Inhibition of C. albicans dimorphic switch by cobalt(II) complexes with ligands derived from pyrazoles and dinitrobenzoate: Synthesis, characterization and biological activity

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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 µg mL\(^{-1}\). The complexes were more active against C. krusei, showing MIC values between 31.25 and 62.5 µg mL\(^{-1}\). In addition, some ligands (L1?L6) and complexes (5 and Co(OAc)\(_2\) · 4H\(_2\)O) significantly reduced the yeast to hypha transition of C. albicans at 500 µg 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. © 2019 by the authors.
Antifungal activity

Cobalt(II) complexes

Crystal structure

Cytotoxicity

Dimorphic switch

Pyrazole and dinitrobenzoate ligands

Trypanosoma cruzi

2,6 bis(3,5 dimethyl 1 pyrazolyl)pyridine

2,6 bis(3,5 dimethyl 4 nitro1pyrazolyl)pyridine

3,5 bis(3,5 dimethyl 4 nitropyrazol 1 ylmethyl)toluene

benznidazole

bis(3,5 dimethyl 1 pyrazolyl)methane

bis(3,5 dimethyl 4 nitro 1 pyrazolyl)methane

bis(dinitrobenzoate o,o?)

cobalt complex

dinitrobenzoate

dinitrobenzoate[2,6 bis(3,5 dimethyl 4 nitro pyrazol 1 ylmethyl)pyridine]

dinitrobenzoate[2,6 bis(3,5 dimethylpyrazol 1 ylmethyl)pyridine]

dinitrobenzoate[3,5 bis(3,5 dimethyl 4 nitro pyrazol 1 ylmethyl)toluene]

dinitrobenzoate[3,5 bis(3,5 dimethylpyrazol 1 ylmethyl)toluene]

dinitrobenzoate[bis(3,5 dimethyl 4 nitro pyrazol 1 yl)methane]

dinitrobenzoate[bis(3,5 dimethylpyrazol 1 yl)methane]

itraconazole

nitrobenzoic acid derivative

pyrazole
unclassified drug
antiinfective agent
cobalt
coordination compound
ligand
nitrobenzene derivative
pyrazole derivative
animal cell
antibiotic sensitivity
antifungal activity
Article
bioassay
biological activity
broth dilution
Candida albicans
Candida tropicalis
carbon nuclear magnetic resonance
controlled study
crystal structure
crystallization
cytotoxicity
drug synthesis
electrospray
elemental analysis
Fourier transform infrared spectroscopy
fungus hyphae
gas chromatography
germ tube inhibition assay
growth inhibition
IC50
infrared spectroscopy
mass spectrometry
melting point
minimum inhibitory concentration
MTT assay
nonhuman
Pichia kudriavzevii
proton nuclear magnetic resonance
Raman spectrometry
Trypanosoma cruzi
ultraviolet visible spectrophotometry
Vero cell line
X ray diffraction
animal
Candida albicans
cell survival
chemical structure
chemistry
Chlorocebus aethiops
drug effect
microbial sensitivity test
structure activity relation
synthesis

X ray crystallography

Animals

Anti-Bacterial Agents

Candida albicans

Cell Survival

Chlorocebus aethiops

Cobalt

Coordination Complexes

Crystallography, X-Ray

Dinitrobenzenes

Ligands

Microbial Sensitivity Tests

Molecular Structure

Pyrazoles

Structure-Activity Relationship

Vero Cells