



Örebro 28 August 2015

Examiner's report on:

Dissertation thesis:

**Interactions of muscarinic receptors and choline esterases:
Functional examinations of esterase inhibitors in the rat.**

Candidate: Uday Kumar Killi, MSc

The current dissertation thesis concerns an investigation of some aspects of muscarinic signaling in the control of heart and the urinary bladder. Although it is an experimental work in rat, the issue under investigation has a great interest also in human biology, since disturbances of heart rhythm as well as of bladder storage, and emptying capacity, respectively, are of marked clinical significance. This thesis, therefore, concerns highly relevant biological problems. The theoretical coverage, the methodological approach, and the analyses of the results obtained, are all in general satisfactory.

Below, my specific comments on the thesis will follow.

The thesis comprises 106 pages.

The *Abstract* (pp.4-8) is written English as well as in Czech, and provides a main summary of the background, the current aims, the methodology used, and the chief results obtained and the interpretations of these.

One appreciates the ensuing list of the *Abbreviations* (pp10-11) that follows.

The *Contents* (pp.12-14) is very detailed, and gives in itself a brief overview of the entire project that has been conducted.

The *Introduction* (pp. 15-62) is a detailed account of the field under study, providing a proper background of the current research topic, and describing in detail the autonomic nervous system,

its signaling molecules and their receptors and respective signal transduction systems. In particular, acetylcholine as a very important messenger, and its synthesis and degradation systems, as well as the (so far) five different receptor subtypes and their respective ligands are covered in depth. Especially, cholinergic drugs (agonists, antagonists, and reactivators) are thoroughly discussed.

The four different *Aims* of the current project (p.63) are clearly stated.

The *Materials* and *Experimental Methods* (pp. 64-67) are listed in short.

The main *Results* obtained in the current investigation with some relevant comments (pp. 68-81) are summarized; despite the complicated nature of some of the findings, the candidate manages to present these in an understandable fashion.

In the *Discussion* (pp. 82-88), the results obtained are analysed and are put into perspectives.

Finally, a *Conclusion* (p. 89) summarizes the main findings of the doctorate project.

It should be mentioned that throughout the thesis, there are a large number of explanatory figures and graphs which improve the text considerably.

The *References* (pp.91-106) cover the important background for the thesis project.

In conclusion, the current dissertation thesis is, as already stated, satisfactory. I have some comments about the thesis that I would like to discuss with the candidate, which, if properly dealt with, would markedly improve the text. Moreover, provided that the presentation and the defense will be conducted acceptably, I will recommend giving the candidate the title of PhD.

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