Scientific Research Publishing

Open Journal of Medicinal Chemistry, 2025, 15(3), 33-44
https://www.scirp.org/journal/ojmc
ISSN Online: 2164-313X
ISSN Print: 2164-3121

Antifungal Activities of 2-Styrylbenzimidazoles against *Candida glabrata*

Songuigama Coulibaly[1], Jean-Paul Deto Ursul N'Guessan[1], Alain Kacou[1], Etienne Kpongbo Angora[2], Mahama Ouattara[1*]

[1]Unité Pédagogique de Chimie Thérapeutique et Chimie Organique, UFR Sciences Pharmaceutiques, Université FHB, Abidjan, Côte d'Ivoire
[2]Unité Pédagogique de Parasitologie-Mycologie-Zoologie Structurale, UFR Sciences Pharmaceutiques, Université FHB, Abidjan, Côte d'Ivoire
Email: *mahama.dpm@gmail.com, songuigama@gmail.com

How to cite this paper: Coulibaly, S., N'Guessan, J.-P.D.U., Kacou, A., Angora, E.K. and Ouattara, M. (2025) Antifungal Activities of 2-Styrylbenzimidazoles against *Candida glabrata*. *Open Journal of Medicinal Chemistry*, **15**, 33-44.
https://doi.org/10.4236/ojmc.2025.153003

Received: August 1, 2025
Accepted: September 1, 2025
Published: September 30, 2025

Abstract

Candidiasis is one of the most widespread fungal infections globally. The efficacy of antifungal chemotherapy has become a public health concern due to the emergence and proliferation of drug-resistant Candida strains. It is within this context that we proposed to design, synthesize, and evaluate the antifungal activities of a new series of 2-styrylbenzimidazoles against a clinical strain of *Candida glabrata*. The objective of this work was to identify a potential antifungal lead compound to initiate its medicinal chemistry development. The 2-styrylbenzimidazoles used were conceptualized using medicinal chemistry techniques involving the hybridization of chemical entities with potential antifungal properties. The antifungal activities of the compounds were expressed as Minimum Inhibitory Concentrations (MICs), determined in vitro against a clinical strain of *C. glabrata* using the microplate dilution technique. All 10 evaluated compounds exhibited antifungal activity against the clinical strain of *Candida glabrata*. Furthermore, the derivative chlorinated at the 2-position of the benzene ring stood out for its particular efficacy against Candida, with an MIC of 12.26 µM. In conclusion, the derivative chlorinated at position 2 can be selected as the "hit molecule" from which further pharmacomodulations can be undertaken to obtain a drug candidate for the medicinal chemistry development of a new class of antifungals based on the 2-styrylbenzimidazole profile.

Keywords

2-Styrylbenzimidazoles, *Candida glabrata*, Anticandidal, Antifungal, Microplate Dilution

1. Introduction

Candidiasis is a common fungal infection that can affect both superficial and deep organs of the human body [1]. It is caused by yeasts of the Candida genus, which include species such as *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida auris*, etc. [2]. Among these, *Candida albicans* remains the most frequently encountered species in human pathology. However, in recent years, there has been an emergence of species that were previously less common, such as *Candida glabrata*, *Candida tropicalis*, and *Candida auris* [3] [4]. In sub-Saharan Africa, superficial candidiasis poses a major challenge for people living with HIV/AIDS [5]. These fungal infections, which cause oropharyngeal candidiasis, complicate swallowing, thereby exacerbating malnutrition and reducing adherence to treatment. This can lead to potentially life-threatening therapeutic failures [6]. Over the past three decades, the frequency of these fungal infections has increased alarmingly, alongside the emergence of previously rare fungal species [7] [8]. Although *Candida albicans* remains the primary agent, accounting for 80% of cases, non-albicans species such as *Candida glabrata* and *Candida tropicalis* are gaining ground. These species are often more resistant to conventional antifungal treatments [9]. Once highly effective, azole antifungals now face growing resistance from Candida strains [10] [11]. This situation represents a significant global public health challenge, with the threat of a fungal pandemic for which effective treatment options could become nonexistent. In response to this situation, we have proposed to contribute to the development of several 2-styrylbenzimidazoles as potential new anticandidal agents.

