

Opinion

Data Review on the Variation in Sensitivity to Aquaculture Chemotherapeutants in Some Crustacean Life Stages

Sarah Marteinson ¹, Melanie Kingsbury ^{2,*}  and Dounia Hamoutene ²

¹ National Contaminants Advisory Group, Fisheries and Oceans Canada, Ottawa, ON K2P 2J8, Canada; sarah.marteinson@dfo-mpo.gc.ca

² St. Andrews Biological Station, Fisheries and Oceans Canada, St. Andrews, NB E5B 0E4, Canada; dounia.hamoutene@dfo-mpo.gc.ca

* Correspondence: melanie.kingsbury@dfo-mpo.gc.ca

Abstract: Aquaculture chemotherapeutants used to control sea lice in finfish aquaculture can disperse into the marine habitat and have the potential to affect non-target species like crustaceans. Some of the compounds used (especially in Canada) include in-feed drugs such as emamectin benzoate (EMB), and ivermectin (IVER), as well as bath pesticides such as azamethiphos (AZA) and hydrogen peroxide (HP). Despite the paucity of data, crustacean life cycle stages appear to have varying sensitivities to these compounds. This data review sets out to examine the intraspecies variation in sensitivity within life stages for lobster (*Homarus*) and prawn (*Pandalus*) species. Despite limited information, it appears that prawn eggs, adults, and juveniles are less sensitive to AZA and EMB compared with larvae, whereas for lobster the opposite is true: adults and juveniles are more sensitive than larvae to AZA (there was insufficient data to assess EMB). For HP, the sensitivity of prawn eggs appears comparable to larvae, but hatching success data suggest that this important stage of development is less impacted than eggs themselves as indicated by one study. These differences are important considerations for toxicity threshold determination processes and risk assessments, which ideally are environmentally relevant, and highlight the need for more data.

Keywords: aquaculture; life stage; crustaceans; anti-sea lice chemotherapeutants; toxicity

Key Contribution: This paper explores the variation in life stage sensitivity of crustaceans to drugs and pesticides used in aquaculture and highlights the need for relevant data when determining thresholds and risk assessments.



Citation: Marteinson, S.; Kingsbury, M.; Hamoutene, D. Data Review on the Variation in Sensitivity to Aquaculture Chemotherapeutants in Some Crustacean Life Stages. *Fishes* **2024**, *9*, 273. <https://doi.org/10.3390/fishes9070273>

Academic Editors: Aoife Elizabeth Parsons and Ann-Lisbeth Agnalt

Received: 10 June 2024

Revised: 4 July 2024

Accepted: 10 July 2024

Published: 11 July 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Salmon cage aquaculture production can result in the release of anti-sea lice drugs and pesticides into marine water and/or sediment matrices if they are released as either a bath or as in-feed medication. Azamethiphos (AZA), an organophosphate pesticide, and hydrogen peroxide (HP) are administered as baths and tend to stay in the water column [1]. AZA acts by inhibiting the activity of the enzyme acetylcholinesterase (AChE), affecting muscle stimulation in lice (e.g., [2–4]). The mode of action of HP is not well understood, however, since it is a strong oxidizer, it has been suggested that mechanisms occurring through peroxidation by hydroxyl radicals, and inactivation of enzymes and DNA replication can result in mechanical paralysis [5]. Mechanical paralysis can also occur with the formation of bubbles in the organism caused by the decomposition of HP into water and O₂ gas [6]. In-feed drugs EMB and IVER are avermectins, which function as neurotoxins by binding to the invertebrate glutamate-gated chloride ion channels, interrupting nerve impulses [7]. Both compounds are poorly soluble in water with a tendency to sorb to particles and sediment [8,9]. EMB also has the additional potential to function as an endocrine disruptor affecting the molt-inhibiting hormone in crustaceans [10].

Understanding the exposure risks of non-target species to these chemotherapeutants is complicated by the different niches they inhabit during their life cycle. Many crustaceans live in the pelagic zone as larvae and in benthic environments as adults. DNA barcoding has confirmed that planktonic larval stages in many cases are spatially separated from the benthic adults [11–13], wherein, larvae and adults are found in different areas [14] with distinct vertical distributions in the water column (e.g., [14,15]). For instance, decapod larvae are planktonic suspension feeders exhibiting swimming behavior, adult lobsters are benthic predators/scavengers utilizing legs for locomotion, while juveniles are benthic feeders, similar to adults, but inhabiting shallower areas closer to shore [16] at different depths [15]. Consequently, exposure to anti-sea lice compounds will vary not only by the drug administered and its behavior in the marine environment (e.g., water column for bath pesticides, sediments for in-feed drugs) but also by species and life cycle stages due to the differences in the zones occupied as well as sensitivity to a particular toxicant [17]. While for many species, younger animals are more sensitive than adults [18], this may not always be the case (e.g., [19]). In a review of EC50 and NOEC values for aquatic invertebrates, it was determined that for only 66% of compounds, EC50s of larvae were greater than or equal to those of juveniles [20,21].

