Brazilian Journal of Microbiology
https://doi.org/10.1007/s42770-022-00777-3

CLINICAL MICROBIOLOGY - RESEARCH PAPER

In vitro antifungal activity of heterocyclic organoboron compounds against *Trichophyton mentagrophytes* and *Microsporum canis* obtained from clinical isolates

Meryem Pir[1] · Fatma Budak[2] · Kemal Metiner[3]

Received: 4 February 2022 / Accepted: 11 May 2022
© The Author(s) under exclusive licence to Sociedade Brasileira de Microbiologia 2022

Abstract
The aim of this study was to investigate the in vitro activity of thirty-eight heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) against clinically isolated dermatophytes *Trichophyton mentagrophytes* and *Microsporum canis*. Minimum inhibitory concentrations (MICs) of compounds (1a–o, 2a–j, 3a–m) were determined according to published protocol Clinical and Laboratory Standards Institute (CLSI) M38–A2 broth microdilution method. The minimum fungicidal concentrations (MFCs) for both *T. mentagrophytes* and *M. canis* were found by subculturing each fungal suspension on potato dextrose agar. According to the results, heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) were found to be more effective against dermatophyte *M. canis* (MIC = 3.12–25 µg/ml) than *T. mentagrophytes* (MIC = 12.5–100 µg/ml). Our findings showed that 7–membered heterocyclic organoboron compounds (3a–m) (MIC = 12.5–50 µg/ml) have stronger in vitro antifungal activity against *T. mentagrophytes* than 5–membered heterocyclic organoboron compounds (1a–o, 2a–j) (MIC = 25–100 µg/ml). The MFC values for all compounds ranged from 6.25 to 200 µg/ml. The limited number of systemic antifungal agents used in the treatment of dermatophyte infections and the presence of side effects have led to the search for new treatment resources in recent years. Therefore, investigation of the effect of heterocyclic organoboron compounds against dermatophytes will be promising for the discovery of new antifungal compounds that have gained great importance today.

Keywords Antifungal activity · Dermatophyte · MFC · MIC · *Microsporum canis* · Organoboron compounds · *Trichophyton mentagrophytes*

Introduction

Dermatophytoses are superficial fungal infections caused by dermatophytes that multiply in hot, humid, and unhygienic environments and affect structures such as skin, hair, and nails. The dermatophyte species commonly seen in cats and dogs is primarily *Microsporum canis* (*M. canis*), but also carrier of other species such as *M. nanum*, *M. gypseum*, *Trichophyton mentagrophytes* (*T. mentagrophytes*), and *T. terrestre*. Dermatophytoses cause fungal lesions on the skin and head area, infecting people in contact with contaminated environments and animals. Dermatophytoses are seen in both humans and animals globally [1, 2].

Zoophilic species benefit by infecting keratin-rich tissues in the human or animal host. Humans can become infected with zoophilic species through direct contact [3–6]. When dermatophytes infect humans, they colonize the keratinized outermost layer of the skin, and usually do not invade the living tissue [7–9].

Treatment of dermatomycosis is delayed by the patient owners due to their long duration and expensiveness, which leads to new searches for treatment. Few antifungal agents are available and licenced for use in veterinary practice, and the use of systemic drugs is limited in livestock due to the problems of residues in products intended for human consumption [10]. Systemic antifungal drugs used in animals with dermatophytosis include griseofulvin, itraconazole, and

Responsible Editor: Rosana Puccia

✉ Fatma Budak
fatmabudak2@gmail.com

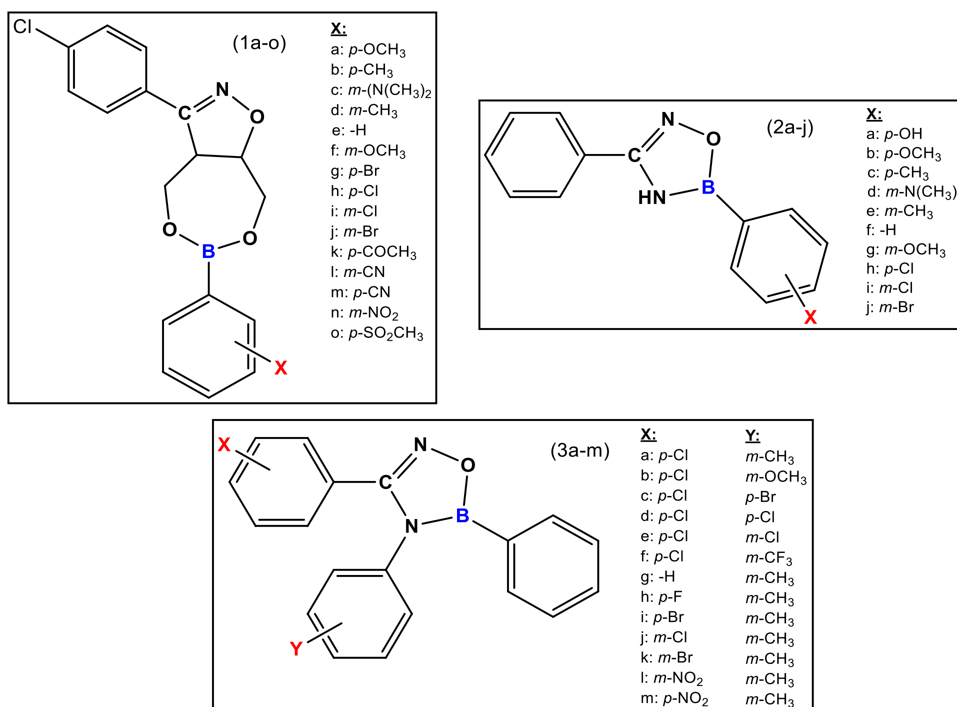
[1] Chemistry and Chemical Processing Technology, Kocaeli Vocational School, Kocaeli University, Kocaeli, Turkey

