Activity of porphyrin compounds against *Nosema ceranae* microsporidia causing honeybee nosemosis

N. ceranae spores cause nosemosis, which impairs digestion and nutrient absorption, and thus contributes to deterioration of health and death of entire colonies. Despite the significant advances in research to control infections caused by *N. ceranae*, this disease remains a serious problem in beekeeping. Therefore, there is a need to search for effective agents to combat *Nosema* microsporidia.

In this dissertation, the efficiency of PP-IX derivatives in inactivation of microsporidia both *in vitro* and *in vivo* was tested. Porphyrins PP[Lys(TFA)-Asp(OH)-OH]$_2$, PP[Lys(TFA)-OH]$_2$, PP[Asp(ONa)-ONa]$_2$, and PP[Lys(TFA)-Lys(TFA)-OH]$_2$ (st. 10-50 μM) caused a 47-80% reduction in spore counts, compared to the control. Irradiation of porphyrins did not result in higher activity against *N. ceranae*; therefore, the mechanism of action of these compounds on microsporidia is different from the photosensitizing mechanism of PDT known to date. The 24-h action of porphyrins on microsporidia resulted in a small number of viable spores (1.6 to 4.3%) in the samples. In addition, porphyrins have been shown to penetrate the interior of viable spores and destroy them most likely by interacting with the internal structures of microsporidia. Since porphyrins did not accumulate in dead spores, it was concluded that porphyrin uptake occurs via active transport. The length of the side chain and the type of the substituent in the PP-IX molecule were also found to have a significant effect on the activity of these compounds. In *in vivo* tests, it was shown that spores treated with porphyrin compounds have a lower infective capacity. Bees infected with spores preincubated with porphyrins had lower infection rates than bees infected with porphyrin-untreated spores. In addition, bees with higher infection levels were found to ingest more food than bees with lower infection levels. Porphyrins PP[Lys(TFA)-OH]$_2$ and PP[Lys(TFA)-Lys(TFA)-OH]$_2$ reduced the number of spores in *N. ceranae*-infected bees with no effect on the lifespan of healthy bees. Only porphyrin complexed with Zn^{2+} ions resulted in reduced lifespan, indicating the need for more detailed studies to assess the toxicity of metalloporphyrins. The results of the study presented in this dissertation provide the basis for concluding that PP-IX derivatives are promising compounds for the control of nosema infection in conditions that do not require a light source, which creates a real opportunity for their use in beekeeping practice.

Keywords: honeybees, *Nosema ceranae*, nosemosis, microsporidia, protoporphyrin IX

Bucek Katarzyna