

Antifungal Properties of 3-(Morpholin-4-yl)propane-2,3-dione 4-Phenylthiosemicarbazone and Its Mixed Ligand-Copper(II) Complexes Toward *Cryptococcus neoformans*

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INTRODUCTION & AIM

The rising incidence of fungal infections and the limited effectiveness of current antifungal drugs emphasize the need for new active substances. *Cryptococcus neoformans* is a major opportunistic pathogen, responsible for cryptococcal meningitis in immunocompromised patients and associated with high mortality worldwide. Thiosemicarbazones and their metal complexes are reported to exhibit diverse biological activities, including antifungal effects.

The aim of our work is to study the antifungal activity towards fungi *Cryptococcus neoformans* of 3-(morpholin-4-yl)propane-2,3-dione 4-phenylthiosemicarbazone and its mixed ligand-copper(II) complexes.

METHOD

For our study, we have synthesized 3-(morpholin-4-yl)propane-2,3-dione 4-phenylthiosemicarbazone (HL) (Figure 1) and its mixed ligand-copper(II) complexes [CuL(Im)NO₃], [CuL(Py)NO₃], [CuL(β-Pic)NO₃], and [CuL(γ-Pic)NO₃]. The composition and structure of all compounds were confirmed using ¹H and ¹³C NMR spectroscopy, FTIR spectroscopy, elemental analysis, molar conductivity measurements, and X-ray crystallographic analysis.

The antifungal activity of all synthesized compounds was evaluated towards *Cryptococcus neoformans* (CECT 1043) using the broth microdilution method.

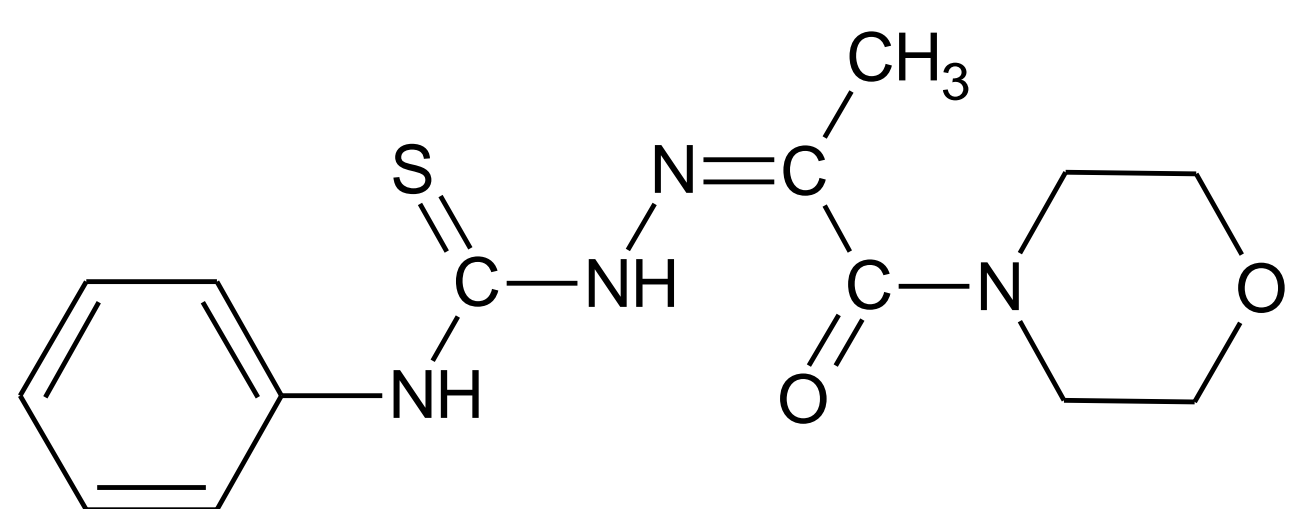


Figure 1. The structural formula of HL

RESULTS & DISCUSSION

The mixed-ligand copper(II) complexes exhibited higher activity compared to both the HL and the copper(II) nitrate complex from which they were obtained (Figure 2). This finding confirms that the introduction of an additional ligand into the inner coordination sphere can enhance biological activity. The most active compound was [CuL(γ-Pic)NO₃], which showed MIC and MBC values of 7.81 µg/mL and 15.63 µg/mL, respectively.

