

STATEMENT

by

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on a research dissertation for conferring the educational and scientific degree of

Doctor of Philosophy

Higher education area: 4. "Natural sciences, mathematics and informatics"

Professional area: 4.3. "Biological Sciences"

Doctoral Programme in "Medical Biochemistry"

Author: Maria Atanasova Choneva

Type of doctoral studies: individual preparation

Department: "Medical Biochemistry"

Topic: *"Effects of Prebiotic Oligosaccharides and Aerobic Training on Metabolic and Behavioural Impairments in an Experimental Model of Type 1 Diabetes"*

Doctoral advisor:

Assoc. Prof. Anelia Veselinova Bivolarska, MD, PhD – Department of Medical Biochemistry, Faculty of Pharmacy, Medical University - Plovdiv

1. Presentation of the procedure and the PhD student

The materials presented to me in electronic version are in conformity with the Procedure for Obtaining the Educational and Scientific Degree of Doctor of Philosophy at Medical University - Plovdiv and include the following documents:

– Application Form addressed to the Rector of MU - Plovdiv to initiate a procedure for defence of a doctoral thesis; CV in European format; Rector's orders for entering doctoral studies and striking off with the right to defend a dissertation; proceedings from the Department Meeting on the preliminary discussion of the doctoral thesis, the dissertation paper itself; synopsis of the latter; a list of the research publications relevant to the dissertation topic; a list of the participations in research forums; statement on the originality and authenticity of the submitted documents.

The PhD student has submitted 3 (three) full text publications on the dissertation topic, 3 of which published in peer-reviewed journals. She has also had 6 participations in research forums with reported announcements on the topic.

Maria Atanasova Choneva graduated as a Master of Pharmacy at Medical University - Plovdiv in 2018. He worked in a pharmacy until June 2019, and from February 2020 as an assistant at the Department of Medical Biochemistry of the Faculty of Pharmacy, MU - Plovdiv. From November 2020 enrolled as a specialist in "Biochemistry" in the same department. In July 2023, she was enrolled as an individual preparation doctoral student at the Department of Medical Biochemistry and after a successful internal defence procedure in April 2024 obtained the right of official defence.

2. Topicality of the research

The dissertation examines the effect of two types of prebiotic oligosaccharides - XOS and GOS, and aerobic training on metabolic and behavioural disorders in rats with STZ-induced diabetes. The diabetic syndrome resulting from the administration of a high dose of STZ is characterized by hyperglycaemia, impaired growth, hyperlipidaemia, and oxidative stress. Behavioural testing revealed anxiety, depressive symptoms, and cognitive deficits. The study focused on the antidiabetic effects of XOS and GOS, which were manifested in significant improvement of hyperglycaemia and hypercholesterolemia, as well as lowering of serum MDA concentrations. A similar hypolipidemic and antioxidant effect was also observed as a result of aerobic training. In terms of neurological

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symptoms, oligosaccharides and aerobic training, alone and in combination, exert significant anxiolytic and antidepressant effects. A positive effect was also found on cognitive deficits, with improved passive learning, short-term and long-term memory being observed. Prebiotics and aerobic exercise also overcome impairments in spatial and recognition memory in diabetic animals. The results of the study support the thesis that oligosaccharides and aerobic exercise would be a useful part of a comprehensive strategy for the prevention and treatment of diabetes and its complications.

3. Knowledge of the problem

The doctoral student is familiar with the modern aspects of the developed topic in depth. A large part - 193 publications, which is 63% of the 307 sources used) is from the last 10 years. The literature review presents expertly analysed and concisely presented information on the state of the problem, which is summarized in several main conclusions at the end of this section. On this basis, the goal is set and the tasks are formulated.

4. Methods of study

An experimental design was used using male Wistar rats randomly assigned to 8 groups. Five of them have a model of diabetes, being distributed in subgroups: treated with xylooligosaccharides (XOS), galactooligosaccharides (GOS), application of aerobic training, alone or in combination for 10 weeks. A set of methods was applied: the blood glucose level was measured weekly, somatometric indicators of the animals were measured, behavioural tests were conducted, microbiological analysis and analysis of biochemical indicators were performed. The obtained data were processed with selected appropriate statistical methods.

All this gives me reason to state that the chosen research methods fully allow achieving the set goal and obtaining an adequate answer to the tasks solved in the dissertation work.

