GSC Advanced Research and Reviews
eISSN: 2582-4597 CODEN (USA): GARRC2
Cross Ref DOI: 10.30574/gscarr
Journal homepage: https://gsconlinepress.com/journals/gscarr/

(RESEARCH ARTICLE)

# Design, synthesis, and anticandidal evaluation of benzimidazole and imidazopyridine-based *N*-Acylhydrazones

Tchambaga Etienne CAMARA [1], Songuigama COULIBALY [2], Patrick-Armand ACHI [1, 3], Evrard ABLO [1, 3], Souleymane COULIBALY [1, *] and COULIBALI Siomenan [1]

[1] *Laboratory of Constitution and Reaction of Matter, UFR Sciences of the Structures of Matter and Technology, Félix Houphouët-Boigny University, Abidjan, Ivory Coast, 22 BP 582 Abidjan 22.*
[2] *Department of Therapeutic Chemistry and Organic Chemistry, UFR Pharmaceutical and Biological Sciences, FHB University, 01 BP V34 Abidjan, Côte d'Ivoire.*
[3] *Institute National Polytechnique Félix Houphouët-Boigny, Yamoussoukro, Ivory Coast.*

GSC Advanced Research and Reviews, 2025, 24(02), 213-223

Publication history: Received on 05 July 2025; revised on 16 August 2025; accepted on 19 August 2025

Article DOI: https://doi.org/10.30574/gscarr.2025.24.2.0240

## Abstract

A novel series of benzimidazole and imidazo[1,2-a]pyridine-based *N*-acylhydrazones was designed, synthesized, and evaluated for antifungal activity against a clinical strain of *Candida albicans*. Structural elucidation was performed using $^{1}H$ and $^{13}C$ NMR spectroscopy and High-Resolution Mass Spectrometry (HRMS). *In vitro* antifungal testing revealed that several compounds exhibited moderate to strong anticandidal activity, with minimum inhibitory concentrations (MICs) ranging from 26.009 µM to 70.034 µM, compared to fluconazole as the reference drug. Structure–activity relationship (SAR) analysis demonstrated that lipophilic aryl substituents, particularly naphthalen-2-ol and aryl sulfane moieties, play a key role in enhancing antifungal efficacy, likely by promoting membrane permeability through increased hydrophobic interactions. Notably, compound **6a**, bearing a naphthalen-2-ol fragment, emerged as the most potent derivative. The results highlight the promising potential of *N*-acylhydrazone scaffolds, particularly those integrating sulfur-containing or polycyclic aromatic groups, as leads for the development of new antifungal agents targeting resistant *Candida albicans* strains.

**Keywords:** *N*-acylhydrazones; Benzimidazole; Imidazo[1,2-a]pyridine; Antifungal activity; *Candida albicans*

## 1. Introduction

Fungal infections remain a significant threat to human health, particularly among immunocompromised individuals. *Candida albicans* (*C. albicans*), a common fungal species in humans, is typically benign but can become pathogenic under certain conditions, leading to candidiasis [1]. It is the most frequent cause of fungemia worldwide and a leading opportunistic infection among individuals with HIV [2].

Although several antifungal therapies are available, treatment options remain limited to five major drug classes: allylamines, azoles, echinocandins, polyenes and pyrimidine analogs [3] [4] [5]. These treatments face growing challenges, including rising drug resistance undesirable side effects, and limited effectiveness against biofilm-associated infections [6] [7] [8]. Biofilms, which often develop on medical devices, significantly hinder treatment by creating barriers that conventional antifungal agents struggle to penetrate [9].

Despite antifungal treatment, *Candida* infections are associated with high mortality rates, sometimes reaching up to 40% [10] [11]. Particularly concerning is the increasing and spreading resistance to widely used antifungal agents such

* Corresponding author: Souleymane COULIBALY

as fluconazole and echinocandins [12] [13]. The declining efficacy of fluconazole, especially among AIDS patients [14], highlights the urgent need for novel antifungal agents. To address these limitations, recent research has focused on developing compounds and therapeutic strategies, including agents that can target both fungal cells and their biofilms, to meet these challenges [15]. Benzimidazole derivatives have demonstrated a wide range of pharmacological properties, including antifungal, antibacterial, antiviral and anticancer activities [16] [17] [18] [19] [20]. Similarly, imidazopyridines have shown important therapeutic potential, such as calcium antagonists [21], anticancer agents [22] [23], antifungals [24], anti-inflammatory and analgesic activity [25]. Additionally, phenylhydrazone-based molecules are known for their anti-infective and antifungal properties, and are present in drugs such as zinoconazole and other experimental compounds [26] [27]. The present study focuses on the design, synthesis and antifungal evaluation of benzimidazole and its isostere imidazopyridine-based N-acylhydrazones derivatives. These hybrid molecules were developed by combining the pharmacologically active cores of benzimidazole or imidazo[1,2-a]pyridine with the phenylhydrazone moiety, aiming to enhance their antifungal efficacy [28] [29]. By structurally integrating these bioactive fragments, this work seeks to develop new antifungal agents capable of overcoming the limitations of existing therapies. The study contributes to ongoing efforts to discover safer and more effective treatments for fungal infections, particularly those complicated by resistance and biofilm formation.

## 2. Materials and methods

### 2.1. Materials

#### *2.1.1. Chemistry Material*

All chemicals were purchased from Aldrich Chemical, Fischer Scientific (France), and were used without further purification unless otherwise stated. The reactions were followed by TLC on pre-coated Merck 60 F254 silica gel plates and revealed using a UV lamp (6 W, 254 nm, and/or 365 nm). The purification of the products was carried out on a Merck G60 silica gel column. Melting points (m.p., °C) were determined using a temperature gradient (40-265°C) Kofler bench. For all compounds, the Nuclear Magnetic Resonance (NMR) spectra of proton $^{1}H$ and carbon $^{13}C$ were recorded on a Brucker 300 or 400 advance device. Tetramethylsilane (TMS) was used as a reference for chemical displacements expressed in δ (ppm). The NMR spectra description uses the following symbols: s (singlet), d (doublet), dd (double doublet), t (triplet), q (quadruplet), m (multiplet). The mass spectra were recorded on a JEOL JMS DX300 spectrometer in ESI mode (electrospray/quadripolar ionization or ESI mass).

#### *2.1.2. Biological materials*

The antifungal activity of the synthesized compounds was evaluated using a clinical strain of *Candida albicans,* obtained from Angré University Hospital Center in Côte d'Ivoire. To assess the sensitivity of this strain, an antifungal susceptibility profile was established using the agar diffusion method [30], as illustrated in Figure 1.


**Figure 1** Antifungal susceptibility profile

A series of ten (10) benzimidazole or imidazopyridine–*N*-acylhydrazones derivatives were synthetized and evaluated for their antifungal activity.

## 2.2. Method

*2.2.1. Chemical Method*

Compounds **2** (sel d'isothiouronium-1*H*-benzimidazole, **3** (2-((benzylthio)methyl)-1*H*-benzimidazole), **4** (ethyl 2-(2-((benzylthio)methyl)-1*H*-benzo[d]imidazol-1-yl)acetate), **5** (2-(2-((benzylthio)methyl)-1*H*-benzimidazol-1-yl)acetohydrazide), **8** (2-(3-nitroimidazo[1,2-a]pyridin-2-yl)isothiouronium) **9** (ethyl 2-((3-nitroimidazo[1,2-a]pyridin-2-yl)thio)acetate) and **10** (3-nitroimidazo[1,2-a]pyridin-2-yl)thio)acetohydrazide) have already been reported [31,32].

