

**Title: ANALYSIS OF THE ANTIFUNGAL POTENTIAL OF METAL COMPLEXES WITH 2-THIAZOLINE-2-THIOL-DERIVATIVE LIGANDS AGAINST YEASTS OF THE *Candida* GENUS**

**Authors:** Souza, J. de P.<sup>1</sup>, Braga, A. V.<sup>1</sup>, Herrera, K. M. S.<sup>1</sup>, Andrade, J. T.<sup>1</sup>, Ferreira, L. S.<sup>1</sup>, Sousa, C. D. F.<sup>1</sup>, Leonel, C. A.<sup>1</sup>, Chagas, R. C. R.<sup>1</sup>, Ferreira, J. M. S.<sup>1</sup>

**Institution:**<sup>1</sup> UFSJ – Universidade Federal de São João Del-Rei (400 Sebastião Gonçalves Coelho street, Chanadour, Divinópolis, Minas Gerais, Brazil, Zip Code 35501-296)

**Summary:**

The species of the *Candida* genus cause opportunistic infections in immunocompromised individuals and are significantly responsible for increasing the incidence of invasive fungal infections. The species of *Candida albicans*, *Candida parapsilosis*, *Candida glabrata*, *Candida tropicalis*, and *Candida krusei* account for about 90% of the fungal infections in hospitals. Furthermore, these species are largely associated with the emergence of strains that are resistant to the current antifungal agents. Thus, it is important to intensify the search for new antifungal substances. Currently, metal complexes with ligands derived from the 2-thiazoline-2-thiol molecule have been studied and reported as compounds that present several biological activities. In this context, it was determined the Minimum Inhibitory Concentration (MIC) of 16 compounds of this class against *C. albicans* ATCC 14053, *C. glabrata* ATCC 2001 and *C. krusei* ATCC 34135. The selected compounds were constituted by the ligands hydrotris(2-mercaptothiazolyl)borate (L1) or 1,2-Bis(2-thiazolin-2-ylsufalnyl)ethane (L2) complexed with cobalt, copper, zinc, silver, nickel, chromium, iron, or manganese. The concentrations of 500, 250, 125, 62.5, 31.25, 15.63, 7.81, and 3.90 µg/mL were tested by broth microdilution method, as described by CLSI (2003). Then, it was performed the plating of the MIC experiment samples to evaluate the Minimal Fungicidal Concentration (MFC). According to the results, L1 showed fungistatic activity against the three tested yeasts when it was complexed with cobalt, copper and nickel, with MIC values ranging from 31.25 to 500 µg/mL. This ligand also showed fungicidal activity against the three yeasts when it was complexed with copper, with MFC values ranging from 31.25 to 500 µg/mL. The L2 ligand presented fungistatic and fungicidal activity against at least one of the three yeasts when it was complexed with cobalt, nickel and silver. However, the MIC and MFC values were higher for the complexes derived from L2 comparing to the complexes derived from L1. The results of the L1 ligand complexed with copper are highlighted since this compound presented the lowest MIC and MFC values and was more effective in inhibiting *C. krusei* (MIC = 31.25µg/mL) than the ketoconazole (MIC = 125µg/mL), which was used as positive control. The next step is to perform the cytotoxicity tests of these compounds in mammalian cell cultures to evaluate their viability as potential antifungals for human use.

**Keywords:** antifungal, *Candida*, metal complexes, 2-thiazoline-2-thiol

**Financial support:** CNPq, FAPEMIG