RESEARCH PAPER

Aquatic Toxicity of the Triazole Fungicide Tebuconazole: Environmental Occurrence, Molecular Mechanisms, and Risk Assessment

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ABSTRACT

Tebuconazole, a commonly used triazole fungicide, is extensively applied in agriculture to control a wide range of fungal diseases. However, its repeated use and environmental persistence have raised growing concerns about contamination, particularly in aquatic ecosystems where non-target organisms are continuously exposed. Increasing evidence suggests that tebuconazole exerts toxicity through multiple interconnected mechanisms. These include the generation of oxidative stress, disruption of cytochrome P450-dependent metabolic processes, mitochondrial dysfunction, endocrine interference, and the activation of apoptotic pathways. Among these, oxidative stress appears to play a central role by initiating a cascade of cellular damage and physiological disturbances. Studies on aquatic organisms, especially fish, have reported significant changes in biochemical biomarkers, enzyme activities, and tissue structure following exposure. However, these responses are not uniform and vary with species, concentration, and duration of exposure. Environmental monitoring has detected tebuconazole in aquatic systems at concentrations ranging from ng/L to µg/L, emphasizing the importance of interpreting laboratory findings in relation to real-world exposure conditions. Its detection in water, sediments, and living organisms also indicates a moderate potential for bioaccumulation and possible transfer across trophic levels. This review brings together current knowledge on the physicochemical characteristics, environmental distribution, mechanisms of toxicity, biomarker responses, and ecological risks associated with tebuconazole in aquatic systems. Unlike earlier descriptive reviews, the present study focuses on comparing findings across studies, linking mechanistic pathways, and evaluating exposure under environmentally relevant conditions. It also identifies key research gaps and suggests future directions to improve ecological risk assessment and promote more sustainable pesticide use.

Keywords: Tebuconazole; Triazole fungicide; Aquatic toxicity; Oxidative stress; Biomarkers; Ecotoxicology; Fish; Environmental contamination

How to cite this article: Manaswitha B, Harinath P, Sujatha B, Veeresh K, Savithri Y, Ravi Sekhar P, Rathnamma VV. Aquatic Toxicity of the Triazole Fungicide Tebuconazole: Environmental Occurrence, Molecular Mechanisms, and Risk Assessment. Int J Drug Deliv Technol. 2026;16(51s): 911-922. DOI: 10.25258/ijddt.16.51s.76

Source of support: Nil.

Conflict of interest: None

1. Introduction

Importance of Fungicides in Agriculture

Fungicides are an essential component of modern agricultural practices, as they help prevent and manage fungal diseases that can severely reduce crop yield and quality. Plant pathogenic fungi are responsible for significant global losses, affecting a wide range of crops including cereals, fruits, vegetables, and ornamental plants. With the global population continuing to grow, the demand for increased food production has led to more intensive farming practices. As a result, the use of chemical pesticides, particularly fungicides, has increased to ensure crop protection and maintain food security (Sharma et al., 2020; Singh et al., 2022). Today, fungicides represent a substantial share of total pesticide usage due to the persistent and widespread nature of fungal infections.

At the same time, the extensive and repeated application of fungicides has raised important environmental concerns. Many of these compounds are relatively persistent and can move through soil and water systems, leading to their accumulation in different environmental compartments. Residues have been detected in soil, surface water, and sediments, posing potential risks to non-target organisms and overall ecosystem health (Santos et al., 2018). In addition, long-term exposure to low concentrations may cause subtle but significant physiological stress in both aquatic and terrestrial organisms, potentially leading to broader ecological imbalances (Khan et al., 2020). These issues underline the importance of understanding the environmental behavior and toxicological effects of widely used fungicides.

Tebuconazole Usage and Environmental Relevance

Tebuconazole is a systemic triazole fungicide belonging to the group of sterol demethylation inhibitors (DMIs). It is widely applied in agriculture to control fungal diseases affecting cereals, fruits, vegetables, oilseed crops, and ornamental plants. Its antifungal activity is primarily attributed to the inhibition of sterol 14-α-demethylase, a cytochrome P450-dependent enzyme essential for ergosterol biosynthesis. By interfering with this pathway, tebuconazole disrupts fungal cell membrane integrity and function (Wang et al., 2019). Owing to its broad-spectrum effectiveness and relatively high persistence, it has become one of the most commonly used fungicides worldwide (Mu et al., 2023; Dong et al., 2023).

However, the biochemical pathways targeted by tebuconazole are not unique to fungi. Similar mechanisms exist in non-target organisms, raising concerns about unintended toxic effects. This is particularly important in aquatic environments, where organisms may experience continuous exposure. The widespread use of tebuconazole has led to its detection in multiple environmental compartments, suggesting a potential for long-term ecological impact (Dong et al., 2024).

