

STATEMENT

by Assoc. Prof. Elisaveta Georgieva Apostolova, PharmD, PhD

Department of Pharmacology, Toxicology and Pharmacotherapy,

Faculty of Pharmacy, Medical University - Plovdiv

regarding a Ph.D. thesis for awarding the educational and scientific degree 'doctor'

professional direction 4.3. "Biological Sciences",

Ph.D. program "Medical Biochemistry".

Author: Maria Atanasova Choneva

Form of doctoral program: independent preparation

Department: Medical biochemistry

Topic: Effects of prebiotic oligosaccharides and aerobic training on metabolic and behavioral impairments in an experimental model of type 1 diabetes

Scientific supervisor:

Assoc. Prof. Anelia Bivolarska, MD, PhD - Medical University - Plovdiv

1. General presentation of the procedure and the doctoral student

I received a set of materials on an electronic medium, which is in accordance with Art. 70 (1) of Section I. Acquisition of educational and scientific degree "DOCTOR" and scientific degree "DOCTOR OF SCIENCES" at MU-Plovdiv; Regulations of the MU-Plovdiv from 28.01.2021 and includes the following documents: application to the Rector of the MU-Plovdiv, curriculum vitae, copy of a higher education diploma, orders of enrollment and termination of the doctoral studies, a protocol for passing the exam "Doctoral minimum in the specialty", a certificate for completed education course in the "Doctoral school", dissertation work, abstract, list and copies of scientific publications on the topic of the dissertation, declaration of originality and authenticity of documents. The Ph.D. student has attached a list of 7 publications, of which 5 are full-text articles and 2 are abstracts from scientific conferences.

The documents meet the requirements of the regulations for starting a dissertation defense procedure.

Maria Atanasova Choneva graduated from the Medical University - Plovdiv in 2018, achieving the degree Master of Pharmacy. During the period 01.11.2016 - 30.10.2019, she worked in a

Pharmacy "Protea 2000". Maria Choneva began her academic career on February 18, 2020, when she was appointed as an assistant at the Department of Medical Biochemistry of the Medical University of Plovdiv. She teaches biochemistry to students from the specialties "Medicine", "Dental Medicine" and "Pharmacy" in Bulgarian and English, conducts colloquiums, and participates in examination sessions. Assistant Choneva participated in 3 courses to improve her qualifications and holds a C1 level English language certificate. On November 15, 2020, she started the postgraduate specialty in "Biochemistry". Maria Choneva actively participates in conferences and seminars (a list of 6 participations is presented). She is a member of the scientific teams of 3 projects, of which 1 is national, financed partially by the European Union.

2. Relevance of the topic

Diabetes mellitus is a socially significant disease that is one of the leading causes of mortality worldwide. It is characterized by metabolic disorders leading to various clinical complications. Type 1 diabetes is a chronic autoimmune disease, the prevalence of which is constantly increasing, and effective preventive and therapeutic strategies are currently lacking. Complications in this disease are observed despite the administration of insulin and control of blood glucose levels. These data indicate the need for an adjuvant therapeutic strategy including appropriate diet and physical activity. Henceforth, the study of the influence of two oligosaccharides - XOS and GOS, and of aerobic training, on metabolic and behavioral parameters in rats with experimentally induced type 1 diabetes is particularly relevant. Functional oligosaccharides and aerobic training have the potential to influence intestinal and systemic immunity, as well as the metabolic disturbances occurring during the progression of the disease. The results of a study of the influence of prebiotics and probiotics, and aerobic training on an animal model of type 1 diabetes in rats would provide scientific justification for their possible application in medical practice, prevention of the disease and its complications, and have significant scientific-applied importance.

