

1 **Supplementary Information:**

2 **Zhao et al.,**

3 **(1-aryloxy-2-hydroxypropyl)-phenylpiperazine derivatives suppress**

4 ***Candida albicans* virulence by interfering with morphological transition**

5

6

7

8

9

10

11

12

13

14

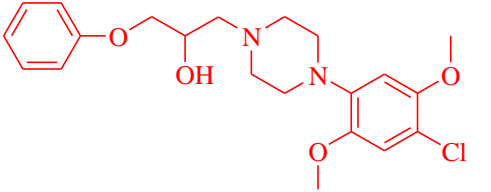
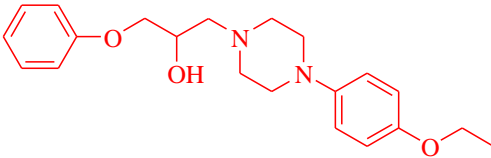
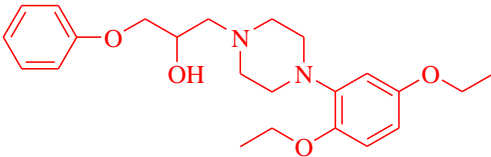
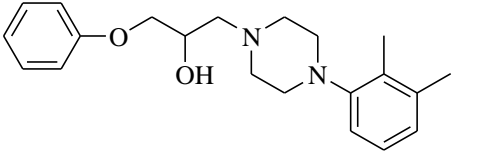
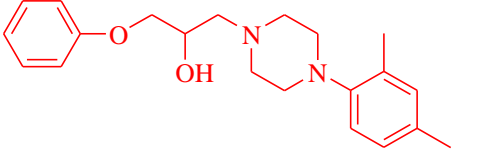
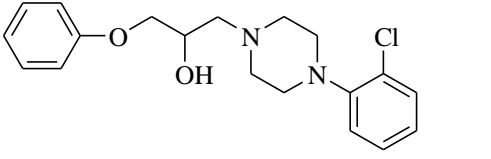
15

16

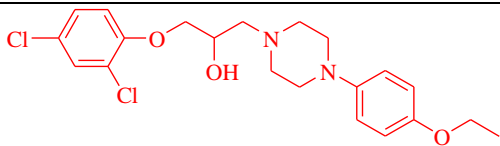
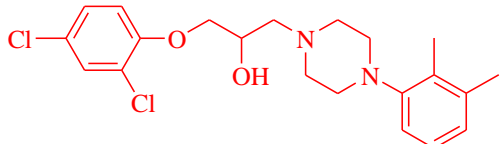
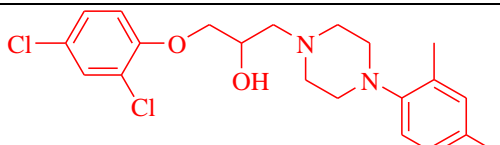
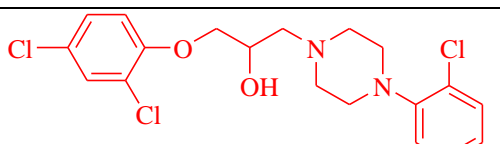
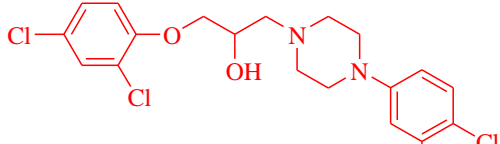
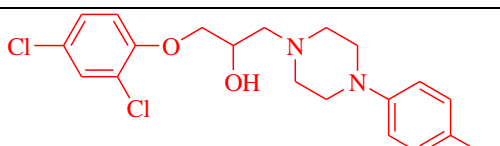
17

