



Review Report on PhD Thesis of Anna Simonova

Thesis title: *New Redox Labels for DNA*

Supervisor: prof. Ing. Michal Hocek, CSc., DSc.

Anna Simonova submitted the doctoral dissertation dealing with the synthesis of the modified 2'-deoxyribonucleoside triphosphates bearing electrochemically oxidizable labels (2,3-dihydrobenzofuran, 2-methoxyphenol, phenothiazine, or ferrocene derivatives) and their incorporation into DNA for the application in bioanalysis.

The PhD Thesis of Anna Simonova is well structured and correctly presented. It consists of 6 main chapters written in English (Introduction, Specific Aims of the Thesis, Results and Discussion, Conclusions, List of Publications, and Experimental Section). The PhD Thesis is written on 143 pages altogether, and enriched by number of figures (58), equations, schemes (43), and tables (18). The theoretical principles as well as the research part were validated with 178 valuable references (see chapter 8).

In chapters 1 and 2, Anna Simonova introduces the reader to the dissertation topic. It is worth to note that the Author has studied carefully the research subject with critical view and used appropriate number of bibliographical sources. It is an evident fact that Anna Simonova deeply understands the theoretical knowledge and the discussed problems.

Chapter 3 (Results and Discussion) represents the most extensive part of the dissertation and reveals the story (based mainly on the Author's peer reviewed publications in *ChemPlusChem*, *Organic and Biomolecular Chemistry*, *Bioorganic and Medicinal Chemistry Letters*, and *Electrochimica Acta*, see chapter 5 – List of Publications) behind the research conducted by Anna Simonova, being clearly summarized in chapter 4 (Conclusions).

In chapter 6 (Experimental Section), instrumentation, materials, and chemicals used to carry out the research work outlined in this dissertation are described. According to my opinion, all the important information to understand and repeat the conducted experiments are presented here.

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This PhD Thesis is greatly written and very well documented. There are almost no typing errors and the text is written in clear and concise manner. The figures and tables are shown properly as well. The hypothesis and arguments are well formulated with meritorious conclusions based on valuable and actual literature. The conclusions confirm that the formed objective of the work was successfully finished.

However, there are mine very minor comments regarding the places in the dissertation which could be improved:

1. There are some heterogeneities in style of the text: a style used once is sometimes not kept when the same style should be applied (e.g., *N*- vs. *N*-, 3'- vs. 3'-, etc.).
2. When some unusual abbreviations are used in figures/schemes, they should be introduced/explained in the figure/scheme caption and/or in the text.
3. Application of paragraph indents could provide better differentiation of individual paragraphs, especially the short ones.
4. All square-wave voltammograms, which were corrected to baseline (e.g., in Figure 29), should be differentiated from those without the baseline correction applied (e.g., by simple note in the figure caption: "Baseline-corrected AdTS square-wave voltammograms of...", like in Figure 45).
5. Graphical quality of some figures, especially those showing electrochemical results, could be better.

There are listed my specific questions to the Defendant to be answered/discussed in the framework of the oral PhD Thesis defense:

1. Chapter 1.4.1: Is liquid mercury the only one electrode material which can be successfully used for investigation of electrochemical reduction of DNA nucleobases?
2. Chapter 1.4.2: Which electrochemical signals resulting from electro-oxidation of DNA nucleobases were observed at silver, copper, and mercury electrodes (that are not suitable for measurements in anodic region of potentials because of electrochemical dissolution of their material at those potentials)?
3. Chapter 3.1.4: How did the Author recognize from square-wave voltammetric recordings that the voltammetric signals in Figure 24 are irreversible, or in Figure 55 reversible (both mentioned in the text)? Or, was there any other investigation criterion applied?

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4. In Figure 55, square-wave voltammetric peaks of dC^{FcM} and dA^{FcM} at potentials around 1.1 V to 1.2 V are not discussed. Does the Author have any idea what redox transformation is behind those signals? Why they are not observable for dC^{Fc} and dA^{Fc} ?
5. Could the Author say a few words about possible applications of her results in clinical and/or medical practice, or in bioanalysis in general?

To sum up, the PhD Thesis represents high level scientific work. It seems to be an interesting material for scientists working with chemically modified DNA bases and investigating their electrochemical behavior. All experiments are well arranged and measurement techniques and methods are correctly applied. It is generally well presented and very interesting to read. The explanations are suitable and focused on the relevant topics.

In my opinion, the reviewed PhD Thesis fulfills all requirements posed on theses aimed for obtaining PhD degree and demonstrates the Author's ability of critical thinking and scientific teamwork in organic chemistry, biochemistry, and electrochemistry. This PhD Thesis is ready to be defended orally, in front of respective committee.

I would like also to propose to reward Anna Simonova's doctoral dissertation due to the following aspects: scientific novelty, an extensive range of research, meritorious presentation and discussion of obtained results, outstanding scientific activity confirmed by papers published in commonly known and highly ranked scientific journals.

Sincerely

doc. RNDr. Vlastimil Vyskočil, Ph.D.

Prague, December 3, 2018

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