**Objectives**: *Candida albicans* is responsible for invasive fungal infections associated with high morbidity and mortality. Resistance to antifungal drugs, namely the azole class, is increasing, making it urgent to develop new therapeutic alternatives. Azole drug resistance can result from several mechanisms, including overexpression of genes encoding efflux pumps. In this work, we used an *in silico* repurposing strategy to identify already approved drugs associated with potential therapeutic targets, involved in membrane transport, in *C. albicans.* The specific objectives were: (i)to create a virtual library of potential therapeutic targets and associated drugs using publicly available databases; (ii) to determine the antimicrobial activity of candidate drugs against a *C. albicans* reference strain; (iii) to evaluate potential adjuvant effect of candidate drugs on the activity of fluconazole (FLU) and ethidium bromide (EtBr), a common efflux pump substrate; and (iv) to assess the potential inhibitory activity of the selected drugs on EtBr efflux in *C. albicans*.

**Materials & Methods:** Predicted *C. albicans* targets and associated approved drugs were identified using an *in silico* repurposing strategy that uses the publicly available data bases Uniprot and KEGG (to identify potential membrane transport targets) and DrugBank (to identify associated approved drugs). Inclusion and exclusion criteria were applied to select representative compounds from different chemical classes for experimental validation. Minimum inhibitory concentrations (MICs) of selected drugs against *C. albicans* ATCC®90028™ were determined by microdilution according to EUCAST guidelines. In addition, the potential adjuvant effect of selected drugs on the activity of FLU and EtBr, was also evaluated by microdilution. Finally, the efflux inhibitory activity of the candidate drugs was evaluated by an optimized/newly developed real-time fluorometric EtBr accumulation assay and the Relative Final Fluorescence (RFF) parameter was determined.

**Results:** *In silico* analysis generated a total of 245 predicted targets associated with 607 drugs in *C. albicans*. A total of 59 drugs, representative of each chemical superclass, was selected for *in vitro* activity evaluation. The drug miltefosine showed the lowest MIC (2 mg/L), while amlodipine and procainamide demonstrated a potential adjuvant effect by decreasing the MICFLU by 8-fold or 4-fold, respectively. The two latter drugs, and additional other eleven drugs, were able to reduce the MICEtBr by at least 4-fold. Fluorometric assays revealed amlodipine, fluvoxamine and fluoxetine as potential efflux inhibitors in *C. albicans.*

**Conclusions:** Fluvoxamine, fluoxetine and amlodipine showed potential efflux inhibitory activity, with amlodipine also modulating the susceptibility of *C. albicans* to fluconazole. In the future, these drugs may contribute to the research and development of lead compounds and new therapeutic alternatives that may be used in the fight against antifungal resistance in *C. albicans*.

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