AgriCos e-Newsletter
ISSN: 2582-7049 www.agricosemagazine.com
Volume: 01 Issue: 02 June 2020 Article No: 26

Synthesis of Promising Fungicide from *Strobilurus Tenacellus*

Bijeeta Thangjam[1*], Bandana Mayanglambam[2] and Tusi Chakma[1]
[1] Ph.D Scholar, Department of Plant Pathology, CAU, Imphal, Manipur
[2] Ph.D Scholar, Department of Plant Pathology, BCKV, Mohanpur, West Bengal, India.
Corresponding Author*: bijeetathangjam@gmail.com

SUMMARY

In present day, environmental sustainability has become the need of the hour and Strobilurin, a derived fungicide, being discovered from naturally occurring fungus S*trobilurus tenacellus*, is one of the world's biggest selling fungicides. The fungus has natural active product Strobilurin-A. This natural compound breaks down rapidly in light and is, therefore, not reliable for disease control. Therefore, different strobilurin analogues were developed with the knowledge of their structures and physical properties. The derived fungicide has broad spectrum and high efficiency in control of plant diseases. In addition to this, they are eco-friendly, have low rate of application and less residual effect. The arrival of this fungicide may be considered 'providential'. They have novel mode of action, which act by halting the synthesis of ATP in respiration process of the pathogens and with different mobility. The first strobilurin derived compound, Azoxystrobin, was made commercially available in 1996. Besides, the fungicidal activity as well as the crop physiology can also be improved. Efficacy of the fungicide is sometimes reduced due to single site mutation in the cytochrome 'b' protein of the pathogen. In order to maintain the efficacy of fungicide, integrated disease management strategy is essential. In this review, the synthesis of the fungicide, biochemical mode of action, agricultural uses, risk factor and strategies for overcoming the limitations are discussed.

INTRODUCTION

In 1977, Anke and Steglich isolated Strobilurins from wood rotting fungus *Strobilurus tenacellus*, a basidiomycete growing on pine cones. The fungus produces the natural antibiotic Strobilurin A, which was reported as a novel compound. It was found that they are highly effective against yeasts and filamentous fungi, but ineffective against bacteria (Anke *et al*,1977). It becomes an important class of agricultural fungicide. The fungus is resistant to its own chemical, because its ubihydroquinone has modified three amino acid sequence that prevent the strobilurins from binding (Sauter *et al*, 1999). Because of their sensitivity to light, and high vapour pressure that causes them to rapidly disappear when applied to the surface of a leaf, chemically unmodified strobilurins are not useful as fungicides for agricultural use. In order to overcome this limitation, strobilurins analogues were developed. The strobilurin-derived compound, azoxystrobin, first made commercially available in 1996, was designed to overcome these limitations. It is the world's biggest-selling fungicide.(Sauter, Steglich & Anke, 1999; Bartlett *et al*., 2002;).

Biosynthesis of Fungicides

From the phenylalanine of the fungus by shikimic acid cycle, the products are biosynthesized. Isolation of the natural strobilurins was done by chromatographic means, and their molecular formulae have been identified by high resolution mass spectrometry. Further, spectroscopic analyses were applied to determine their molecular structures (Schramm et al).With the knowledge of the structure and physical properties led to the discovery of synthetic strobilurins. Chemical formula of natural strobilurin A is methyl (E)-3-methoxy-2-(5-phenylpenta-2,4-dienyl) acrylate.

Snythetic Strobilurin used in Agriculture are:

1. Azoxystrobin-Methyl (E)-2-2-[6-(2-cyanophenoxy) pyrimidin-4yloxy] phenyl-3-methoxyacrylate
2. Kresoxim-methyl- Methyl (E)-methoxyimino [2-(o-tolyloxymethyl) phenyl] acetate
3. Trifloxystrobin- Methyl (E)-methoxyimino-(E)-[1-(α,α,α,-trifluoro-m-tolyl) ethylideneaminooxy] otolyl acetate
4. Metominostrobin- (E)-2-methoxyimino-N-methyl-2- (2-phenoxyphenyl) acetamide
5. Fluoxastrobin- (E)-2-[6-(2-chlorophenoxy)-5-fluoropyrimidin-4-yloxy]phenyl (5,6-dihydro-1,4,2-dioxazin-3-yl) methanone O-methyloxime
6. Pyraclostrobin Carbamate -Methyl-N-2-[1-(4-chlorophenyl)-1H-pyrazol-3 yloxymethyl] phenyl (N-methoxy)-carbamate
7. Picoxystrobin- Methyl (E)-3-methoxy-2-[2-(6-trifluoromethyl-2-pyridyloxymethyl) phenyl] acrylate
8. Dimoxystrobin- (E)-2-(methoxyimino)-N-methyl-2-[(2,5-xylyloxy)-o-tolyl] cetamide.

Mode of Action

The target site of strobilurin-derived fungicides involve the component of the respiratory electron transfer chain, namely, complex III [quinone outside (Qo) portion] in the mitochondria. Therefore, strobilurin-derived fungicides are called Qo inhibitors (QoIs). Fungicide inhibit pathogen respiration by binding to the cytochrome b complex III at the Q_0 site and block electron transfer between cytochrome b and cytochrome c1 in mitochondrial respiration and also decrease the transfer of electron from inner mitochondrial matrix to outside inner mitochondrial space thereby decreasing the proton motive force which is required for activation of ATP synthetase. This disrupts the energy cycle within the pathogen by halting the production of ATP.

Mobility

It defines the fungicide movement when applied to plant. The synthetic analogues have same mode of action but different mobilities. All of the Q_oI fungicides exhibit translaminar movement which means across the lamina, or leaf blade. When these fungicides are applied, most of the active ingredients are initially held on or within the waxy cuticle of plant surfaces. Some of the active ingredients leak into the underlying plant cells. The fungicide Azoxystrobin and Picoxystrobin moves translaminarly as well as systemically in the plant's vascular system. Trifloxystrobin and Kresoxim methyl fungicides move translaminarly as well as vapour movement but not systemically and have affinity for the waxy cuticle and the active ingredients that leak all the way through the lamina quickly rebind to the cuticle on the far side of the leaf blade and found on both leaf surfaces, even if only one leaf surface was treated. As they move in the vapor phase, they readily re-bind to the cuticle. Metominostrobin and Fluoxastrobin exhibit systemic movement only . Pyraclostrobin– Carbamate and Dimoxystrobin exhibit translaminar movement

Agricultural Uses

The main use of strobilurins as agrochemical in the field of agriculture is to control plant diseases. Strobilurins derived fungicides are effective against Basidiomycetes, Deuteromycetes, Ascomycetes amd Omycetes.It is used in the control of wide range of plant diseases such as Powdery mildew of grapes, Apple scab, Late blight of potato, Downy mildew of grape and Cucurbits, Brown rust of wheat and barley and many other plant diseases. Not only used as foliar fungicides they are also used in seed treatment and furrow application for soil borne pathogens. They have rapid activities and kill the germination of the fungal spores. Besides the fungicidal activity, it also improves the crop physiology of the plant by adding

more healthy green colour to the plant known as the "greening effect" which leads to significant increase in crop harvest both in volume and quality. They are eco-friendly with less residual effect, as they degrade readily, being derived from natural product. They are used at low rates, no cross-resistance to others, have preventative and post-infection curative activity, low mammalian toxicity and low risk to non-targets.

Risk Development

Resistance against the fungicides are developed due to continuous use of the fungicides in control of the same pathogen. The primary mechanism of QoI resistance is target site-based and involves mutations in the mitochondrial cytochrome *b* gene, resulting in peptide sequence change that prevents fungicide binding (Gisi *et al*., 2002). G143A is the most common form of strobilurin resistance **(**Kraiczy et al., 1996**)**. Mutation starts with a single-base pair change in mitochondrial DNA in which Guanine (G) is replaced by Cytosine (C). This changes the genetic message (codon) from GGA to GCA. The corresponding amino acid also changes from Glycine (GLY) to Alanine (Ala) in the cytochrome protein. The cytochrome protein with the Gly143Ala (G143A) amino acid change is resistant to strobilurins. Mechanism of resistance to QoI fungicides is also mediated by the induction of an alternative cyanide-resistant respiration that is sustained by alternative oxidase (AOX). Induction of AOX allows the fungus to recover the ability to synthesize ATP and regain the metabolic activities.

