



CRITICAL REVIEW

by Assoc. Prof. Milka Asparuhova Nashar

Department of Biochemistry, Molecular Medicine and Nutrigenomics, Faculty of Pharmacy
Medical University "Prof. Dr Paraskev Stoyanov" - Varna,

about a procedure for the award of the educational and scientific degree "Doctor"

Field of higher education: 4. Natural Sciences, Mathematics and Informatics

Professional field: 4.3. Biological Sciences

Doctoral programme: *Medical Biochemistry*

Author: Mariya Atanasova Choneva

Department: Department of Biochemistry, Faculty of Pharmacy, Medical University of Plovdiv

Dissertation title: „Effects of prebiotic oligosaccharides and aerobic training on metabolic and behavioural impairments in an experimental model of type 1 diabetes“.

Supervisor: Assoc. Prof. Anelia Bivolarska, MD, PhD, Head of the Department of Medical Biochemistry, Faculty of Pharmacy, Medical University of Plovdiv

1. Overall presentation of the procedure and the doctoral student

I have been assigned as a member of the Scientific Jury for the awarding of a Doctoral Degree to Mariya Choneva (order No. R-1045/04.04.2024 of the Medical University - Plovdiv Rector). At the first meeting of the Scientific Jury, I was assigned to prepare this review. The set of materials is by the Law of the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), and the specific requirements of the Regulations for the development of the academic staff in the Medical University of Plovdiv and includes all required documents.

The doctoral student has attached 3 full-text publications related to the dissertation work.

2. Brief biographical data for the doctoral student

Mariya Choneva graduated from the Medical University - Plovdiv with excellent grades as a Master of Pharmacy in 2018. Since 2020, she has been an assistant at the Department of "Medical Biochemistry" of the Faculty of Pharmacy. Leads practical classes in biochemistry for students in "Medicine", "Dental Medicine" and "Pharmacy" in Bulgarian and English, and takes part in holding colloquiums and final exams. In the short time since she joined the department until now, Mariya has already been a member of the teams of three scientific projects and has completed several qualification courses, which presents her as an ambitious and active young scientist with the

potential to develop and contribute actively to the department scientific and publication activity. She is fluent in English, and since 2020 she has been enrolled on a Biochemistry specialization.

3. Relevance of the topic and expediency of the aim and tasks

The dissertation submitted for review highlights the role of diet and physical activity in the control of diabetes mellitus. This disease has a leading role in morbidity and mortality worldwide. Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease, with the genetic component being a major factor in its onset at an early age. The search for effective therapeutic and preventive strategies is of utmost importance to control the disease and to prevent its complications, which are the main cause of disability and mortality.

The dissertation developed by Mariya Choneva is a multidisciplinary study dedicated to revealing the mechanisms by which prebiotic supplementation and aerobic training positively influence the glycemic index, lipid profile and redox status. In addition, they have a beneficial effect on the intestinal microbiota, stimulating the growth of beneficial intestinal bacteria separately and in combination. It can be hypothesized that this may be a crucial factor in improving cognitive functions and managing conditions, such as depression and anxiety, encountered in diabetic patients. I am convinced that the results of this scientific work will find application in the development of therapeutic programmes for patients with T1DM.

4. Understanding of the problem

The in-depth and analytical literature review presents Choneva as a well-informed and competent researcher. In the first chapter, the author makes a thorough description of T1DM, from the point of view of the epidemiology and etiology of the disease. In the next chapter, the role of the intestinal microbiota in energy homeostasis, endocrine regulation, immune protection and, last but not least, its role in correct communication in the gut-brain axis is explained in a logical sequence and build-up. The skilful handling of terminology and the ease with which the doctoral student handles the description of the mechanisms behind this complex communication are impressive. The role of dysbiosis as a factor associated with the development of metabolic disorders, including diabetes, is convincingly presented. Further on in the literature review, the importance of prebiotics and physical activity as factors that positively influence the composition and function of the intestinal microflora, and hence their beneficial effect in the control of T1DM, has been consistently clarified. Despite the complexity of the topic, the literature review is a fascinating read, which proves the excellent awareness and ability of the doctoral student to handle, analyze and interpret scientific literature.

5. Research methodology

A wide range of pharmacological, biochemical, behavioural and microbiological methods and tests were applied to evaluate the effects of xylooligosaccharides and galactooligosaccharides, as well as aerobic training in experimental animals with induced diabetes. The chosen methods are sufficiently specific and informative and adequate to the set aim and tasks.