Antifungal activity toward *Cryptococcus neoformans*

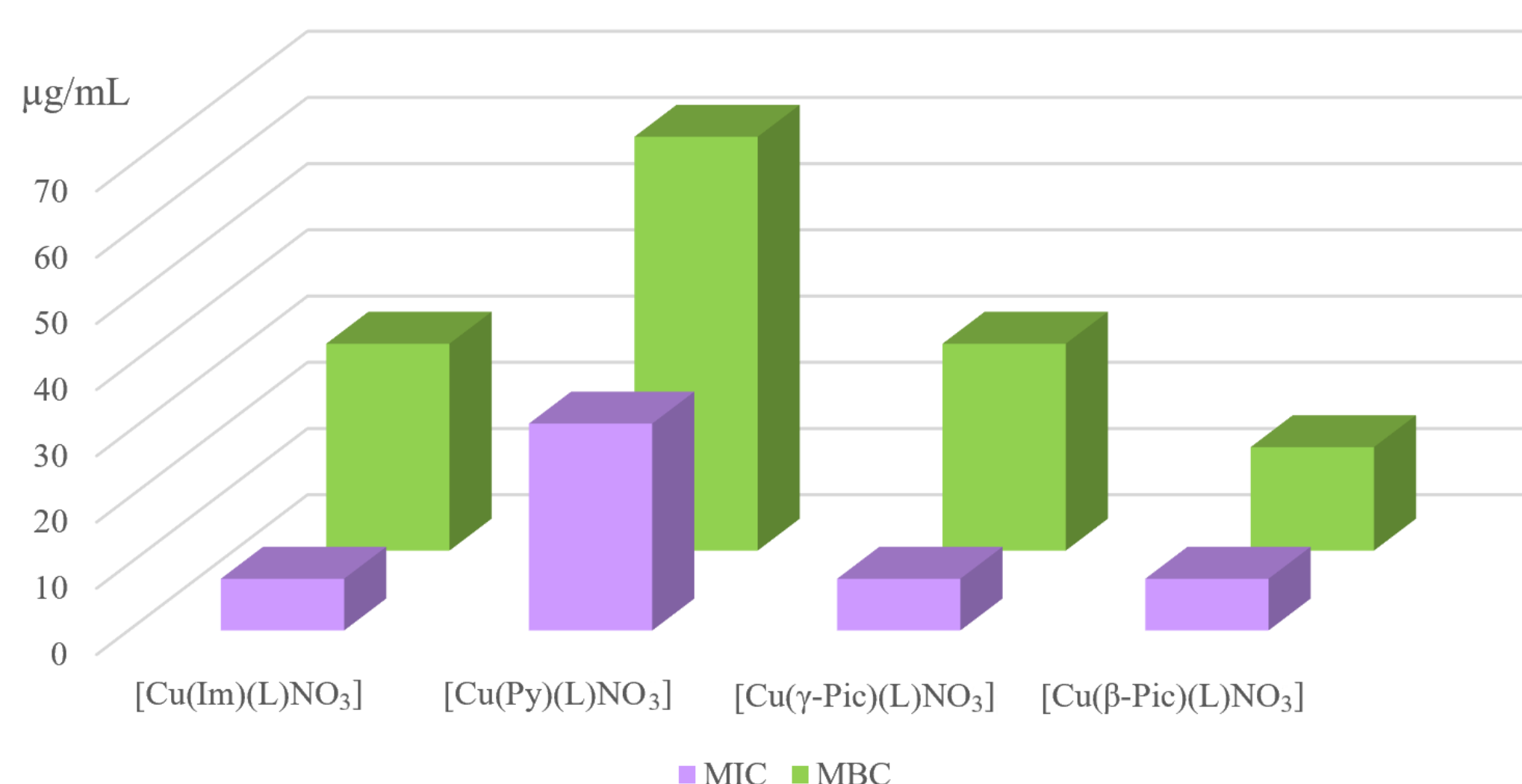


Figure 2. The activity of copper(II) complexes

CONCLUSION

These results highlight the potential of mixed ligand-copper(II) complexes as promising leads for the development of new antifungal agents, particularly against pathogenic fungi such as *Cryptococcus neoformans*. Moreover, it is important to note that the incorporation of N-heteroaromatic bases into the structure of the copper nitrate complex significantly enhanced its antifungal activity, making these complexes more active than both the thiosemicarbazone itself and its copper(II) nitrate complex.

ACKNOWLEDGEMENT

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