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The impact of anti-sea lice pesticides, azamethiphos and deltamethrin, on European lobster (*Homarus gammarus*) larvae in the Norwegian marine environment☆

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ABSTRACT

Anti-sea lice pesticides, used in the salmonid aquaculture industry, are a growing environmental concern due to their potential to adversely affect non-target crustaceans. Azamethiphos and deltamethrin are two bath treatment pesticides used on salmon farms in Norway, however, limited information is available on their impact on European lobster (*Homarus gammarus*) larvae in the Norwegian marine environment. Here, we firstly report the lethal (LC_{50}) and effective (EC_{50}) concentrations of azamethiphos and deltamethrin for stage I and stage II larvae, following 1-h exposures. Using a hydrodynamic model, we also modelled the dispersal of both compounds into the marine environment around selected Norwegian farms and mapped the potential impact zones (areas that experience LC_{50} and EC_{50} concentrations) around each farm. Our data shows that azamethiphos and deltamethrin are acutely toxic to both larval stages, with LC_{50} and EC_{50} values below the recommended treatment concentrations. We also show that the azamethiphos impact zones around farms were relatively small (mean area of 0.04–0.2 km^2), however deltamethrin impact zones covered much larger areas (mean area of 21.1–39.0 km^2). These findings suggest that deltamethrin poses a significant risk to European lobster in the Norwegian marine environment while the impact of azamethiphos may be less severe.

1. Introduction

In the past three decades, global aquaculture production has expanded rapidly, from 5.2 million tonnes in 1981 to 110.2 million million tonnes in 2016 (FAO, 2018). This expansion has led to growing environmental concerns over the industry's impact on water quality, natural ecosystems and human health (Liu et al., 2017; Páez-Osuna, 2001). Norway is the largest producer of farmed Atlantic salmon (*Salmo salar*) in the world, with 1.2 million tonnes produced annually (FAO, 2018). Sea lice (*Lepeophtheirus salmonis*) infestations are common in the salmonid aquaculture industry, reducing the general welfare of the farmed fish and causing significant economic losses to the industry (Pike et al., 1999; Wagner et al., 2008; Burka et al., 1997). Chemotherapeutic drugs and pesticides applied either as in-feed additives or bath treatments are one of several methods for controlling these infestations on salmonid farms. Bath treatments involve surrounding fish cages with a tarpaulin or transferring the fish to well-boats so they are enclosed. The recommended treatment concentration for the pesticide is added, and salmon are held in the bath for the recommended treatment time. Following the treatment, the enclosed water is directly released into the surrounding aquatic environment (Burridge et al., 2010). Azamethiphos and deltamethrin are important bath treatment pesticides used in major regions of salmonid aquaculture worldwide (Burridge et al., 2010; Scottish Environmental Protection Agency (SEPA), 2019; Folkehelseinstituttet, 2019). Azamethiphos, the active ingredient in the commercial formulations Salmosan Vet® and Trident Vet®, is a neurotoxic insecticide, causing acetylcholinesterase (AChE) inhibition which consequently results in paralysis and eventual mortality of the target organism (Baillie et al., 1985). On salmon farms, a

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20–40 min azamethiphos treatment is recommended with a target concentration of 100 μg L^{-1}. Deltamethrin, a synthetic pyrethroid insecticide, is the active ingredient in the commercial formulation AlphaMax®. It interacts with the sodium (Na+) channels of nerve membranes, resulting in depolarisation of nerve endings and over-stimulation of cells and eventual paralysis (Miller and Adams, 1982). A 30-min deltamethrin treatment is recommended with a target concentration of 2 μg L^{-1}. The use of azamethiphos and deltamethrin, along with other delousing pesticides, was widespread on Norwegian fish farms between 2010 and 2015, as a result of increased resistance amongst sea lice to the different pesticide compounds. The current annual consumption of azamethiphos and deltamethrin is relatively low in comparison to previous years, with only 154 kg and 10 kg (active substance) used in 2019, respectively (Folkehelseinstituttet, 2019).

Given the growing evidence showing that anti-sea lice pesticides are toxic to non-target species, particularly crustaceans, their direct release into the marine environment is an increasing cause for concern (Burridge et al., 2010; Urbina et al., 2019). To better assess the impacts of azamethiphos and deltamethrin on non-target species in the Norwegian marine environment, a greater understanding of their toxicity and environmental concentrations around fish farms is required. To date azamethiphos and deltamethrin acute toxicity tests using marine crustaceans have mostly involved 24, 48 and 96 h exposure periods (Burridge et al., 1999; Ernst et al., 2001; Ernst et al., 2014; Oliveira et al., 2012; Adam et al., 2010), which do not reflect the highly acute exposures expected to occur in the marine environment following the release of bath treatment effluents (Ernst et al., 2001; Burridge et al., 2014; Bruno and Raynard, 1994; Tomlin, 1997; Scottish Environmental Protection Agency (SEPA), 2005). Currently, there also is limited information available on the dispersal of azamethiphos and deltamethrin in the marine environment around Norwegian fish farms. Consequently, it is difficult to assess whether threshold concentrations, calculated from laboratory based toxicity tests, are likely to pose a risk to non-target species living in the wild near aquaculture facilities. While mathematical models have been developed for assessing the dispersal of bath treatment compounds from farming systems located in shallow estuarine, semi-enclosed (e.g. sea lochs) and coastal environments in Scotland and Ireland (Falconer and Hartnett, 1993; Gillibrand and Turrell, 1997; Gillibrand and Turrell, 1999; Scottish Environmental Protection Agency (SEPA), 2008), the environmental conditions in Norway's fjords are considerably different. Therefore there is an urgent need to apply a hydrodynamic model to assess the dispersal of bath treatment compounds specifically in the Norwegian marine environment (Rico et al., 2019).

The main aim of this study was to assess the potential impact of azamethiphos and deltamethrin on a native non-target crustacean species in the Norwegian marine environment. Our first objective was to examine the toxicity of both compounds to European lobster *(Homarus gammarus)* larvae following an environmentally relevant exposure period (1 h) and establish threshold concentrations associated with exposure. *H. gammarus* is an important commercial species in many coastal regions of Europe, including Norway, and is often located near salmon aquaculture sites. *H. gammarus* larvae are pelagic and remain in the surface layers and therefore can move with pesticide plumes following the operational release of bath treatment effluents. Consequently, the larvae are potentially more vulnerable to exposure than benthic invertebrates such as adult lobsters. The second objective of this study was to use a hydrodynamic model to simulate the dispersal of azamethiphos and deltamethrin into the marine environment at multiple Norwegian fish farms. Using the simulated dispersal data, we subsequently mapped the areas around each of the farms which experience pesticide concentrations exceeding the lethal and effective threshold concentrations calculated here for *H. gammarus* larvae.