Environmental Contamination and Exposure Pathways

Tebuconazole enters aquatic systems mainly through agricultural runoff, spray drift, leaching, and wastewater discharge (Syafrudin et al., 2021; Zhu et al., 2022). Monitoring studies have consistently reported its presence in surface water, groundwater, sediments, and soils, often at concentrations ranging from ng/L to µg/L, indicating its widespread environmental distribution (Carena et al., 2022; Aragão et al., 2021).

Its persistence in the environment depends on several factors, including temperature, pH, microbial activity, and light exposure. Under certain conditions, degradation may be slow, resulting in prolonged environmental residence and continuous exposure of aquatic organisms (Guo et al., 2020). In addition, degradation processes can generate transformation products that may retain biological activity or exhibit different toxicity profiles, complicating ecological risk assessments (Chen et al., 2024). The presence of multiple pesticides in the environment may further increase ecological risk through additive or synergistic interactions (Backhaus and Faust, 2021).

Impacts on Aquatic Ecosystems

Aquatic ecosystems are particularly vulnerable to pesticide contamination, as they often act as final sinks for agricultural pollutants. Aquatic organisms can absorb contaminants directly through gills and skin or indirectly through food intake. Exposure to tebuconazole has been linked to a range of toxic effects, including oxidative stress, endocrine disruption, metabolic imbalance, neurotoxicity, and structural damage to tissues (Jiang et al., 2020; Rodrigues et al., 2023).

These effects can negatively influence growth, reproduction, and survival, ultimately affecting population dynamics and ecosystem stability. Fish, commonly used as bioindicators, have shown behavioral changes, physiological stress responses, and tissue damage following exposure. Similarly, invertebrates, algae, and amphibians exhibit growth inhibition, reproductive impairment, and developmental toxicity, which may disrupt trophic interactions and ecological balance (Ortiz-Santaliestra et al., 2020; Qian et al., 2020; Acquaroni et al., 2024).

Need for Mechanistic and Ecological Evaluation

Although tebuconazole is generally regarded as moderately toxic under acute exposure conditions, growing evidence suggests that chronic exposure can lead to significant biochemical and physiological disturbances. These effects are mediated through interconnected mechanisms, including oxidative stress, mitochondrial dysfunction, cytochrome P450 interference, and endocrine disruption (Dong et al., 2024; Wang et al., 2023).

Toxic responses are often influenced by species differences, developmental stage, exposure concentration, and environmental conditions, making direct comparisons between studies difficult. Moreover, organisms in natural environments are typically exposed to mixtures of contaminants rather than single compounds, which may enhance toxicity beyond what is predicted from individual exposures (Zhang et al., 2023). This highlights the need for more integrated and critical evaluations of both mechanistic pathways and ecological relevance in toxicity studies.

Aim of the Review

Given the extensive use and environmental persistence of tebuconazole, there is a clear need for a comprehensive and critical synthesis of existing knowledge. This review aims to integrate current understanding of its physicochemical properties, environmental occurrence, molecular mechanisms of toxicity, and biological effects, with particular emphasis on aquatic organisms. In addition to summarizing available studies, it provides a comparative analysis of findings, considers environmentally relevant exposure scenarios, and identifies key research gaps. The review also discusses biomarker responses and ecological risk assessment to support improved environmental safety evaluation and more sustainable pesticide management.

2. Physicochemical Properties and Environmental Fate of Tebuconazole

The physicochemical characteristics and environmental behavior of pesticides play a key role in determining their distribution, persistence, bioavailability, and ecological risk. Tebuconazole possesses properties that promote both persistence and mobility in the environment, influencing its exposure pathways and toxicokinetic behavior in aquatic organisms (Guo et al., 2020; Li et al., 2021). A clear understanding of these properties is essential for linking environmental presence with biological effects.

Chemical Structure and Molecular Characteristics

Tebuconazole is a systemic triazole fungicide classified under sterol demethylation inhibitors (DMIs). Its chemical structure, (RS)-1-(4-chlorophenyl)-4,4-dimethyl-3-(1H-1,2,4-triazol-1-ylmethyl)pentan-3-ol ($C_{16}H_{22}ClN_3O$; molecular weight 307.8 g/mol), includes a triazole ring and a chlorinated aromatic group. These structural features contribute to its biological activity, chemical stability, and lipophilic nature (PPDB, 2022).

While these characteristics are essential for its antifungal function, they also enable interactions with biological membranes in non-target organisms. Its moderate molecular size and hydrophobic nature facilitate diffusion across membranes, allowing uptake through gills, skin, and the gastrointestinal tract. These properties ultimately influence absorption, distribution, metabolism, and elimination processes, shaping its toxicokinetic profile (Suominen et al., 2023).

Solubility and Partitioning Behavior

Tebuconazole exhibits moderate water solubility (30–40 mg/L) and a relatively high octanol–water partition coefficient (log $K_ow \approx 3.7$), indicating its lipophilic character (PPDB, 2022; Guo et al., 2020). These properties promote its adsorption to organic matter and biological tissues, thereby affecting its environmental distribution and bioavailability.

