

ABSTRACT

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Title of diploma thesis: Identification and quantification of anthelmintics and their metabolites in tapeworms by LC/MS

Biotransformation of anthelmintics, as well as the activity of biotransformation enzymes, represents areas that are not yet so much explored at the tapeworms. However especially biotransformation enzymes can to a certain extent protect organism of the parasite against effects of anthelmintics (and xenobiotics in general). The ability of the parasite to metabolize administered anthelmintic drug to an inactive metabolite can represent a convenient defence mechanism that may contribute to the formation of resistance. The aim of my thesis was to evaluate the metabolism of selected anthelmintics (albendazole sulphoxide, flubendazole, mebendazole) in *Hymenolepis diminuta*. Results of metabolism show that the rat tapeworm is unable to oxidize or reduce albendazole sulphoxide. Tapeworm is able to reduce mebendazole and flubendazole. For mebendazole and flubendazole reduction the kinetic parameters were determined. It was shown that the rate of conversion to reduced metabolites of flubendazole is twenty times slower than for mebendazole reduction, but the affinity of reductases is seven times higher to flubendazole. The only phase II metabolites were two methylated derivatives of reduced flubendazole. In one case methylation took place on benzimidazole core (C-methylation), in second on the side chain (N-methylation). Metabolites were detected and identified using HPLC with spectrofluometric detector, UV detector and mass spectrometer. Compared with the results of the metabolism in other helminths, it was shown that the biotransformation of xenobiotics is different not only in different helminths within individual classes, but also among tapeworms themselves.