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CHAPTER : 06

Advances in Fungal Disease Management: The Role of Succinate Dehydrogenase Inhibitors (SDHIs)

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Abstract

Succinate Dehydrogenase Inhibitors (SDHIs) are a class of fungicides that play a significant role in managing a wide range of fungal diseases in crops. These fungicides specifically target the succinate dehydrogenase enzyme, disrupting the energy production of fungi, ultimately causing their death. Over the years, SDHI fungicides have evolved, with modern formulations like fluopyram, boscalid and fluxapyroxad providing broader-spectrum action and increased effectiveness. However, the widespread use of SDHIs has raised concerns about resistance development in fungal pathogens, making it essential to adopt resistance management strategies. SDHIs continue to be vital in sustainable agriculture, contributing to healthier crops and improved yields. Future developments in this class of fungicides promise more effective and environmentally friendly solutions for disease control in various crops.

Keywords Crop protection, Fungal diseases Fungicides, Resistance management, Succinate dehydrogenase inhibitors

1. Introduction

For centuries, farmers have relied on pesticides to protect their crops from diseases and pests. While alternative methods of disease control, like biological control and cultural practices, are being developed and used, synthetic pesticides still play a major role in managing plant diseases. Over the last 100 years, the use of chemical pesticides has increased significantly. This growth has been boosted by advancements in farming practices and the expansion of global trade. Today, nearly a thousand different chemicals are used worldwide to improve crop yields, ensure multiple harvests from the same fields and protect plants from various threats. In 2019, about 4.19 million metric tons of pesticides were used worldwide. China used the most, with 1.76 million tons, followed by the United States with 408 thousand tons, Brazil with 377 thousand tons and Argentina with 204 thousand tons (Fernández, 2021). According to the Food and Agriculture Organization (FAO), pesticide usage is expected to reach 4.41 million tons by 2027. These chemicals work by interfering with the vital biological functions of pests and

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pathogens, inhibiting their growth and spread.

However, while pesticides are effective in managing plant diseases, their widespread use comes with concerns. They can pollute the air, water and soil, potentially causing harm to the environment and human health (Pereira *et al.*, 2016). This has led scientists to focus on developing more targeted and environmentally friendly ways to control diseases.

A major innovation in this area is the development of Succinate Dehydrogenase Inhibitors (SDHIs) (Inaoka *et al.*, 2015, Ren *et al.*, 2018, Sakai *et al.*, 2012). SDHIs are a class of fungicides that specifically target the succinate dehydrogenase enzyme in fungi. This enzyme is crucial for the fungi's energy production and by blocking its activity, SDHIs stop the fungi from growing, eventually killing them.

In this chapter, the role of SDHI fungicides as a key tool in managing fungal diseases will be discussed. Their mode of action, effectiveness and differences from other fungicides will be explained. Some of the latest SDHI fungicides, along with their trade names, will also be introduced. Challenges such as the potential for fungi to develop resistance and the environmental impact of SDHIs will also be addressed.

As agriculture moves towards more sustainable practices, understanding how SDHIs and similar fungicides can manage diseases in a safer and more efficient way is crucial. This chapter will provide insights into the advances in SDHIs, including their role in promoting healthier crops, a cleaner environment and the introduction of new formulations to the market.

2. The History of SDHI Fungicides

The journey of SDHI fungicides began in the 1960s with the launch of Carboxin, an innovative product that specifically targeted certain fungi, including *Rhizoctonia* species and other basidiomycetes (Sierotzki and Scalliet, 2013). This marked the first significant step in the development of this class of fungicides. Between 1971 and 1997, a second generation emerged, featuring compounds like Benodanil, Fenfuram, Furametpyr, Mepronil, Flutolanil and Thifluzamide. These fungicides were particularly effective against smut diseases in cereals caused by fungi such as *Ustilago nuda* and *U. hordei.*

The evolution continued with the introduction of newer SDHI fungicides, offering a broader spectrum of action. An important example is boscalid, which received approval in 2002 for its ability to combat both basidiomycetes and ascomycetes, including the common soil-borne fungus *Sclerotinia sclerotiorum* (Li *et al.*, 2022). Recently, new SDHI fungicides have become popular in agriculture because they are highly effective against many types of fungi.

