted, weighed, and homogenized. A 1 g subsample of the homogenized tissue was taken, transferred to glass vials, and stored at −28 °C.

2.5. Chemical analyses

Teflubenzuron in the water and mussel tissue was quantified at NIVA (Oslo) as described in detail in Brooks et al. (2019). Briefly, water samples were shaken with acetonitrile and NaCl to salt out the water. The extract was injected into the LC-MS (Waters Acquity UPLC system connected to a Quattro Ultima triple quadrupole mass spectrometer).

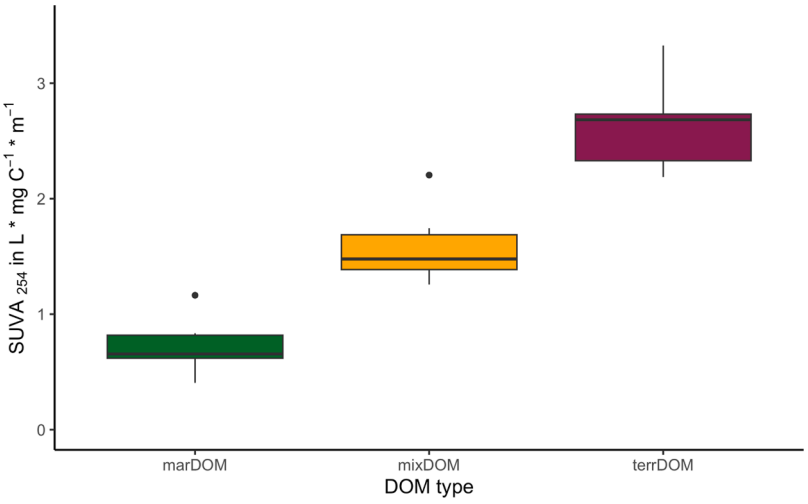

Fig. 2. Specific adsorption at 254 nm ($SUVA_{254}$) for the different DOM types: marine DOM (=marDOM), terrestrial DOM (=terrDOM), and a mixture of aquatic and terrestrial DOM (=mixDOM). $SUVA_{254}$ correlates with the size and aromaticity of DOM, with an increase of 1 in $SUVA_{254}$ representing an increase of 6.52 (intercept: 3.63) in aromaticity as shown by ^{13}C - NMR by *Weishaar et al. (2003)*. The boxplots display median values as a vertical line, the 25 % and 75 % percentiles as hinges, and the 1.5 times interquartile range from the hinge (Wickham, 2016).

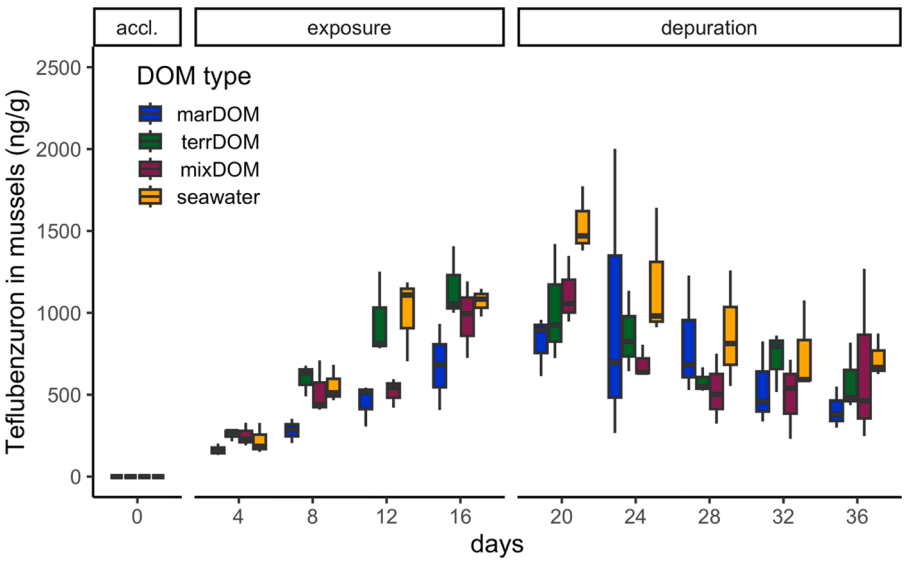

Fig. 3. Teflubenzuron in mussel tissue in the 16 days of the exposure phase and the 20 days of the depuration phase. The acclimation phase was 14 days long; however, only the last time point is displayed. Mark that in some cases, the highest concentrations were reached at the beginning of the depuration phase instead of the exposure phase. Neither steady state nor full depuration was reached. The boxplots display median values as a vertical line, the 25 % and 75 % percentiles as hinges, and the 1.5 times interquartile range from the hinge (Wickham, 2016).

