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Isolation and Identification of Water-Soluble Metabolites Produced in Culture by Fungus *Hypocrea* sp.

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Highlights: The production of peptaibols is a defense mechanism, because these peptides have antibiotic activity. The present work aimed at the isolation of water-soluble peptaibols and different secondary metabolites from the fungal strain *Hypocrea* sp. Chromatographic separations and spectroscopic analysis of compounds from the aqueous fraction enabled us to identify the peptaibol trichokonin VI as well as the dipeptides tyrosyl-proline, phenylalanine-proline and Cyclo[Pro-Phe].

During the last century, the discovery of antibiotics led to an increase of human life expectancy [1]. Peptaibols are antibiotic peptides, most of which are produced by fungi, generally being lipophilic, linear and comprising from 4 to 21 amino acids [2]. The Antarctic continent is a unique environment for the discovery of marine-derived microorganisms, with a hostile environment and extreme climate. Moreover, the local marine microbiota is still little explored by man [3].

In the present investigation, we assessed the chemical profile of the aqueous fractions obtained from the fungus *Hypocrea* sp., isolated in the Antarctic continent. Fungal cultures were grown in solid Potato Dextrose Agar and liquid Sabouraud Dextrose Broth medias. After the growth, liquid media was subjected to a liquid/liquid partition with EtOAc to give an organic and an aqueous fraction. The aqueous fraction was fractionated by chromatography and the derived samples were analyzed by UPLC-QToF-MS and NMR-1D and -2D techniques.

Analysis of the fractions obtained indicated mass-to-charge signals compatible with the peptaibol trichokonin VI. This peptaibol has a long chain and has shown antibiotic activity against Gram positive bacteria, healthy and cancer cell lines (MCF-7, MCF-10A, ACP01, HELA and A549) and against the parasite *Plasmodium falciparum* (strain 3D7, sensitive to chloroquine), with IC50 of 0.6 \pm 0.2 μ M [4]. Additionally, three dipeptides, tyrosyl-proline, phenylalanine-proline and Cyclo[Pro-Phe], were isolated and identified by analysis of spectroscopic data. The presentation will show and discuss the strategy to investigate the fungal media aqueous extract for the isolation of secondary metabolites, as well as the identification of the peptides isolated.

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