These modern SDHIs, such as Fluopyram, Flutolanil, Boscalid, Benzovindiflupyr and Fluxapyroxad, not only inhibit fungal growth and spore germination but also reduce the production of harmful mycotoxins like Deoxynivalenol (DON), associated with *Fusarium asiaticum* (Xu *et al.*, 2019). As a result, SDHIs represent a crucial development in the fight against fungal diseases, providing farmers with reliable tools to protect their crops while minimizing the risk of resistance development in pathogens.

3. Mechanism of Action of SDHI Fungicides

SDHI fungicides work by blocking fungi from producing the energy they need to survive. These fungicides target a specific enzyme called succinate dehydrogenase (SDH), which plays a key role in the energy production process of fungal cells.

Fungal cells, like all living organisms, rely on energy for growth and reproduction. This energy is generated through a process that takes place in the mitochondria, known as the tricarboxylic acid (TCA) cycle and the electron transport chain (ETC). The enzyme SDH is crucial in both of these processes. It helps convert a substance called succinate into fumarate in the TCA cycle and assists in transferring electrons in the ETC, which is essential for generating energy.

When SDHI fungicides are applied, they block the activity of the SDH enzyme. This disruption prevents the fungal cells from converting succinate to fumarate and stops the transfer of electrons in the ETC. Without these processes, the fungi can't produce the energy they need, which causes their growth to slow down and eventually leads to their death (Aldera and Govender, 2018).

SDHI fungicides cut off the energy supply of fungal cells by inhibiting the SDH enzyme, making it impossible for them to survive and spread.

4. Common SDHI Fungicides

Succinate dehydrogenase inhibitors (SDHIs) are a class of fungicides that have become essential in modern agriculture for managing a wide range of fungal diseases. These fungicides work by blocking the activity of the enzyme succinate dehydrogenase (SDH), a crucial part of the fungal cell's energy production process. By inhibiting this enzyme, SDHIs disrupt the energy cycle in fungi, leading to their death.

The Fungicide Resistance Action Committee (FRAC) currently lists 24 SDHI fungicides under Group 7, which are classified as inhibitors of complex II in the mitochondrial respiratory chain of fungi.

Despite significant variations in their chemical structures, these compounds share a common feature - an amide bond. SDHIs are further divided into 12 distinct chemical families based on their structural characteristics:

1. Pyrazole-4-carboxamides: This is the largest group, containing fungicides such as Fluxapyroxad, Penflufen, Penthiopyrad, Furametpyr, Bixafen, Benzovindiflupyr, Isopyrazam, Sedaxane, Fluindapyr and Inpyrfluxam.

2. Thiazole-carboxamides: Represented by Thifluzamide, this family is used for its specific action on certain crops and pathogens.

3. Pyrazine-carboxamides: Pyraziflumid is the main compound in this class, known for its distinctive chemical backbone.

4. N-methoxy-(phenylethyl)-pyrazole-carboxamides: Pydiflumetofen belongs to this group, offering a unique molecular structure contributing to its mode of action.

5. N-cyclopropyl-N-benzyl-pyrazole-carboxamides: Isoflucypram is a key member of this class, featuring a Cyclopropyl and benzyl group in its structure.

6. Furan-carboxamides: Fenfuram is the primary representative of this family, characterized by a furan ring attached to the Carboxamide group.

7. Oxathiin-carboxamides: Carboxin and Oxycarboxin fall under this family, widely used due to their early development and effectiveness.

8. Pyridine-carboxamides: Boscalid is a well-known fungicide from this family, commonly applied in controlling various plant diseases.

9. Phenylbenzamides: This class includes Flutolanil, Mepronil and Benodanil, each with distinct properties for targeting specific fungi.

10. Pyridinyl-ethyl-benzamides: Fluopyram is the key fungicide in this group, used for its broad-spectrum activity.

11. Phenyl-cyclobutylpyridineamides: Cyclobutrifuram, a newer addition to the SDHI family, features a Cyclobutyl ring attached to a Pyridineamide structure.

12. Phenyl-oxo-ethylthiophene amides: Isofetamid belongs to this group, distinguished by its Phenyl-oxo-ethylthiophene structure, making it effective in managing specific fungal pathogens.

