CHARLES UNIVERSITY
FACULTY OF PHARMACY IN HRADEC KRALOVE

Department Pharmaceutical Chemistry and Pharmaceutical Analysis

Study program: Pharmacy

Opinion of the Opponent of the Diploma Thesis

Year of the defense: 2023

Student:	**Amirhossein Fekri**
Thesis Tutor:	Assoc. prof. PharmDr. Jan Zitko, Ph.D.
Consultant:	Mgr. Vinod Sukanth Kumar Pallabothula
Opponent:	Assoc. prof. PharmDr. Miroslav Miletin, Ph.D.
Thesis title:	**DESIGN, SYNTHESIS AND EVALUATION OF HETEROCYCLIC COMPOUNDS WITH POTENTIAL ANTIMICROBIAL ACTIVITY IV**

Scope of work, number of 71 pages, 17 figures, 3 tables, 55 citations

Evaluation of the work:

a)	Processing of the theoretical part:	Excellent
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:	Very good
i)	Meeting the objectives of the work:	Very good
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:

Student Amirhossein Fekri elaborated a diploma thesis titled " HETEROCYCLIC COMPOUNDS WITH POTENTIAL ANTIMICROBIAL ACTIVITY IV. The thesis is arranged in the usual way.

The aim of the study was to design, synthesize, and test two series/types of pyrazineamide derived compounds. The thesis includes very detailed research part concerning compound of structural types of interest prepared by the authors research group or other researchers. Based on the obtained information, in the Experimental part the new derivatives were designed, explored in silico, synthesized and tested in in vitro biological essays. The prepared compounds are well characterized by physical and spectral methods. Unfortunately, the assay results wero not much successful, but some interesting structure-activity relations were found.

Both chemical methods of synthesis and biological assays results are discussed and in Conclusion part possible outcomes of the thesis are summarized.

The work is formally and graphically very well processed, with only a few misspellings and minor deficiencies, some of which are listed below.

Plagiarism detection software shown up to 21% similarity with other texts, the highest values with other studies of the same group, but is concerns the titles, general chemical synthetic and analytical methods, biological essays, literature citations. Some short similar texts in theoretical part were correspondingly cited. Therefore, the work can be considered original.

Overall, the thesis is of a very good level, it is a contribution to scientific work in the field, and it fully meets the requirements for qualification work of this type, so I recommend it for the defense.

Questions and comments to student:

Comments, errors and typos:

The page numbering is missing. Even if in the electronic version it does not seem to be a big problem, the orientation in the work is a bit complicated and in a printed version it is significantly uncomfortable.

Page 12, Fig. 1: Error in description of the left down formula. Additionally, the R1 and R2 substituents in the right down should be explained similarly to the R in the left formula.

Page 14: The formula of rifampicin is drawn unclearly, even if maybe correctly.

Generally to the INN in the text: They should be written with lowercase initial letter.

Page 22 and possibly elsewhere: the names of microorganisms should be written with capital initial letter and in italic. Here Plasmodium falciparum, page 32 Mycolicibacterium smegmatis.

Page 25, Fig. 6: The angles of bonds on carbon in upper part of formula seems to be too sharp.

Page 29, Step 1 description, 1st line: Missing bracket ending.

Questions:

Page 24, Fig. 5 and comments: While in text comments the note is about alkyl/methyl in position 2´, in the Fig. 5 formula 14b it is in position 4´. What is correct?

Page 25, discussion about substituent in position 4´: Could you explain if it is even necessary or advantageous?

Page 29, generally to acylation: The acyl chlorides used were commercial or did you synthesize them?

Page 29, reaction 2.2.1.(b) and elsewhere: Didn´t you experience of reaction the ester with hydrazine hydrate? Was the ester bond stable?

Page 34: Why the m.p. was not determined at compound 1?

Page 48 and following: Could you refer more in detail how you have optimized the conditions for the acylation reactions? Have you gradually increased reaction temperature possibly to find the optimal one for monoacylation?

Page 62 and following, Conclusions: You mention halogen and short alkyl as advantageous substituents, however, in the Thesis only chlorine, fluorine ad methyl were studied. Have you tested or found in literature another substituent of these types (bromine, -CF3, C2-C4 alkyls, etc.)?

Evaluation of the thesis: Excellent		**For the defense: Recommend**
In Hradec Kralove	11. září 2023	signature of the opponent