2. Material and methods

2.1. Animal collection and maintenance

This experiment was approved by the Norwegian Food Safety Authority (ID 15510) and has been carried out according to The Code of Ethics of the World Medical Association for animal experiments (The Norwegian Ministry of, 2010; The Norwegian Ministry of, 2015). Six ovigerous *H. gammarus* females were purchased from a local lobster dealer on 22 May 2018 and transferred to the Institute of Marine Research (IMR) field station at Austevoll, located outside Bergen (N60°05′15.36″, E5°15′54″). They were initially kept in holding tanks (1.5 m × 1.5 m x 1 m) supplied with filtrated seawater from 160 m depth at a flow of 30 L min^{-1} (salinity of 34.7 ppt and temperature of 8 °C). Females were fed frozen shrimp twice per week and the temperature was kept low to postpone and control hatching. Experiments were conducted at the same location in August–November 2018. The ovigerous females were transferred to holding tanks with 16 °C to stimulate hatching.

When spawning occurred larvae were removed from the hatching tanks every morning and transferred to 40 L fibreglass incubators (plankton Kreisler tanks) (Hughes et al., 1974), which were supplied with oxygenated seawater (15–16 °C) at a rate of 8–10 L min^{-1} and kept in a 16:8 h light: dark cycle. Maximum density for each incubator was set to 50 larvae L^{-1}. The incubators were treated for the bacteria *Leucatrix minor* with chloramine-T (every third day at 0.02 g L^{-1} for 1 h). Larvae were fed frozen artemia twice a day and checked daily to determine the stage of development. The larvae were staged I-II according to Sars (1874). Briefly, stage I larvae are characterised by the lack of pleopods while stage II larvae had developed pleopods. At the selected water temperature, the approximate number of days required to pass through the stage I to stage II larval stages were 4 and 5 days, respectively. The larvae used in each lethality test were of the same stage and approximate age. The mean carapace length for stage I and stage II larvae was 2.3 mm ± 0.1 and 3.3 mm ± 0.1, respectively.

2.2. Acute toxicity tests

H. gammarus larvae (5 larvae per tank, 3–4 replicates per concentration) were exposed to a range of concentrations of azamethiphos (1–1000 μg L^{-1}) and deltamethrin (0.01–200 ng L^{-1}) in 700 mL of test solution for 1 h to generate cumulative mortality curves. Each assay was repeated twice (approx. 40 larvae per concentration). The chosen concentrations were based on LC_{50} values estimated for *H. americanus* lobster larvae (Burridge et al., 2014). Azamethiphos (Trident Vet 500 mg g^{-1} powder) was purchased from Neptune Pharma Ltd. (London, UK) and deltamethrin (AlphaMax 10 mg ml^{-1}) from Pharmaq A/S, (Overhalla, Norway). Stock solutions (1 μg L^{-1} and 10 mg L^{-1}, respectively) of azamethiphos and deltamethrin were prepared using the stock formulations and filtered seawater (0.2 μm). Test concentrations were prepared by serial dilutions of stock solutions. All experimental units and equipment for preparing stock solutions were made of glassware (as deltamethrin is known to readily bind to the walls of plastic test vessels). After each exposure, the larvae were placed in 1 L recovery units supplied with fresh seawater. The number of mortalities and immobile larvae were recorded at 0 h and 24 h post-exposure in each tank. Lobsters were considered immobile if they sank to the bottom of the tank, i.e. normal swimming behaviour was absent and considered dead when there was no movement of pleopods even after gentle prodding. Larvae were fed

compound fish feed (Otohime C, Marubeni Nisshin Feed Company, Japan) during the 24 h recovery period. Water temperatures ranged between 13.5 and 17.7 °C. Lethal and total effect dose-response curves were generated for each individual assay (as each pesticide assay was repeated twice) as well as the data combined (i.e. assay one and two were combined). For each of the dose-response curves, LC_x and EC_x values, based on mortality and total effect (mortality + immobility) after the 24 h recovery period, were calculated, respectively.

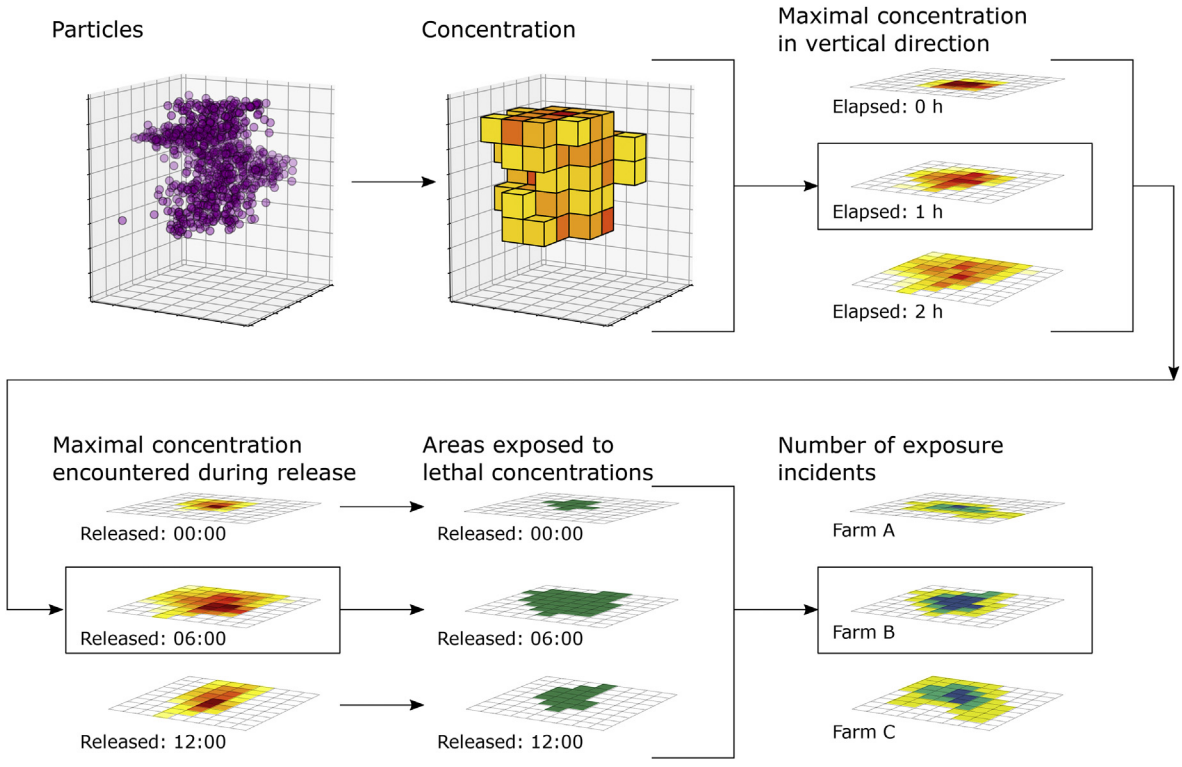
2.3. Modelling pesticide dispersal and impact zones

The dispersal of azamethiphos and deltamethrin into the marine environment around Norwegian fish farms was simulated for a 24 h period post bath treatment effluent release using a hydrodynamical model. The dispersal data was subsequently used to map the potential impact zones around fish farms. Impact zones are defined as areas around fish farms which are exposed to the lethal and effective concentrations of azamethiphos and deltamethrin (as per the 1 h toxicity tests carried out with *H. gammarus* larvae in the present study) at any point during the 24 h simulation. A schematic of the procedure used for computing impact zones is outlined in Scheme 1.