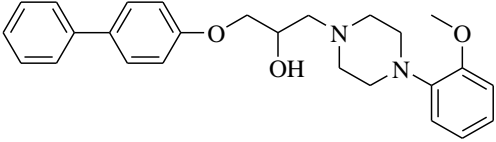
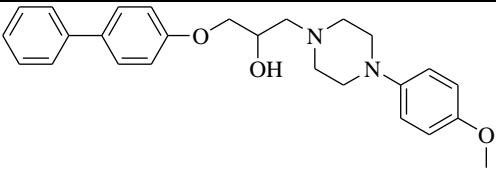
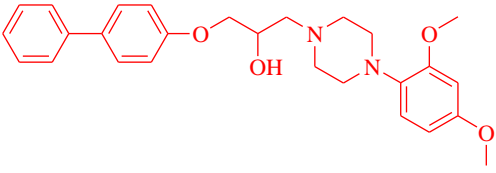
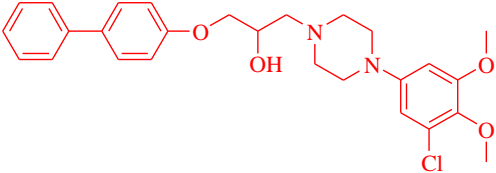
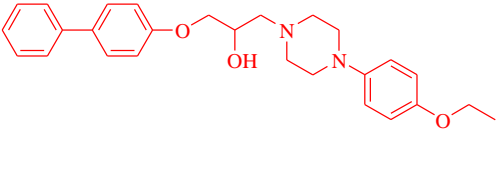
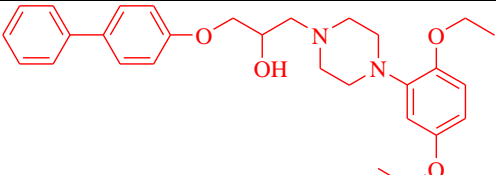
18 Table S1. Analysis of chemical structures of piperazine derivatives

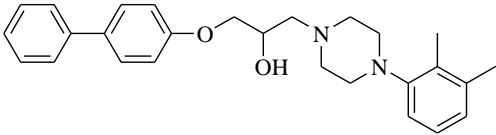
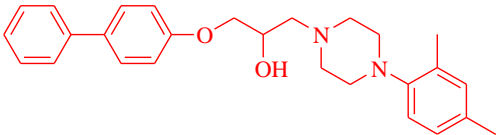
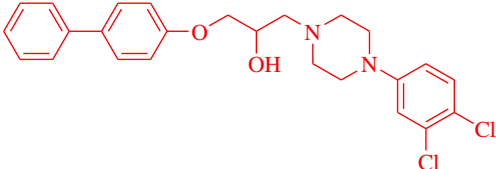
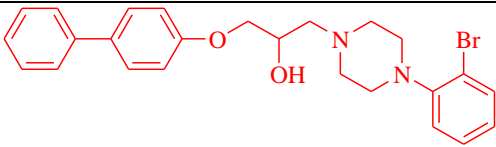
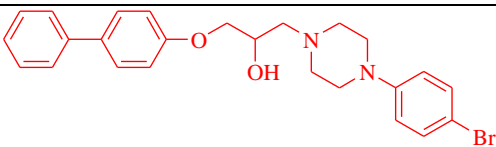
Com. No.	Structure	Description of Mass Spectra	Description of NMR Spectra
1c		ESI (<i>m/z</i>): [M+H] ⁺ 343.3. HRESIMS <i>m/z</i> : 343.2026 (M ⁺ +H, calcd for C ₂₀ H ₂₇ N ₂ O ₃ , 343.1943).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.79-7.29 (m, 9H, ArH), 3.96-3.98 (m, 2H, - OCH ₂ -), 3.85-3.88 (m, 1H, - CH-OH), 3.66 (s, 3H, -OCH ₃ -), 3.50 (brs, 2H, -CH ₂ -N), 2.97-2.99 (brs, 4H, piperazinyl right H), 2.54- 2.62 (m, 4H, piperazinyl left H).
2c*		ESI (<i>m/z</i>): [M+H] ⁺ 373.3. HRESIMS <i>m/z</i> : 373.2123 (M ⁺ +H, calcd for C ₂₁ H ₂₉ N ₂ O ₄ , 373.2049).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.91-7.40 (m, 9H, ArH), 3.99-4.01 (m, 2H, - OCH ₂ -), 3.87-3.91 (m, 1H, - CH-OH), 3.57 (s, 2H, -CH ₂ - N), 2.97 (brs, 4H, piperazinyl right H), 2.63 (m, 4H, piperazinyl left H), 2.50-2.55 (m, 2H, -CH ₂ -N).
3c		ESI (<i>m/z</i>): [M+H] ⁺ 373.3. HRESIMS <i>m/z</i> : 373.2132 (M ⁺ +H, calcd for C ₂₁ H ₂₈ ClN ₂ O ₄ , 373.2049).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.40-7.29 (m, 8H, ArH), 3.96-3.98 (m, 2H, - OCH ₂ -), 3.83-3.87 (m, 1H, - CH-OH), 3.72 (s, 3H, - OCH ₃), 3.68 (s, 3H, -OCH ₃), 3.57 (s, 2H, -CH ₂ -N), 2.84 (brs, 4H, piperazinyl right H), 2.55 (m, 4H, piperazinyl left H).
4c*		ESI (<i>m/z</i>): [M+H] ⁺ 373.3. HRESIMS <i>m/z</i> : 373.2132 (M ⁺ +H, calcd for C ₂₁ H ₂₉ N ₂ O ₄ , 373.2049).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.41-7.28 (m, 8H, ArH), 3.96-3.98 (m, 2H, - OCH ₂ -), 3.84-3.88 (m, 1H, - CH-OH), 3.69 (s, 3H, - OCH ₃), 3.65 (s, 3H, -OCH ₃), 2.94 (brs, 4H, piperazinyl right H), 2.57 (m, 4H, piperazinyl left H), 2.47-2.51 (m, 2H, -CH ₂ -N).
5c*		ESI (<i>m/z</i>): [M+H] ⁺ 407.3. HRESIMS <i>m/z</i> : 407.1738 (M ⁺ +H, calcd for C ₂₁ H ₂₈ ClN ₂ O ₄ , 407.1659).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.76-7.30 (m, 7H, ArH), 3.98-4.00 (m, 2H, - OCH ₂ -), 3.85-3.89 (m, 1H, - CH-OH), 3.82 (s, 6H, - OCH ₃ ×2), 2.87 (brs, 4H, piperazinyl right H), 2.56- 2.59 (brs, 4H, piperazinyl left H), 2.48-2.52 (brs, 2H, -CH ₂ - N).