**General procedure for the synthesis of *N*-acylhydrazones benzimidazoles (6a-f) or *N*-acylhydrazones imidazo[1,2-a]pyridine 11a-b**

In a 10 mL flask equipped with a magnetic stirrer, 2-(2-((benzylthio)methyl)-*1H*-benzimidazol-1-yl)acetohydrazide **5** (1eq, 1.123 mol) or 3-nitroimidazo[1,2-a]pyridin-2-yl)thio)acetohydrazide **10** (1eq, 1.23 mol) was dissolved in methanol. Benzaldehyde derivatives were added and two drops of concentrated hydrochloric acid (HCl). The reaction mixture was refluxed for one hour. After cooling to room temperature, the precipitate formed was filtered, dried and purified by silica column chromatography to give compounds **6** and **11**.

***(E)-2-(2-((benzylthio)methyl)-1H-benzimidazol-1-yl)-N-((3-hydroxynaphthalen-2-yl)methylene)acetohydrazide (11e)***

Yellow powder, yield= 80% m.p = 170-175°C, $^{1}$H NMR (300 MHz, DMSO-*d6*) δ (ppm) : 11.74 (ap+sp) (s, 1H, NH), 9.27 ap, 8.96 sp (s, 1H, CH=N), 8.85 (d, *J = 8.6 Hz*, 1H, $H_{Ar}$), 8.36 (ap+sp) (d, *J = 8.6 Hz*, 1H, $H_{Ar}$), 7.97 – 7.14 (m, 13H, $H_{Ar}$), 5.61sp, 5.21ap (s, 2H, N-$CH_2$), 4.03 ap (s, 25H), 3.98 sp (s, 2H, $CH_2$), 3.76 ap, 3.73 sp (s, 2H, $CH_2$). $^{13}$C NMR (75 MHz, DMSO-*d6)* δ (ppm) : 167.85 sp, 163.47 ap (C=O), 158.40, 157.41, 146.98, 143.81 ap, 142.43 sp (N=CH), 138.45, 133.42, 133.06, 131.97, 131.80, 129.56, 129.48, 128.82, 128.34, 127.37, 124.03, 122.90, 122.70, 122.29, 122.05, 121.74, 119.22, 110.78, 109.04, 45.54ap, 45,16sp ($CH_2$-N), 35.17, 27.14. HRMS(ESI): Calc for $C_{28}H_{24}N_4NaO_2S$ $(M+Na)^+$: 503.1222; Found: 503.1226.

**(E)-2-(2-((benzylthio)methyl)-1*H*-benzimidazol-1-yl)-*N*-(2-hydroxybenzylidene) acetohydrazide (6b)**

Beige powder, yield= 94% m.p = 186-188°C, $^{1}$H NMR (300 MHz, DMSO-*d6*) δ (ppm): 11.70 ap, 10.94 sp (s, 1H, NH), 10.09 (ap+sp) (s, 1H, OH), 8.48 ap, 8.38 sp (s, 1H, N=CH), 7.88 – 6.86 (ap+sp) (m, 13H, $H_{Ar}$), 5.51 sp, 5.15 ap (s, 2H, N-$CH_2$), 3.98 ap, 3.95 sp (s, 2H, $CH_2$), 3.74 ap, 3.72 sp (s, 2H, $CH_2$). $^{13}$C NMR (75 MHz, DMSO-*d6*) δ (ppm): 168.22 (C=O), 157.89, 156.89, 151.91, 148.00, 142.36 (N=CH), 141.97, 138.49, 132.04, 131.77, 129.55, 129.48, 128.83, 127.37, 122.66, 122.00, 120.61, 119.87, 119.10, 116.65, 110.85, 45.45, 35.19, 27.12. HRMS(ESI): *Calc for* $C_{24}H_{22}N_4NaO_2S$ $(M+Na)^+$: 453.1821; Found: 453.1822

**(E)-2-(2-((benzylthio)methyl)-*1H*-benzimidazol-1-yl)-*N*-(3-bromobenzylidene) acetohydrazide (6c)**

Beige powder, yield= 82% m.p.= 218-220°C, $^{1}$H NMR (300 MHz, DMSO-*d6*) δ (ppm) : 11.89 (ap+sp) (s, 1H, NH); 8.24 ap, 8.06 sp (s, 1H, CH=N); 7.78 (ap+sp) (d, *J = 7.8 Hz*, 2H, $H_{Ar}$); 7.68–7.59 (ap+sp) (m, 1H, $H_{Ar}$); 7.54–7.15 (ap+sp) (m, 10H, $H_{Ar}$); 5.56 sp, 5.13 ap (s, 2H, N-$CH_2$); 3.98 (ap+sp) (s, *2*H, $CH_2$); 3.74 ap, 3.71 sp (s, 2H, $CH_2$). $^{13}$C NMR (75 MHz, DMSO-*d6*) δ (ppm): 168.79 sp, 163.91 ap (C=O), 151.99, 142.84, 142.39 (N=CH), 138.49, 136.97, 136.86, 133.05, 131.43, 129.49, 128.82, 127.38, 126.87, 122.75, 122.66, 122.02, 119.17, 110.86, 45.08, 35.19, 27.13. HRMS(ESI): Calc for $C_{24}H_{21Br}N_4NaOS$ $(M+Na)^+$: 515.0628; Found: 515.0619

**(E)-2-(2-((benzylthio)methyl)-1*H*-benzimidazol-1-yl)-*N*-(4-nitrobenzylidene)acetohydrazide (6d)**

Yellow powder, yield= 90% m.p. = 224-226°C, $^{1}$H NMR (300 MHz, DMSO-*d6*) δ (ppm) : 8.38 ap, 8.19 sp (s, 1H, N=CH), 8.33 (ap+sp) (d, *J = 8.7 Hz*, 2H, $H_{Ar}$), 8.07 (ap+sp) (d, *J = 8.7 Hz*, 2H, $H_{Ar}$), 7.99 (ap+sp) (d, *J = 8.7 Hz*, 1H, $H_{Ar}$), 7.69 – 7.61 (ap+sp) (m, 1H, $H_{Ar}$), 7.56 – 7.47 (ap+sp) (m, 1H, $H_{Ar}$), 7.44 – 7.16 (ap+sp) (m, 6H, $H_{Ar}$), 5.59 sp, 5.16 ap (s, 2H, N-$CH_2$), 3.97 (ap+sp) (s, 2H, $CH_2$), 3.74 ap (s, 2H, $CH_2$), 3.71 sp (s, 2H, $CH_2$). $^{13}$C NMR (75 MHz, DMSO-*d6*) δ (ppm): 169.05 (C=O), 152.00, 148.33, 145.56, 142.38 (N=CH), 142.17, 140.80, 138.48, 136.85, 129.49, 128.83, 128.47, 127.39, 124.51, 122.75, 122.05, 119.21, 110.81, 45.06, 35.17, 27.10. HRMS (ESI): Calc for $C_{24}H_{21}N_5NaO_3S$ $(M+Na)^+$: 482.1123; Found: 482.1128