The objective of the present review is to discuss differences in sensitivity between life stages for common marine crustacean genera used in toxicity tests for AZA, HP, EMB, and IVER. We considered published toxicity data recently used to develop Species Sensitivity Distributions (SSDs) for the determination of thresholds for these compounds [22–24]. For most compounds, there were only sufficient data available for *Homarus* spp. (lobster) and *Pandalus* spp. (prawn), thus, the discussion is limited to these species.

2. Approach Used for Data Review

Data on toxicity endpoints (EC50, LC50, and NOEC/LOEC) from published studies for the most well-studied taxa available were extracted from previous collection exercises (AZA, HP, EMB, IVER: [22,23]) that incorporated quality assessments [24–26]. These included lobsters (*Homarus gammarus*, *H. americanus*) and prawns (*Pandalus platyceros*, *P. danae*, *P. borealis*) (Supplemental table A.1 for EMB, B.1 for IVER included in Kingsbury et al. [22]; Table S1 for both AZA and HP included in Hamoutene et al. [24]). For each compound, we grouped data by species, endpoint, exposure type (water or sediment), and life stage (Tables 1 and 2). Though the option was thoroughly explored, for most data sets, other than one, there was insufficient sample size to run meaningful statistical comparisons and, therefore, our focus was on a qualitative commentary. Life stages for prawns were divided into egg (egg and egg to stage I), larvae (stage I–V), juvenile, and adult. Life stages for lobsters were divided into larvae (stage I–IV; largely planktonic), juvenile (V; mostly benthic), and adult. These stages were based on how they were classified in the studies referenced. Values were averaged and presented along with the maximum and minimum values and number of endpoints. Only one data set had enough values to conduct statistical analyses: LC50 for lobster exposed to AZA in water. Life stages for this endpoint were compared using a *t*-test: (larvae ($n = 18$) vs. juvenile (stage V)/adults ($n = 9$)).

Table 1. Summary of published data using *Pandalus* spp. For emamectin benzoate (EMB), azamethiphos (AZA), and hydrogen peroxide (HP) water exposures (summarized and quality controlled as per [22,23]).

Drug	Endpoint	<i>n</i>	Life-Stage	Endpoint Response	Concentration Min–Max (Average) in $\mu\text{g L}^{-1}$	Exposure Timeframe (min, h, d)
EMB	NOEC/LOEC	4	egg to stage 1	hatch success	300–1000 (650)	1–3 h
	NOEC/LOEC	6	juvenile	survival	100–500 (300)	24 h
	NOEC/LOEC	6	adult	survival	100–500 (300)	24 h
	EC50	2	egg	hatch success	>1200	1–3 h
	EC50	2	egg to stage 1	hatch success	605–926 (765.5)	1–3 h
	EC50	6	larvae	morbidity	321–489 (403.5)	1–3 h
	EC50	2	juvenile	morbidity	1321–1532 (1425.5)	1–3 h
	LC50	3	juvenile	mortality	482–670 (576.3)	24 h
	LC50	3	adult	mortality	738–927 (852.7)	24 h

Table 1. Cont.

Drug	Endpoint	<i>n</i>	Life-Stage	Endpoint Response	Concentration Min–Max (Average) in $\mu\text{g L}^{-1}$	Exposure Timeframe (min, h, d)
AZA	NOEC/LOEC	4	larvae	morbidity	110 (10–300)	1–3 h
	EC50	2	egg	hatch success	187–220 (203.5)	1–3 h
	EC50	2	egg to stage 1	hatch success	52–69 (60.5)	1–3 h
	EC50	6	larvae	morbidity	10–47 (28.3)	1–3 h
	EC50	2	juvenile	morbidity	178–236 (207)	1–3 h
	LC50	3	adult	mortality	17.1–39.8 (28)	3 × 1 h
HP	NOEC/LOEC	2	larvae	mobility	1000–3000 (2000)	1–3 h
	EC50	2	egg	hatch success	73,000–74,000 (73,500)	1–3 h
	EC50	2	egg to stage 1		118,000–249,000 (183,500)	1–3 h
	EC50	6	larvae		77,000–433,000 (209,833.3)	1–3 h
	EC50	2	juvenile		765,000–809,000 (787,000)	1–3 h
	LC50	2	adult	mortality	530–2700 (1615)	24–48 h

Table 2. Summary of published data using lobster (*Homarus* spp.) For emamectin benzoate (EMB), and azamethiphos (AZA) water exposures (summarized and quality controlled as per [22,23]).