6c*		<p>ESI (<i>m/z</i>): [M+H]⁺ 407.3.</p> <p>HRESIMS <i>m/z</i>: 407.1742 (M⁺+H, calcd for C₂₁H₂₈ClN₂O₄, 407.1659).</p>	<p>¹H NMR (500 MHz, DMSO), δ (ppm): 6.63-7.30 (m, 7H, ArH), 3.97-4.01 (m, 2H, - OCH₂-), 3.86-3.88 (m, 1H, - CH-OH), 3.79 (s, 3H, - OCH₃), 3.74 (s, 3H, -OCH₃), 3.00 (brs, 4H, piperazinyl right H), 2.59 (brs, 4H, piperazinyl left H), 2.50-2.52 (m, 2H, -CH₂-N).</p>
7c*		<p>ESI (<i>m/z</i>): [M+H]⁺ 357.3.</p> <p>HRESIMS <i>m/z</i>: 357.2178 (M⁺+H, calcd for C₂₁H₂₉N₂O₃, 357.21).</p>	<p>¹H NMR (500 MHz, DMSO), δ (ppm): 6.83-7.28 (m, 9H, ArH), 3.96-3.98 (m, 4H, - OCH₂-x2), 3.86 (brs, 1H, - CH-OH), 2.95 (brs, 4H, piperazinyl right H), 2.58 (brs, 4H, piperazinyl left H), 2.43 (m, 2H, -CH₂-N), 1.31 (t, 3H, -CH₃).</p>
8c*		<p>ESI (<i>m/z</i>): [M+H]⁺ 401.3.</p> <p>HRESIMS <i>m/z</i>: 401.2440 (M⁺+H, calcd for C₂₃H₃₃N₂O₄, 401.2362).</p>	<p>¹H NMR (500 MHz, DMSO), δ (ppm): 6.39-7.30 (m, 8H, ArH), 3.97-4.00 (m, 2H, - OCH₂-), 3.90-3.95 (m, 4H, - OCH₂CH₃x2), 3.87-3.88 (m, 1H, -CH-OH), 2.98 (brs, 4H, piperazinyl right H), 2.59 (brs, 4H, piperazinyl left H), 2.52 (m, 2H, -CH₂-N), 1.27- 1.31 (m, 6H, -CH₃x2).</p>
9c		<p>ESI (<i>m/z</i>): [M+H]⁺ 341.3.</p> <p>HRESIMS <i>m/z</i>: 341.2233 (M⁺+H, calcd for C₂₁H₂₉N₂O₂, 341.2151).</p>	<p>¹H NMR (500 MHz, DMSO), δ (ppm): 6.82-7.28 (m, 8H, ArH), 3.96-4.00 (m, 2H, - OCH₂-), 3.85-3.88 (m, 1H, - CH-OH), 2.76 (brs, 4H, piperazinyl right H), 2.59 (brs, 4H, piperazinyl left H), 2.42-2.53 (m, 2H, -CH₂-N), 2.17 (s, 3H, -CH₃), 2.12 (s, 3H, -CH₃).</p>
10c*		<p>ESI (<i>m/z</i>): [M+H]⁺ 341.3.</p> <p>HRESIMS <i>m/z</i>: 341.2233 (M⁺+H, calcd for C₂₁H₂₉N₂O₂, 341.2151).</p>	<p>¹H NMR (500 MHz, DMSO), δ (ppm): 6.88-7.30 (m, 8H, ArH), 3.99-4.01 (m, 2H, - OCH₂-), 3.86-3.90 (m, 1H, - CH-OH), 2.78 (brs, 4H, piperazinyl right H), 2.59 (brs, 4H, piperazinyl left H), 2.50-2.54 (m, 2H, -CH₂-N), 2.19 (s, 6H, -CH₃x2).</p>
11c		<p>ESI (<i>m/z</i>): [M+H]⁺ 347.2.</p> <p>HRESIMS <i>m/z</i>: 347.1533 (M⁺+H, calcd for C₁₉H₂₄ClN₂O₂,</p>	<p>¹H NMR (500 MHz, DMSO), δ (ppm): 6.91-7.40 (m, 9H, ArH), 3.99-4.01 (m, 2H, - OCH₂-), 3.87-3.91 (m, 1H, - CH-OH), 3.57 (s, 2H, -CH₂- N), 2.97 (brs, 4H, piperazinyl right H), 2.63 (m, 4H, piperazinyl left H), 2.50-2.55</p>