**(E)-*N*-(4-(benzylthio)benzylidene)-2-(2-((benzylthio)methyl)-1*H*-benzimidazol-1-yl)acetohydrazide (6e)**

Khaki powder, yield= 82% m.p. = 178-180°C, $^{1}$H NMR (300 MHz, DMSO-*d6*) δ (ppm) : 11.87 ap, 11.77 sp (s, 1H, NH), 8.24 ap, 8.05 sp (s, 1H, CH=N), 7.68 (ap+sp) (d, *J* = 8.8 Hz, 3H, $H_{Ar}$), 7.59 – 7.13 (ap+sp) (m, 15H, $H_{Ar}$), 5.54 sp, 5.13 ap (s, 2H, N-$CH_2$), 4.33 (ap+sp) (s, 2H, $CH_2$), 3.98 (ap+sp) (s, 2H, $CH_2$), 3.76 ap, 3.73 sp (s, 2H, $CH_2$). $^{13}$C NMR (75 MHz, DMSO-*d6*) δ (ppm) : 168.49 sp (C=O); 152.00; 144.04 ap; 142.42 sp (CH=N); 139.43; 138.48; 137.65; 136.87; 131.80; 129.50; 129.31; 128.92; 128.84; 128.15; 128.03; 127.93; 127.65; 127.39; 122.70; 122.04; 119.20; 110.81; 45.00; 36.48; 35.24; 27.15. HRMS (ESI) **:** Calc for $C_{31}H_{28}N_4NaOS_2$ $(M+Na)^+$ : 559.1943 ; Found : 559.1946

**(E)-2-(2-((benzylthio)methyl)-1H-benzimidazol-1-yl)-N-((2-hydroxynaphthalen-2 yl)methylene)acetohydrazide (6f)**

Yellow powder, yield= 80% m.p. = 170-175°C, $^{1}$H NMR (300 MHz, DMSO-*d6*) δ (ppm) : 11.74 (ap+sp) (s, 1H, NH), 9.27 ap, 8.96 sp (s, 1H, CH=N), 8.85 (d, *J = 8.6 Hz*, 1H, $H_{Ar}$), 8.36 (ap+sp) (d, *J = 8.6 Hz*, 1H, $H_{Ar}$), 7.97 – 7.14 (m, 13H, $H_{Ar}$), 5.61 sp, 5.21 ap (s, 2H, N-$CH_2$), 4.03 ap (s, 25H), 3.98 sp (s, 2H, $CH_2$), 3.76 ap, 3.73 sp (s, 2H, $CH_2$). $^{13}$C NMR (75 MHz, DMSO-*d6)* δ (ppm) : 167.85 sp, 163.47 ap (C=O), 158.40, 157.41, 146.98, 143.81ap, 142.43 sp (N=CH), 138.45, 133.42, 133.06, 131.97, 131.80, 129.56, 129.48, 128.82, 128.34, 127.37, 124.03, 122.90, 122.70, 122.29, 122.05, 121.74, 119.22, 110.78, 109.04, 45.54 ap, 45,16 sp ($CH_2$-N), 35.17, 27.14. HRMS(ESI): Calc for $C_{28}H_{24}N_4NaO_2S$ $(M+Na)^+$: 503.1222; Found: 503.1226

**(E)-2-(3-Nitro-*H*-imidazo[1.2-a]pyridin-2-ylthio)-*N*-benzylideneacetohydrazide (11a)**

Orange powder. m..p = 232–234°C; yield = 79%, $^{1}$H NMR (300 MHz, DMSO-d6) δ (ppm) 11.77 ap, 11.67 sp (s, 1H; NH), 9.34 (sp + ap) (dt. J = 6.9, 1.1 Hz, 1H; HAr), 8.22 ap, 8.05 sp (s, 1H; N=CH), 7.90 – 7.77 (sp + ap) (m, 2H; HAr), 7.71 (sp + ap) (td, J = 3.8; 2.2 Hz, 2H; HAr), 7.51–7.34 (sp + ap) (m, 4H; HAr), 4.63 sp, 4.22 ap (s, 2H, S-$CH_2$). $^{13}$C NMR (75 MHz, DMSO-d6) δ (ppm) 169.39 sp, 164.18 ap (C=O), 153.54 sp, 153.15 ap (N=CH), 147.44, 146.23, 144.16, 134.53, 134.48, 133.52sp, 133.46 ap (CAr), 130.60 sp, 130.44 ap (CAr), 129.29, 128.65 sp, 128.40 ap (CAr), 127.58, 127.34, 11697 sp, 116.87 ap (CAr), 116.79, 33.95 ap, 33.08 sp ($SCH_2$). HRMS (ESI):Calc for [M + Na+] $C_{16}H_{13}N_5NaO_3S$ = 378.0521. Found = 378.0525.

**(E)-N-(2-Hydroxybenzylidene)2-(3-nitro-*H*-imidazo[1.2-a]pyridin-2-ylthio) acetohydrazide (11b)**

Brown powder, m.p. = 238–240°C, yield = 69%, $^{1}$H NMR (300 MHz, DMSO-d6) δ (ppm) 11.64 sp (s, 1H; OH), 11.14 ap, 11.01 sp (s, 1H; NH), 10.13 ap (s, 1H, OH), 9.35 (sp-ap) (m, 1H; HAr), 8.44 ap, 8.36 sp (s, 1H; N=CH), 7.90–7.77 (sp-ap) (m, 4H; HAr), 7.70 (sp-ap) (ddd, J = 8.1, 4.8, 1.6 Hz, 1H, HAr), 7.54 (dd, J = 8.0, 1.7 Hz, 1H; HAr), 7.49–7.35 (m, 2H; HAr),

7.35–7.20 (m, 2H, HAr), 7.03–6.80 (m, 5H, HAr), 4.61 sp, 4.23 ap(s, 2H, S-$CH_2$).$^{13}$C NMR (75 MHz, DMSO-d6) δ (ppm) 169.03 sp, 164.07 ap (C=O), 163.28 ap, 159.10 sp (C-OH), 157.73, 156.89, 153.54 sp, 153.06 ap (N=CH), 147.65, 146.24, 141.78, 133.72, 133.53, 133.47, 131.94, 131.72, 131.32, 129.68, 128.54, 126.86, 120.51, 120.09, 119.91, 119.84, 119.08, 118.64, 116.99, 116.80, 116.64, 33.67ap, 33.12sp ($SCH_2$), HRMS (ESI): Calc for [M + H+] $C_{16}H_{14}N_5O_4S$ = 372.0843. Found = 372.0839.