Drug	End Point	<i>n</i>	Endpoint Response	Life-Stage	Concentration Min–Max (Average) in $\mu\text{g L}^{-1}$	Exposure Timeframe
EMB	LC50	1	mortality	larvae (IV)	>589	7 d
	LC50	1	mortality	adult	644	7 d
AZA	NOEC/LOEC	3	n/a, survival, behaviour	larvae (I–IV)	1–11.5 (7.8)	1 h–5 × 1 h
	NOEC/LOEC	2	n/a, behaviour	adult	1.03–2.9 (2.0)	30 min–1 h
	EC50	3	n/a	larvae (IV)	0.36–1.25 (0.7)	24–96 h
	LC50	18	Mortality	larvae (I–IV)	0.9–50.4 (16.3)	5 min–48 h
	LC50	1	Mortality	juvenile (V)	0.5	96 h
	LC50	8	Mortality	adult	0.216–24.8 (4.3)	1 h–48 h

3. Results and Discussion

Overall, this exercise highlights the paucity of data for all these aquaculture chemotherapeutants. For IVER, there was only data available for sediment exposure of stage IV lobster larvae, so no life stage comparisons could be discussed. HP had sufficient data for prawn to discuss EC50 endpoints. For EMB and AZA, both lobster and prawn had some data that could be commented on for differences in life-stage sensitivities for water exposures, but there was insufficient data for EMB sediment exposures. The lack of data for benthic life stages is noteworthy as EMB water exposures are not as environmentally relevant considering that EMB tends to sorb to particulate matter [10,27] and is thus expected to accumulate in sediment. This is supported by one study where 89% of EMB partitioned into sediment within the first 24 h in a water–sediment system [9].

Our data review suggests that there are differences in sensitivity between the life stages of lobster and prawn for all aquaculture therapeutants to varying degrees. For prawn, broadly speaking, it appears that eggs, adults, and juveniles are less sensitive to AZA and EMB compared with larvae (Table 1), whereas for lobster the opposite is true, adults and juveniles are more sensitive than larvae for AZA only (Table 2) with insufficient data to assess EMB. For HP, we can note that the sensitivity of prawn eggs appears comparable to that of larvae, but hatching success data suggest that this important stage of development was less impacted than eggs themselves as per the data generated by Mill and colleagues [28].

3.1. Prawn Data

Eggs appear to be less sensitive than other post-hatching life stages for both EMB and AZA EC50 data generated from water exposures and based on hatching success and morbidity as indicators. Conversely, sensitivity to HP decreases from egg to juvenile.

For post-egg stages, sensitivity to AZA seems to increase as prawns develop in the larval phases followed by a decrease in the juvenile stages [9,28]. Similar trends have been observed for smaller crustacean species. A recent study on life stages for *Gammarus pulex* and *Asellus aquaticus* exposed to imidacloprid, an agricultural insecticide, and one of its metabolites shows that for *G. pulex*, neonates were the most sensitive and that sensitivity decreased with an increase in age/size [29].

Low sensitivity to AZA in eggs might be attributed to the amount of the nervous system enzyme AChE present in the embryo, which is the target site for AZA's mode of action. A study by Lund et al. [30] found that there was no measurable AChE present up to stage IV embryos and concentrations of the enzyme were not significant until stages VI and VII. Consequently, the effects of organophosphate pesticide (chlorpyrifos or malathion) exposure were not apparent in prawn eggs until the later embryonic developmental stages close to hatching [30]. This is comparable to the results presented by Mill et al. [28] in terms of egg and egg-to-stage I sensitivity to AZA. In addition, eggs have protective layers and an ability to selectively osmoregulate [31,32]. The permeability of eggs changes at distinct stages of development from where little water enters (stage III) to an increase in water content as the egg develops to stage IV [31–33]. Permeability changes can influence the potential for exposure to chemicals depending on the length and timing of exposure and the exact phase of egg development [30].

Similar to the trends observed for AZA, sensitivity to EMB seems to increase as prawns develop in the larval phases followed by a decrease in the juvenile stages (Table 1; [28,34]). However, as stated above, in real-world settings, exposure to EMB in water is unlikely due to the chemical properties of EMB which cause it to sorb into sediment or onto particles quickly.