[2] Department of Microbiology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey

[3] Department of Microbiology, Faculty of Veterinary Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey

Published online: 13 June 2022

Scheme 1 Structures of tested compounds 6-substituted phenyl-3-(4-chlorophenyl)-3a,4,8,8a-tetrahydro-[1,3,2]dioxaborepino[5,6-d]isoxazoles (1a-o), 3,5-disubstituted 4,5-dihydro-1,2,4,5-oxadiazaboroles (2a–j), and 3,4,5-trisubstituted 4,5-dihydro-1,2,4,5-oxadiazaboroles (3a–m)



terbinafine [11]. In humans, dermatophytoses can be treated topically or systemically with azoles or allylamines. Since dermatophyte infections can be recurrent and chronic, they require long-term treatment with antifungal agents. Moreover, some widely used antifungal agents, such as terbinafine and azole-like compounds, have liver and cardiac side effects and drug–drug interactions that prevent the prolonged usages. Hence, fungal infections have an important cause of the decline in the quality of human living standards. New antifungal agents that selectively inhibit a single fungal species are urgently needed and will help to overcome the above problems. However, emerging resistance to current drugs highlights the importance of molecular studies of antifungal resistance, which may be valuable in curing the disease [8, 12–15].

The number of patients with clinically resistant dermatophytosis is increasing, indicating the increasing clinical importance of antifungal susceptibility testing (AFST) in situations where resistance is common [16]. The presence of natural or synthetic products among the new antifungal targets are seen as advances that facilitate the development of new strategies for antifungal therapy [17, 18]. In addition, with the development of technology in recent years, the latest technological innovations for the prevention of diseases are used by using smart clothes in the field of health. In this way, by combining drug therapy with technological devices and clothing, usable product design for treatment approaches that are thought to be more effective becomes a necessity. It is seen that there are many reactive fungal wearable product studies developed for this purpose [19–22].

When the antifungal studies on dermatophytes in the literature are examined, the following publications stand out: topical application of boric acid and ozonated olive oil [6], antifungal potential of ozone [23], antidermatophytic oxaborole-6-benzene sulphonamide [24], antifungal activity of some plants [25–27], antioxidant and antidermatophytic activities of essential oil and extracts [28–40], antifungal effect of silver nanoparticles [41], antifungal activity of gelatin-stabilized selenium oxide nanoparticles [42], antifungal activity of lichen compounds [43], and hormonal effects on fungal growth [44]. For this reason, heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m), which we synthesized in our previous studies [45–47], have given very good activity results, as new drug discovery researches are increasing.

Materials and methods

Antifungal agents and fungal strains

The structure of thirty-eight heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) with synthesis and analysis results are included in the literature [45–47] is shown in Scheme 1. 6-Substituted phenyl-3-(4-chlorophenyl)-3a,4,8,8a-tetrahydro-[1,3,2]dioxaborepino[5,6-d]isoxazoles (1a-o), 3,5-disubstituted 4,5-dihydro-1,2,4,5-oxadiazaboroles (2a–j), and 3,4,5-trisubstituted 4,5-dihydro-1,2,4,5-oxadiazaboroles (3a–m) were synthesized by reacting different starting materials and phenylboronic acid derivatives.

Compounds (1a–o, 2a–j, 3a–m) to be tested were dissolved in sterile 100% ethanol (Sigma) to obtain stock solution of 2000 µg/ml. The final desired concentration (1600 µg/ml) was prepared with RPMI 1640 medium for compounds (1a–o, 2a–j, 3a–m). The tested concentrations ranged from 1600 to 0.04 (1600, 800, 400, 200, 100, 50, 25, 12.5, 6.25, 3.12, 1.56, 0.78, 0.39, 0.19, 0.09, and 0.04) µg/ml. In the studied concentrations, ethanol did not effect the microorganisms.

