ANTIFUNGAL ACTIVITY OF POLYGODIAL ISOLATED FROM *polygonum acuminatum* AND OF THE BIOTRANSFORMATION PRODUCT

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INTRODUCTION
The current interest in the development of new antifungal agents can partially be due to the dramatic rise in the number of patients with suppression of their immune system. Otherwise, the emergence of fungal resistance to available antifungal agents, leads to an increasing need for new and effective structures.(1) *Polygonum acuminatum* (Polygonaceae) is used to heal infected wounds in the traditional Argentinean medicine.(2) This study was carried out to evaluate the antifungal properties of this plant to give support to its ethnopharmacological use, and to isolate the compound(s) responsible for its activity. In addition, a fungal biotransformation of the main compound was performed.

MATERIALS AND METHODS
Aerial parts of *P. acuminatum* were collected at Puerto Gaboto (Argentine) and once dried, they were powdered. 100 g of the vegetal material was successively extracted by maceration with petroleum ether (Hex), dichloromethane (DCM), ethyl acetate (EtOAc) and methanol (MeOH). After filtration and evaporation 1.3, 2.0, 1.2 and 2.7 g of each extract were obtained respectively.

For antifungal evaluation, strains from the American Type Culture Collection (ATCC) and Centro de Referencia en Micología (CEREMIC) were used. Minimum Inhibitory Concentration (MIC) of each extract or compound was determined by using broth microdilution techniques according to the guidelines of the CLSI(3) for yeasts (M27-A2) and for filamentous fungi (M38A).

For biotransformation experiments, suspensions of conidia (5x10^6 CFU/mL) of *Aspergillus fumigatus* ATCC 26934 were used to inoculate flasks containing Czapek medium (250 mL). The cultures were incubated at 30 ºC for 72 h. The substrate (70 mg) in DMSO (3 mL) was poured into flasks containing the fungal biomass and the reaction mixtures were incubated. The mixtures were filtered, and the aqueous phases were extracted with ethyl acetate. The organic phases were dried and analyzed by TLC and GC.

RESULTS
The four extracts of *P. acuminatum* were evaluated against a panel of human opportunistic and pathogenic fungi. Results showed that all yeasts and dermatophytes, but not *Aspergillus* spp., were sensitive to *P. acuminatum* extracts. DCM extract displayed the broadest spectrum of action, inhibiting 6/9 fungi tested (MICs: 31.25 - 500 µg/mL). Hex and EtOAc extracts inhibited 4/9 fungi (MICs: 125 - 500 µg/mL) and MeOH extract was inactive (MIC > 500 µg/mL).

The bioguided fractionation of the DCM extract led to the isolation of polygodial (1), which have been previously isolated from another natural sources.(2,4) Biotransformation of (1) by *A. fumigatus* led to the obtainment of decahydropyranofuran-1-ol (2) known as isodrimeninol.(5) Both compounds were evaluated for antifungal activity and results showed that (1) possessed the strongest antifungal activity (MICs: 3.9 - 62.5 µg/mL) meanwhile (2) was less active (MICs: 31.2 - 250 µg/mL).

CONCLUSIONS
DCM extract of *P. acuminatum* possessed antifungal activity against yeasts and dermatophytes, giving support to its ethnopharmacological use in Argentine.(6) The sesquiterpene polygodial was the main compound responsible for this activity. Its biotransformation major product (isodrimeninol) possessed lower activity, suggesting that *A. fumigatus* modifies (1) to the antifungal compound (2), with lower antifungal capacity, as a defense mechanism.

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