

## Evaluation review of dissertation thesis

**Charles University in Prague, Faculty of Pharmacy in Hradec Králové**

**Workplace:** Department of Pharmaceutical Botany

**Name of student:** Latifah Ajaj Al Shammari, MSc.

**Title of dissertation:** Alkaloids of the genus *Hippeastrum* (Amaryllidaceae): isolation, identification, biological activity

**Reviewer:** prof. PharmDr. Karel Šmejkal, Ph.D.

**Workplace of reviewer:** Department of Natural Drugs, Faculty of Pharmacy, MU

### Text of review:

Latifah Ajaj Al Shammari's dissertation is written on the topic of isolation, structural analysis and testing of biological active natural substances. It is concentrated on the analysis of alkaloids obtained from plants of the family Amaryllidaceae, in particular from *Hippeastrum* spp. At the workplace, she isolated a series of alkaloids typical of Amaryllidaceae plants, using classical chromatographic methods. A combination of various analytical techniques, in particular nuclear magnetic resonance and mass spectroscopy, was used to identify the substances. Thus, she isolated 18 different alkaloids and tried to determine their relative representation in the analyzed plant. These substances were evaluated for biological activity towards enzymes of interest in the treatment of Alzheimer's disease, as well as for the evaluation of potential cytotoxicity.

Isolation of natural substances from plant material is a very traditional pharmacognostic discipline. It has long provided a description of thousands of structurally diverse compounds that serve as drugs or as models for the synthesis of more active compounds. At present, the discipline may be somewhat underestimated because it requires patience, the results are often not fantastic, and the result is suitable for publication often only when needs to be combined with extensive biological activity testing, which makes the outcomes of the whole process more attractive. The work performed by the author is a typical representative of the phytochemical analysis described here. She isolated a series of substances in an amount sufficient both for testing biological activity and for the potential preparation

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of semi-synthetic derivatives. One compound was described in plant material for the first time. Tests of activity in connection with Alzheimer's disease did not show significant activity, but the potential in the field of cytotoxic activity and subsequently the activity of semi-synthetic derivatives promise interesting results.

Graphically, the work is at a standard level. Part of the work is also an overview of used literature. The author was the first author or participated in the publication of a series of works, an overview of which is given. The works are published in renowned and quality magazines and there is no need to doubt their quality. Overall, I evaluate the work positively, it contains a lot of new information, and within the studied issues it is necessary for further research in this area. I have some general comments and questions:

*Formal comments:*

Use constantly symbol L or l for litres

I recommend to use electron impact ionization instead electron ionization to describe the MS ionization method

*m/z* should be in italics

Fonts should be uniform in size through the text

x or × should be used constantly through the text

*Questions*

- 1) Page 28: its written, that 64 Hippeastrum alkaloids were fully characterised, later 69 structures are mentioned. Which compounds make the difference and how were they identified?
- 2) I do not fully understand the Chapter 4.6 – the amount of extract was the amount processed? The first number the amount of processed bulbs?
- 3) Could you please explain which „additional physical properties“ were used to identify the isolated compounds, for example in chapter 4.6 ?
- 4) Page 47 – 360 fractions with volume of 500 mL, means you used 180 liters of solvents?
- 5) 5.2.6. The presented ismin belongs to phenantridine type of alkaloids? Could you explain the biosynthetic pathways behind this compound?
- 6) Why do you use assignment of signals in <sup>13</sup>C NMR for some compounds, and for some not?
- 7) 5.2.18 „The ESI-HRMS of this compound showed a molecular ion peak [M+H]<sup>+</sup> at *m/z* 304.1550, corresponding to the formula C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub><sup>+</sup> (calc. 304.1543). (Fig. 32).“ the value is corresponding to M<sup>+</sup> not to M+H<sup>+</sup>

## **Conclusion**

The student has demonstrated creative skills in the field of research, the work meets the requirements of standard dissertation in the field. I recommend the thesis for defence before the commission for state doctoral examinations and defence of dissertations.

**Datum:** 22/05/2021

**Signature:** Karel Šmejkal