The T. mentagrophytes (isolated from dog) and M. canis (isolated from cat) strains were clinical isolates obtained from skin and hair samples taken with the suspicion of cutaneous mycosis and kept in the Faculty of Veterinary Medicine, Department of Microbiology Culture Collection, Istanbul University–Cerrahpasa. Isolation and identification were done by conventional methods. At the time of testing, the isolates were subcultured twice to achieve exponential growth and to ensure purity.

C. albicans (ATCC 90,028) strain was used as a quality control.

Inoculum preparation and AFST

The broth microdilution (BMD) method was performed in accordance with the Clinical and Laboratory Standards Institute (CLSI) M38–A2 [48]. RPMI 1640 broth with L–glutamine without sodium bicarbonate was used. The medium was buffered to pH 7.0 at 25 °C with 0.165 M morpholinepropanesulfonic acid (MOPS) (Sigma). Preparation of inoculum suspensions of dermatophytes were based mainly to the CLSI guidelines [48] and the procedure in the literature [49]. The microdilution assay was performed in multiwell microdilution plates (sterile, disposable 96 U–shaped wells). Fluconazole (Sigma) was used as the control antimicotic (MIC = 2 µg/ml), which was also obtained from the manufacturer.

In our previous studies, we used *C. albicans* (ATCC 90,028) for antifungal activity [45–47]. The broth microdilution method was performed in accordance with the CLSI M27–A2 [50]. The MIC was defined as the lowest compound concentration that caused 100% inhibition of visible fungal growth. The MIC results for *C. albicans* (ATCC 90,028) obtained in our previous studies [45–47] are 50–100 µg/ml for (1a–o), 25–200 µg/ml for (2a–j), and 50–800 µg/ml for (3a–m).

Before antifungal susceptibility testing, *T. mentagrophytes* and *M. canis* were subcultured onto potato dextrose agar (PDA) plates were incubated at a temperature of 25 ± 1 °C for a period of 7–14 days. All tested strains grew well during this period. The fungal colonies were covered with ca. 10 ml of distilled sterile water, and suspensions were prepared by gently probing the surface with the tip of a Pasteur pipette. The resulting mixtures of conidia and hyphal fragments were withdrawn and transferred to a sterile tube. They were incubated at room temperature for 30 min to precipitate heavy particles and the upper homogeneous suspensions were collected and mixed with a vortex mixer for 15 s (Fig. 1). The density of these suspensions was adjusted with a spectrophotometer at a wavelength of 530 nm to obtain inoculum quantification (65 to 75% T). These stock suspensions were diluted 1:50 in RPMI 1640 medium to obtain the final inoculum size, which range from 0.4×10^4 to 5×10^4 CFU/ml (colony forming unit). For susceptibility tests, 100 µl of each organoboron compounds (1a–o, 2a–j, 3a–m) solutions was added in microdilution plates containing 100 µl of RPMI 1640 medium buffered to pH 7.0 with 0.165 M MOPS; then, microdilution plates were inoculated with 100 µl of the previously obtained inocula. Microdilution plates were incubated at 25 ± 1 °C for a period of 7–14 days and were examined daily for the presence of fungal colonies. MICs corresponded to the lowest concentration that showed 100% growth inhibition which is determined with the naked eye (Table 1). All tests were performed in duplicate.

The minimum fungicidal concentrations (MFCs) of the compounds were obtained by a subculture of 100 µl from minimum inhibitory concentration (MIC-2) wells, without visible growth, placed in Petri dishes containing potato dextrose agar medium [15]. MFC values represent the lowest concentration of compound that produces a 99.9% end point reduction (Table 1).

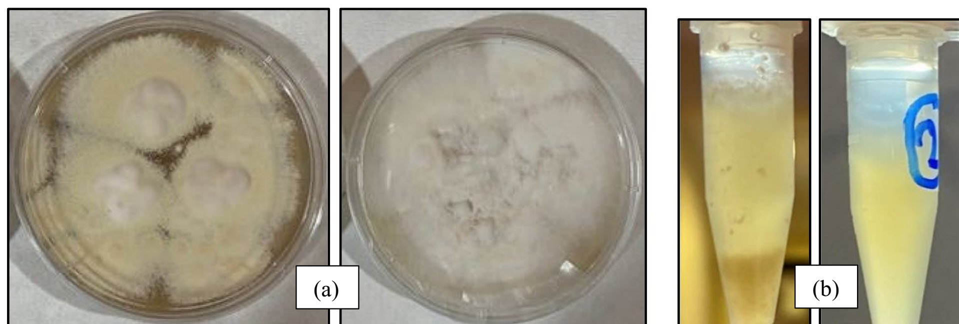


Fig. 1 a Fungal colonies (left T. mentagrophytes, right M. canis) were poured with sterile distilled water and gently examined with the tip of a Pasteur pipette, b first and final preparation of fungal colonies in the sterile tube

Table 1 In vitro antifungal activity data of compounds (1a–o, 2a–j, 3a–m)