2. Experimental Section

2.1. Pharmacochemical Design

Among the medicinal chemistry strategies for developing new molecules, the concept of molecular juxtaposition is currently one of the most rapidly growing strategies. It involves combining two or more biologically active entities to obtain new molecules with high anti-infective potential. The application of this concept has led to the development of numerous drug molecules such as trioxaquines (antimalarials), vancomycins (antibiotics), etc. This so-called "dual-shot" strategy was developed with the aim of reducing the emergence of drug-resistant pathogens [12] [13]. Having proven its effectiveness, we have adopted this research method in our work to discover new molecules with anti-infective properties. Thus, we have designed a hybrid chemical profile resulting from the judicious combination of the benzimidazole heterocycle and the styryl functional chain. The choice of benzimidazole is justified by its role as the pharmacophore vector in several drugs used in therapy. Furthermore, it possesses numerous anti-infective activities, including anthelmintic, antibacterial, antiviral, and antifungal properties [14]-[17]. As for the styryl chain or aryl α,β-ethylene group, it is a functional chain that acts as a modulator of biological activities, particularly anti-infective ones (antibacterial, antifungal, antiparasitic, and antiviral) [18]-[21]. It is characterized by the

ability of the π electrons of the ethylene bond to conjugate with those of the aryl ring, especially when the latter bears electron-withdrawing or electron-donating groups. This is why we have undertaken our research work around the benzimidazole nucleus and the styryl chain, due to their multiple pharmacological potentials, particularly antifungal. Thus, by applying the medicinal chemistry concepts of juxtaposing bioactive entities, it seemed logical to us to design a new chemical profile combining the styryl and benzimidazole groups. These styryl derivatives could themselves possess potential antifungal activities, provided they are judiciously attached to the benzimidazole pharmacophore vector of Chlormidazole [22] (**Figure 1**).

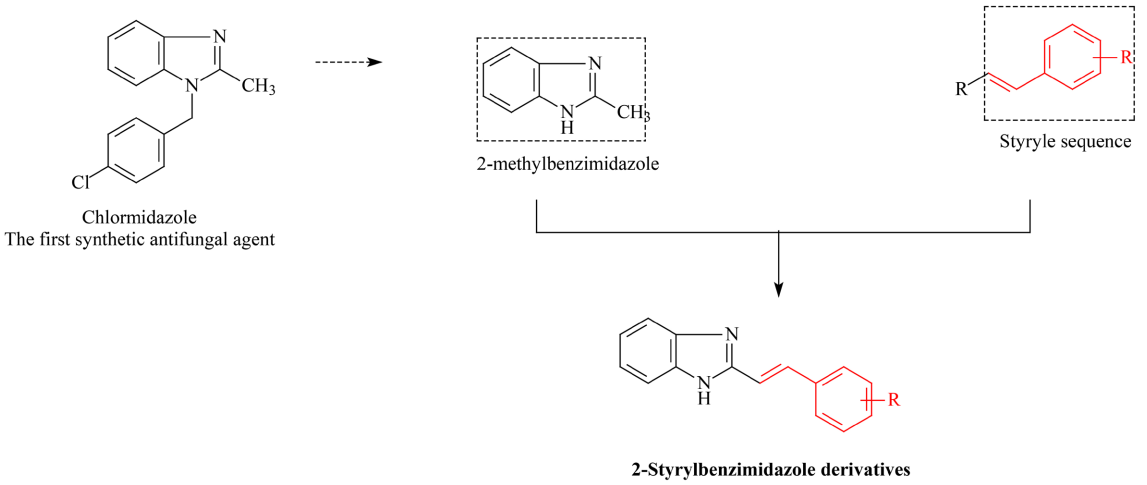


Figure 1. Design of 2-styrylbenzimidazoles.

2.2. Chemistry

The synthesis of the 2-styrylbenzimidazoles was carried out in two main steps: the construction of 2-methylbenzimidazole and its condensation with aldehydes to yield the 2-styrylbenzimidazoles. The construction of 2-methylbenzimidazole required the prior synthesis of ortho-phenylenediamine via the reduction of 2-nitroaniline. This reduction was performed according to the method described by Ramaiah and colleagues [23]. It involves treating 2-nitroaniline with zinc powder in methanol in the presence of ammonium chloride. After cooling, the reaction mixture is filtered to remove insoluble impurities, and the filtrate is evaporated to dryness using a rotary evaporator. The crude ortho-phenylenediamine obtained from the reduction was used without purification in a condensation reaction with acetic acid in the presence of diluted hydrochloric acid (4N) under reflux for 5 hours. After cooling, the reaction mixture was neutralized with an ammonium hydroxide (NH_4OH) solution. The 2-methylbenzimidazole was isolated and purified by recrystallization in water. This compound was then subjected to a solvent-free condensation reaction with benzaldehyde or its derivatives, following a Knoevenagel-type reaction [24]. The reaction mixture was heated to between 170 and 200˚C for 3 hours. After cooling, the resulting solid was dissolved in 2-propanol,

and the target 2-styrylbenzimidazole was obtained by adding an oxalic acid solution followed by neutralization with ammonia.

