Carbamate and Pyrethroid Pesticide Toxicity in Fish: Biochemical and Molecular Perspectives

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***Abstract*— Carbamate and pyrethroid insecticides threaten aquatic ecosystems despite their agricultural importance. This review synthesizes biochemical and molecular mechanisms of their toxicity in fish. Carbamates inhibit acetylcholinesterase, disrupting neurotransmission, while pyrethroids alter sodium channel function, causing neuronal hyperexcitation. Both induce oxidative stress through lipid peroxidation and antioxidant depletion. Molecular studies reveal modulation of detoxification enzymes (CYPs, GSTs), stress proteins, and inflammatory pathways, with histopathological damage observed in liver, gills, and kidneys. Critically, chronic exposures, pesticide mixtures, and environmental co-stressors produce synergistic effects overlooked by conventional toxicity testing. We emphasize integrating biochemical biomarkers, molecular endpoints, and multi-omics approaches for early detection of sublethal impacts. Given fish populations' ecological and economic value, sustainable pest management and comprehensive monitoring are essential for protecting aquatic biodiversity and ensuring food security.**

***Keywords*— Carbamates, Fish toxicity, Acetylcholinesterase, Oxidative stress.**

I. INTRODUCTION

Aquatic ecosystems are increasingly vulnerable to chemical contamination from agricultural runoff, industrial discharge, and domestic wastewater. Among environmental pollutants, pesticides constitute a particularly insidious threat due to their deliberate design for biological activity and their widespread use across terrestrial and aquatic landscapes (Bradbury & Coats, 1989). Fish, as important components of aquatic food chain and sentinels of ecosystem health, are highly susceptible to pesticide exposure. Their sensitivity, coupled with their ecological and economic importance, makes them ideal bio-indicators for deciding the environmental impacts of agrochemical contamination.

Two pesticide classes—carbamates and pyrethroids—are globally used insecticide and have attracted significant eco-toxicological attention. Carbamates, synthetic derivatives of carbamic acid, function primarily as reversible acetylcholinesterase (AChE) inhibitors, damaging cholinergic neurotransmission essential for coordinated neuromuscular activity (Abou-Donia et al., 1986). While often perceived as less persistent than organophosphates, carbamates show high acute toxicity to aquatic organisms and can cause cumulative biochemical disruption following repeated sub-lethal exposures (Ram et al., 1988; David et al., 2004).

Pyrethroids, synthetic analogues of naturally found pyrethrins made from Chrysanthemum flowers, represent one of the fastest-growing insecticide classes. These lipophilic compounds target voltage-gated sodium channels in nerve membranes, prolonging channel opening and causing sustained depolarization, neuronal hyperexcitation, and eventual paralysis (Bradbury & Coats, 1989). Because of their high lipophilicity and efficient uptake across gill epithelia, pyrethroids are extraordinarily toxic to fish, often at concentrations orders of magnitude lower than those affecting terrestrial organisms (Velisek et al., 2006). Beyond acute neurotoxicity, pyrethroids causes oxidative stress, immunosuppression, endocrine disruption, and genotoxic damage (Yang et al., 2022; Li et al., 2025).

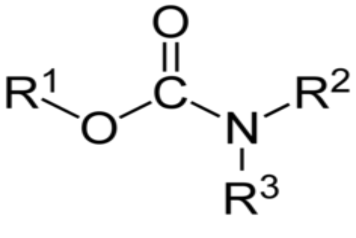

Fig. 1 Carbamate

At the biochemical level, both pesticide classes disrupt key enzymatic systems. Carbamates irreversibly compromise AChE activity, leading to acetylcholine aggregation and cholinergic overstimulation (El-Sayed et al., 2011; Singh & Sharma, 2012).

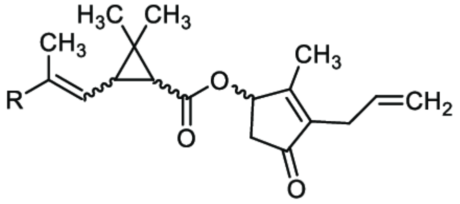

Fig. 2 Pyrethroids

Pyrethroids, while primarily targeting sodium channels, also provoke profound oxidative stress by overwhelming antioxidant defense mechanisms, resulting in lipid peroxidation, protein oxidation, and DNA damage (Korkmaz et al., 2009; Yildirim et al., 2006). These biochemical perturbations manifest as alterations in blood chemistry, enzyme activities, and metabolic homeostasis.

