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Review Article/ Derleme Makalesi

Toxic Effects of lambda-cyhalothrin and acetamiprid on aquatic species: What we know so far

Lambda-cyhalothrin ve acetamiprid'in sudaki türler üzerindeki toksik etkileri: Şimdiye kadar bilinenler

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Abstract
Worldwide, two families of phytopharmaceutical products are the most represented in daily use. These are the pyrethroid family of insecticides and the neonicotinoid family of insecticides. Studies show that these two families of pesticides can have a negative impact on aquatic species such as fish, amphibians and aquatic invertebrates due to their toxicity to these species. The literature review conducted on the toxic effects of Lambda-cyhalothrin and Acetamiprid on aquatic organisms highlights the potential environmental risks associated with the use of these insecticides. The studies reviewed indicate that both Lambda-cyhalothrin and Acetamiprid have toxic effects on a wide range of aquatic organisms, including fish, invertebrates, and algae. The effects can range from acute toxicity to sublethal effects such as changes in behavior, reproduction, and growth. However, it also highlighted the lack of studies on the impacts of these insecticides on mussels' species. This lack of research highlights the need for further studies to be conducted to fully understand the potential risks of these insecticides on mussels and other aquatic organisms.
Key Words : lambda-cyhalothrin, acetamiprid, aquatic species, toxicity

Öz
Dünya çapında, günlük kullanımda en çok temsil edilen iki fitofarmasötik ürün ailesi bulunmaktadır. Bunlar piretroid insektisit ailesi ve neonikotinoid insektisit ailesidir. Araştırmalar, bu iki pestisit ailesinin, bu türlere toksisiteleri nedeniyle balıklar, amfibiler ve suda yaşayan omurgasızlar gibi suda yaşayan türler üzerinde olumsuz bir etkisi olabileceğini göstermektedir. Lambda-sitalotrin ve Asetamipridin suda yaşayan organizmalar üzerindeki toksik etkileri üzerine yapılan literatür taraması, bu insektisitlerin kullanımıyla ilişkili potansiyel çevresel riskleri vurgulamaktadır. Gözden geçirilen çalışmalar, hem Lambda-cyhalothrin hem de Asetamiprid'in balıklar, omurgasızlar ve algler dahil olmak üzere çok çeşitli suda yaşayan organizmalar üzerinde toksik etkilere sahip olduğunu göstermektedir. Etkiler, akut toksisiteden davranış, üreme ve büyümedeki değişiklikler gibi ölümcül olmayan etkilere kadar değişebilir. Bununla birlikte, bu böcek öldürücülerin midye türleri üzerindeki etkileri üzerine yapılan çalışmaların eksikliğine de dikkat çekti. Bu araştırma eksikliği, bu böcek öldürücülerin midye ve diğer suda yaşayan organizmalar üzerindeki potansiyel risklerini tam olarak anlamak için daha ileri çalışmaların yapılması gerektiğini vurgulamaktadır.

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INTRODUCTION

Pesticides represent a major discovery in the field of agriculture, making it more modern and productive. The importance of these chemicals is verifiable by the figure they represent in the world market reaching millions of dollars[1]. This makes their massive use throughout the world not without consequences for our environment. Indeed, during the application of these chemicals on crops, it has been noted significant losses in nature of the order of 10% to 70% towards the soil against a dispersion in the air of the order of 30% to 50%[2].

According to the annual reports of the WHO, the cases of intoxication are constantly increasing with several thousand cases of mortality. These observations are most often made in rural areas where there is a lack of appropriate monitoring systems and where local communities do not have a good understanding of the rules of application, the doses to be applied, the protective tools, etc.[3,4] As an example of a pesticide-related tragedy, we have the poisoning that occurred in 1999 in the Republic of Benin, which cost the death of several people in the Borgou area, in the north-east of the country[5]. Similarly, in Chad, more than a dozen people met a tragic fate west of the capital city of Ndjamena, following the feeding of contaminated vegetables (salads) to the population[4]. Because of the existence of several families of insecticides, it is not always easy for users to have the best control of what they use. Worldwide, two families of phytopharmaceutical products are the most represented in daily use. These are the pyrethroid family of insecticides and the neonicotinoid family of insecticides[6].