✓ **Synthesis Procedure for *ortho*-Phenylenediamine**

In a round-bottom flask containing 2-nitroaniline (a) (7.2 mmol), zinc powder (144.9 mmol), ammonium chloride (36.23 mmol), and 20 ml of methanol were added (Figure 2). The reaction mixture was heated under reflux for 6 hours. After cooling, the mixture was filtered, and the filtrate was evaporated to dryness using a rotary evaporator. The resulting ortho-phenylenediamine (b) was used without further purification in the subsequent reaction step.

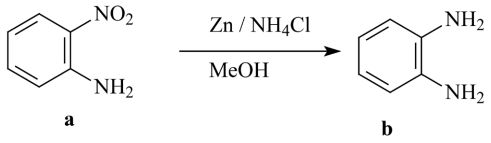


Figure 2. Reduction of 2-nitroaniline to ortho-phenylenediamine.

✓ **Procedure for the synthesis of 2-methylbenzimidazole**

The ortho-phenylenediamine (b) (46 mmol) obtained from the previous synthesis was dissolved in 50 mL of diluted (4N) HCl in a 150 mL round-bottom flask. Acetic acid (c) (64 mmol) was added to this solution. The reaction mixture was brought to reflux for 5 hours (Figure 3). Subsequently, the mixture was cooled, and the pH of the solution was adjusted to 8 using ammonia. The resulting solid was filtered under vacuum and recrystallized in 50 mL of distilled water to yield the expected 2-methylbenzimidazole (d) with an 87% yield.

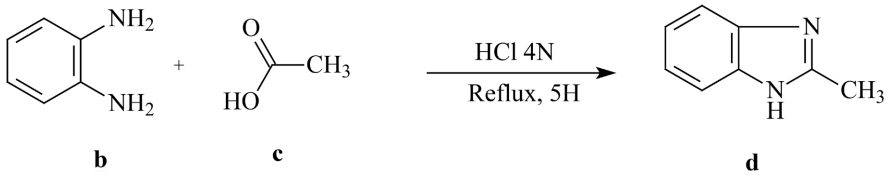


Figure 3. Synthesis of 2-methylbenzimidazole.

✓ **Procedure for the synthesis of 2-styrylbenzimidazoles**

In a round-bottom flask, 0.5 g of 2-methylbenzimidazole (d) (3.8 mmol) and 3.8 mmol of benzaldehyde or its derivative (e) were added. The reaction mixture was heated without solvent at a temperature between 170˚C and 200˚C for 3 hours (Figure 4). After cooling, the resulting brown mass was dissolved in 10 mL of isopropanol. To this solution, 0.56 g of oxalic acid in 5 mL of isopropanol was added while stirring. The precipitated solid was filtered under vacuum and washed with ice-cold water. This precipitate was then suspended in ice-cold water, and the resulting suspension was treated with aqueous ammonia (NH_4OH) to adjust the pH to between 8 and 10. The solid obtained was filtered, washed with hexane, and dried to yield the expected 2-styrylbenzimidazole derivatives (1-10).

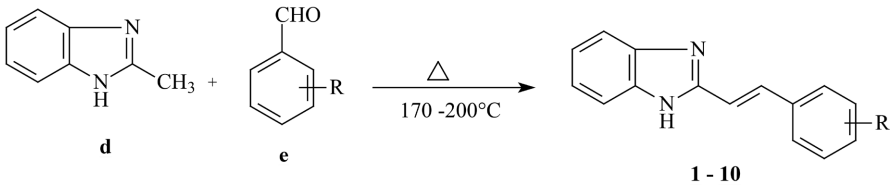


Figure 4. Synthesis of 2-styrylbenzimidazoles.

2.3. Biology

The antifungal activity of 2-styrylbenzimidazoles was evaluated using the microplate dilution method against the clinical strain *Candida glabrata* (U3538) of vaginal origin from the University Hospital Center (CHU) of Angré (Ivory Coast).

