SYNTHETIC ORGANOtellurides MEDIATED REVERSAL OF FLUCONAZOLE RESISTANCE IN CLINICAL ISOLATES OF CANDIDA ALBICANS

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INTRODUCTION AND OBJECTIVES: Candida albicans is a human pathogen responsible for most opportunistic fungal infections. Fluconazole is widely used to treat these infections, the fluconazole resistance mediated by efflux pumps arises as a serious public health problem. The main efflux pumps associated with this phenotype in C. albicans are CaCdr1; CaCdr2 and CaMdr1. This study aims to evaluate the ability of synthetic organotellurides compounds to reverse this resistance phenotype presented by C. albicans clinical isolates that overexpress the efflux pumps. MATERIALS AND METHODS The following fluconazole-resistant strain isolated from clinical material were used: 95-142 (overexpression of CACDR1 and CACDR2); 96-25 (overexpression of CAMDR1) and 12-99 (overexpression of CACDR1, CACDR2 and CAMDR1). Initially it was performed the chemosensitization assay “Spot Test” (Reis de Sá et al. 2014) to verify which compounds (final concentration 100 µM) could inhibit the growth of yeast strains when combined with sub MIC fluconazole concentrations. Thereafter the checkerboard assay was conducted (Niimi et al. 2004) to quantify the synergistic effect between those compounds and fluconazole through the FICI index. The Real Time PCR assay was conducted to evaluate the effect of compounds on CACDR1, CACDR2 and CAMDR1 transcription. RESULTS AND DISCUSSION: Two of five compounds were able to reverse the fluconazole resistance expressed in three strains and demonstrated a synergism with fluconazole (FICI ≤ 0.5). However, the compounds exposure did not markedly affect the expression of the transporters CaCdr1, CaDdr2 and CaMdr1 in strain 12-99. CONCLUSIONS: These two synthetic compounds seem to be promising as reversers of azole resistance mediate by efflux pumps. Probably they act mainly as efflux pump blockers once the transcription levels of CACDR1, CACDR2 and CAMDR1 genes were not affected by compounds.

Key Words: Candida albicans; Efflux pumps; Synthetic organotellurides.
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