

Abstract

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Bc. Kateřina Junková

Supervisor: prof. RNDr. Lenka Skálová, Ph.D.

Consultant: Mgr. Josef Krátký, PharmDr. Thuy Linh Nguyen, Ph.D.

Title of diploma thesis: **Testing of the efficacy and toxicity of new potential anthelmintics I**

Haemonchus contortus, a blood-feeding nematode of ruminants, causes significant economic losses in livestock production worldwide. Despite anthelmintic therapy being crucial for haemonchosis control, the emergence of anthelmintic resistance in *H. contortus* is increasingly compromising the efficacy of available drugs. Therefore, there is an urgent need for novel anthelmintics effective against resistant *H. contortus* strains.

The theoretical part of this thesis provides a concise overview of current treatment options for haemonchosis, including the mode of action of commonly used anthelmintics. Alternative measures for haemonchosis prevention and control, including plant-derived anthelmintics, vaccines, and biological control, are also presented in the context of their potential to replace or supplement anthelmintic therapy and thereby mitigate the risk of resistance development.

The experimental part of this thesis evaluated the efficacy of two novel potential anthelmintics, OMK1 and OMK2, synthesized in the laboratory of Prof. Kurz at Heinrich Heine University Düsseldorf. The anthelmintic activity of OMK1 and OMK2 against eggs, larvae, and adults of both susceptible and anthelmintic-resistant *H. contortus* strains was assessed in our laboratories. Additionally, the potential toxicity of these compounds was tested in liver slices.

The results demonstrated that OMK1 had no ovicidal effect, while OMK2 inhibited egg hatching at a concentration of 1 μM . The effect of these compounds on xL3 larvae

was inconclusive. Promising anthelmintic activity of OMK1 and OMK2 was observed against adult *H. contortus*. OMK1 reduced the viability of ISE strain males and females at concentrations of 0,1 and 1 μM , respectively. In IRE strain females, OMK1 did not affect viability, but was effective against males at a concentration of 0,1 μM . The OMK1 derivative did not reduce the motility of ISE strain females; however, a significant decrease in motility was observed in males exposed to OMK1. The OMK2 derivative reduced the viability of adults of both sexes and strains at concentrations of 0,1 and 1 μM . A decrease in motility was also observed in both males and females exposed to OMK2. Neither derivative exhibited toxicity to sheep liver slices.

The results suggest that both novel derivatives, particularly OMK2, hold promise as potential anthelmintics against *H. contortus*.