The antifungal susceptibility test performed on the clinical strain of *Candida glabrata* showed sensitivity to fluconazole, nystatin, and amphotericin B, and resistance to econazole and miconazole. As fluconazole is the most commonly used molecule in the treatment of fungal infections in our country, we chose it as the reference molecule in our study. The microplate dilution method involves exposing a Candida inoculum to serial dilutions of the test compound in 96-well microplates (12 rows of 8 wells). The inhibition of fungal growth is assessed by colorimetric detection of dehydrogenase activity in the yeast cells using Methyl Thiazolyl Tetrazolium chloride (MTT). This (purple) coloration originates from the activity of mitochondria in viable, metabolically active cells. The MIC (Minimum Inhibitory Concentration) is determined as the lowest concentration that prevents the change from the yellow color of MTT [25]-[30].

✓ **Preparation of the inoculum**

The preparation of the inoculum began by subculturing the Candida strain on Sabouraud glucose agar (Sabouraud 4% glucose agar, Fluka®) in a Petri dish. After 24 hours of incubation at 37˚C, one to three colonies were inoculated into 50 mL of Tryptone Soya Broth (OXOID®) and left at room temperature for 12 - 24 hours to yield broth1. Then, 5 mL of broth1 was transferred into 25 mL of Tryptone Soya Broth (OXOID®) and placed under agitation for 6 hours (the time required to reach exponential growth of Candida) to yield broth2. At the time of the test, 2.5 mL of broth2 was added to 25 mL of Tryptone Soya Broth (OXOID®) to obtain an inoculum containing approximately 10^5 cells/mL [25]-[30]. The colony-forming unit count in the inoculum was confirmed using a Malassez counting chamber.

✓ **Determination of minimum inhibitory concentrations**

The test was performed using 96-well microplates. Stock solutions of the different compounds were prepared in Dimethyl Sulfoxide (DMSO) at a concentration of 1 mg/mL and then diluted with Tryptone Soya Broth (OXOID®) to obtain solutions concentrated at 100 µg/mL. 100 µL of this dilution was deposited into the wells of the first row. Then, 50 µL of Tryptone Soya Broth (OXOID®) was distributed into all other wells. A serial dilution was performed using 50 µL from the first row's wells. 50 µL of broth3 containing the inoculum was distributed into all wells. The plates were incubated at 30˚C for 48 hours. For the revelation of the prepared

microplates, 40 µL of an aqueous solution of Methyl Thiazolyl Tetrazolium chloride (MTT) at a concentration of 2.5 mg/mL was distributed into the wells and incubated for an additional 2 hours at room temperature. The aqueous MTT solution is yellow in color. Wells containing still viable cells turn purple due to the dehydrogenase activity of the mitochondria. The MIC determination, which is the lowest concentration at which no color change was observed, was made visually. [25]-[30]. All samples were tested in duplicate, and the tests were repeated twice. The minimum inhibitory concentrations, initially expressed in µg/mL (mass/volume), were converted to µM (number of molecules/volume). This conversion is justified because two molecules with the same MIC in µg/mL can exhibit very different biological activities if their molar masses differ. Conversion to µM normalizes the data in terms of the number of active molecules, providing a more accurate relative potency for each compound.

3. Results and Discussion

3.1. Results

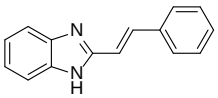
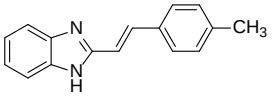
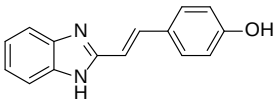
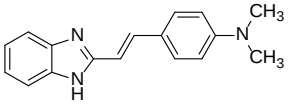
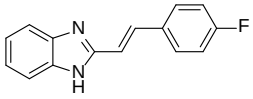
✓ **Chemistry**

The synthesis of the 2-styrylbenzimidazole derivatives was carried out using established methods, yielding two intermediates and ten final compounds. The characterization of the chemical structures of the various synthesized derivatives has been described in a previous article [31].

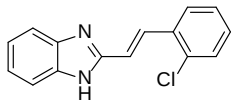
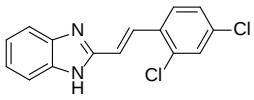
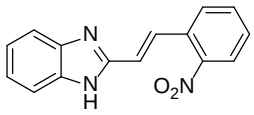
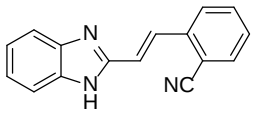
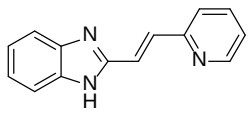
✓ **Antifungal activity**

The Minimum Inhibitory Concentrations of the 2-styrylbenzimidazole derivatives against the clinical strain of *Candida glabrata* are summarized in **Table 1** below.

