Abstract

The growing phenomenon of antimicrobial resistance in pathogenic microorganisms presents an emerging issue given the lack of methods alternative to antibiotic treatment to combat infections. In recent years there has been growing interest in developing techniques of limiting the spread of pathogenic microorganisms by disrupting the activity of their virulence factors – mechanisms enabling them to effectively infect the host organism. In several infectious strains such is the role of urease – an enzyme of the hydrolase class that catalyzes the hydrolysis of urea. Mechanisms of virulence that involve expression and activity of urease in microorganisms are numerous and include but are not necessarily limited to: utilizing urea as a nitrogen source for growth, changing the pH of the cell environment for survival, or complex inflammatory processes as a host reaction to the very presence of urease protein, catalytically active or not, that facilitate tissue colonization.

This thesis presents the results of research on the possibilities to control ureolytic activity of bacterial and fungal pathogenic strains in which urease constitutes diverse virulence factors leading to various consequences to the host's health. The studies included *C. neoformans* for which the role of urease and control mechanisms of its activity has not been fully characterized so far. Within this study, a protocol of ureolysis induction in the *C. neoformans* cells as well as the properties of the isolated yeast enzyme were described.

The main part of the thesis consists of the analysis of microbial urease inhibition studies conducted for over 200 structurally various chemicals. Among the studied compounds were e.g. analogues of catechol, ebselen derivatives, phosphonic structures, thiourea derivatives (reaction substrate analogue) and hybrid, mulitfunctional compounds. The most active structures were additionally studied for their potential inhibitory activity towards other pivotal enzymes such as thioredoxin reductase that is a part of a mechanism controlling oxidative stress in microbial cells. Their influence on the growth and viability of bacterial biofilm, a structure known for its enhanced resistance to commonly used antibiotics, was also studied. For numerous effective inhibitors their ability to impair ureolysis in the whole cells of microorganisms was also confirmed.