**(E)-2-(3-Nitro-*H*-imidazo[1.2-a]pyridin-2-ylthio)-*N*-(4-[benzylthio] benzylidene)acetohydrazide (11c)**

Khaki powder; m.p. = 250–252°C; yield = 72%. $^{1}$H NMR (300 MHz, DMSO-d6) δ (ppm) 11.77 ap, 11.62 sp (s, 1H, NH), 9.35 (sp + ap) (d, J = 6.8 Hz, 1H, HAr). 8.17 ap, 8.00 sp (s, 1H, N=CH-), 7.91–7.80 (sp + ap) (m, 2H, HAr), 7.66–7.56 (sp + ap) (m, 2H, HAr), 7.46–7.39(sp + ap) (m, 5H, HAr), 7.34–7.27 (sp + ap) (m, 2H, HAr), 7.27–7.23 (sp + ap) (m, 1H, HAr), 4.62 sp, 4.31 ap (s, 2H, S-$CH_2$), 4.39 sp, 4.21 ap (s, 2H, S-$CH_2$). $^{13}$C NMR (75 MHz, DMSO-d6) δ (ppm) 168.80 sp, 163.57 ap (C=O), 153.07 sp, 152.69 ap (N=CH-), 146.35 sp, 145.76 ap (CAr), 143.10, 139.10 sp, 138.82 ap (CAr), 137.15 sp, 137.09 ap (CAr), 133.00, 131.32, 129.85, 128.86 sp, 128.83 ap (CAr), 128.53 sp, 128.44 ap (CAr), 128.22, 127.96, 127.66, 127.54 sp, 127.51 ap (CAr), 127.27 sp, 127.16 ap (CAr), 126.43, 116.50 sp, 116.33 ap (CAr), 35.92, 33.49 ap, 32.58 sp (S-$CH_2$). HRMS (ESI): Calc for [M + Na+] $C_{23}H_{19}N_5NaO_3S_2$ = 500.1021. Found = 500.1025.

**(E)-2-(3-Nitro-*H*-imidazo[1.2-a]pyridin-2-ylthio)-N'-(4-[4-methylbenzyloxy] benzylidene) acetohydrazide (11d)**

Khaki powder; m.p. = 216–218°C; yield = 72%; $^{1}$H NMR (300 MHz, DMSO-d6) δ (ppm) 11.65 ap, 11.55 sp (s, 1H, NH), 9.33 (sp + ap) (dt, J = 6.9, 1.1 Hz, 1H, HAr), 8.15 ap, 7.98 sp (s, 1H, N=CH-), 7.88–7.75 (sp + ap) (m, 2H, HAr), 7.62 (sp + ap) (dd, J = 8.8, 2.2 Hz, 2H, HAr), 7.40 (sp + ap) (ddd, J = 6.6, 5.4, 2.9 Hz, 1H, HAr), 7.33 (sp + ap) (d, J = 7.7 Hz, 2H, HAr),

7.18 (sp + ap) (d, J = 7.8 Hz, 2H, HAr), 7.05 (sp + ap) (dd, J = 8.9, 2.2 Hz, 2H, HAr), 5.08 (sp +- ap) (s, 2H, O-$CH_2$), 4.60 sp, 4.19 ap (s, 2H, S-$CH_2$), 2.29 sp, 2.08 ap (s, 3H, $CH_3$), $^{13}$C NMR (75 MHz, DMSO-d6) δ (ppm) 168.65 sp,163.39 ap (C=O), 159.99 sp, 159.82 ap (CAr), 153.15 sp, 152.74 ap (N=CH-), 146.80, 145.77, 143.48, 137.20, 133.69, 133.05 sp, 132.99 ap (CAr), 129.01, 128.71, 128.44, 128.20, 127.94 sp, 127.87 ap, 126.76, 116.49, 116.39 sp, 116.33 ap (CAr), 115.18, 69.27, 33.52 ap, 32.63 sp (S-$CH_2$), 20.79. HRMS (ESI): Calc for [M + H+] $C_{24}H_{22}N_5O_4S$ = 476.0956. Found = 476.0952.

*2.2.2. Biological Methods*

The compounds were solubilized using either dimethyl sulfoxide (DMSO) or distilled water, and tested against a clinical strain of *Candida albicans*. Fluconazole was used as the reference antifungal agent. The fungal strain was supplied and identified by the Parasitology-Mycology Unit of the Medical Biology Department at Angré University Hospital. Antifungal activity of our compounds was determined using the broth microdilution method in 96-well microplates, following a standard procedure to establish the Minimum Inhibitory Concentrations (MICs) of the compounds. This method involves exposing *Candida albicans* inoculum to a series of compound dilutions and monitoring fungal growth inhibition through a colorimetric assay of germ dehydrogenase activity using Methyl Thiazolyl Tetrazolium (MTT) chloride. This coloration (violet) comes from the mitochondrial activity of active living cells. From 7-day-old colonies of *Candida albicans* grown on Sabouraud chloramphenicol agar, a stock Conidia suspension was vortexed vigorously for 15-20 secondes in 5 mL of Tryptone Soy Broth (OXOID®). The conidial concentration was determined using a Malassez counting chamber, and adjusted to give a turbidity of 0.5 McFarland (0.4-5 × $10^6$ spores/mL). A 50-fold dilution of this suspension was prepared to obtain a working concentration of approx. 0.08-1 × $10^5$ CFU/mL [33]. Stock solutions of the test compounds were prepared in dimethylsulfoxide (DMSO) or water at 1 mg/mL. In the first row of each microplate, 100 µL of the stock solution was added. All remaining wells received 50 µL of Tryptone Soy Broth. Serial dilutions were performed by transferring 50 µL from one well to the next across the row. Each well then received 50 µL of the diluted fungal inoculum. The 96-well plates were incubated at 37°C for 7 days. After incubation, 40 µL of an aqueous solution of MTT aqueous solution at a concentration of 2.5 mg/mL was added to each well, followed by an additional 24-hours incubation at 37°C. The MTT solution, which is initially yellow turns purple in wells where fungal cells remain viable, due to mitochondrial dehydrogenase activity (Figure 2).

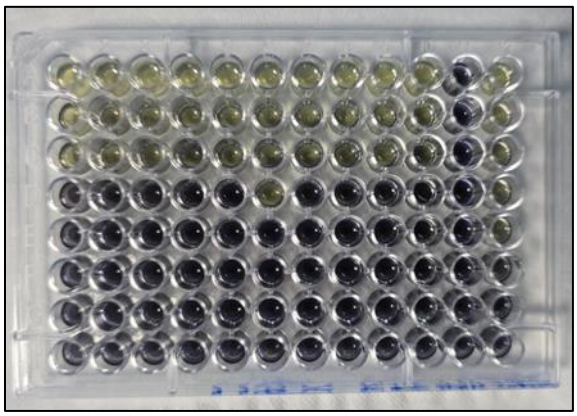


**Figure 2** Dilution on microplates in liquid medium

The MIC was defined as the lowest concentration of the compound that prevented this color change, indicating complete growth inhibition [34] [35] [36]. All samples were duplicated and the tests were repeated and improved twice.

## 3. Results and Discussion

### 3.1. Chemistry

We successfully synthesized two series of *N*-acylhydrazones derivatives: benzimidazole-based (6a-f) and imidazo[1,2-a]pyridine-based *N*-acylhydrazones (11a-d) (as outlined in Figure 3 and Figure 4). The synthetic route to the benzimidazole derivatives began with the preparation of the isothioureonium salt (2), following the procedure reported by Farid et *al* [31]. Specifically, 2-chloromethyl *1H*-benzimidazole (1) was reacted with thiourea under reflux in acetonitrile for 1.5 hours, yielding salt (2) in 89% yield. Next intermediate (3) was obtained according to a method described by Oleynik et *al.* [32]. Salt (2) underwent alkylation with benzyl chloride in a water-ethanol mixture in the presence of sodium hydroxide (NaOH). Ester intermediate (4) was then synthesized by a nucleophilic substitution between compound (3) and ethyl 2-chloroacetate using potassium carbonate ($K_2CO_3$) in dimethylformamide (DMF).

