Extracts from Argentinian native plants reverse fluconazole resistance in Candida species by inhibiting the efflux transporters Mdr1 and Cdr1

Gil, Florimar, Laiolo, Jerónimo

, Bayona-Pacheco, Brayan and Cannon, Richard D.

(2022) *Extracts from Argentinian native plants reverse fluconazole resistance in Candida species by inhibiting the efflux transporters Mdr1 and Cdr1.* BMC Complementary Medicine and Therapies, 22 (1). ISSN 2662-7671

Resumen

Background: The development of multidrug resistance (MDR) associated with the overexpression of the efflux transporters Mdr1 and Cdr1 in Candida species impedes antifungal therapies. The urgent need for novel agents able to inhibit the function of both pumps, led us to evaluate this property in 137 extracts obtained from Argentinian plants. Methods: The ability of the extracts to reverse efflux pump-mediated MDR was determined with an agar chemosensitization assay using fluconazole (FCZ) resistant Mdr1- and Cdr1-overexpressing clinical isolates of Candida albicans and Candida glabrata as well as Saccharomyces cerevisiae

strains selectively expressing Mdr1 (AD/CaMDR1) or Cdr1 (AD/CaCDR1). The resistance-reversing activity of the most potent extracts was further confirmed using a Nile Red accumulation assay. Results: Fifteen plant extracts overcame the FCZ resistance of Candida albicans 1114, which overexpresses CaMdr1 and CaCdr1, and AD/CaMDR1, with those from Acalypha communis and Solanum atriplicifolium being the most effective showing 4- to 16-fold reversal of resistance at concentrations ≥ 25 µg/mL. Both extracts, and to a lesser extent that from Pterocaulon alopecuroides, also restored FCZ sensitivity in CgCdr1-overexpressing C. glabrata 109 and in AD/CaCDR1 with fold reversal values ranging from 4 to 32 and therefore demonstrating a dual effect against Mdr1 and Cdr1. Both, A. communis and S. atriplicifolium extracts at concentrations ≥ 12.5 and ≥ 25 µg/mL, respectively, increased the intracellular Nile Red accumulation in all yeast strains overexpressing efflux pumps. Conclusions: The non-toxic and highly active extracts from A. communis and S. atripicifolium, provide promising sources of compounds for potentiating the antifungal effect of FCZ by blocking the efflux function of Mdr1 and Cdr1 transporters.

TIPO DE DOCUMENTO: Artículo

DOI: https://doi.org/10.1186/s12906-022-03745-4

PALABRAS CLAVE: Candida albicans. Candida glabrata. Fármacos. Terapias antifúngicas.

TEMAS: R Medicina > R Medicina (General)

R Medicina > RM Terapéutica. Farmacología

UNIDAD ACADÉMICA: Universidad Católica de Córdoba > Unidad Asociada a CONICET