5. Characteristics and evaluation of the dissertation paper and its contributions

The dissertation covers 148 pages and is structured according to generally accepted requirements in the following sections – introduction, literature review, aim and objectives, material and methods, results and discussion, conclusion, conclusions, contributions.

The introduction briefly and clearly touches on the main aspects of the study - the social significance of type 1 diabetes mellitus (T1DM) due to the development of oxidative stress and inflammation in the body and severe complications such as cerebrovascular disease, coronary artery disease, neuro-, nephro- and retinopathy. The potential of prebiotics to control glycaemic control has been noted, as has the effect of exercise to favourably influence weight and impaired metabolic function.

The literature review is divided into separate chapters that examine in detail the available information on the topic: T1DM, gut microbiota, prebiotics and aerobic training. A sufficient volume of literary sources has been used, a large part of which is from recent years. At the end of the review, based on the examined data, a conclusion was made and the state of the problem was summarized, based on which the goal and tasks were derived.

The aim is clearly formulated, there are seven tasks and they cover the main aspects of the considered scientific issues and the conducted research.

In the "*Materials and methods*" section, the experimental model is described in detail, represented by a visual time graph; the 8 groups of experimental animals used for the purposes of the

study; the measured somatometric parameters, the conducted behavioural tests, microbiological analysis and biochemical analysis, applied analytical, morphometric and statistical methods.

The "*Results*" section is merged with the "*Discussion*" section and spans 53 pages. It is arranged logically and tightly, according to the tasks performed. 20 figures and 3 tables are presented. Charts visualize data from statistical analysis and are expertly crafted. The results are authentic and credible, and the figures are sufficiently informative. The obtained results are analysed and skilfully interpreted. The changes in the model of T1DM, as well as the changes in the individual parameters and markers, occurring during the administration of prebiotics and aerobic training were monitored. The conclusion drawn covers all aspects of the study conducted and the results presented.

The conclusions are organized into seven groups, which are logically connected with the set tasks. Three contributions are presented as original, which are based on the obtained results and do not repeat those in the available literature. Three contributions of a scientific and applied nature have also been presented.

6. Evaluation of the publications and the personal contribution of the PhD student

The publications that reflect the results of the dissertation are 3 articles in publications referenced in international databases with an impact factor (Open Medicine, Z Naturforsch C J Biosci) and one in *KNOWLEDGE* - International Journal. The articles are in English. The PhD student Maria Choneva is the first author of 2 of the full-text publications. 6 citations are also presented, which confirms the importance of the dissertation student's scientific activity.

There are six participations in scientific forums: presentations at two international scientific forums and four conferences in Bulgaria.

The dissertation student is familiar with the main stages of the experiment in detail and actively participated in taking the material, processing it, preparing and conducting the tests and analyses. The processing of the results, the analysis, the documentation through figures and diagrams of the obtained data were carried out with skill and experience.

Critical notes and recommendations

I have no critical remarks. For a more optimal perception of the results in blood glucose changes, I would recommend that Figure 7 be presented with the places of the groups and the weekly glucose changes reversed. This would make interpretation easier. In the future, the dissertation student can expand the field of research on the topic of the current dissertation, publish other research results and apply some of the obtained results in practice.

7. Synopsis of the dissertation

The abstract is comprehensive and presents the main parts of the dissertation work - introduction, aim and tasks, material and methods, results and discussion, conclusion, conclusions, contributions and a list of publications, citations and participations related to the topic. Three original contributions are noted, as well as three of a scientific-applied nature.

In conclusion, the abstract is done as required and reflects the main results achieved in the dissertation.

CONCLUSION

The dissertation *contains scientific, applied science and applied results, representing an original contribution to science and meeting all requirements* of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations on the application of the above-mentioned law and the Regulations of MU – Plovdiv.

The dissertation shows that the doctoral student Maria Choneva **possesses** in-depth theoretical knowledge and professional skills in the doctoral program "Medical Biochemistry", **demonstrating** qualities and skills for independent conduct of scientific research.

On the basis of the above-mentioned facts, I am deeply convinced in giving my **positive assessment** of the reviewed dissertation, synopsis, results obtained and contributions and **propose to the honourable Research Council to confer the educational and scientific degree of Doctor of Philosophy** on Maria Atanasova Choneva in the doctoral programme in "Medical Biochemistry".

20 April, 2024

Statement prepared by: .

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Prof. **Dr. Elena Ivanova**, PhD