Studies show that these two families of pesticides can have a negative impact on aquatic species such as fish, amphibians, and aquatic invertebrates due to their toxicity to these species. Neonicotinoids can also disrupt the development and reproduction of these species, as well as their immune systems. In addition, they can disrupt aquatic ecosystems by reducing biodiversity and altering food chains[7]. Pyrethroids are pesticides derived from the plant Pyrethrum, which are used to control insects in agriculture and in homes. Pyrethroids can affect the nervous system of aquatic species, resulting in behavioral disturbances and mortality. They can also interfere with the development and reproduction of these species, as well as their immune systems. Pyrethroids can also disrupt aquatic ecosystems by reducing biodiversity and altering food chains[8]. Some countries have taken steps to reduce the use of these pesticides to protect aquatic species[9].

Among these different groups, Lambda-cyhalothrin and Acetamiprid are recognized as the two most used pesticides throughout the world and particularly in many developing and developed countries, whether by large cotton producers or by certain producers of cereals and vegetables.[10,11,12]

GENERAL PROPERTIES OF NEONICOTINOIDS AND ACETAMIPRID

Neonicotinoid insecticides are synthetic analogues of nicotine, which is a naturally occurring alkaloid extracted from tobacco leaves, used for centuries as an insecticide[13]. Like almost all available insecticides, neonicotinoids are neurotoxicants: their target is the postsynaptic acetylcholine receptor, the blockage of which induces paralysis and death of the insect[14]. The approach adopted to develop neonicotinoids, i.e. to reproduce the pharmacological activity of nicotine by increasing the selectivity towards insects in order to limit the toxicity in mammals, was in all respects similar to the one conducted with pyrethroids, analogues of the natural pyrethrins present in the flowers of certain varieties of chrysanthemums[15].

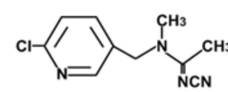
To obtain agriculturally usable compounds, chemists have had to increase the light stability and hydrophobicity of the molecules, which is necessary to penetrate the chitin envelope of pests.[14]. Very little resistance has developed in insects, unlike what has been observed with other classes, including pyrethroids. The neonicotinoids are a group of chemical substances used exclusively for their insecticidal action in agriculture and for their biocidal action in the domestic and professional fields. Seven neonicotinoid substances are (or have been) exploited since their market introduction in the used exclusively for their insecticidal action in agriculture and for their biocidal action in the domestic and professional fields. Seven neonicotinoid substances are (or have been) exploited since their market introduction in the 1990s: clothianidin, dinotefuran, imidacloprid, nitenpyram, thiacloprid, thiamethoxam, and acetamiprid[16,17].

Although the leader of the neonicotinoids is imidacloprid, ACE has become a staple in pesticide use since its synthesis in 1989 and its release in 1995 under the commercial formulation Supreme® for foliar application.[18]

Its importance stems from the fact that it is used in the overall protection of a variety of crops due to its broad spectrum of efficacy, systemicity, translaminar action, residual activity, and unique mode of action[19]. Thus, it is used in the Beninese cotton crop to control pests[11]. Studies have shown that acetamiprid is a mobile compound, rapidly biodegradable in soil[20].

Acetamiprid is a systemic insecticide, meaning that after treatment, it penetrates plants (via their root or foliar systems) and is transported throughout the plant's organism[21].It is used in the treatment of fruit trees, rose bushes, cereal and beet seeds, as well as in the treatment of buildings or domestic animal premises.[22] Against a large number of sucking insects (aphids, white flies, thrips, leafhoppers), butterfly caterpillars. Its versatile use makes it a widely used insecticide throughout the world. The following table presents the main physical-chemical and biological properties of this product.