5. Field Applications of SDHI Fungicides

SDHI fungicides are widely used in agriculture to control a variety of fungal diseases across different crops. Their mode of action, which targets the mitochondrial respiratory chain in fungal cells, makes them effective against a broad range of pathogens. A new generation of succinate dehydrogenase inhibitors (SDHIs) has been developed in recent years (Inaoka *et al.*, 2015; Ren *et al.*, 2018; Sakai *et al.*, 2012), including fungicides like thifluzamide (1997), boscalid (2005), isopyrazam (2010), fluopyram (2012), fluxapyroxad (2012), benzovindiflupyr (2013) and pydiflumetofen (2017). These newer SDHIs have broader activity compared to the older ones like carboxin and oxycarboxin and they are effective in controlling various diseases such as rusts, Rhizoctonia, leaf spots, powdery mildew and fruit diseases in crops like wheat, maize, vegetables, soybeans, potatoes and groundnut. SDHIs are the second-largest group of fungicides used in agriculture and are now a major focus of research globally. Below are some key field applications of SDHI fungicides based on specific crops and diseases:

5.1. Rice

Bakanae disease, caused by the fungus *Fusarium fujikuroi*, has emerged as a significant problem in rice cultivation. The effectiveness of a new succinate dehydrogenase inhibitor (SDHI) fungicide, penflufen, was tested and showed strong bioactivity against *F. fujikuroi* (Sun *et al.*, 2021).

5.2. Barley

• *Brown Rust* (*Pucciniahordei*): SDHI fungicides are used to control brown rust, a major foliar disease that reduces yield and grain quality in barley.

• *Net Blotch* (*Pyrenophorateres*): These fungicides are also applied to manage net blotch, which causes leaf damage and hinders photosynthesis.

• *Ramularia Leaf and Awn Spot* (*Ramulariacollo-cygni*): SDHIs are effective in preventing the spread of ramularia, which impacts barley leaves and awns, reducing crop productivity.

• *Scald* (*Rhynchosporiumsecalis*): SDHIs help manage scald, a common barley disease that leads to large lesions on leaves.

5.3. Wheat

• *Leaf Rust* (*Pucciniarecondita*): SDHIs are essential for controlling leaf rust in wheat, a disease that leads to early defoliation and reduced grain quality.

• *Stripe Rust* (*Pucciniastriiformis*): These fungicides are applied to manage stripe rust, a serious threat that can result in significant yield loss.

• *Speckled Leaf Blotch* (*Mycosphaerellagraminicola*): SDHI fungicides help control speckled leaf blotch, which causes brown lesions on wheat leaves.

5.4. Apple

• *Scab* (Venturiainaequalis): SDHIs are used in apple orchards to manage scab, a disease that affects fruit quality and yield.

• *Powdery Mildew* (*Podosphaeraleucotricha*): SDHI fungicides manage powdery mildew on apple leaves and fruit, maintaining the commercial value of apples.

• *Dry Eye Rot* (*Botrytis cinerea*): These fungicides are applied to control Botrytis rot, which causes post-harvest losses in apples.

5.5. Pear

• *Black Spot (Scab)* (*Venturia pyrina*): SDHI fungicides are effective against pear scab, a common disease that reduces fruit quality.

5.6. Grapes

• *Botrytis Bunch Rot (Grey Mould)* (*Botrytis cinerea*): SDHI fungicides are widely used to control grey mould, which can significantly impact grape yields and wine quality.

• *Powdery Mildew* (*Erysiphenecator*): SDHIs are applied to manage powdery mildew in grapes, ensuring better fruit quality and yield.

• *Stonefruit* (Peaches, Plums, etc.)

• *Blossom Blight/ Brown Rot* (*Monilinia fructicola*): SDHI fungicides are used to control blossom blight and brown rot, common diseases that can cause pre- and post-harvest fruit decay.

• *Grey Mould* (*Botrytis cinerea*): SDHIs are also effective in managing grey mould in stonefruit.

5.7. Squash and Pumpkin

• *Gummy Stem Blight* (*Didymella bryoniae*): SDHI fungicides are essential for controlling gummy stem blight, which causes significant crop losses in cucurbits.

• *Powdery Mildew* (*Sphaerotheca fuliginea, Erysiphe cichoracearum*): These fungicides are applied to control powdery mildew, a common disease in squash and pumpkins.

5.8. Kiwifruit

• Sclerotinia Blossom and Fruit Rot (*Sclerotinia sclerotiorum*): SDHIs are used to manage Sclerotinia rot in kiwifruit, a disease that causes blossom and fruit decay.

SDHI fungicides are versatile tools in controlling a wide range of fungal diseases across cereals, fruits and vegetable crops. Their ability to target key pathogens helps in maintaining crop health, increasing yields and ensuring the quality of agricultural produce.

