

Supplementary Materials

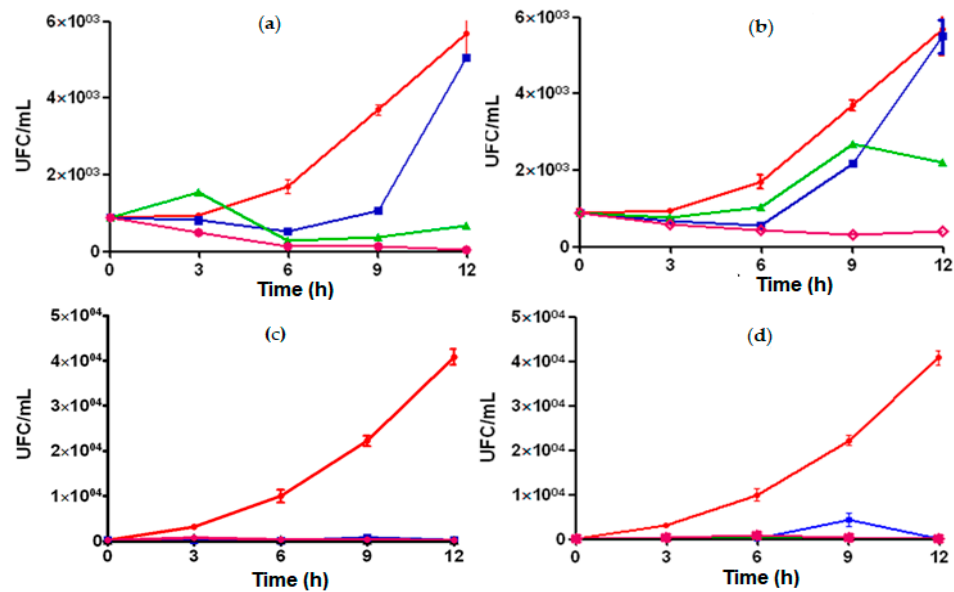


Figure S1. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with simvastatin and fluconazole. The yeasts (2x10⁴ cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μM (fushia lines) of simvastatin (a,c) and fluconazole (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

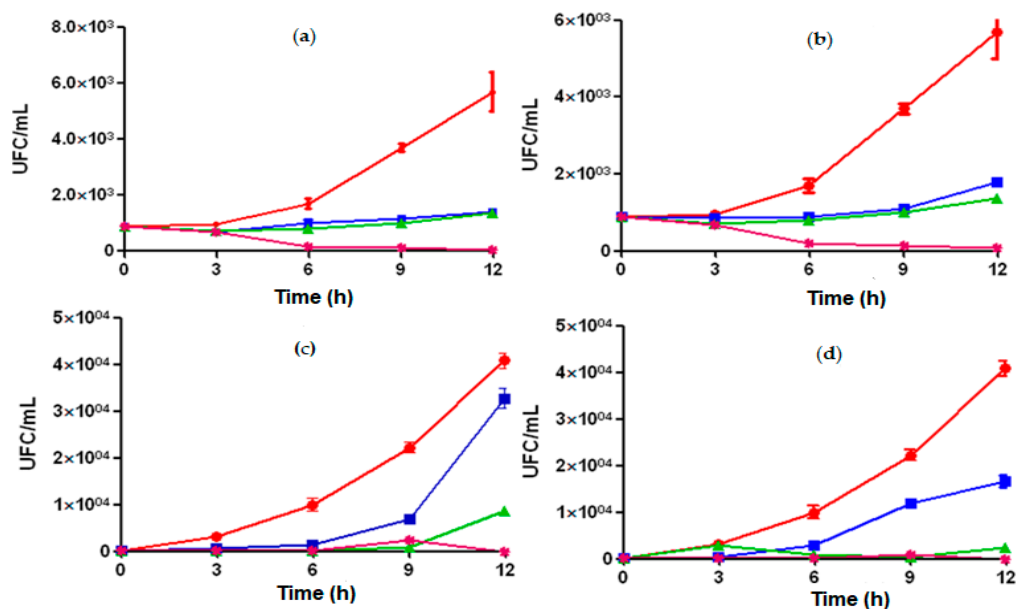


Figure S2. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 1a and 1b. The yeasts (2x10⁴ cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μM (fushia lines) of 1a (a,c) and 1b (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

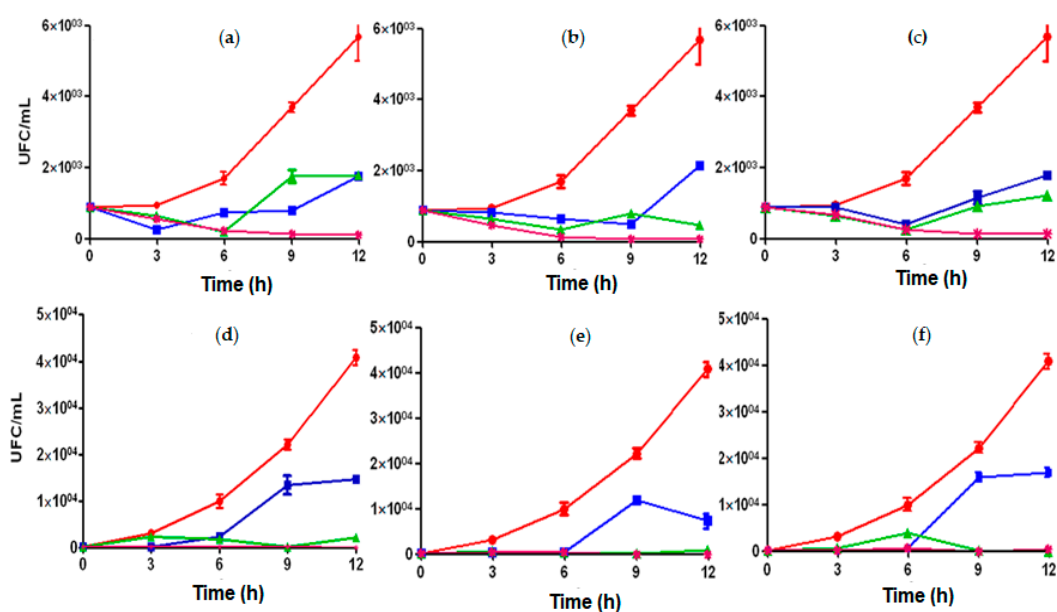


Figure S3. Growth inhibition of *C. glabrata* (a-c) and *C. albicans* (d-f) with 2a, 2b and 2c. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 2a (a,d), 2b (b,e) and 2c (c,f) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

