

**Acetamiprid & Cypermethrin Exposure Mediated Toxicity: A Review of
Its Effect on Ecosystem Health**

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Abstract

The widespread use of acetamiprid, a neonicotinoid insecticide, and cypermethrin, a synthetic pyrethroid, has raised significant environmental concerns due to their frequent co-occurrence in agricultural landscapes. While acetamiprid targets insect nicotinic acetylcholine receptors, causing neural overstimulation, cypermethrin disrupts sodium channel function, leading to rapid neurotoxicity. Their distinct mechanisms of action and persistent environmental presence make their combined impact on non-target organisms and ecosystems particularly complex and underexplored. This review systematically synthesizes current scientific findings on the joint environmental and toxicological effects of acetamiprid and cypermethrin, with an emphasis on ecosystem health. Drawing exclusively from PubMed-indexed research, it examines their occurrence in soil, water, and air, evaluates their individual and combined toxicity to aquatic life, terrestrial wildlife, and livestock, and explores mechanisms of synergistic, additive, and antagonistic interactions. The review also assesses the environmental fate, degradation dynamics, bioaccumulation potential, and the risk of biomagnification through food webs. Given the prevalence of pesticide mixtures in the environment, reliance on single-compound risk assessments may underestimate ecological threats. By focusing on the combined effects of these two widely used pesticides, this review highlights the need for more integrative and realistic environmental risk assessment frameworks. Ultimately, it aims to support the development of more effective management strategies for mitigating the adverse ecological impacts of pesticide mixtures.

Keywords: Acetamiprid, cypermethrin, Ecosystem health, Synergic toxicity, bioaccumulation, biomagnification

Introduction:

Acetamiprid, a widely employed neonicotinoid insecticide, acts by selectively binding to and activating the postsynaptic nicotinic acetylcholine receptors (nAChR) in insects.¹ This interaction leads to an overstimulation of the nervous system, resulting in abnormal excitation, convulsions, paralysis, and ultimately, mortality in target pests.¹ Its systemic properties allow for effective control of a broad spectrum of sucking insects across various agricultural crops.⁵ The perceived lower toxicity of acetamiprid to mammals in comparison to older classes of insecticides has contributed to its increased adoption in modern agricultural practices.⁵ Cypermethrin, a synthetic pyrethroid insecticide, is recognized for its broad-spectrum activity against a wide range of insect pests.⁷ Its primary mode of action involves disrupting the normal functioning of the insect nervous system by interfering with the kinetics of voltage-gated sodium channels in nerve cell membranes.⁸ This disruption leads to a rapid onset of neurotoxic symptoms, including incoordination, paralysis, and death.⁷ Despite its effectiveness in pest

control, cypermethrin is known for its high toxicity to aquatic organisms, raising environmental concerns regarding its use, particularly in proximity to water bodies.⁷

The distinct biochemical targets and modes of action of acetamiprid and cypermethrin suggest that their co-occurrence in the environment could lead to complex toxicological outcomes. Acetamiprid's influence on cholinergic neurotransmission contrasts with cypermethrin's impact on sodium channel dynamics. Understanding these fundamental differences is essential for predicting the potential interactions and combined effects when these compounds are present simultaneously in ecosystems. The possibility of additive, synergistic, or antagonistic effects underscores the need to move beyond single-compound risk assessments to evaluate the ecological hazards posed by their combined exposure.

In contemporary agricultural landscapes, the application of multiple pesticides, either concurrently or sequentially, is a common practice.¹² This results in the frequent co-occurrence of various pesticidal compounds, including acetamiprid and cypermethrin, in environmental matrices such as soil, water, and air.¹² Consequently, non-target organisms in these ecosystems are often exposed to complex mixtures of pesticides rather than single compounds in isolation. The toxicological effects of pesticide mixtures on organisms and ecosystem processes can deviate substantially from the effects observed when individual compounds are studied in isolation.² Interactions within these mixtures can lead to synergistic effects, where the combined toxicity is greater than the sum of the individual toxicities, or antagonistic effects, where the combined toxicity is less than expected.² Such synergistic interactions can amplify the risks to ecosystem health, potentially causing more severe impacts on non-target organisms and ecological functions than anticipated from assessments of single pesticide exposures. Given the widespread agricultural use of both acetamiprid and cypermethrin, a comprehensive understanding of their combined impact on non-target organisms and ecosystem processes is crucial for informed environmental management and the development of effective risk mitigation strategies.¹⁵ Therefore, evaluating the ecological risks associated with these pesticides in isolation may not accurately reflect the real-world threats posed to ecosystem health due to the common occurrence of pesticide mixtures in the environment. A focused investigation into their combined effects is essential for a more realistic and protective assessment of ecological risks.