From the BarentsWatch database, we selected a sample of 23 Norwegian fish farms (referred to here as farms A-W) that carried out delousing bath treatments with azamethiphos or deltamethrin in the period 2017–2018 (BarentsWatch, 2019) (Fig. S1 of the Supporting Information). Particle tracking software LADiM (Myksvoll et al., 2018) was used to simulate the release and dispersal of both pesticides from each farm. Ocean current data, based on the NorFjords hydrodynamic model, was entered into the particle tracking software. The NorFjords model, an implementation of the Regional Ocean Model System (ROMS) (Shchepetkin and McWilliams, 2005; Haidvogel et al., 2008) has a resolution of 160 m × 160 m and 35 vertical levels, and includes recorded input data from atmosphere, tides and rivers (Isachsen, 2014; Storesund et al., 2017). The model is based on the NorKyst800 model (Albretsen et al., 2011) which has a horizontal resolution of 800 m × 800 m. The release sites span a wide geographical region, with latitudes in the range 59.5 °N - 70.5 °N (Fig. S1). Various types of hydrodynamic regimes are represented including sheltered locations with modest tidal currents (Farms A, R, V), larger fjords with more pronounced tidal activity (Farms D-H, J-M, Q, S, W), open-ended fjords with a dominant current direction (Farms B, C, I, O, T, U) and exposed locations that are highly influenced by the Norwegian coastal current (Farms N, P). Chemical plumes released in sheltered areas tend to disperse and move slowly. In exposed regions, turbulent currents dissolve released plumes quickly and disperse contaminants over a large area in a short time.

The released pesticide was represented by 100,000 particles, initially dispersed within a volume of 50 m × 50 m x 10m, which is roughly equal to the size of a typical large Norwegian fish cage (Fiskeridirektoratets og Mattilsynets anbefalinger, 2010). The particles were tracked for 24 h. A rectangular grid (100 m × 100 m in the horizontal direction, 1 m in the vertical direction) was constructed around the cage, and the *particle density* was calculated from the grid block volume and the number of particles within each block. From this we computed the maximal particle density in the vertical direction and stored the result on a 2D grid, for each time step. The data was combined into a dilution map, where each point represents the largest particle density encountered during the simulation (Fig. S2).

The BarentsWatch database does not specify the date or time of bath treatments, only the week in which the treatment was performed. Because of this, and to study the effect of varying weather and tide conditions on pesticide dispersal, we simulated a pesticide release at 00:00, 06:00, 12:00 and 18:00 for each day the treatment was performed for all 23 locations under consideration. This



Scheme 1. Schematic representation of the procedure for computing bath treatment impact zones.

resulted in a total of 28 releases per location, and therefore 28 dilution maps per farm. The releases were not cumulative; the location was assumed pristine before each release. In order to create maps of the impact zones around each fish farm, each of the dilution maps were then related to the EC_{50} and LC_{50} values for the combined data (i.e. the data from the two repeat assays combined) reported here. For instance, if the LC_{50} value of a pesticide corresponds to N % of the recommended treatment concentration, the LC_{50} impact zone for that drug is the portion of the dilution map that exceeds N % of the initial particle density. The impact zones for each farm were subsequently overlaid and the resulting maps show the proportion of releases that result in areas around the farms experiencing lethal or effective concentrations of the pesticides.

The impact zones vary in shape and size depending on the pesticide, location and time of release. In order to summarize the data, we computed radial and areal extent of the impact zone for each of the simulated releases. The radial extent is defined as the largest distance from the fish farm to the edge of the impact zone, while the areal extent is simply the area of the impact zone.

2.4. Statistical analyses

All statistical analyses were conducted in R Studio (3.4.3) (RStudio Team, 2016). LC_{50} and EC_{50} values, and their 95% confidence intervals (CI), for each pesticide were calculated using generalised linear models (GLM) within the *ecotox* R package (Hlinaet al., 2019), with binomial error structures and probit links according to Finney (1971). Pesticide concentrations were log transformed (log_{10}) to linearise the data. Dose-response data were plotted using the *ggplot2* R package (Wickham, 2009). The dose-response curves for the repeated assays were compared statistically using ratio tests within the *ecotox* R package, as well as the confidence interval overlap method. Dispersal models were performed in Python and exposure areas were plotted using the package *holoviews* with the backend *matplotlib* (Hunter, 2007).

3. Results and discussion

3.1. Acute toxicity of azamethiphos and deltamethrin

A summary of the azamethiphos and deltamethrin LC_{50} and EC_{50} values, and their corresponding 95% CIs, for each of the repeated assays as well as the combined data are provided in Table S1 and Table S2. One hour exposures to azamethiphos were acutely toxic to both stage I and stage II *H. gammarus* larvae, with both mortality and immobility increasing in a dose dependent manner (Table S3). For both stage I and stage II larvae, there was a significant difference in the mortality dose-response curves for each of the azamethiphos assays performed and the associated lethal threshold concentrations (Fig. S3; Ratio Test, $p < 0.001$). For stage I and stage II larvae, the 1h-LC_{50} values for azamethiphos ranged from 23.8 to 75.7 μg L^{-1} and 8.5–75.7 μg L^{-1}, respectively. As the two assays were performed with larvae hatched from two different females, the differences in mortality levels between assays may be suggestive of differences in inherited tolerance. Interestingly, however, there was no significant difference in the total effect dose-response curves for the two repeated assays, as well as the estimated effective threshold concentrations (Ratio Test, $p > 0.05$), which suggests that the overall effect of azamethiphos between different populations may not be drastically dissimilar. When the data from the two assays were combined, the 1h-LC_{50} values (95% CIs) for stage I and II larvae were 43.1 μg L^{-1} (13.0–131.0 μg L^{-1}) and 20.5 μg L^{-1} (13.2–30.9 μg L^{-1}), respectively, representing approximately 2- and 5-fold dilutions of the treatment concentrations used on Norwegian fish farms (Fig. 1). Our results are in line with a recent study which found that azamethiphos (10–500 μg L^{-1}) induced significant mortalities in crab larvae (*Metacarcinus edwardsii*), following short term exposures (30-min) (Gebauer et al., 2017). In contrast, 1-h exposures to azamethiphos, at similar concentrations to those tested here, did not lead to a significant increase in mortalities amongst exposed *H. americanus* lobster larvae (stage I and III) and several shrimp species (*M. stenolepsis*, *C. septemspinosa*, *P. flexuosus, P. elegans)* (Ernst et al., 2014; Burridge et al., 2014). In addition, limited mortalities were observed amongst northern shrimp (*Pandalus borealis*) exposed to azamethiphos for a 2 h period, however, it should be noted that exposure concentrations in these studies were relatively low (100–200 ng L^{-1}) (Bechmann et al., 2020; Frantzen et al., 2019). It is interesting to observe here that stage II larvae were slightly more sensitive to azamethiphos exposure than stage I larvae. It has been hypothesised that stage-specific differences in crustacean sensitivity to pesticides is a result of differences in metabolism, moulting frequency, detoxification mechanisms and allometric differences (i.e., surface area to volume), with adult life stages often less sensitive than earlier life stages (Medina et al., 2002; Willis and Ling, 2004). Similar to our findings, however, higher sensitivity in later life stages has more recently been observed in several crustaceans including copepods (*Acartia hudsonica)* and krill (*Calanus* spp.) (Van Geest et al., 2014a; Escobar-Lux et al., 2019), though no plausible explanation has yet to be determined.

