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

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Background: We studied the antifungal activity of SCY-078 (an orally bioavailable 1,3-beta-D-glucan synthesis inhibitor) and MYC 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 (Table).

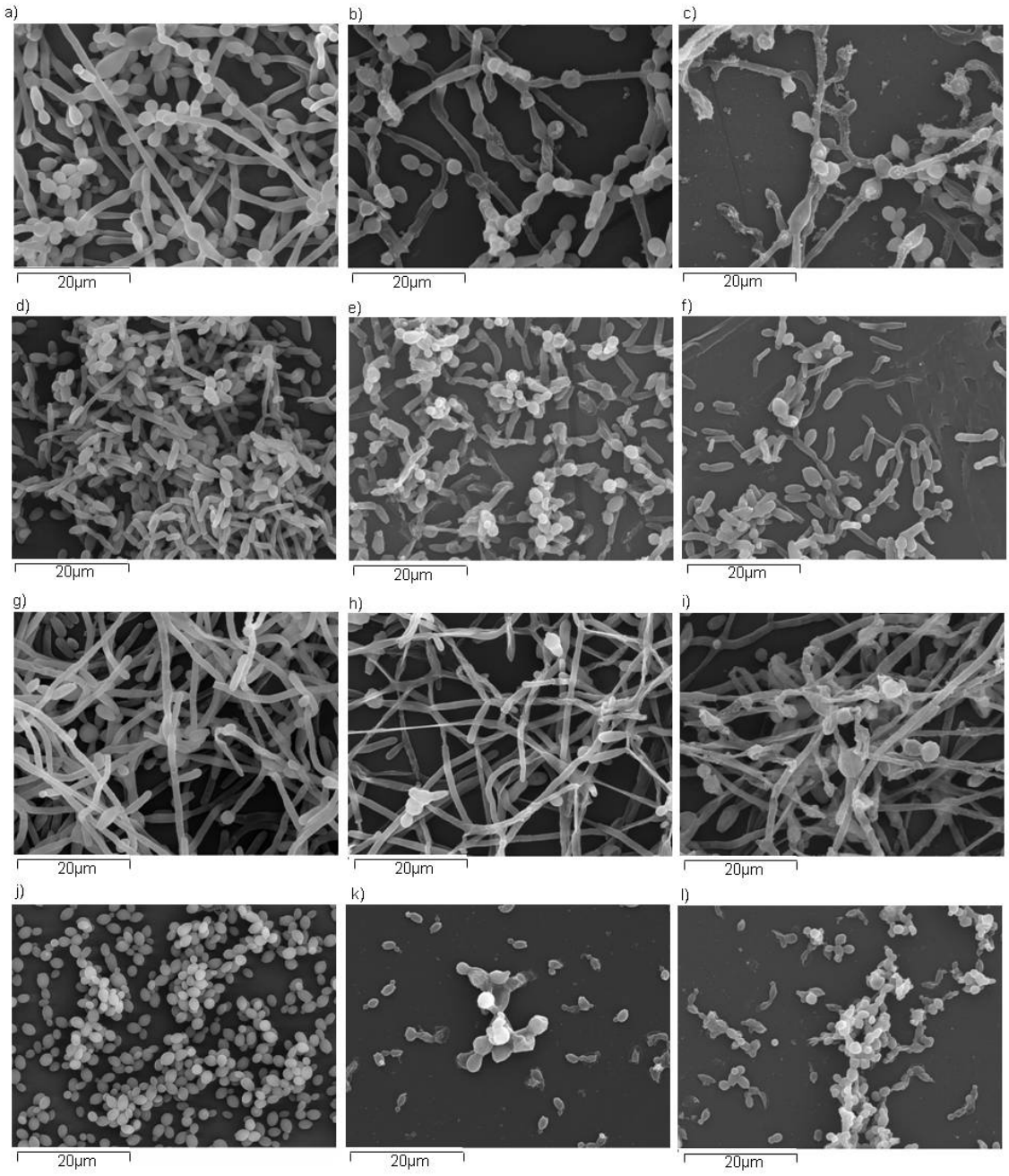
Material/methods: The *in vitro* activity of SCY-078, and MYC against the biofilms was obtained by means of the XTT reduction assay. The sessile MIC (SMIC) was defined as an 80% reduction in the metabolic activity of the biofilm treated with the antifungal compared with the control well. Values reaching statistical significance (P<0.05) are shown in **bold**. Four isolates (*C. albicans* n=1, *C. parapsilosis* n=1, *C. glabrata* n=1, *C. tropicalis* n=1) were randomly selected for scanning electronic microscopy analysis to study the impact of MYC and SCY-078 exposure on the biofilm structure.

Results: SCY-078 and MYC showed essentially the same activity, expressed in µg/ml, against the biofilms [GM (**2.04 vs 1.1**); $SMIC_{50}$ (4 vs 1); $SMIC_{90}$ (≥32); range (≤0.015 - ≥32)].

Species	GM (MYC/SCY-078)	$SMIC_{50}$ (MYC/SCY-078)	$SMIC_{90}$ (MYC/SCY-078)	Range (MYC/SCY-078)
C. albicans (n=55)	0.75/1.007	1/0.125	≥32	(≤0.015 - ≥32)

C. parapsilosis (n=33)	8.3/11.81	16/≥32	≥32	(0.5/0.25 - ≥32)
C. glabrata (n=31)	**0.072/0.431**	≤0.015/0.25	2/16	(≤0.015 - ≥32)
C. tropicalis (n=8)	4.8/2.3	≥32/16	≥32	(≤0.015/0.062 -≥32)
C. krusei (n=12)	0.187/0.567	0.125/0.5	0.5/16	(0.125/0.25 - 0.5/16)
Candida spp. (n=26)	1.7/4.9	2/8	≥32	(0.031/0.062 - ≥32)
Non-*Candida* (n=13)	≥32/27.3	≥32	≥32	(≥32/4 - ≥32)
Fluconazole-R *Candida* isolates (n=24)	**0.33/1.33**	0.125/0.5	≥32	(≤0.015/0.125 - ≥32)
fks-mutant *Candida* isolates (n=9)	1.9/2.5	1/8	≥32	(0.125/0.062 - ≥32)

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 (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).



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