

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

Department Pharmaceutical Chemistry and Pharmaceutical Analysis

Study program: choose study program

Opinion of the Opponent of the Diploma Thesis

Year of the defense: 2024

Student: **Parinaz Tabarestani**
Thesis Tutor: Assoc. prof. PharmDr. Jan Zitko, Ph.D.
Consultant: PharmDr. Priam-Amedeo HOUNGBEDJI
Opponent: Assoc. prof. PharmDr. Miroslav Miletin, Ph.D.
Thesis title: **Design, synthesis, and biological evaluation of pyrazinamide derivatives containing 1,2,3-triazole linker II.**

Scope of work, number of 79 pages, 21 figures, 8 tables, 79 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): | Very good |
| d) The quality of the experimental data obtained: | Very good |
| e) Processing of results (clarity): | Good |
| f) Evaluation of results, including statistical analysis: | Very good |
| g) Discussion of results: | Excellent |
| 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): | Very good |
| l) Formal level of the work (text structure, graphic design): | Good |

I recommend the thesis for recognition as a rigorous thesis

Comments on the evaluation:

Student Parinaz Tabarestani elaborated a diploma thesis titled Design, synthesis, and biological evaluation of pyrazinamide derivatives containing 1,2,3-triazole linker II. The thesis is arranged in the usual way. The aim of the study was to design, synthesize, and test two series/types of pyrazinamide derived compounds, bearing phenyl substituent attached via triazole ring. The thesis includes 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 new derivatives were designed, synthesized and tested in in vitro biological essays. The prepared compounds are well characterized by physical and spectral methods. Antimycobacterial assays results were partly successful, 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.

Plagiarism detection software shown 11% (Theses), resp. 21% (Turnitin) similarity with other texts, mainly with other studies of the same group, but is concerns the titles, general

chemical synthetic and analytical methods, biological assays, literature citations. Some short similar texts in theoretical part were correspondingly cited. Therefore, the work can be considered original.

The experimental part of the thesis is on a very good level. However, the formal arrangement is much worse, with many typing errors, missing or abundant spaces, wrongly written uppercase and lowercase letters, etc. The work is graphically not quite well processed, with deficiencies, some of which are listed below.

Questions and comments to student:

General about the schemes: the formulas are of different size and many are very blurry. The formulas descriptions in the schemes are of different size even within the same scheme (e.g. Fig. 1).

Typing errors and inaccuracies:

Abbreviations: *Candida albicans* not in italic

List of Tables: Table 5 name with lowercase letter.

P. 18, 6.4-6.6: Wrongly lowercase letters.

P. 21, ciprofloxacin: INN should be with lowercase letter.

P. 28., 10.1: Merck is located in Schneldorf; Varian in Palo Alto.

P. 34, Table 2: Different font types in the Table.

In chapters 10.4.1-10.4.20 there are number of formal errors (missing colons, spaces in places other than where they belong, lowercase letters instead of uppercase, missing "measured" in Elemental analysis, etc.). Some formulas are of a very low quality.

P. 55, 11.1.4, second line: Huisgen cycloaddition should always be with uppercase letter.

P. 65, Table 6: in description antibacterial should be in lowercase letter.

P. 70: Eight trains with uppercase letter.

Etc.

Notes and questions:

P. 18, point 4: Click reaction is not necessarily stereospecific.

P. 27, Fig. 13: The formula o morphaznamide is written to be taken from Wikipedia. Where you can it verify?

P. 29., Step 2: Exactly how the gradient was performed (time course)?

In general on CuAAC reactions: yields were very variable and sometimes very low. This may be related to the different solubility of the reactants - while the components are lipophilic, the catalyst is strongly polar. Have you considered using a catalyst for CuAAC in a lipophilic medium? For example, what system could be used?

Generally to the Thesis: Which experiments were carried out directly by the author of the Thesis?

P. 37, 38: Table 5 and onwards: it does not make sense to introduce a CAS No. column for newly synthesised substances. Tables 5 and 6 could be in one common table, except for the CAS No. it is unnecessary to indicate mmol and mg in the same table.

Chapter 11.2: It was not necessary to insert NMR spectra directly in this type of work, but if they are already inserted, their description should be correct. There are a number of inaccuracies and errors in the descriptions given in this chapter. As an example, in the description of Fig. 16 (there are analogous errors in the others):

The hydrogens of the pyrimidine are discussed, but there is no pyrimidine in the molecule. Probably pyrazine was meant (?). But then the other points don't match:

Signal at 8.99 ppm (C): This doublet corresponds to the proton in position 5 of the pyrimidine ring.... (there is Cl in the position 5 of compound 19).

Signal at 8.85 ppm (D): This doublet corresponds to the proton in position 4 of the pyrimidine ring....(there is no hydrogen in case of pyrazine).

Signal at 4.59 ppm (H): This singlet corresponds to the protons on the alkyne group ($\text{C}\equiv\text{CH}$)... (the alkyne reacted to triazole, or not?)

Description of protons of the methylene group connecting amide nitrogen and triazole is missing.

At least this part of Thesis should be corrected in an errata.

Despite of the mentioned mistakes and inaccuracies, as already noted, the experimental part of the thesis is on a very good level, it brings a reasonable contribution to scientific work in the field, and it meets the requirements for qualification work of this type. Therefore, I recommend it for the defence, provided the major mistakes will be corrected.

Evaluation of the thesis: Very good

**For the
defense:**

Recommend

In Hradec Kralove

9. září 2024

signature of the opponent