One hour exposures to deltamethrin were considerably more toxic than azamethiphos to both stage I and stage II *H. gammarus* larvae, with both mortality and immobility increasing in a dose-dependent manner (Fig. 1, Table S4). There was no significant difference in the lethal and total effect dose-response curves, as well as the estimated threshold concentrations for the two repeated deltamethrin assays (Ratio Test, $p > 0.05$; Fig. S4). For the combined data, the 1h-LC_{50} values (with 95% CIs) for stage I and II larvae were estimated to be 2.6 ng L^{-1} (0.6–11.0 ng L^{-1}) and 2.9 ng L^{-1} (1.5–5.7 ng L^{-1}), representing approximately 800-fold dilution of the treatment concentration. These results are consistent with those reported for stage I *H. americanus* lobster larvae (3.4 ng L^{-1}), though reduced sensitivity was also observed in adults (19 ng L^{-1}) and stage III larvae (36.5 ng L^{-1}) (Burridge et al., 2014; Fairchild et al., 2010). Lobster species appear to be more sensitive to deltamethrin compared to many other taxonomic groups, with higher 1h-LC_{50} values reported for shrimp (105.1–142 ng L^{-1}), *mysid* (13.9 ng L^{-1}), amphipod (13.1–70 ng L^{-1}) and crab larvae (1300 ng L^{-1}) (Burridge et al., 2014; Fairchild et al., 2010; Van Geest et al., 2014b; Parsons et al.). In two recent studies examining the toxicity of deltamethrin to *P. borealis*, high levels of mortality were observed amongst individuals exposed to low concentrations of deltamethrin (0.2–6 ng L^{-1}) for short time period (2 h), however LC_{50} values were not estimated, therefore, direct comparisons with these studies cannot be made (Bechmann et al., 2020; Frantzen et al., 2019). These results demonstrate that there are species-specific and life-stage specific differences in sensitivity to azamethiphos and deltamethrin amongst crustaceans. *H. gammarus* larvae appear to be one of the most sensitive crustacean species tested to date and therefore the present results should be included in any future ecological risk assessments investigating the risks of pesticides to the marine environment (Vaal et al., 2000).

Here, we reported EC_{50} values based on the combination of lethality and immobility, which previously has been shown to be a highly sensitive and potentially more environmentally relevant endpoint for assessing neurotoxic compound (Fairchild et al., 2010; Van Geest et al., 2014b). Indeed, we found that EC_{50} values for both azamethiphos and deltamethrin were substantially more sensitive than LC_{50} values based on mortality. The EC_{50} threshold values for azamethiphos were 15.5 μg L^{-1} (9.3–24.5 μg L^{-1}) and 9.2 μg L^{-1}

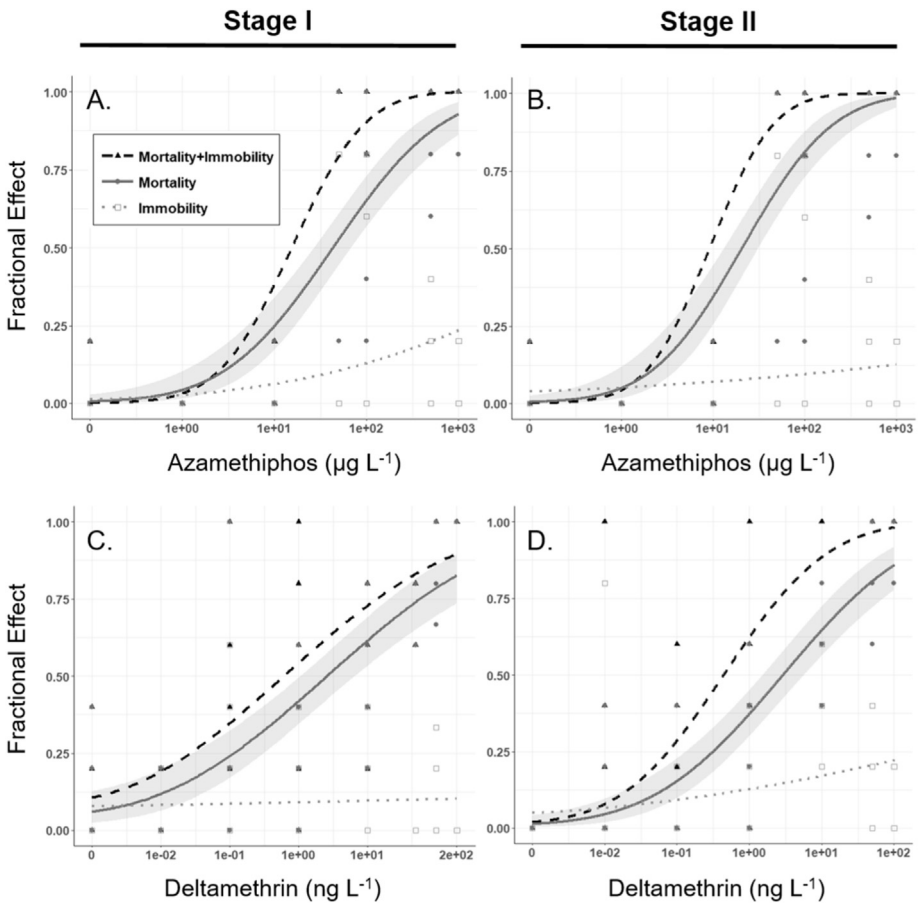


Fig. 1. The toxicity of azamethiphos and deltamethrin to stage I and stage II *H. gammarus* larvae following a 1 h exposure and a 24 h recovery period. Dose-response curves showing (▲) total effect (mortality + immobility, (●) mortality and (■) immobility amongst larvae exposed to nominal concentrations of (A–B) azamethiphos (1–1000 µg L^{-1}) and (C–D) deltamethrin (0.01–200 ng L^{-1}). Each point on the graphs represents an individual replicate glass dish containing 5 larvae and the lines represent the best fit model for the data, calculated using a binomial log-probit GLM in R (model output summarised in Tables S1 and S2).

(5.7–14.1 µg L^{-1}) for stage I and II larvae, respectively, which are 2.2- and 2.7-fold lower than the respective calculated LC_{50} values and approximately 10-fold lower than the recommended treatment concentrations. For deltamethrin, the 1h-EC_{50} values for stage I and II larvae were estimated to be 0.6 ng L^{-1} (0.2–2.1 ng L^{-1}) and 0.4 ng L^{-1} (0.2–1.1 ng L^{-1}), respectively, which are 4.3- and 7.3-fold lower than the respective calculated LC_{50} values and approximately 4000-fold lower than the recommended treatment concentrations. Given that immobile larvae are incapable of maintaining their position in the water column, unable to avoid predators and unable to feed, these larvae are considered to be ecologically dead (Van Geest et al., 2014b) and therefore the data presented here suggested that both azamethiphos and deltamethrin are considerably more toxic than previous published studies have suggested.