Mussel homogenates were extracted twice with acetonitrile and were then centrifuged and combined. Next, the water was salted out with NaCl, and the acetonitrile was diluted further before analysis. The validation of the method showed that the average recovery of the three spiked seawater samples was 87 % (RSD of 3.5 %), and the average recovery of the three spiked mussel samples was 92 % (RSD of 2.1 %). The limit of detection was 1.0 ng/g (w.w.).

2.6. Calculations and statistical analyses

The data consisted of an exposure (days 0–16) and a depuration phase (days 17–36).

The mussel condition index was calculated as follows using the mussel wet tissue weight (MW in g) and the shell dry weight (SW in g) (Beyer et al., 2017; Davenport and Chen, 1987) (Eq. (1)):

$$CI = \left(\frac{MW}{SW}\right) 100 \quad (1)$$

Due to the small sample size, random effect factors, and the non-normal response variable, we adopted a Bayesian approach. Our candidate model for teflubenzuron dynamics was based on Ratier et al. (2022), in which the rate of change in mussel concentration is given by the balance between absorption and elimination:

$$\frac{dx}{dt} = k_1\ u - k_2\ x,\ x(0) = 0 \quad (2)$$

Here, x(t) is the teflubenzuron concentration in mussel tissue, $x(0)$ is the concentration at timepoint 0, and u(t) is the concentration in the environment. The experimental design entails that the environment concentration u(t) will be a step function that is equal to a constant value u_0 in the exposure phase $t \leq t_0$ and zero in the depuration phase $t > t_0$, which can be written as $u(t) = u_0 \times (t \leq t_0)$, with k_1 as the absorption rate constant (including all absorption processes; in L/kg/d) and k_2 as the elimination rate constant (including all elimination processes; in d^{-1}). The analytical solution (Eq. (3)) for the differential equation was used as the basic formula in the Bayesian model:

$$x(t) = u_0 \left(\frac{k_1}{k_2}\right) \left(e^{(k_2 \min(t,t0))} - 1\right)\ e^{(-k_2 t)} \quad (3)$$

This equation describes an asymptotic increase up to time t_0 (the exposure phase) and the exponential decay thereafter during the depuration phase. Since the parameters k_1 and u_0 appear only as a product in Eq. (3), they cannot be identified independently. Therefore, we reparametrized the model with only two parameters, k_2 and $k_u = k_1\ u_0$, which are both identifiable. We can recover the absorption rate coefficient k_1 by dividing the fitted compound parameter by the nominal exposure concentration, $k_1 = k_u / u_0$. This also allowed us to calculate the bioaccumulation factor $BAF = k_1 / k_2$ based on Arnot and Gobas (2006).

Priors were set as follows: normal distribution with a non-negative constraint (mean 200 and SD 200) for the compound parameter k_u and log-normal with a log-mean of 0 for the elimination rate constant k_2. These weakly informative priors were based on previous data (Brooks et al., 2019). We assumed that both parameters could vary by a random effect between aquaria and that k_u also had a fixed effect of DOM type. We fitted the model with the brms package (Bürkner, 2017), a front-end for the Bayesian computation environment Stan (Stan Development Team, 2021) using four chains with 10,000 iterations each and an adapt delta of 0.99 with a max tree depth of 15. The chains converged well, with a Rhat of 1.00.

In the Bayesian statistical framework, p-values are not calculated; instead, visual distributions are used to address uncertainties. Combined with contextual knowledge, they provide a visual tool to estimate the biological relevance of the results (Shoemaker et al., 1999). To simplify interpretation, we also calculated the percentage of overlap of the posterior BAF distributions based on regular integrals.

All statistical analyses were performed in R Studio (R Core Team, 2019: the R foundation for statistical computing; R version 4.0.3, RStudio version 1.4.1106 "Tiger Daylily"). Further R packages that were used for visualization purposes: ggplot2 (Wickham, 2016); cowplot (Wilke, 2020); dplyr (Wickham et al., 2022); RcolorBrewer (Neuwirth, 2022); tidyverse (Wickham et al., 2019); plyr (Wickham, 2011); tidybayes (Kay, 2023); and Rstan (Stan Development Team, 2021).