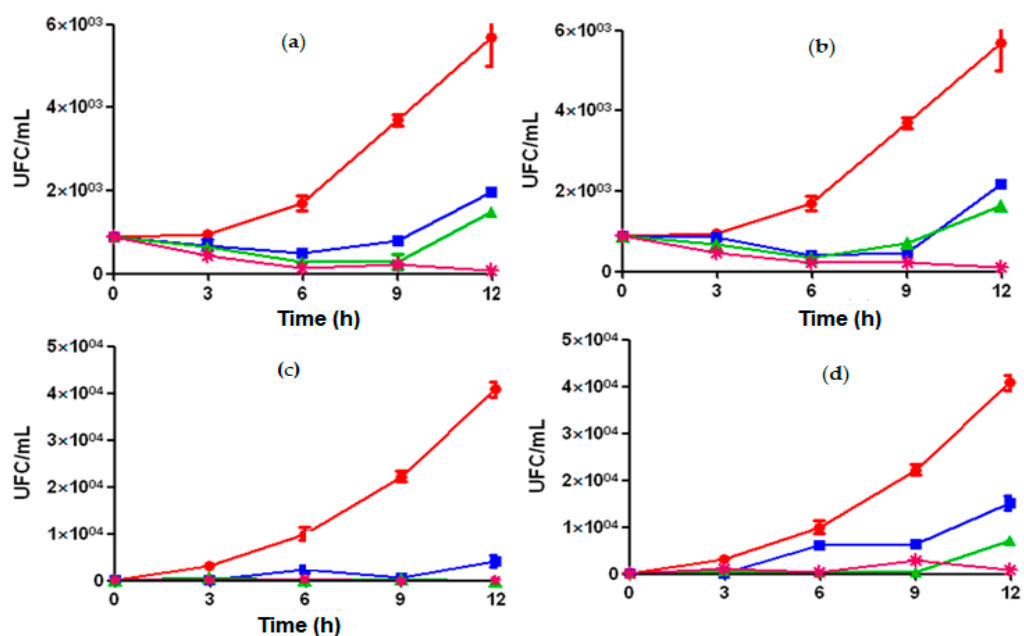


Figure S4. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 3a and 3b. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 3a (a,c) and 3b (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

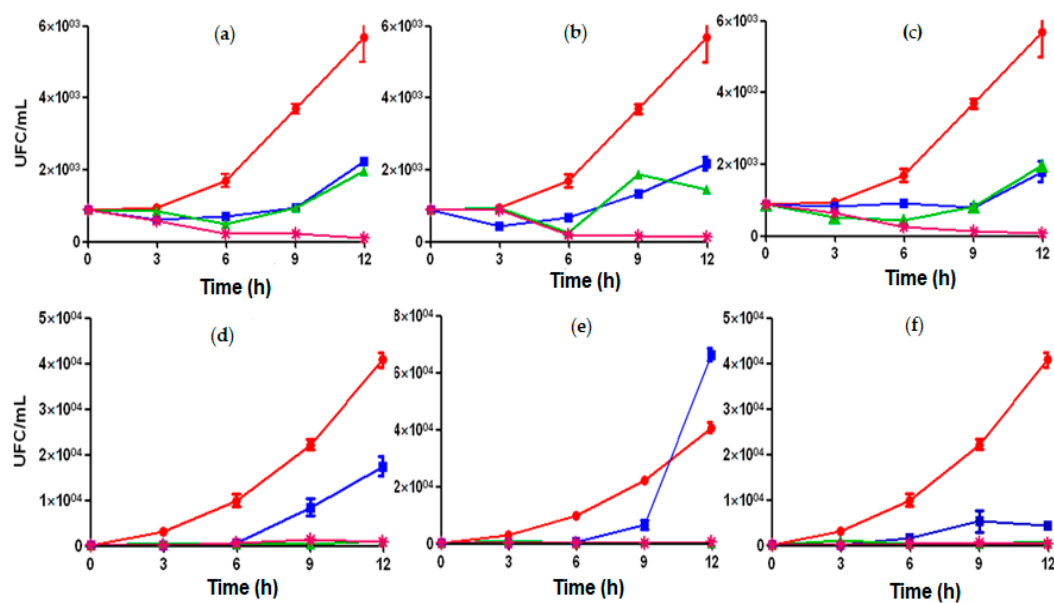


Figure S5. Growth inhibition of *C. glabrata* (a-c) and *C. albicans* (d-f) with 4a, 4b and 4c. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 4a (a,d), 4b (b,e) and 4c (c,f) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