Given that the exposure period in this study was extremely short, the larvae were monitored both immediately after the 1 h exposure period and 24 h post exposure, allowing us to assess whether immobilised larvae could recover. In both azamethiphos and deltamethrin assays, larvae that were immobilised at 0 h post exposure typically did not recover by 24 h post exposure and consequently died (Tables S3 and S4). This lack of recovery and delayed mortality may be explained by the mode of action of the two toxicants. Azamethiphos covalently binds to AchE via phosphorylation and while the enzyme remains phosphorylated, its activity is inhibited. Consequently, ACh accumulates in cholinergic synapses, leading to unregulated excitation at neuromuscular junctions of skeletal muscle, preganglionic neurotransmitters and postganglionic nerve endings of the autonomic nervous system, and neurotransmitters in the brain or CNS. The phosphorylated AchE is typically very stable and may persist for days or weeks. The AchE activity is only slowly reactivated by spontaneous hydrolysis of the phosphate ester and recovery usually depends on new enzyme synthesis (Fulton and Key, 2001). Studies in fish, birds, mammals and invertebrates have shown a direct relationship between levels of AChE inhibition in the brain and subsequent mortality (Russom et al., 2014), which may explain the delayed mortality observed here at 24 h post exposure. While there are differences in sensitivity between species and life stage to various AChE inhibiting chemicals, it is evident that upon reaching a critical inhibition threshold, mortality is highly likely. Mortality may arise as a result of adverse physiological responses at the organ level such as altered respiratory activity, altered heart rates, altered blood pressure levels and seizures (Russom et al., 2014). Deltamethrin, on the other hand, inhibits the activity of voltage-gated sodium channels, resulting in depolarisation and prolonged permeability of the nerve to sodium. This consequently produces a series of repetitive nerve signals in sensory organs, sensory nerves, and muscles resulting in eventual paralysis (Soderlund, 2012). As a type II pyrethroid pesticide, deltamethrin contains an α-cyano group that induces long-lasting inhibition of the sodium channel activation gate which again likely explains the lack of recovery observed amongst lobster larvae in the present study.

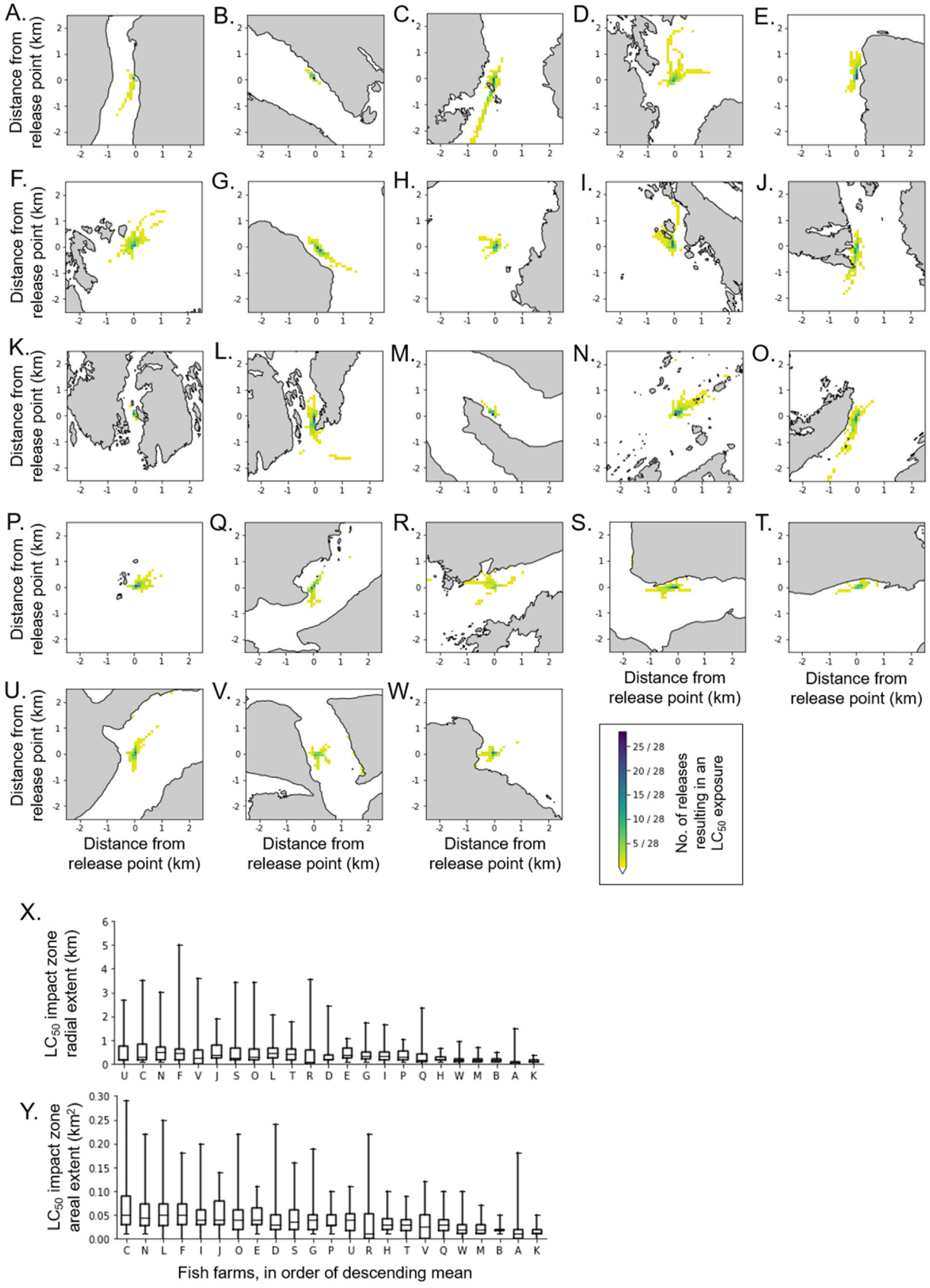


Fig. 2. Azamethiphos LC_{50} impact zones. (A–W) Maps illustrating the areas around 23 Norwegian fish farms which, based on multiple dispersal simulations (covering a range of tide and weather conditions), experienced lethal concentrations of azamethiphos (20 μg L^{-1}) in the 24 h after the simulated release of a bath treatment effluent from a standard size salmon pen which had been treated at the recommended dose of 100 μg L^{-1}. The colour legend displays the number of releases which have resulted in an area experiencing a lethal concentration of azamethiphos. The dark blue colour indicates an area which has experienced lethal concentration of azamethiphos in a high proportion of simulated releases (i.e.

Table 1
Summary of the total areal and radial extent of the azamethiphos and deltamethrin LC_{50} and EC_{50} impact zones for the Norwegian fish farms. Minimum, maximum and mean (±SD) values are shown.

Bath Treatment Pesticide	Lethal and Effective Threshold	Areal Extent of Impact Zones (km^2)			Radial Extent of Impact Zones (km)		
		Min	Max	Mean	Min	Max	Mean
Azamethiphos	LC_{50}	0.0	0.3	0.04 (±0.04)	0.0	5.0	0.04 (±0.04)
	EC_{50}	0.01	1.3	0.2 (±0.2)	0.1	18.5	1.3 (±1.4)
Deltamethrin	LC_{50}	0.1	87.9	21.1 (±13.9)	0.2	28.2	10.6 (±5.6)
	EC_{50}	0.1	144.2	39.0 (±26.5)	0.2	28.2	12.2 (±6.0)

Table 2
Summary of the areal and radial extent of the azamethiphos and deltamethrin LC_{50} impact zones around the selected fish farms. Minimum, maximum and mean (±SD) values are shown.