This literature review aims to systematically analyze and synthesize the existing scientific knowledge regarding the combined effects of acetamiprid and cypermethrin exposure on ecosystem health. By exclusively utilizing research articles indexed in PubMed, this review will critically evaluate the current understanding of the environmental risks associated with this specific pesticide mixture. The scope of this review will encompass the examination of studies that address environmental contamination in soil, water, and air; the toxicity to various animal groups, including aquatic organisms, terrestrial wildlife, and livestock; the mechanisms of toxic action, with a focus on synergistic, additive, and antagonistic interactions; the environmental fate and degradation pathways of the mixture; the potential for bioaccumulation and biomagnification in food chains; and an overview of any existing review articles that specifically address the hazards of acetamiprid and cypermethrin mixtures to ecosystem health.

Environmental Contamination by Acetamiprid and Cypermethrin Mixture:

Studies have demonstrated that acetamiprid can persist in soil environments and negatively influence key soil properties, including biochemical characteristics and the activity and diversity of soil microbial communities.¹ These impacts can manifest as a reduction in microbial diversity, alterations in the structural composition of microbial communities, and inhibition of essential soil processes such as respiration and enzymatic activities.¹ Cypermethrin, a synthetic pyrethroid insecticide widely used in agriculture, is also recognized as a persistent contaminant of soil, posing potential risks to both environmental and human health.²⁴ The environmental persistence of cypermethrin in soil is influenced by a variety of factors, including the soil's physicochemical properties and the metabolic activity of soil microorganisms, with reported half-lives varying depending on these conditions.²⁴

Research suggests that the presence of certain metal ions in soil can modulate the degradation of both acetamiprid and cypermethrin.²⁵ For instance, copper has been observed to stabilize acetamiprid, potentially prolonging its persistence in soil, while chromium and nickel may facilitate its degradation. Similarly, the presence of copper ions in soil has been shown to influence the degradation of cypermethrin by affecting the activity of soil microorganisms.²⁵ Interestingly, studies on the cucumber phyllosphere have indicated that cypermethrin treatment can lead to an increase in the total microbial biomass, particularly bacterial biomass dominated by Gram-negative species, while simultaneously causing a decrease in the abundance of fungi.²⁶ This observation suggests that cypermethrin, or its degradation products, might serve as a nutrient source for specific groups of soil microbes.

The simultaneous presence of acetamiprid and cypermethrin in soil could therefore result in complex and potentially opposing effects on soil microbial communities. While acetamiprid tends to exhibit inhibitory effects on overall microbial activity and diversity, cypermethrin might selectively stimulate the growth of certain bacterial groups while suppressing others. This interplay could lead to significant shifts in soil nutrient cycling processes, potentially impacting plant health and the overall functionality of the soil ecosystem.

Contamination of Water:

The contamination of aquatic ecosystems by pesticides, including pyrethroid insecticides such as cypermethrin, is a well-documented phenomenon that can induce harmful effects on the production, reproduction, and survival of a broad spectrum of aquatic organisms, ranging from microscopic algae and aquatic plants to invertebrates and fish.⁷ Cypermethrin is particularly recognized for its high acute toxicity to aquatic life, with numerous studies reporting significant mortality in fish and aquatic invertebrates even at relatively low concentrations.⁷ The classification of cypermethrin as a priority substance under the European Commission Water Framework Directive highlights the regulatory concerns associated with its presence and potential impacts on water quality and aquatic biodiversity.¹⁰ Acetamiprid, due to its water-soluble nature, can readily enter both surface water and groundwater systems through agricultural runoff from treated fields and spray drift during application.³ Although generally considered to have lower acute toxicity to aquatic organisms compared to cypermethrin, the widespread use of acetamiprid in agriculture has led to its frequent detection in various aquatic environments worldwide.²⁷

The co-occurrence of acetamiprid and cypermethrin, along with other pesticides, in aquatic habitats is a common scenario in agricultural regions. Research has demonstrated that mixtures containing neonicotinoids like acetamiprid and pyrethroids like cypermethrin can exert combined toxic effects on aquatic organisms. Notably, these effects often involve synergistic interactions, where the combined toxicity of the mixture is greater than the sum of the toxicities of the individual components, posing an elevated risk to aquatic ecosystem health.¹⁴

The simultaneous contamination of water resources by acetamiprid and cypermethrin thus presents a significant and multifaceted threat to the health and stability of aquatic ecosystems. The inherent high toxicity of cypermethrin to aquatic life, coupled with the potential for endocrine disruption by acetamiprid and the documented synergistic toxic effects of neonicotinoid-pyrethroid mixtures, suggests that the combined presence of these insecticides in aquatic environments could lead to severe consequences for aquatic biodiversity and the overall functioning of these vital ecosystems.