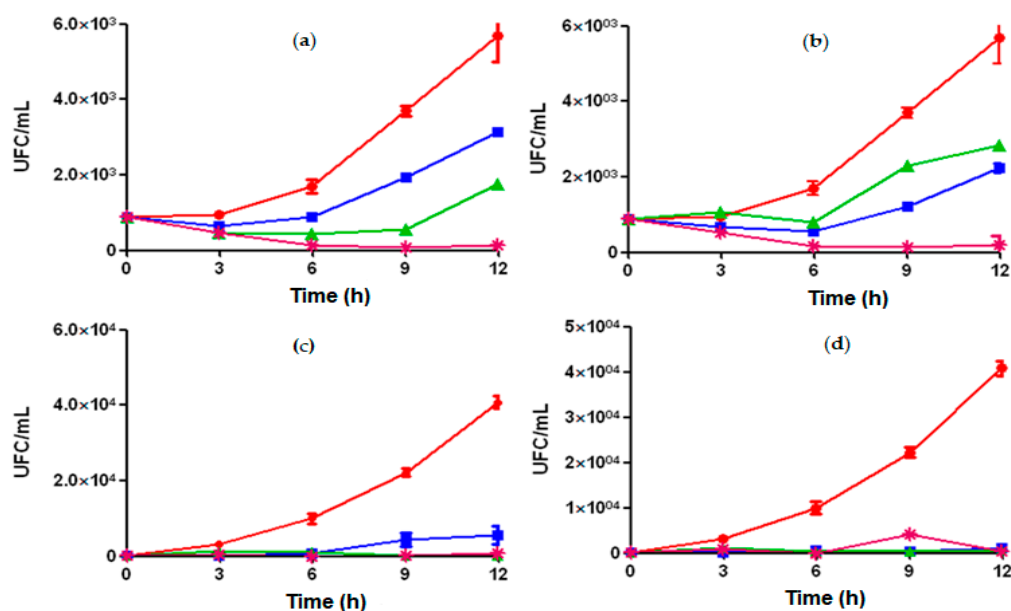


Figure S6. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 5a and 5b. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 5a (a,c) and 5b (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

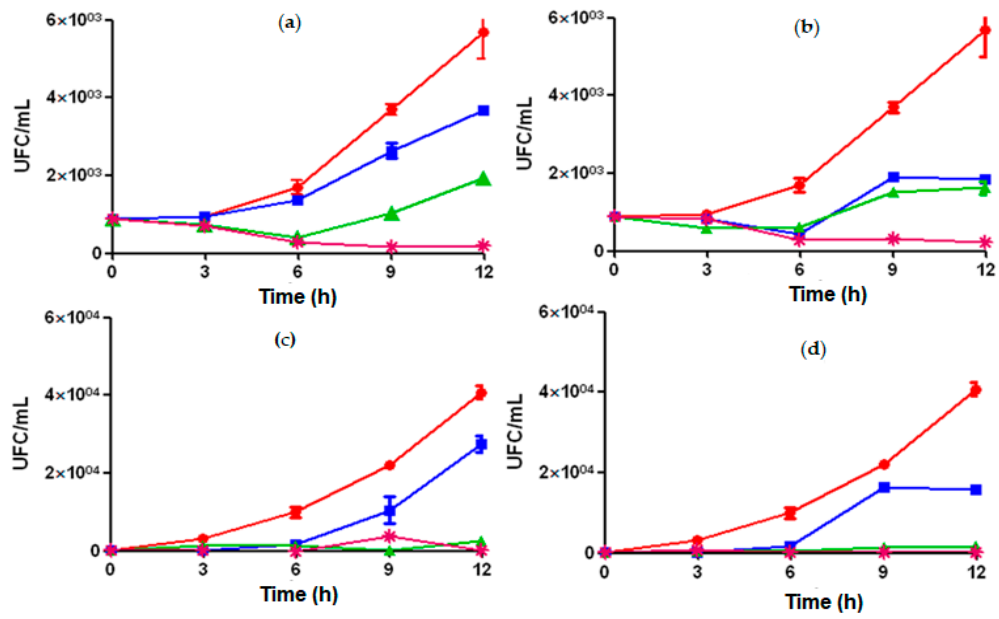


Figure S7. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 6a and 6b. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 6a (a,c) and 6b (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

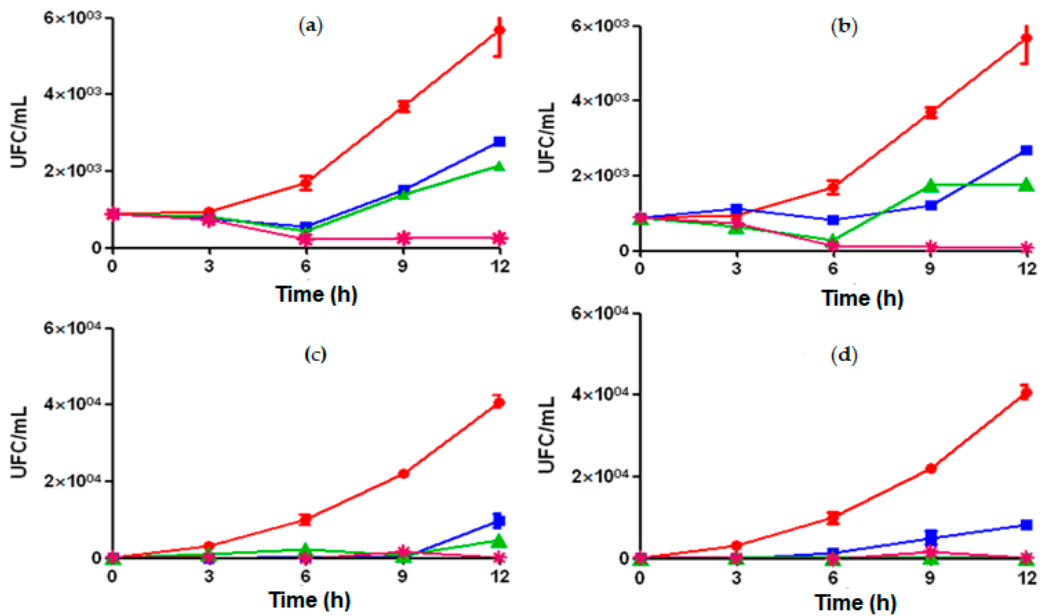


Figure S8. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 6c and 6d. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 6c (a,c) and 6d (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

