

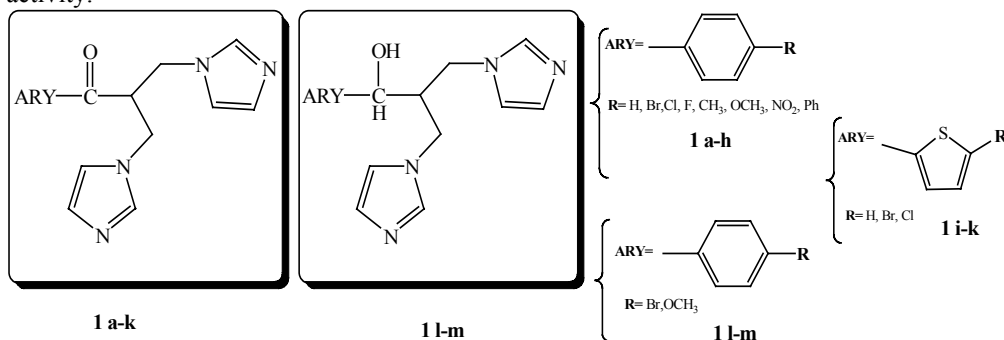
Synthesis, antifungal and antimycobacterial activities of new bis-imidazole derivatives.

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Considering the increased incidence of severe opportunistic fungal infections in immunocompromised patients together with the development of resistance among pathogenic *Candida spp.*, there is a great need for new antifungal compounds.

On the other hand, the increase of tuberculosis due to emergence of multidrug-resistant strains (MDR) of *Mycobacterium tuberculosis*, together with the increased incidence of severe disseminated infections produced by mycobacteria other than tuberculosis (MOTT) in immunocompromised patients, have prompted the search for new antimycobacterial drugs.

Because many imidazole derivatives showed potent antifungal activity associated with good antimycobacterial activity, we synthesized a series of compounds **1 a-m** characterized by the simultaneous presence of two imidazole rings linked together by a propane bridge connected with a variously substituted aromatic ring with the aim of modulate the lipophilic character of the corresponding molecules in consideration of the importance of this parameter for the activity.



The synthesized compounds reached MIC₉₀ values of 8 µg/ml against *Mycobacterium tuberculosis* H₃₇Rv strain and 2-4 µg/ml against *Candida albicans* e *Candida glabrata* strains.

Further, we performed a molecular modeling study in order to rationalize the possible interactions between the synthesized compounds and the active site of the target enzyme, cytochrome P450-dependent lanosterol 14 α -demethylase, and we quantified these interactions by comparing the calculated binding free energy values of compounds to their experimental MIC values.