

ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Bc. Karolína Štěřbová

Supervisor: prof. RNDr. Lenka Skálová Ph.D.

Title of diploma thesis: Changes in expression of biotransformation enzymes in nematodes affected by albendazole

Barber's pole worm (*Haemonchus contortus*) is highly pathogenic parasitic nematode, which assaults gastrointestinal system of small ruminants. Disease. Which caused is named by the agent haemonchoses. Long-term infection leads to develop of anaemia, lose weight of host and often even death. For treatment of this disease, synthetic antiparasitic drugs called anthelmintics are used. However, worldwide problem is growth of resistance against all used anthelmintics. Cause of this problem is probably common and unreasonable using of anthelmintics and the exposure of the parasites to sub-lethal doses. This thesis is focused on study of the mechanisms of resistance of barber's pole worm to albendazole, anthelmintic belonging to benzimidazoles group. The increased expression of biotransformation enzymes could contribute to resistance development.

In our study, the influence of albendazole on expression of selected genes in adults of *H. contortus* from the ISE (Inbred Susceptible Edinburgh) strain was studied. Worms were isolated from the sheep's abomasum and exposed to three different concentration of albendazole (0,01 μM , 0,1 μM , 1 μM). The incubations lasted 4 or 12 hours. Expression of the selected genes of cytochromes P450 (CYP) and UDP-glukosyltransferases (UGT) were analysed by quantitative PCR. The results were normalized by reference gene GAPDH and related to control (0 μM ABZ). Significant albendazole-induced differences were observed in the expression of CYPs and UGTs. Both sexes differed in the constitutive expression of genes as well as in the response to albendazole. As the most upregulated gene was UGT367A1, this enzyme might be related to resistance of barber's pole worms to albendazole.