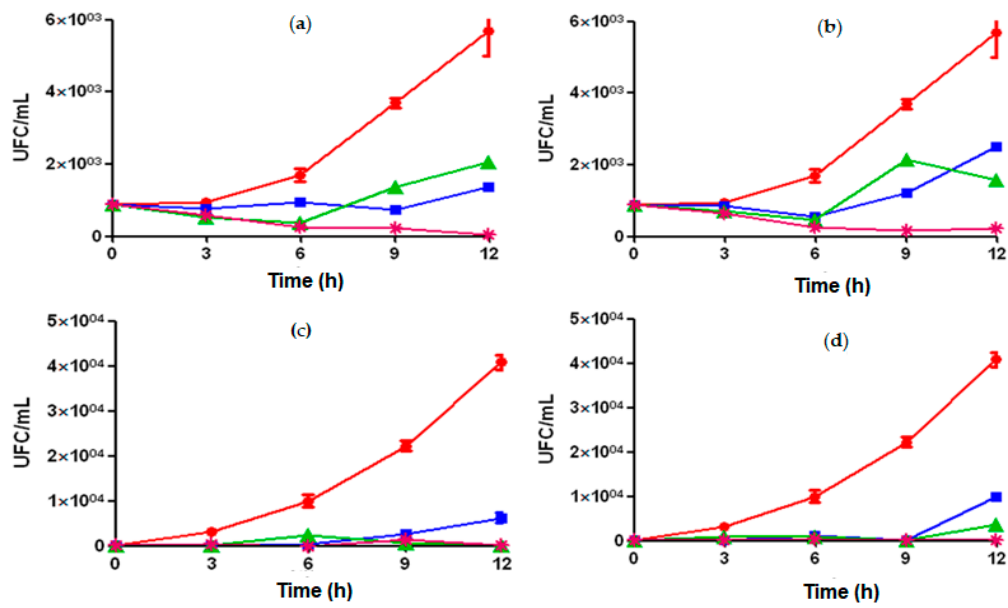


Figure S9. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 6e and 6f. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 6e (a,c) and 6f (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

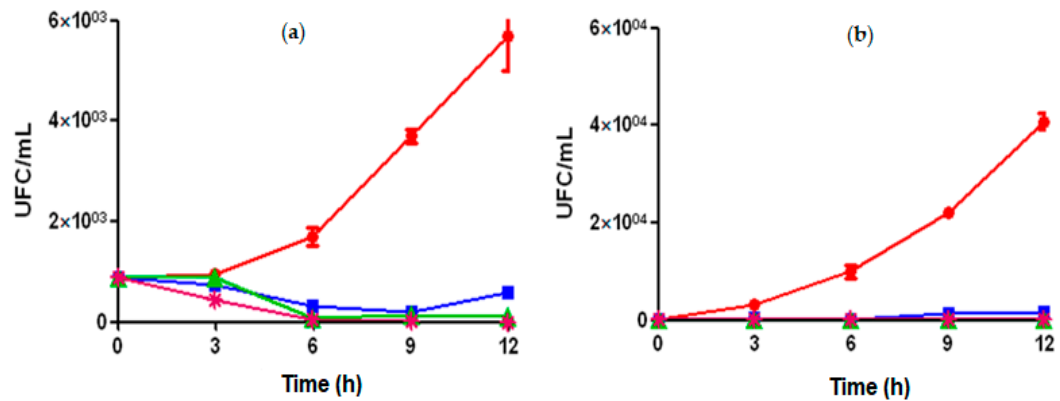


Figure S10. Growth inhibition of *C. glabrata* (a) and *C. albicans* (b) with 6g. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 6g (a,b) 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

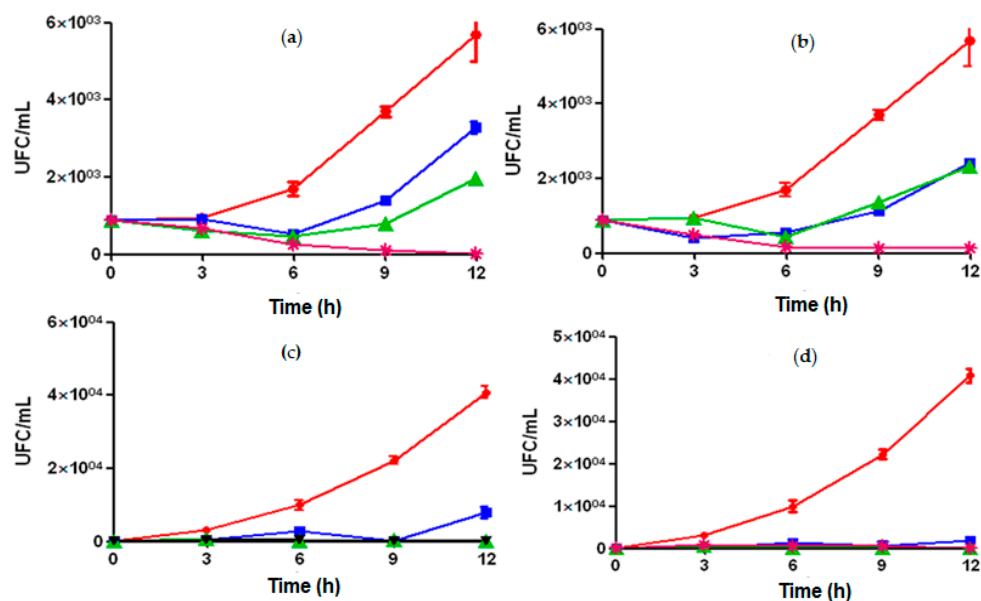


Figure S11. Growth inhibition of *C. glabrata* (a-b) and *C. albicans* (c-d) with 7a and 7b. The yeasts (2×10^4 cells/mL) were grown in absence (red lines) and presence of 100 (blue lines), 300 (green lines) and 600 μ M (fushia lines) of 6e (a,c) and 6f (b,d) for 3, 6, 9 and 12 h at 37 °C. After treatment, they were inoculated on YPD agar plates and incubated for 24 h to determine the number of UFC/mL.

