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Identification of new peptaibols in the strain of *Trichoderma amazonicum* MMSRG 38A isolated from açaí fruit.

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Highlights: The objective of this study was to prospect peptaibols of *Trichoderma amazonicum* MMSRG 38A. Among the peptaibols found were hypomuricins A3 and A4 and four new putative sequences of 14-residue peptaibols. The genome has 63 BGCS being a 14-module NRPS hybrid responsible for the biosynthesis of peptaibols.

Trichoderma are recognized as an abundant source of non-ribosomal peptides (NRPs), which belong to the class of peptaibols. These secondary metabolites have amphipathic characteristics with action on the membrane and with a wide range of effects such as: antimicrobial, cytotoxic, and inducing resistance in plants. Thus, the diversity and versatility of peptaibols make them a promising source for the development of new drugs and bioinputs. Recently, approaches such as genomic mining that allows the identification of BGCs (Biosynthetic Gene Clusters) related to NRPSs (Non-ribosomal Peptide Synthase) and the characterization of adenylation domains responsible for the incorporation of amino acids in combination with LC-MS/MS data has helped in the prediction of the NRPs. In this study, we present the identification of new 15-residue peptaibols produced by a strain of *T. amazonicum* isolated from açaí. For this purpose, an approach combining genomic mining, phylogenetic analysis of adenylation domains and liquid chromatography coupled with mass spectrometry was used. The LC-MS/MS analyzes were performed with a Thermo Scientific Dionex Ultimate 3000 liquid chromatography system chromatograph coupled to a Thermo ScientificTM Q ExactiveTM Plus high-resolution mass spectrometer (Waltham, MA, USA). Product ion spectra (MS/MS) were analyzed and organized into molecular networks using the GNPS platform (http://gnps.ucsd.edu). The genome was used to predict BGCs via the FungiSMASH platform. Sixty-three BGCs were identified, seven related to NRPS-like, six NRPSs and six NRPs-PKS hybrids. Of these, an NRPS of 14 modules, the first presenting a KS domain (ketosynthase) located in scaffold 62, was identified as responsible to produce peptaibols of 14 residues. The generated molecular network showed several connected nodes, referring to monocharged ions with *m/z* between 1095 and 1495, indicative of molecules with high molecular weight. Crude extract analysis showed a chemically diverse set of 15 residue peptaibols. The MS/MS analyzes identified 4 new peptaibols with *m/z* 1436, 1478,1481 and 1495. And the fragmentation through the product ion scanning experiment allowed the sequencing of the peptaibols of 14 residues. Amino acid prediction, based on phylogenetic analysis of adenylation domains, allowed extensive annotation of mass spectral properties related to 14-residue peptaibols. These results demonstrate the potential of combining molecular and chemical approaches for the discovery of new natural products. Our results provide four new chemical entities that could be useful in medicine and agriculture.

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