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Bioefficacy and Management Potential of Strobilurin-Based Fungicides against Rice Blast Disease

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SUMMARY

Strobilurin fungicides have been cornerstone in rice blast management owing to their systemic protection, broad-spectrum nature, and positive impact on yield. Their favourable safety profile and effectiveness make them key components of integrated disease management systems. However, their long-term sustainability is threatened by the evolution of fungal resistance, predominantly through G143A mutations in the cytochrome b gene. Effective resistance management strategies includes rotating fungicides with diverse modes of action, using fungicides mixtures with compatible partners like triazoles, and avoiding excess reliance on single-chemistry molecules. Future research should prioritize on the discovery of next-generation strobilurins, monitoring of molecular resistance, and adoption of environmentally safe formulations. A holistic approach that integrates host resistance, agronomic practices, and prudent use of fungicide will remain crucial in sustainable management of rice blast disease.

INTRODUCTION

Rice (*Oryza sativa* L.) is one of the primary staple food crops for more than half of the world's population (FAO, 2024). Rice importance as a primary food source is closely associated to its contribution in food security, especially in Asia, Africa, and portions of Latin America (Khush, 2013). However, rice production is seriously hampered by biotic stresses, especially rice blast disease caused by the fungal pathogen *Magnaporthe oryzae* (Yadav et al., 2019, Jeevan et al., 2023). Globally, rice blast is documented as the most destructive disease of rice worldwide, causing 10% to 30%, yield losses under normal conditions and up to 70% under severe epidemics (Skamnioti and Gurr, 2009; Dean et al., 2012). It infects several parts of the rice plant (leaves, stems, nodes, and panicles), resulted in significant yield reduction and considerable economic losses (Panda et al., 2017, Sahu et al., 2017). The rapid genetic evolution, remarkable adaptability and wide virulence spectrum, have made its management more complex. These factors make this disease as a consistent problem to sustainable rice production. Consequently, implementing effective management practices is essential for rice blast to safeguards rice yields, guarantee food security, and sustain the income of millions of growers (Susan et al., 2019). This calls for an integrated strategies that includes agronomic management, host resistance, and fungicidal treatments, with special focus on effective and environmentally sustainable chemical intervention such as strobilurin based fungicides (Kumar et al. 2020).

1. Overview of Strobilurin Fungicides

Chemical Nature and Classification

Strobilurins fungicides are derived from β-methoxyacrylate derivatives that were first isolated from *Strobilurus tenacellus* (Bartlett et al., 2002). They are categorized under QoI (quinone outside inhibiting) category, designated as FRAC Group 11, owing to their unified mode of action (FRAC, 2024). Structurally, they share a hallmark of *O-methoxyacrylate* or *O-methoxyiminoacetate* pharmacophore, which confers broad-spectrum antifungal activity (Bartlett et al., 2002; Balba, 2007). Commercial formulation of strobilurins includes, azoxystrobin, kresoxim-methyl, picoxystrobin, pyraclostrobin, trifloxystrobin, and metominostrobin (most recent), each differ slightly in their substituent groups and physicochemical traits (Kumar et al., 2020).

Mode of Action: Inhibition of Mitochondrial Respiration via Cytochrome *bc*1 Complex

Strobilurins fungicides exert their effect by inhibiting mitochondrial respiration through binding with the Qo (Quinol-Oxidation) site of the cytochrome *bc*1 complex (complex III) within mitochondria of fungus (Bag et al., 2016, FRAC, 2024). This interaction inhibits electron transfer from ubiquinol to cytochrome *c*1, disrupting

ATP synthesis and inducing quick energy depletion in fungal cells (Musso et al., 2020). The site-directed inhibition accounts for their potent fungicidal effectiveness; however, it also adds to the development of resistance primarily through mutations in the *cytb* gene, notably through G143A substitution mechanism (Gisi et al., 2002; FRAC, 2024).

Systemic and Protective Attributes

Although, mainly protective in nature, several members in strobilurin group represents translaminar movement and xylem mobility, enabling partial systemic protection of newly emerged leaves (Bartlett et al., 2002). For instance, azoxystrobin represents strong protective and antisporulant effect but limited curative action (Balba, 2007). Additionally, these fungicides also displayed delayed plant senescence and promote physiological processes like chlorophyll preservation and enhanced photosynthetic efficiency, leading to a "greening effect" and better yield stability (Grossmann and Retzlaff, 1997).