Contamination of Air:

Pesticides, as a broad class of compounds, can contaminate the atmospheric environment through several pathways, including spray drift that occurs during application, volatilization of the compounds from treated surfaces such as plants and soil, and long-range atmospheric transport that can lead to deposition in areas far removed from the original application sites.

Studies have indicated that a significant proportion of applied pesticides, often exceeding 90%, does not reach the intended target pests. Instead, this fraction enters various environmental compartments, with the atmosphere being a notable sink for off-target pesticide contamination.³⁰

The extent to which a pesticide volatilizes into the air is influenced by its specific physicochemical properties, particularly its vapor pressure, as well as prevailing environmental conditions such as temperature and humidity.¹² Pesticides with higher vapor pressures tend to volatilize more readily.

Once in the atmosphere, pesticides can be transported by air currents, potentially traveling over considerable distances. Eventually, these airborne pesticides can be deposited back onto terrestrial and aquatic ecosystems through processes such as rainfall, dry deposition of particles, and gravitational settling. This atmospheric deposition can contribute to the contamination of non-target environments, exposing organisms to pesticides through inhalation, direct contact with contaminated surfaces, or ingestion of pesticide-laden food or water.

While the provided research material does not contain specific data on the combined levels of acetamiprid and cypermethrin air contamination, the general understanding of pesticide environmental fate suggests that both insecticides are likely to be present in the air following agricultural applications. Their presence in the atmosphere could lead to the exposure of terrestrial wildlife, including beneficial insects like pollinators, through inhalation of contaminated air or deposition of pesticide residues onto their foraging habitats and food sources.

Toxicity of Acetamiprid and Cypermethrin Mixture to Animal Groups:

Aquatic Organisms:

Cypermethrin is well-established as a highly toxic insecticide to a wide array of aquatic organisms, including various species of fish and invertebrates.⁷ Its neurotoxic mode of action leads to a range of adverse effects in fish, including alterations in behavior, impairments in reproductive function, histopathological changes in vital organs such as gills and liver, disturbances in haemato-biochemical parameters, inhibition of key enzymes like acetylcholinesterase, induction of genotoxicity resulting in DNA damage, promotion of oxidative stress, and even suppression of the immune system.⁷

In contrast, acetamiprid generally exhibits lower acute toxicity to aquatic organisms when compared to cypermethrin.¹⁸ However, chronic exposure to acetamiprid at concentrations that are environmentally relevant has been demonstrated to impair endocrine functions in aquatic vertebrates such as zebrafish. This can manifest as feminization of male fish, significant alterations in the levels of sex hormones, and changes in the expression of genes involved in the hypothalamic-pituitary-gonad (HPG) axis, which plays a crucial role in reproduction.³⁸

Notably, research has indicated that mixtures of acetamiprid with other agrochemicals, including cypermethrin and other pyrethroid insecticides, can result in synergistic toxic effects on aquatic organisms like zebrafish (*Danio rerio*) and the water flea (*Daphnia magna*).² Synergistic toxicity implies that the combined effect of the insecticide mixture is significantly greater than the sum of the toxic effects of the individual components when they act in isolation. This phenomenon suggests that the co-occurrence of acetamiprid and cypermethrin in aquatic environments could pose a considerably higher risk to aquatic life than would be predicted based on the toxicity of each insecticide alone.

Terrestrial Wildlife:

Acetamiprid is recognized as posing a potential toxicity risk to various non-target terrestrial organisms, including ecologically important groups such as bees, as well as birds and mammals.¹ Sublethal exposure of honeybees to acetamiprid has been shown to negatively impact both larvae and adult bees, particularly affecting their learning and memory abilities, which are essential for successful foraging and the overall survival of the bee colony.²¹

Cypermethrin is also known to be highly toxic to bees, further contributing to the potential for harm to pollinator populations when these two insecticides are used in agricultural settings.⁸

Studies have demonstrated that mixtures of acetamiprid with pyrethroid insecticides, such as cypermethrin or deltamethrin, can cause significantly higher mortality rates and impair cognitive functions like learning and memory in honeybees.¹⁵ The prevalence of synergistic interactions in these neonicotinoid-pyrethroid mixtures amplifies their toxicity to pollinators, raising serious concerns about the potential for negative impacts on pollination services that are vital for both wild plant communities and agricultural productivity.