		347.1448).	(m, 2H, -CH ₂ -N).
12c		ESI (<i>m/z</i>): [M+H] ⁺ 381.3. HRESIMS <i>m/z</i> : 381.1139 (M ⁺ +H, calcd for C ₁₉ H ₂₃ Cl ₂ N ₂ O ₂ , 381.1058).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.86-7.35 (m, 8H, ArH), 3.94-3.99 (m, 2H, - OCH ₂ -), 3.84-3.88 (m, 1H, - CH-OH), 3.12 (brs, 4H, piperazinyl right H), 2.53- 2.58 (m, 4H, piperazinyl left H), 2.47-2.52 (m, 2H, -CH ₂ - N).
13c*		ESI (<i>m/z</i>): [M+H] ⁺ 391.2. HRESIMS <i>m/z</i> : 391.1021 (M ⁺ +H, calcd for C ₁₉ H ₂₄ BrN ₂ O ₂ , 391.0943).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.92-7.55 (m, 9H, ArH), 3.97-3.99 (m, 2H, - OCH ₂ -), 3.87 (brs, 1H, -CH- OH), 2.93 (brs, 4H, piperazinyl right H), 2.61 (brs, 4H, piperazinyl left H), 2.51 (m, 2H, -CH ₂ -N).
14d		ESI (<i>m/z</i>): [M+H] ⁺ 411.2. HRESIMS <i>m/z</i> : 411.1244 (M ⁺ +H, calcd for C ₂₀ H ₂₅ Cl ₂ N ₂ O ₃ , 411.1164).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.77-7.51 (m, 7H, ArH), 4.03-4.06 (m, 1H, -CH- OH), 3.97-4.02 (m, 2H, - OCH ₂ -), 3.65 (s, 3H, - OCH ₃), 2.95 (brs, 4H, piperazinyl right H), 2.52- 2.57 (m, 4H, piperazinyl left H), 2.50 (brs, 2H, -CH ₂ -N).
15d*		ESI (<i>m/z</i>): [M+H] ⁺ 475.3. HRESIMS <i>m/z</i> : 475.0962 (M ⁺ +H, calcd for C ₂₁ H ₂₆ Cl ₂ N ₂ O ₄ , 475.088).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.71-7.48 (m, 5H, ArH), 4.03-4.05 (m, 1H, -CH- OH), 3.96-3.98 (m, 2H, - OCH ₂ -), 3.79 (s, 6H, - OCH ₃ ×2), 2.83 (brs, 4H, piperazinyl right H), 2.54 (m, 4H, piperazinyl left H), 2.50 (brs, 2H, -CH ₂ -N).
16d*		ESI (<i>m/z</i>): [M+H] ⁺ 441.3. HRESIMS <i>m/z</i> : 441.1350 (M ⁺ +H, calcd for C ₂₁ H ₂₇ Cl ₂ N ₂ O ₄ , 441.127).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.38-7.49 (m, 6H, ArH), 4.04-4.05 (m, 1H, -CH- OH), 3.98 (brs, 2H, -OCH ₂ -), 3.72 (s, 3H, -OCH ₃), 3.67 (s, 3H, -OCH ₃), 2.82 (brs, 4H, piperazinyl right H), 2.54 (m, 4H, piperazinyl left H), 2.50 (brs, 2H, -CH ₂ -N).
17d*		ESI (<i>m/z</i>): [M+H] ⁺ 475.3. HRESIMS <i>m/z</i> : 475.0959 (M ⁺ + H, calcd for C ₂₁ H ₂₆ Cl ₂ N ₂ O ₄ , 475.088).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.60-7.52 (m, 5H, ArH), 4.05-4.07 (m, 1H, -CH- OH), 3.98-4.00 (m, 2H, - OCH ₂ -), 3.77 (s, 3H, - OCH ₃), 3.72 (s, 3H, -OCH ₃), 2.97 (brs, 4H, piperazinyl right H), 2.56 (brs, 4H, piperazinyl left H), 2.50 (brs,

