Abstract

Charles University
Faculty of Pharmacy in Hradec Králové
Department of Biochemical Sciences
Candidate: Bc. Martina Salvová
Supervisor: prof. RNDr. Lenka Skálová, Ph.D.

Title of diploma thesis: **The changes in flubendazole metabolism during life cycle of nematode**

The nematode barber's pole worm (*Haemonchus contortus*) is an infectious pathogen that causes gastrointestinal haemonchosis in ruminants. Its life cycle consists of egg, larval (L1, L2 and L3) and adult stages. Haemonchosis is a common and widespread disease of farm animals, which causes significant global economic losses.

Whereas the treatment of haemonchosis is mainly based on pharmacotherapy using anthelmintics, the increasing drug resistance of barber's pole worm to these drugs is a big problem. Hence, the study of the mechanisms of the development of drug resistance in this parasite is in the foreground of scientific interest. One of the mechanisms of resistance may be an increased ability to deactivate the anthelmintics. In the case of the benzimidazole anthelmintic flubendazole, deactivation is based on a reduction of the carbonyl group by the enzymes aldo-ketoreductases and short-chain dehydrogenases/reductases. The metabolite with decreased anthelmintic efficacy is produced by the reduction of flubendazole, and in this way, nematodes protect themselves against the toxic effect of anthelmintic.

The aim of this study was to monitor the reduction of flubendazole in eggs, L1 larvae and adults of barber's pole worm of strain ISE (susceptible to anthelmintics) and strain IRE (resistant to benzimidazole anthelmintics). A solid phase extraction method was used for sample preparation before the analysis. Reduced flubendazole was quantified by HPLC analysis with mass spectrometric detection.

Understanding the abilities of development stages to inactivate flubendazole may help in the fight against anthelmintic resistance.