The decrease in sensitivity observed as prawns mature could be because immature forms are more susceptible to chemical disruptions as a result of their thinner, less complex carapaces [35] and the onset of rapid morphological changes that occur as adult structures form [18]. Crustacean larvae might also be more susceptible to toxic effects if they lack the systems required to eliminate toxins from the body [18]. This vulnerability, however, may cease once they are fully developed as is typical in crustaceans [18].

Exposure to HP exhibited a similar trend as EMB and AZA with larvae being more sensitive than juveniles; however, eggs exposed to HP were more sensitive than both larvae and juveniles, which was not the case for eggs exposed to either EMB or AZA. One possible explanation for the difference in sensitivity between these compounds could be the size of the molecules [36]. EMB has a molecular weight of ~1000 g/mol [7] (depending on the homolog) and AZA 325 g/mol [37], while the molecular weight of HP is 34 g/mol [38], which might make it easier for it to pass into eggs during osmoregulation. One study by Frantzen et al. [39] on the effects of HP on egg-carrying prawn found low sensitivity of the eggs; however, the concentration used in this study was low (1.6 mg L⁻¹) compared to 10 mg L⁻¹ used by Mill et al. [28], who observed eggs to be the most sensitive when looking at life stage differences. In addition, one study on HP exposure to sea lice eggs that used higher concentrations ([40]; 470–2000 mg L⁻¹) determined that there could be a direct effect on the egg membrane, disrupting the integrity of the egg sac and embryo [40], which presents a second possible explanation. They also observed that less mature eggs were more successful when hatching than eggs that were exposed closer to hatching [40]. This could have also been a factor in the results observed in the other study [28], as they were looking at hatch success and would have exposed more mature eggs.

3.2. Lobster Data

For AZA exposures, larval forms appear to be less sensitive than juveniles (stage V) or adults on average (LC50 and NOEC/LOEC endpoints—Table 2), which was confirmed with statistical analyses for LC50 only ($n = 10$ for juveniles/adults and $n = 18$ for larvae; $p = 0.003$). There were not enough data to explore the effects of the duration of exposure, though we can note an increase in sensitivity between short and prolonged exposures,

which is expected and noted by others (e.g., [41]). Burrridge et al. [42] showed no significant differences between LC50s of larvae and adult lobsters but a tendency towards a higher tolerance for AZA by larvae, which we can support herein with the results of additional studies. This trend may not be the same for sublethal impacts, however. In a study exploring environmentally relevant scenarios of exposures (pulse exposures, recovery), de Jourdan et al. [43] found that lobster larvae from all stages exhibited immobilization responses when exposed to greater than $2.0 \mu\text{g L}^{-1}$ of AZA with latent mortality and effects on molting less than 5 days after exposure. In the trials conducted with adults, all lobsters behaved normally while exposed to sublethal azamethiphos ($<0.09 \mu\text{g L}^{-1}$), but over the 21 days they were monitored, an increase in aggressive responses was recorded [43].

There is a complex interplay in lobster life histories that can affect the sensitivity of lobsters to AZA such as a balance between age, sex, life stage, timing of molting [34], and the amount of AChE present. Cenov et al. [44] determined that activity levels of AChE in Norway lobster (*Nephrops norvegicus*) can change due to seasonal variation and that there is a negative correlation with carapace length. They also suggest that there could be sex-related differences in the presence of this enzyme associated with behavior and the reproductive cycle of adults [44]. This variation in AChE levels throughout a lobster's life could imply that they might be more sensitive during periods of higher AChE activity such as during increased molting in young, small lobsters or spawning and incubation of females [44]. This could be part of the explanation for the higher sensitivity of advanced life stages in this species alongside other sublethal mechanisms of toxicity.

4. Conclusions and Recommendations

Despite limited information, this review highlights that there are life stage variations in sensitivity to aquaculture chemotherapeutants and it is dependent on the species, the compound, and its mode of action. Adult/juvenile lobsters are most sensitive (AZA) whereas for prawn, it is the larval stages that appear to have greater sensitivity compared with adults, juveniles, or eggs (except in the case of HP). Thus, in the context of crustacean life histories, caution should be taken before considering using endpoints from either larval, juvenile, or adult stages only as representative of the whole species. For example, the only available data for IVER were stage IV juvenile lobsters exposed in sediment and it may be problematic to use this single endpoint. This highlights the complexity of defining a species' sensitivity to exposures when they have complex life histories. In addition, the context of exposure scenarios in situ should be considered to incorporate other modifiers that we have discussed.