3. Knowledge of the problem

The literature review represents an in-depth study of the problem and lays the theoretical background for the experiments performed. It includes data on the epidemiology of the disease, the complications appearing during its progression, and the environmental factors that influence its occurrence. The composition of the intestinal microbiota, its relation to the immune and cognitive functions, as well as the relationship between this composition and the development of type 1 diabetes mellitus are examined. A detailed analysis of the available literature data on the role of prebiotics, diet, and aerobic training on metabolic disorders and cognitive functions is also included. The literature review shows knowledge of the problem, and its summary testifies to the doctoral student's abilities to evaluate creatively the available material.

4. Research methodology

The formulated tasks correspond to the set aim. The chosen research methodology allows achieving the aim and obtaining an adequate answer to the tasks solved in the dissertation work. The experimental settings are illustrated with figures that are the author's contribution of the doctoral student.

5. Characterization and evaluation of the dissertation work and contributions

The dissertation is written on 14 standard pages and contains an introduction – 2 pages, literature review – 43 pages, aim and tasks – 1 page, material and methods – 15 pages, results and discussion – 54 pages, conclusions – 2 page, contributions - 1 page, publications – 3 pages, and bibliography - 28 pages. The results are presented in 4 tables and illustrated with 26 figures and 9 photographs. The literature review includes 307 sources in English, of which 61 are from the last 5 years.

The **literature review** demonstrates knowledge of the literature and provides a theoretical background for the chosen research methods. **The aim** is clearly formulated, and **the tasks** are logically related to the set aim. The "**Materials and Methods**" section contains a detailed description of the experimental settings and they are appropriately selected according to the tasks set. The statistical methods guarantee a correct assessment of the confidence of the obtained experimental data. **The results** include studies of blood glucose levels, somatometric indicators, and markers of inflammation. The choice of experimental setups and biomarkers is well justified. The role of inflammation, oxidative stress, and dyslipidemia in the development of complications is discussed, as well as the specific biochemical molecules and intracellular pathways involved in the pathophysiological changes in diabetes mellitus. The effects of different approaches on the cognitive functions and composition of the gut microbiota of rats were investigated. The statistical analysis shows the reliability and originality of the obtained results. Results are appropriately interpreted and substantiated with treatment-induced changes. **The conclusions** are supported by the obtained results and fully meet the set tasks and objectives. Seven conclusions and 6 contributions were formulated, of which 3 are original and 3 are of scientific and practical importance.

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

A list of 3 full-text publications related to the dissertation is presented, of which 2 are articles in journals referenced in the Scopus and Web of Science databases with an impact factor, and 1 is published in a non-referenced journal. Evidence of the high scientific value of the dissertation work is the noted citations - 6 in total, all of which are in journals with an impact factor. Assistant Professor Choneva is the first author of 2 of the publications. The doctoral student has participated in 6 scientific conferences on the subject of the dissertation work. The scientific production of the doctoral student fully covers the quantitative criteria specified in the Regulations of the MU - Plovdiv.

Based on the presented declaration of originality and credibility and my personal impressions of the doctoral student, I believe that she participated in the conduct of the experiments described in the dissertation, and the obtained results and formulated conclusions, and contributions are her personal merit.

I have no critical remarks about the doctoral student.

7. Abstract

The submitted abstract contains 60 pages and meets the requirements of the regulations for its preparation. It includes a description of the materials and methods, and reflects the main results, conclusions and contributions of the dissertation work.

CONCLUSION

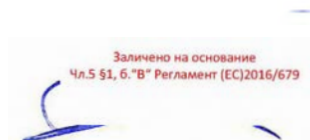
The dissertation **contains scientific, scientific-applied, and applied results**, which represent an **original contribution** to science and **meet all the requirements** of the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of LDASRB and the Regulations of the MU - Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements included in the Regulations of the Ministry of Education - Plovdiv for the application of the LDASRB.

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

Due to the above, **I confidently give my positive assessment** of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results, and contributions, and I propose to the honorable scientific jury **to award** the educational and scientific degree "doctor" to Maria Atanasova Choneva in a doctoral program in Medical biochemistry.

12.04.2024

Prepared by:



/Assoc. Prof. Elisaveta Apostolova, MPharm, PhD/