Exploring the antimicrobial potential of natural compounds inducing oxidative stress on Rhodococcus fascians

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Mycoredoxins (Mrxs), a type of thiol disulphide oxidoreductases, have been demonstrated to play a crucial role in redox homeostasis in different species of *Actinobacteria*. Our research group previously showed that mycoredoxins are very important for maintaining redox homeostasis during macrophage infection in the animal pathogen *Rhodococcus equi* 'Previously published in: Mourenza Á et al. (2019) Antibiotics (Basel) 8(11), 558'. Subsequently, to explore the implications of mycoredoxins in other actinobacterial phytopathogens, genes coding for mycoredoxins were identified in *Rhodococcus fascians* through gene homology. Using optimized protocols for unmarked gene deletion, we generated several *R. fascians* mutants lacking genes coding for mycoredoxins (*mrx*). Interestingly, mutants lacking the three identified genes displayed phenotypic differences under oxidative stress conditions compared to the wild-type strain. Capitalizing on this finding, both strains were utilized to identify natural compounds that potentially exert their antimicrobial activity by inducing oxidative stress. We screened a commercial library comprising more than 3,000 natural compounds (MedChemExpress). The identified compounds ideally have the potential to replace conventional pesticides in a sustainable and environmentally friendly manner. Furthermore, we are not only investigating the individual activity of the compounds but also exploring their efficiency in combinations, seeking synergies. In this study, we present the antimicrobial activity of oxidative stress-inducing natural compounds alone and in combination, tested against different *R. fascians* mycoredoxin mutants. As a result, we discern the antimicrobial potential of the selected natural compounds, and concurrently, the distinct role of individual mycoredoxins in regulating intracellular oxidative stress in *R. fascians* and potentially in other phytopathogens.

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