NEW OXICONAZOLE ANALOGUES AS ANTIFUNGAL AGENTS

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The incidence of systemic fungal infections in immunocompromised patients has increased greatly during the last 20 years. Despite the growing list of antifungal agents, their clinical value has been limited by toxicity, pharmacokinetic deficiency or insufficiency in antifungal activity, partly imputable to the emergence of drug resistance.

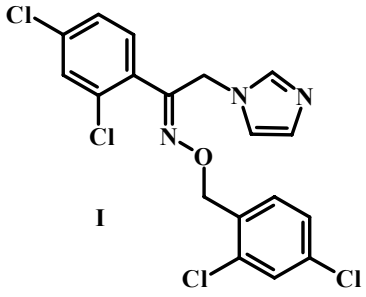
Among antifungal agents, azole derivatives are still a viable lead structure in pursuit of a more efficacious, broad spectrum, systemic antifungal drug.

They act by inhibiting the cytochrome P450-dependent lanosterol 14α-demethylase ($P450_{14DM}$, CYP51), a key enzyme in the fungal ergosterol-biosynthesis pathway [1].

Among the azole antifungals, oxiconazole (I) is a well-known agent with a broad spectrum of activity [2], structurally characterized by an oxime ether group.

Previously we reported 1,4-benzothiazine and 1,4-benzoxazine azole compounds that are active against an experimental model of systemic candidiasis [3].

As part of this research project, this work focuses on the synthesis and evaluation of new oxiconazole analogues, structurally characterized by a 1,4-benzothiazine or 1,4-benzoxazine moiety (II).



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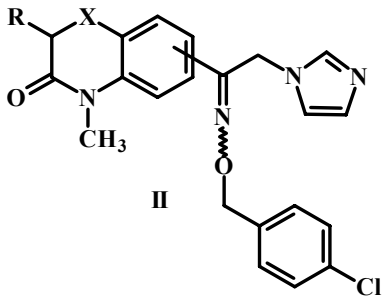

II

Synthesis, docking studies and microbiological evaluation will be discussed.

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