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Assoc. Prof. Silvia Gancheva, MD, PhD

Chairman of the Scientific Jury

Procedure for acquiring an ESD "Doctor"

Specialty "Pharmacology (incl. pharmacokinetics and chemotherapy)"

OPINION

by Assoc. Dr. Galya Tsvetanova Stavreva-Marinova, MD

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According to the procedure for acquiring the **educational and scientific degree "Doctor"** in

Field of higher education: 7. "Health and sports"

Professional direction: 7.1. "Medicine"

PhD program: Pharmacology (incl. pharmacokinetics and chemotherapy)

Author: Dr. Mehmed Reyzov Abtulov

Form of doctoral studies: full-time doctoral student

Dissertation topic: "PHARMACOLOGICAL INVESTIGATION OF THE EFFECTS OF ARONIA MELANOCARPA FRUIT JUICE IN AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME".

Research supervisor: Prof. Dr. Stefka Valcheva-Kuzmanova, MD, DSc.

I present the opinion in my capacity as a member of the Scientific Jury, established by the Order of the Rector of the University of Varna (No. R-109-282/07.08.2022) and the decision of the 1st absent meeting of the Scientific Jury held on 13.07. 2022. I declare that I have no conflict of interest, including co-authorship with the PhD student Mehmed Reyzov.

General presentation of the procedure

The presented set of materials on an electronic medium is in accordance with the requirements of Art. 69 of the Regulations for the Development of the Academic Staff at the Medical University - Varna. On the basis of the set of materials and documents, I declare that the rules and conditions for the defense of a dissertation work for the acquisition of the ESD "Doctor" have been complied with, in accordance with the Act on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its application and the Regulations for the Development of the Academic Staff at the Medical University – Varna.

Education and qualification

The dissertation candidate Dr. Mehmed Reyzov Abtulov is a Master of Medicine (diploma No. 005060/31.10.2017 from Medical University – Varna). Since October 2018, he is currently working as an assistant at the Department of Pharmacology and Clinical Pharmacology and Therapy of the University of Varna. By Order of the Rector of MU-Varna (No. P-109-253 of 01.08.2019) Dr. Reyzov enrolled as a doctoral student in full-time study and the topic of the dissertation work "Pharmacological investigation

of the effects of *Aronia melanocarpa* fruit juice in an experimental model of metabolic syndrome" and scientific supervisor Prof. Dr. Stefka Valcheva-Kuzmanova.

Dr. Reyzov finished PhD program with the right of defense by order of the Rector of MU-Varna No. R-109-282/08.07.2022. He completed training in pedagogy and andragogy (October, 2021). He participated in a project funded by the MU-Varna on the topic: "Investigation of the bioflavonoid fustin for antitumor, anti-inflammatory and gastro-entero-hepatoprotective action in experimental pharmacological models". He is fluent in Turkish and English, has the skills to work with a computer and analytical equipment.

The dissertation work, presented for review consists of 157 pages and contains 27 tables and 30 figures. All the main elements of the generally accepted in our country structure for presenting a dissertation work are included: title page – 2 pages; abbreviations – 3 pages; table of contents – 4 pages; introduction – 2 pages; literature review – 40 pages, aim and tasks – 1 page; materials and methods – 10 pages; results and discussions – 56 pages; conclusions - 4 pages; contributions - 2 pages; references – 33 pages, including 409 sources in Latin and 1 in Cyrillic, with 112 articles published after 2017. An impression is made by the good technical execution of the dissertation work and the precision in citing the used literary sources in the academic "Vancouver Style".

Relevance of the topic and appropriateness of the aim and tasks

Metabolic syndrome (MS) is a relatively new clinical entity whose incidence has increased exponentially over the past few decades in all ages. The most widely recognized metabolic risk factors are atherogenic dyslipidemia, elevated blood pressure, and elevated plasma glucose. Individuals with these characteristics typically exhibit a prothrombotic and proinflammatory state. MS is associated with an increased risk of developing not only diabetes and cardiovascular disease, but also obesity, nonalcoholic fatty liver disease, sleep apnea, hypertension, stroke, reproductive problems, and cancer. Control is always based on healthy lifestyle choices, but should also be supported by pharmacological treatment. The focus of therapeutic efforts is mainly on the treatment of obesity, insulin resistance and hypertension. In recent years, a number of preclinical and clinical studies have demonstrated the role of biologically active substances of plant origin in the control of body mass, hyperglycemia and dyslipidemia.

The fruits of *Aronia melanocarpa* are extremely rich in biologically active substances. They contain carbohydrates, proteins, fats, organic acids, vitamins, minerals and polyphenols. There is strong evidence for the effects of *Aronia melanocarpa* and its products (leaves, fruit, juice, nectar, extract) on body weight, lipid metabolism, glycemic control, hypertension, oxidative imbalance and chronic inflammation.