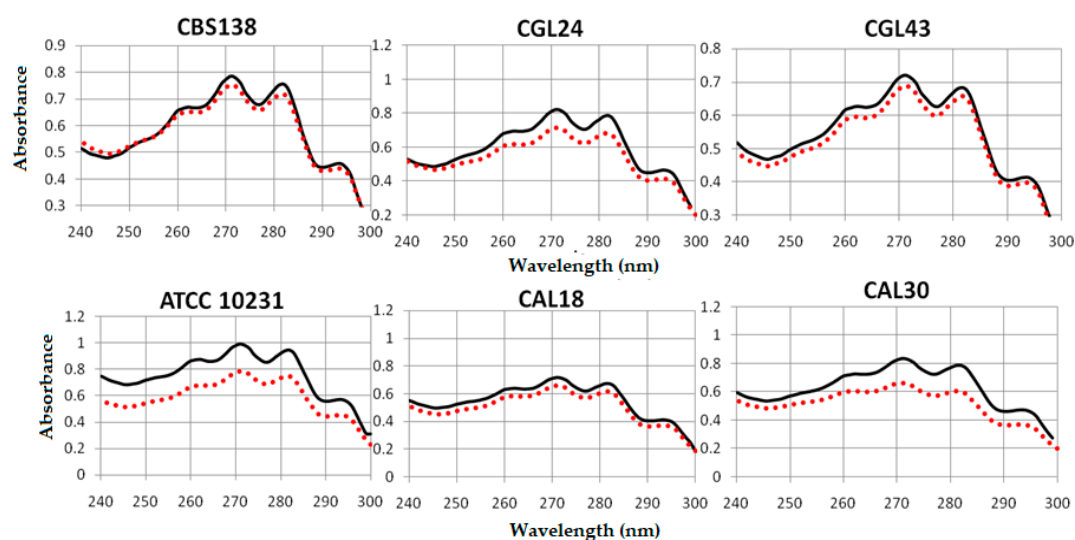


Figure S12. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without simvastatin (black line) and with 100 μ M of simvastatin (res dashed line). Followed by ethanolic extraction with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the "x" axes and the wavelengths (nm) in the absorption spectrum on the "y" axes.

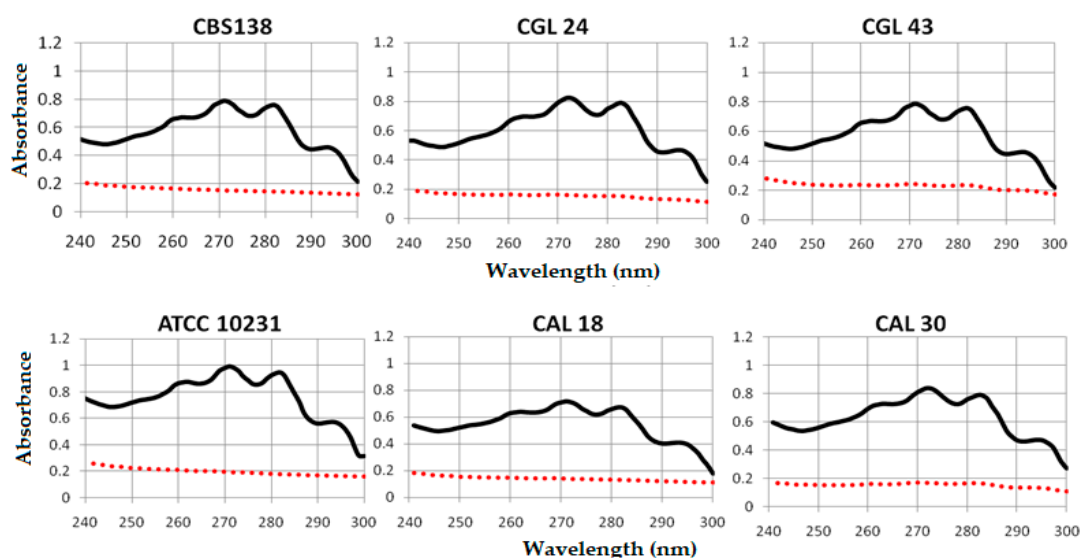


Figure S13. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without fluconazole (black line) and with 100 μ M of fluconazol (red dashed line). Followed by ethanolic extraction with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass.

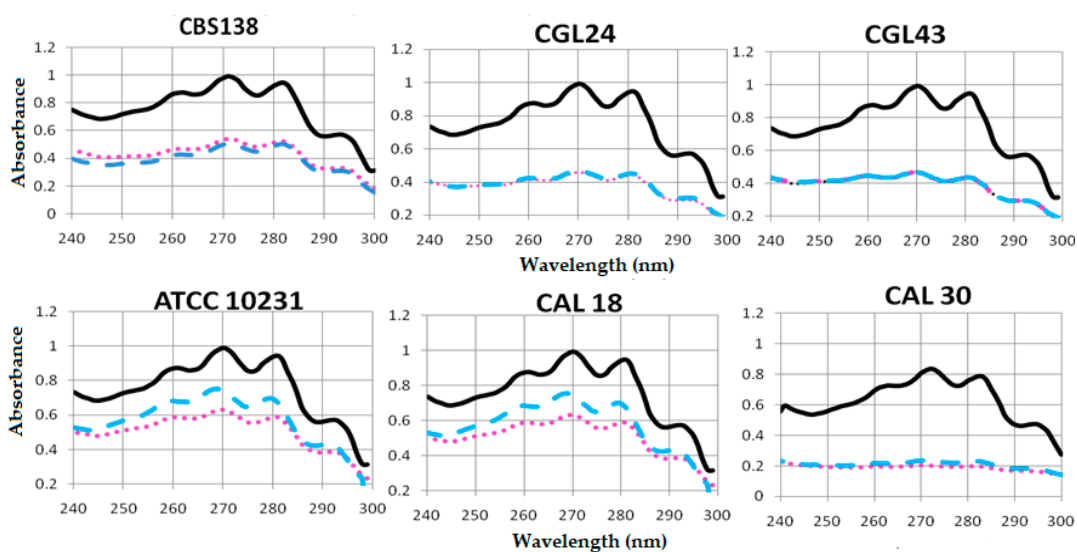


Figure S14. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 1a (fushia dashed line) and of 1b (blue dashed line). Followed by ethanolic extraction with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the "x" axes and the wavelengths (nm) in the absorption spectrum on the "y" axes.

