Emerging Challenges of Fungicide Resistance in Plant Pathogens

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Fungicides have been in use in the agriculture sector for over 200 years to protect plants against diseases. It is a chemical compound which has the ability to kill or inhibit fungi and their spores. It has become a vital component of crop protection such that certain diseases can only be managed through the use of fungicides.

When site-specific fungicides were introduced through benzamidoles in the 1960's, the pathogens started showing a new phenomenon called fungicide resistance. Fungicide resistance has a long and well documented history. Several reports of fungicide resistance have been reported in India over years. Resistance of *Rhizoctonia bataticola* to carbendazim was reported by Kumar and Shastry in 1979. Basu Chaudhary and Putto reported mancozeb resistance of *Venturia inequalis* in 1984. *Venturia inequalis* was also reported to be resistant to carbendazim which was demonstrated by two scientists, Gangawane and Reddy in 1985.

Fungicide resistance- while the term appears to be simple, it has significantly disrupted the foundation of crop protection. Recent fungicides such as benomyl, carbendazim, thiabendazole, carboxim were considered as highly promising alternatives to the regularly used fungicides as these were site specific, selective in their biochemical action and safer to use. Researches have been conducted to find the root cause for fungicide resistance as it was not only affecting the farming community but also the manufacturers. Initially, people associated the failure of fungicides with the emergence of resistance without considering other possible factors such as wrong time of application, inadequate dosage, wrong choice of fungicides or unfavourable environmental conditions such as heavy rains as the fungicides gets washed off on application. Studies have proved that fungicide applications do not cause resistance. Resistant fungal strains arise through genetic mutation within the fungal population. The application of fungicides eliminates the sensitive population, allowing the resistant mutants to survive and multiple. As a result, the fungal population gradually becomes dominated by resistant strains. Thus, resistance develops through natural selection of mutants under fungicide pressure. In addition to the genetic mechanism, biochemical processes also play a role in the development of fungicide resistance.

To better understand the dynamics of fungicide resistance, it is necessary to know the two primary types of resistance that is qualitative and quantitative resistance. Quantitative resistance, linked to a single gene mutation which results in a complete loss of sensitivity. In contrast, quantitative resistance involves multiple genes. Hence, the mutation in one gene leads to a gradual reduction in sensitivity. Additionally cross resistance, where resistance to one fungicide confers the resistance to other fungicides with a similar mode of action, can further complicate disease management strategies.

Fungicide resistance is frequently associated with alterations in the permeability of the fungal cell membrane, particularly in the case of site-specific fungicides. Reduced membrane permeability can limit the uptake of the fungicide, thereby decreasing its intracellular concentration and overall effectiveness. As a result, the fungicide is unable to reach its target site within the fungal cell, leading to reduced sensitivity and the development of resistance. In *Botrytis cinerea*, resistance to the fungicide fludioxonil has been linked to reduced membrane permeability. The resistant strains show decreased absorption of the fungicide due to changes in membrane transport proteins. These proteins, which usually help bring fludioxonil into the fungal cells, are less active or altered, so the fungicide can't reach its target inside the fungus, leading to reduced control. Another strategy involves enhanced detoxification, where the fungus metabolizes the fungicide into a less toxic or inactive form. Another resistance mechanism is the failure to activate pro-fungicides. Some fungicides are applied in an inactive state and require enzymatic conversion within the fungal cell to become toxic. If the fungus lacks or alters the necessary enzymes, the activation does not occur. Additionally, resistance can develop through changes at the target site of the fungicide. These alterations may involve point mutations in genes encoding the target protein, thereby reducing the fungicide's ability to bind and

disrupt the intended biochemical process. Another important resistance mechanism involves the action of efflux pumps, which actively transport fungicides out of the cell before they reach toxic concentrations. In fungi, the most common of these are ATP-binding cassette (ABC) transporters. While many fungicides are still able to reach effective levels inside fungal cells despite the presence of efflux systems, the activity of these transporters can significantly reduce the intracellular accumulation of fungicides, thus lowering the sensitivity of the pathogen. Together, these mechanisms significantly reduce the efficacy of fungicides and present a major challenge in the management of fungal diseases.

Fungicide resistance can be managed through an integrated approach that combines several strategies to reduce the selection pressure and delay resistance development. To minimize the risk of fungicide resistance and ensure effective disease control, fungicides should not be used in isolation. Instead, they should be applied as a mixture with one or more fungicides that have a different mode of action. For instance, combining a site-specific fungicide with a broad-spectrum, multisite protectant—such as a mix of azoxystrobin with chlorothalonil—can improve efficacy and delay resistance development. Alternating fungicides with different modes of action is also essential; for example, rotating a systemic fungicide like tebuconazole with a contact fungicide such as copper oxychloride helps in breaking the disease cycle. Effective spraying practices are equally important. Limit the use of high and medium-risk fungicides, apply the correct dosage based on the disease severity, and rotate among different classes of fungicides to avoid selection pressure. Consecutive applications of products with the same mode of action should be avoided. For example, if seeds are treated with a triazole-based fungicide, follow-up foliar applications should use a product from a different chemical group. Repeating the same active ingredient, such as treating seeds with thiophanate-methyl and following up with a foliar spray of the same, should be avoided to prevent resistance, particularly in crops like beans. Economic and strategic spraying is also important—avoid unnecessary applications when pathogen pressure is low, as this not only wastes resources but also promotes the development of resistant strains. Additionally, early and late-season sprays should be minimized unless necessary. Always adhere to the manufacturer's recommended dose, even under low disease pressure, as sub-lethal doses can encourage resistance. Finally, fungicides should be a part of an integrated disease management approach. This includes planting disease-resistant varieties, implementing cultural practices such as canopy management and sanitation, using protectant fungicides to delay disease onset, and integrating biological control agents with site-specific fungicides for a more sustainable and effective management strategy.

In conclusion, fungicides are widely used in the agricultural sector and have become almost unavoidable. Unlike in developed countries, most fungicides used in India are contact or multisite types, which helps reduce the development rate of resistant strains and by keeping the above management strategies in mind such as using the recommended doses, rotating with fungicides of different modes of actions, it is possible to slow down the development of fungicide resistance. A thoughtful and proactive approach not only preserves the efficacy of existing fungicides but also ensures sustainable disease management in the long term.

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