Based on the long-term experience of the department's team with *Aronia melanocarpa* and the data from the scientific literature, it is logically hypothesized that the application of *Aronia melanocarpa* fruit juice will improve the disturbances in the lipid profile, glucose metabolism, body weight and behavioral changes in rats with experimental model of diet-induced MS. The aims and objectives are adequate to investigate and generalize the pharmacological effects of *Aronia melanocarpa* fruit juice (AMFJ) in rats with an experimental model of MS.

Research methodology

The set of experimental methods makes a good impression, they are described briefly and precisely. A high-fat, high-fructose 10-week diet to induce MS, a carrageenan model of inducing inflammation,

behavioral research methods, biochemical, histological and immunohistochemical methods were used. Methods for statistical analysis of data are adequate. The selected, presented and applied methodical approaches allowed Dr. Reyzov to fulfill the tasks of the research and achieve the set aim.

The presented results of the dissertation work show that the study was not only well planned, but also successfully executed. The research data are described briefly and clearly, well-illustrated with 27 tables and 30 figures. From the obtained results and the discussion presented after the results of each task, it can be concluded that the PhD student knows the methods used, skillfully and comprehensibly presents the obtained data. The discussion of the results by tasks introduces some disproportionality into the overall structure of the thesis, but makes the results easier to understand. The discussion is done in a good scientific style, calmly handling the data of other authors and comparing them with one's own results. An advantage of the work would be the presentation of a comprehensive, concise, concluding discussion summarizing those made on the individual tasks.

In the conducted research, the most noticeable behavioral changes in the MS group were the pronounced anxious behavior and memory impairment. Administration of AMFJ effectively normalized the behavior of rats at the lowest dose used, which may also be associated with suppression of oxidative stress and inflammation. AMFJ improves impaired glucose control and decreased sensitivity to insulin in the periphery, dose-dependently reduces triglyceride levels, as well as the amount of retroperitoneal adipose tissue, favorably affects SOD activity. All doses of PSAM improved histopathological changes associated with metabolic syndrome in adipose tissue, myocardium, blood vessels, liver, as well as many of the MS-induced immunohistochemical changes in adipose tissue and liver.

The conclusions correspond to the tasks set and are a logical reflection of the results obtained. The conclusions are accurate and comprehensive.

Contributions and significance of the development for science and practice

I accept the contributions formulated by the PhD student, which I qualify as scientific-theoretical and scientific-applied:

Abstract of the doctoral thesis

The abstract meets the requirements both in terms of content and layout. It accurately and correctly reflects the essence of the dissertation work. It is illustrated with highly informative figures and tables. It reflects the methodology, the main results with their discussion and the relevant conclusions, contributions and publications related to the work.

Assessment of the publications in connection with a dissertation

The results of the dissertation work have been published in 3 articles, with another 1 article accepted for publication in journals, indexed and referenced in WoS. In all published articles, Dr. Mehmed Reyzov is the first author. The presented articles reflect and are fully related to the subject of his research work.

CONCLUSION

The dissertation intiled "Pharmacological investigation of the effects of *Aronia melanocarpa* fruit juice in an experimental model of metabolic syndrome" contains scientific-theoretical and scientific-applied


results that represent an original contribution to science. The work meets all the requirements of the Act on Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its Implementation and the relevant Regulations of the Medical University "Prof. Dr. P. Stoyanov" - Varna. The presented materials and dissertation results fully correspond to the specific requirements of the University.

The dissertation shows that the PhD student Dr. Mehmed Reyzov Abtulov has bibliographic culture at a scientific level, has mastered experimental models and methods, is able to analyze, synthesize results and formulate conclusions, has in-depth theoretical knowledge and professional skills in the specialty of Pharmacology. From the above, it follows that the two qualifying tasks of the doctorate have been fulfilled - educational and scientific, and the completed written work can receive a well-deserved positive evaluation.

The results of Dr. Mehmed Reyzov's dissertation enrich the long-term research of biologically active substances of plant origin conducted in the department. Confirmations and new evidence are convincing that substances contained in aronia berries possess insulin-sensitizing and anti-inflammatory activity, favorably affecting the various components of MS (hypertriglyceridemia, hyperglycemia, obesity, arterial hypertension). These results and those of the team's previous research should lead to the creation/implementation of supplements/medications to prevent and influence MS.

Due to the above, I confidently give my positive assessment and propose to the respected members of the Scientific Jury to award the ESD "Doctor" to Dr. Mehmed Reyzov Abtulov in the doctoral program in Pharmacology (incl. pharmacokinetics and chemotherapy), Professional direction 7.1. Medicine.

21.08.2022
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Signature: 
/Assoc. Dr. Galya Stavreva-Marinova, MD/