At the molecular level, contemporary research has unveiled complex transcriptional and post-transcriptional responses to pesticide exposure. Studies employing RNA-sequencing, proteomics, and targeted gene expression analyses demonstrate that both carbamates and pyrethroids modulate the expression of genes encoding detoxification enzymes (cytochrome P450 superfamily, glutathione S-transferases), stress-response proteins (heat shock proteins), inflammatory cytokines, and apoptosis regulators (Yang et al., 2022; Fernandes et al., 2021; Li et al., 2024). These molecular signatures not only elucidate mechanistic pathways of toxicity but also provide sensitive biomarkers for environmental monitoring and risk assessment.

Importantly, emerging evidence suggests that real-world exposure scenarios—characterized by chronic low-dose exposures, pesticide mixtures, pulsed contamination events, and interactions with environmental co-stressors such as microplastics and hypoxia—produce toxicological outcomes that differ markedly from those predicted by single-compound acute toxicity tests (Okogwu et al., 2022; Laetz et al., 2009; Morales-Rivera et al., 2021). This complexity underscores the inadequacy of traditional risk assessment paradigms and highlights the need for integrative, multi-tiered ecotoxicological approaches.

This review aims to synthesize the current understanding of carbamate and pyrethroid toxicity in fish, with emphasis on biochemical and molecular mechanisms. By consolidating findings from laboratory, mesocosm, and field studies, we seek to identify consistent patterns of toxicity, highlight knowledge gaps, and propose directions for future research. Ultimately, this synthesis is intended to inform evidence-based regulatory policies and promote sustainable pesticide management practices that protect aquatic biodiversity and human food security.

II. MODES OF ACTION: NEUROTOXIC MECHANISMS

A. CARBAMATES: ACETYLCHOLINESTERASE INHIBITION

Carbamate insecticides works primarily through reversible inhibition of acetylcholinesterase (AChE), a serine hydrolase enzyme important for terminating cholinergic neurotransmission by hydrolyzing the neurotransmitter acetylcholine (ACh) at synaptic junctions (Abou-Donia et al., 1986). Whereas organophosphates, which form stable covalent bonds with the enzyme's active site, carbamates carbamylate the serine residue transiently, allowing spontaneous reactivation of AChE over time. However, the period of inhibition is sufficient to cause acetylcholine accumulation, continuous stimulation of cholinergic receptors, and impaired neuromuscular functioning.

Numerous studies have documented robust AChE inhibition in fish exposed to carbamate pesticides. Singh and Sharma (2012) reported significant dose-dependent suppression of AChE activity in brain and muscle tissues of *Labeo rohita* following sub-lethal carbofuran exposure, correlating with behavioral abnormalities such as erratic swimming and loss of equilibrium. Similarly, Glusczak et al. (2007) observed persistent cholinesterase inhibition in *Leporinus obtusidens*, accompanied by increased plasma glucose levels indicative of metabolic stress. El-Sayed et al. (2011) demonstrated that carbaryl exposure in Nile tilapia (*Oreochromis niloticus*) resulted in pronounced AChE depression alongside oxidative stress markers and histopathological lesions in liver and gill tissues.

Importantly, Jablonski et al. (2022) highlighted the vulnerability of early life stages to carbamate toxicity. Zebrafish embryos and larvae exposed to methomyl exhibited dose-dependent mortality, skeletal deformities, pericardial edema, and impaired swimming performance, all correlated with significant AChE inhibition. The heightened sensitivity of developing fish reflects their limited detoxification capacity and the critical role of cholinergic signalling in neural development.

The ecological implications of AChE inhibition extend beyond direct neurotoxicity. Impaired cholinergic function compromises essential behaviours such as predator avoidance, foraging efficiency, and social interactions, ultimately reducing fitness and survival in natural environments (Satyavardhan & Sharma, 2016; Nair & Sreenivasan, 2013). Furthermore, the behavioral endpoints often manifest at lower concentrations and earlier time points than biochemical markers, positioning behavioral assays as sensitive early-warning indicators in environmental monitoring programs.

