

DEPSIDE DEPSIDONE SYNTHESIS IN LICHENIZED FUNGI: INSIGHTS FROM *Pseudevernia furfuracea*

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Abstract

Depside and depsidones are polyphenolic compounds with important ecological and pharmaceutical implications, but many details of their biosynthesis are still under investigation. We describe a molecular analysis of the two chemotypes of *Pseudevernia furfuracea*, one producing the depside olivetoric acid, and the other the corresponding depsidone physodic acid. Using genomics and transcriptomics, we detect a biosynthetic gene cluster putatively involved in olivetoric/physodic biosynthesis in *Pseudevernia furfuracea*. This cluster has similarity to a cluster in *Cladonia grayi* associated with the synthesis of the depside/depsidone pair 4-*O*-demethylsphaerophorin/grayanic acid. The putative *P. furfuracea* cluster contains a non-reducing polyketide synthase (*NR-PKS*) and a cytochrome p450 (*cyt p450*). This supports that the PKS synthesizes and joins both aromatic rings of the depside, and that *cyt p450* converts the depside to the corresponding depsidone. This is the first study to identify the putative physodic and olivetoric acid gene cluster. We also propose a specific mechanism of depside synthesis by the PKS. Our study contributes to the understanding of natural product synthesis in lichenized fungi.