In aquatic systems, tebuconazole partitions between the water column and sediments. Although adsorption to sediments may reduce its immediate availability in water, it creates a reservoir of contamination that can persist over time. Resuspension processes may subsequently release these bound residues back into the water, leading to prolonged and intermittent exposure (Li et al., 2021; Zhu et al., 2022). This is particularly important for benthic organisms, which may experience continuous exposure under realistic environmental conditions.

Persistence and Environmental Stability

The persistence of tebuconazole is influenced by environmental factors such as temperature, pH, microbial activity, and light exposure. It is generally considered moderately persistent, with reported half-lives ranging from weeks to several months depending on conditions (Guo et al., 2020; Li et al., 2021).

Repeated application in agricultural settings may result in accumulation within environmental compartments, increasing the likelihood of chronic exposure in non-target organisms. In aquatic environments, degradation may be slower due to reduced microbial activity and limited photodegradation, further extending exposure duration (Dong et al., 2024). Such persistence is ecologically significant, as long-term low-level exposure may lead to sublethal effects that are not captured in short-term toxicity studies.

Bioaccumulation Potential

The lipophilic nature of tebuconazole contributes to its potential to accumulate in aquatic organisms through both direct exposure and dietary intake. Studies have shown that triazole fungicides can accumulate in fish tissues, particularly in lipid-rich organs such as the liver and muscle (Suominen et al., 2023; Wang et al., 2022).

Although tebuconazole is not considered highly bioaccumulative compared to persistent organic pollutants, its continuous environmental input and persistence may lead to moderate but ecologically relevant accumulation. This potential varies across species and exposure conditions, making comparisons between studies challenging. Additionally, the possibility of trophic transfer raises further concern, as residues may move across food webs and affect higher trophic level organisms, including birds and mammals (Luo et al., 2022).

Degradation Pathways and Transformation Products

Tebuconazole is degraded in the environment through microbial activity, photolysis, and, to a lesser extent, chemical hydrolysis. Microbial degradation is the dominant pathway, resulting in the formation of metabolites through oxidation and structural modification processes (Chen et al., 2024).Photodegradation in surface waters can produce transformation products with toxicity profiles that differ from the parent compound, whereas hydrolysis generally plays a minor role under neutral conditions (Li et al., 2021). Importantly, some degradation products may remain biologically active or even exhibit increased toxicity, highlighting a limitation of risk assessments that focus only on the parent compound (Dong et al., 2024). Therefore, both parent compounds and their metabolites should be considered in ecological evaluations.

Environmental Transport and Distribution

The movement and distribution of tebuconazole in the environment are governed by its physicochemical properties and surrounding environmental conditions. Agricultural runoff is a major pathway through which it enters aquatic systems, particularly during rainfall events. Spray drift and leaching further contribute to contamination of nearby surface and groundwater bodies (Syafrudin et al., 2021).

Once present in aquatic systems, tebuconazole distributes among water, sediments, and living organisms, creating complex exposure pathways. Sediments can act as secondary sources, releasing previously adsorbed residues back into the water column and prolonging exposure (Carena et al., 2022; Zhu et al., 2022). This dynamic behavior underscores the importance of considering both immediate and long-term exposure scenarios in ecological risk assessments.

3. Occurrence of Tebuconazole in Aquatic Environment

The presence of tebuconazole in aquatic environments has been widely documented, largely due to its extensive agricultural use and environmental persistence. It enters water bodies through several pathways, including agricultural runoff, spray drift, leaching, and wastewater discharge (Syafrudin et al., 2021; Zhu et al., 2022). As a result, it has been consistently detected in surface water, groundwater, and sediments, particularly in regions with intensive agricultural activity.

Environmental monitoring studies report tebuconazole concentrations typically ranging from ng/L to µg/L. Although these levels are often below acute toxicity thresholds, their continuous input can create conditions of chronic exposure, especially for sensitive aquatic species (Carena et al., 2022). Seasonal patterns in pesticide application and rainfall further influence its environmental distribution, with higher concentrations frequently observed during peak agricultural periods (Dong et al., 2023). Such variability makes comparisons between studies difficult and highlights the importance of standardized monitoring strategies.

Sediments play a significant role in the environmental behavior of tebuconazole. Due to its affinity for organic matter, the compound readily adsorbs to sediments, reducing its immediate availability in the water column. However, this does not eliminate risk; instead, sediments act as long-term reservoirs that can gradually release the compound back into the water, leading to sustained exposure for benthic organisms (Li et al., 2021). This aspect is particularly important when evaluating long-term ecological risks.

Wastewater treatment plants also contribute to environmental contamination. Conventional treatment processes may not fully remove fungicide residues, allowing tebuconazole to persist in treated effluents and continuously enter aquatic systems (Aragão et al., 2021). Its detection in groundwater further indicates its ability to move through soil layers, raising concerns about both environmental and potential human exposure (Zhu et al., 2022).

Transformation processes add another layer of complexity to its environmental occurrence. Microbial degradation and photochemical reactions can produce metabolites that persist in aquatic systems and may differ in toxicity from the parent compound (Chen et al., 2024; Dong et al., 2024). However, information on the environmental concentrations and ecological effects of these transformation products remains limited, representing a key research gap.