B. PYRETHROIDS: SODIUM CHANNEL DISRUPTION

Pyrethroid insecticides act primarily on voltage-gated sodium channels in nerve axons, delaying channel inactivation and prolonging sodium influx during action potential generation. This results in repetitive neuronal firing, hyperexcitation, and eventual paralysis—a syndrome termed "knockdown" in insects and "CS syndrome" (choreoathetosis with salivation) in mammals (Bradbury & Coats, 1989). Pyrethroids are classified into two types based on their chemical structure and symptomatology: Type I (lacking an α-cyano group) produce tremors, while Type II (containing an α-cyano group) induce choreoathetosis and salivation. In fish, pyrethroid neurotoxicity manifests as behavioral disturbances, loss of equilibrium, increased opercular movements, and erratic swimming patterns. Velisek et al. (2006) documented rapid onset of neurotoxic symptoms in common carp (*Cyprinus carpio*) exposed to permethrin, including hyperactivity followed by lethargy, surface breathing, and lateral positioning. Biochemical assays confirmed AChE inhibition and electrolyte imbalance, suggesting that pyrethroids induce secondary cholinergic disruption beyond their primary sodium channel effects.

Liu et al. (2025) demonstrated a strong correlation between neurobehavioral abnormalities and AChE inhibition in deltamethrin-exposed zebrafish, confirming that pyrethroids engage multiple neural pathways. Interestingly, Blanc et al. (2021) showed that embryonic permethrin exposure induced persistent changes in gene expression related to nervous system development, with behavioral abnormalities observed in subsequent unexposed generations. This suggests heritable epigenetic modifications or germline transmission of molecular imprints, expanding the temporal scope of pyrethroid neurotoxicity beyond immediate exposure windows.

The lipophilic nature of pyrethroids facilitates their rapid uptake across gill membranes and bioaccumulation in lipid-rich tissues such as brain, liver, and adipose depots (Wang et al., 2018). This efficient partitioning into neural tissues underlies their extreme toxicity to fish, often exceeding that of organophosphates by several orders of magnitude. Moreover, species-specific variations in sensitivity exist, with salmonids exhibiting greater vulnerability compared to warm-water species, likely due to differences in metabolic detoxification capacity (Bradbury & Coats, 1989; Velisek et al., 2009).

III. OXIDATIVE STRESS AND ANTIOXIDANT RESPONSES

A. MECHANISMS OF OXIDATIVE STRESS INDUCTION

Oxidative stress—an imbalance between reactive oxygen species (ROS) production and antioxidant defences—has emerged as a central mechanism of both carbamate and pyrethroid toxicity in fish. ROS, including superoxide anion ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), and hydroxyl radical (•OH), are normally generated during aerobic metabolism but are tightly regulated by enzymatic (superoxide dismutase, catalase, glutathione peroxidase) and non-enzymatic (glutathione, vitamins C and E) antioxidant systems. Pesticide exposure disrupts this homeostasis, leading to oxidative damage to cellular macromolecules.

Li et al. (2025) investigated oxidative stress in Japanese flounder (Paralichthys olivaceus) exposed to deltamethrin and observed marked increases in malondialdehyde (MDA), a lipid peroxidation product, alongside suppression of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities. Metabolomic profiling revealed disruptions in energy metabolism, indicating that deltamethrin impairs both cellular defences and bioenergetics. Similarly, Korkmaz et al. (2009) demonstrated cypermethrin-induced oxidative damage in freshwater fish, characterized by elevated lipid peroxidation and decreased glutathione levels, with histopathological lesions in gills and liver tissues.

