

The novel oral glucan synthase inhibitor SCY-078 shows *in vitro* activity against *Candida* spp. biofilms

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INTRODUCTION AND PURPOSE

SCY-078 (formerly MK-3118) is a new semi-synthetic derivate of the terpenoid enfumafungin, a potent, but structurally different to echinocandins, inhibitor of 1,3-b-D-glucan synthase. SCY-078 is available for IV/oral administration showing similar activity to caspofungin against *Candida* spp. and *Aspergillus* spp. isolates mostly collected in the USA.

Hypothetically the mechanism of action of SCY-078 predicts antifungal activity against *Candida* biofilms although its activity has been studied exclusively against planktonic forms.

We studied the antifungal activity of SCY-078 and micafungin against the sessile forms of 178 *Candida* and non-*Candida* isolates causing fungemia in patients recently admitted to a large European hospital in Madrid, Spain.

METHODS

ISOLATES

C. albicans n= 55
C. parapsilosis n= 33
C. glabrata n=31
C. tropicalis n= 8
C. krusei n=12
Candida spp. n=26
Non-*Candida* yeasts n=13
Fluconazole resistant isolates n= 24
Echinocandin resistant isolates n= 9

Biofilm susceptibility to micafungin and SCY-078 by XTT
Determination of sessile MIC (SMIC₈₀) as 80% reduction of metabolic activity in comparison with untreated control

Scanning electron microscopy of 4 randomly chosen isolates.
C. albicans n=1
C. parapsilosis n=1
C. glabrata n=1
C. tropicalis n=1

RESULTS

The anti-biofilm activity of the drugs tested is shown in Table 1, SMIC₈₀ values for SCY-078 and micafungin were essentially the same against the biofilms generated by the different *Candida* spp. with the exception of *C. glabrata* in which micafungin had significantly lower SMIC values ($P < 0.001$).

The impact of the SCY-078 and micafungin exposure on the preformed biofilm structure was assessed by SEM (Figure 1).

C. albicans biofilms appeared with swollen blastospores and thin hyphae after exposure to micafungin (figure 1b) or SCY-078 (figure 1c).

The effect of micafungin against *C. parapsilosis* biofilms was slight and only a small reduction on the amount of yeast was observed (figure 1e), whereas the reduction in the amount of blastospores was more prominent after SCY-078 exposure (figure 1f).

C. tropicalis biofilm was very dense and thick (figure 1g) but micafungin (figure 1h) and SCY-078 (figure 1i) led to the presence of thin hyphae and swollen blastospores.

C. glabrata biofilm (figure 1j) was formed by a layer of clumped blastospores that became damaged after micafungin treatment (figure 1k) whereas SCY-078 treatment led to a lower effect (figure 1l).

Table 1. Antifungal susceptibility of biofilms to micafungin and SCY-078.

Species	SMIC ₈₀ (Micafungin/SCY-078)		
	Percentile 50	Percentile 90	Range
<i>C. albicans</i>	1/0.125	≥32	≤0.015 - ≥32
<i>C. parapsilosis</i>	16/≥32	≥32	0.5/0.25 - ≥32
<i>C. glabrata</i>	≤0.015/0.25	2/16	≤0.015 - ≥32
<i>C. tropicalis</i>	≥32/16	≥32	≤0.015/0.062 - ≥32
<i>C. Kirusei</i>	0.125/0.5	0.5/16	0.125/0.25 - 0.5/16
<i>Candida</i> spp.	2/8	≥32	0.031/0.062 - ≥32
Non- <i>Candida</i>	≥32	≥32	≥32/4 - ≥32
Fluconazole-R	0.125/0.5	≥32	≤0.015/0.125 - ≥32
<i>Candida fks</i> -mutant	1/8	≥32	0.125/0.062 - ≥32