Table 1: Molecular structure and physicochemical properties of Acetamiprid (ACE) [23, 24]

Parameters	**Common name**	**CAS**	**Chemical name**	**Chemical formula**	**Molecular structure**
Molecular characteristics	Acetamiprid (ACE)	35410-20-7	(*E*)-*N*1-[(6-chloro-3-pyridyl)methyl]-*N*2-cyano-*N*1-methylacetamidine	C10H11ClN4	
Physicochemical properties of Acetamiprid	**Molecular weight (g/mol)**	**Pressure of vapour (mm Hg)**	**Henry's constant (atm m3 mol-1)**	**Solubility (mg/l)**	**Log Koc**
	222.7	4.4x10-5	6.9 x 10-8	2950 – 4200	2.12 – 2.43
	Log Koe	**pKa**	**TD50 soil (days)**	**TD50 hydrolysis water (days)***	**TD50 photolysis water (days)**
	0.80	0.7	2 – 450	Stable ; 420 (pH=9)	34

Under acidic or neutral pH conditions, the compounds are stable to hydrolysis, while under alkaline conditions (pH 9), hydrolysis may occur. Koc = organic carbon/water partition coefficient; Kow = octanol/water partition coefficient; pKa = dissociation coefficient; TD50 soil = half-life of neonicotinoids in soil; TD50 sediment = half-life of neonicotinoids in sediment; TD50 hydrolysis water = half-life of neonicotinoids by hydrolysis in water; TD50 photolysis water = half-life of neonicotinoids by photolysis in water.

Jeschke et al.[13] identified a potential harmful effect on the development of neurons and brain structures in a fetus or young child. Cardiac and respiratory failure results in death within hours. Inhalation of acetamiprid dust results in mouth and lung irritation with bronchial hypersecretion[25]. The Canadian Pest Management Regulatory Agency (CPMA) considers acetamiprid to be a potential endocrine disruptor and suspects reproductive effects in mammals and birds primarily affecting the thyroid[13,26,27].

Due to its high solubility, acetamiprid (ACE) may persistent in aquatic environment. Residues of acetamiprid (2 ng/L to 410 µg/L) were detected in surface water bodies around the world[28,29]. In addition, neonicotinoid pesticides pose a risk to non-target aquatic organisms because of their solubility in water and ease of transmission to aquatic environments[30]. Numerous studies have been conducted to evaluate the effects of ACE on non-target organisms, particularly aquatic organisms. This has resulted in a variety of responses over different exposure periods at different dose levels.

Neonicotinoid insecticide acetamiprid is frequently used in agriculture to control a wide range of pests, such as leafhoppers, aphids, and pests of leafy vegetables[31]. Only 2–20% of acetamiprid, which is primarily applied as a foliar spray, is absorbed by plants; the remainder is released into the environment[32]. Acetamiprid is highly water soluble and mobile, has a half-life of 420 days in water, and can contaminate the surface of water bodies through drift, soil runoff, and rainwater washout. Acetamiprid is one of the most common neonicotinoids detected in aquatic ecosystems and its residual concentrations in surface water are 2–410 µg/L worldwide, threatening the health of aquatic untargeted organisms[33,34,35]. Ma et al.[33] found that acetamiprid impairs growth and causes morphological abnormalities in zebrafish embryos. Cossi et al.[12] reported that, after 14 days of exposure to both 150 µg/L and 1500 µg/L CEA, a significant increase in carboxylase activity, glutathione S-transferase activity, glutathione content, and a decrease/inhibition of catalase activity, oxygen species levels and superoxide dismutase at both concentrations were observed in the freshwater gastropod *Biomphalaria straminea* (adult). Acetamiprid primarily affects antioxidant and detoxification biomarkers, according to Cossi et al.[12], indicating that toxicity pathways are connected to the metabolism of detoxification and oxidation in *Biomphalaria straminea*. Demirci and Güngördü[36] determined that acetamiprid can significantly affect the activity of biochemical marker enzymes, for example, carboxylesterase, in *Gambusia holbrooki.* Turan and Ergenler[37] investigated the genotoxic effect of acetamiprid on *Cyprinus carpio* and found that the frequency of micronuclei and DNA strand breaks was significantly increased, demonstrating the genotoxic potential of acetamiprid in fish.