6. Resistance Management Strategies

To manage resistance to SDHI fungicides effectively, preventive strategies are essential to prevent or delay the development of resistant strains in crops (McKay *et al.*, 2011). Fungicides like benodanil, bixafen, boscalid, carboxin and fluopyram belong to the same cross-resistance group, so careful management is necessary to avoid resistance.

There is a moderate to high risk of resistance developing against SDHIs, with resistant strains already observed in pathogens such as *Botrytis cinerea*, *Corynespora cassiicola*, *Alternaria alternata* and *Aspergillus oryzae* (Avenot *et al.*, 2020). In China, mutants of *Sclerotinia sclerotiorum* resistant to boscalid have also been reported due to repeated fungicide exposure.

To delay resistance, it is crucial to implement effective disease control practices. This includes applying SDHI fungicides at the recommended rates and intervals. Limiting the number of applications per season is also important, as overuse increases the risk of resistance. A key strategy is to combine SDHI fungicides with others that have different modes of action. Using mixtures or combined products with another fungicide that can control the disease on its own helps reduce the chances of resistance. For best results, SDHI fungicides should be used preventively or at the early stages of disease development. This approach not only improves their effectiveness but also helps extend the useful life of these fungicides, ensuring continued protection for crops.

7. Future Perspectives in SDHI Fungicide Development

The future of SDHI fungicides is promising, with the development of several new products since 2010, except for boscalid, which was introduced in 2003. These fungicides are gaining popularity due to their effectiveness against a wide range of plant diseases and various companies continue to innovate in this space.

For example, penthiopyrad (Affet® SC, Gaia® WDG) by Mitsui Chemicals Agro, isofetamid (Kenja®) by Ishihara Sangyo Kaisha, pyraziflumid (Parade®) by Nihon Nohyaku and inpyrfluxam (Indiflin™) by Sumitomo Chemical have already reached the market, showing strong disease control across multiple crops. Pyrapropoyne by Nissan Chemical is still under development but holds similar potential. Isofetamid, registered in Canada, the USA and Japan, has broad-spectrum activity against fungi such as *Botrytis*, *Sclerotinia*, *Alternaria* and *Venturia*. It remains effective against some SDHI-resistant pathogens, which adds to its value in resistance management strategies.

Another important development is pyraziflumid, which was registered in Japan in 2018 and can be used for different crops like rice and some horticultural crops. Its unique pyrazine carboxamide structure makes it highly effective against a broad range of fungal diseases. Similarly, inpyrfluxam has shown impressive results in controlling major plant diseases like brown rust in wheat, net blotch in barley and black scurf in potatoes in the European market.

Multinational agrochemical companies are carefully promoting their SDHI fungicides by creating products for specific crops and types of diseases. Syngenta, for instance, has developed multiple SDHI fungicides, each designed for different applications, such as isopyrazam (Reflect®) for foliar application on wheat, sedaxane (Vibrance®) for seed treatments and pydiflumetofen (Adepidyn™) for diseases like powdery mildew and Alternaria on vegetables and fruits. Bayer is also contributing to this field with products like bixafen (Aviator® Xpro™), penflufen (EverGol® Prime) and fluopyram (Luna®). Bayer's isoflucypram, still under development, has shown promising results against leaf spot diseases across many crops.

In the future, SDHI fungicides are expected to become more important in crop protection, with advancements aimed at targeting specific diseases and regions. These fungicides are likely to be part of integrated disease management programs, combined with other modes of action to slow down the development of resistance. With ongoing research, there is potential to improve their effectiveness, making SDHI fungicides an important tool in managing plant diseases.

8. Conclusion

Succinate Dehydrogenase Inhibitors (SDHIs) represent a major advancement in fungal disease management, offering farmers new and effective ways to protect their crops. Their unique mechanism of action, which disrupts key processes in fungal cells, has proven to be highly effective in controlling a range of fungal diseases. Moreover, SDHIs have shown a lower risk of resistance development compared to other fungicides, making them reliable tools for long-term disease control. As part of integrated disease management strategies, SDHIs can play a key role in enhancing crop protection while also promoting sustainable agricultural practices. By combining SDHIs with other control methods, farmers can not only reduce disease pressure but also minimize the environmental impact of chemical use. This makes SDHIs an important part of the future of crop protection, contributing to healthier crops and more resilient agricultural systems.

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