

## Publication

A Review of Current Knowledge of Resistance Aspects for the Next-Generation Succinate Dehydrogenase Inhibitor Fungicides

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The new broad-spectrum fungicides from the succinate dehydrogenase inhibitor (SDHI) class have been quickly adopted by the market, which may lead to a high selection pressure on various pathogens. Cases of resistance have been observed in 14 fungal pathogens to date and are caused by different mutations in genes encoding the molecular target of SDHIs, which is the mitochondrial succinate dehydrogenase (SDH) enzyme. All of the 17 marketed SDHI fungicides bind to the same ubiquinone binding site of the SDH enzyme. Their primary biochemical mode of action is the blockage of the TCA cycle at the level of succinate to fumarate oxidation, leading to an inhibition of respiration. Homology models and docking simulations explain binding behaviors and some peculiarities of the cross-resistance profiles displayed by different members of this class of fungicides. Furthermore, cross-resistance patterns among SDHIs is complex because many mutations confer full cross resistance while others do not. The nature of the mutations found in pathogen populations varies with species and the selection compound used but cross resistance between all SDHIs has to be assumed at the population level. In most of the cases where resistance has been reported, the frequency is still too low to impact field performance. However, the Fungicide Resistance Action Committee has developed resistance management recommendations for pathogens of different crops in order to reduce the risk for resistance development to this class of fungicides. These recommendations include preventative usage, mixture with partner fungicides active against the current pathogen population, alternation in the mode of action of products used in a spray program, and limitations in the total number of applications per season or per crop.

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