Beyond direct chemical presence, tebuconazole may also influence ecological processes. Fungicides have been shown to affect aquatic microbial communities, potentially disrupting nutrient cycling and overall ecosystem functioning (Roman et al., 2021). These indirect effects can extend through food webs and impact higher trophic levels.

Bioaccumulation further contributes to its ecological relevance. Aquatic organisms can accumulate tebuconazole through both direct exposure and dietary intake. Although accumulation levels are generally moderate, continuous exposure may facilitate trophic transfer within aquatic food webs, increasing ecological risk (Suominen et al., 2023; Luo et al., 2022).Importantly, tebuconazole rarely occurs alone in natural environments. It is often present alongside other pesticides, and such mixtures may produce additive or synergistic toxic effects that are not adequately captured in single-compound studies (Backhaus and Faust, 2021). Additionally, environmental factors such as temperature, pH, and dissolved organic matter can influence its behavior and toxicity, further complicating real-world exposure scenarios (Zhang et al., 2023).

Overall, the widespread occurrence of tebuconazole, combined with its persistence, moderate bioaccumulation potential, and interaction with environmental variables, underscores the need for integrated monitoring and comprehensive risk assessment approaches. A clearer understanding of its environmental distribution is essential for developing effective strategies to mitigate its ecological impact.

4. Mechanisms of Toxicity of Tebuconazole

The toxic effects of tebuconazole in non-target organisms arise from a complex interplay of biochemical and molecular processes that disrupt normal cellular function. Although its primary mode of action involves inhibition of sterol 14-α-demethylase (a cytochrome P450 enzyme) in fungal pathogens, similar enzymatic systems are present in aquatic organisms. As a result, interference with these conserved pathways can lead to unintended toxic effects across multiple levels of biological organization.Rather than acting through a single pathway, tebuconazole induces a network of interconnected responses. These include oxidative stress, disruption of cytochrome P450-mediated metabolism, mitochondrial dysfunction, endocrine interference, neurotoxicity, genotoxicity, and apoptosis (Dong et al., 2024; Zhao et al., 2024). Among these, oxidative stress is widely recognized as a central mechanism that initiates downstream cellular damage.

Exposure to tebuconazole can lead to excessive production of reactive oxygen species (ROS), overwhelming the organism's antioxidant defense systems. This imbalance results in oxidative damage to lipids, proteins, and DNA. At the cellular level, elevated ROS can disrupt mitochondrial membrane integrity by inducing permeability changes, leading to loss of membrane potential and reduced ATP production. Mitochondrial dysfunction, in turn, can further increase ROS generation, creating a self-amplifying cycle of cellular damage.Oxidative stress also plays a key role in activating intracellular signaling pathways. ROS-mediated damage can trigger pathways such as p53, JNK, and caspase cascades, ultimately leading to programmed cell death (apoptosis). This highlights that oxidative stress is not only a damaging factor but also a regulator of cellular signaling processes involved in stress response and cell fate.

In addition to oxidative stress, inhibition of cytochrome P450 enzymes disrupts metabolic homeostasis and detoxification pathways. This can lead to the accumulation of toxic intermediates within the organism. Since these enzymes are also involved in steroid hormone synthesis, their disruption is closely associated with endocrine interference. Alterations in hormone regulation

Taken together, these mechanisms demonstrate that tebuconazole toxicity is not the result of isolated effects but rather a coordinated network of interacting pathways. Understanding these interactions is essential for linking molecular-level changes to organism-level outcomes and for improving the accuracy of ecological risk assessments.

Oxidative Stress and Redox Imbalance

Oxidative stress is widely regarded as one of the primary mechanisms underlying the toxicity of tebuconazole and often represents an early event in cellular injury. Exposure to this fungicide has been shown to increase the production of reactive oxygen species (ROS), including superoxide anions, hydrogen peroxide, and hydroxyl radicals. These reactive molecules can damage essential cellular components, leading to lipid peroxidation, protein oxidation, enzyme dysfunction, and DNA damage (Er et al., 2025; Feng et al., 2022).

Under normal conditions, cells maintain redox balance through antioxidant defense systems such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione-S-transferase. However, prolonged or high-level exposure to tebuconazole can overwhelm these defenses, resulting in oxidative damage and disruption of cellular function. Importantly, oxidative stress does not act in isolation; it serves as a central mechanism linking multiple toxic pathways.

At the mechanistic level, excessive ROS can compromise mitochondrial membrane integrity by inducing permeability changes, which leads to loss of membrane potential and reduced ATP production. ROS can also activate stress-related signaling pathways such as p53 and JNK, which are involved in regulating apoptosis and cellular stress responses. These interactions highlight the dual role of oxidative stress—as both a direct damaging factor and a regulator of downstream processes such as inflammation, mitochondrial dysfunction, and programmed cell death (Monteiro et al., 2021; Shi et al., 2023).