This step provided ester (4) in 92% yield. Hydrazide (5) was subsequently prepared by refluxing ester (4) with hydrazine monohydrate in ethanol for 5 hours, affording the product in 90% yield. Condensation of hydrazide (5) with a series of substituted aromatic aldehydes under reflux in methanol for 1 hour gave the desired *N*-acylhydrazone derivatives (**6a-f**), with yields ranging from 50 to 94% (Figure 3).

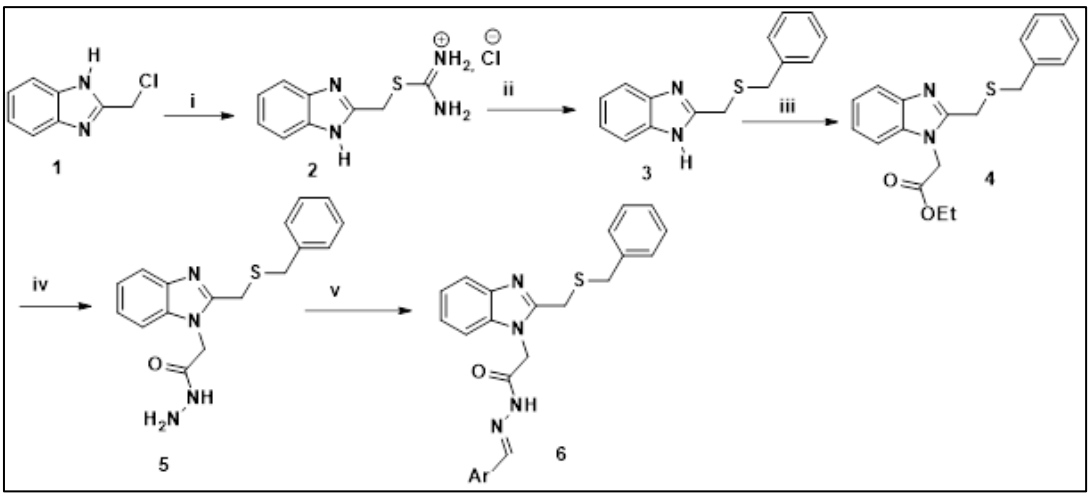



**Figure 3** Synthesis route of benzimidazole-*N*-acylhydrazones derivatives

Reaction conditions: *(i) Thiourea, MeCN, reflux, 2h; (ii) Benzyl chloride, NaOH, EtOH/$H_2O$, reflux 2h; (iii) $ClCH_2CO_2Et$, $K_2CO_3$, DMF, 2h; (iv) $NH_2$-$NH_2$, EtOH, reflux 5h; (v) Ar-COH, MeOH, reflux 1h*

The imidazo[1,2-a]pyridine-based *N*-acylhydrazone derivatives (**11a–d**) were synthesized through a four-step pathway starting from a 3-nitro-substituted imidazo[1,2-a]pyridine scaffold (Figure 4). The introduction of a nitro group (–$NO_2$) at position 3 served to electronically deactivate position 2, thereby promoting aromatic nucleophilic substitution reaction. In the first step, 2-chloro-3-nitroimidazo[1,2-a]pyridine (**7**) was reacted with thiourea under conditions analogous to those used for the benzimidazole series. This reaction afforded the isothioureonium salt of 3-nitro imidazo[1,2-a]pyridine (**8**) in 96% yield [31]. Subsequently, salt (**8**) was treated with ethyl 2-chloroacetate under basic conditions in a refluxing water-ethanol mixture, leading to the formation of thioester (**9**) in 73% yield. Conversion of the ester (**9**) to the corresponding hydrazide (**10**) was achieved through reaction with hydrazine hydrate, yielding in 52% yield.

Finally, the condensation of hydrazide (**10**) with a series of substituted aromatic aldehydes in methanol under reflux for 1 hour gave the target *N*-acylhydrazone derivatives (**11a–d**). The reactions proceeded smoothly, affording products in moderate to good yields ranging from 52% to 82% (Figure 4).

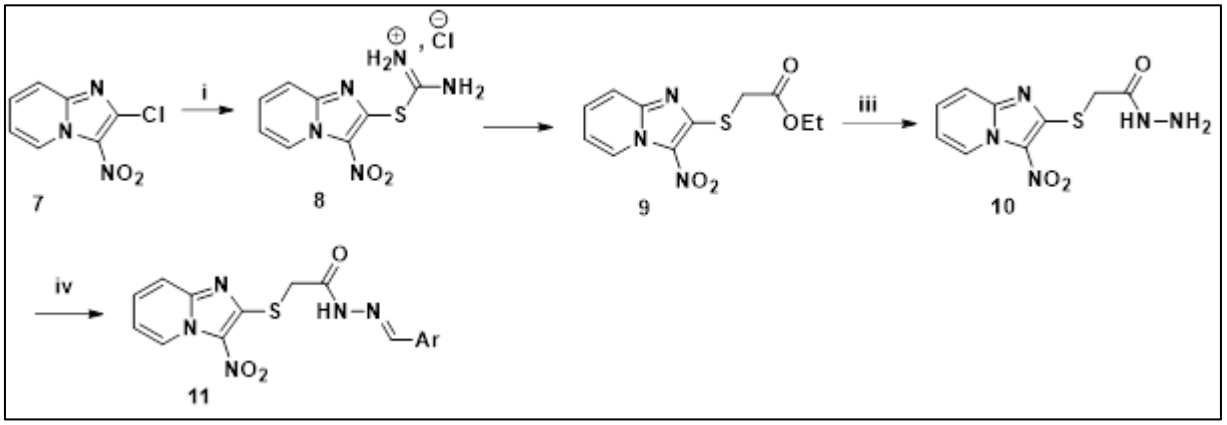



**Figure 4** Synthesis route of N-acylhydrazone imidazo[1,2-a]pyridine derivatives

Reaction conditions: *(i) Thiourea, MeCN, reflux; 48 h; (ii) $ClCH_2CO_2Et$, NaOH, EtOH/$H_2O$, reflux 1h; (iii) $NH_2$-$NH_2$, EtOH, reflux 5h; (iv) Ar-COH, MeOH, reflux 1h.*

The structures of key intermediates and final benzimidazole-based derivatives (compounds 3, 4, 5 and 6a-f) were confirmed using spectroscopic analyses such as $^{1}H$ NMR, $^{13}C$ NMR and High-Resolution Mass spectrometry (HRMS). In the $^{1}H$ NMR spectrum of compound (3), two singlets were observed at 3.71 and 3.93 ppm, corresponding to the two methylene protons ($CH_2$). These assignments were supported by $^{13}C$ NMR spectrum. The spectrum which showed two distinct signals at 27 and 35 ppm, confirming the presence of two methylene ($CH_2$) carbons. For compound (4), the $^{1}H$ NMR spectrum showed characteristic signals of an ethoxy group: a quadruplet at 4.20 ppm ($-CH_2-$) and a triplet at 1.26 ppm ($-CH_3$), confirming successful ester formation. In compound (5), analysis of the $^{1}H$ NMR spectrum shows the disappearance of ethoxy signals and the appearance of new peaks supported the conversion to the hydrazide. Specifically, two signals, one at 9.54 ppm attributable to the hydrazide NH proton, and another at 4.39 ppm assigned to $NH_2$ protons, confirming successful hydrazinolysis of the ester.

