

ABSTRACT

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Title of diploma thesis: The study of possible use of sertraline against gastrointestinal nematodes

Haemonchus contortus is a widespread parasitic nematode infecting the gastrointestinal tract of many small ruminants that causes enormous damage to animal production every year. It is responsible for a disease in its host called Haemonchosis the main characteristic of which is anaemia caused by severe blood loss. This is responsible for the reduced productivity of the animal, and in some cases results in the death of the host. A relatively limited range of anthelmintic drugs is used for the treatment of Haemonchosis with new substances rarely being added to the list of treatments. Due to the massive use of the same anthelmintic drugs and the parasites adaptability, extensive resistance is pervasive with current treatments being no longer effective. For this reason it has become necessary to look for new effective drugs that have a different mechanism of action (MOA). One possibility is to test the anthelmintic efficacy of common drugs from other therapeutic groups.

In this work, the potential anthelmintic effect, metabolism and toxicity of sertraline was investigated. Sertraline is a commonly prescribed drug for the treatment of depressive and anxiety disorders in humans. Our results showed that sertraline possessed anthelmintic activity against *H. contortus*, with females proving to be less sensitive than males. The metabolism of sertraline in *H. contortus* was studied using high performance liquid chromatography. Hydroxylated metabolites were found, but most of the parent compound remained unmetabolized. Metabolism did not differ significantly between strains sensitive or resistant to other anthelmintics, it was also seen that strain gender did not have any effect on outcome. In sheep hepatocytes, sertraline did not show toxicity at concentrations sufficient for the anthelmintic effect and toxicity being only evident at higher levels.

Based on this work, sertraline appears to be potentially useful for the treatment of haemonchosis. However, its effects must be further investigated *in vivo*.