3. Results

Teflubenzuron concentrations in mussel tissue were below the detection limit (<1 ng/g w.w.) in all controls throughout the experiment. In the DOM treatments with teflubenzuron, the concentrations increased throughout the exposure period and did not correlate with mussel size (Fig. S2). Concentrations peaked in the early depuration phase treatments except for marDOM, for which concentrations peaked during the end of the exposure phase (Figs. 3, 4). We did not reach full depuration during our experimental timeline nor did we reach steady state during exposure.

The uptake rate constants k_1 (median; 2.5 % and 97.5 % percentile)

were highest in the mixDOM treatment with a k_1 of 5 (4; 6); followed by a k_1 of 4 in marDOM (3; 6); a k_1 of 4 in terrDOM (3; 5); and a k_1 of 3 in seawater (2; 4) but overlapped between treatments. TerrDOM and seawater had similarly low uptake rates of teflubenzuron with considerable overlap, while marDOM and mixDOM had higher uptake rates with less overlap.

The mussels in the DOM replicates (Fig. 4) responded similarly except for one seawater replicate. This exception was a high tissue concentration measured in the seawater treatment on day 24 during the depuration phase, which was not repeated elsewhere. This high value did not correlate with high teflubenzuron concentration in the water during that day, nor were any higher levels of teflubenzuron found in the water in the depuration phase. However, this measurement was not excluded from the dataset. Both the data point and the high standard deviation (SD) of the respective model reflect that outlier in the single aquarium. The SD was lowest in the marDOM models (Fig. 4).

The kinetic bioaccumulation factor (BAF) (median; 2.5 % and 97.5 % percentile) varied as follows: 106 L/kg (69 L/kg; 160 L/kg) for the treatment with seawater; 121 L/kg (82 L/kg; 186 L/kg) for terrDOM; 144 L/kg (102 L/kg; 221 L/kg) for marDOM; and 165 L/kg (117 L/kg; 244 L/kg) for mixDOM (Fig. 5). The overlap between the posterior distributions of terrDOM with the distribution for seawater was 75 %, 45 % between marDOM and seawater, and 27 % between mix and seawater.

The mussel condition index did not differ between the exposure types (teflubenzuron or control) or DOM treatment types (Figs. S3, S4).

4. Discussion

We generally observed a high degree of overlap in teflubenzuron uptake rates between the DOM treatments. However, there was a tendency for mussels to exhibit higher uptake rates in the DOM treatments than in the seawater treatment. The highest teflubenzuron uptake rates were found in the mixDOM treatment followed by the marDOM treatment. The terrDOM treatment had a slightly higher median uptake rate than the seawater treatment with high distribution overlap, reflecting the surprisingly low capacity of terrDOM to function as a contaminant vector in the investigated setting.

4.1. DOM as a vector for lipophilic contaminants

Teflubenzuron bioaccumulation rates appeared higher in all DOM treatments compared to seawater. Thus, all types of DOM seemed to act as contaminant vectors. Against expectations, the bioaccumulation rates in the terrDOM treatment were not higher than in the other DOM types and had the highest degree of distribution overlap with the seawater treatment. Studies focusing only on non-feeding-related uptake have reported that terrDOM can reduce direct contaminant uptake from water, which is called bioconcentration. Presumably, the large contaminant-DOM complexes cannot penetrate membranes directly, leading to the observed reduction of uptake (Akkanen and Kukkonen, 2003; Lu et al., 2018). Thus, unexpectedly finding higher bioaccumulation patterns in DOM treatments in a feeding-related experiment focusing on bioaccumulation highlights the importance of food-related uptake in filter feeders.

Our finding that terrDOM was a less effective contaminant vector for blue mussels compared to other DOM types suggests more complex associations between DOM, lipophilic contaminants, bioavailability, and uptake than our hypothesis considered. For example, to act as a pseudo-micelle and thus, as an effective vector for a particular chemical, a DOM molecule must have a specific size and molecular configuration (Chiou et al., 1986). Furthermore, factors such as the inherent alkalinity of seawater may prevent pseudo-micelle formation (see de Melo et al. 2016). In addition, the water's hardness can impact the binding properties between DOM and the contaminant, and the presence of metal ions can affect the formation and stability of pseudo-micelles (Akkanen and Kukkonen, 2003; von Wandruszka, 1999).