Compounds substituents: X, Y, and control	Fungi isolates/antifungal activity — MIC and MFC values in µg/ml					
	T. mentagrophytes			*M. canis*		
	MIC–0	MIC–2	MFC	MIC–0	MIC–2	MFC
1a *p*-OCH_3	50	50	100	12.5	25	50
1b *p*-CH_3	50	50	100	12.5	25	50
1c *m*-$(N(CH_3)_2$	50	50	100	25	25	50
1d *m*-CH_3	50	50	100	25	25	50
1e -H	50	50	100	12.5	25	50
1f *m*-OCH_3	50	50	100	25	25	50
1 g *p*-Br	25	25	50	6.25	6.25	12.5
1 h *p*-Cl	25	25	50	6.25	6.25	12.5
1i *m*-Cl	12.5	25	50	6.25	6.25	12.5
1j *m*-Br	12.5	25	50	3.12	6.25	12.5
1 k *p*-$COCH_3$	25	50	100	12.5	12.5	25
1 l m-CN	25	25	50	3.12	3.12	6.25
1 m *p*-CN	25	25	50	12.5	12.5	25
1n *m*-NO_2	25	25	50	12.5	12.5	25
1o *p*-SO_2CH_3	25	50	100	12.5	25	50
2a *p*-OH	50	100	200	12.5	12.5	25
2b *p*-OCH_3	50	100	200	12.5	12.5	25
2c *p*-CH_3	25	25	50	25	25	50
2d *m*–$N(CH_3)_2$	25	50	100	25	25	50
2e *m*-CH_3	50	100	200	25	25	50
2f -H	50	100	200	12.5	12.5	25
2 g m-OCH_3	25	50	100	12.5	12.5	25
2 h *p*-Cl	25	25	50	6.25	6.25	12.5
2i *m*-Cl	25	25	50	6.25	6.25	12.5
2j *m*-Br	25	25	50	25	25	50
3a *p*-Cl, *m*-CH_3	12.5	12.5	25	6.25	12.5	25
3b *p*-Cl, *m*-OCH_3	25	25	50	12.5	12.5	25
3c *p*-Cl, *p*-Br	50	50	100	12.5	12.5	25
3d *p*-Cl, *p*-Cl	50	50	100	6.25	6.25	12.5
3e *p*-Cl, *m*-Cl	6.25	12.5	25	6.25	6.25	12.5
3f *p*-Cl, *m*-CF_3	12.5	25	50	6.25	6.25	12.5
3 g -H, *m*-CH_3	25	25	50	12.5	25	50
3 h *p*-F, *m*-CH_3	25	25	50	25	25	50
3i *p*-Br, *m*-CH_3	6.25	12.5	25	6.25	12.5	25
3j *m*-Cl, *m*-CH_3	12.5	12.5	25	12.5	12.5	25
3 k m-Br, *m*-CH_3	6.25	12.5	25	12.5	12.5	25
3 l m-NO_2, *m*-CH_3	25	50	100	25	25	50
3 m *p*-NO_2, *m*-CH_3	25	25	50	25	25	50
P	+	+		+	+	

P, positive control (just medium, RPMI 1640); fluconazole as the negative control agent (standard drug; MIC = 2 µg/ml)

Best MIC results are indicated with bold font

Results and discussion

The *T. mentagrophytes* and *M. canis* isolates were isolated from skin and hair samples taken from cats and dogs with hair loss, skin crusting, and redness. Healthy animals also carry this factor without showing any symptoms. It also poses a risk to humans as it is zoonotic.

Our previous studies with heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) have shown their antifungal

activity against *C. albicans* with MIC ranged from 25 to 800 µg/ml [45–47].

The heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) have been tested for their antifungal effects against two pathogenic fungi in this study. The antifungal activity results of all the compounds (1a–o, 2a–j, 3a–m) are given in Table 1. The results were compared with the standard drug, fluconazole.

The microplates were incubated at 25 ± 1 °C and were read at 7 days and 14 days of incubation. The MICs were determined by visual inspection of the macroscopic growth inhibition of each well compared with that of the growth control (drug–free) well. Two MIC end points were determined for each isolate. The wells were given a numerical score as follows: (i) 0, 100% inhibition of growth (at 7 days) (designated MIC–0); and (ii) 2, 100% inhibition of growth (at 14 days) (designated MIC–2). For *T. mentagrophytes*: (i) MIC–0: 6.25–50 µg/ml and (ii) MIC–2: 12.5–100 µg/ml and for *M. canis*: (i) MIC–0: 3.12–25 µg/ml and (ii) MIC–2: 3.12–25 µg/ml, respectively. The values given in Table 1 (in other words MIC–2) were accepted as the final MIC values of compounds (1a–o, 2a–j, 3a–m).

