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ORIGINAL

Application of Bioassay-Guided Fractionation Coupled with a Molecular Approach for the Dereplication of Antimicrobial Metabolites

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Abstract A systematically delineated dereplication approach was described based on genome mining and bioassay-guided fractionation using endophytic fungus *Xylaria psidii* FPL-52(S) isolated from leaves of *Ficus pumila* Linn., (Moraceae). A polyketide synthase gene-based molecular screening strategy by a degenerate oligonucleotide primer polymerase chain reaction technique coupled with a bioinformatic phylogenomic approach revealed the presence of an iterative polyketide synthase gene within the genome of *Xylaria psidii* FPL-52(S). Chemical dereplication of ethyl acetate extract derived from a submerged fermentation culture broth of *Xylaria psidii* FPL-52(S) by bioassay-guided chromatographic and hyphenated analytical spectroscopic techniques led to the identification of polyketide mycoalexin 3-*O*-methylmellein. Antimicrobial profiling and minimal inhibitory concentration values for 3-*O*-methylmellein were determined by disc diffusion and microbroth dilution techniques. Gram-positive bacteria, dermatophytic and phytopathogenic fungi were susceptible in terms of inhibition zone and minimum inhibitory concentration values when compared to co-assayed standards. Herein, we highlight and demonstrate an improved approach which facilitates efficient dereplication and effect-guided fractionation of antimicrobial metabolite(s). The present work flow serves as a promising dereplication tool to survey the biosynthetic potential of endophytic fungal diversity, thereby identifying the most promising strains and prioritizing them for novel polyketide-derived antimicrobial metabolite discovery.

Keywords Bioprospecting · Hyphenated techniques · High-throughput · Polyketides · Polyketide synthase gene · Phylogenomics · Dereplication · Bioautography · Strain prioritization

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Introduction

Microbial natural products are represented as a "prolific source" of diverse molecular frameworks and chemical scaffolds with a remarkable and wide range of biological activities [1–4]. Their value has been recognized since the serendipitous discovery of penicillin from *Penicillium notatum* by Alexander Fleming. Microbial natural products from various sources provide a wide variety of applications in medicine, industries and agriculture. Natural antimicrobial secondary metabolites of microbial origin from various sources are still playing a key and enormous role in microbial natural product-based drug discovery [5–10]. One such intriguing prolific microbial bioresource is "endophytes", microbes residing in