Biological factors that potentially reduce bioaccumulation in blue mussels include reduced filtration rates and a lack of filtration induction due to the small size class of DOM compared to the target size of the filtration apparatus (Kach and Ward, 2008). However, neither observations during the experiment nor the measured mussel condition index indicated a structured difference between the treatments in this regard. Other factors include an increase in feeding selectivity and the production of pseudo-feces, which are constituted of particles that are rejected prior to digestion (see Beninger et al. 1999) and that can be induced by particles in the micro- and macro-size range. However, the tendency of particles to induce pseudo-feces production seems to decrease strongly between 1000 μm and 19 μm; therefore, the DOM size class should not be relevant (Ward et al., 2019). In other words, since

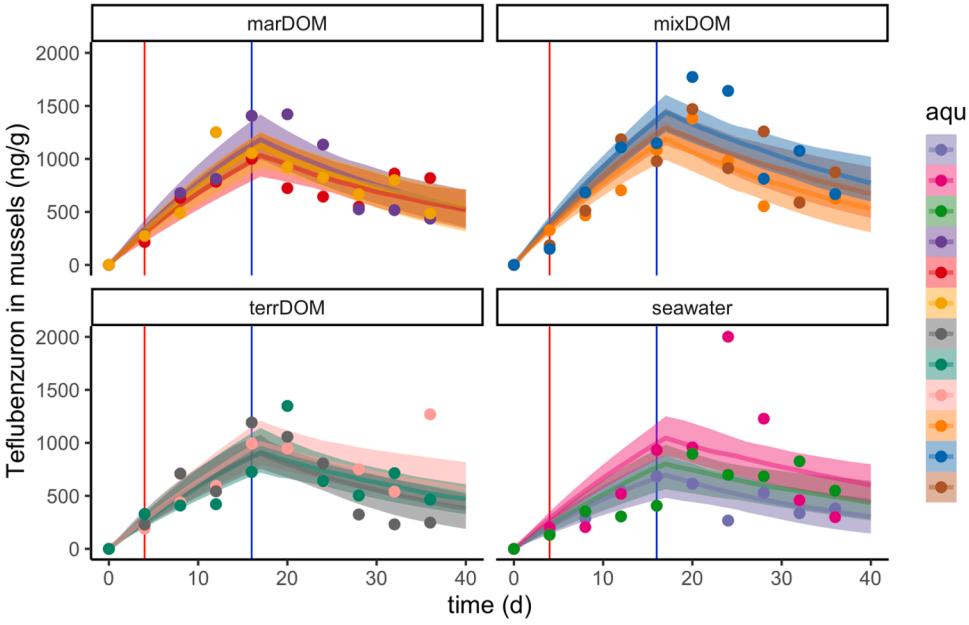

Fig. 4. Teflubenzuron content in mussel tissue by aquaria (aqu color represent different aquaria) and DOM type (the line represents the median and the ribbon the 95 % confidence interval based on the Bayesian model, while the dots are the individual measured data plots). The red vertical line denotes the start of the exposure phase, and the blue vertical line the start of the depuration phase. The mussels in the different aquaria of the same treatment had relatively similar teflubenzuron concentrations within the different sampling time points, except for one aquarium in the seawater treatment that had higher levels.

