ABSTRACT

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Title of Doctoral Thesis	**The use of LC/MS for the study of biotransformation of xenobiotics in helminths**

Annually, parasites cause many losses regarding not only human lives but also the livestock. One of the most effective weapons that can be used against them are anthelmintics. However, in many cases anthelmintics cease to work and resistance development occurs. One of the possible mechanisms of resistance is the biotransformation of the drug to ineffective or less active products by the parasite.

The aim of this work was to bring new knowledge about the biotransformation of drugs in helminths. Emphasis was given to the relationship between biotransformation and the resistance of parasites against anthelmintic drugs. A possible technique to achieve this goal is to study directly the products of biotransformation, i.e. metabolites. As this issue is nowadays most frequently solved by liquid chromatography and mass spectrometry, we used this technique to meet our goals.

Biotransformation was studied in representatives of tapeworms, flukes and roundworms. Where possible, economically important representatives as Barber's pole worm (*Haemonchus contortus*) or lancet fluke (*Dicrocoelium dendriticum*) were in the centre of our attention. In the group of tapeworms, model rat tapeworm (*Hymenolepis diminuta*) was used.

Substances from groups of benzimidazoles, macrocyclic lactones and pyrazinoisoquinolines were studied. The ability of parasites to inactivate drugs was confirmed in the group of benzimidazoles, especially for drugs containing a carbonyl group. In the case of Barber's pole worm, the relationship between the resistance and the activity of biotransformation enzymes was further confirmed.

Acquired information confirms that the parasites are able, under certain conditions, to inactivate the drug and thus resist the treatment. Data measured in this work are potentially usable in further studies of the relationship between biotransformation and resistance in helminths, as well as in possible design of new drugs.