Warsaw, 22.05.2022

Prof. dr hab. Dorota Maciejewska

ul. Szwankowskiego 4a m 12

01-318 Warszawa

The review of PhD thesis

titled

Molecularly imprinted polymers-based chemosensors for selective determination of chosen food toxins

written by **Viknasvarri Ayerdurai**

Although the idea to use the molecularly imprinted polymers (MIP) to the bioanalysis is not really new, the research objective is topical, because of increased of public awardees concerned the food contaminants, and increasing demands from the food industry for rapid toxin determination, which has prompted the development of the analytical devices. New analytical systems for the food toxins examinations, can have a positive impact on the safety of the consumers. The proposed electrochemical sensors coated with imprinted polymer layer as the tools to the realization of the scientific goals should result in the efficient, bioanalytical devices. The planned use the sensors in the presence of the interferences and developing of the electrochemical method to measure their recognition properties are serious challenge. Therefore, the solution of the problems and the positive outcome of the research have a strong potential to fulfil the requirements for the PhD project.

The presented PhD thesis has a classical organization on 192 pages. First, data about the scientific activity of PhD student are given. She is the co-author of 2 papers (Σ IF = 10.652), 1 patent application, 4 oral and 7 poster presentations at scientific conferences. She was the participant of 2 short training programs. I should mention that there are also 2 manuscripts prepared to publish. All these achievements are joined with PhD research, and reflect well her activity and level of her work.

Next, the main goals and the final results are showed in the Abstract. She experimentally verify the possibility of the determination in complex biological matrices two substances: tyramine and 2-amino-3,7,8-trimethyl-3*H*-imidazo[4,5-*f*]quinoxaline (7,8-DiMeIQx) by using the chemosensors covered with the molecularly imprinted polymer

layers. Chapter 1 and also Section 2.2 in Chapter 2 can be described as the literature review or the introduction. Section 1.1 summarizes the idea of the molecular imprinting in the polymeric matrices, the MIP preparation procedures, and the significance of the computational simulations. Section 1.2 concerns the construction of the electrochemical MIP chemosensors and their application in food and pharmaceuticals analysis. Section 1.3 comprises knowledge about the compounds of interest and about their determinations using MIPs. There are also data about MIPs mimicking dsDNA interactions. Section 2.2 contains the information about the electrochemical and the physicochemical techniques, especially these which are used in PhD dissertation. Sections 2.1 and 2.3 include the experimental information with the recipes details. In all these parts a lot of abbreviations are used, and the data are presented as the text and additionally as the figures. The illustrations repeat the information from the text, but are made very professionally. Unfortunately, the errors creep into the text. I am showing few of them which are joined with the theme of PhD thesis.

Page 48, Scheme 1.3-3 – improper chemical formulas of quinoxalines (fortunately, formula of 7,8-DiMeIQx in the rest of the thesis is given properly).

Page 62, Table 2.1-4 – improper chemical formula of urea.

Pages 57 and 158 – the information "two cancer triggering food toxins ... ". It is not true for tyramine. Tyramine is not the carcinogenic substance. It is trace biogenic amine joined with the hypertension crisis, the intracranial hemorrhage, the cardiac failure and many more.

Pages 144 and 160 – the information about IR spectra measurements differs. The text should be carefully corrected because of the mistakes also in the main part *i.e.* Chapter 3 and 4.

To sum up, Chapters 1 and 2 direct our attention to the methods or the research which are crucial for the realization of the PhD project. The data are well referenced.

Chapter 3 elaborates the examinations of tyramine determination published in *Bioelectrochemistry* **2021**, 138, 107695, so comprises the data which were already reviewed, what simplifies the reviewer work. Nevertheless, I want to ask some questions, add some comments, and indicate some discrepancies in the text.

The computational simulations were performed only for two systems, and their significance is limited in the analysis of the molecular recognition. The author proposed cationic form of the template and the anionic form of the monomer. Is it good assumption?

Both substances are solved in acetonitrile, and the monomer is a weak acid.

The number of significant digits of the errors should be one, and the measured values should have as many significant figures as are consisted with the estimated errors. This rule is not satisfied in some part of PhD thesis for example in Tables 3.2-4 and 3.2-5.

A comment to the PM IRRAS spectra – the vibration band present at 3260 cm^{-1} can be assigned to water, which was adsorbed in the pores of polymer layer during extraction.

To sum up, Chapter 3 presents the results which can stimulate the future research. For example, the Author:

– used a non-linear regression to construct calibration line for tyramine sorption in real samples, what allowed for the elimination of the interferences impact on the analysis

– proposed the monomer with the corona ether substituent, what is an interesting proposition, because the template can create many intermolecular interactions during imprinting process

– showed the essential role of the post-polymerization treatment for the physicochemical properties of the sensor surface.

Chapter 4 concerns the determination of 2-amino-3,7,8-trimethyl-3*H*-imidazo[4,5-*f*]quinoxaline (7,8-DiMeIQx) published in *J. Agric. Food Chem.* **2021**, 69, 14689-14698, what means that discussed studies are accepted by the scientific community, and makes also the reviewer task more complicated.

The Author utilized the adenine- and tymine-functionalized monomers to the synthesis of the polymer's layer. It is a clever idea because the MIP-chemosensor can mimic the interactions with DNA, which are responsible for the toxicity of 7,8-DiMeIQx. The computational simulations have predicted the possibility of successful creation of the selective adsorption cavities for the pre-polymerization complexes, defined by the Author. However one should remember, that the polymerization and the sorption processes are performed in the different conditions (solvents, ions, temperature), and that the predictions are dependent on the choice of the modeled systems. The new materials obtained during synthetic procedures were sensitive for the extraction/washing steps, and their successful optimization was made by the Author. The Author performed the time-consuming examinations to understand the differences in the electrochemical properties of MIP- and NIP-coated chemosensors, as well as the dependence of their detection signals on the post-polymerization treatment.

My comments to Chapter 4 are as follows:

– the improper number of significant digits of the errors is also in this chapter (Tables 4.2-4, 4.2-5 and 4.2-6).

– the interpretation of the FTIR spectra – may be pronounced band at 2900 cm^{-1} can be assigned to CH_3 groups from trimethylamine, which was adsorbed during extraction?

– the 7,8-DiMeIQx are found in the biological samples at nanograms/g, but the limit of detection is 15.5 μM for the constructed sensor. It needs comment.

Both Chapters, 3 and 4, do not include information about the amount of experiments done to get each measured point.

To sum up, the goals of PhD thesis were carried out. New electrochemical sensors were constructed for tyramine and 2-amino-3,7,8-trimethyl-3*H*-imidazo[4,5-*f*]quinoxaline, and their selectivity was sufficient to the analysis in complex matrices.

The presented PhD dissertation meets the requirements of article 187 of the act from 20.07. 2018 "Low of Higher Education and Science' (A.R. From 2018, it.1668 with changes). I submit the proposal to the Scientific Council of the Institute of Physical Chemistry of the Polish Academy of Science to admit Viknasvarri Ayerdurai to the next steps of PhD procedure.

Prof. dr hab. Dorota Maciejewska