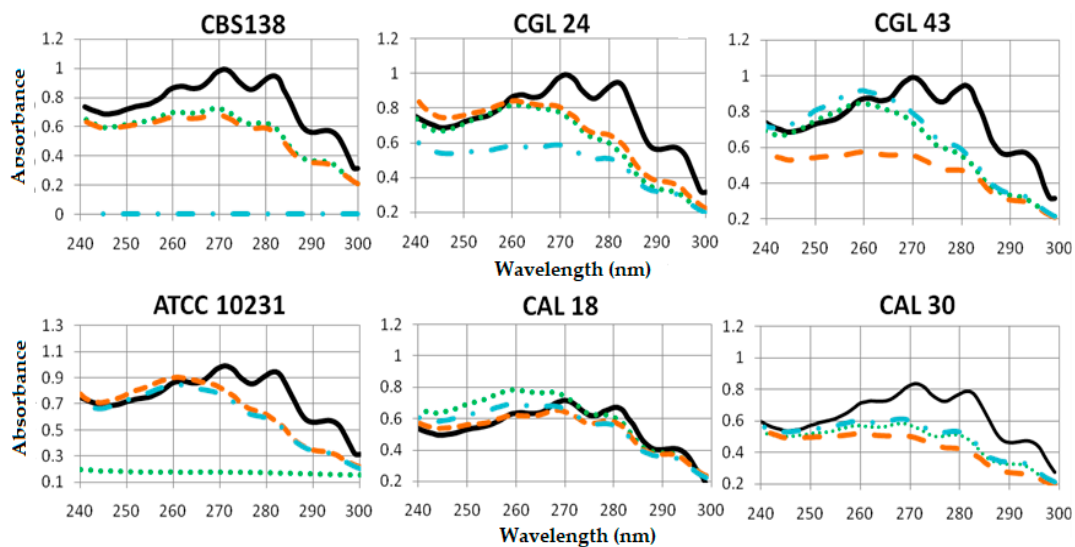


Figure S15. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 2a (green line) , 2b (orange dashed line) and of 2c (blue dashed line). Followed by ethanolic extraction with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the “x” axes and the wavelengths (nm) in the absorption spectrum on the “y” axes.

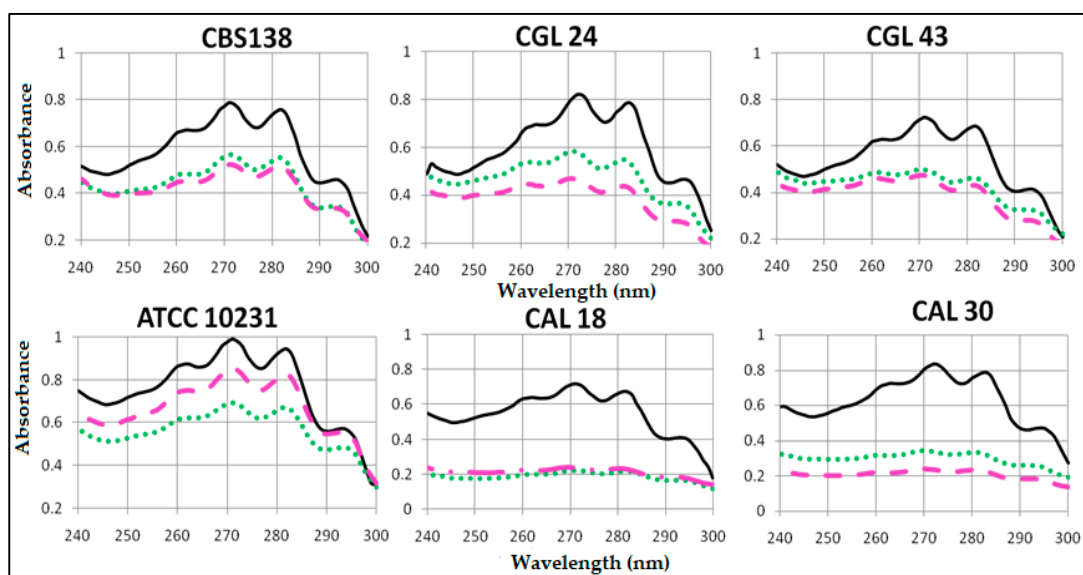


Figure S16. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 3a (green line) and 3b (fushia dashed line). Followed by ethanolic extracción with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the “x” axes and the wavelengths (nm) in the absorption spectrum on the “y” axes.

