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Abstract

Novel Imidazole Derivatives as Antifungal Agents: Synthesis, Biological Evaluation, ADME Prediction and Molecular Docking Studies †

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The incidence of infection from opportunistic and pathogenic fungi has continued to rise in recent years. Azoles are an extensive and comparatively new class of synthetic compounds including imidazoles and triazoles and this group is most commonly applied in clinical treatment [1]. Azoles are administered against C14α-demethylase in the ergosterol pathway [2]. Ergosterol is a principal component of the fungal cell wall, which plays a significant role in membrane fluidity, enzyme activity, cell morphology, membrane permeability and cell cycle progression [3]. On the other hand, a literature review shows that the compounds that include dithiocarbamates have significant antifungal and anti-bacterial effects [4,5].

In light of the above findings, a series of compounds with imidazole and dithiocarbamate scaffolds was designed and synthesized. The structures of the synthesized compounds were elucidated using FT-IR, ^{1}H-NMR, ^{13}C-NMR, and HRMS spectral data. The target compounds were screened for in vitro anticandidal activity against Candida species by broth microdiluation methods. The results of in vitro anti-Candida activity, a docking study and ADME prediction revealed that the newly synthesized compounds have potential anti-Candida activity and evidenced the most active derivative, **5b**, which can be further optimized as a lead compound.

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References

1. Iman, M.; Peroomian, T.; Davood, A.; Amini, M.; Sardari, S.; Azerang, P. Design, Synthesis and Evaluation of New Azoles as Antifungal Agents: A Molecular Hybridization Approach. *Pharm. Chem. J.* **2016**, *49*, 1354–1359.
2. Lupetti, A.; Danesi, R.; Campa, M.; Del Tacca, M.; Kelly, S. Molecular basis of resistance to azole antifungals. *Mol. Med.* **2002**, *8*, 77–81.
3. Jacob, K.S.; Ganguly, S.; Kumar, P.; Poddar, R.; Kumar, A. Homology model, molecular dynamics simulation and novel pyrazole analogs design of Candida albicans CYP450 lanosterol 14 α-demethylase, a target enzyme for antifungal therapy. *J. Biomol. Struct. Dyn*. **2016**, *35*, 1–44.

4. Yurttaş, L.; Özkay, Y.; Duran, M.; Turan-Zitouni, G.; Özdemir, A.; Cantürk, Z.; Küçükoğlu K.; Kaplancıklı, Z.A. Synthesis and antimicrobial activity evaluation of new dithiocarbamate derivatives bearing thiazole/benzothiazole rings. *Phosphorus Sulfur Silicon Relat. Elem*. **2016**, *191*, 1166–1173.
5. Zou, Y.; Yu, S.; Li, R.; Zhao, Q.; Li, X.; Wu, M.; Huang, T.; Chai, X.; Hu, H.; Wu, Q. Synthesis, antifungal activities and molecular docking studies of novel 2-(2,4-difluorophenyl)-2-hydroxy-3-(1H-1,2,4-triazol-1-yl) propyl dithiocarbamates. *Eur. J. Med. Chem.* **2014**, *74*, 366–374.