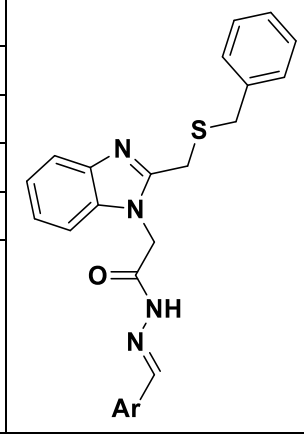
The imidazo[1,2-a]pyridine-based (11a-d) were also characterized by $^{1}H$ NMR, $^{13}C$ NMR and HRMS. In the $^{1}H$ NMR spectrum of intermediate (9) a singlet at 4.12 ppm was observed, corresponding to the two methylene protons located between the sulfur atom and the ester function (S-$CH_2$-COOEt). The ethoxy group protons of the ester function appeared as a quadruplet at 4.24 ppm ($-CH_2-$) and a triplet at 1.30 ppm ($-CH_3$), confirming the presence of the ester functionality. These changes clearly indicated successful conversion of the ester into the hydrazide. For hydrazide (10), the $^{1}H$ NMR spectrum revealed the disappearance of the ethoxy signals and the appearance of two broad singlets at 4.32 and 7.42 ppm, corresponding to the amine ($-NH_2$) and hydrazide ($-NH-C=O$) protons, respectively.

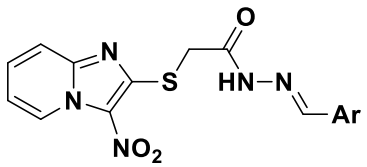
In the final *N*-acylhydrazone derivatives (6a-f and 11a-d), $^{1}H$ NMR spectra exhibited a notable duplication of signals associated with three adjacent groups in the acylhydrazone moiety: the amide NH, the azomethine (N=CH), and the methylene group (-$CH_2$-CO-) [37].This duplication is consistent with the presence of two conformers: *syn*-periplanar (sp E) and *anti*-periplanar E (ap E) in an approximate 66:34 % ratio, respectively. Interestingly, in compounds featuring an ortho-hydroxy substituent on the aromatic acyl group, the ap E conformer became slightly predominant. This shift is likely due to additional stabilization through intramolecular hydrogen bonding, involving the ortho-hydroxyl proton and both the azomethine nitrogen and the adjacent carbonyl oxygen lone pairs. Such conformational behavior reflects the dynamic structural versatility of the *N*-acylhydrazone motif, which may influence biological activity.

### 3.2. Anticandidal activities

The anticandidal activity of the synthetized compounds was compared with the reference drug Fluconazole. Minimum Inhibitory Concentrations (MICs) were initially determined in µg/mL (mass/volume) but were subsequently converted to micromolar (µM) to enable a more accurate comparison of biological activity. This conversion is essential because MIC values expressed in mass per volume (µg/mL) do not account for molecular weight differences among compounds. Expressing MICs in µM allows for normalization based on molecular concentration, thus providing a more precise evaluation of antifungal efficacy on a per-molecule basis. The results of the anticandidal activity obtained after evaluation of benzimidazole *N*-acylhydrazones (**6a-f**) and imidazo[1,2-a]pyridine *N*-acylhydrazones (**11a-d**) against the clinical strain of *Candida Albicans* are presented in Table 1.

**Table 1** Anticandidal activity of *N*-acylhydrazones derivatives (**6a-f** and **11a-d**)

| Compounds | General structure | Ar | Molecular weight (g/mol) | MIC (µg/mL) | MIC (µM) |
|---|---|---|---|---|---|
| 6a |  | Naphtalen-2-ol | 480.586 | 12.5 | 26.009 |
| 6b | | 4-Hydroxyphenyl | 430.526 | 25 | 58.068 |
| 6c | | 2-Hydroxyphenyl | 430.526 | 25 | 58.068 |
| 6d | | 4-Nitrophenyl | 459.524 | 25 | 54.404 |
| 6e | | 3-Bromophenyl | 493.423 | 25 | 50.666 |
| 6f | | (4-methylbenzyl)(phenyl)sulfane | 550.739 | 25 | 45.393 |

| | | | | | |
|---|---|---|---|---|---|
| 11a |  | Phenyl | 355.372 | 25 | 70.034 |
| 11b | | 2-Hydroxyphenyl | 371.371 | 25 | 67.318 |
| 11c | | (4-methylbenzyl)(phenyl)sulfane | 491.584 | 25 | 50.856 |
| 11d | | 1-methyl-4-(phenoxymethyl)benzene | 461.496 | 25 | 54.171 |
| Fluconazole | | | 306.276 | 25 | 81.62 |

The antifungal evaluation demonstrated that both benzimidazole *N*-acylhydrazone (**6a-f**) and imidazo[1,2-a]pyridine *N*-acylhydrazone (**11a-d**) derivatives exhibit significant activity against the clinical strain of *Candida albicans*, with MICs ranging from 26.009 μM to 70.034 μM. To gain further insight into the molecular features influencing antifungal efficacy, a structure–activity relationship (SAR) analysis was undertaken. The aim is to establish correlations between specific structural elements and observed biological activity, in order to identify functional groups or scaffolds that contribute to the induction or enhance antifungal potential. For this discussion, MIC values expressed in micromolar units are used as a direct indicator of antifungal potency: the lower the MIC, the more active the compound. Our findings indicate that both the heterocyclic core (benzimidazole *vs.* imidazo[1,2-a]pyridine) and the nature of the aromatic ring attached *via* the hydrazone linkage significantly influence biological activity against *C. Albicans* strains. Within the benzimidazole *N*-acylhydrazone series (**6a–f**), variation in antifungal efficacy was clearly observed, suggesting that substituents on the aryl moiety play a pivotal role. Analysis of this series reveals that:

Compound **6a**, bearing a naphthalen-2-ol moiety at the hydrazone position showed the highest antifungal activity in the series with an MIC of 26.009 μM. This strong performance is likely due to the extended π-system and high lipophilicity of the naphthyl ring, which may promote favorable van der Waals or hydrophobic interactions with the lipid-rich fungal membrane.

Substitution of the naphthyl group with its monocyclic analogs, 2-hydroxyphenyl (compound **6b**) and 4-hydroxyphenyl (compound **6c**), led to a marked decrease in activity, both exhibiting identical MICs of 58.068 μM. These results suggest that the reduction in molecular volume and increased hydrophilicity of the phenolic moieties diminish antifungal efficacy. The hydroxylated derivatives proved 2 times less effective than compound **6a**. The presence of hydroxyl groups, capable of hydrogen bonding, appears unfavorable in this scaffold.

Replacing the hydroxyl group in **6c** with a nitro group in compound **6d** (4-nitrophenyl) slightly improved activity (MIC = 54.404 μM). This modest gain may be attributed to the intrinsic antimicrobial properties of nitro groups, as evidenced in related nitroimidazole-based drugs.

Further modification by introducing a halogenated phenyl in compound **6e** (3-bromophenyl) did not significantly alter antifungal potency, with an MIC also at 54.404 μM. This suggests that, unlike in some azole antifungals, halogenation at this position does not enhance efficacy in this series.