6. Characteristics and evaluation of the dissertation

The dissertation is written on 147 pages, illustrated with 26 figures, 4 tables and 9 photographs. It is structured according to the requirements for this type of scientific work, with a balanced volume between the main sections, as follows: Table of Contents - 2 pages, Abbreviations used in Bulgarian and English - 4 pages, Introduction - 2 pages, Literature review with conclusion - 34 pages, Aim and tasks - 1 page, Materials and methods - 16 pages, Results and discussion - 54 pages, Conclusions - 2 pages, Contributions - 1 page, List of scientific publications and participation in conferences related with the dissertation work and noted citations – 3 pages, Bibliography – 28 pages. The reference list includes more than 300 literary sources, which is enough for dissertation work and is a confirmation of the solid theoretical awareness of the author.

Logically, the most extensive part of the dissertation is the chapter "Results and Discussions". In a rat model of streptozotocin-induced T1DM, the effect of two oligosaccharides, in combination or separately with anaerobic training, on blood glucose levels, lipid profile, markers of oxidative stress was analyzed and evaluated. A large set of behavioral tests were also performed to assess the effect of treatment on anxiety and cognitive processes in diabetic animals and healthy controls. The sheer volume of work done and the large volume of results with input are impressive. A hypoglycemic effect of the two oligosaccharides after several weeks of treatment has been proven, a beneficial effect of aerobic training on the lipid profile, an antioxidant effect of the oligosaccharides alone and in combination with aerobic training, as well as their positive effect in some of the behavioural tests, such as the desire to exploring a new environment, lowering the anxiety index and a positive effect on learning and memory.

The results are competently and thoroughly discussed, with skilfully argued conclusions about the probable mechanisms underlying the observed effects.

The conclusions are formulated clearly and are logically derived based on the obtained results, and their number is adequate for the tasks set.

7. Contributions and significance of the dissertation for science and practice

Contributions are divided into original contributions and scientific-applied contributions. I agree with the author's assessment of the indisputable prospect of applying the obtained results in practice, with a contribution to health. The antidiabetic effects of the two oligosaccharides would be

of interest, both in the development of programmes for the prevention and treatment of diabetes and its complications and in the creation of a new generation of nutritional supplements and synbiotics.

8. Evaluation of publications on the dissertation work

The results have been reported in 3 full-text publications, two of which have an impact factor and Q3, which fulfils the minimum requirements for awarding the Doctoral degree. The doctoral student is the first author in two of the publications, which proves her contribution to the research, analysis and summarization of the results. The publications have already been cited several times, which is proof of their quality and the reliability of the results. A list of six participations in scientific forums, three of them international, is presented.

9. Personal participation of the doctoral student

The personal participation of the doctoral student in the conducted research is indisputable. The results discussed and the contributions formulated are entirely her contribution, of course under the expert guidance of her supervisor.

10. Abstract

The abstract is a total of 60 pages, is made according to the requirements and reflects the main results achieved in the dissertation.

11. Critical remarks and recommendations

I have no remarks or recommendations on the presented final version of the dissertation work. I note with satisfaction that Assistant Professor Choneva complied with all the notes and recommendations addressed to the dissertation project when she was enrolled.

12. Personal impressions

I do not know Mariya Choneva personally, but I have excellent impressions of her theoretical and experimental work and the confident and competent interpretation of the results.

13. Recommendations for future application of contributions and results

Given the importance of the topic, I advise the doctoral student to continue and expand her research in collaboration with clinical specialists and companies producing food and supplements. The development of new prebiotics and synbiotics with a beneficial effect on the glycemic index, lipid profile and healthy composition of the intestinal microbiota will contribute to the general well-being and quality of life, not only for diabetics but also for individuals with metabolic syndrome and cardiovascular diseases.

CONCLUSION

The dissertation entitled „Effects of prebiotic oligosaccharides and aerobic training on metabolic and behavioural impairments in an experimental model of type 1 diabetes“ meets all the requirements of the Law of the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for application of LDASRB and the respective Regulations of MU-Plovdiv.

The dissertation contains scientific and scientific-applied results that represent an original contribution to science and presents Associate Professor Mariya Choneva as a young scientist with the skills to formulate a scientific problem and research goals and work thoroughly to achieve them. In the overall presentation of the state of the problem, as well as in the interpretation and discussion of the results, the doctoral student shows in-depth theoretical knowledge and demonstrates a scientifically sound research approach.

Due to the above, I confidently give my positive assessment of the scientific work, presented by the above-reviewed dissertation, abstract, achieved results and contributions, and I propose to the honourable scientific jury to award the educational and scientific degree "Doctor" to Mariya Atanasova Choneva in a doctoral programme "Medical biochemistry".

Заличено на основание
Чл.5 §1, б. "В" Регламент (ЕС)2016/679

Reviewer:

Assoc. Prof. Milka Nashar, Ph.D.

April 22, 2024