Furthermore, research has detected residues of a wide range of pesticides, including both neonicotinoids and pyrethroids, in wild small mammals inhabiting agricultural landscapes.⁴¹ This indicates that terrestrial wildlife is frequently exposed to complex mixtures of these agricultural chemicals in their natural environments. The long-term ecological consequences of such widespread exposure to pesticide mixtures on terrestrial food webs and overall biodiversity are areas of ongoing investigation and concern.

Livestock:

While acetamiprid is generally considered to have relatively low toxicity in mammals, including livestock species, the ingestion of large quantities can lead to acute poisoning. Symptoms observed in livestock such as buffalo following accidental ingestion of acetamiprid include severe gastrointestinal disturbances and respiratory distress.⁴² Similarly, cypermethrin is typically regarded as having low toxicity to mammals at the concentrations used in commercial products for pest control.⁸

However, it has been shown that the presence of elevated levels of pesticide residues, including organophosphates and pyrethroids, in the dietary constituents of livestock can be linked to adverse health outcomes, such as alterations in birth weight and other developmental parameters in newborn animals.²² This suggests that indirect exposure through contaminated feed and water sources could pose a risk to livestock health.

In the context of managing insect pests that can affect livestock, mixtures of insecticides containing pyrethroids and neonicotinoids, such as cypermethrin and acetamiprid, have been explored for their efficacy. These mixtures can sometimes exhibit additive or synergistic effects on the target insect pests, potentially enhancing their control.¹⁷

Mechanisms of Toxicity of Acetamiprid and Cypermethrin Mixture:

Synergistic, Additive, or Antagonistic Interactions:

In vitro studies have demonstrated that a specific mixture of acetamiprid and alpha-cypermethrin induces synergistic genotoxic and cytotoxic effects in human peripheral blood lymphocytes.¹⁶ This synergy is evidenced by increased chromosomal aberrations, sister chromatid exchange, and micronucleus formation, along with a reduction in mitotic and proliferation indices, indicating enhanced DNA damage and inhibition of cell division compared to the individual compounds.

Research on honeybees has also revealed that mixtures of acetamiprid with other pyrethroids, such as deltamethrin, can lead to synergistic increases in mortality.²¹ Furthermore, acetamiprid in combination with various other pesticides, including cypermethrin and other pyrethroids, often exhibits synergistic toxic interactions in honeybees, suggesting that these mixtures can be particularly harmful to pollinator insects.¹⁵ The prevalence of synergistic effects underscores the importance of evaluating the combined toxicity of pesticides rather than relying solely on the toxicity profiles of individual compounds for ecological risk assessment.

Neurotoxicological Effects:

Acetamiprid exerts its insecticidal action by acting as a potent agonist at the postsynaptic nicotinic acetylcholine receptors (nAChR) in the insect central nervous system.¹ This interaction leads to an overstimulation of the cholinergic system, resulting in a cascade of neurological effects including tremors, convulsions, paralysis, and ultimately, death. The selectivity of acetamiprid for insect nAChRs over mammalian subtypes is thought to contribute to its relatively lower mammalian toxicity. Cypermethrin, as a pyrethroid insecticide, disrupts nerve function by interfering with the voltage-gated sodium channels in nerve cell membranes.⁸ It acts by prolonging the opening of these channels, leading to a continuous flow of sodium ions into the nerve cell, which causes repetitive nerve firing, muscle spasms, and paralysis in insects. The combined exposure to acetamiprid and cypermethrin could potentially lead to a

more severe and complex disruption of the nervous system in both target insect pests and non-target organisms. The simultaneous action on both cholinergic receptors and sodium channels might overwhelm the nervous system's capacity to regulate nerve impulse transmission, potentially resulting in enhanced neurotoxic effects.

Genotoxic and Cytotoxic Effects:

As previously mentioned, a specific mixture of acetamiprid and alpha-cypermethrin has demonstrated genotoxic effects in human peripheral blood lymphocytes *in vitro*.¹⁶ These effects include an increase in chromosomal aberrations, sister chromatid exchanges, and micronucleus formation, indicating the potential for DNA damage. The same mixture also exhibited cytotoxic effects by significantly reducing the mitotic index, proliferation index, and nuclear division index in the treated lymphocytes, suggesting an inhibition of cell growth and proliferation.¹⁶

Endocrine Disrupting Effects:

Long-term exposure to acetamiprid alone has been shown to impair endocrine functions in zebrafish, leading to feminization of males, altered levels of sex hormones, and changes in the expression of steroidogenic genes.³⁸ While the endocrine disrupting potential of cypermethrin or the combined effects of acetamiprid and cypermethrin mixture are not explicitly detailed in the provided snippets, the known ability of neonicotinoids to interfere with hormonal systems suggests that the mixture could also have implications for endocrine regulation in various animal groups.