Farm	Azamethiphos						Deltamethrin					
	Areal extent (km^2)			Radial extent (km)			Areal extent (km^2)			Radial extent (km)		
	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.	Mean
A	0.00	0.2	0.02 ± 0.03	0.0	1.5	0.1 ± 0.3	3.5	29.4	8.6 ± 6.2	3.2	23.9	7.9 ± 5.6
B	0.01	0.1	0.02 ± 0.01	0.1	0.5	0.2 ± 0.1	8.5	37.4	20.8 ± 7.5	7.6	20.1	14.1 ± 3.4
C	0.01	0.3	0.07 ± 0.07	0.1	3.5	0.7 ± 0.9	16.9	87.9	42.2 ± 15.0	7.9	28.2	19.9 ± 6.5
D	0.00	0.2	0.05 ± 0.06	0.0	2.5	0.5 ± 0.6	8.4	26.5	15.7 ± 4.9	3.6	13.0	8.0 ± 2.9
E	0.01	0.1	0.05 ± 0.03	0.1	1.1	0.5 ± 0.3	16.6	52.0	31.0 ± 7.3	7.1	17.6	11.7 ± 2.7
F	0.00	0.2	0.06 ± 0.04	0.0	5.0	0.6 ± 1.0	12.5	59.0	23.5 ± 11.1	4.7	18.0	10.0 ± 3.9
G	0.01	0.2	0.04 ± 0.03	0.1	1.7	0.4 ± 0.4	14.6	57.3	30.0 ± 10.7	6.2	25.2	12.9 ± 5.1
H	0.01	0.1	0.03 ± 0.02	0.1	0.7	0.2 ± 0.2	16.0	79.7	36.9 ± 15.3	3.9	20.7	10.5 ± 4.2
I	0.00	0.2	0.06 ± 0.05	0.0	1.7	0.4 ± 0.4	0.1	51.9	28.7 ± 10.9	0.2	23.2	14.6 ± 5.5
J	0.00	0.1	0.05 ± 0.04	0.0	1.9	0.6 ± 0.5	7.8	79.6	31.7 ± 17.4	4.7	23.1	15.0 ± 5.5
K	0.00	0.1	0.02 ± 0.01	0.0	0.4	0.1 ± 0.1	3.8	24.5	8.0 ± 5.0	3.4	15.6	5.9 ± 2.7
L	0.00	0.3	0.06 ± 0.05	0.0	2.1	0.5 ± 0.4	7.4	43.9	25.1 ± 10.9	5.2	22.0	11.2 ± 4.5
M	0.01	0.1	0.02 ± 0.01	0.1	0.7	0.2 ± 0.1	10.3	36.8	21.2 ± 7.7	4.9	20.2	12.2 ± 5.0
N	0.01	0.2	0.06 ± 0.05	0.1	3.0	0.7 ± 0.7	16.1	52.8	30.6 ± 10.9	5.4	20.5	12.0 ± 4.6
O	0.00	0.2	0.05 ± 0.05	0.0	3.4	0.6 ± 0.3	6.2	38.5	16.1 ± 7.4	3.9	22.2	9.3 ± 4.7
P	0.01	0.1	0.04 ± 0.02	0.1	1.1	0.4 ± 0.3	12.7	51.7	27.1 ± 10.3	3.2	21.8	13.6 ± 6.4
Q	0.00	0.1	0.03 ± 0.03	0.0	2.4	0.4 ± 0.5	4.0	28.0	14.4 ± 5.2	2.5	18.0	11.7 ± 3.7
R	0.00	0.2	0.03 ± 0.05	0.0	3.6	0.5 ± 0.9	2.4	20.4	6.4 ± 3.8	1.8	8.2	4.4 ± 1.7
S	0.00	0.2	0.05 ± 0.04	0.0	3.5	0.6 ± 0.8	6.3	56.4	22.6 ± 14.9	3.9	24.3	12.2 ± 5.4
T	0.00	0.1	0.03 ± 0.02	0.0	1.8	0.5 ± 0.5	0.5	21.3	9.3 ± 5.7	1.6	10.7	6.5 ± 2.8
U	0.00	0.1	0.04 ± 0.03	0.0	2.7	0.7 ± 1.0	7.1	36.1	19.0 ± 7.0	3.2	18.4	10.0 ± 4.2
V	0.00	0.1	0.03 ± 0.03	0.0	3.6	0.6 ± 0.9	1.4	7.0	4.1 ± 1.7	1.5	6.7	4.6 ± 1.7
W	0.00	0.1	0.03 ± 0.02	0.0	1.0	0.2 ± 0.2	2.9	33.6	13.2 ± 7.2	2.3	14.6	6.8 ± 2.9