Interestingly, compound 6f, which incorporates a 4-methylbenzyl(phenyl)sulfane moiety, displayed the second-best activity (MIC = 45.393 μM). This result likely reflects the increased lipophilicity imparted by the methyl and sulfane functionalities, which may enhance membrane permeability and compound diffusion through the fungal cell wall.

Replacing the benzimidazole core with the isosteric imidazo[1,2-a]pyridine scaffold, and repositioning the acetothiohydrazide functionality to position 2, resulted in derivatives (11a–d) that retained antifungal activity, albeit with generally higher MIC values (50.856–70.034 μM), suggesting slightly reduced potency compared to their benzimidazole counterparts. In addition, the structure-activity relationships undertaken enabled us to establish:

Compound 11a, bearing an unsubstituted phenyl ring, displayed the lowest activity in the series (MIC = 70.034 μM). The limited efficacy may be due to the absence of lipophilic or electron-donating substituents that enhance cell permeability. A minor improvement was observed in compound 11b, where substitution with a 2-hydroxyphenyl group lowered the MIC to 67.318 μM. However, as in the benzimidazole series, the presence of hydrophilic hydroxyl groups did not significantly enhance activity.

Introduction of a 4-methylbenzyl(phenyl)sulfane moiety in compound 11c resulted in a notable increase in antifungal activity (MIC = 50.856 μM), mirroring the trend observed in compound 6f. The result reinforces the beneficial role of the sulfane group in enhancing lipophilic interactions with fungal membranes.

Compound 11d, bearing a closely related 1-methyl-4-(phenyl)sulfanylbenzene group, also showed good activity (MIC = 54.171 μM), confirming the pharmacological relevance of aryl sulfur-containing substituents in promoting antifungal efficacy.

## 4. Conclusion

This study reports the successful design and antifungal evaluation of two novel series of *N*-acylhydrazone derivatives based on benzimidazole and imidazo[1,2-a]pyridine scaffolds. Spectroscopic analyses confirmed the structures and conformational behavior of the synthesized compounds, which were obtained as mixtures of E-conformers. Biological assessment against *Candida albicans* revealed variable antifungal activities, strongly influenced by both the nature of the heterocycle and the substituents on the acylhydrazone moiety. Among the benzimidazole derivatives, compound 6a, featuring a naphthalen-2-ol group, demonstrated the most potent activity, underscoring the importance of bulky, lipophilic aromatic systems in facilitating interaction with fungal membranes. Similarly, derivatives incorporating sulfur-based aryl substituents (6f, 11c, and 11d) displayed enhanced antifungal efficacy, supporting their relevance in pharmacomodulation strategies.

These findings provide valuable insights into the structure–activity relationships of *N*-acylhydrazone compounds and pave the way for the development of optimized antifungal agents with improved potency and selectivity. Future work will focus on broadening the antifungal spectrum, assessing cytotoxicity, and exploring molecular mechanisms of action.

## Compliance with ethical standards

### *Acknowledgments*

The authors would like to thank the Angré University Hospital Center in Côte d'Ivoire where the antifungal tests were performed. We wish to thank the laboratory (Laboratoire de Méthodologie et Synthèse de Produits Naturels) of the University of Quebec in Montreal (Canada) for providing us the chemical reagents and material for the spectroscopic analyzes

### *Disclosure of conflict of interest*

No potential conflict of interest was reported by the authors.

### *Author contributions*

T.E.C., P.A.A and E.A performed the synthesis, purification of all the compounds and contributed to the writing of the manuscript. S.C. conceptualized the biological study, SC participated in the design and conceptualization of the work, and revised the manuscript, while C.S supervised the overall project.

## References

[1] J. Kim, P. Sudbery, Candida albicans, a major human fungal pathogen, J Microbiol. 49 (2011) 171–177. https://doi.org/10.1007/s12275-011-1064-7.

[2] W. Nittayananta, Oral fungi in HIV : challenges in antifungal therapies, Oral Diseases 22 (2016) 107–113. https://doi.org/10.1111/odi.12394.

[3] S. Campoy, J.L. Adrio, Antifungals, Biochemical Pharmacology 133 (2017) 86–96. https://doi.org/10.1016/j.bcp.2016.11.019.

[4] M. Kneale, J.S. Bartholomew, E. Davies, D.W. Denning, Global access to antifungal therapy and its variable cost, J. Antimicrob. Chemother. 71 (2016) 3599–3606. https://doi.org/10.1093/jac/dkw325.

[5] D.S. Perlin, Current Perspectives on Echinocandin Class Drugs, Future Microbiol. 6 (2011) 441–457. https://doi.org/10.2217/fmb.11.19.

[6] D. Sanglard, F.C. Odds, Resistance of Candida species to antifungal agents: molecular mechanisms and clinical consequences, The Lancet Infectious Diseases 2 (2002) 73–85. https://doi.org/10.1016/S1473-3099(02)00181-0.

[7] P. Vandeputte, S. Ferrari, A.T. Coste, Antifungal Resistance and New Strategies to Control Fungal Infections, International Journal of Microbiology 2012 (2012) 1–26. https://doi.org/10.1155/2012/713687.

[8] D.S. Perlin, Echinocandin Resistance in Candida, Clinical Infectious Diseases 61 (2015) S612–S617. https://doi.org/10.1093/cid/civ791.

[9] C. Williams, G. Ramage, Fungal Biofilms in Human Disease, in: G. Donelli (Ed.), Biofilm-Based Healthcare-Associated Infections, Springer International Publishing, Cham, 2015: pp. 11–27. https://doi.org/10.1007/978-3-319-09782-4_2.

[10] B.J. Kullberg, M.C. Arendrup, Invasive Candidiasis, N Engl J Med 373 (2015) 1445–1456. https://doi.org/10.1056/NEJMra1315399.

[11] J. Talapko, M. Juzbašić, T. Matijević, E. Pustijanac, S. Bekić, I. Kotris, I. Škrlec, Candida albicans—The Virulence Factors and Clinical Manifestations of Infection, JoF 7 (2021) 79. https://doi.org/10.3390/jof7020079.

[12] M.C. Fisher, N.J. Hawkins, D. Sanglard, S.J. Gurr, Worldwide emergence of resistance to antifungal drugs challenges human health and food security, Science 360 (2018) 739–742. https://doi.org/10.1126/science.aap7999.

[13] D. Sanglard, F.C. Odds, Resistance of Candida species to antifungal agents: molecular mechanisms and clinical consequences, The Lancet Infectious Diseases 2 (2002) 73–85. https://doi.org/10.1016/S1473-3099(02)00181-0.

[14] E. Siikala, R. Rautemaa, M. Richardson, H. Saxen, P. Bowyer, D. Sanglard, Persistent Candida albicans colonization and molecular mechanisms of azole resistance in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) patients, Journal of Antimicrobial Chemotherapy 65 (2010) 2505–2513. https://doi.org/10.1093/jac/dkq354.

[15] E. Borghi, G. Morace, F. Borgo, R. Rajendran, L. Sherry, C. Nile, G. Ramage, New strategic insights into managing fungal biofilms, Front. Microbiol. 6 (2015). https://doi.org/10.3389/fmicb.2015.01077.

