Cytotoxic and antifungal activities of melleolide antibiotics follow dissimilar structure-activity relationships.

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Details

Abstract

The fungal genus Armillaria is unique in that it is the only natural source of melleolide antibiotics, i.e., protoilludene alcohols esterified with orsellinic acid or its derivatives. This class of natural products is known to exert antimicrobial and cytotoxic effects. Here, we present a refined relationship between the structure and the antimicrobial activity of the melleolides. Using both agar diffusion and broth dilution assays, we identified the Δ(2,4)-double bond of the protoilludene moiety as a key structural feature for antifungal activity against Aspergillus nidulans, Aspergillus flavus, and Penicillium notatum. These findings contrast former reports on cytotoxic activities and may indicate a different mode of action towards susceptible fungi. We also report the isolation and structure elucidation of five melleolides (6'-dechloroarnamial, 6'-chloromelleolide F, 10-hydroxy-5'-methoxy-6'-chloroarmillane, and 13-deoxyarmellides A and B), along with the finding that treatment with an antifungal melleolide impacts transcription of A. nidulans natural product genes.

Beteiligte Forschungseinheiten

__ Infektionsbiologie Peter F. Zipfel ___ Mehr erfahren __

__ Molekulare und Angewandte Mikrobiologie Axel Brakhage ___ Mehr erfahren __

__ Microbiome Dynamics Gianni Panagiotou ___ Mehr erfahren __

__ Pharmazeutische Mikrobiologie Dirk Hoffmeister ___ Mehr erfahren __

Leibniz-HKI-Autor*innen

Markus Bohnert

[Details](#)

Axel A. Brakhage

Details

Hans-Martin Dahse

Details

Dirk Hoffmeister

[Details](#)

Fabian Horn

Details

Hans W. Nützmann

Details

Volker Schroeckh

Details

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