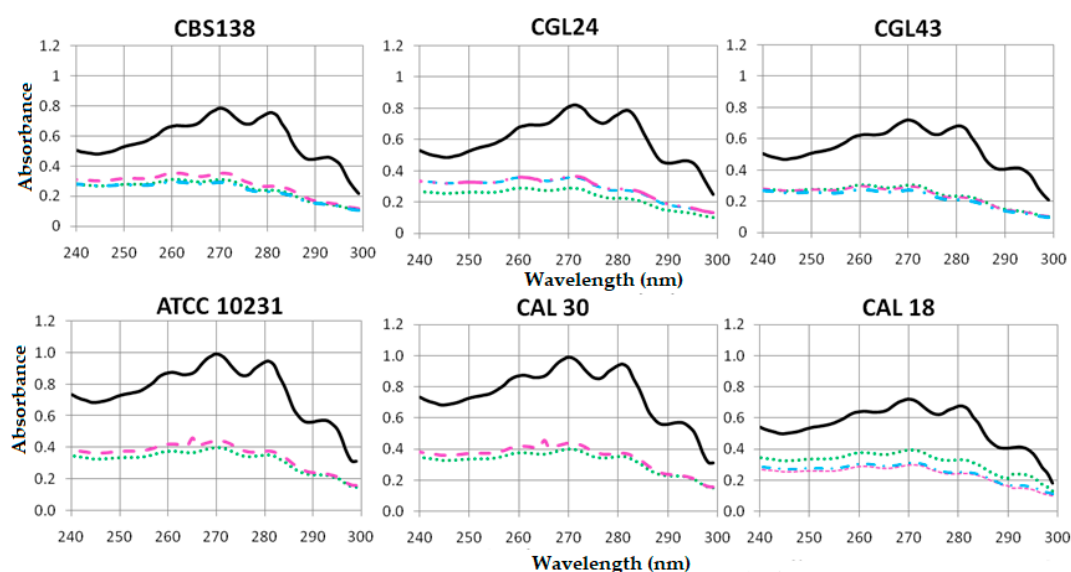


Figure S17. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 4a (green dashed line), 4b (fushia dashed line) and 4c (blue dashed line). Followed by ethanolic extracción with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the “x” axes and the wavelengths (nm) in the absorption spectrum on the “y” axes.

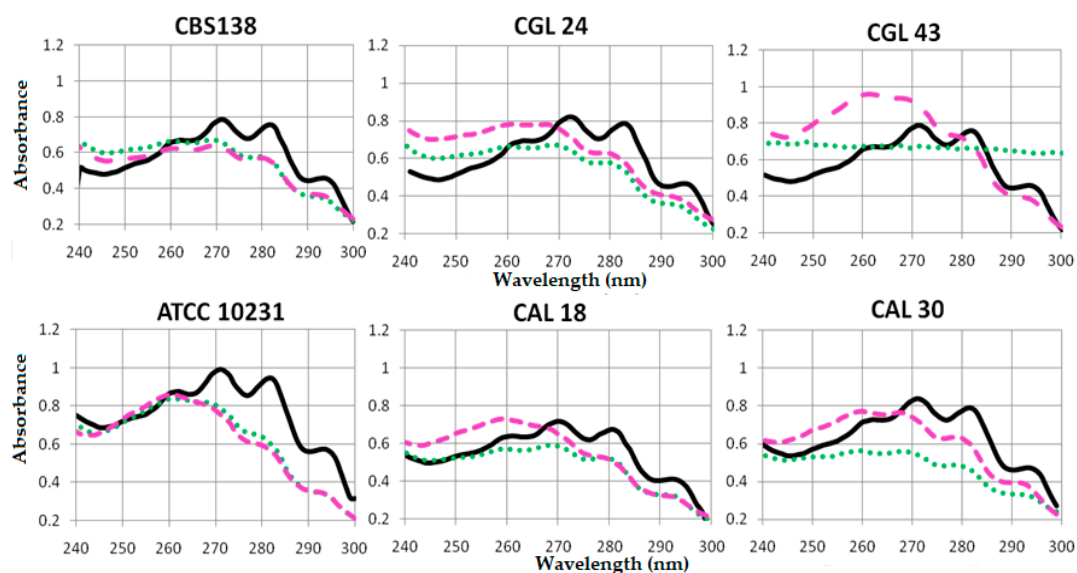


Figure S18. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 5a (green dashed line) and 5b (fushia dashed line). Followed by ethanolic extracción with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the “x” axes and the wavelengths (nm) in the absorption spectrum on the “y” axes.

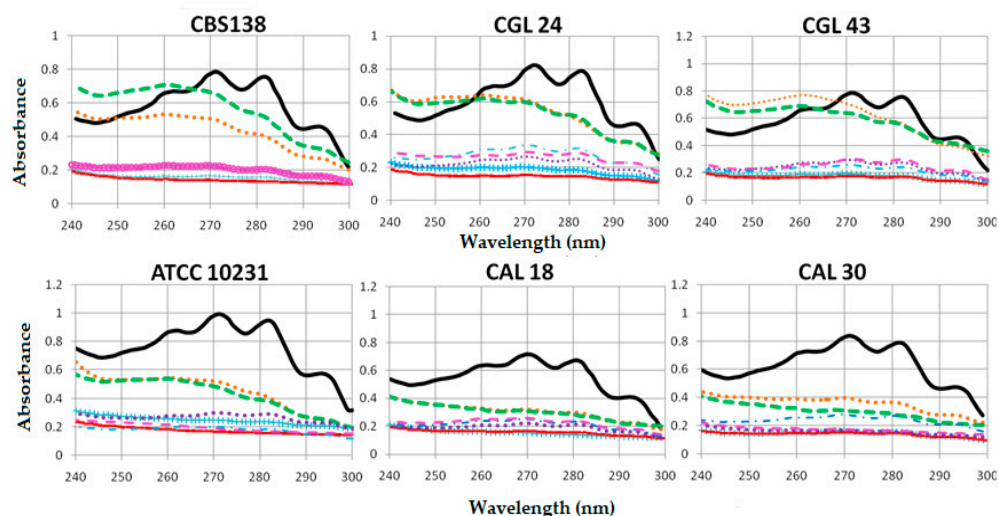


Figure S19. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 6a (orange dashed line), 6b (green dashed line), 6c (light blue dashed line), 6d (red dashed line), 6e (purple dashed line), 6f (dark blue dashed line) and 6g (fushia dashed line). Followed by ethanolic extracción with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the “x” axes and the wavelengths (nm) in the absorption spectrum on the “y” axes.