Table 1. Activity of 2-styrylbenzimidazoles against the clinical strain of *Candida glabrata*.

Compound number	Chemical Structures	Molar Mass (g/mol)	Calculated LogP	MIC (µg/mL)	MIC (µM)
1		220.28	3.65	12.5	56.74
2		234.30	4.14	6.25	26.67
3		236.27	3.36	6.25	26.45
4		263.34	3.94	6.25	23.73
5		238.27	3.81	6.25	26.23

Continued

6		254.72	4.21	3.125	12.26
7		289.16	4.77	6.25	21.61
8		265.27	4.04	12.5	47.12
9		245.29	3.69	6.25	25.48
10		221.26	2.74	6.25	28.24
	Fluconazole	306.27		6.25	20.40

These results indicate that the 2-styrylbenzimidazoles exhibit anticandidal activity against the clinical strain of *Candida glabrata* used. Compound 1 (unsubstituted 2-styrylbenzimidazole) and compound 8 (2-nitro derivative) are the least active derivatives against *Candida glabrata*, with MICs of 56.74 µM and 47.12 µM, respectively. Compounds 2 (benzenic ring para-methyl derivative), 3 (para-hydroxy), 4 (para-dimethylamino), 5 (para-fluoro), 7 (2,4-dichloro), 9 (2-cyano), and 10 (pyridinyl derivative) induced antifungal activities close to that of Fluconazole, with MICs between 20 µM and 30 µM. Compound 6 (2-chloro derivative) demonstrated the best anticandidal efficacy, with an MIC of 12.26 µM.

3.2. Discussion

Following the evaluation of the antifungal activities of our 2-styrylbenzimidazole derivatives against *Candida glabrata*, we undertook a structure-activity relationship (SAR) discussion. The objective is to establish a correlation between the structure and antifungal activities in order to identify the structural elements that contribute to inducing, or even enhancing, the expected antifungal effects. In this discussion, we use the minimum inhibitory concentration (MIC) to quantify the anticandidal efficacy of each compound; that is, a compound is considered more effective if its MIC is lower. According to the results, it is evident that 2-styrylbenzimidazoles can inhibit Candida strains, particularly *Candida glabrata*. These results once again confirm the antifungal properties of the benzimidazole nucleus, as reported by Wolley in 1944 [22]. Furthermore, the results reveal that the efficacy of these 2-styrylbenzimidazole derivatives varies depending on the nature of the substituent on the benzenic ring. Therefore, our discussion aims to compare the antifungal efficacy of the different molecules based on the nature of the

substituent on the benzenic ring. Analysis of the obtained results established that linking the benzimidazole heterocycle to the styryl functional group at position 2 yields compound 1, which possesses anticandidal activity against *C. glabrata* with an MIC of 56.74 μM. The presence of the styryl group at position 2 of the benzimidazole appears favorable for the emergence and maintenance of antifungal activities. Given this result, various structural modifications were undertaken around the benzenic ring of compound 1 to improve its activity. These modifications allowed us to establish that: Introducing a small alkyl radical like a methyl group at position 4 (compound 2) leads to an improvement in antifungal activity, with an MIC of 26.67 μM. This performance is twice that of compound 1 (MIC = 56.74 μM) and is on the same order of magnitude as the reference drug, Fluconazole (MIC = 20.40 μM). This result with the methyl group could be partially explained by the greater lipophilicity imparted by the methyl group compared to the hydrogen atom. Replacing the methyl with a hydroxyl group (compound 3) maintains the anticandidal efficacy, with an MIC of 26.45 μM. This efficacy, equivalent to compound 2, could be explained by the ability of the hydroxyl group to form additional hydrogen bonds with the biological target. Furthermore, the hydroxyl group at position 4 was replaced by a more electron-donating dimethylamino group (compound 4) to verify the impact of this effect. The antifungal result of compound 4 (MIC = 23.73 μM) shows that the dimethylamino group leads to a slight improvement in antifungal activity, thus confirming the benefit of electron-donating groups in enhancing antifungal activities. Such modulation of antifungal activities by electron-donating groups appears favorable for maintaining these anticandidal activities. Replacing the hydroxyl group with a halogen atom at position 4, specifically fluorine (compound 5), results in the same efficacy observed with compounds 3 and 4, with an MIC of 26.23 μM. The presence of the fluorine atom, considered a modulator of the anticandidal performance of Fluconazole in the conazole series [32], does not appear to be relevant in the 2-styrylbenzimidazole series. In contrast, introducing a chlorine atom at position 2 (compound 6) leads to potent anticandidal activity with an MIC of 12.26 μM. This 2-chloro derivative exhibited the best anticandidal performance in the chemical series of 2-styrylbenzimidazoles, with efficacy superior to the reference drug, Fluconazole (MIC = 20.40 μM). Such performance confirms the ability of chlorine atoms to improve anticandidal activities, as reported with first-generation conazoles [32]. Duplicating the chlorine atom at positions 2 and 4 (compound 7) did not improve the anticandidal performance. Indeed, compound 7, with an MIC of 21.61 μM, proved less effective than its monochloro analogue; however, this performance is comparable to that of the reference drug, Fluconazole (MIC = 20.40 μM). Ultimately, the modulation of antifungal performance by halogen atoms proves more judicious with a chlorine atom at position 2 of the benzenic ring of the 2-styrylbenzimidazoles. Replacing the chlorine atom at position 2 with an electron-withdrawing nitro group yields compound 8. The latter, with an MIC of 47.12 μM, exhibited efficacy nearly equivalent to the unsubstituted compound 1 and lower than that of the other derivatives obtained by chemical modulation of the benzenic ring. The nitro