Begum (2005) provided early evidence of carbamate-induced oxidative stress, reporting elevated lipid peroxidation and reduced antioxidant enzyme activities in *Clarias batrachus* exposed to carbofuran. Uner et al. (2006) extended these findings in common carp, noting dose-dependent MDA elevation and antioxidant suppression, with liver tissue being more vulnerable than muscle or gill tissues. These observations highlight organ-specific susceptibilities and support the use of hepatic biomarkers in ecotoxicological evaluations.
The molecular basis of oxidative stress involves both direct ROS generation by pesticides and indirect effects mediated through mitochondrial dysfunction. Yuan et al. (2023) demonstrated that deltamethrin exposure in crucian carp (*Carassius auratus*) triggered endoplasmic reticulum (ER) stress alongside oxidative stress, disrupting protein folding and cellular homeostasis. Santos et al. (2019) employed proteomics to characterize deltamethrin-induced alterations in sea bream (*Sparus aurata*), revealing changes in mitochondrial proteins involved in oxidative phosphorylation and the unfolded protein response.

B. ANTIOXIDANT DEFENCE MODULATION

Fish respond to pesticide-induced oxidative stress by modulating antioxidant enzyme expression and activity, though chronic exposure often overwhelms these adaptive mechanisms. Singh et al. (2010) reported that cypermethrin exposure in *Labeo rohita* suppressed catalase, SOD, and glutathione reductase activities, creating an imbalance that favored oxidative damage. Yildirim et al. (2006) observed similar patterns in Nile tilapia exposed to deltamethrin, with reductions in antioxidant enzymes accompanied by hematological disturbances including decreased RBC counts and hemoglobin content.

Interestingly, Korkmaz et al. (2009) demonstrated that dietary supplementation with ascorbic acid (vitamin C) significantly reduced oxidative stress markers and alleviated tissue injury in cypermethrin-exposed fish. This finding suggests that nutritional interventions may serve as protective strategies in polluted environments or aquaculture settings. Patel and Kaur (2020) further explored this concept, showing that selenium and vitamin E supplementation attenuated deltamethrin-induced oxidative stress, histopathological damage, and stress-related gene expression in rainbow trout, with improved survival and growth metrics.

The ecological relevance of oxidative stress extends beyond cellular damage. Oxidative disruption impairs immune function, reproductive performance, and tolerance to environmental stressors such as hypoxia and temperature fluctuations. Yuan et al. (2023) found that deltamethrin-exposed crucian carp had reduced hypoxia tolerance, demonstrating how pesticide-induced oxidative stress compromises adaptive capacity in natural habitats characterized by fluctuating environmental conditions.

IV. MOLECULAR AND GENOMIC RESPONSES

A. DETOXIFICATION ENZYME MODULATION

Fish possess sophisticated xenobiotic detoxification systems comprising Phase I (functionalization), Phase II (conjugation), and Phase III (transport) enzymes. Cytochrome P450 monooxygenases (CYPs) catalyse oxidative biotransformation of lipophilic pesticides, while glutathione S-transferases (GSTs) facilitate conjugation reactions that enhance water solubility and excretion. Pesticide exposure typically induces these detoxification pathways; though chronic exposure may lead to enzyme saturation or inhibition.

Yang et al. (2022) employed transcriptomic analysis to investigate deltamethrin effects in channel catfish (*Ictalurus punctatus*), revealing differential expression of genes encoding CYP enzymes, GSTs, and other detoxification proteins within six hours of exposure. Fernandes et al. (2021) utilized RNA-seq in juvenile seabass (*Dicentrarchus labrax*) chronically exposed to pyrethroids, identifying dose-dependent regulation of multiple CYPs, UDP-glucuronosyltransferases (UGTs), and genes involved in mitochondrial function and neurodevelopment. Network analysis linked altered transcriptional modules to observed phenotypes including reduced growth and behavioural impairments.

Zhang et al. (2016) investigated molecular responses in grass carp (*Ctenopharyngodon idella)* exposed to cypermethrin and found upregulation of Phase II detoxification enzymes (GST) alongside downregulation of genes involved in energy metabolism (PPARα, CPT1), suggesting metabolic resource diversion toward detoxification at the expense of growth. This trade-off has important implications for aquaculture productivity and wild population fitness.

B. STRESS RESPONSE PATHWAYS

Heat shock proteins (HSPs) are molecular chaperones that protect cellular proteins from denaturation and facilitate proper protein folding under stress conditions. Pesticide exposure commonly induces HSP expression as an adaptive response. Li et al. (2024) documented upregulation of HSP70 in methomyl-exposed zebrafish hepatic tissue, indicating activation of stress-response pathways. Patel and Kaur (2020) showed that antioxidant supplementation partially normalized HSP70 expression in deltamethrin-exposed rainbow trout, suggesting that nutritional interventions can modulate stress-response gene regulation.