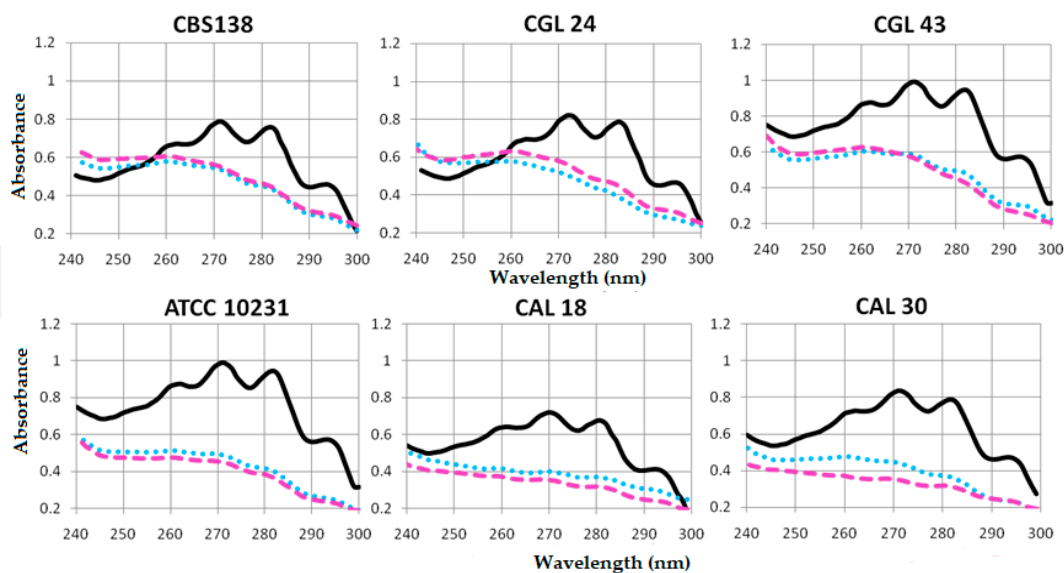


Figure S20. Reduction in ergosterol levels with simvastatin. The strains of *C. glabrata* (CBS, CGL24 and CGL43) and *C. albicans* (ATCC10231 CAL18 and CAL30) were grown in YNB without compound (black line) and with 100 μ M of 7a (blue dashed line) and 7b (fushia dashed line). Followed by ethanolic extracción with KOH, the fraction corresponding to sterols was scanned from 240 to 300 nm. The quantities taken correspond to equal cell mass. The graph shows the absorbance values on the “x” axes and the wavelengths (nm) in the absorption spectrum on the “y” axes.

Table S1. Calculated physicochemical properties of simvastatin, fluconazole, a-asarone, and the series of test compounds 1a–b, 2a–c, 3a–b, 4a–c, 5a–b, 6a–g, and 7a–b.

Compound	MW(g/mol)	Log P	Log S	HA	HD
Simvastatin	418.572	4.4608	-4.75	5	1
Fluconazole	306.275	-0.1089	-2.175	7	1
a-asarone	212.288	1.6008	-1.545	3	0
1a	283.279	1.3698	-2.788	7	0
1b	254.281	1.9457	-2.032	5	1
2a	193.245	1.9329	-2.636	3	1
2b	194.229	2.2645	-2.264	3	1
2c	212.675	3.2162	-3.296	2	0
3a	238.326	3.5723	-2.983	3	0
3b	224.299	3.1179	-2.713	2	0
4a	236.266	2.1059	-2.267	4	0
4b	267.236	0.7564	-2.599	7	1
4c	250.293	2.5122	-2.567	4	0
5a	345.825	4.0878	-4.337	4	1
5b	345.825	4.15	-4.533	4	1
6a	194.229	1.8977	-2.181	3	0
6b	180.202	1.4914	-1.881	3	0
6c	194.229	1.907	-2.04	3	0
6d	208.256	2.3133	-2.34	3	0
6e	194.229	1.907	-2.04	3	0
6f	222.239	1.425	-2.521	4	0
6g	253.253	1.3917	-2.8	6	0
7a	196.245	2.3878	-2.129	3	1
7b	194.220	2.2023	-2.068	3	1

MW, molecular weight; Log P, partition coefficient; Log S, water solubility; H-A, hydrogen-bond acceptors and H-D, hydrogen-bond donors.

Table S2. Determination of the respiratory capacity of *petite* mutants of *C. glabrata* y *C. albicans* in YPD, YPG and YNB + glycerol. Presence or absence of mitochondrial genes.

Lane	Origin	Growth			Fragment (pb)	Loss DNAm
		YPD	YPG	YNB + Glycerol		
1	Ca6f	+	-	-	-	Total
2	Ca6f	+	-	-	-	Total
3	Ca4c	+	+	+	1250	Partial
4	Ca6g	+	-	-	-	Total
5	Ca6b	+	+	+	-	Partial
6	Ca6b	+	-	-	-	Total
7	Ca6b	+	+	+	-	Partial
8	Ca3a	+	+	+	-	Partial
9	Ca5a	+	+	+	1250, 1000	Partial
10	Ca5a	+	+	+	1250, 1000	Partial
11	Cg2b	+	+	+	-	Total
12	Cg6d	ND	ND	ND	-	ND
13	Cg7a	+	+	-	-	Total
14	Cg2b	+	+	+	+	No loss
16	Cg4b	ND	ND	ND	-	ND
17	Cg5im	+	-	-	1500, 1250, 1000	Partial
18	Cg7a	+	-	-	-	Total
19	Cg3b	+	-	-	-	Total
20	Cg7a	+	-	-	1500, 1250, 1000	Parcial
21	Cg2b	+	+	+	+	No loss
22	Cg6f	+	+	+	+	No loss
23	Cg5im	+	-	-	-	Total
24	Cg5im	ND	ND	ND	-	ND
25	Cg5im	+	-	-	1500	Partial
26	Cg5im	+	-	-	1500, 1250, 1000	Partial
27	Cg5im	+	-	-	1500, 1250	Partial
15	CBS138	+	+	+	1500, 1250, 1000	No loss
28	ATCC10231	+	+	+	1500, 1250, 1000	No loss

+, growth, -, no growth, ND; undetermined