

**UNIVERZITA KARLOVA V PRAZE
FARMACEUTICKÁ FAKULTA V HRADCI KRÁLOVÉ**

Katedra farmaceutické chemie a kontroly léčiv

Studijní program: Farmacie

Posudek oponenta diplomové práce

Oponent/ka: **Doc. PharmDr. Miroslav Miletín, Ph.D.**

Rok obhajoby: 2015

Autor/ka práce: **Jeřábek Jakub**

Název práce:

Design and Synthesis of Hybrid Compounds Based on Tacrine/Resveratrol Derivatives

Rozsah práce: počet stran: 39, počet grafů: 0, počet obrázků: 4,

počet tabulek: 1, počet citací: 42

Práce je: experimentální

- a) Cíl práce je: zcela splněn
- b) Jazyková a grafická úroveň: velmi dobrá
- c) Zpracování teoretické části: výborné
- d) Popis metod: výborný
- e) Prezentace výsledků: výborná
- f) Diskuse, závěry: velmi dobré
- g) Teoretický či praktický přínos práce: výborný

Případné poznámky k hodnocení:

Jakub Jeřábek elaborated his diploma thesis named "Design and Synthesis of Hybrid Compounds Based on Tacrine/Resveratrol Derivatives" at University of Bologna, Faculty of Pharmaceutical Sciences, Department of Pharmaceutical Chemistry.

The thesis comprises usual parts, including also list of abbreviations which is helpful in reading the text because of specific abbreviations used in this area.

As a Theoretical part he performed literature search for causes of the Alzheimer disease and described recent trends in the development of drugs studied or already marketed as real or potential agents for treatment of dementias. He classified the drugs according to their mechanism of action.

In Experimental part of the Thesis he describes in detail the syntheses performed, the biological screening methods are mentioned as well.

The Thesis is finalized by Discussion, Conclusions and list of References.

The thesis corresponds in its extend and content to the task as well as to the convention in this type of work.

Dotazy a připomínky:

I have following questions and comments:

Generally in the Thesis: in some cases capital letters are used inappropriately (p. 16 - Sarin, Tabun; p. 23 Scheme 4 - several cases, page 25 Scheme 2 - Crown, p. 32 Anthranilic acid)

Confusing numbering of Schemes: Scheme 1 to 4 until page 23 and then again Scheme 1 to 3.

Ad p. 20: Could you explain the mechanism of brain lipids peroxidation in more details?

p. 21: A mistakenly written very common word - vine should be wine...

Are there available convincing clinical trials confirming positive effects of antioxidants in treatment of AD?

p. 23, 24: Wrong drawing of indexes at R substituents - should be as upper index not lower ones.

The same pages: Schemes of synthesis would be better to arrange logically as the syntheses proceeded, so first intermediates, then final compounds. The same is for the descriptions of synthetic procedures.

Page 25 resp. 31 - the chemical used is Tin(II) chloride dihydrate not dehydrate (as written at p.31).

Ad Discussion: Have you got already some results of antioxidant activity testing?

General question to the topic: is there really demonstrated advantage of use of multi-target-directed-ligands above use of the separate constituents? What about balancing dosage of the active principles? What about optimization of pharmacokinetics etc.?

Despite of the above notes and comments the thesis fully complies with requirements for such type of work and I recommend it to defence.

Celkové hodnocení: výborně, k obhajobě: doporučuji

V Hradci Králové dne 15.9. 2015

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podpis oponentky / oponenta