The lipophilic nature of neonicotinoids such as acetamiprid facilitates their passage through all biological barriers[38]. The digestive distribution is rapid and complete, and the plasma peak is obtained at the second hour

Veedu et al.[35] investigated the toxicity of ACE to freshwater fish (*Catla catla*) based on biochemical indices and antioxidant enzyme activities. After 96 h of exposure to ACE concentrations of 00.5 mg/L and 1 mg/L, they concluded that the LPO level in gill tissues of exposed fish increased significantly, while the levels of glutathione peroxidase (GPx), catalase (CAT), glutathione-S-transferase (GST) and reduced glutathione (GSH) in the gills decreased significantly. Acetamiprid and its formulations (Mospilan) at 0.01 and 0.1 mg/mL inhibited VD4-RPeD1 in the freshwater gastropod *Lymnaea stagnalis*[39].

The study by Jiao et al.[40] on *Xenopus laevis* focused on the biochemical and histopathological responses of this species following exposure to ACE concentrations in the range of 1/10 and 1/100 LC_{50}, with an LC_{50} equivalent to 64.48 mg/L. The results demonstrated that, after 28 days of exposure at those concentrations, acetamiprid exposure significantly changed the oxidant status of and caused histological damage to the liver. Furthermore, the untargeted metabolomic analysis based on liquid chromatography-tandem mass spectrometry (LC-MS/MS) identified the endogenous metabolites that were significantly altered. There were 89 differential metabolites compared to the controls. The molecular details of the hepatotoxic effects of acetamiprid on *X. laevis* were revealed by the disruption of sixteen pathways, mostly related to amino acid metabolism and lipid metabolism, including sphingolipid metabolism, glycerophospholipid metabolism, and histidine metabolism.

ACE treatments on zebrafish brain and liver exposure on zebrafish brain and liver resulted in oxidative effects in both fish organs, with the greatest adverse effects in the brain compare to the results obtained with other compounds (Carbamazepine and cadmium) during the same experiments.[4]

Table 2: Potential Effects of Acetamiprid on Aquatic Organisms[42]

Organisms	Parameters	Duration of exposure	Value (mg/L)
		Aquatic invertebrates	
Aedes aegypti	LC_{50}	24 h	0.65
		48 h	0.329
	LC_{50}	24 h	1.11
Americamysis bahia	LC_{50}	24 h	0.066
Cheumatopsyche brevilineata	EC_{50} (mobility)	96 h	0.00335
Chironomus tepperi	LC_{50}	48 h	0.0022
Culex pipiens	LC_{50}	48 h	0.454
		72 h	0.18 0.296 0.1 0.026
Daphnia magna	EC_{50} (mobility)	24 h	50
Gammarus fossarum	LC_{20}	7 days	0.02134 0.329
Gammarus pulex	LC_{50}	96 h	0.05
Hexagenia sp.	LC_{25}	96 h	0.055
	LC_{50}		0.78
Simulium latigonium	LC_{50}	96 h	0.00373
Fish			
Cyprinodon variegatus	LC_{50}	96 h	100
Danio rerio embryos			13.33
Danio rerio juveniles			36.91
Lepomis macrochirus			> 119.3
Oncorhynchus mykiss			> 100

EC50: concentration of a substance that affects 50% of the test organisms; LC20: lethal concentration of a substance to 20% of test organisms; LC25: the lethal concentration of a substance in 25% of the test organisms; LC_{50}: the lethal concentration of a substance in 50% of the test organisms.

GENERAL PROPERTIES OF LAMBDA-CYHALOTHRIN

Lambda-cyhalothrin (LCH or λ-cyhalothrin) is a chemical compound, which belongs to the family of synthetic pyrethroids (type II), used as an active ingredient in several insecticides. It is commonly used against crop pests (wheat, grapevine, cotton, etc.) across several agricultural areas but also against some external pests, e.g. domestic insects[43]. It is used for the control of various vineyard pests, including moths, leafrollers, leafhoppers and thrips.