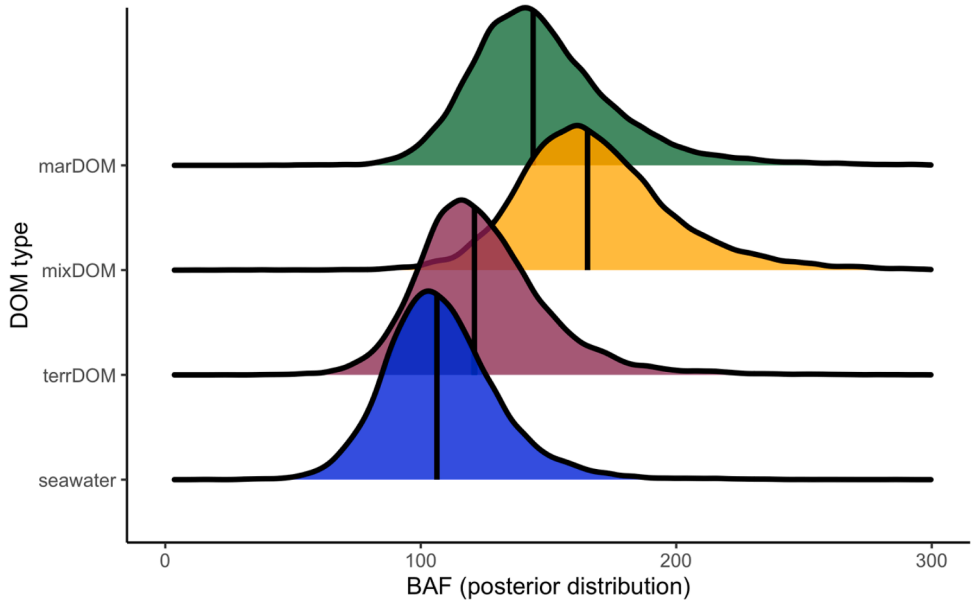

Fig. 5. Bioaccumulation factor (BAF) by DOM type according to a Bayesian model. The black vertical lines display the median values. While there is some considerable overlap in BAF between the DOM types, there is a pattern of increased BAF in the mixDOM and marDOM than the terrDOM treatments, which again has a tendency towards a slightly higher BAF than the seawater.

DOM is considerably smaller, it would be unlikely to induce pseudo-feces production, and definitely should not lead to different degrees of induction in the marDOM and terrrDOM treatments. Differences may also exist in the digestibility and intestinal uptake efficiency of the DOM-contaminant complex, which can be affected by the strength of the interaction between the DOM molecule and the contaminant and thus, may differ with DOM type (de Melo et al., 2016 and references therein).

While the current study did not measure these processes, bacterial abundance and production potentially influence uptake patterns in filter feeders. It is known that different qualities of DOM can have a profound effect on bacterial production (Creed et al., 2018). Indeed, we observed in an initial test phase that our marDOM preparation became cloudy after just a day in the refrigerator, while the terrDOM remained clear for days. We resolved the issue by using an entirely sterile filtration set, which seemed to confirm that bacteria had been an issue in the earlier marDOM preparation.

The removal rate of bacteria from water is not efficient in blue mussels (Jacobs et al., 2015). However, even with a low retention rate, bacteria may become an essential factor when abundant and when the mussels' water filtration rates are high. This is especially true in our setup, in which the mussels filtered the entire volume of water within the aquaria multiple times per day. MarDOM is considered a higher-quality food source for many bacteria since terrDOM is more bio-refractory (Boyd and Osburn, 2004; Creed et al., 2018; Hopkinson et al., 1998; Pérez and Sommaruga, 2006). Bacteria could serve as an effective contaminant vector since they are known to feed on DOM and thus, would also take up associated contaminants (e.g., Larsson and Hagström 1979). Compared to DOM, bacteria have a larger size class, and thus, blue mussels could harvest them more effectively via their filtration apparatus (Kach and Ward, 2008; Rosa et al., 2018). In addition to bacteria directly feeding on DOM and associated contaminants, an affinity may exist between the contaminants and bacterial lipids, DOM-mediated or otherwise (Creed et al., 2018; Widenfalk et al., 2008). Thus, an unequal distribution of bacterial biomass between DOM treatment types may have contributed to the higher bioaccumulation in treatments with algae-based DOM (mixDOM and marDOM).

The high bioaccumulation in the mixDOM treatment suggests a combined effect of different mechanisms that are additive or interactive. Further experiments are needed to identify and understand the various drivers in these bioaccumulation processes.

4.2. *Bioaccumulation factor of teflubenzuron*

The bioaccumulation factor (BAF) of teflubenzuron in blue mussels in the present study was two orders of magnitude below BAFs of concern (BAF > 2000 L/kg) based on the EU REACH (Registration, evaluation, authorization, and restriction of chemicals) regulation (European Commission, 2006). Furthermore, our experiment's measured BAF was lower than that measured for blue mussels' direct uptake of teflubenzuron without food (Brooks et al., 2019), for which a kinetic bioconcentration factor (BCF) of 1304 at 35 % salinity was reported. Brooks et al. (2019) conducted an experiment without DOM exposure under flow-through conditions and teflubenzuron saturation of the water, and their high BCF suggests that our study's exposure method did not saturate the water with teflubenzuron. In our experiment, steady state and full depuration were not reached; this was not essential for our modeling approach and did not affect the calculated BAF. However, the blue mussel bioconcentration study mentioned above (Brooks et al., 2019) did reach steady state at approximately 1500 ng/g w.w, which is close to the peak concentrations reached in our experiment.

Peak concentrations of teflubenzuron in the mussels were reached in most aquaria on the first sampling day of the depuration phase. The delay in reaching peak concentrations to post-exposure may be due to using the same aquaria for both the exposure and depuration phases rather than replacing the used aquaria with clean ones in the depuration phase. Hence, teflubenzuron, which is lipophilic, may have attached to the glass aquaria during the exposure phase and subsequently leached back into the water at the beginning of the depuration phase (see Arnot et al. 2010). The risk of uptake of teflubenzuron from feces and pseudofeces was minimized in these experiments as the mussels were placed in net cages that allowed feces to sink to the bottom of the aquaria.