group, known in medicinal chemistry as a modulator of anti-infective activities in the 5-nitroimidazole series and analogues [33], does not appear conducive to enhancing the expected antifungal activities. Substituting the nitro group at position 2 with another electron-withdrawing group, a nitrile (compound 9), leads to a slight improvement in antifungal activities, with an MIC of 25.48 µM. This performance is superior to that of the unsubstituted compound 1 and comparable to that of the 4-methyl, 4-hydroxy, and 4-fluoro derivatives. Replacing the benzenic ring of the unsubstituted compound 1 with a hexagonal heteroaryl group like 2-pyridinyl (compound 10) maintains the expected antifungal activities, with an MIC of 28.24 µM. While this is slightly lower than that of the reference drug, Fluconazole (MIC = 20.40 µM), it remains twice as high as that obtained with the unsubstituted compound 1 (MIC = 56.74 µM). Such structural variation using heterocycles appears favorable for a slight increase in anticandidal activities.

4. Conclusion

This medicinal chemistry work is part of the development of new drug candidates to combat fungal diseases. The evaluation of the antifungal activities of the 2-styrylbenzimidazole derivatives against a Fluconazole-sensitive strain of *Candida glabrata* demonstrated that 2-styrylbenzimidazoles possess anticandidal activity against the clinical strain of *C. glabrata*, with minimum inhibitory concentrations ranging between 12.26 and 56.74 µM. The best performance against *C. glabrata* was achieved with the 2-chloro derivative (compound 6), exhibiting an MIC of 12.26 µM. Furthermore, the chemical modifications undertaken revealed that substituting the benzenic ring of the unsubstituted styrylbenzimidazole with chemical modulators such as hydroxyl, fluorine, chlorine, dimethylamino, and nitrile groups contributes to an increase in anticandidal performance. Additionally, replacing the benzenic ring of the unsubstituted styrylbenzimidazole with a pyridine ring is also favorable for improving the anticandidal activity. The best antifungal profile against the *C. glabrata* strain was obtained with the 2-chloro derivative. This derivative is characterized by potent anticandidal activity superior to that of the reference drug substance, Fluconazole. These results allow us to validate the 2-styrylbenzimidazole chemical profile as a new potential antifungal pharmacophore. However, it is necessary to elucidate the mechanism of action of these 2-styrylbenzimidazoles on *Candida glabrata*, determine their cytotoxicity, and extend the antifungal evaluation to other fungal species in order to determine the antifungal spectrum of these molecules.

Acknowledgements

The authors of this article wish to express their sincere gratitude to the National Public Health Laboratory of Côte d'Ivoire and to the Parasitology and Mycology Laboratory of the University Hospital Center (CHU) of Angré (Côte d'Ivoire) for the characterization of the chemical compounds and the evaluation of the antifungal activities, respectively.

Conflicts of Interest

The authors of this article declare that they have no conflicts of interest in the production of this work.

References

[1] Valeix, N. (2019) Parasitology and Mycology. De Boeck Supérieur, 133 p.