Table 1: Description of Lambda-cyhalothrin[44]

Parameter	Name or number
Common name	Lambda-cyhalothrin
Chemical name	1:1 mixture of (*S*)-α-cyano-3-phenoxybenzyl (*Z*)-(1*R*,3*R*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate and (*R*)-α-cyano-3-phenoxybenzyl (*Z*)-(1*S*,3*S*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate
CAS number	91465-08-6
Mode of action	Pyrethroid: interaction with pre-synaptic sodium channels.

LCH is a substance capable of either killing or repelling the pests. It is one of the most widely utilized pyrethroids in the world[44] due to its advantages in terms of effectiveness and less toxicity[46]. This active substance consists of two of the four enantiomeric forms of cyhalothrin.

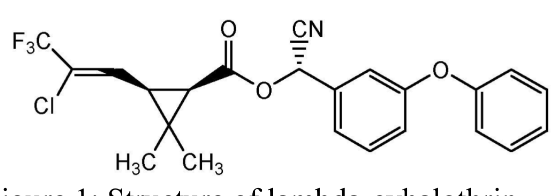


Figure 1: Structure of lambda-cyhalothrin

Lambda cyhalothrin is mainly used to control defoliator caterpillars (caterpillars that eat leaves). It is also used to control tomato moth, aphids, leafhoppers and cucurbit flies (melon, squash). Lambda cyhalothrin is more rarely offered for control of thrips and whitefly.

Table 2: Lambda-cyhalothrin physico-chemical proprieties[44]

Parameter	Unit	Value	Remark
Molecular weight	[g/mol]	449.9	
Water solubility	[mg/L]	0.004	20°C, pH 5
		0.005	20°C, pH 6.5
		0.004	20°C, pH 9.2
pK_a	[-]	>9	No dissociation at environmentally relevant pH values
Log K_{ow}	[-]	7	20°C
Log K_{oc}	[-]	5.20	Mean of 4.58, 4.68, 5.30 and 5.54
Vapour pressure	[Pa]	$2x10^{-7}$	20°C, extrapolated
Melting point	[°C]	49.2	
Boiling point	[°C]	-	No measurable boiling point (decomposes)
Henry's law constant	[Pa.m3/mol]	0.02	20°C

TOXICITY OF LAMBDA-CYHALOTHRIN ON AQUATIC SPECIES

Pyrethroids have been linked to a variety of organic effects in fish, as well as the induction of morpho functional changes in several tissues[47]. Due to the lipophilicity, pyrethroids have a raised absorption in the gill, which contribute to the fish sensibility. These, in turn, seem to be deficient in enzymatic pathways that hydrolyze the pyrethroids[48].

Zhan et al.[48] reported that LCH showed a toxicity of the order of 0.0074 mg/L, corresponding to the 72-hour LC_{50} value. As an enzymatic response to this effect, the antioxidant enzyme CAT and the apoptotic enzyme caspase 3 were significantly altered; likewise, more significant changes were found in the mRNA expression of five genes. With a 96h-LC_{50} equal to 1.48 µg/L and during a 45-day exposure to environmentally relevant concentrations of Lambda-cyhalothrin, organisms of the species *Cyprinus carpio* L. suffered from an alteration of their acute survivability and activity of hematological, plasma biochemical, and enzymological and stress parameters (in gills and liver) [49]. After an examination of the 96 h LC_{50} value of lambda-cyhalothrin to *Tubifex tubifex* that is 0.13 mg/L, Chatterjee et al.[50] concluded that the different concentrations of lambda-cyhalothrin (0.013 and 0.026 mg/L) caused significant alterations in growth rate and oxidative stress enzymes in *T. tubifex* during 14 days exposure period. This insecticide has the potential to cause effects on aquatic life with the ability to perturb the normal trophic balance through the toxicity study of this compound on the fish organism. In fact, the median lethal concentration (LC_{50}) of LCH on guppy fish (*Poecilia reticulata* Peters, 1859) is 81.83 µg/L[51]. After chronic exposure of *Oreochromis niloticus* to the sublethal dose (0.86 µg/L) of lambda-cyhalothrin, there was an impairment of neuronal motor function in fish[47].