C. APOPTOSIS AND CELL DEATH PATHWAYS

Chronic pesticide exposure activates programmed cell death pathways, contributing to tissue degeneration and organ dysfunction. Li et al. (2024) demonstrated that methomyl exposure upregulated apoptotic markers (caspase-3, Bax) while suppressing anti-apoptotic genes (Bcl-2) in zebrafish liver, indicating that carbamate exposure triggers apoptosis. Notably, the study revealed sex-dependent differences, with female zebrafish exhibiting stronger induction of apoptotic genes compared to males, suggesting hormonal or metabolic modulation of toxicological responses.

Oliveira et al. (2022) investigated combined permethrin and methomyl exposure in juvenile seabass and found potentiation of apoptosis regulators in co-exposed groups through transcriptomic analysis, despite largely additive effects on traditional biomarkers. This highlights the value of molecular endpoints in detecting interaction effects not captured by conventional biochemical assays.

D. IMMUNE AND INFLAMMATORY RESPONSES

Pesticide exposure can compromise fish immune function, increasing susceptibility to infectious diseases. Yang et al. (2022) demonstrated that deltamethrin exposure altered expression of immune-related genes including interleukins and complement proteins in channel catfish. Li et al. (2024) observed increased expression of inflammatory cytokines (IL-1β, TNF-α) in methomyl-exposed zebrafish, indicating activation of inflammatory responses.

Hosseini et al. (2018) specifically examined immunotoxicity of deltamethrin in zebrafish, reporting reduced lysozyme activity, decreased macrophage phagocytic capacity, and altered cytokine expression. Importantly, these immunological impairments correlated with higher susceptibility to bacterial infection in challenge tests, demonstrating that pyrethroid exposure translates to increased disease risk in natural and aquaculture environments. Liu et al. (2025) corroborated these findings, showing that deltamethrin suppressed phagocytic ability of immune cells alongside neurobehavioral and oxidative stress effects.

E. ENDOCRINE DISRUPTION

Emerging evidence suggests that both carbamates and pyrethroids can interfere with endocrine signaling pathways. Fernandez-Lopez et al. (2015) investigated carbaryl effects on reproductive fitness in guppies (*Poecilia reticulata*), finding that chronic exposure produced fewer and smaller offspring, disrupted ovarian histology, and altered expression of estrogen receptor (ERα) and vitellogenin genes. These results indicate endocrine-mediated reproductive impairment by carbamates, with potential population-level consequences.

Khan et al. (2024) explored permethrin toxicity in zebrafish with focus on metabolic pathways, discovering that permethrin disrupted lipid metabolism by interfering with KRAS-PPAR-GLUT signalling. Exposure led to abnormal lipid accumulation, altered glucose uptake, and metabolic stress, linking pyrethroid toxicity to metabolic dysfunction beyond neurotoxicity.

V. HISTOPATHOLOGICAL ALTERATIONS

A. HEPATOTOXICITY

The liver, as the primary organ for xenobiotic metabolism, is particularly vulnerable to pesticide-induced damage. Histopathological studies consistently report hepatocellular alterations following carbamate and pyrethroid exposure.

Ram et al. (1988) conducted one of the earliest long-term studies, exposing *Channa punctatus* to carbofuran for six months. Despite sublethal dosing, progressive hepatic degeneration occurred, characterized by necrosis, vacuolation, and fatty changes. The study revealed that chronic low-dose exposure produces cumulative toxic effects not predicted by acute toxicity tests, emphasizing the importance of chronic exposure scenarios in risk assessment.

Li et al. (2025) documented hepatocellular vacuolation and necrosis in Japanese flounder exposed to deltamethrin, alongside biochemical markers of oxidative stress and metabolic disruption. Zhang et al. (2016) observed vacuolation and mild fibrosis in grass carp liver following chronic cypermethrin exposure, correlating with impaired growth and altered energy metabolism gene expression.