[2] Dodé, G., Jean, D. and Dante, B. (1984) Treatise on Medical Mycology. Payot, 482 p.

[3] Whaley, S.G., Berkow, E.L., Rybak, J.M., Nishimoto, A.T., Barker, K.S. and Rogers, P.D. (2017) Azole Antifungal Resistance in *Candida albicans* and Emerging Non-*Albicans candida* Species. *Frontiers in Microbiology*, **7**, Article 2173. https://doi.org/10.3389/fmicb.2016.02173

[4] Krcmery, V. and Barnes, A.J. (2002) Non-*Albicans candida* spp. Causing Fungaemia: Pathogenicity and Antifungal Resistance. *Journal of Hospital Infection*, **50**, 243-260.

[5] Mushi, M.F., Bader, O., Taverne-Ghadwal, L., Bii, C., Groß, U. and Mshana, S.E. (2017) Oral Candidiasis among African Human Immunodeficiency Virus-Infected Individuals: 10 Years of Systematic Review and Meta-Analysis from Sub-Saharan Africa. *Journal of Oral Microbiology*, **9**, Article ID: 1317579. https://doi.org/10.1080/20002297.2017.1317579

[6] Taverne-Ghadwal, L., Kuhns, M., Buhl, T., Schulze, M.H., Mbaitolum, W.J., Kersch, L., *et al.* (2022) Epidemiology and Prevalence of Oral Candidiasis in HIV Patients from Chad in the Post-Haart Era. *Frontiers in Microbiology*, **13**, Article 844069. https://doi.org/10.3389/fmicb.2022.844069

[7] Aydemir, Ö., Demiray, T., Köroğlu, M., *et al.* (2017) Emerge of Non-*Albicans candida* Species; Evaluation of *Candida* Species and Antifungal Susceptibilities According to Years. *Biomedical Research*, **28**, 2820-2825.

[8] Ben-Ami, R. and Kontoyiannis, D.P. (2021) Resistance to Antifungal Drugs. *Infectious Disease Clinics of North America*, **35**, 279-311. https://doi.org/10.1016/j.idc.2021.03.003

[9] Denning, D.W. (2022) Antifungal Drug Resistance: An Update. *European Journal of Hospital Pharmacy*, **29**, 109-112. https://doi.org/10.1136/ejhpharm-2020-002604

[10] Meunier, B. (2011) Hybrid Molecules as a Strategy for Creating New Anti-Infective Agents. *Comptes Rendus Chimie*, **14**, 400-405.

[11] Shaveta, S., Mishra, S. and Singh, P. (2016) Hybrid Molecules: The Privileged Scaffolds for Various Pharmaceuticals. *European Journal of Medicinal Chemistry*, **124**, 500-536.

[12] N'Guessan, D.J.P. (2018) Anticandidosic Activities of New Chalcones Vectorised by Benzimidazole against a Strain of *Candida albicans* Pharmacoresistance to Azoles. *IOSR Journal of Pharmacy and Biological Sciences*, **13**, 11-16.

[13] Songuigama, C., Ndu, J.P., Mahama, O. and Mamidou, K.W. (2019) Synthesis and Antifungal Activities of Benzimidazolyl-Arylpropenone Scaffolds as Promising Inhibitors of Azole-Resistant *Candida* Strains. *European Journal of Biomedical and Pharmaceutical Sciences*, **6**, 19-25.

[14] Tahlan, S., Kumar, S. and Narasimhan, B. (2019) Antimicrobial Potential of 1*H*-Benzo[*d*]Imidazole Scaffold: A Review. *BMC Chemistry*, **13**, Article No. 18. https://doi.org/10.1186/s13065-019-0521-y

[15] Padalkar, V.S., Borse, B.N., Gupta, V.D., Phatangare, K.R., Patil, V.S., Umape, P.G., *et al.* (2016) Synthesis and Antimicrobial Activity of Novel 2-Substituted Benzimidazole,

Benzoxazole and Benzothiazole Derivatives. *Arabian Journal of Chemistry*, **9**, 1125-1130.

[16] De Filippis, B., Ammazzalorso, A., Amoroso, R. and Giampietro, L. (2019) Stilbene Derivatives as New Perspective in Antifungal Medicinal Chemistry. *Drug Development Research*, **80**, 285-293.

