

## Review Report on the Ph.D. thesis

submitted to the Charles University,  
Faculty of Pharmacy in Hradec Králové, Department of Biochemical Sciences

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

PhD candidate: **Mgr. Markéta Zajíčková**

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

*Dear Vice-Dean,*

*I thank you for the invitation to review the Ph.D. thesis, written by Markéta Zajíčková, which I have accepted and herein submit the review report as requested. Doctoral candidate submitted her Ph.D. thesis which generally deal with chemical control of gastrointestinal nematodes (GINs) in ruminants relating to anthelmintic resistance. The efficacy of the traditional anthelmintic control of GINs is limited, and moreover, this chemical approach contributes to environmental (and subsequently food sources) contamination by xenobiotics. From this point of view, this topic is relevant in the context of the One Health approach and is highly welcomed. This thesis consists of a collection of four research papers and one review; the candidate is the first author on three of these papers. All of the papers have been published in high impact scientific journals; three papers even belongs to the first decile. The presented results could be valuable to both scientists (veterinarians, parasitologists, pharmacologists, etc.) and practitioners (veterinarians and ruminant health specialists).*

*The structure of this PhD thesis conforms to principles and requests of scientific work and I have just one comment to this point. Even if in this case it is rather complicated to summarize all the methodological approaches used in the research, the thesis should contain*

*a chapter Material and methods. In this section, it would be possible to generally describe the experimental/analytical methods applied and the biological material used, and possibly refer to published papers.*

*In my opinion, the literature review is in some respects far too generalized. In the introduction I would expect more detailed information concerning the impact of the most important GINs (trichostrongylids) on ruminant livestock health, welfare and production, instead of knowledge regarding human hosts and their nematode parasites. Some inaccurate and misleading information, mostly in parasitological nomenclature, can be find in the chapter Theoretical background. Specific comments are listed below:*

- *All GINs infections are not classified as soil transmitted helminthiasis. The later term should be restricted only for infections caused by nematodes transmitted through contaminated soil (e.g. ascarids *Ascaris* sp., whipworms *Trichuris* sp., or hookworms *Ancylostoma* sp.) – see page 2*
- *The general term "roundworm" is commonly used for all the nematodes; however, hookworms, whipworms and pinworms are common names of specific group of nematodes – see page 2*
- **Strongyloides stercoralis* is commonly classified as a threadworm, not a pinworm – see page 3*
- *Infective stage of all ascarids are the eggs containing the third larval stage; the description of the *A. lumbricoides* life cycle on the page 3 is somewhat misleading*
- *The candidate should use only accepted common names of GINs – e.g. barber's pole worm (*Haemonchus* spp.) or black scour worms (*Trichostrongylus colubriformis* and *T. vitrinus*) – see page 5*
- *The fifth larval stage (L<sub>5</sub>) in the schema of *H. contortus* life cycle is missing – see figure 2*
- *The photomicrographs presented in figure 3 do not provide any basic morphological features for *H. contortus* identification (e.g. male gubernaculum, spicule tips and individual rays of bursal lobes or neodont morphology in the buccal cavity in both sexes) and this figure should be omitted*

- *The correct name of a spiroindole anthelmintic drug is "derquantel" not "draquantel" – see page 17 and in the later pages*
- *In my opinion, the section focused on anthelmintic resistance detection methods (page 21) is overly simplistic and misleading; at the very least the methods should be divided into in vivo and in vitro techniques because they provide different results*
- *The larval development test (LDT) as the most universal in vitro method for the detection of anthelmintic resistance which is applicable to all anthelmintic classes should be included to this section*
- *Based on the current knowledge/recommendations, the benzimidazole resistant nematode strains are present if a medium effective dose  $ED_{50}$  exceed the concentration of  $0.2 \mu\text{g TBZ.ml}^{-1}$  – see page 21*

*Notwithstanding the minor shortcomings mentioned above, the literature review section provides a solid background for understanding the issue and to the experimental part of thesis. There are no other weaknesses which require further attention.*

*Whereas all the presented papers have undergone an international peer-review process conducted by several specialists in the given topic, it can be assumed that the methods and techniques applied in this PhD thesis can produce results that achieve the stated aims. Although the aims of this thesis are clearly stated, the scientific hypotheses are absent.*

*The chapter Results and Discussion is divided according to the individual topics of the papers and summarizes the findings of the research included in this PhD thesis. Only relevant data and findings (without bias or misinterpretation) that connect with the goal of the thesis are presented to avoid overwhelming a reader. The candidate put her results in the context with appropriate research topics and highlighted larger implications of her research.*

*Markéta Zajíčková has demonstrated the ability to perform research in a specific field in order to achieve and present scientific results. Her PhD thesis meets all of the standard requirements*

*and I find this thesis adequate for defence in front of a respective committee with the aim of receiving a Doctor of Philosophy (Ph.D.) degree.*

*Questions for the defence:*

- 1. Haemonchus contortus is a popular model for parasitological research around the world. Do you have an idea how prevalent is this pathogenic nematode amongst small ruminants in the Czech Republic? And what is the current importance of H. contortus for ruminant livestock production in the CR?*
- 2. What is your opinion on non-chemical approaches to control GINs in the conditions of the CR? Discuss both the real pros and cons of these alternative control practices.*

Prague, August 29, 2023

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***doc. Ing. Jaroslav Vadlejch, Ph.D.***

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