B. BRANCHIAL PATHOLOGY

Gills serve as the primary interface for respiratory gas exchange, ion regulation, and contaminant uptake in fish, making them highly susceptible to pesticide toxicity. Common histopathological lesions include epithelial lifting, lamellar fusion, hyperplasia, edema, and necrosis, all of which compromise respiratory efficiency and osmoregulation.

Li et al. (2025) reported epithelial lifting and lamellar fusion in gills of deltamethrin-exposed Japanese flounder. Sharbidre et al. (2011) documented significant gill damage in *Oreochromis mossambicus* exposed to cypermethrin, including lamellar fusion and epithelial lifting that impaired gas exchange. Velisek et al. (2006) confirmed similar lesions in common carp exposed to permethrin, alongside neurotoxic symptoms and metabolic disturbances.

C. NEPHROTOXICITY

Kidneys play critical roles in osmoregulation, nitrogenous waste excretion, and xenobiotic elimination. Pesticide-induced renal damage compromises these essential functions, potentially leading to systemic physiological collapse.

Yang et al. (2022) observed kidney histopathological damage in channel catfish exposed to deltamethrin for only six hours, including tubular necrosis and epithelial degeneration. Dorlikar and Thengare (2025) focused specifically on renal pathology in *Clarias gariepinus* following sublethal cypermethrin exposure, revealing tubular degeneration, glomerular shrinkage, and interstitial edema. Such structural damage compromises osmoregulation and excretory function, critical for survival in freshwater environments.

VI. CHRONIC, LOW-DOSE, AND MIXTURE EXPOSURES

A. CHRONIC EXPOSURE EFFECTS

Real-world pesticide exposures are typically chronic and low-dose rather than acute and high-concentration, yet most toxicity testing relies on short-term acute protocols. Several studies have addressed this discrepancy by investigating chronic exposure scenarios.

Velisek et al. (2009) examined long-term permethrin effects in rainbow trout and found that chronic exposure resulted in growth retardation, reduced condition factor, histological alterations in liver and gills, and impaired hematological parameters. Almeida and Pereira (2020) investigated pulsed carbofuran exposure simulating agricultural runoff, finding episodic but recurrent AChE suppression, repeated oxidative stress spikes, and cumulative histological damage over time. Notably, fish did not fully recover between pulses, resulting in progressive physiological decline and reduced hypoxia tolerance.

Zhang et al. (2016) demonstrated that chronic low-dose cypermethrin exposure in grass carp shifted energy budgets, reducing growth and triggering long-term sublethal effects at environmentally realistic concentrations. The integrated physiological and molecular dataset illustrated how chronic pyrethroid exposure can impact aquaculture productivity and wild population fitness.

B. PESTICIDE MIXTURE TOXICITY

Natural aquatic environments rarely contain single pesticides; instead, fish encounter complex mixtures that may produce additive, synergistic, or antagonistic effects. Mixture toxicity represents a critical gap in standard risk assessment frameworks. Okogwu et al. (2022) investigated combined cypermethrin and dimethoate toxicity in juvenile *Clarias gariepinus*, revealing pronounced synergistic effects. Fish exposed to the pesticide mixture exhibited greater behavioral disturbances, stronger AChE inhibition, and more severe oxidative stress compared to single-compound exposures, accompanied by histological damage to gills and liver. The study underscores that aquatic organisms face complex mixtures in nature, and single-pesticide models drastically underestimate true environmental risks.

Laetz et al. (2009) provided comprehensive evidence of mixture toxicity in salmonids, demonstrating that sublethal concentrations of multiple pesticides in agricultural runoff produced synergistic neurotoxic effects unpredicted by individual compound assessments. Pesticide mixtures amplified AChE inhibition and impaired swimming performance, reducing predator avoidance and foraging efficiency. This influential work challenged regulatory reliance on single-compound thresholds and emphasized the need for cumulative risk assessment frameworks.

Oliveira et al. (2022) examined combined permethrin and methomyl exposure in juvenile seabass, finding largely additive effects on growth and oxidative biomarkers but potentiation of stress-response pathways and apoptosis regulators at the transcriptomic level. This highlights the importance of molecular endpoints in detecting interaction effects not apparent through traditional biochemical assays.