			2H, -CH ₂ -N).
18d*		ESI (<i>m/z</i>): [M+H] ⁺ 425.3. HRESIMS <i>m/z</i> : 425.1393 (M ⁺ +H, calcd for C ₂₁ H ₂₇ Cl ₂ N ₂ O ₃ , 425.132).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.82-7.51 (m, 7H, ArH), 3.94-3.99 (m, 4H, - OCH ₂ -x2), 4.04-4.06 (brs, 1H, -CH-OH), 2.94 (brs, 4H, piperazinyl right H), 2.57 (brs, 4H, piperazinyl left H), 2.43 (m, 2H, -CH ₂ -N), 1.30 (t, 3H, -CH ₃).
19d*		ESI (<i>m/z</i>): [M+H] ⁺ 409.3. HRESIMS <i>m/z</i> : 409.1442 (M ⁺ +H, calcd for C ₂₁ H ₂₇ Cl ₂ N ₂ O ₂ , 409.1371).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.83-7.53 (m, 6H, ArH), 4.05-4.07 (m, 1H, -CH- OH), 3.99-4.00 (m, 2H, - OCH ₂ -), 2.75 (brs, 4H, piperazinyl right H), 2.56 (brs, 4H, piperazinyl left H), 2.46 (brs, 2H, -CH ₂ -N), 2.17 (s, 3H, -CH ₃), 2.12 (s, 3H, - CH ₃).
20d*		ESI (<i>m/z</i>): [M+H] ⁺ 409.3. HRESIMS <i>m/z</i> : 409.1453 (M ⁺ +H, calcd for C ₂₁ H ₂₇ Cl ₂ N ₂ O ₂ , 409.1371).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.83-7.50 (m, 6H, ArH), 4.04-4.06 (m, 1H, -CH- OH), 3.97-4.01 (m, 2H, - OCH ₂ -), 2.73 (brs, 4H, piperazinyl right H), 2.55 (brs, 4H, piperazinyl left H), 2.44 (brs, 2H, -CH ₂ -N), 2.16 (s, 3H, -CH ₃), 2.15 (s, 3H, - CH ₃).
21d*		ESI (<i>m/z</i>): [M+H] ⁺ 415.2. HRESIMS <i>m/z</i> : 415.0752 (M ⁺ +H, calcd for C ₁₉ H ₂₂ Cl ₃ N ₂ O ₂ , 415.0669).	¹ H NMR (500 MHz, DMSO), δ (ppm): 7.00-7.53 (m, 7H, ArH), 4.05-4.07 (m, 1H, -CH- OH), 3.99 (brs, 2H, -OCH ₂ -), 2.94 (brs, 4H, piperazinyl right H), 2.61 (brs, 4H, piperazinyl left H), 2.55 (brs, 2H, -CH ₂ -N).
22d*		ESI (<i>m/z</i>): [M+H] ⁺ 449.1. HRESIMS <i>m/z</i> : 449.0364 (M ⁺ + H, calcd for C ₁₉ H ₂₁ Cl ₄ N ₂ O ₂ , 449.0279).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.83-7.47 (m, 6H, ArH), 4.03-4.04 (m, 1H, -CH- OH), 3.97-4.02 (m, 2H, - OCH ₂ -), 3.10 (brs, 4H, piperazinyl right H), 2.54 (brs, 4H, piperazinyl left H), 2.44 (brs, 2H, -CH ₂ -N).
23d*		ESI (<i>m/z</i>): [M+H] ⁺ 461.1. HRESIMS <i>m/z</i> : 461.0223 (M ⁺ +H, calcd for C ₁₉ H ₂₂ BrCl ₂ N ₂ O ₂ , 461.1922).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.81-7.49 (m, 7H, ArH), 4.02-4.05 (m, 2H, - OCH ₂ -), 3.96-4.01 (m, 1H, - CH-OH), 3.05-3.06 (brs, 4H, piperazinyl right H), 2.55- 2.56 (m, 4H, piperazinyl left H), 2.50 (brs, 2H, -CH ₂ -N).