Disruption of Cytochrome P450 and Metabolic Homeostasis

As a sterol demethylation inhibitor, tebuconazole targets cytochrome P450 enzymes that play a crucial role in xenobiotic metabolism, detoxification, and the synthesis of endogenous compounds such as steroid hormones. In non-target organisms, inhibition of these enzymes can impair detoxification processes, leading to the accumulation of reactive or harmful intermediates (Wang et al., 2023).

Beyond detoxification, disruption of cytochrome P450 activity can affect lipid metabolism, carbohydrate utilization, and overall energy balance. These changes may result in physiological stress and reduced organismal fitness. Notably, inhibition of steroidogenic enzymes connects metabolic disturbances with endocrine disruption, emphasizing that these effects are closely interrelated rather than independent (Dong et al., 2024).

Endocrine Disruption and Hormonal Imbalance

Tebuconazole is increasingly recognized as a potential endocrine disruptor due to its ability to interfere with hormone synthesis and signaling pathways. Changes in gene expression related to steroidogenesis and hormone metabolism may lead to altered levels of sex hormones and impaired reproductive function (Ma et al., 2024).

In aquatic organisms, such disruption can manifest as abnormal gonadal development, altered reproductive behavior, reduced fertility, and developmental defects. Importantly, these effects have been observed even at environmentally relevant concentrations, suggesting that long-term, low-level exposure may have significant ecological consequences. The close link between cytochrome P450 inhibition and hormonal imbalance further highlights the integrated nature of tebuconazole toxicity.

Mitochondrial Dysfunction and Energy Metabolism Impairment

Mitochondria are central to ATP production and cellular energy regulation. Exposure to tebuconazole can interfere with the electron transport chain, reducing ATP synthesis and impairing overall energy metabolism (Feng et al., 2022).

This mitochondrial impairment is closely associated with oxidative stress. Disruption of electron transport can enhance ROS generation, creating a feedback loop that amplifies cellular damage. Reduced energy availability can, in turn, affect essential biological processes such as growth, reproduction, and immune function. These findings indicate that mitochondrial dysfunction works in concert with oxidative stress to drive toxicity.

Neurotoxicity and Behavioral Alterations

Neurotoxic effects of tebuconazole have been documented in several aquatic species, often appearing as changes in behavior such as altered swimming patterns, reduced feeding activity, and impaired predator avoidance. These effects are commonly linked to oxidative damage in neural tissues and disruption of neurotransmitter systems (Lin et al., 2021; Rodrigues et al., 2023).Alterations in acetylcholinesterase (AChE) activity, a key enzyme involved in neurotransmission, are frequently reported and may contribute to impaired neural signaling. From an ecological perspective, such behavioral changes are significant because they can reduce survival and reproductive success, ultimately affecting population dynamics.

Genotoxicity and DNA Damage

Tebuconazole exposure has been associated with genotoxic effects, including DNA strand breaks, chromosomal abnormalities, and micronucleus formation. These effects are largely attributed to oxidative stress and interference with DNA repair mechanisms (Zhang et al., 2020; Li et al., 2020).

Genetic damage is particularly concerning because it can lead to mutations, developmental abnormalities, and long-term impacts at the population level. The persistence of such damage links molecular-level effects to broader ecological consequences.

Apoptosis and Programmed Cell Death

Apoptosis induced by tebuconazole occurs through multiple interconnected pathways, including oxidative stress, mitochondrial dysfunction, and activation of caspase signaling cascades. Additional factors such as disruption of calcium homeostasis and endoplasmic reticulum stress may further contribute to programmed cell death (Li et al., 2020; Dong et al., 2024).

While apoptosis initially serves as a protective mechanism to eliminate damaged cells, excessive activation can result in tissue injury and organ dysfunction, particularly in vital organs such as the liver, gills, and kidney.

Integrated Toxicity Pathways

The toxic effects of tebuconazole are best understood as a network of interacting mechanisms rather than isolated processes. For example, oxidative stress can trigger mitochondrial dysfunction, which in turn increases ROS production and activates apoptotic pathways. Similarly, cytochrome P450 inhibition links metabolic disruption with endocrine imbalance.

This interconnected framework highlights the importance of viewing toxicity as a cascade of linked events. Such an integrated approach is essential for connecting molecular responses to organism-level outcomes and for improving ecological risk assessment models.

5. Toxic Effects of Tebuconazole in Aquatic Organisms

Aquatic ecosystems are particularly susceptible to pesticide contamination due to continuous inputs from agricultural and other sources. Exposure to tebuconazole has been associated with a wide range of biological effects, including oxidative stress, metabolic disturbances, endocrine disruption, neurotoxicity, histopathological damage, and reproductive impairment.

The severity and nature of these effects vary depending on factors such as exposure concentration, duration, species sensitivity, and environmental conditions. This variability underscores the importance of carefully comparing experimental conditions and considering environmentally realistic exposure scenarios when interpreting toxicological findings.