[16] A. Koné, C. Souleymane, M. Kalo, C. Tchambaga Etienne, S. Collet, D. Sissouma, Synthesis of novel benzimidazole-based retrochalcones and their anticancer activity against breast and colon cancer, Synthetic Communications 55 (2025) 175–182. https://doi.org/10.1080/00397911.2024.2440026.

[17] C. Souleymane, C. Siomenan, A. Evrard, C. Bakary, C.T. Etienne, A. Ane, Influence of N-methyl piperidine on Antibacterial Activity of 2-(thioalkyl)-1H methylbenzimidazole Derivatives, ChemXpress 14 (2022) 9–18.

[18] A. Evrard, C. Siomenan, C.T. Etienne, T. Daouda, C. Souleymane, S. Drissa, A. Ané, Design, Synthesis and in Vitro Antibacterial Activity of 2-thiomethyl-benzimidazole Derivatives, Advances in Biological Chemistry 11 (2021) 165–177. https://doi.org/10.4236/abc.2021.114012.

[19] O. Mahama, N.D. Jean-Paul, C. Songuigama, S. Drissa, K.W. Mamidou, Design and Pharmacochemical Development of New Anthelmintics with Benzimidazolyl Arylpropenone Profile: Structure-Activity Relationship, Pharmacophore 11 (2020) 58–66. https://doi.org/10.51847/OG0uAs7.

[20] L. El Ouasif, A. Bouyahya, R. Zniber, M. El Ghoul, R. Achour, H. Chakchak, A. Talbaoui, H. El Boury, N. Dakka, Y. Bakri, Novel 2-mercaptobenzimidazole derivatives: synthesis and evaluation of its antibacterial and antioxidant activities, Mediterr.J.Chem., 6 (2017) 77–87. https://doi.org/10.13171/mjc63/01704032355-elghoul.

[21] N.S. Rao, C. Kistareddy, Synthesis and antibacterial activity of novel imidazo[1,2-a]pyrimidine and imidazo[1,2-a]pyridine chalcones derivatives, Der Pharma Chemica 6 (2012) 2408-2415

[22] R. Fu, Q. You, L. Yang, W. Wu, C. Jiang, X. Xu, Design, synthesis and bioevaluation of dihydropyrazolo[3,4-b]pyridine and benzo[4,5]imidazo[1,2-a]pyrimidine compounds as dual KSP and Aurora-A kinase inhibitors for anti-cancer agents, Bioorganic & Medicinal Chemistry 18 (2010) 8035–8043. https://doi.org/10.1016/j.bmc.2010.09.020.

[23] A. Lauria, C. Patella, I. Abbate, A. Martorana, A.M. Almerico, Lead optimization through VLAK protocol: New annelated pyrrolo-pyrimidine derivatives as antitumor agents, European Journal of Medicinal Chemistry 55 (2012) 375–383. https://doi.org/10.1016/j.ejmech.2012.07.046.

[24] Y. Rival, G. Grassy, A. Taudou, R. Ecalle, Antifungal activity in vitro of some imidazo[1,2-a]pyrimidine derivatives, European Journal of Medicinal Chemistry 26 (1991) 13–18. https://doi.org/10.1016/0223-5234(91)90208-5.

[25] K. Adingra, K. Alain, S. Coulibali, C. Tchambaga, S. Coulibaly, M. Ouattara, D. Sissouma, Synthesis and Anticandidosic Activities of Imidazo[1,2-a]pyridinehydrazone Derivatives, ChemXpress 14 (2022) 1–8. https://doi.org/10.37532/ 2320-1967.2022 .14(1).1-8

[26] Z.-C. Dai, Y.-F. Chen, M. Zhang, S.-K. Li, T.-T. Yang, L. Shen, J.-X. Wang, S.-S. Qian, H.-L. Zhu, Y.-H. Ye, Synthesis and antifungal activity of 1,2,3-triazole phenylhydrazone derivatives, Org. Biomol. Chem. 13 (2014) 477–486. https://doi.org/10.1039/C4OB01758G.

[27] A. Ayati, M. Falahati, H. Irannejad, S. Emami, Synthesis, in vitro antifungal evaluation and in silico study of 3-azolyl-4-chromanone phenylhydrazones, DARU J Pharm Sci 20 (2012) 46. https://doi.org/10.1186/2008-2231-20-46.

[28] D.U.J.-P. N'Guessan, L.A.C. Kablan, A. Kacou, C. Bories, S. Coulibaly, D. Sissouma, P.M. Loiseau, M. Ouattara, Synthesis and Biological Profiles of Some Benzimidazolyl-chalcones as Anti-leishmanial and Trypanocidal Agents, CSIJ (2021) 47–56. https://doi.org/10.9734/CSJI/2021/v30i830249.

[29] Drissa Sissouma, Synthesis and in vitro nematicidal activity of new chalcones vectorised by imidazopyridine, Afr. J. Pharm. Pharmacol. 5 (2011). https://doi.org/10.5897/AJPP11.550.

[30] P. Badiee, A. Abdolvahab, M. Moeini, P. Haddadi, S. Farshad, A. Japoni, M. Ziyaeyan, Antifungal susceptibility of the Aspergillus species by Etest and CLSI Reference Methods, Arch. Iran. Med. (2012) 429-432

[31] F.M. Ibatullin, S.I. Selivanov, A.G. Shavva, A General Procedure for Conversion of S-Glycosyl Isothiourea Derivatives into Thioglycosides, Thiooligosaccharides and Glycosyl Thioesters, Synthesis (2001) 0419–0422. https://doi.org/10.1055/s-2001-11443.

[32] A.S. Oleynik, N.Y. Pevneva, N.V. Kandalintseva, A.E. Prosenko, O.M. Khoshchenko, Synthesis and Biological Activity of Hydrophilic Alkylphenols, Chem Sus Chem (2008) 551-556.

[33] C. Lass-Flörl, S. Perkhofer, In vitro susceptibility-testing in Aspergillus species, Mycoses 51 (2008) 437–446. https://doi.org/10.1111/j.1439-0507.2008.01510.x.

[34] A. Espinel-Ingroff, B. Arthington-Skaggs, N. Iqbal, D. Ellis, M.A. Pfaller, S. Messer, M. Rinaldi, A. Fothergill, D.L. Gibbs, A. Wang, Multicenter Evaluation of a New Disk Agar Diffusion Method for Susceptibility Testing of Filamentous Fungi with Voriconazole, Posaconazole, Itraconazole, Amphotericin B, and Caspofungin, J Clin Microbiol 45 (2007) 1811–1820. https://doi.org/10.1128/JCM.00134-07.

[35] E. Cantón, A. Espinel-Ingroff, J. Pemán, Trends in antifungal susceptibility testing using CLSI reference and commercial methods, Expert Review of Anti-Infective Therapy 7 (2009) 107–119. https://doi.org/10.1586/14787210.7.1.107.

[36] S. Arikan, Current status of antifungal susceptibility testing methods, Med Mycol 45 (2007) 569–587. https://doi.org/10.1080/13693780701436794.

[37] P.-A. Achi, S. Coulibali, K.Y.G. Molou, S. Coulibaly, S. Kouassi, D. Sissouma, L. Ouattara, A. Ané, Stereochemical design and conformation determinations of new benzimidazole-N-acylhydrazone derivatives, Synthetic Communications 52 (2022) 1306–1317. https://doi.org/10.1080/00397911.2022.2084417.