C. INTERACTIONS WITH ENVIRONMENTAL CO-STRESSORS

Pesticide toxicity can be modulated by environmental factors and co-stressors. Morales-Rivera et al. (2021) explored whether microplastics enhance pyrethroid toxicity by serving as vectors for hydrophobic pesticides. Juvenile tilapia exposed to deltamethrin sorbed to polyethylene microbeads accumulated higher liver residues and exhibited stronger oxidative stress responses compared to dissolved pesticide alone at equivalent nominal concentrations. This supports the "vector hypothesis" and indicates that microplastic pollution may amplify ecological risks of lipophilic pesticides.

Yuan et al. (2023) found that deltamethrin-exposed crucian carp had reduced hypoxia tolerance, demonstrating that pesticide-induced stressors compromise fish ability to adapt to fluctuating environmental oxygen levels. This interaction between chemical stressors and natural environmental variability has important implications for predicting population-level impacts in dynamic aquatic ecosystems.

VII. KNOWLEDGE GAPS AND FUTURE RESEARCH DIRECTIONS

Despite substantial progress in understanding carbamate and pyrethroid toxicity in fish, several critical knowledge gaps remain:

A. TRANSGENERATIONAL AND EPIGENETIC EFFECTS

Blanc et al. (2021) provided compelling evidence of transgenerational effects following embryonic permethrin exposure, but the molecular mechanisms underlying epigenetic inheritance remain poorly understood. Future research should investigate:
DNA methylation, histone modification, and microRNA patterns in pesticide-exposed fish and their offspring Germline transmission mechanisms and stability of epigenetic marks across generations Population-level consequences of transgenerational effects on fitness and adaptation

B. INTERACTIONS WITH CLIMATE CHANGE AND ENVIRONMENTAL STRESSORS

Climate change is altering aquatic environments through warming temperatures, ocean acidification, hypoxia, and altered precipitation patterns. Understanding how these changes interact with pesticide toxicity is critical:
Temperature effects on pesticide metabolism, bioaccumulation, and toxicity Combined stressor impacts (pesticides + hypoxia, thermal stress, acidification) Implications for species range shifts and ecosystem restructuring

C. MICROBIOME-PESTICIDE INTERACTIONS

Yang et al. (2022) demonstrated deltamethrin-induced microbiome disruption, opening a new research frontier:

Mechanistic understanding of how pesticides alter fish microbiomes Consequences of microbiome dysbiosis for host health, immunity, and metabolism Potential for probiotic interventions to mitigate pesticide impacts

D. NANOPESTICIDES AND EMERGING FORMULATIONS

Novel pesticide formulations including nanoencapsulated products may exhibit altered environmental fate and toxicity profiles requiring investigation:

Comparative toxicity of conventional vs. nanoformulations Uptake mechanisms and tissue distribution of nanoparticles Interactions between nanomaterials and pesticide active ingredients

VIII. DISCUSSION

The collective body of evidence reviewed herein unequivocally demonstrates that carbamate and pyrethroid pesticides pose significant threats to fish health across multiple levels of biological organization. From molecular and biochemical perturbations to organismal dysfunction and potential population-level consequences, the impacts of these widely used insecticides extend far beyond their intended target organisms.

A. CONVERGENT AND DIVERGENT MECHANISMS

While carbamates and pyrethroids differ in their primary molecular targets—AChE inhibition versus sodium channel disruption—they converge on common downstream pathways, particularly oxidative stress. This mechanistic convergence has important implications: biomarkers of oxidative damage (lipid peroxidation, antioxidant enzyme suppression) provide broadly applicable indicators of pesticide exposure regardless of specific compound class. However, the distinct primary mechanisms necessitate compound-specific biomarkers (AChE for carbamates, sodium channel dysfunction indicators for pyrethroids) for exposure confirmation and mechanistic attribution.

B. SUBLETHAL EFFECTS AND ECOLOGICAL RELEVANCE

A critical theme emerging from the reviewed literature is that sublethal exposures producing no overt mortality nonetheless induce biochemical, molecular, and behavioral alterations that compromise ecological fitness. Impaired predator avoidance, reduced foraging efficiency, suppressed immune function, and disrupted reproduction can reduce survival and reproductive success in natural environments even when laboratory mortality tests suggest "safe" exposure levels. This disconnect between traditional toxicity endpoints and ecologically relevant impacts underscores the inadequacy of LC50-based risk assessments and the necessity of incorporating sublethal endpoints into regulatory frameworks.