2. Efficacy of Strobilurins against Rice Blast

Numerous field and laboratory investigations showed stronger effectivity of strobilurins against rice blast disease. *In–vitro* study showed that, azoxystrobin and trifloxystrobin effectively inhibits spore germination and mycelial growth of *M. oryzae* (Kumar et al., 2020). Field trials azoxystrobin spray demonstrated reduced blast severity (up to 70%) and improved grain yield compared to control experiment (Kongcharoen et al., 2020). Similarly, strobilurin-based combinations achieved reductions in blast disease (both leaf and neck) incidences across varying environmental conditions (Xu et al., 2023).

Comparative Analysis of Strobilurins: Azoxystrobin, Trifloxystrobin, and Metominostrobin

Name of fungicide	Characteristics	Effectivity	Reference
Azoxystrobin (first commercial strobilurin)	Broad-spectrum activity and partial systemicity	Rice blast	Kongcharoen et al., 2020
Trifloxystrobin	High lipophilicity, shows excellent residual and translaminar activity	Leaf and panicle blast	Ogoshi et al., 2018
Metominostrobin	Broad-spectrum activity	Leaf and neck blast	Gaikwad and Balgude, 2018

Impact on Disease Severity Reduction and Yield Improvement

Field trials showed strobilurin applications considerably reduced rice blast severity (40–70%) based on disease pressure and timing (Kumar et al., 2020; Xu et al., 2023). Field application of azoxystrobin or trifloxystrobin + tebuconazole during critical growth stages showed better yield gains (10–25%) (Kongcharoen et al., 2020). Beyond reducing disease severity, strobilurins aid plants in enhanced physiological performance, delayed senescence, and better grain filling, thus enhancing overall yield stability (Balba, 2007). However, attributable to their single-site action, emergence of resistance in *M. oryzae* populations is a serious concern. Thus, this issue can be minimised by fungicidal rotation or its combination with fother ungicides having different modes of action (e.g. triazoles or SDHIs), to maintain their efficacy (FRAC, 2024; Gisi et al., 2002).

1. Mechanisms of Action and Resistance

Inhibition of Fungal Mitochondrial Processes

Strobilurin fungicides functions as quinone outside inhibitors (QoIs), directly acting on the cytochrome *bc*1 complex (complex III) within mitochondrial electron transport chain (Bartlett et al., 2002). Specifically, they attach to the Qo site on cytochrome *b*, where cytochrome *c1* is normally getting electrons from ubiquinol. This binding halts the electron transfer, altering proton gradient formation across the inner mitochondrial membrane and thus obstructing ATP synthesis (Musso et al., 2020). Consequently, energy production fails, which ultimately leads to suppression of spore germination as well as mycelial growth (Balba, 2007). The strobilurins fungicide mechanism of site-specific inhibition explains about their high potency but with limited curative activity.

Resistance development: Mutations Such as G143A

In spite of their broad efficacy, resistance against QoIs have developed globally, caused by point mutations in the mitochondrial cytochrome *b* gene (*cytb*) (Gisi et al., 2002). The most common mutation, G143A, (substitution of glycine with alanine) occur at position 143 within the Qo-binding site, that prevent strobilurin binding without hampering mitochondrial function (Sierotzki et al., 2000). Other mutations (F129L and G137R) that confer lower resistance levels than common mutation (G143A) have also been reported (FRAC, 2024). The resistance observed among fungus is often qualitative, means mutant fungal isolates exhibit near-total insensitivity against all QoI fungicides (Bartlett et al., 2002). Resistance once established within fungal population remains stable and persistent due to the mitochondrial inheritance of *cytb* gene (Gisi et al., 2002). Thus, effectiveness of QoIs based fungicides can be long-lasting by employing strategies like resistance alleles monitoring and use of fungicides rotation.

Structural and Molecular Insights Into Resistance Mechanisms

Structural analyses of the *bc*1 complex have demonstrated both mechanism; strobilurins interaction at the Qo site and disruption of binding due to G143A mutation. High-resolution crystallography, revealed that mutation causes formation of bulky alanine residue at position 143 which physically blocks QoI molecules from entering their binding site resulting in eliminating their inhibitory effect (Sierotzki et al., 2000). Computational modelling also support alteration in local conformations due to these mutations and lessen hydrophobic interactions decisive for binding of fungicide (Musso et al., 2020). Such molecular insights have been helpful in developing next-generation QoIs fungicides with better binding elasticity and reduced cross-resistance (Xu et al., 2023).