24e		ESI (<i>m/z</i>): [M+H] ⁺ 419.3. HRESIMS <i>m/z</i> : 419.2340 (M ⁺ +H, calcd for C ₂₆ H ₃₁ N ₂ O ₃ , 419.2256).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.85-7.59 (m, 13H, ArH), 4.00-4.04 (m, 4H, - OCH ₂ -), 3.90-3.93 (m, 1H, - CH-OH), 3.74 (s, 3H, - OCH ₃), 2.94 (brs, 4H, piperazinyl right H), 2.59 (brs, 4H, piperazinyl left H), 2.44 (m, 2H, -CH ₂ -N).
25e		ESI (<i>m/z</i>): [M+H] ⁺ 419.3. HRESIMS <i>m/z</i> : 419.2235 (M ⁺ +H, calcd for C ₂₆ H ₃₁ N ₂ O ₃ , 419.2256).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.80-7.62 (m, 13H, ArH), 4.00-4.06(m, 2H, - OCH ₂ -), 3.92-3.95 (m, 1H, - CH-OH), 3.67 (s, 3H, - OCH ₃), 3.00-3.02 (m, 4H, piperazinyl right H), 2.56- 2.65 (brs, 4H, piperazinyl left H), 2.41-2.45 (m, 2H, -CH ₂ - N).
26e*		ESI (<i>m/z</i>): [M+H] ⁺ 449.3. HRESIMS <i>m/z</i> : 449.2440 (M ⁺ +H, calcd for C ₂₇ H ₃₃ N ₂ O ₄ , 449.2362).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.39-7.59 (m, 12H, ArH), 4.00-4.03 (m, 2H, - OCH ₂ -), 3.89-3.92 (m, 1H, - CH-OH), 3.72 (s, 3H, - OCH ₃), 3.67 (s, 3H, -OCH ₃), 3.61 (s, 2H, -CH ₂ -N), 2.85 (brs, 4H, piperazinyl right H), 2.56 (brs, 4H, piperazinyl left H).
27e*		ESI (<i>m/z</i>): [M+H] ⁺ 483.3. HRESIMS <i>m/z</i> : 483.2049 (M ⁺ +H, calcd for C ₂₇ H ₃₂ BrN ₂ O ₄ Cl, 483.1972).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.73-7.59 (m, 11H, ArH), 3.99-4.02 (m, 2H, - OCH ₂ -), 3.89-3.92 (m, 1H, - CH-OH), 3.80 (s, 6H, - OCH ₃ ×2), 2.85 (brs, 4H, piperazinyl right H), 2.56 (brs, 4H, piperazinyl left H), 2.44 (brs, 2H, -CH ₂ -N).
28e*		ESI (<i>m/z</i>): [M+H] ⁺ 433.3. HRESIMS <i>m/z</i> : 433.2497 (M ⁺ +H, calcd for C ₂₇ H ₃₃ N ₂ O ₃ , 433.2413).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.84-7.59 (m, 13H, ArH), 3.94-4.03 (m, 4H, - OCH ₂ -×2), 3.91-3.93 (m, 1H, -CH-OH), 2.96 (brs, 4H, piperazinyl right H), 2.59 (brs, 4H, piperazinyl left H), 2.44 (m, 2H, -CH ₂ -N), 1.31 (t, 3H, -CH ₃).
29e*		ESI (<i>m/z</i>): [M+H] ⁺ 477.4. HRESIMS <i>m/z</i> : 477.2755 (M ⁺ +H, calcd for C ₂₉ H ₃₇ N ₂ O ₄ , 477.2675).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.37-7.58 (m, 12H, ArH), 4.01-4.03 (m, 2H, - OCH ₂ -), 3.85-3.92 (m, 4H, - OCH ₂ CH ₃ ×2), 3.64 (s, 2H, - CH ₂ -N), 2.96 (brs, 4H, piperazinyl right H), 2.57 (brs, 4H, piperazinyl left H), 2.40-2.43 (m, 1H, -CH-OH),

