

ABSTRACT

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Title of diploma thesis: Metabolism of monepantel in parasites and their hosts

Monepantel (MOP) belongs to a new class of anthelmintic drugs - amino-acetonitrile derivatives. They differ from the commonly used broad-spectrum drugs (makrocyclic lactones, benzimidazoles and imidazothiazoles) in chemical structure and mechanism of action. Because of frequent use of these classes the resistance in many pathogenic parasites was developed. The aim of this study was identification and comparison of phase I and II metabolites of MOP biotransformation in parasites (*Haemonchus contortus* – sensitive strain ISE and multi-resistant strain WR) and in their hosts - sheep (*Ovis aries*) through *in vivo* and *ex vivo* study. Ultra-high performance liquid chromatography with tandem mass spectrometry technique (UHPLC-MS/MS) was used for identification of MOP metabolites. In sheep, 13 metabolites of phase I and II biotransformation of MOP were detected in *in vivo* study, 7 of them have not been described previously. In parasites *ex vivo*, only 4 metabolites of phase I MOP biotransformation were found. Following biotransformation reactions of MOP were detected: S-oxidation, hydroxylation, hydrolysis of nitril to amide, glucuronidation and conjugation with glutathione which was subsequently transformed to conjugate with acetylcysteine. Based on the obtained results, scheme of metabolism of the metabolic pathways of MOP in parasites and in their hosts have been proposed.