

Antifungal activity of clotrimazole against *Candida albicans* depends on carbon sources, growth phase, and morphology.

Kasper L, Miramón P, Jablonowski N, Wisgott S, Wilson D, Brunke S, Hube B (2015) Antifungal activity of clotrimazole against *Candida albicans* depends on carbon sources, growth phase, and morphology. *J Med Microbiol* 64, 714-723.

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Abstract

Vulvovaginal candidiasis (VVC), a superficial infection predominantly caused by the pathogenic fungus *Candida albicans*, is frequently treated with clotrimazole. Some drug formulations contain lactate for improved solubility. Lactate may modify *C. albicans* physiology and drug sensitivity by serving as a carbon source for the fungus and/or affecting local pH. Here we explored the effects of lactate, in combination with pH changes, on *C. albicans* proliferation, morphology and clotrimazole sensitivity. Moreover, we determined the influence of growth phase and morphology per se on drug sensitivity. We show that utilisation of lactate as a carbon source does not promote fast fungal proliferation or filamentation. Lactate had no influence on clotrimazole-mediated killing of *C. albicans* in standard fungal cultivation media but had an additive effect on the fungicidal clotrimazole action under in vitro vagina-simulative conditions. Moreover, clotrimazole-mediated killing was growth-phase and morphology-dependent. Post-exponential cells were resistant to the fungicidal action of clotrimazole, while logarithmic cells were sensitive, and hyphae showed

highest susceptibility. Finally, we show that treatment of preformed *C. albicans* hyphae with sub-lethal concentrations of clotrimazole induced a reversion to yeast phase growth. As *C. albicans* hyphae are considered the pathogenic morphology during mucosal infections, these data suggest that elevated fungicidal activity of clotrimazole against hyphae plus clotrimazole-induced hyphae-to-yeast reversion may help to dampen acute vaginal infections by reducing the relative proportion of hyphae and thus shifting to a non-invasive commensal-like population. In addition, lactate as an ingredient of clotrimazole formulations may potentiate clotrimazole killing of *C. albicans* in the vaginal microenvironment.

Involved units

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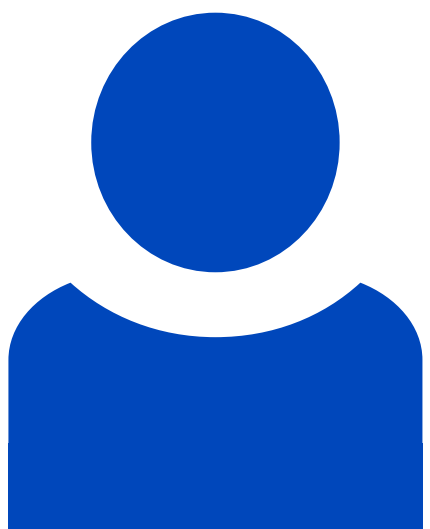
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