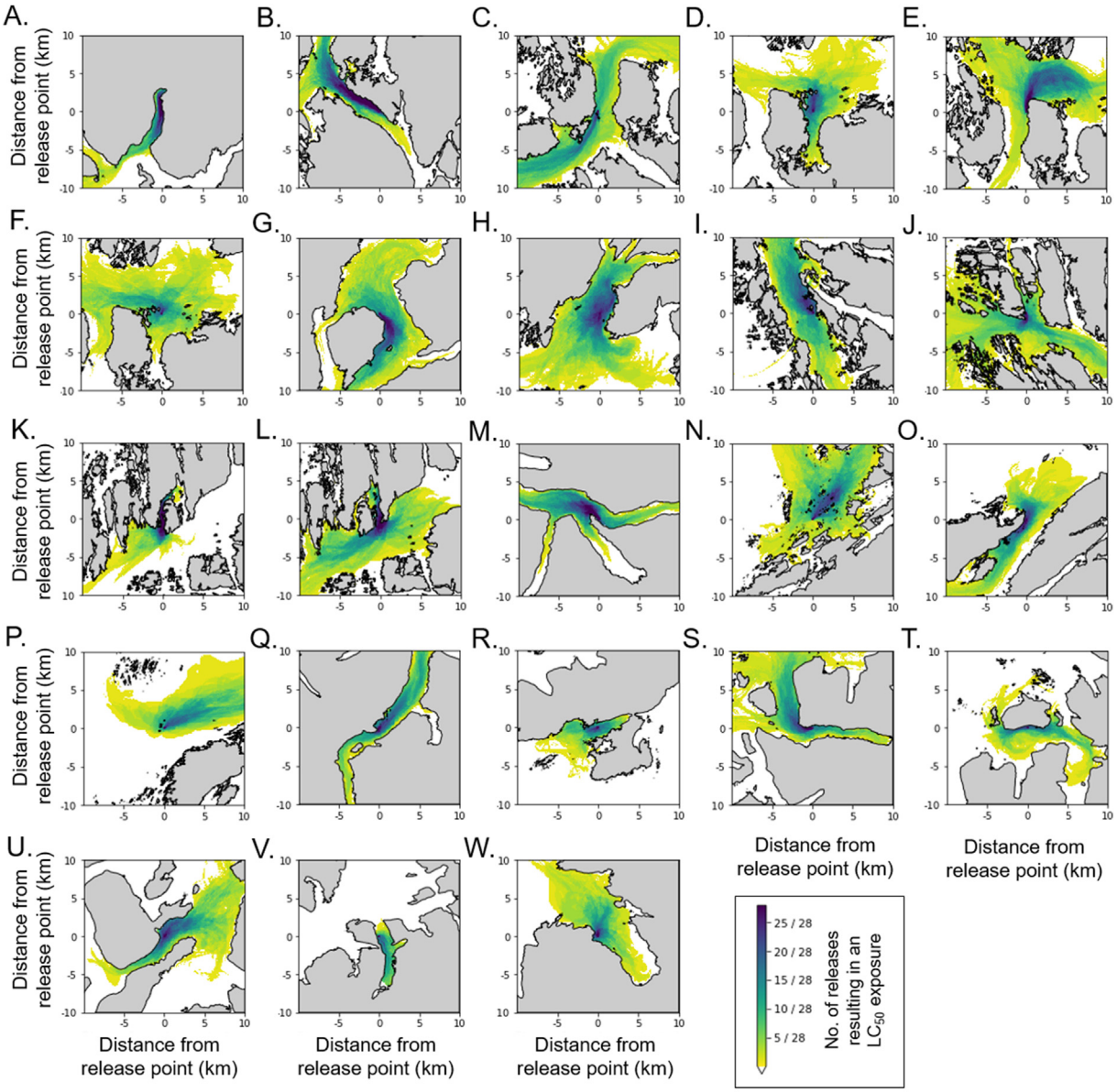
It is important to note that water chemistry was beyond the scope of the current study and therefore dose-response curves and the associated lethal and effective threshold concentrations were generated based on nominal concentrations and not measured concentrations. Previous studies, however, recovered and measured azamethiphos at concentrations consistent with the nominal concentrations (Burridge et al., 2014; Bechmann et al., 2020), which would suggest that the lobster larvae here were exposed to concentrations similar to the nominal concentrations. In contrast, in several studies deltamethrin was either not detected, below the limit of detection or measured at much lower concentrations than the nominal concentrations (Ernst et al., 2014; Burridge et al., 2014; Bechmann et al., 2020). Given that the larvae were severely affected after the 1 h exposure period in the present study, this suggests that deltamethrin was in fact present in the treatment water, however it should be considered that the threshold concentrations estimated here may underestimate the toxicity of deltamethrin.

3.2. Azamethiphos and deltamethrin impact zones

When all farms were considered together, the areas at risk of exposure to lethal concentrations of azamethiphos (corresponding to a dilution limit of 20%) were relatively small (Fig. 2, Table 1). For example, the mean (±SD) areal and radial extent of the azamethiphos LC_{50} impact zones were 0.04 (±0.04) km^2 and 0.4 (±0.6) km, respectively. The areas at risk of exposure to effective azamethiphos concentrations (corresponding to a dilution limit of 10%) were only slightly larger (Fig. S5, Table 1), with the mean (±SD) areal and radial extent of the EC_{50} impact zones calculated to be 0.2 (±0.2) km^2 and 1.3 (±1.4) km, respectively. A summary of the areal and radial extent of the lethal and effective azamethiphos impact zones for each farm is presented in Table 2 and Table S5, respectively.

While field measurements were beyond the scope of this study, previous studies have also shown the dispersal of azamethiphos from fish farms to be limited (Ernst et al., 2014; Langford et al., 2015). Very low concentrations of azamethiphos (26 ng L^{-1}), well below the lethal concentrations reported here for *H. gammarus*, were measured at the edge of a Norwegian fish farm 1 week following a bath treatment procedure and concentrations were reported to decrease with increasing distance from the farm (0.5 ng L^{-1} at 1000 m). It should be noted, however, that the long period between treatment and sampling may explain the low concentrations observed (Langford et al., 2015). The dispersal of azamethiphos from a Canadian fish farm was also limited in the 2–3 h after bath treatment releases. While relatively high

under various environmental conditions) whereas the yellow colour indicate areas which have experienced lethal concentrations of azamethiphos in a low proportion of simulated releases (i.e. under only very specific weather conditions). (X–Y) Boxplots showing the variation in the extent (areal and radial) of the LC_{50} impact zones at each farm (28 simulated releases were performed per farm). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)


A.
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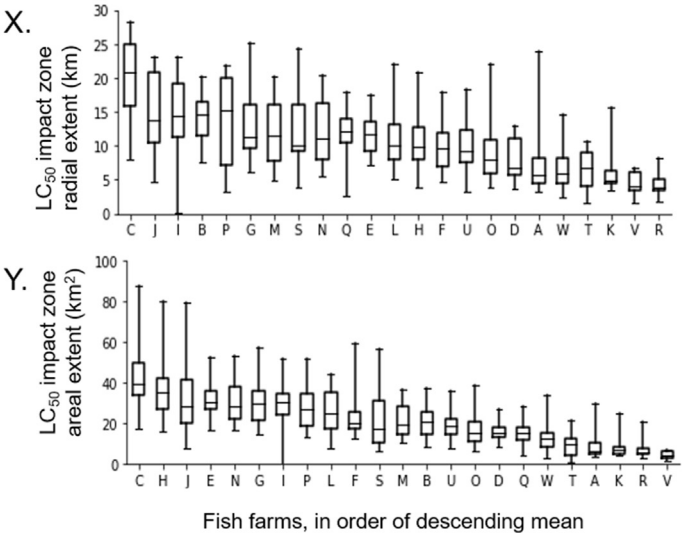
S.
T.
U.
V.
W.
Distance from release point (km)
Distance from release point (km)
25 / 28
20 / 28
15 / 28
10 / 28
5 / 28
No. of releases resulting in an LC50 exposure


X.
LC50 impact zone radial extent (km)
C J I B P G M S N Q E L H F U O D A W T K V R
Y.
LC50 impact zone areal extent (km2)
C H J E N G I P L F S M B U O D Q W T A K R V
Fish farms, in order of descending mean

concentrations of azamethiphos (25 μg L^{-1}), similar to the lethal concentrations observed in the present study, were measured in water sampled very close (within 1 m) to the edge of the pen, concentrations decreased significantly with increasing distance from the farm (approx. 1 μg L^{-1} was detected 1000 m from the cage) (Ernst et al., 2014). While our results are generally in line with these field based studies, in that areas likely to be exposed to high concentrations of azamethiphos appear to be small, the field studies may underestimate the size of the impacted areas. For instance, our results show that, on average, lethal concentrations of azamethiphos dispersed 400 m from a fish farm, in comparison to the field studies in which similar concentrations were only detected 1 m from a farm. This discrepancy is likely a result of the fact that concentrations measured don't necessarily reflect the maximum concentration that might occur in any given area. Water samples are taken at a single point in time and location, and any slight deviations from these may lead to a very different measurement. The discrepancy could also be a result of differences in the topography, geography, geology and ocean currents between Norwegian and Canadian farm sites. Indeed, we also found that the extent (both areal and radial) of the zones varied greatly between the Norwegian farms selected for this study. For example, the mean radial extent of the azamethiphos LC_{50} and EC_{50} impact zones varied between 0.1-0.7 km and 0.4–2.9 km across the selected farms, respectively. In addition, the extent of the impact zones varied substantially within the selected farms. For example, on Farm C the radial extent of the azamethiphos LC_{50} and EC_{50} impact zone varied between 0.1-3.5 km and 0.3–18.5 km, respectively (Table 1). This between-farm and in-farm variation in the extent of the impact zones suggests that the degree to which azamethiphos will negatively affect non-target species in the wild is likely to vary substantially between geographical regions and under different environmental conditions (e.g. ocean currents and weather).