As can be seen from Table 1, all heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) showed antifungal effect, ranging from very good to moderate, with minimum inhibitory concentrations of 3.12–100 µg/ml. According to all microbial results, compound (1 l) has the best activity with MIC value of 3.12 µg/ml to *M. canis*. The second best activity belongs to compounds (1 g, 1 h, 1i, 1j, 2 h 2i, 3d, 3e, and 3f) with the MIC value of 6.25 µg/ml on the same dermatophyte. When these MIC results are compared with the standard drug fluconazole (MIC = 2 µg/ml), it can be seen that a very good antifungal value with MIC = 3.12 µg/ml is obtained especially for compound (1 l) against *M. canis*.

Compound (1 l) has the MIC value of 25 µg/ml to *T. mentagrophytes*. As can be seen from Table 1, the best effect is the 12.5 µg/ml with compounds (3a, 3e, 3i, 3j, and 3 k) to *T. mentagrophytes*. The other compounds have a moderate effect on the fungi, i.e., 25, 50, and 100 µg/ml. 7–Membered heterocyclic organoboron compounds (3a–m) are found to be more effective against *T. mentagrophytes* with MIC values of 12.5–50 µg/ml.

Table 1 shows the MFCs of heterocyclic organoboron compounds (1a–o, 2a–j, 3a–m) against *T. mentagrophytes* and *M. canis*. All the tested compounds showed MIC and MFC values, which support their antifungal activity against fungi. The MFC values varied from 6.25 to 200 µg/ml. The results obtained are important in combating fungal diseases, especially those caused by the fungus *T.mentagrophytes*, which are difficult to treat and are increasing in prevalence worldwide.

Studies on the chemistry of boron atom containing compounds have gained even greater importance today, with the demonstration of its biological properties, such as inhibitors of dipeptidyl peptidase IV (DPP IV), anticoagulants, and inhibitors of thrombin, potent hypolipemic agents, boron neutron capture therapy (BNCT) agents, anticancer agents, antibacterial agents, antiviral agents, and antiparasitic agents [51, 52]. In this study, it was concluded that the organoboron compounds (1a–o, 2a–j, 3a–m) that we synthesized may have an important place in antifungal activity. When the studies on dermatophytes were examined, it was seen that there were no studies on heterocyclic boron compounds, but mostly on thiophene derivative, quinolines derivatives, essential oil, and chitosan nanoparticles [53–58].

Conclusion

This paper is the first presented study to investigate the in vitro antifungal effects of organoboron compounds against dermatophytes. The results showed that heterocyclic organoboron compounds have in vitro antifungal activity against *T. mentagrophytes* and *M. canis*. Therefore, further studies should be carried out to confirm the usefulness of these organoboron derivatives in vivo. Thus, it can be concluded that organoboron compounds could be used as a new antidermatophytic agents to control superficial human fungal infections. Boron compounds, which we think will have an important effect in antifungal therapy, will be derivatized in future studies and new compound syntheses will be made.

Complementary investigations should be conducted to evaluate the efficacy of these compounds on more clinical isolates per fungal species. We believe that by performing toxicity tests, the antifungal effects of compounds can be indicated with more reliable results. This will reveal more precisely whether the compounds will be used in therapy in the future.

Funding This work was supported by Kocaeli University Scientific Research Projects Coordination Unit. Project Number: FHD–2021–2437.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Hanedan B, Bilgili A, Uysal MH (2021) Health risks that fungal infections of skin in cats and dogs cause in humans, control and treatment choices. Icontech International Journal 5(2):10–17. https://doi.org/10.46291/ICONTECHvol5iss2pp10-17
2. Gräser Y, Monod M, Bouchara JP, Dukik K, Nenoff P, Kargl A, Kupsch C, Zhan P, Packeu A, Chaturvedi V, Hoog S (2018)

New insights in dermatophyte research. Med Mycol 56(1):2–9. https://doi.org/10.1093/mmy/myx141