One instance where more complete information for a species is critical is in the development of species sensitivity distributions (SSDs) that are used to determine environmental quality standard (EQS) thresholds. These models are only as good as the data employed in their development, which can only be further strengthened by using protocols to select suitable and quality data [25] and adequate sample size and species representation [45–47]. However, SSD guidance dictates taking the lowest endpoint per species highlighting the potential of either overprotecting or underprotecting species when not enough data are available on the particular life stages that are most environmentally relevant for species with life stage differences [48,49].

Even beyond determining EQS, risk assessment of a toxic compound should include evaluation of various life stages along with the type of exposure expected (e.g., via water or sediment) based on the properties and environmental partitioning of the drug used to ensure toxicity data best reflects real-world scenarios (e.g., [50]). For species where life cycle stages are spatially separated, those with a higher potential for exposure to a contaminant would ideally be selected for inclusion. For example, benthic organisms could be exposed to plumes of a bath pesticide in shallow areas or to hydrophobic compounds via particles carrying a toxicant for in-feed compounds and water/sediment equilibrium timelines should also be considered. In general, there is a lack of sufficient toxicity data on aquaculture chemotherapeutants to accomplish this at this time, highlighting the need for

relevant research, which will improve our understanding of the unintended effects of these chemicals and allow for stronger statistical models.

Author Contributions: Conceptualization, D.H.; Formal Analysis, M.K., D.H. and S.M.; Data Curation, M.K.; Writing—Original Draft Preparation, M.K.; Writing—Review and Editing, S.M., M.K. and D.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Fisheries and Oceans Canada, CSRF AQ-22-01-06 (D. Hamoutene).

Institutional Review Board Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study.

Conflicts of Interest: The authors declare no conflicts of interest.