Toxicity in Fish

Fish are widely used as model organisms in ecotoxicology due to their ecological relevance and direct exposure to waterborne contaminants. Tebuconazole exposure has been linked to behavioral changes such as erratic swimming, reduced activity, increased mucus secretion, and impaired feeding. These responses are often early indicators of physiological stress and neurotoxicity (Rodrigues et al., 2023; Lin et al., 2021).

At the biochemical level, oxidative stress is one of the most consistently observed effects. Increased ROS production leads to enhanced lipid peroxidation and altered antioxidant enzyme activity, including changes in superoxide dismutase, catalase, and glutathione-related enzymes (Monteiro et al., 2021; Rana et al., 2024). However, the extent of these responses varies across species and experimental conditions.

Metabolic disturbances are also common. Changes in enzymes such as alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase indicate tissue damage and metabolic imbalance, particularly in the liver and muscle (Huang et al., 2022). Since the liver is central to detoxification, its impairment can significantly disrupt physiological homeostasis. Alterations in glucose and glycogen levels further reflect changes in energy metabolism, especially under chronic exposure.

Histopathological studies provide clear evidence of organ-level damage. Structural changes in the liver, gills, kidney, and brain—such as cellular degeneration, necrosis, and inflammation—have been widely reported (Rodrigues et al., 2023). These alterations can compromise essential functions like respiration, ion regulation, and detoxification.

Reproductive effects have also been observed, including hormonal imbalance, impaired gonadal development, and reduced reproductive performance (Liang et al., 2022). Notably, such effects may occur even at relatively low exposure levels, raising concerns about long-term population impacts.

6. Genotoxic and Molecular Biomarkers

Genotoxic biomarkers are important tools for assessing DNA damage and cellular toxicity in organisms exposed to contaminants. Common indicators include DNA strand breaks, micronucleus formation, chromosomal abnormalities, and responses observed through comet assays (Zhang et al., 2020; Li et al., 2020). These markers are particularly valuable because genetic damage can lead to mutations, developmental defects, and long-term consequences at the population level.

Molecular biomarkers provide deeper insight into the underlying mechanisms of toxicity. Changes in gene expression related to oxidative stress, apoptosis, detoxification pathways, and stress proteins help reveal how organisms respond at the cellular level. Advances in techniques such as transcriptomics and proteomics have made it possible to detect early and sensitive molecular responses to contaminants (Tang et al., 2021). However, interpreting these responses requires careful consideration of exposure conditions, species differences, and experimental design, as these factors can strongly influence the results.

Integrated Biomarker Approaches

Evaluating multiple biomarkers across different levels of biological organization—biochemical, physiological, and molecular—offers a more complete understanding of pesticide toxicity than relying on a single endpoint. Multi-biomarker approaches help identify exposure pathways, clarify mechanisms of action, and better link observed effects to ecological outcomes (Kaur et al., 2023).

Such integrated strategies also improve the connection between laboratory findings and real-world environmental conditions, thereby strengthening ecological risk assessments. In addition, biomarker indices can provide quantitative measures of organism health and environmental stress, making them useful for monitoring programs. For these reasons, multi-biomarker approaches are increasingly recommended for assessing the complex effects of pesticides in aquatic ecosystems.

7. Ecological Risk Assessment of Tebuconazole

Ecological risk assessment plays a key role in evaluating the potential environmental impacts of pesticide contamination. The risk associated with tebuconazole depends on several factors, including its environmental concentration, persistence, bioavailability, bioaccumulation potential, species sensitivity, and duration of exposure. Given its widespread use and persistence, tebuconazole is increasingly recognized as a contaminant of concern in aquatic environments (Luo et al., 2022; Zhu et al., 2022).

Risk assessment typically involves comparing predicted environmental concentrations (PEC) with predicted no-effect concentrations (PNEC). Available evidence suggests that triazole fungicides may pose moderate to high risks, particularly to sensitive organisms such as algae and aquatic invertebrates. Although acute toxicity may appear relatively low, chronic exposure—even at environmentally relevant concentrations—can lead to sublethal effects such as oxidative stress, reproductive impairment, and developmental abnormalities. These effects may ultimately influence population dynamics over time (Silva et al., 2019).

Environmental Exposure and Risk Characterization

Tebuconazole enters aquatic systems mainly through agricultural runoff, spray drift, leaching, and wastewater discharge. These pathways contribute to contamination of both surface waters and sediments, with concentrations often varying seasonally depending on agricultural practices and rainfall patterns (Syafrudin et al., 2021).

Sediments can act as secondary sources of contamination by releasing previously adsorbed residues back into the water column, thereby prolonging exposure. As a result, aquatic organisms may experience both short-term high exposures and long-term low-level exposure. Risk characterization studies indicate that sublethal effects can occur at concentrations lower than those causing mortality, highlighting the importance of including chronic endpoints in ecological assessments (Pettersen et al., 2022).