3. Mignon B, Monod M (2011) Zoonotic infections with dermatophyte fungi. Clinical Practice and Public Health Control, Oxford Textbook of Zoonoses-Biology
4. Baumgardner DJ (2017) Fungal infections from human and animal contact. J Patient Cent Res Rev 4(2):78–89. https://doi.org/10.17294/2330-0698.1418
5. Iorio R, Cafarchia C, Capelli G, Fasciocco D, Otranto D, Giangaspero A (2007) Dermatophytoses in cats and humans in central Italy: epidemiological aspects. Mycoses 50(6):491–495. https://doi.org/10.1111/j.1439-0507.2007.01385.x
6. Gezer AH, Acar A (2020) Effects of boron compounds and ozonated olive oil on experimental Microsporum canis infection in rats. Turk J Vet Anim Sci 44:258–265. https://doi.org/10.3906/vet-1910-51
7. Ferguson L, Fuller LC (2017) Spectrum and burden of dermatophytes in children. J Infect 74(1):54–60. https://doi.org/10.1016/S0163-4453(17)30192-5
8. Martinez-Rossi NM, Peres NTA, Rossi A (2008) Antifungal resistance mechanisms in dermatophytes. Mycopathologia 166:369–383. https://doi.org/10.1007/s11046-008-9110-7
9. Hayette MP, Sacheli R (2015) Dermatophytosis, trends in epidemiology and diagnostic approach. Curr Fung Infect Rep 9(3):164–179. https://doi.org/10.1007/s12281-015-0231-4
10. Chermette R, Ferreiro L, Guillot J (2008) Dermatophytoses in animals. Mycopathologia 166:385–405. https://doi.org/10.1007/s11046-008-9102-7
11. Moriello KA (2004) Treatment of dermatophytosis in dogs and cats: review of published studies. Vet Dermatol 15(2):99–107. https://doi.org/10.1111/j.1365-3164.2004.00361.x
12. Gupta AK, Foley KA, Versteeg SG (2017) New antifungal agents and new formulations against dermatophytes. Mycopathologia 182(1–2):127–141. https://doi.org/10.1007/s11046-016-0045-0
13. Elewski BE (1998) Onychomycosis: pathogenesis, diagnosis, and management. Clin Microbiol Rev 11(3):415–429. https://doi.org/10.1128/CMR.11.3.415
14. Bao Y, Wan Z, Li R (2013) In vitro antifungal activity of Micafungin and Caspofungin against dermatophytes isolated from China. Mycopathologia 175:141–145. https://doi.org/10.1007/s11046-012-9571-6
15. Yamaguchi MU, Silva APB, Ueda-Nakamura T, Filho BPD, Silva CC, Nakamura CV (2009) Effects of a thiosemicarbazide camphene derivative on Trichophyton mentagrophytes. Molecules 14(5):1796–1807. https://doi.org/10.3390/molecules14051796
16. Dogra S, Shaw D, Rudramurthy SM (2019) Antifungal drug susceptibility testing of dermatophytes: laboratory findings to clinical implications. Indian Dermatol Online J 10(3):225–233. https://doi.org/10.4103/idoj.IDOJ_146_19
17. Noguchi H, Matsumoto T, Hiruma M, Kimura U, Kano R, Yaguchi T, Fukushima S, Ihn H (2019) Tineaunguium caused by terbinafine-resistant Trichophyton rubrum successfully treated with fosravuconazole. J Dermatol 46(12):e446–e447. https://doi.org/10.1111/1346-8138.15033
18. Negri M, Salci TP, Shinobu-Mesquita CS, Capoci IR, Svidzinski TI, Kioshima ES (2014) Early state research on antifungal natural products. Molecules 19:2925–2956. https://doi.org/10.3390/molecules19032925
19. Adamatzky A, Nikolaidou A, Gandia A, Chiolerio A, Dehshibi MM (2021) Reactive fungal wearable. BioSystems 199:104304. https://doi.org/10.1016/j.biosystems.2020.104304
20. Wang L, Lou Z, Jiang K, Shen G (2019) Bio-multifunctional smart wearable sensors for medical devices. Advanced Intelligent Systems 1(5):1900040. https://doi.org/10.1002/aisy.201900040
21. Mondal S, Zehra N, Choudhury A, Iyer PK (2021) Wearable sensing devices for point of care diagnostics. ACS Appl Bio Mater 4(1):47–70. https://doi.org/10.1021/acsabm.0c00798