References

- Page, F.H.; Losier, R.; Haigh, S.; Bakker, J.; Chang, B.D.; McCurdy, P.; Beattie, M.; Haughn, K.; Thorpe, B.; Fife, J.; et al. *Transport and Dispersal of Sea Lice Bath Therapeutants from Salmon Farm Net-Pens and Well-Boats*; DFO Canadian Science Advisory Secretariat Research Document 2015/064; Canadian Science Advisory Secretariat (CSAS): Ottawa, ON, Canada, 2015; p. xviii + 148.
- Ernst, W.; Doe, K.; Cook, A.; Burrige, L.; Lalonde, B.; Jackman, P.; Aubé, J.G.; Page, F. Dispersion and Toxicity to Non-Target Crustaceans of Azamethiphos and Deltamethrin after Sea Lice Treatments on Farmed Salmon, *Salmo Salar*. *Aquaculture* **2014**, *424–425*, 104–112. [[CrossRef](#)]
- Kallander, D.B.; Fisher, S.W.; Lydy, M.J. Recovery Following Pulsed Exposure to Organophosphorus and Carbamate Insecticides in the Midge, *Chironomus Riparius*. *Arch. Environ. Contam. Toxicol.* **1997**, *33*, 29–33. [[CrossRef](#)] [[PubMed](#)]
- Canty, M.N.; Hagger, J.A.; Moore, R.T.B.; Cooper, L.; Galloway, T.S. Sublethal Impact of Short-Term Exposure to the Organophosphate Pesticide Azamethiphos in the Marine Mollusc *Mytilus Edulis*. *Mar. Pollut. Bull.* **2007**, *54*, 396–402. [[CrossRef](#)] [[PubMed](#)]
- Refseth, G.H.; Nøst, O.A.; Evensen, A.; Tassara, L.; Espenes, H.; Drivdal, M.; Augustin, S.; Samuelsen, O.; Agnalt, A.L. Risk Assessment and Risk Reducing Measures for Discharges of Hydrogen Peroxide (H₂O₂). Tromsø, Norway. 2019. Available online: <https://www.fhf.no/prosjekter/prosjektbasen/901416/> (accessed on 19 September 2023).
- Escobar-Lux, R.H.; Parsons, A.E.; Samuelsen, O.B.; Agnalt, A.L. Short-Term Exposure to Hydrogen Peroxide Induces Mortality and Alters Exploratory Behaviour of European Lobster (*Homarus Gammarus*). *Ecotoxicol. Environ. Saf.* **2020**, *204*, 111111. [[CrossRef](#)]
- Roberts, T.R.; Hutson, D.H. Macrocytic Insecticides. In *Metabolic Pathways of Agrochemicals: Part 2: Insecticides and Fungicides*; The Royal Society of Chemistry: Cambridge, UK, 1999; pp. 87–94, ISBN 9788578110796.
- Jacova, R.; Kennedy, C. Avermectin Toxicity to Benthic Invertebrates Is Modified by Sediment Organic Carbon and Chemical Residence Time. *Environ. Toxicol. Chem.* **2022**, *41*, 1918–1936. [[CrossRef](#)] [[PubMed](#)]
- Strachan, F.; Kennedy, C.J. The Environmental Fate and Effects of Anti-Sea Lice Chemotherapeutants Used in Salmon Aquaculture. *Aquaculture* **2021**, *544*, 737079. [[CrossRef](#)]
- Lumaret, J.; Errouissi, F.; Floate, K.; Römbke, J.; Wardhaugh, K.; Rombke, J.; Wardhaugh, K. A Review on the Toxicity and Non-Target Effects of Macrocytic Lactones in Terrestrial and Aquatic Environments. *Curr. Pharm. Biotechnol.* **2012**, *13*, 1004–1060. [[CrossRef](#)] [[PubMed](#)]
- Maslakova, S.; Ellison, C.I.; Hiebert, T.C.; Conable, F.; Heaphy, M.C.; Venera-Pontón, D.E.; Norenburg, J.L.; Schwartz, M.L.; Moss, N.D.; Boyle, M.J.; et al. Sampling Multiple Life Stages Significantly Increases Estimates of Marine Biodiversity. *Biol. Lett.* **2022**, *18*, 20210596. [[CrossRef](#)] [[PubMed](#)]
- Collin, R.; Venera-Pontón, D.E.; Driskell, A.C.; Macdonald, K.S.; Geyer, L.B.; Lessios, H.A.; Boyle, M.J. DNA Barcoding of Echinopluteus Larvae Uncovers Cryptic Diversity in Neotropical Echinoids. *Invertebr. Biol.* **2020**, *139*, e12292. [[CrossRef](#)]
- Palecanda, S.; Feller, K.D.; Porter, M.L. Using Larval Barcoding to Estimate Stomatopod Species Richness at Lizard Island, Australia for Conservation Monitoring. *Sci. Rep.* **2020**, *10*, 10990. [[CrossRef](#)]
- Katz, C.H.; Cobb, J.S.; Spaulding, M. Larval Behavior, Hydrodynamic Transport, and Potential Offshore-to-Inshore Recruitment in the American Lobster *Homarus Americanus*. *Mar. Ecol. Prog. Ser.* **1994**, *103*, 265–274. [[CrossRef](#)]
- Queiroga, H.; Blanton, J. Interactions between Behaviour and Physical Forcing in the Control of Horizontal Transport of Decapod Crustacean Larvae. In *Advances in Marine Biology*; Academic Press: San Diego CA, USA, 2004; Volume 47, ISBN 0120261480.
- Cobb, S. *The American Lobster: The Biology of Homarus Americanus*; University of Rhode Island: Kingston, RI, USA, 1976.
- Spurgeon, D.; Lahive, E.; Robinson, A.; Short, S.; Kille, P. Species Sensitivity to Toxic Substances: Evolution, Ecology and Applications. *Front. Environ. Sci.* **2020**, *8*, 588380. [[CrossRef](#)]
- Mohammed, A. Why Are Early Life Stages of Aquatic Organisms More Sensitive to Toxicants than Adults? In *New Insights into Toxicity and Drug Testing*; IntechOpen: Rijeka, Croatia, 2013. [[CrossRef](#)]
- Tangwancharoen, S.; Burton, R.S. Early Life Stages Are Not Always the Most Sensitive: Heat Stress Responses in the Copepod *Tigriopus Californicus*. *Mar. Ecol. Prog. Ser.* **2014**, *517*, 75–83. [[CrossRef](#)]
- Länge, R.; Hutchinson, T.H.; Scholz, N.; Solbé, J. Analysis of the ECETOC Aquatic Toxicity (EAT) Database II—Comparison of Acute to Chronic Ratios for Various Aquatic Organisms and Chemical Substances. *Chemosphere* **1998**, *36*, 115–127. [[CrossRef](#)]