Bioaccumulation and Trophic Transfer Risks

Bioaccumulation is an important factor in determining ecological risk, as it influences how contaminants are retained and transferred within food webs. Due to its lipophilic nature, tebuconazole can accumulate in aquatic organisms, particularly in lipid-rich tissues such as the liver and muscle (Suominen et al., 2023; Wang et al., 2022).

Although its bioaccumulation potential is generally considered moderate, continuous environmental exposure may lead to gradual buildup in organisms over time. This accumulation can be transferred across trophic levels, potentially affecting predators such as birds and mammals that rely on aquatic organisms for food (Whitfield et al., 2024). These processes highlight the importance of considering not only direct exposure but also food web dynamics in ecological risk assessments.

Mixture Toxicity and Environmental Interactions

In natural environments, organisms are rarely exposed to a single chemical. Instead, they encounter complex mixtures of pesticides and other contaminants. Agricultural runoff, in particular, often contains multiple compounds, and combined exposure can produce additive or even synergistic effects that increase overall toxicity beyond what would be expected from individual substances (Backhaus and Faust, 2021). This represents a significant limitation of many laboratory studies, which typically assess single-compound toxicity under controlled conditions.

Environmental factors such as temperature, pH, salinity, and dissolved oxygen also play an important role in influencing pesticide behavior, bioavailability, and organism sensitivity. Changes in climate, including rising temperatures and altered rainfall patterns, may further affect degradation rates and exposure dynamics (Zhang et al., 2023). Together, these interactions highlight the need to incorporate realistic environmental conditions into ecological risk assessments to better reflect field scenarios.

Sensitivity of Aquatic Organisms

The sensitivity of aquatic organisms to tebuconazole varies widely depending on species, life stage, and physiological characteristics. Early developmental stages are generally more vulnerable, as their detoxification systems are not fully developed and their metabolic demands are higher (Acquaroni et al., 2024). Primary producers such as algae may also show high sensitivity, since fungicides can directly interfere with cellular processes involved in growth and metabolism.

Differences in sensitivity among fish, amphibians, and invertebrates suggest that single-species studies may not adequately represent ecosystem-level responses. Such variability can lead to shifts in species composition and ecological function following pesticide exposure, underscoring the importance of multi-species and multi-level approaches in toxicity assessment (Pettersen et al., 2022).

8. Ecological Implications and Environmental Management

The ecological effects of tebuconazole extend beyond individual organisms to influence population dynamics and ecosystem functioning. Chronic exposure may result in reduced growth, impaired reproduction, and increased mortality, which can gradually alter community structure. In particular, impacts on primary producers and invertebrates may disrupt food web interactions, nutrient cycling, and overall ecosystem stability (Whitfield et al., 2024).

To mitigate these risks, effective environmental management strategies are essential. These may include optimizing pesticide application practices, developing safer formulations, improving wastewater treatment processes, and implementing continuous environmental monitoring. Regulatory frameworks should also consider both acute and chronic toxicity, along with mixture effects and environmental variability, to support sustainable pesticide use while protecting aquatic ecosystems (Silva et al., 2019).

9. Conclusion

Tebuconazole is one of the most widely used triazole fungicides in modern agriculture, and its extensive application has led to increasing environmental contamination, particularly in aquatic systems. Its physicochemical properties, including persistence and moderate lipophilicity, contribute to its widespread distribution, prolonged environmental presence, and potential for bioaccumulation in aquatic organisms.

This review highlights that tebuconazole induces a broad range of toxic effects, including oxidative stress, endocrine disruption, neurotoxicity, metabolic disturbances, and histopathological changes. These effects arise from interconnected mechanisms involving cytochrome P450 inhibition, mitochondrial dysfunction, excessive reactive oxygen species production, and activation of apoptotic pathways. Understanding these integrated mechanisms is essential for linking molecular-level changes to organismal and ecological outcomes.

A key strength of this review is its comparative and integrative approach, which brings together findings across studies while highlighting variability in species sensitivity, exposure conditions, and experimental design. Evidence suggests that early life stages and certain groups, such as algae and invertebrates, may be particularly sensitive, emphasizing the need for life-stage-specific and multi-species assessments. Furthermore, consideration of environmentally relevant concentrations and chronic exposure scenarios reveals that sublethal effects can have significant long-term ecological consequences.

Biomarkers provide valuable tools for early detection and mechanistic interpretation of toxic effects, while ecological risk assessment underscores the importance of incorporating chronic toxicity, bioaccumulation, trophic transfer, and mixture effects. These findings demonstrate that real-world exposure scenarios are more complex than laboratory conditions and require integrated evaluation approaches.

Despite advances in understanding, several knowledge gaps remain, particularly regarding long-term chronic exposure, the toxicity of transformation products, and the combined effects of multiple environmental stressors. Future research integrating molecular, biochemical, and ecological perspectives will be essential for improving predictive models and strengthening risk assessment frameworks.

Overall, a comprehensive and mechanistic understanding of tebuconazole toxicity is crucial for developing effective environmental management strategies and ensuring sustainable pesticide use while minimizing risks to aquatic ecosystems and biodiversity. This review contributes to that goal by linking mechanistic insights with ecological relevance under realistic exposure conditions.