22. Mohankumar P, Ajayan J, Mohanraj T, Yasodharan R (2021) Recent developments in biosensors for healthcare and biomedical applications: a review. Measurement 167:108293. https://doi.org/10.1016/j.measurement.2020.108293
23. Ouf SA, Moussa TA, Abd-Elmegeed AM, Eltahlawy SR (2016) Antifungal potential of ozone against some dermatophytes. Braz J Microbiol 47(3):697–702. https://doi.org/10.1016/j.bjm.2016.04.014
24. Abdel-Shafi S, Al-Mohammadi A, Almanaa TN, Moustafa AH, Saad TMM, Ghonemey A, Anacarso I, Enan G, El-Gazzar N (2020) Identification and testing of antidermatophytic oxaborole-6-benzene sulphonamide derivative (OXBS) from Streptomyces atrovirens KM192347 isolated from soil. Antibiotics 9(4):176. https://doi.org/10.3390/antibiotics9040176
25. Asgarpanah J, Hashemi SJ, Hashemi E, Askari K (2017) *In vitro* antifungal activity of some traditional Persian medicinal plants on pathogenic fungi. Chin J Integr Med 23(6):433–437. https://doi.org/10.1007/s11655-015-2181-7
26. Ye L, Lin P, Du W, Wang Y, Tang C, Shen Z (2018) Preparation, antidermatophyte activity and mechanism of methylphloroglucinol derivatives. Front Microbiol 9:2262. https://doi.org/10.3389/fmicb.2018.02262
27. Mousavi SAA, Kazemi A (2015) *In vitro* and *in vivo* antidermatophytic activities of some Iranian medicinal plants. Med Mycol 53(8):852–859. https://doi.org/10.1093/mmy/myv032
28. Bajpai VK, Yoon JI, Kang SC (2009) Antioxidant and antidermatophytic activities of essential oil *and extracts of Metasequoia glyptostroboides Miki ex* Hu. Food Chem Tox 47(6):1355–1361. https://doi.org/10.1016/j.fct.2009.03.011
29. Rezgui M, Majdoub N, Mabrouk B, Baldisserotto A, Bino A, Ben Kaab LB, Manfredini S (2020) Antioxidant and antifungal activities of marrubiin, extracts and essential oil from *Marrubium vulgare* L. against pathogenic dermatophyte strains. J Mycologie Medicale 30(1):100927. https://doi.org/10.1016/j.mycmed.2020.100927
30. Khayyat S, Al-Kattan M, Basudan N (2018) Phytochemical screening and antidermatophytic activity of lavender essential oil from Saudi Arabia. Int J Pharmacol 14(6):802–810. https://doi.org/10.3923/ijp.2018.802.810
31. Trifan A, Bostănaru AC, Luca SV, Grădinaru AC, Jităreanu A, Aprotosoaie AC, Miron A, Cioancă O, Hăncianu M, Ochiuz L, Bujor A, Aelenei P, Mareș M (2020) Antifungal potential of *Pimpinella anisum, Carum carvi* and *Coriandrum sativum* extracts. A comparative study with focus on the phenolic composition. Farmacia 68(1):22–27. https://doi.org/10.31925/farmacia.2020.1.4
32. Choi KD, Kim HY, Shin IS (2017) Antifungal activity of isothiocyanates extracted from horseradish (*Armoracia rusticana*) root against pathogenic dermal fungi. Food Sci Biotechnol 26(3):847–852. https://doi.org/10.1007/s10068-017-0104-4
33. Sharma M, Tiwari M (2012) A study of dermatophytes in dogs and *in vitro* response of *Psoralea corylifolia* essential oil. Jeobp 15(3):445–453. https://doi.org/10.1080/0972060X.2012.10644071
34. Bajpai VK, Yoon JI, Kang SC (2009) Antifungal potential of essential oil and various organic extracts of *Nandina domestica* Thunb. against skin infectious fungal pathogens. Appl Microbiol Biotechnol 83:1127–1133. https://doi.org/10.1007/s00253-009-2017-5
35. Soković M, Ristić M, Grubišić D (2004) Chemical composition and antifungal activity of the essential oil from *Juniperus excelsa* berries. Pharm Biol 42(4–5):328–331. https://doi.org/10.1080/13880200490511936