2. Synergistic and Combined Use

Benefits of combining strobilurins with other fungicides

Strobilurins are often mixed with different fungicides having modes of action, especially triazoles (demethylation inhibitors) to lessen the resistance emergence and broaden disease management (Bartlett et al., 2002; Gisi et al., 2002). Triazoles acts by inhibiting the C14-demethylase enzyme which is involved in ergosterol biosynthesis, thus affecting membrane integrity, whereas strobilurins act by disrupting mitochondrial respiration. Their mixing offers complementary and synergistic effects as strobilurins is preventive in action, and triazoles showed curative and antisporulant activity (Balba, 2007; Xu et al., 2023). Further, such combination helps in reducing selection pressure on target site individually, delay in the resistance development and recuperating the longevity of both active ingredients (FRAC, 2024).

Examples of Commercial Formulations and Their Synergistic Effects

Numerous commercial products combine QoIs and triazoles for management of rice blast and other cereal diseases. Examples includes; trifloxystrobin + tebuconazole**,** azoxystrobin + difenoconazole, and pyraclostrobin + epoxiconazole (Kongcharoen et al., 2020; Ogoshi et al., 2018). Field trials showed that, these mixture combinations surpass single applications, providing better disease suppression as well as yield stability. For instance, panicle blast severity and improved grain yield was found with trifloxystrobin + tebuconazole treatments as compared to individual application of fungicides (Ogoshi et al., 2018). Similarly, azoxystrobin + difenoconazole showed better control of both leaf and neck blast under high disease pressure (Xu et al., 2023).

Strategies for Resistance Management

For better resistance management, strategies mostly focus on rotation and fungicidal mixtures with different FRAC codes to minimise the risk of development of resistant populations (FRAC, 2024). Recommended practices mostly include restraining QoI applications with only two or three per season, using combination of systemic partners (e.g., triazoles, SDHIs), and integrating non-chemical approaches such as proper field sanitation and growing resistant cultivars (Gisi et al., 2002; Kumar et al., 2020). The combined and careful utilization of strobilurins within the framework of an integrated disease management is crucial for effective blast management and fungicide efficacy over sustainable period.

Environmental and Toxicological Aspects

Strobilurin fungicides are mostly recognised as eco-friendly owing to their low usage rates, quick degradation and low toxicity against mammals and beneficial organisms (Bartlett et al., 2002; Balba, 2007). Further, their low acute toxicity (mammals and birds), and rapid degradation (in soil and water) reduces their long-term persistence in the environmental (Li et al., 2011). However, temporary accumulation in sediments occurs due to their lipophilic nature, and few formulations are harmful to aquatic organisms (especially fish and crustaceans) (Gisi et al., 2002). Study on effects on non-target organisms (including beneficial soil microbes and mycorrhizae) elucidated that their effect often transient and varied based on fungicides dose and environmental conditions (Komárek et al., 2010). Soil microbial dynamics can be altered through long-term or excessive use which directly affects nutrient cycling and soil fertility. Therefore, soil health and ecological integrity can be sustained through monitoring environmental residues and adopting balanced use strategies.

Recent Advances and Future Perspectives

Recent research has concentrated on synthesizing innovative hybrid formulations with better delivery systems to improve the constancy, bioavailability, and activity spectrum of strobilurin fungicides. For example, hybrid compounds integrating strobilurin with triazole groups have demonstrated greater fungicidal activity and lowered potential of resistance risks development (Xu et al., 2023). Molecular modeling and docking analysis aid to provide better insights on fungicide target interactions within the cytochrome *bc1* complex, facilitating the rational development of new analogues with better efficacy against resistant *M. oryzae* strains (Wang et al., 2021). Furthermore, formulations based on nanotechnology have also improved their foliar adhesion and controlled release, minimizing drift hazard and improving field efficiency. In the future, designing new strobilurin analogues that effectively target resistant fungal populations, combined with modern agriculture technologies, hold promise for sustainable and adaptive management solutions. Integrating biochemical, molecular, and ecological data will be imperative to optimize fungicide usage within climate-resilient and environmentally sound disease management strategies.

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