Through their investigation of the effect of Lambda-cyhalothrin on the activity and variables like heart rate and thoracic limb activity. In the brackish water system, it was found that LCH can affect the organism of fish. Indeed, following exposure of *Sarotherodon melanotheron* to the 96 h LC_{50} of HCLs (9 mg/L), alterations in the gills of the species were observed[53]. For *Oreochromis niloticus*, the LC_{50} (96 h) value of lambda-cyhalothrin was determined as 2.901 µg/L. After exposure of this fish to 0.48 µg/L (1/6 of the 96-h LC_{50}) lambda-cyhalothrin, this pesticide caused oxidative stress in the liver of *Oreochromis niloticus* with adaptive response supplied against oxidative stress by GSH metabolism[54]. Alvim et al.[55] reported that LCH caused DNA damage in different tissues and ENA in erythrocytes of *Prochilodus lineatus* after exposure to 0.15 µg/L. In the same experiment, LCH was found to be the most toxic insecticide, even at much lower concentrations than imidacloprid, causing DNA damage in all tissues analyzed, indicating that the effect of the mixture is mainly due to the presence of the pyrethroid.

According to some studies, the insecticide LC is extremely toxic to various fish species, as indicated by the values of the mean lethal concentration (LC_{50} – 96 h), which range from 0.008 µg/L for the sheepshead minnow *Cypronodum variegatus* up to 0.24 µg/L for the rainbow trout *Oncorhynchus mykiss*[43].

Table 5: Effects of lambda-cyhalothrin on selected freshwater species[44]

Chronic[a] **Taxonomic group**	Unit **NOEC/EC_{10} (µg/L)**	**Acute**[a] **Taxonomic group**	Remark **L(E)C_{50} (µg/L)**
Algae		Algae	
Pseudokirchneriella subcapitata	> solubility	*Pseudokirchneriella subcapitata*	> solubility
Crustacea		Crustacea	
Daphnia magna	**0.002**[b]	*Asellus aquaticus*	0.0248[c]
		Cyclops sp.	0.3
		Daphnia galeata	0.117
		Daphnia magna	0.39
		Hyalella azteca	0.0023
		Ostracoda	3.3
		Simocephalus vetulus	0.957
		Insecta	
		Caenis horaria	0.0136
		Corixa sp.	0.03
		Sialis lutaria	0.028
		Arachnida	
		Hydrocarina	0.047
		Pisces	
		Cyprinus carpio	0.50
		Gasterosteus aculeatus	0.49
		Ictalurus punctatus	0.16
		Lepomis macrochirus	0.21
		Leucistus idus	0.08
		Onchorhynchus mykiss	0.24
		Oryzias latipes	1.60
		Pimephales promelas	0.70

CONCLUSION

In conclusion, the literature review conducted on the toxic effects of Lambda-cyhalothrin and Acetamiprid on aquatic organisms highlights the potential environmental risks associated with the use of these insecticides. The studies reviewed indicate that both Lambda-cyhalothrin and Acetamiprid have toxic effects on a wide range of aquatic organisms, including fish, invertebrates, and algae. The effects can range from acute toxicity to sublethal effects such as changes in behavior, reproduction, and growth. These findings suggest that the use of these insecticides in areas near aquatic habitats can have negative impacts on aquatic organisms and the ecosystem as a whole.

However, it also highlighted the lack of studies on the impacts of these insecticides on mussel's species. Despite mussels being an important part of aquatic ecosystems, little is known about the potential effects of these insecticides on these organisms. This lack of research highlights the need for further studies to be conducted to fully understand the potential risks of these insecticides on mussels and other aquatic organisms. Additionally, it is important for decision-makers and stakeholders to consider the use of alternative pest management methods, such as integrated pest management, to reduce the use of insecticides near aquatic habitats and to protect the aquatic biodiversity. It is imperative to consider the impacts of these insecticides on all aquatic species, including mussels, to have a comprehensive understanding of the effects on aquatic ecosystems.

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