CHARLES UNIVERSITY
FACULTY OF PHARMACY IN HRADEC KRALOVE

Department pharmaceutical chemistry and pharmaceutical analysis

Study program: Pharmaceutical Sciences

Opinion of the Opponent of the Diploma Thesis

Year of the defense: 2023

Student:	**Nechirwan Taimur Abdalrahman, B.Sc.**
Thesis Tutor:	doc. PharmDr. Jan Zitko, Ph.D.
Consultant:	
Opponent:	doc. PharmDr. Veronika Nováková, Ph.D.
Thesis title:	**Design, synthesis and evaluation of heterocyclic compounds with potential antimicrobial activity VI**

Scope of work, number of 64 pages, 13 figures, 3 tables, 41 citations

Evaluation of the work:

a)	Processing of the theoretical part:	Very good
b)	The complexity of the methods used:	Excellent
c)	Preparation of the methodological part (clarity, comprehensibility):	Excellent
d)	The quality of the experimental data obtained:	Excellent
e)	Processing of results (clarity):	Very good
f)	Evaluation of results, including statistical analysis:	Excellent
g)	Discussion of results:	Very good
h)	Clarity, conciseness, and adequacy of conclusions:	Excellent
i)	Meeting the objectives of the work:	Excellent
j)	Quantity and up to date of references:	Excellent
k)	Language level (stylistic and grammatical level):	Excellent
l)	Formal level of the work (text structure, graphic design):	Excellent

I recommend the thesis for recognition as a rigorous thesis ☐

Comments on the evaluation:

The work of Nechirwan Taimur Abdalrahman deals with synthesis of a series of 3-(arylureido)pyrazine-2-carboxamide derivatives, its antimicrobial evaluation and computational methods describing the interaction with the homology model of Mycobacterial prolyl-tRNA synthetase. Theoretical part is devoted to tuberculosis, the possibility of its treatment and the issue of resistance. The flow of the text could be better, some paragraphs seem to be unrelated to the previous text. Overall, however, this chapter is clear and provides an up-to-date overview of the issue studied. Experimental part describes procedures of the reactions as well as for computational and antimicrobial studies. However, it is not clear which experiments were performed by the student and which were done as a service. The next chapter Results and Discussion describes shortly the story of chemical experimental part. Student mentions that some of the final products were purified by flash chromatography, but nothing like that is described in the Experimental section. The repeatability of the described reactions may therefore be questionable. The student also mentions that the substitution conditions were optimized, but the specific procedures tried (e.g., reactants, solvents, times, etc.) and yields given are not listed anywhere in the Diploma

Thesis. In my opinion, this part of discussion could have been more detailed, e.g. it could have compared the methods used with those described in the literature, optimization reactions could have been mentioned, etc. The discussion on antimicrobial activity, on the other hand, is precisely elaborated, as is the description of the in silico simulations. The next chaper Conclusion summarizes the work done within the Diploma Thesis, which is followed by the list of references in a uniform format. Overall, the Diploma Thesis is at a great level, both in terms of content and formality. The Theses programme and Turnitin have found quite a lot of agreement with other documents, but in general these are parts where this can be tolerated (e.g. description of the methodology for the determination of antimicrobial activity).

Questions and comments to student:

Notes: page numbers are missing; HPLC purity was not assessed only for fluorine samples as student mentions, but also for sample 3-MeO-VZN;

1) Which experiments were performed by the student and which were done as a service?

2) Why did you decided to use urea as a linker? Is there any obvious reason for this?

3) Could you compare your procedure for the synthesis of 3-aminopyrazine-2-carboxamide with published procedures?

4) How did you assign the signals in H-NMR to the individual hydrogens in the molecule? How do you explain that each of the hydrogens on CONH2 has its own signal?

5) The signal at 3.33 ppm in the H-NMR of intermediate-2 (in DMSO) is probably not the signal of the NH2 protons. Could you correct it and suggest where the NH2 signal might appear?

6) The substitution reaction yields are approximately 25% for almost all compounds of the series. Do you have any idea why the yields are so low? Could you summarize the optimization procedures mentioned in the discussion (what compound was used, what were the yields, etc.). What do you mean by the statement "carbonation was another problem"? (on page 50).

Evaluation of the thesis: Excellent		**For the defense:** **Recommend**
In Hradec Kralove	8. září 2023	signature of the opponent