ABSTRACT

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Title of diploma thesis: Relation between alkali-metal-cation homeostasis and resistance to antimycotics in *Candida* species

The family of *Candida species*, normally a harmless human commensal of the gastrointestinal and genitourinary tract, can become a human pathogen under certain circumstances. Mainly in immunocompromised patients, *Candida* cause a wide range of infections and are the most prevalent pathogenic yeast. In this work we have focused on the most common *Candida species* (*C. albicans*, *C. parapsilosis* and *C. glabrata*) and we included *C. dubliniensis* as well. *Candida species* differ in their resistance to azole-antimycotics and their halotolerance.

Azoles form the most important group of drugs with antifungal activity. They destabilise plasma membrane of *Candida* cells. The essential function of plasma membrane is regulation of cation homeostasis. The combination of subinhibition concentrations of fluconazole and NaCl is known to inhibit the growth of both fluconazole-sensitive and fluconazole-resistant) *C. albicans* strains.

We have found that all tested *Candida* species can generaly tolerate high concentrations of fluconazole or salts separately, but the combination of both compounds inhibites their growth effectively. Subinhibition concentrations of salts amplified sensitivity to another cell barriers disrupting drugs (other azoles, calcofluor white, sodium dodecylsulfate). Toxic sodium cations potentiated the activity of all antimycotics very strongly. The higher concentration of potassium cations and higher sorbitol-mediated osmotic pressure affected only the resistance to anitmycotics of *C. dubliniensis.* The species *C. glabrata* was able to compensate salt- and toxic-stress the most effectively.

Project aims to deeper understand the mechanism of action of antifungal agents and the development of resistance to antimycotics.