STROBILURINS - QUINONE OUTSIDE INHIBITORS: DEVELOPMENT, APPLICATIONS, AND RESISTANCE

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STROBILURINS	
methoxy-acrylates	• azoxystrobin • coumoxystrobin • enoxastrobin • flufenoxystrobin • picoxystrobin • pyraoxystrobin
methoxy-acetamide	• mandestrobin
methoxy-carbamates	• pyraclostrobin • pyrametostrobin • triclopyricarb
dihydro-dioxazines	• fluoxastrobin

Introduction

Strobilurins are a class of fungicides mostly derived from natural substances produced by wood-decaying mushrooms, particularly from the genus Strobilurus. The discovery of strobilurins dates back to the 1970s when researchers identified their unique fungicidal properties. This discovery led to the synthesis of various strobilurin analogs. Thanks to their broad-spectrum activity and relatively low toxicity to humans and animals, strobilurins have become some of the most widely used fungicides globally. They are effective against a wide range of fungal pathogens, including those causing powdery mildew, rusts, leaf spots, and blights, and are used in various crops such as cereals, field crops, fruits, tree nuts, vegetables, turfgrasses, and ornamentals. These fungicides exhibit systemic properties, meaning they can be absorbed by plant tissues and translocated throughout the plant, which provides protection to both treated and new growth, enhancing their effectiveness in disease management. Strobilurins are compatible with many other agricultural chemicals, including insecticides and herbicides, allowing them to be integrated easily into existing pest management programs. This compatibility facilitates their use in tank mixes, reducing the number of applications needed and saving time and resources for farmers. In some cases, they are also found to enhance plant growth. In this review, the properties of strobilurins such as their synthesis, biochemical mode of action, fungicidal activity, resistance risk, and human and environmental safety are discussed in detail.

Strobilurins, introduced in 1996, have become the second largest chemistry group of fungicides, primarily due to their widespread use on cereals and, more recently, on soybeans. The market reached $600 millions in 2004. Companies have also promoted the plant health benefits of these fungicides for soybeans and corn. Strobilurin fungicides are highly effective, possess a broad spectrum of activity, and are suitable for a wide range of crops. However, issues with disease resistance, such as Septoria in wheat in Europe and challenges in the U.S. turf market, have impacted sales. Consequently, companies are adjusting their usage recommendations by developing mixtures and exploring alternative applications, including seed treatments.

STROBILURINS	
oximino-acetates	• kresoxim-methyl • trifloxystrobin
oximino-acetamides	• dimoxystrobin • fenaminstrobin • metominostrobin • orysastrobin
oxazolidine-diones	• famoxadone
imidazolinones	• fenamidone
benzyl-carbamates	• pyribencarb

MODE OF ACTION

Strobilurins exert a site-specific mode of action by inhibiting fungal respiration at the Qo site within the mitochondria. In essence, strobilurins disrupt mitochondrial respiration in fungi by blocking electron transport within the cytochrome bc1 complex (Complex III of the electron transport chain) between cytochrome b and cytochrome c1, specifically at the Qo site. By inhibiting ubiquinol-cytochrome c-oxidoreductase, they impair the respiratory process, depriving the fungal cell of its energy supply (ATP), ultimately leading to its death. Consequently, strobilurins are also referred to as QoIs or inhibitors of the bc1 complex. Given that this complex is present in all eukaryotic organisms, strobilurins, such as pyraclostrobin and azoxystrobin, partially inhibit electron transport in plants upon contact, as observed in mitochondria isolated from wheat plants..

FUNGICIDAL ACTIVITY

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RESISTANCE

Strobilurins posses a high risk of development of resistant pathogen subpopulations because they are *site-specific* and interfere with just one, very specific biochemical site in the fungal cell. This is important because a single mutation at the biochemical target site of the fungicide can often result in a fungicide-resistant strain. If such a resistant strain emerges, repeated application of QoI fungicides can lead to the appearance of of a subpopulation of strobilurine-resistant pathogens.

ENVIRONMENTAL FATE

The strobilurin fungicides are relatively easily degraded, ensuring low persistence in any environment. Hydrolysis is not typically a major route of environmental dissipation, while adsorption, microbial degradation, and photolysis are significant. Strobilurins generally follow a typical soil degradation pattern, forming metabolites that are potentially more mobile but usually less toxic than the parent compound. They generally posses low toxicity and pose a minimal risk to birds, mammals, and bees, with no toxicity observed at limit doses, except for metominostrobin, which shows some toxicity toward mammals. They also present a low risk to other terrestrial organisms, including non-target arthropods, earthworms, non-target plants, and soil microorganisms. Regarding aquatic organisms, strobilurin toxicity is variable, increasing from metominostrobin, azoxystrobin, kresoxim-methyl, picoxystrobin, and trifloxystrobin, to pyraclostrobin. This correlates with their increasing lipophilicity, represented by their log P_{ow} values. Aquatic toxicity is measured in terms of the external concentration in the surrounding water, while effects largely depend on the dose, represented by the internal concentration in the organism. Compounds with higher lipophilicity are more readily taken up by aquatic organisms, leading to higher toxicity compared to less lipophilic compounds with similar intrinsic toxicity.

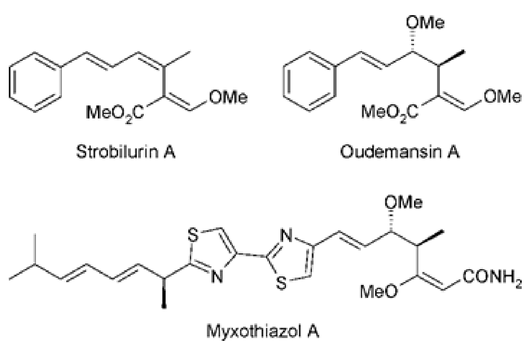

Fig. 1 Representative natural strobilurins

CONCLUSION

Strobilurins demonstrate excellent properties in several areas, including biology, biokinetics, and human and environmental safety. Each strobilurin possesses distinctive technical properties with varying strengths and weaknesses compared to other strobilurins. In the future, selecting the appropriate strobilurin will involve matching its technical profile to the specific agronomic challenge. Strobilurin fungicides have been highly successful due to their numerous benefits and are considered one of the most valuable classes of single-site fungicides discovered by the agrochemical industry. If recommended usage patterns are maintained, the reliance on strobilurins for crop protection is likely to continue for many years to come.