

Review of dissertation thesis

Title: Study Of Pyridine Derivatives As Potential Antimycobacterial Active Drugs
Author: Mgr. Daria Nawrot
Supervisor: Prof. PharmDr. Martin Doležal, Ph.D.
Consultant: Assoc. Prof. PharmDr. Jan Zitko, Ph.D.
Reviewer: Prof. PharmDr. Kamil Musílek, Ph.D.

Author submitted the dissertation thesis (commentary on published articles) written on 34 pages. The thesis is divided into reasonable chapters and 95 literature sources are referenced. Author published 3 experimental articles related to the thesis topic plus 2 more (review, article) not directly related to the thesis.

The introductory part is standard, when it is reflecting the thesis/topic. But the direct thesis aims are missing or they are somehow incorporated into introductory or other chapters. I think these should be clearly defined as a separate chapter. The chapters related to commentaries of published articles are well prepared with some issues/drawbacks (see comments/questions). Author published 2 experimental articles as the first author (Q3 and Q1 based on impact factor) and 1 experimental article as co-author (Q2 based on impact factor). Two articles were published in journals with standard per-review processes, one in journal with questionable per-review processes. Two other published works, where author is on the first position are somehow related to the thesis topic. The author had also multiple presentations on the international scientific meetings.

Comments:

1. There are multiple typographical errors that could be corrected by author.
2. The Czech abstract was most probably not correct by native speaker, but it should be.
3. Artemisinin-resistant malaria should not be listed in chapter Antimicrobial resistance.
4. Fig. 8/9/11/15/16/17 – the substitution R/R¹/R² should be better given in the figures to better depict the structural motifs used for derivatization.
5. The author's contribution should be given for each publication listed on p. 31/32, although it is mostly written in the previous sections.

Questions:

6. What means: According to the literature [ref] ... ; ... in immunodeficient patients [ref]. (p. 14)?
7. Is HepG2 carcinoma cell line good model for cytotoxicity evaluation? What are its advantages or disadvantages?
8. Why the data from biological evaluation are not listed in the thesis? Such data are commented in the text, but one has to check the published articles (not directly attached to the thesis) to find them. I think this is the major drawback of the thesis. Especially, if the unpublished data from *in vitro* evaluation are commented in the thesis without showing them.
9. I.e. the Conclusions section contains the extracted activity data (in text or figure) that were not depicted before. How can one find the rationality of selecting those compounds are the most promising? Please, show the complex bioactivity data during the thesis defence and rationalize the selection of the most promising compounds.

In summary, the dissertation thesis of Mgr. Daria Nawrot contains interesting results that are important for further research in this field. Author most probably did a huge amount of experimental work that was published in impacted journals indexed in Web of Science. The thesis could be improved in many directions according to the comments/questions of the reviewer. But in general, thesis fulfils the criteria for dissertation theses and I recommend it for defence in front of board of experts, where student should explain and answer comments and question raised by the reviewer.

In Hradec Králové 21st March 2024

prof. PharmDr. Kamil Musílek, Ph.D.