Compared to azamethiphos, the deltamethrin LC_{50} impact zones (corresponding to a dilution limit of 0.1%) were extensive (Fig. 3, Table 1). When all farms were considered together, the mean (±SD) areal and radial extent of the deltamethrin LC_{50} impact zones were 21.1 (±13.9) km^2 and 10.6 (±5.6) km, respectively. Our results also show that even larger areas are at risk of exposure to effective concentrations of deltamethrin (Fig. S6, Table 1), with the mean (±SD) areal and radial extent of the EC_{50} impact zones (corresponding to a dilution limit of 0.02%) reaching 39.0 (±26.5) km^2 and 12.2 (±6.0) km, respectively. The areal and radial extent of the lethal and effective deltamethrin impact zones for each farm is presented in Table 2 and Table S5, respectively. Earlier field measurement studies from Canada have suggested that low levels of deltamethrin may disperse into large areas around fish farms, however our results suggest that the deltamethrin impact zones could be far larger than previously predicted. For example, low concentrations of deltamethrin (approx. 1 ng L^{-1}), similar to the lethal and effective concentrations observed here, were measured in water sampled 1000 m from a Canadian fish farm after bath treatment release (Ernst et al., 2014). Our results on the other hand indicate that these low levels of deltamethrin could disperse to a distance approximately 10x greater than that sampled in the Canadian study. Since the extent of the deltamethrin impact zones, like the azamethiphos impact zones, varied considerably both between and within farm sites, the impact on non-target species will depend on the specific geographical region and the weather conditions occurring at the time of treatment.

It is important to discuss our findings in relation to the underlying assumptions and limitations of the hydrodynamic model. It should be stressed that several of the assumptions assigned to the model could result in worst case scenario impact zones. For example, the model assumes that deltamethrin remains in the water and does not adsorb to organic matter for 24 h post release. Deltamethrin, however, has a high Log K_{ow} value (5.43) and therefore is likely to partition to the particulate phase soon after bath treatment releases (International Programme on Chemical Safety & World Health Organization, 1990; Muir et al., 1985). Particle-bound deltamethrin has a greater tendency to sequester to sediments and therefore some of the pesticide would adhere to the seafloor rather than transported over large distances. Consequently, the current model may overestimate the dispersal of deltamethrin and the extent of the potential impact zones. In addition, the model does not consider the length of time of pesticide exposure, but simply maps the areas around the farms that experience lethal/effective concentrations of the pesticides at any point during the 24 h simulation. The threshold concentrations selected here were based on a 1 h toxicity test but some areas around farms may experience these concentrations for much shorter periods of time. If this is the case, the impacts on non-target species in these areas may be less than the model predicts.

While the previous assumptions may result in the overestimation of the extent of the impact zones, other assumptions of the model may lead to an underestimation of their extent. For example, we have assumed the ocean to be pristine after each release, therefore there is no residual levels of the compound left in the water by the time the next release occurs. In reality, delousing operations with azamethiphos and deltamethrin can involve the concurrent and sequential applications of many pens within a single fjord. These treatment methods may result in cumulative loading of the pesticides and subsequently higher concentrations and larger impact zones around the farms. Future studies are necessary to further advance the model described here by incorporating absorption coefficients and allowing for multiple bath treatment releases, which would better reflect dispersal situations in the Norwegian marine environment. Finally, future work that robustly models the interactions between lobster larvae and contaminated plumes of water that are released from aquaculture sites would greatly increase our understanding of the impact of bath treatment pesticides on wild lobster populations. The hydrodynamic model described in this paper does, however, provides a first order estimate of the dispersal of both azamethiphos and deltamethrin into the Norwegian marine environment and their potential risk to wild lobster larvae after bath treatment releases from fish farms. Our results clearly demonstrate that large areas around aquaculture facilities are exposed to lethal and effective concentrations of deltamethrin following anti-sea lice treatments, and therefore this compound is likely to have widespread adverse effects on sensitive non-target crustacean species living in areas close to farms delousing with this compound. It is important to highlight, however, that the consumption of deltamethrin on Norwegian fish farms has reduced dramatically in recent years, with

Fig. 3. Deltamethrin LC_{50} impact zones. (A–W) Maps illustrating the areas around 23 Norwegian fish farms which, based on multiple dispersal simulations (covering a range of tide and weather conditions), experienced lethal concentrations of deltamethrin (2 ng L^{-1}) in the 24 h after the simulated release of a bath treatment effluent from a standard size salmon pen which had been treated at the recommended dose of 2 μg L^{-1}. The colour legend displays the number of releases which have resulted in an area experiencing a lethal concentration of deltamethrin. The dark blue colour indicates an area which has experienced lethal concentration of deltamethrin in a high proportion of simulated releases (i.e. under various environmental conditions) whereas the yellow colour indicate areas which have experienced lethal concentrations of deltamethrin in a low proportion of simulated releases (i.e. under only very specific weather conditions). (X–Y) Boxplots showing the variation in the extent (areal and radial) of the LC_{50} impact zones at each farm (28 simulated releases were performed per farm). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

only 10 kg of the active substance used in 2019 (Folkehelseinstituttet, 2019). Therefore, the use of deltamethrin may have population level effects on *H. gammarus* but only in very specific regions where the consumption is highest. In contrast to deltamethrin, the areas exposed to lethal and effective concentrations of azamethiphos are relatively small and therefore the impact of this compound will likely be less severe. These findings should be considered by legislators both in Norway and in other salmonid aquaculture regions around the world when carrying out future environmental risk assessments of these compounds and in assessing the potential risks associated with the expansion of aquaculture into new sites and increasing production at existing sites.

4. Conclusion

It is clear from the present study that deltamethrin is extremely toxic to *H. gammarus* larvae, in line with various other studies on non-target marine crustaceans. For the first time, we have demonstrated that azamethiphos is also acutely toxic to *H. gammarus* larvae following short 1 h exposures. The hydrodynamic model described in this paper assesses the dispersal of both azamethiphos and deltamethrin into the Norwegian marine environment and their potential risk to wild lobster larvae after bath treatment releases from fish farms. Our results clearly demonstrate that large areas around aquaculture facilities are exposed to lethal and effective concentrations of deltamethrin following anti-sea lice treatments, and therefore this compound is likely to have widespread adverse effects on sensitive non-target crustacean species living in these areas. On the other hand, the areas exposed to lethal and effective concentrations of azamethiphos are relatively small in comparison and therefore the impact of this compound is likely to be less severe.

Author contribution

The project was conceived and designed by all authors. AP, OS, REL, ALA carried out the exposure studies and AP performed data analysis. PNS performed mathematical modelling analyses. AP and PNS wrote the manuscript, with input from OS, REL and ALA.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2020.114725.

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