Other Mechanisms:

Exposure to acetamiprid has been shown to induce oxidative stress in rats, characterized by an increase in oxidant levels and a decrease in antioxidant defense mechanisms.⁴⁶ Similarly, cypermethrin exposure can lead to oxidative stress injury in various fish species.⁷ Therefore, it is plausible that the combined exposure to acetamiprid and cypermethrin could exacerbate oxidative stress in exposed organisms.

Environmental Fate and Degradation of Acetamiprid and Cypermethrin Mixture:

Degradation Pathways in Soil, Water, and Air:

Acetamiprid in soil undergoes biodegradation primarily through microbial activity, involving pathways such as N-demethylation and oxidative cleavage of the cyanoimino group, often facilitated by soil fungi like *Aspergillus heterochromaticus*.¹ Cypermethrin degradation in soil is also largely microbially mediated, with bacteria like *Bacillus cereus* playing a significant role.²⁴ Additionally, the use of biochar has been shown to enhance cypermethrin degradation in soil. Both pesticides can also undergo photodegradation when exposed to sunlight in the environment.

Influence of Environmental Factors:

The degradation rates of acetamiprid and cypermethrin are influenced by various environmental factors, including pH, temperature, sunlight, and the activity of microorganisms.⁴⁸ Soil properties such as moisture content and mineral composition also play a role in their degradation in soil.²⁵ Climatic conditions, such as evapotranspiration, can affect the dissipation of these pesticides from crops.⁵⁰

Formation and Toxicity of Degradation Products:

Acetamiprid degradation results in the formation of metabolites like N-desmethyacetamiprid (IM-2-1) and IM-1-3, some of which can still exhibit toxicity.¹ Cypermethrin degradation can lead to the formation of 3-phenoxybenzoic acid and potentially cyanohydrin, which can inhibit ion channels and increase oxidative stress.²⁴

Bioaccumulation and Biomagnification of Acetamiprid and Cypermethrin Mixture:

Acetamiprid has been shown to bioaccumulate in aquatic organisms, including zebrafish, and can be transferred from exposed adults to their offspring.³⁹ Cypermethrin, being lipophilic, has a potential for bioaccumulation in aquatic organisms, particularly in fatty tissues.⁷ Pesticides, in general, can biomagnify along food chains, leading to higher concentrations in organisms at higher trophic levels.²⁸ The bioaccumulation of these pesticides in aquatic organisms can pose risks to human health through the consumption of contaminated fish.²⁸

Review of Existing Literature on Acetamiprid and Cypermethrin Mixture Hazards to Ecosystem Health:

Studies have investigated the combined effects of acetamiprid with other pyrethroids like deltamethrin on honeybees²¹ and the genotoxic effects of acetamiprid and alpha-cypermethrin mixtures on human lymphocytes.¹⁶ Reviews also discuss the combined toxicity of insecticides and fungicides, including neonicotinoids and pyrethroids, on pollinators¹⁴ and the general impacts of pesticides on ecosystems.³ However, a comprehensive review specifically addressing the hazards of the combined exposure to acetamiprid and cypermethrin on overall ecosystem health appears to be limited in the provided snippets.

Conclusion:

The combined exposure to acetamiprid and cypermethrin presents a complex array of potential hazards to ecosystem health. Evidence suggests that these insecticides can interact synergistically, enhancing their toxicity to various organisms, particularly aquatic life and pollinators. The contamination of soil, water, and air by this mixture can have far-reaching consequences, affecting microbial communities, non-target invertebrates, and vertebrates across different trophic levels. While both compounds have individual mechanisms of toxicity, their co-occurrence can lead to enhanced neurotoxicological, genotoxic, cytotoxic, and potentially endocrine-disrupting effects. The environmental fate and degradation of the mixture are influenced by a multitude of factors, and the formation of toxic degradation products further complicates the risk assessment. Moreover, the potential for bioaccumulation and biomagnification in food chains raises concerns about long-term impacts on ecosystem stability and potential risks to human health. Further research is warranted to fully elucidate the chronic and sublethal effects of this pesticide mixture on a wider range of species and ecosystem processes, as well as to develop effective strategies for monitoring and mitigating the associated environmental risks.

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