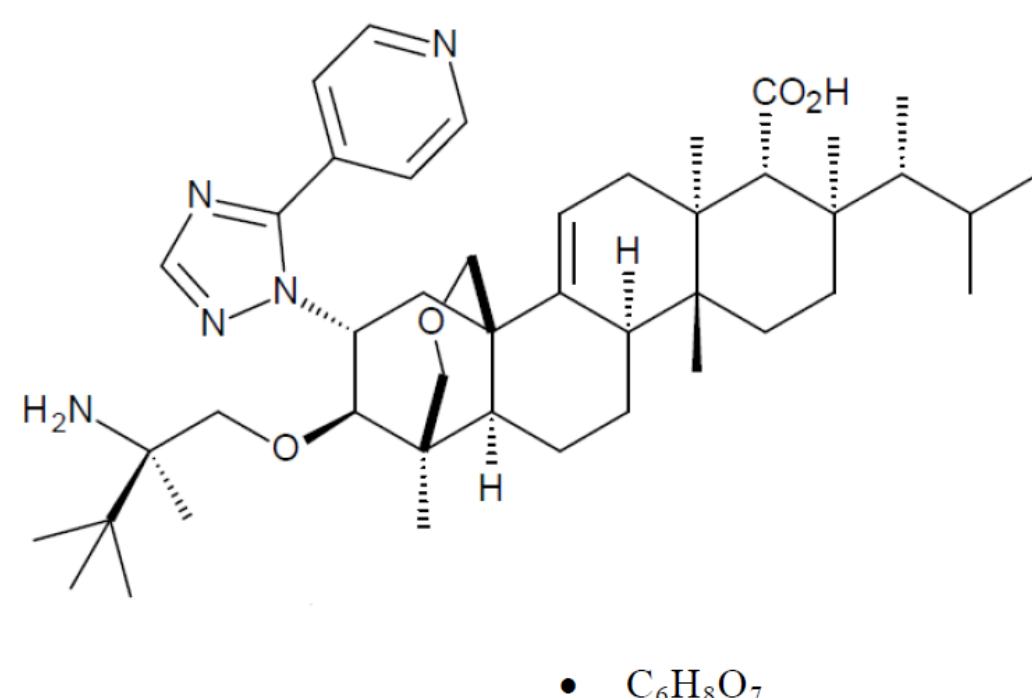


INTRODUCTION

- SCY-078 is an oral and intravenous semi-synthetic triterpenoid antifungal glucan synthase inhibitor, in development for the treatment of invasive and mucocutaneous fungal diseases.



- SCY-078 has fungicidal activity against *Candida*, is available in an oral formulation and exhibits an extensive tissue distribution, making it a suitable candidate for the treatment of vulvovaginal candidiasis (VVC).
- Normal pH of the vagina is between, 4.0 – 4.5, a slightly acidic environment. *In vitro* testing of antifungals are normally performed at a pH of 7.0. Previous studies have found that the test medium pH in *in vitro* susceptibility testing can alter the azole MIC for *Candida* species and that an acidic pH tends to increase the MICs of fluconazole for selected *Candida* species.

OBJECTIVE

The purpose of this study was to determine whether changes in pH of the test medium affect the *in vitro* susceptibility of *Candida glabrata* and *Candida albicans* vaginal isolates to SCY-078 using fluconazole and micafungin as comparators.

METHODS: STUDY DESIGN

Ten strains each of vaginal *C. albicans* and *C. glabrata* isolates from a recent clinical trial were tested. Susceptibility testing was performed using a broth microdilution method according to CLSI M27-A3 guidelines. A 0.1-ml of 0.5-2.5 x 10³ blastospores/ml in RPMI 1640 medium was added to each microdilution well. Antifungal susceptibility testing was carried out in RPMI 1640 at pH 7 (to mimic RPMI medium used by the CLSI M-27A3 document), pH 5.72 (to mimic the pH of Sabouraud Dextrose broth and Yeast Nitrogen Base media), and pH 4.5 (to mimic the pH of the vaginal cavity). Buffering was achieved with morpholinepropanesulfonic acid (MOPS; 0.165 M). Inhibition endpoints were read as a 50% reduction in growth compared to growth control after 24 hours incubation at 35° C.

CONCLUSION

SCY-078 demonstrates *in vitro* efficacy against *C. glabrata* and *C. albicans* in neutral and low pHs. MIC values for SCY-078 were lower at the lowest pH tested whereas the MIC values of micafungin seem to be unaffected by pH and the MIC values of fluconazole may be inversely affected by pH, especially for *C. glabrata*. This data corroborates the activity observed with SCY-078 in patients with VVC.

RESULTS

Table 1. MIC ranges for compounds against two *Candida* species at various pH.

<i>C. glabrata</i>	pH		
	7.0	5.72	4.5
SCY-078	0.5 - 1	0.5	0.031 - 0.063
Micafungin	0.25 - 0.5	0.25	0.25
Fluconazole	0.5 - 2	2 - 16	1 - 16
<i>C. albicans</i>	pH		
	7.0	5.72	4.5
SCY-078	0.125 - 0.5	0.125-0.25	<0.016 - 0.031
Micafungin	0.25	0.063 - 1	0.25 - 0.5
Fluconazole	<0.125 - 1	<0.125 - 1	0.25 - 8

Table 2. MIC₅₀ and MIC₉₀ compounds against two *Candida* species at various pH.

<i>C. glabrata</i>	pH					
	7.0		5.72		4.5	
	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀
SCY-078	1	1	0.5	0.5	0.063	0.063
Micafungin	0.25	0.5	0.25	0.25	0.25	0.25
Fluconazole	1	2	8	16	8	16
<i>C. albicans</i>	pH					
	7.0		5.72		4.5	
	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀
SCY-078	0.25	0.5	0.25	0.25	<0.016	<0.016
Micafungin	0.25	0.25	1	1	0.5	0.5
Fluconazole	0.25	0.25	<0.125	0.25	0.25	1