			1.24-1.27 (m, -6H, -CH ₃ ×2).
30e		ESI (<i>m/z</i>): [M+H] ⁺ 417.3. HRESIMS <i>m/z</i> : 417.2543 (M ⁺ +H, calcd for C ₂₇ H ₃₃ N ₂ O ₂ , 417.2464).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.88-7.61 (m, 12H, ArH), 4.01-4.07 (m, 2H, -OCH ₂ -), 3.92-3.95 (m, 1H, -CH-OH), 2.79 (brs, 4H, piperazinyl right H), 2.60 (brs, 4H, piperazinyl left H), 2.43-2.52 (m, 2H, -CH ₂ -N), 2.19 (s, 6H, -CH ₃ ×2).
31e*		ESI (<i>m/z</i>): [M+H] ⁺ 417.3. HRESIMS <i>m/z</i> : 417.2546 (M ⁺ +H, calcd for C ₂₇ H ₃₃ N ₂ O ₂ , 417.2464).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.82-7.59 (m, 12H, ArH), 4.01-4.04 (m, 2H, -OCH ₂ -), 3.90-3.93 (m, 1H, -CH-OH), 2.76 (brs, 4H, piperazinyl right H), 2.60 (brs, 4H, piperazinyl left H), 2.43-2.50 (m, 2H, -CH ₂ -N), 2.17 (s, 3H, -CH ₃), 2.11 (s, 3H, -CH ₃).
32e*		ESI (<i>m/z</i>): [M+H] ⁺ 457.3. HRESIMS <i>m/z</i> : 457.1451 (M ⁺ +H, calcd for C ₂₅ H ₂₇ Cl ₂ N ₂ O ₂ , 457.1371).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.89-7.60 (m, 12H, ArH), 4.01-4.04 (m, 2H, -OCH ₂ -), 3.90-3.93 (m, 1H, -CH-OH), 3.15 (brs, 4H, piperazinyl right H), 2.57 (m, 4H, piperazinyl left H), 2.40-2.52 (m, 2H, -CH ₂ -N).
33e*		ESI (<i>m/z</i>): [M+H] ⁺ 467.2. HRESIMS <i>m/z</i> : 467.1334 (M ⁺ +H, calcd for C ₂₅ H ₂₈ BrN ₂ O ₂ , 467.1256).	¹ H NMR (500 MHz, DMSO), δ (ppm): 6.94-7.60 (m, 13H, ArH), 4.00-4.05 (m, 2H, -OCH ₂ -), 3.91-3.93 (m, 1H, -CH-OH), 2.95 (brs, 4H, piperazinyl right H), 2.63 (brs, 4H, piperazinyl left H), 2.43-2.52 (m, 2H, -CH ₂ -N).
34e*		ESI (<i>m/z</i>): [M+H] ⁺ 467.1. HRESIMS <i>m/z</i> : 467.1334 (M ⁺ +H, calcd for C ₂₅ H ₂₈ BrN ₂ O ₂ , 467.1256).	¹ H NMR (500 MHz, CDCl ₃), δ (ppm): 6.79-7.56 (m, 13H, ArH), 4.15-4.19 (m, 1H, -CH-OH), 4.06-4.07 (m, 2H, -OCH ₂ -), 3.18-3.21 (m, 4H, piperazinyl right H), 2.83-2.87 (m, 2H, -CH ₂ -N), 2.60-2.70 (m, 4H, piperazinyl left H).

19 **Note: Structures with * are novel compounds.**

20

21

22

23

24 **Table S2. PCR primers used in this study**

Primer	Sequence (5'-3')
GSP1-F ^a	TGAAGTCCATCCATTAGGAT
GSP1-R	ATCTCTATGCCAGTTTGGAA
RAS1-F	GGCCATGAGAGAACAATATA
RAS1-R	GTCTTTCCATTTCTAAATCAC
CDC35-F	TTCATCAGGGGTTATTTTAC
CDC35-R	CTCTATCAACCCGCCATTTT
PDE2-F	ACCACCACCACTACTACTAC
PDE2-R	AAAATGAGTTGTTCTGTCC
EFG1-F	TATGCCCCAGCAAACAACCTG
EFG1-R	TTGTTGTCCTGCTGTCTGTC
TEC1-F	AGGTTCCCTGGTTTAAGTG
TEC1-R	ACTGGTATGTGTGGGTGAT
CST20-F	TTCTGACTTCAAAGACATCAT
CST20-R	AATGTATATTTCTGGTGGTG
HST7-F	ACTCCAACATCCAATATAACA
HST7-R	TTGATTGACGTTCAATGAAGA
CEK1-F	AGCTATACAACGACCAATTAA
CEK1-R	CATTAGCTGAATGCATAGCT
CPH1-F	ATGCAACACTATTTATACCTC
CPH1-R	CGGATATTGTTGATGATGATA
ALS3-F	CTAATGCTGCTACGTATAATT

ALS3-R	CCTGAAATTGACATGTAGCA
HWP1-F	TGGTGCTATTACTATTCCGG
HWP1-R	CAATAATAGCAGCACCGAAG
ECE1-F	GCTGGTATCATTGCTGATAT
ECE1-R	TTCGATGGATTGTTGAACAC

