

**TITLE:** EVALUATION OF NEW POTENTIAL COMPOUNDS FOR THE TREATMENT OF CHROMOBLASTOMYCOSIS

**AUTHORS:** COELHO, R.A.; JOFFE, L.S.; FIGUEIREDO-CARVALHO, M.H.G.; BRITO-SANTOS, F.; RODRIGUES, M.L.; ALMEIDA-PAES, R.

**INSTITUTION:** FUNDAÇÃO OSWALDO CRUZ, INSTITUTO NACIONAL DE INFECTOLOGIA EVANDRO CHAGAS, RIO DE JANEIRO, RJ, BRASIL.

**ABSTRACT:**

Chromoblastomycosis (CBM) is a chronic fungal infection of the cutaneous and subcutaneous tissue caused by traumatic implantation of several species of black fungi into the host. The most common agents of CBM are *Fonsecaea pedrosoi*, *Fonsecaea nubica*, *Fonsecaea monophora*, *Phialophora verrucosa*, *Cladophialophora carrionii*, *Rhinocladiella aquaspersa*, *Rhinocladiella similis*, *Exophiala dermatitidis*, and *Exophiala jeanselmei*, among others. There is no standard CBM treatment to follow. Therapy usually requires more than one drug to be administered and, sometimes, physical methods such as surgery or cryosurgery are necessary to improve the therapeutic response. Itraconazole (ITZ) and terbinafine (TRB) are the antifungal drugs most commonly used to treat patients with CBM. Due to the paucity of antifungal drugs that can be used in the treatment of this mycosis, the refractoriness of some cases and potential recurrences this mycosis, a preclinical study involving compounds already established for the treatment of other diseases and with known cytotoxicity will allow the discovery of potential new drugs that may be included in clinical trials for the treatment of CBM in the future. Thus, the objective of this study was to evaluate the antifungal activity of 400 molecules present in Pathogen box against CBM agents. An initial screening with the compounds of the Pathogen box diluted at 1 $\mu$ M in RPMI 1640 was performed with a *F. pedrosoi* clinical strain according to the EUCAST guidelines for filamentous fungi. The compounds that inhibited more than 70% of the growth of this strain were further tested against other seven etiologic agents of CBM in concentrations ranging from 10 to 0.039  $\mu$ M. Two compounds were highlighted in the screening: MMV021013 and MMV688978. When they were tested against different CBM agents, MIC values (100% inhibition) between 1.25-5 $\mu$ M and 1.25-2.5 $\mu$ M were found, respectively. The analysis of potential synergism of these compounds with the drugs already used in the treatment of this disease (ITZ and TRB) was also performed and synergism was observed for some CBM agents. These results reveal promising new drugs to be tested in the treatment or prophylaxis of CBM in the future.

**Keywords:** Chromoblastomycosis, *Pathogen box*, antifungal activity

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