TITLE: *IN VITRO* ANTIFUNGAL ACTIVITY OF RALTEGRAVIR OBTAINED FROM THE COMPUTATIONAL DRUG REPOSITIONING

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ABSTRACT:

Drug repositioning using computer techniques is a strategy for finding a new indication for an already approved drug. This methodology is growing rapidly, reducing the time for identification, characterization and structure-optimization for novel drug candidates with economic benefits. *Candida* spp., *Cryptococcus* spp. and *Paracoccidioides* spp. are three pathogenic fungi that can cause systemic mycoses and are of high clinical importance, especially since it affects immunocompromised individuals and to the restricted market of conventional antifungal drugs and the limitations its present for treatment these diseases. This study aimed the *in vitro* antifungal activity of raltegravir, used for the treatment of HIV-1 infection, obtained from the drug repositioning through of similarity with the small molecule F2832-0099 (Life Chemicals) that has action in thioredoxin reductase enzyme from *C. albicans*. Raltegravir was obtained from the Targetmol provider and the *in vitro* susceptibility tests were performed against isolates of *P. lutzii* (Pb01), *P. brasiliensis* (Pb18), *C. albicans* (ATCC 90028), *C. parapsilosis* (ATCC 22019), *C. glabrata* (ATCC 90030), *C. tropicalis* (ATCC 750), *C. krusei* (ATCC 6258) and *C. neoformans* (INCQS). The *in vitro* antifungal activity of raltegravir was determined by Minimum Inhibitory Concentration (MIC) in accord with the broth microdilution methods developed by the Clinical and Laboratory Standards Institute M27-A3. The fungi most susceptible of raltegravir were *P. brasiliensis and P. lutzii*, with MIC value of 16 and 32 µg/mL, respectively. In addition, this drug also presented antifungal activity against some *Candida* species: *C. albicans* (MIC 128 µg/mL), *C. tropicalis* (MIC 256 µg/mL) and *C. glabrata* (MIC 128 µg/mL). With reduced risk and decreased time to market due to availability of preclinical data, the compounds from drug repositioning are promising. As raltegravir showed antifungal activity *in vitro* satisfactory mainly for the genus *Paracoccidioides*, our next tests, both *in vitro* and *in vivo*, will be conducted objecting to confirm its activity in paracoccidioidomycosis.

Keywords: antifungal activity, raltegravir, drug repositioning, systemic mycoses, paracoccidioidomycosis

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