

ABSTRACT

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Title of Dissertation Thesis: **Metabolism and efficacy of new potential anthelmintics**

Overpopulation of gastrointestinal nematodes represents global health and economical problem. Therefore, suitable solution in the form of effective anthelmintic treatment is needed. Several anthelmintics with distinct mechanism of action are available on the market, however, the widespread resistance limits their efficacy. As a consequence, finding a new possible alternative becomes important. In present dissertation thesis, the novel anthelmintic candidates were selected and their effect against model parasitic nematode *Haemonchus contortus* was examined. The studies encompassed three approaches within the field of drug discovery: new molecular entity identification and structure modification, drug repurposing, and medicinal plants screening. Newly synthesized compounds designated as BLK127, HBK4 and BLK127 derivatives, already known antipsychotic drug sertraline (SRT) and the extracts from eight European ferns species from genus *Dryopteris*, *Athyrium* and *Blechnum* were the subjects of our interests. Two developmental stages, eggs and adults, of drug-sensitive and drug-resistant strains of *H. contortus* were used for anthelmintic efficacy screening. In order to improve the anthelmintic testing in adult worms, a biochemical method based on the measurement of ATP level was adopted and optimized. BLK127 and several of its derivatives, SRT and three fern extracts: *Athyrium distentifolium*, *Dryopteris aemula*, and *Dryopteris cambrensis* proved anthelmintic activity as they significantly decreased the level of ATP in adults of both, sensitive and resistant strains. Consequently, the hepatotoxicity of all compounds was evaluated, and with the exception of HBK4, which was subsequently eliminated as a potential candidate, none of the compounds exhibited harm to the ovine liver. Lastly, biotransformation of SRT and BLK127 in adult *H. contortus* and sheep liver was assessed. The results revealed extensive biotransformation in sheep liver, whereas *H. contortus* exhibited limited metabolic activity with only traces of metabolized product detected. Some of the obtained results are really promising, and they could be a basis for further studies, including *in vivo* testing.