Highlights

- Tebuconazole is widely detected in aquatic environments due to intensive agricultural use.
- Toxicity is driven by interconnected mechanisms, particularly oxidative stress and mitochondrial dysfunction.
- Sensitivity varies among species and life stages, with early developmental stages showing higher vulnerability.
- Biomarkers provide effective tools for early detection and mechanistic understanding of toxicity.
- Chronic exposure, bioaccumulation, and mixture effects significantly increase ecological risk in aquatic systems.

Table 1. Physicochemical properties and environmental behavior of tebuconazole

Parameter	Value / Characteristics	Environmental Significance	References
Chemical name	(RS)-1-(4-chlorophenyl)-4,4-dimethyl-3-(1H-1,2,4-triazol-1-ylmethyl)pentan-3-ol	Triazole fungicide with systemic activity	PPDB, 2022
Molecular formula	$C_{16}H_{22}ClN_3O$	Determines stability and transport behavior	PPDB, 2022
Molecular weight	307.8 g/mol	Influences absorption and distribution	PPDB, 2022
Water solubility	30–40 mg/L	Moderate mobility in aquatic systems	Guo et al., 2020
Log Kow	~3.7	Indicates lipophilicity and bioaccumulation potential	Li et al., 2021
Soil half-life	Several weeks to months	Persistence increases exposure duration	Dong et al., 2023
Environmental fate	Runoff, leaching, sediment adsorption	Major pathways to aquatic ecosystems	Syafrudin et al., 2021
Degradation pathways	Microbial metabolism, photolysis	Formation of transformation products	Chen et al., 2024

Table 2. Occurrence of tebuconazole in aquatic environments

Environmental Matrix	Concentration Range	Source of Contamination	References
Surface water	ng/L–µg/L levels	Agricultural runoff and spray drift	Carena et al., 2022
Groundwater	Trace concentrations	Leaching through soil profile	Zhu et al., 2022
Sediments	Accumulated residues	Adsorption to organic matter	Li et al., 2021
Wastewater effluents	Detectable residues	Incomplete removal during treatment	Aragão et al., 2021
Agricultural drainage	Elevated seasonal concentrations	Intensive pesticide application	Dong et al., 2023

Table 3. Mechanisms of toxicity of tebuconazole in aquatic organisms

Mechanism	Biological Effects	Key Indicators	References
Oxidative stress	ROS generation, lipid peroxidation, cellular damage	SOD, CAT, MDA	Li et al., 2020; Er et al., 2025
Cytochrome P450 inhibition	Metabolic disruption, endocrine effects	CYP enzyme alterations	Wang et al., 2023
Endocrine disruption	Hormonal imbalance, reproductive toxicity	Steroid hormones, GSI	Ma et al., 2024
Mitochondrial dysfunction	Reduced ATP,	Mitochondrial enzyme activity	Feng et al., 2022

Mechanism	Biological Effects	Key Indicators	References
	energy imbalance		
Neurotoxicity	Behavioral alterations	AChE activity	Lin et al., 2021
Genotoxicity	DNA damage	Micronucleus, comet assay	Zhang et al., 2020
Apoptosis	Programmed cell death	Caspase activation	Dong et al., 2024

Table 4. Toxic effects of tebuconazole in aquatic organisms

Organism	Exposure Type	Observed Effects	References
Zebrafish (*Danio rerio*)	Acute and chronic	Hepatotoxicity, oxidative stress, apoptosis	Li et al., 2020
Freshwater fish species	Sublethal exposure	Behavioral abnormalities, metabolic disturbance	Rodrigues et al., 2023
Common carp (*Cyprinus carpio*)	Chronic exposure	Oxidative stress, tissue damage	Rana et al., 2024
Aquatic invertebrates	Chronic exposure	Reduced survival and reproduction	Barata et al., 2020
Algae	Growth inhibition tests	Photosynthesis impairment	Qian et al., 2020
Amphibians	Developmental exposure	Developmental abnormalities	Ortiz-Santaliestra et al., 2020

Table 5. Biomarkers used for assessment of tebuconazole toxicity

Biomarker Category	Parameters	Toxicological Significance	References
Oxidative stress	SOD, CAT, GPx, GST, MDA	Cellular oxidative damage	Monteiro et al., 2021
Metabolic enzymes	ALT, AST, LDH	Liver and tissue injury	Huang et al., 2022
Neurotoxicity	AChE activity	Nervous system impairment	Lin et al., 2021
Hematological	RBC, WBC, hemoglobin	Physiological stress	Kaur et al., 2023
Genotoxicity	DNA damage, micronucleus	Genetic toxicity	Zhang et al., 2020
Endocrine	Hormone levels, GSI	Reproductive disruption	Ma et al., 2024

The toxic effects of tebuconazole involve interconnected molecular and physiological pathways that collectively contribute to organism-level and ecological consequences

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