

CHARLES UNIVERSITY
FACULTY OF PHARMACY IN HRADEC KRALOVE

Department: of Pharmaceutical Chemistry and Pharmaceutical Analysis

Master's degree program in Pharmacy

Opponent's review of Master's thesis

Student's name: Cristina Paredes de la Red

Mentor of the thesis: prof. PharmDr. Martin Doležal, Ph.D.

Year of the thesis
defense: 2018

Opponent of the thesis: PharmDr. Marta Kučerová, Ph.D.

Title of the thesis:

Synthesis and antiinfective evaluation of substituted N-(pyrazin-2-yl)benzenesulfonamides

Formal comments: number of pages: 58, number of figures: 7, number of tables: 5, number of references: 34.

Type of work: Experimental work

- a) The aim of the thesis is: Fulfilled
- b) Language and graphic level: Excellent
- c) Processing of the theory: Excellent
- d) Methods description: Excellent
- e) Results description: Excellent
- f) Discussion and conclusions: Excellent

I recommend Diploma thesis for the recognition as Rigorous thesis .

Opponent's comments:

Survey

Cristina Paredes de la Red dealt with the synthesis of molecules combining pyrazine ring and arylsulfonamide moiety. The compounds were obtained by sulfonylation of aminopyrazine or 6-chloroaminopyrazine and they differed further in the aryl part. In total, eight compounds have been synthesized either in a flask or in the microwave reactor. All the substances have been obtained in sufficient purity and characterized by melting points and NMR spectra as a contribution to a larger series of twenty one compounds in total prepared previously. The compounds have been evaluated for antibacterial and antifungal activity and partly on antimycobacterial effects. The comparison of biological activity of the whole series is provided (in case results were available) Some selected descriptors of the compounds have been included, e.g. Rule of five, lead likeness.

In the theoretical part of the diploma thesis, tuberculosis treatment is described and the design of the synthesized compounds is elucidated.

Comments:

p. 6 - I would recommend to write Food and Drug Administration in initials capitals from the reason being an institution name.

p. 8, line 2 - in the chemical name, letter e is abundant (pyrazine-2-yl)

p. 14 - I do not recommend to denote sulfonamides as antibiotics. Even if the public mixes the terms antibiotics and synthetic antibacterial agents, it should be distinguished in a scientific text. Whereas Paul Ehrlich - the Father of chemotherapy synthesized arsphenamin (Salvarsan) as the first antibacterial (antimicrobial) compound, the very first antibiotic used in therapy was streptomycin isolated from soil microorganisms. Sulfonamides are pure synthetic compounds and they are not bacterial products.

It is usual to write the units for NMR spectra - they are ppm and the signals are related to tetramethylsilane via the characteristic solvent signals.

In references, either the abbreviation of journal titles (e.g. ref. 3, 10, 20) should be used or the full journal title, not the mixed style.

Questions:

1. When you described the mechanism of action of sulfonamides on the page 16, you mentioned the competition with para-aminobenzoic acid. Do you know which enzyme is inhibited by sulfonamides during the biosynthesis of folic acid in bacteria?
2. Could you please comment on the discrepancies between the chemical formula on the page 21 in the third line below the structure and in the paragraph Elemental analysis?
3. Have you dried your compounds after chromatography and before characterization?
4. Could you please elucidate the characterization of compounds by IR and NMR spectra (see page 18).
5. In the discussion, I miss any synthetic remarks - complications, novelty of the compounds (reference melting points) and other matters like comments on methods of characterization.

To sum up my evaluation, the student was able to accomplish the work and write the diploma thesis at very high quality and in very short time. In addition, Cristina Paredes de la Red succeeded in Students Scientific Conference at the Faculty of Pharmacy in Hradec Kralove (April 18th 2018) with the second prize in the chemical section. I would like to congratulate Cristina and express my admiration.

Evaluation of Master's thesis: Excellent

Recommendations for the thesis defense: Recommended

In Hradec Kralove May 27th, 2018

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Opponent's signature