21. Hutchinson, T.H.; Solbé, J.; Kloepper-Sams, P.J. Analysis of the ECETOC Aquatic Toxicity (EAT) Database. III—Comparative Toxicity of Chemical Substances to Different Life Stages of Aquatic Organisms. *Chemosphere* **1998**, *36*, 129–142. [CrossRef]
22. Kingsbury, M.; Marteinson, S.; Ryall, E.; Hamoutene, D. Considerations and Data Update for the Inference of Environmental Quality Standards for Two Avermectins Widely Used in Salmon Aquaculture. *Mar. Pollut. Bull.* **2024**, *201*, 116213. [CrossRef] [PubMed]
23. Hamoutene, D.; Marteinson, S.; Kingsbury, M.; McTavish, K. Species Sensitivity Distributions for Two Widely Used Anti-Sea Lice Chemotherapeutants in the Salmon Aquaculture Industry. *Sci. Total Environ.* **2023**, *857*, 159574. [CrossRef]
24. Hamoutene, D.; Ryall, E.; Porter, E.; Page, F.H.; Wickens, K.; Wong, D.; Martell, L.; Burrridge, L.; Villeneuve, J.; Miller, C. *Discussion of Environmental Quality Standards (EQS) and Their Development for the Monitoring of Impacts from the Use of Pesticides and Drugs at Marine Aquaculture Sites*; DFO Canadian Science Advisory Secretariat Research Document 2022/066; Canadian Science Advisory Secretariat (CSAS): Ottawa, ON, Canada, 2022; p. v + 68 + Lii.
25. Moermond, C.T.A.; Kase, R.; Korkaric, M.; Ågerstrand, M. CRED: Criteria for Reporting and Evaluating Ecotoxicity Data. *Environ. Toxicol. Chem.* **2016**, *35*, 1297–1309. [CrossRef]
26. CCME. A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life. In *Canadian Environmental Quality Guidelines*, 1999; Canadian Council of Ministers of the Environment: Winnipeg, MB, Canada, 2007.
27. Bright, D.A.; Dionne, S. *Use of Emamectin Benzoate in the Canadian Finfish Aquaculture Industry: A Review of Environmental Fate and Effects*; Environment and Climate Change Canada: Ottawa, ON, Canada, 2005; 74p.
28. Mill, K.; Sahota, C.; Hayek, K.; Kennedy, C.J. Effects of Sea Louse Chemotherapeutants on Early Life Stages of the Spot Prawn (*Pandalus platyceros*). *Aquac. Res.* **2021**, *53*, 109–124. [CrossRef]
29. Huang, A.; Roessink, I.; van den Brink, N.W.; van den Brink, P.J. Size- and Sex-Related Sensitivity Differences of Aquatic Crustaceans to Imidacloprid. *Ecotoxicol. Environ. Saf.* **2022**, *242*, 113917. [CrossRef]
30. Lund, S.A.; Fulton, M.H.; Key, P.B. The Sensitivity of Grass Shrimp, *Palaemonetes pugio*, Embryos to Organophosphate Pesticide Induced Acetylcholinesterase Inhibition. *Aquat. Toxicol.* **2000**, *48*, 127–134. [CrossRef]
31. Bas, C.C.; Ituarte, R.B.; Kittlein, M.J. Decapod Egg Membranes: Powerful Barriers or Regulatory Structures. *J. Exp. Biol.* **2022**, *225*, jeb244165. [CrossRef]
32. Charmantier, G.; Charmantier-Öaures, M. Ontogeny of Osmoregulation in Crustaceans: The Embryonic Phase1. *Am. Zool.* **2001**, *41*, 1078–1089. [CrossRef]
33. Charmantier, G.; Aiken, D.E. Osmotic Regulation in Late Embryos and Prelarvae of the American Lobster *Homarus americanus* H. Milne-Edwards, 1837 (Crustacea, Decapoda). *J. Exp. Mar. Bio. Ecol.* **1987**, *109*, 101–108. [CrossRef]
34. Mill, K.; Kennedy, C.J. Lethal and Sublethal Effects of the Anti-Sea Lice Formulation Salmosan® on the Pacific Spot Prawn (*Pandalus platyceros*). *J. World Aquac. Soc.* **2021**, *52*, 1243–1258. [CrossRef]
35. Anger, K. Contributions of Larval Biology to Crustacean Research: A Review. *Invertebr. Reprod. Dev.* **2006**, *49*, 175–205. [CrossRef]
36. Escher, B.I.; Berger, C.; Bramaz, N.; Kwon, J.H.; Richter, M.; Tsinman, O.; Avdeef, A. Membrane-Water Partitioning, Membrane Permeability, and Baseline Toxicity of the Parasitocides Ivermectin, Albendazole, and Morantel. *Environ. Toxicol. Chem.* **2008**, *27*, 909–918. [CrossRef]
37. Pest Management Regulatory Agency (PMRA). *Proposed Registration Decision PRD2016-25 Azamethiphos*; Pest Management Regulatory Agency: Ottawa, ON, Canada, 2016.
38. Solvay. Safety Data Sheet INTEROX® PARAMOVETM 50 Ver 1.04; Vol. 1.04. 2015. Available online: <https://www.solvay.com/en/downloadDocument?fileId=16381100&fileName=INTEROX%C2%AE%20PARAMOVE%C2%AE%2050&base=RCSEHS> (accessed on 27 June 2022).
39. Frantzen, M.; Bytingsvik, J.; Tassara, L.; Reinardy, H.C.; Refseth, G.H.; Watts, E.J.; Evenset, A. Effects of the Sea Lice Bath Treatment Pharmaceuticals Hydrogen Peroxide, Azamethiphos and Deltamethrin on Egg-Carrying Shrimp (*Pandalus borealis*). *Mar. Environ. Res.* **2020**, *159*, 105007. [CrossRef] [PubMed]
40. Aaen, S.M.; Aunsmo, A.; Horsberg, T.E. Impact of Hydrogen Peroxide on Hatching Ability of Egg Strings from Salmon Lice (*Lepeophtheirus salmonis*) in a Field Treatment and in a Laboratory Study with Ascending Concentrations. *Aquaculture* **2014**, *422–423*, 167–171. [CrossRef]
41. Pahl, B.C.; Opitz, H.M. The Effects of Cypermethrin (Excis) and Azamethiphos (Salmosan) on Lobster *Homarus americanus* H. Milne Edwards Larvae in a Laboratory Study. *Aquac. Res.* **1999**, *30*, 655–665. [CrossRef]
42. Burrridge, L.E.; Haya, K.; Zitko, V.; Waddy, S. The Lethality of Salmosan® (Azamethiphos) to American Lobster (*Homarus americanus*) Larvae, Postlarvae, and Adults. *Ecotoxicol. Environ. Saf.* **1999**, *169*, 165–169. [CrossRef] [PubMed]
43. de Jourdan, B.; Benfey, T.; Burrridge, L.; Surette, M.; McCarthy, A.F.; Barria-Araya, A.M.; Daoud, D. Evaluating Non-Lethal and Latent Effects of the Anti-Sea Lice Pesticide Azamethiphos on Larvae and Adults of the American Lobster (*Homarus americanus*). *Aquac. Res.* **2022**, *53*, 6355–6368. [CrossRef]
44. Cenov, A.; Linšak, D.T.; Perić, L.; Žurga, P.; Lušić, D.V.; Traven, L.; Linšak, Ž.; Pupavac, S.M.; Hamer, B.; Pelikan, J.; et al. Acetylcholinesterase Activity in Muscle Tissue of Norway Lobster *Nephrops norvegicus*: Importance of Body Size, Season, Sex and Naturally Occurring Metals. *Mar. Pollut. Bull.* **2024**, *200*, 116067. [CrossRef] [PubMed]
45. Carr, G.J.; Belanger, S.E. SSDs Revisited: Part I—A Framework for Sample Size Guidance on Species Sensitivity Distribution Analysis. *Environ. Toxicol. Chem.* **2019**, *38*, 1514–1525. [CrossRef]

