

Impact of the exposure of clinical relevant yeasts to agricultural azoles in terms of antifungal resistance

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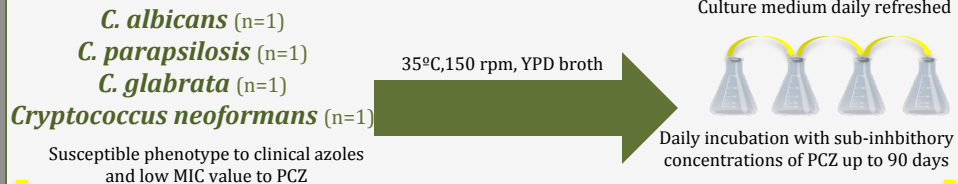
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Introduction

Antifungals similar to those used in human therapy are widely used in agriculture and resistance to such antifungals is also increasing. Azoles also represent first line options for human antifungal therapy. The acquisition of azole resistance in nature may thus result in a significant, yet undetermined, impact regarding human health. The main goal was to assess the development of cross-resistance between Prochloraz (PCZ), an agricultural azole and clinical azoles by *Candida spp.* and *Cryptococcus neoformans*.

Materials and Methods

In vitro induction assay



PCZ MIC was evaluated, according to CLSI M27-A3 (S4) protocol every five days

Whenever a significant increase of PCZ MIC value was found, MIC values of antifungals fluconazole (FLU), voriconazole (VOR), posaconazole (POS) were determined. Afterwards the strains were re-incubated for an additional 90 days, under the same conditions, in absence of PCZ and MIC was re-determined.

Results

Species	Time of exposure (days)	MIC (mg/l)			
		PCZ	FLC	VRC	POS
<i>C. albicans</i>	0	0.5	0.25	0.03	0.03
	90	16	1	0.06	0.5
	Ø90	16	0.5	0.06	0.5
<i>C. parapsilosis</i>	0	2	0.5	0.03	0.03
	90	64	1	0.06	2
	Ø90	64	1	0.06	2
<i>C. glabrata</i>	0	1	1	0.25	0.03
	90	64	64	1	16
	Ø90	64	64	0.25	16
<i>C. neoformans</i>	0	0.03	0.125	0.25	0.125
	90	64	64	1	1
	Ø90	64	64	1	1

PCZ=Prochloraz; FLC=Fluconazole; VRC=Voriconazole; POS=Posaconazole
 Ø= MIC after 90 days of culture in the absence of PCZ.

- The developed MIC value was stable
- *C. albicans* and *C. parapsilosis* did not exhibit cross-resistance to clinical azoles.
- *C. glabrata* developed cross-resistance to FLC and POS but not to VRC.
- *Cryptococcus neoformans* isolates only displayed cross-resistance to FLC.

Conclusions

Our *in vitro* assays suggests that the exposure of clinical relevant fungi to agricultural azole antifungals may be associated to the emergence of stable cross-resistance to clinical azoles, which may results in serious impact in human health.