

Posudek oponenta disertační práce

Univerzita Karlova

Fakulta

Doktorský studijní

program

Farmaceutická fakulta v Hradci Králové

Farmakognosie a nutraceutika

Uchazeč

Pracoviště

Habilitační práce

Abdullah Al Mamun MSc.

Katedra farmakognosie a farmaceutické botaniky

Amaryllidaceae alkaloids of genus *Narcissus* and their biological activity

Oponent

Pracoviště

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The thesis relates to „Amaryllidaceae alkaloids of genus *Narcissus* and their biological activity“. *Narcissus* plants have always been a promising source of Amaryllidaceae alkaloids as primary health remedies by indigenous peoples for many centuries. The thesis is therefore interesting from scientific point of view. Its research part is focused on isolation of alkaloids from different natural sources, identification, and subsequent screening of different biological activities, for example testing enzyme inhibition (hAChE, hBuChE, POP, GSK3 β , and BACE1), cytotoxicity testing on panel of tumour cell lines and antimicrobial activity testing. would like to highlight some of the research results obtained in this thesis:

1) Three novel belladine-type alkaloids named carltonine A, B, and C have been isolated. Carltonine A and B alkaloids exhibited selective hBuChE inhibition. The heterodimer alkaloid narciabduliine inhibited both hAChE and hBuChE. Subsequently, twenty derivatives have been synthesized.

2) Semi-synthetic derivatives of galanthamine have been prepared by substituting its free hydroxyl group in position C-6. Interestingly, all compounds showed significant antimycobacterial activity against all studied *Mycobacterium* strains. The most active derivatives were found to have hepatotoxic effects. Further optimization of the structure is required to improve antibacterial activity with reduced cytotoxicity.

The thesis is classically divided and consists of an Introduction, Aims of the Thesis, Theoretical Part, Overview of the Publications, Conclusion, Abstract, List of Publications, and References. I personally like comments on the published works within the individual chapters and a conclusion with a view to the future. The thesis is based on three original

papers published in international peer-reviewed journals. There are 2 first author papers published in *Biomolecules* and *Int. J. Mol. Sci.* All these journals have very good international reputation. Abdullah Al Mamun also contributed to three other very good articles which are included in the dissertation. There are 3 other articles not included in the thesis where Mr. Manun is also co-author. He also participated in several conferences (5 lectures + 1 poster), in which he is also the first author. Such a record of a publication is a very good student for a doctorate. It shows that Mr. Manun worked in a highly productive team, in which more employees contribute to each of the published contributions. I very much appreciated that the author's contribution is always clearly declared in relation to each published article.

The above-mentioned list also clearly shows very significant share of the author in published works. The dissertation itself is very erudite, written in readable language and even for an occasional pharmacologist it is very easy to understand. This is a very high-quality thesis. Only exceptionally I discovered more complicated and less comprehensible sentences. The essence of the dissertation cannot be criticized in its essence. The work is also tastefully complemented graphically by pictures. There are typos here and there, but they can be forgiven. Also, references are not always uniform. Here and there the full names of journals and elsewhere their abbreviations are used, as well as citations of books or chapters in various styles, etc.

Opponents' questions on the defence of the dissertation

1. You were able to prepare a new series of galanthamine derivatives with significant antimycobacterial activity against different *Mycobacterium* strains which were however hepatotoxic. Do you have some ideas how to get more effective compounds but with limited hepatotoxicity?
2. Your review summarizes recent progress on Amaryllidaceae and further isoquinoline alkaloids in relation to Alzheimer's Disease. You summarised that different research groups used various types of enzymes within biological assays, e.g. electric eel acetylcholinesterase (EeAChE), human acetylcholinesterase (hAChE), mouse brain acetylcholinesterase, equine serum BuChE (EqBuChE), and human BuChE (hBuChE). You just declare this alkaloid has this type of effects while the other one another type of effects. However, I was not able to find any real conclusion. What is really the most interesting target. Would it be interesting to focus on more of these enzymes together?

What about testing on cell level? There are also several Alzheimer's Disease cell line models which could be used to further test potential of your compounds. Some *in vivo* models are known as well. Is there some potential to improve the level of testing in your labs?

Conclusion

In conclusion, I would like to state that the results of the submitted thesis are very interesting and widely published in foreign journals, which significantly increases the prestige of this dissertation. This is an exceptionally good work, in which a high degree of the author's ability to conduct targeted scientific research in the field of molecular Pharmacognosy and Nutraceuticals is clearly observable. The thesis Abdullah Al Mamun MSc. "Amaryllidaceae alkaloids of genus *Narcissus* and their biological activity" meets all the standard requirements for theses in the field of Pharmacognosy and Nutraceuticals. From a scientific point of view, the thesis meets all the criteria for this type of thesis in the sense of Act 111/1998 Coll., and therefore I recommend it for defence.

Olomouc, 10.4.2022

Prof. Ing. Miroslav Strnad, DSc.