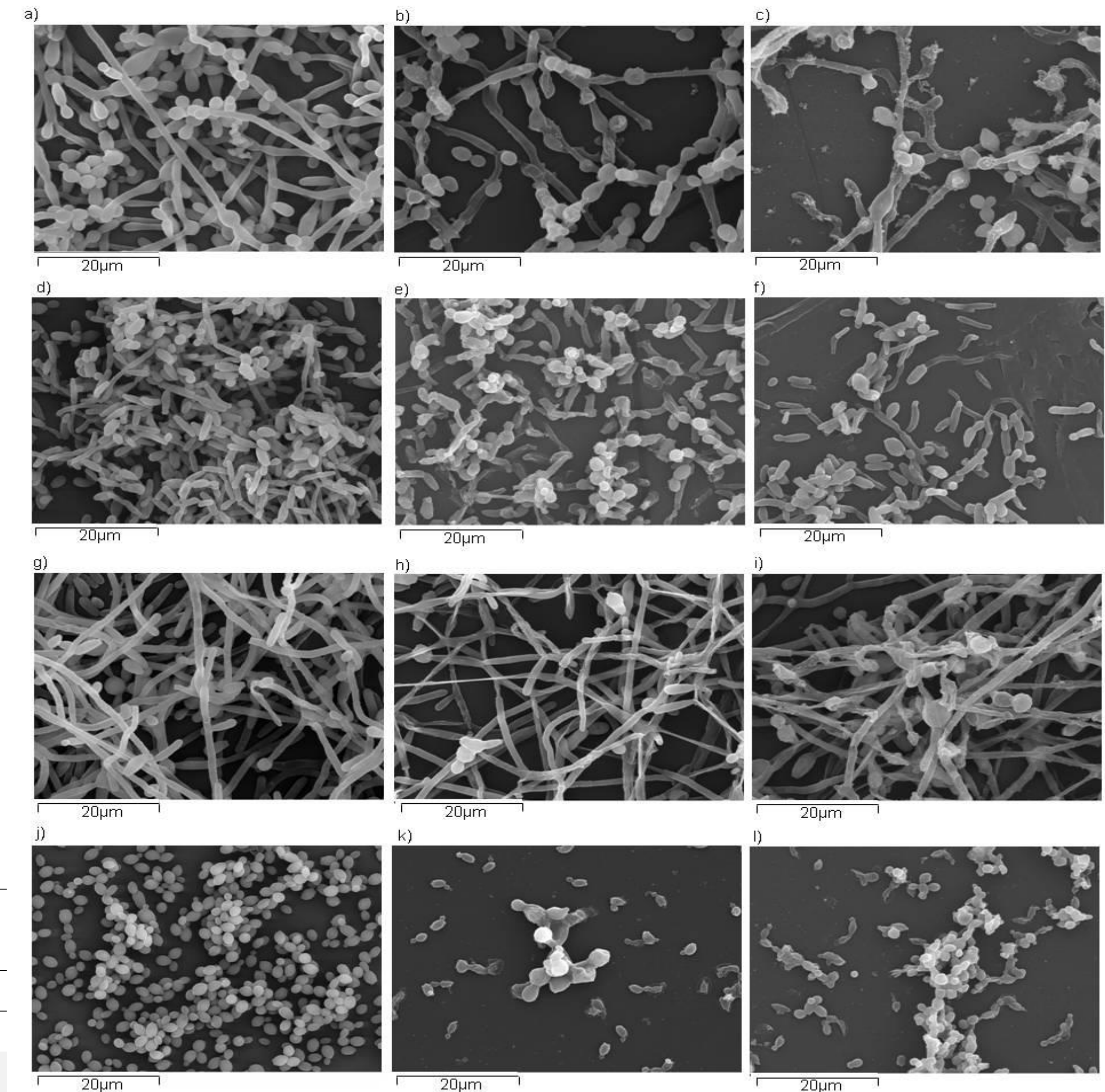


Figure 1. SEM image of the activity of micafungin and SCY-078 against biofilms formed by different species of *Candida*. A concentration equal to SMIC₈₀ was tested. 2000 X magnification. a) *C. albicans* untreated control (b) *C. albicans* treated with micafungin=0.031 mg/L, (c) *C. albicans* treated SCY-078=0.062 mg/L, (d) *C. parapsilosis* untreated control (e) *C. parapsilosis* treated with micafungin=8 mg/L, (f) *C. parapsilosis* treated SCY-078=16 mg/L, (g) *C. tropicalis* untreated control (h) *C. tropicalis* treated with micafungin=16 mg/L, (i) *C. tropicalis* treated with SCY-078=16 mg/L, (j) *C. glabrata* untreated control (k) *C. glabrata* treated with micafungin=0.015 mg/L, (l) *C. glabrata* treated SCY-078=0.25 mg/L.

CONCLUSIONS

Our study showed that SCY-078 has a high *in vitro* activity against *Candida* invasive isolates in sessile forms (biofilms) comparable to micafungin.