Since for all DOM treatments and for seawater, the BAF of teflubenzuron in mussels was below the regulatory threshold, feeding on mussels is likely not an important source of teflubenzuron for natural predators. This study's choice of contaminant was based on its lipophilic properties, making it likely to affiliate with terrDOM, which is composed of large molecules and is rich in humic acid. Thus, teflubenzuron was

chosen for its potential to trace uptake differences under different DOM conditions rather than for directly investigating its hazard potential in aquaculture.

Indeed, most teflubenzuron exposure near aquaculture facilities occurs via two routes: through teflubenzuron-spiked feeding pellets that remain uneaten by the fish in aquaculture or through feces excreted by the fish after they feed on the pellets (Samuelsen et al., 2015). Both the pellets and the feces sink down and can be eaten by organisms living below the fish farm; alternatively, the substances can settle in the sediment, leading to high exposure concentrations (Langford et al., 2011). In blue mussels, the highest measured teflubenzuron concentrations were in organisms sampled in the vicinity of a fish farm (72.4 ng/g ww in Samuelsen et al. 2015). This measurement was far below our lowest measured concentration of 407 ng/g w.w., which was from the seawater treatment on the final day of exposure. In contrast, teflubenzuron concentrations up to 865 g/g w.w. have been measured in the tissues of the predatory brown crab (Cancer pagurus), a species that is vulnerable to teflubenzuron's toxic mechanisms (Neal and Wilson, 2008; Samuelsen et al., 2015).

4.3. Effect of browning on contaminant transport

Our controlled experiment of teflubenzuron uptake in blue mussels showed that terrDOM alone led to lower contaminant uptake and bioaccumulation compared to marDOM. But a natural environment is characterized by complex properties and interactions; thus, extrapolating from the laboratory to the field is challenging. For example, unlike marDOM, terrDOM can introduce contaminants from the terrestrial environment to downstream aquatic systems, potentially carving a new pathway for contaminants to reach an aquatic environment. Depending on the contamination level of the original areas and the pathway terrDOM takes before entering an aquatic system, there may be substantial inputs of terrDOM-associated contaminants from land to coastal waters, including agricultural pesticides and urban contaminants. In a fjord system in western Norway, for example, an increasing input of terrDOM appeared to cotransport the legacy pesticide dichlorodiphenyltrichloroethane (DDT), leading to considerably elevated levels of this chemical in blue mussels (Ruus et al., 2010). In a natural environment, terrDOM eventually mixes with the marDOM already present in an aquatic system, which would simulate conditions approaching our mixDOM treatment, which led to the highest uptake rate in the experiment. Thus, the combination of different DOM types and an overall increase in DOM concentrations could result in higher bioaccumulation levels in filter feeders and thus, should be monitored further in the field.

5. Conclusions

Compared to seawater controls, all types of DOM were associated with a slight increase in bioaccumulation of teflubenzuron in blue mussels. This suggests that when DOM is present, dietary uptake is a exposure route for filter feeders to lipophilic contaminants. However, against expectations, bioaccumulation in terrDOM treatments was less than that in the other DOM treatments. The observed differences between terrDOM and the seawater treatments were negligible, suggesting that terrDOM is of low environmental relevance as a contaminant vector. Overall, the bioaccumulation factors were low for all treatments, the differences between the bioaccumulation factors were small, and the highest bioaccumulation rates were reached in the treatment that combined terrDOM and marDOM.

In this experiment, the exact combination of factors tested had low environmental relevance. However, the overall findings suggest a relevant mechanism that may gain importance in a complex natural system.

CRediT authorship contribution statement

Sabrina Schultze: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Visualization. **Tom Andersen:** Conceptualization, Methodology, Formal analysis, Software, Writing – review & editing, Visualization, Supervision. **Nina Knudtzon:** Investigation, Writing – review & editing. **Anders Ruus:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Funding acquisition. **Jan T. Rundberget:** Methodology, Resources, Writing – review & editing. **Steven J. Brooks:** Conceptualization, Writing – review & editing. **Amanda Poste:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Funding acquisition. **Dag O. Hessen:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Katrine Borgå:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data available in supplementary information

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.aquatox.2023.106696.

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