Strobilurin Resistance Management (FRAC)

1. Use at the early stages of disease development- It has protective action before the population build-up and can control the disease effectively.
2. Limit the number of applications in a given season- Increasing the number of application, the higher is the selection pressure towards the development of a resistant population. Limiting the number of application reduces the opportunity for selection pressure.
3. Limit the number of consecutive applications - Limit the spray to two and switch to equal number of non QoI fungicides with different mode of action.
4. Mixing QoI fungicides with other fungicides- Mixing with fungicides with different mode of action will reduce the rate of regeneration of mutants.

CONCLUSION

Strobilurins are the most preferred group as they are environmentally safe. Strict anti-resistance strategies, including the limitation of treatments and the use of mixtures or alternating compounds, should be followed to maintain the high efficacy of this class of fungicides. If recommended use- patterns are strictly followed, the dependence of crop protection on the QoIs is likely to continue for many years.

REFRENCES

Anke, T., Oberwinkler, F., Steglich, W., & Schramm, G. (1977). The strobilurins-new antifungal antibiotics from the basidiomycete Strobilurus tenacellus (Pers. ex Fr.) Sing. *The Journal of antibiotics*, *30*(10), 806-810.

Bartlett, D. W., Clough, J. M., Godwin, J. R., Hall, A. A., Hamer, M., & Parr-Dobrzanski, B. (2002). The strobilurin fungicides. *Pest management science*, *58*(7), 649-662.

Bartlett, D. W., Clough, J. M., Godwin, J. R., Hall, A. A., Hamer, M., & Parr-Dobrzanski, B. (2002). The strobilurin fungicides. *Pest management science*, *58*(7), 649-662.

Deising, H. B., Reimann, S., & Pascholati, S. F. (2008). Mechanisms and significance of fungicide resistance. *Brazilian Journal of Microbiology*, *39*(2), 286-295.

Delgado, J. A., Lynnes, T. C., Meinhardt, S. W., Wise, K. A., Gudmestad, N. C., Bradley, C. A., ... & Goswami, R. S. (2013). Identification of the mutation responsible for resistance

to QoI fungicides and its detection in Ascochyta rabiei (teleomorph Didymella rabiei). *Plant Pathology*, *62*(3), 688-697.

Lesniak, K. E., Proffer, T. J., Beckerman, J. L., & Sundin, G. W. (2011). Occurrence of QoI resistance and detection of the G143A mutation in Michigan populations of Venturia inaequalis. *Plant disease*, *95*(8), 927-934.

McGrath, M. T., & Shishkoff, N. (2003). First report of the cucurbit powdery mildew fungus (Podosphaera xanthii) resistant to strobilurin fungicides in the United States. *Plant Disease*, *87*(8), 1007-1007.

Morton, V., & Staub, T. (2008). A short history of fungicides. *APSnet Features*.

Sauter, H., Steglich, W., & Anke, T. (1999). Strobilurins: evolution of a new class of active substances. *Angewandte Chemie International Edition*, *38*(10), 1328-1349.

Slusarenko, A. J., Fraser, R. S., & van Loon, L. C. (Eds.). (2012). *Mechanisms of resistance to plant diseases*. Springer Science & Business Media.

Vincelli, P. (2002). Q o I (strobilurin) fungicides: benefits and risks. *Plant Health Instructor*, *DOI*, *10*.

Vincelli, P. (2002). Q o I (strobilurin) fungicides: benefits and risks. *Plant Health Instructor*, *DOI*, *10*.

Zhou, Y., Chen, L., Hu, J., Duan, H., Lin, D., Liu, P., ... & Liu, X. (2015). Resistance mechanisms and molecular docking studies of four novel QoI fungicides in Peronophythora litchii. *Scientific reports*.