[17] Kluska, M., Jabłońska, J. and Prukała, W. (2023) Analytics, Properties and Applications of Biologically Active Stilbene Derivatives. *Molecules*, **28**, Article 4482. https://doi.org/10.3390/molecules28114482

[18] Jain, D.K., Jain, N., Patel, V., Singhal, S. and Jain, S.K. (2015) Synthesis, Characterization and Antimicrobial Activity of Novel Substituted Cis-Stilbene Derivatives. *World Journal of Pharmacy and Pharmaceutical Sciences*, **4**, 1473-1491.

[19] Heck, R.F. and Nolley, J.P. (1972) Palladium-Catalyzed Vinylic Hydrogen Substitution Reactions with Aryl, Benzyl, and Styryl Halides. *The Journal of Organic Chemistry*, **37**, 2320-2322. https://doi.org/10.1021/jo00979a024

[20] Woolley, D.W. (1944) Some Biological Effects Produced by Benzimidazole and Their Reversal by Purines. *Journal of Biological Chemistry*, **152**, 225-232. https://doi.org/10.1016/s0021-9258(18)72045-0

[21] Ramaiah, K. and Ramanatham, J. (2000) Synthesis and Spectral Properties of 2-Styrylbenzimidazoles. *Indian Journal of Chemistry*, **39B**, 904-914.

[22] Jones, G. (2011) The Knoevenagel Condensation. In: *Organic Reactions*, John Wiley & Sons, Inc., 204-599. https://doi.org/10.1002/0471264180.or015.02

[23] Kritikos, A., Neofytos, D., Khanna, N., *et al.* (2018) Accuracy of Sensititre YeastOne Echinocandins Epidemiological Cut-Off Values for Identification of FKS Mutant *Candida albicans* and *Candida glabrata*: A Ten Year National Survey of the Fungal Infection Network of Switzerland (FUNGINOS). *Clinical Microbiology and Infection*, **24**, 1214.e1-1214.e4.

[24] Coulibaly, S., N'guessan, J.P., Kone, M.W., *et al.* (2018) Anticandidosic Activities of New Chalcones Vectorised by Benzimidazole against a Strain of *Candida albicans* Pharmacoresistance to Azoles. *IOSR Journal of Pharmacy and Biological Sciences*, **13**, 11-16.

[25] Coulibaly, S., N'guessan, J.P., Kone, M.W., *et al.* (2014) Anti *Candida* L Activities of New Arylpropenones with Imidazopyridine Scaffold. *Afrique Biomédicale*, **19**, 43-48.

[26] N'Guessan, J.P., Coulibaly, S., Molou, K.Y.G., *et al.* (2014) Anti-*Candida albicans* Activities of Some Benzothiazoles and Structural Analogues with Heteroaryl Scaffold. *Afrique Biomédicale*, **19**, 4-10.

[27] Coulibaly, S., N'guessan, J.P., Ouattara, M., *et al.* (2019) Synthesis and Antifungal Activities of Benzimidazolyl-Arylpropenone Scaffolds as Promising Inhibitors of Azole-Resistant *Candida* Strains. *European Journal of Biomedical and Pharmaceutical Sciences*, **6**, 19-25.

[28] Coulibaly, S., Kone, A., N'guessan, J.P., *et al.* (2020) Design, Synthesis and Anticandidal Activities of Some Retrochalcones with Benzimidazole Nucleus. Journal of Pharmaceutical and Biological Sciences, 21, 5-11.

[29] Ablé, N.C., N'guessan, D.U.J.-P., Yéhé, M.D., Coulibaly, S., *et al.* (2023) Determination of Analytical Parameters of Some 2-Arylvinyl Benzimidazole Derivatives by Liquid Chromatography Coupled with Tandem Mass Spectrometry (LC/MS/MS). *International Journal of Pharmacy and Chemistry*, **9**, 67-77.

[30] Bryskier, A. (1999) Antibacterial and Antifungal Agents. Ellipses, 1216 p.

[31] AFECT (French Association of Teachers of Therapeutic Chemistry) (2000) Treatise

on Therapeutic Chemistry, Volume 5: Main Antifungal and Antiparasitic Agents, Volume 2: Antiparasitics. Tec & Doc, 544 p.

[32] Heeres, J., Meerpoel, L. and Lewi, P. (2010) Conazoles. *Molecules*, **15**, 4129-4188. https://doi.org/10.3390/molecules15064129

[33] Edwards, D.I. (1993) Nitroimidazole Drugs—Action and Resistance Mechanisms II. Mechanisms of Resistance. *Journal of Antimicrobial Chemotherapy*, **31**, 201-210. https://doi.org/10.1093/jac/31.2.201