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

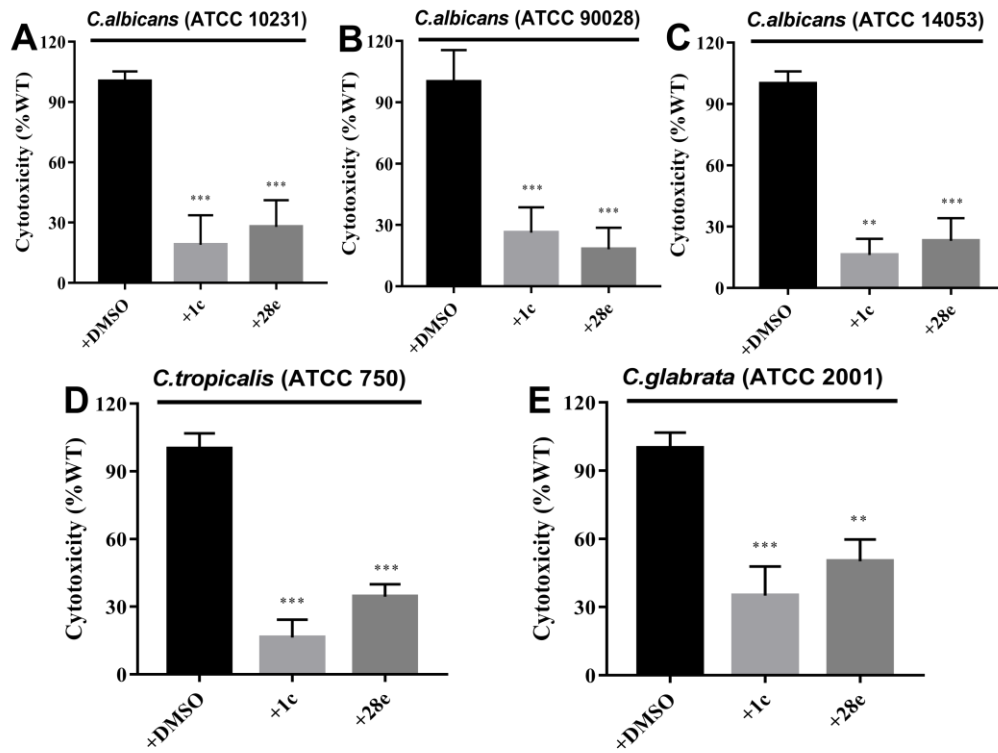
40

41

42

43

44



45

46 **Fig. S1.** Effects of piperazine derivatives on different clinic isolated *C. albicans* strains and other
 47 *Candida* species virulence using a cell line. Cytotoxicity assays were performed with the same
 48 methods as used in Fig 4B. The final concentration of compound 1c and 28e was 100 μ M for the
 49 treatment of five strains. Data are the mean \pm standard deviation of three independent experiments.

50 *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$ (unpaired t test).

51

52

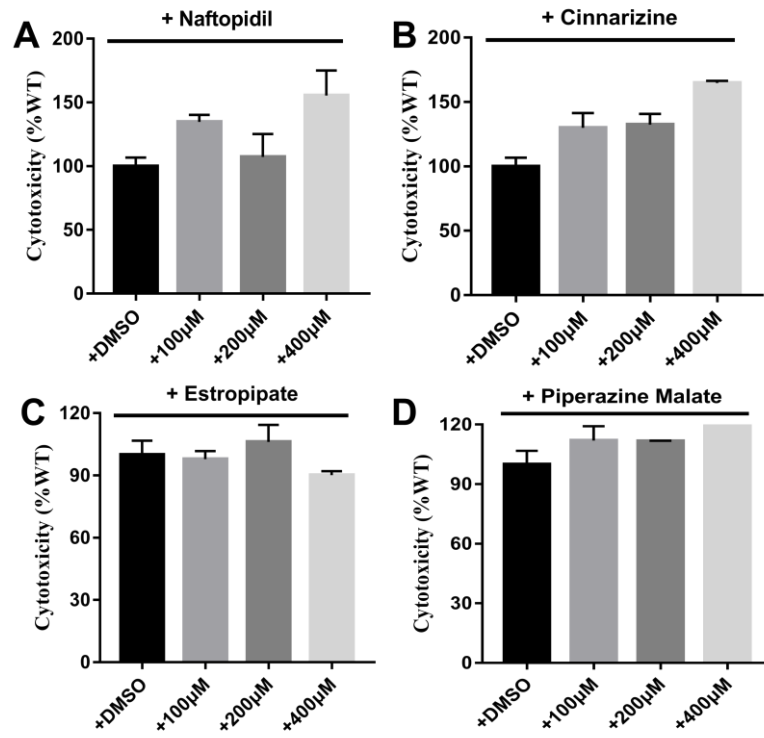
53

54

55

56

57



58

59 **Fig. S2.** Influences of different piperazine compounds on *C. albicans* SC5314 virulence using a cell
 60 line. Data are the mean \pm standard deviation of three independent experiments.

61