36. Patra M, Shahi SK, Midgely G, Dikshit A (2002) Utilization of essential oil as natural antifungal against nail-infective fungi. Flavour Fragr J 17(2):91–94. https://doi.org/10.1002/ffj.1049
37. Noorkorina TKT, Ab Aziz FM, Alojid AAM, Ahmad NN, Salmuna ZN, Asma Hassan S, Hashim S, Harun A (2021) Antifungal effects and phytochemical screening of *Andrographis paniculate* extracts on dermatomycoses. Malays J Microbiol 17(5):576–587. https://doi.org/10.21161/mjm.211144
38. Tiwari N, Pandit R, Gaikwad S, Gade A, Rai M (2017) Biosynthesis of zinc oxide nanoparticles by petals extract of *Rosa indica* L., its formulation as nail paint and evaluation of antifungal activity against fungi causing onychomycosis. IET Nanobiotechnol 11(2):205–211. https://doi.org/10.1049/iet-nbt.2016.0003
39. Najar B, Mecacci G, Nardi V, Cervelli C, Nardoni S, Mancianti F, Ebani VV, Giannecchini S, Pistelli L (2021) Volatiles and antifungal-antibacterial-antiviral activity of South African *Salvia* spp. essential oils cultivated in uniform conditions. Molecules 26(9):2826. https://doi.org/10.3390/molecules26092826
40. Foss SR, Nakamura CV, Ueda-Nakamura T, Cortez DAG, Endo EH, Filho BPD (2014) Antifungal activity of pomegranate peel extract and isolated compound punicalagin against dermatophytes. Ann Clin Microbiol Antimicrob 13:32. https://doi.org/10.1186/s12941-014-0032-6
41. Mousavi SAA, Salari S, Hadizadeh S (2015) Evaluation of antifungal effect of silver nanoparticles against *Microsporum canis*, *Trichophyton mentagrophytes* and *Microsporum gypseum.* Iran J Biotech 13(4):e1302. https://doi.org/10.15171/ijb.1302
42. Kazemi M, Akbari A, Zarrinfar H, Soleimanpour S, Sabouri Z, Khatami M, Darroudi M (2020) Evaluation of antifungal and photocatalytic activities of gelatin-stabilized selenium oxide nanoparticles. J Inorg Organomet Polym 30:3036–3044. https://doi.org/10.1007/s10904-020-01462-4
43. Furmanek L, Czarnota P, Seaward MRD (2019) Antifungal activity of lichen compounds against dermatophytes: a review. J Appl Microbiol 127(2):308–325. https://doi.org/10.1111/jam.14209
44. Brasch J, Flader S (1996) Human androgenic steroids affect growth of dermatophytes *in vitro*. Mycoses 39:387–392
45. Pir M, Agirbas H, Budak F, Sahin O (2017) Synthesis, characterization, antimicrobial activity and QSAR studies of some new 6-substituted phenyl 3-(4-chlorophenyl)-3a,4,8,8a-tetrahydro-[1,3,2]dioxaborepino[5,6-d]isoxazoles. Heteroatom Chem 28(2):e21363. https://doi.org/10.1002/hc.21363
46. Pir M, Agirbas H, Budak F, Ilter M (2016) Synthesis, characterization, antimicrobial activity, and QSAR studies on substituted oxadiazaboroles. Med Chem Res 25(9):1794–1812. https://doi.org/10.1007/s00044-016-1603-1
47. Pir M (2021) Synthesis of some dioxaborepine derivatives and determination of antimicrobial activity. DEUFMD 23(68):501–507. https://doi.org/10.21205/deufmd.2021236813
48. Clinical and Laboratory Standards Institute (CLSI) (2008) Reference method for broth dilution antifungal susceptibility testing of filamentous fungi: approved standard. 2nd ed. M38-A2. Vol 28, No. 16, Wayne, PA, USA.
49. Fernandez-Torres B, Cabanes FJ, Carillo-Munoz AJ, Esteban A, Inza I, Abarca L, Guarro J (2002) Collaborative evaluation of optimal antifungal susceptibility testing conditions for dermatophytes. J Clin Microbiol 40(11):3999–4003. https://doi.org/10.1128/JCM.40.11.3999-4003.2002
50. Clinical and Laboratory Standarts Institute (CLSI) (2002) Reference method for broth dilution antifungal susceptibility testing of yeast: approved standard. 2nd ed. M27-A2. Wayne, PA, USA.
51. Benderdour M, Bui-van T, Dicko A, Belleville F (1998) *In vivo* and *in vitro* effects of boron and boronated compounds. J Trace Elements Med Biol 12:2–7
52. Song S, Gao P, Sun L, Kang D, Kongsted J, Poongavanam V, Zhan P, Liu X (2021) Recent developments in the medicinal chemistry of single boron atom-containing compounds. Acta Pharmaceutica Sinica B 11(10):3035–3059. https://doi.org/10.1016/j.apsb.2021.01.010
53. Neves WW, Neves RP, Macedo DPC, Eleamen GRA, Kretzschmar EAM, Oliveira EE, Mendonça-Junior FJB, Lima-Neto RG (2020) Incorporation of 2-amino-thiophene derivative in nanoparticles: enhancement of antifungal activity. Braz J Microbiol 51:647–655. https://doi.org/10.1007/s42770-020-00248-7
54. Machado GRM, Diedrich D, Ruaro TC, Zimmer AR, Teixeira ML, Oliveira LF, Jean M, Weghe PV, Andrade SF, Gnoatto SCB, Fuentefria AM (2020) Quinolines derivatives as promising new antifungal candidates for the treatment of candidiasis and dermatophytosis. Braz J Microbiol 51:1691–1701. https://doi.org/10.1007/s42770-020-00348-4
55. Silva LC, Miranda MACM, Freitas JV, Ferreira SFA, Lima ECO, Oliveira CMA, Kato L, Soares CMA, Pereira M (2020) Antifungal activity of Copaíba resin oil in solution and nanoemulsion against *Paracoccidioides* spp. Braz J Microbiol 51:125–134. https://doi.org/10.1007/s42770-019-00201-3
56. Araujo DE, Oliveira AA, Cabral MS, CostanAF SBC, Silva LC, Menezes LB, Soares CMA, Amaral AC, Pereira M (2020) Investigation of thiosemicarbazide free or within chitosan nanoparticles in a murine model of vulvovaginal candidiasis. Braz J Microbiol 51:1465–1473. https://doi.org/10.1007/s42770-020-00326-w
57. Pereira FO (2021) A review of recent research on antifungal agents against dermatophyte biofilms. Med Mycol 59:313–326. https://doi.org/10.1093/mmy/myaa114
58. Junior FAS, Brilhante RSN, Cordeiro RA, Brito EHS, Sidrim JJC, Rocha MFG (2007) Glucose improves the in vitro viability of Microsporum canis and Trichophyton mentagrophytes var. Mentagrophytes J Microbiol Methods 69:218–221. https://doi.org/10.1016/j.mimet.2006.12.014

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.