

INVESTIGATION OF ANTIFUNGICAL ACTIVITY AGAINST *Candida auris* FROM FRACTIONS OF *Siparuna glycycarpa* OBTAINED BY COUNTERCURRENT CROMATOGRAPHY

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Candida auris has emerged as a multidrug-resistant fungal pathogen of global concern, associated with severe invasive infections and high mortality rates. Azoles remain the primary class of antifungal drugs used for candidiasis; however, resistance in *C. auris* poses a significant challenge to current therapeutic strategies. *Siparuna glycycarpa* (Siparunaceae), native to the Brazilian Amazon, recognized for its rich and diverse chemical composition, including alkaloids, chalcones, and both free and glycosylated flavonoids. The present study aims to evaluate fractions from *S. glycycarpa* with potential antifungal activity against *C. auris*, focusing on their ability to inhibit efflux pumps, either alone or in combination with fluconazole. A portion of the SGD extract underwent initial cleanup by liquid–liquid extraction using hexane–ethyl acetate–methanol–water (HEMWat, 1:1:1:1, v/v). The upper phase (SGDU) was subsequently fractionated by high-speed countercurrent chromatography (HSCCC) on an HTPrep apparatus equipped with a 112 mL column (2.0 mm i.d.) operated at a flow rate of 2.5 mL/min, using HEMWat 7:3:6:4 as the solvent system. A total of 140 fractions (2 mL each) were collected, 80 during the elution phase and 60 during the extrusion phase. Based on thin-layer chromatography (TLC) profiles, these fractions were combined into 23 subfractions, which were then evaluated *in vitro* against *C. auris*. Of these, seven fractions, in which chalcones (2',6'-di-hidroxi-4,4'-dimetoxi-di-hidrochalcona and 2',6'-di-hidroxi-4'-metoxi-di-hidrochalcona) identified by NMR, demonstrated significant efflux pump inhibitory activity when combined with fluconazole at a concentration of 100 µg/mL. This finding suggests possible synergistic interaction between the compounds present in the fractions and fluconazole, potentially restoring the drug's effectiveness against resistant *C. auris* strains.

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