

**CHARLES UNIVERSITY
FACULTY OF PHARMACY IN HRADEC KRALOVE**

Department of Pharmaceutical Chemistry and Pharmaceutical Analysis

Study program: Pharmacy

Opinion of the Opponent of the Diploma Thesis

Year of the defense: 2024

Student: **Asal Askari**
Thesis Tutor: Assoc. Prof. PharmDr. Jan Zitko, Ph.D.
Consultant: Ghada Bouz, Ph.D.
Opponent: Prof. PharmDr. Petr Zimčik, Ph.D.
Thesis title: **Design, Synthesis, and Evaluation of Heterocyclic Compounds with Potential Antimicrobial Activity V**

Scope of work, number of 56 pages, 14 figures, 10 tables, 60 citations

Evaluation of the work:

- | | |
|---|-----------|
| a) Processing of the theoretical part: | Excellent |
| b) The complexity of the methods used: | Good |
| c) Preparation of the methodological part (clarity, comprehensibility): | Very good |
| d) The quality of the experimental data obtained: | Very good |
| e) Processing of results (clarity): | Very good |
| f) Evaluation of results, including statistical analysis: | Good |
| g) Discussion of results: | Good |
| h) Clarity, conciseness, and adequacy of conclusions: | Very good |
| 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): | Very good |

I recommend the thesis for recognition as a rigorous thesis

Comments on the evaluation:

The presented work focuses on the development of novel heterocyclic compounds with quinazolinone scaffold as potential antistaphylococcal derivatives. The author introduces the readers first to the topic of Staphylococcus infections including their treatment and mechanism of resistance to current antibiotics. Novel antibiotics approved in the last years are reviewed as well. I consider this part of the work to be very informative and comprehensive. Then, the author focuses on the structural motif she investigated - quinazoline and quinazolinone and brings brief overview of them from the chemical point of view and reviews the use of this structural motif in therapeutical agents. This part of the text ends by review of the structure-activity relationships found in the literature between quinazoline derivatives and their activity against Staphylococcus aureus.

The work then follows by description of the work. The student synthesized one starting material (one step reaction) followed by aminolysis of the lactone by substituted benzylamines to obtain eleven target compounds. No optimization of the reaction was performed/needed. Subsequently, the compounds were submitted to biological assays

(antibacterial, antifungal, antimycobacterial). It is however, not clear who performed these experiments. The thesis does not state if the experiments were performed by the student or by any collaborators. Based on previous similar theses, it is expected, that these were performed in other department. If this is true, the discussion of the own results obtained by the student is strongly limited and most of the text is focused on the data obtained by collaborators (although on the compounds the student prepared). I would expect more focus on the work of the student, e.g., problems of the synthesis, reason for choosing the procedures, attempt to explain different yields, possible alternative strategies for the synthesis, etc.

The system for check of plagiarism (Turnitin) resulted in about 51% similarity. Part of the results is given by routine parts of the work (references, acknowledgement etc.) and does not represent any ethic problem. The most problematic from this point of view is text of the biological assays that is completely copied, including e.g., citation of the works from the original source that do not correspond to the current thesis. Unfortunately, proper citation of the original text was done only for chapter 4.3.1. The other three chapters are just copied without any reference (and without any modification). This is on the border of acceptance. I fully understand that the procedures for testing do not change but when the whole text is fully copied from other source, it should be properly cited. I recommend adding "errata" with correct citation.

Questions and comments to student:

- There are few typing errors (e.g., missing dots at the end of sentences, extra dots behind the numbers (Table 3), not correctly divided words at the end of the line, ...) but generally, the text is well written and prepared.
- Figure 7. The rightest structure is not a tautomer. It seems to be incorrectly drawn. Can you present the correct structure?
- How did you determine the amount of oxygen in elemental analysis? This element cannot be determined using the instrumentation available in our department.
- There are some errors in elemental analysis data description: GDM-4 (not complete analysis is mentioned, the data are calculated or determined values?), GDM-7, GDM-2 (the analysis is missing, only calculated data are presented. Is there any reason for that (low amount of sample, not yet completed analysis?)).
- The prepared compounds were not very active. Based on achieved experience and experience of your colleagues working on similar compounds, is it possible to suggest novel structures with potentially improved activity?

Evaluation of the thesis: Very good

**For the Recommend
defense:**

In Hradec Králové

29. května
2024

signature of the opponent