



Article

Inhibition of *C. albicans* Dimorphic Switch by Cobalt(II) Complexes with Ligands Derived from Pyrazoles and Dinitrobenzoate: Synthesis, Characterization and Biological Activity

Daniela Fonseca ¹, Sandra M. Leal-Pinto ², Martha V. Roa-Cordero ² , José D. Vargas ², Erika M. Moreno-Moreno ³, Mario A. Macías ¹, Leopoldo Suescun ⁴ , Álvaro Muñoz-Castro ⁵ and John J. Hurtado ^{1,*}

¹ Department of Chemistry, Universidad de los Andes, Carrera 1 No. 18A-12, 111711 Bogotá, Colombia

² Grupo de Investigación en Manejo Clínico-CLINIQUES, Facultad de Ciencias de la Salud, Universidad de Santander, 680002 Bucaramanga, Colombia

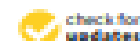
³ Grupo de Investigación en Biotecnología Agroambiente y Salud-MICROBIOTA, Facultad de Ciencias de la Salud, Universidad de Santander, 680002 Bucaramanga, Colombia

⁴ Crysmat-Lab, DETEMA, Facultad de Química, Universidad de la República, Av. 18 de Julio 1824-1830, 11200 Montevideo, Uruguay

⁵ Grupo de Química Inorgánica y Materiales Moleculares, Universidad Autónoma de Chile, El Llano Subercaseaux, Santiago 2801, Chile

* Correspondence: j.hurtado@untandes.edu.co; Tel.: +57-1-3394949 (ext. 3468)

Received: 23 April 2019; Accepted: 18 June 2019; Published: 1 July 2019



Abstract: Seven cobalt(II) complexes of pyrazole derivatives and dinitrobenzoate ligands were synthesized and characterized. The single-crystal X-ray diffraction structure was determined for one of the ligands and one of the complexes. The analysis and spectral data showed that all the cobalt complexes had octahedral geometries, which was supported by DFT calculations. The complexes and their free ligands were evaluated against fungal strains of *Candida albicans* and emerging non-*albicans* species and epimastigotes of *Trypanosoma cruzi*. We obtained antifungal activity with a minimum inhibitory concentration (MIC) ranging from 31.3 to 250 $\mu\text{g mL}^{-1}$. The complexes were more active against *C. krusei*, showing MIC values between 31.25 and 62.5 $\mu\text{g mL}^{-1}$. In addition, some ligands (L1–L6) and complexes (5 and $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$) significantly reduced the yeast to hypha transition of *C. albicans* at 500 $\mu\text{g mL}^{-1}$ (inhibition ranging from 30 to 54%). Finally, the complexes and ligands did not present trypanocidal activity and were not toxic to Vero cells. Our results suggest that complexes of cobalt(II) with ligands derived from pyrazoles and dinitrobenzoate may be an attractive alternative for the treatment of diseases caused by fungi, especially because they target one of the most important virulence factors of *C. albicans*.

Keywords: pyrazole and dinitrobenzoate ligands; cobalt(II) complexes; crystal structure; *Trypanosoma cruzi*; antifungal activity; cytotoxicity; dimorphic switch

1. Introduction

Microorganisms, such as fungi and parasites, cause diseases that have become a public health problem worldwide. Fungal infections caused by opportunistic yeasts of the genus *Candida* are becoming more frequent and are associated with high morbidity and mortality [1]. *C. albicans* is the most frequently isolated species in patients with candidiasis; however, the emergence of non-*albicans* strains, such as *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata*, among others, has become a