C. FROM MOLECULAR SIGNALS TO POPULATION IMPACTS

The advent of omics technologies has provided unprecedented molecular-level resolution of pesticide toxicity mechanisms. However, a critical challenge lies in translating molecular and biochemical biomarkers into predictions of organism fitness and population dynamics. While gene expression changes, protein alterations, and metabolomic shifts provide sensitive early-warning signals, quantitative relationships between these molecular perturbations and apical endpoints (growth, reproduction, survival) require further elucidation. Developing such quantitative linkages through AOPs and mechanistic modelling represents a priority for predictive ecotoxicology.

D. COMPARATIVE PERSPECTIVES AND SPECIES SENSITIVITY

The substantial variation in pesticide sensitivity among fish species reflects differences in physiology, behaviour, habitat use, and detoxification capacity. Salmonids' heightened vulnerability to pyrethroids, for instance, has important conservation implications for threatened salmon and trout populations in agricultural regions. Developing species sensitivity distributions and identifying traits associated with vulnerability or resilience could improve predictive capacity and enable more protective risk assessments for sensitive taxa.

IX. CONCLUSIONS

This comprehensive review synthesizes the current understanding of carbamate and pyrethroid pesticide

toxicity in fish, emphasizing biochemical and molecular mechanisms. Key conclusions include:
Neurotoxicity represents the primary mode of action for both pesticide classes, mediated through AChE inhibition (carbamates) or sodium channel disruption (pyrethroids), resulting in behavioral abnormalities and neuromuscular dysfunction.

Oxidative stress emerges as a critical secondary mechanism, characterized by elevated ROS production, lipid peroxidation, protein oxidation, and suppression of antioxidant defences, leading to cellular damage across multiple organ systems.
Molecular investigations reveal complex transcriptional and post-transcriptional responses, including modulation of detoxification enzymes, stress proteins, inflammatory cytokines, apoptosis regulators, and endocrine signalling pathways, providing mechanistic insights and sensitive biomarkers. Multi-organ histopathological damage affects liver, gills, and kidneys, compromising essential physiological functions including metabolism, respiration, osmoregulation, and excretion.

Chronic low-dose exposures, pesticide mixtures, and environmental co-stressors produce cumulative and synergistic effects not predicted by standard acute toxicity tests, highlighting inadequacies of current risk assessment paradigms. Sub-lethal effects on growth, reproduction, behaviour, and immune function compromise ecological fitness even at exposure levels below acute toxicity thresholds, with potential population-level consequences. Transgenerational effects following developmental exposures suggest epigenetic reprogramming with implications extending across multiple generations.

Species-specific sensitivity variation necessitates protective risk assessments accounting for vulnerable taxa rather than relying solely on standard test species.
Integration of traditional biomarkers with omics technologies provides comprehensive mechanistic understanding and sensitive early-warning indicators suitable for environmental monitoring.
Practical mitigation strategies, including nutritional supplementation, habitat management, and sustainable pest management, offer pathways to reduce pesticide impacts on fish populations.

X. FINAL PERSPECTIVE

Fish populations face mounting pressures from habitat degradation, climate change, overexploitation, and chemical contamination. Pesticides represent one component of this complex stressor landscape, yet one that is amenable to management through informed regulation and sustainable agricultural practices. The biochemical and molecular biomarkers reviewed herein provide powerful tools for detecting and quantifying pesticide impacts, enabling evidence-based decision-making. However, translating scientific understanding into effective environmental protection requires sustained commitment from researchers, regulators, industry, and agricultural stakeholders.

Given the ecological importance of fish as ecosystem engineers, nutrient cyclers, and food resources, and their economic significance for fisheries and aquaculture, protecting fish populations from pesticide impacts serves both environmental and human welfare objectives. As agricultural intensification continues globally to meet food demands of growing human populations, achieving sustainable pest management that safeguards aquatic biodiversity represents one of the paramount environmental challenges of the 21st century.

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