46. TGD European Commission; Directorate-General for Health and Food Safety. *Technical Guidance for Deriving Environmental Quality Standards*; European Commission: Brussels, Belgium, 2018.
47. Warne, M.; Batley, G.; van Dam, R.; Chapman, J.; Fox, D.; Hickey, C.; Stauber, J. *Revised Method for Deriving Australian and New Zealand Water Quality Guideline Values for Toxicants—Update of 2015 Version. Prepared for Revision of the Australian and New Zealand Guidelines for Fresh and Marine Water Quality*; Australian and New Zealand G: Brisbane, QLD, Australia, 2018.
48. Water Framework Directive—United Kingdom Advisory Group (UKTAG). *UKTAG Environmental Quality Standards Recommendation for Emamectin Benzoate*; WFD-UKTAG: Bristol, UK, 2022.
49. Posthuma, L.; Traas, T.P.; Suter, G.W. (Eds.) *Species Sensitivity Distributions in Ecotoxicology*; Lewis Publishers: Boca Raton, FL, USA, 2002; ISBN 1566705789.
50. Sævik, P.N.; Agnalt, A.L.; Samuelsen, O.B.; Myksvoll, M. Modelling Chemical Releases from Fish Farms: Impact Zones, Dissolution Time, and Exposure Probability. *ICES J. Mar. Sci.* **2022**, *79*, 22–33. [[CrossRef](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.