Title: THIOSEMICARBAZONE AND MORPHOLINE COMPOUNDS WITH POTENTIAL ANTIGUNGAL AND ANTIBACTERIAL ACTIVITY

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Abstract:

Thiosemicarbazones are widely employed as metalloenzymes inhibitor due to their ability to form chelates with metals. Morpholines are six-membered heterocycles containing amine and ether functional groups, which are widely used as a building block in the preparation of several drugs. Thiosemicarbazones, morpholines and their derivatives have been associated to a broad spectrum of therapeutic activities, becoming interesting your research as possible antimicrobials. Thus, the aim of this study is to evaluate the antibacterial and antifungal potential of three thiosemicarbazones (TSRT, TSTPHF4, TSTOHF6) and one morpholine (RMF4) derivatives. They were evaluated against *Candida* sp. (*C. albicans* ATCC 10231, *C. glabrata* ATCC 2001, *C. krusei* ATCC 34135 and *C. tropicalis* ATCC 28707) and six bacterial strains: three gram-negatives (*P. aeruginosa* ATCC 25853, *E. coli* ATCC 25922 and *A. baumannii* ATCC19606) and three gram-positives (*Streptococcus agalactiae* ATCC 13813, *Staphylococcus aureus* ATCC 29231 and *Staphylococcus epidermidis* ATCC 12228). The Minimum Inhibitory Concentration (MIC) was determinated by the broth microdilution method. Moreover, the Minimum Bactericidal Concentration (MBC) and Minimum Fungicidal Concentration (MFC) were evaluated by agar microdilution. The compounds were diluted in dimethylsulfoxide (DMSO), and tested in concentrations range of 1000µg/mL to 3.9µg/mL. Streptomycin and ketoconazole were used as positive controls while DMSO was used as a negative one. The data showed that TSRT has a fungistatic activity against *C. albicans* and *C. tropicalis* with MIC 525µg/mL and 125µg/ml, respectively. Furthermore, it has a fungicidal activity against *C. tropicalis*, with MFC of 125µg/mL. The compound RMF4 showed fungistatic activity against four yeasts tested with MIC range of 250µg/mL to 1000µg/mL. In relation to the antibacterial activity tests, TSRT showed bacteriostatic activity against *E. coli*, *S. aureus* and *S. epidermidis* with a MIC range of 65µg/mL to 250µg/mL. RMF4 presented bacteriostatic action on *E. coli* and *A. baumannii* with a MIC range of 250µg/mL and 500µg/mL, respectively. Generally, these compounds showed fungistatic and bacteriostatic activity at low concentrations and may belong to a promising class of antimicrobial agents.

Keywords: Thiosemicarbazones, Morpholines, Antifungal, Antibacterial.

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