

OPINION

by Prof. Aneliya Aleksandrova Dimitrova, MD, PhD

Department of Physiology and Pathophysiology

Faculty of Medicine

Medical University – Pleven

REGARDING: Dissertation thesis for the award of the educational and scientific degree “Doctor” by Dr. Diyana Asparuhova Kyuchukova, full-time doctoral student in the Pathophysiology Sector at the Department of Physiology and Pathophysiology, Faculty of Medicine, Medical University of Varna.

By Order of the Rector of the Medical University of Varna No. R-109-502/16.12.2025 and by decision of the Chair of the Scientific Jury, I have been appointed to present an opinion regarding the dissertation thesis entitled “*Investigation of the Relationship between Obesity and Cardiovascular Damage in an Experimental Model of Metabolic Syndrome*” for the acquisition of the educational and scientific degree “Doctor” under the doctoral program “Pathophysiology”, professional field 7.1 Medicine, area of higher education 7. Health and Sports.

The author of the dissertation is Dr. Diyana Asparuhova Kyuchukova, a full-time doctoral student in the Pathophysiology Sector at the Department of Physiology and Pathophysiology, Faculty of Medicine, Medical University of Varna. The supervisor of the dissertation thesis is Assoc. Prof. Kamelia Zhechkova Bratoeva, MD, PhD.

Dr. Kyuchukova has submitted all the required documents in accordance with the requirements of the Law on the Development of the Academic Staff and the regulations of the Medical University of Varna. I hereby declare that I have no conflict of interest, including co-authorship in the publications with which the candidate participates in the procedure.

Dr. Diyana Kyuchukova was born in 1991. In 2016, she graduated in Medicine from the Medical University “Prof. Dr. Paraskev Stoyanov” – Varna. She worked for several months as

a nurse at the "Filaretova" Hospice, and since 2017 she has been employed as a physician at the Center for Emergency Medical Care – Varna. In 2017, after successfully passing a competitive selection procedure, she began working at the Medical University of Varna, Department of Physiology and Pathophysiology, as an Assistant Professor.

The topic of the dissertation thesis is relevant and addresses the global problem of obesity, which is rapidly spreading and affects millions of adults worldwide. Obesity is a chronic metabolic disorder with a multifactorial etiology, characterized by pathological accumulation of adipose tissue. Its increasing prevalence on a global scale defines it as a socially significant problem. There is convincing evidence that obesity is an independent risk factor for the development of cardiovascular damage and cardiovascular diseases.

The pathogenetic mechanisms linking obesity to cardiovascular pathology are complex and interrelated. Of particular importance is visceral adipose tissue, which functions as an endocrinologically active organ and secretes adipokines, leptin, pro-inflammatory cytokines, and free fatty acids. This leads to chronic low-grade inflammation, endothelial dysfunction, insulin resistance, and disturbances in lipid metabolism, which accelerate atherogenesis and the progression of atherosclerotic vascular changes.

Contemporary scientific research shows that obesity is closely associated with the development of arterial hypertension, dyslipidemia, and type 2 diabetes mellitus, which further increase cardiovascular risk. Due to its high prevalence and multifactorial mechanisms of damage, obesity represents a serious public health problem requiring early prevention, lifestyle modification, and a comprehensive therapeutic approach. Therefore, the study of the causes of obesity and the possibilities for therapeutic intervention is of exceptional importance for the prevention of this socially significant disease.

The literature review is comprehensive and in-depth. It demonstrates extensive use and thorough knowledge of the international scientific literature on the subject. The aim of the study is clearly formulated, and six specific objectives are presented for its achievement.

Eighteen laboratory male white Wistar rats weighing 120–160 g were investigated. The experimental animals were divided into three groups ($n = 6$) according to the substances used and the feeding regimen. The applied methods are appropriate and informative. Zoometric measurements (body weight, length, etc.), biochemical and clinical laboratory methods,

immunological methods, morphological methods (histological and immunohistochemical), as well as statistical methods for data processing were employed.

The results are objective and reliable, and their discussion is competent and thorough. Eleven main conclusions are formulated, which I accept. They accurately and comprehensively reflect the principal achievements of the presented work.

Dr. Kyuchukova demonstrates a significant number of scientific contributions, which are well presented and well substantiated. They are divided into original contributions, five in number. The most important among them are related to a comprehensive investigation of changes in the expression of SOD-1, VCAM-1, NOS3, and RIP3, and their relationship with pathomorphological changes in the endothelial cells of the coronary vessels, interlobar arteries, and cardiomyocytes in experimental animals subjected to a high-fructose diet (HFD).

Another important contribution is the comprehensive study of the effects of supplementation with S-adenosylmethionine (SAM) on morphometric and morphological parameters, as well as on the expression levels of SOD-1, VCAM-1, and NOS3 in the coronary vessels, preglomerular arteries, and cardiomyocytes in experimental animals subjected to an HFD. Among the confirmatory contributions, the association between HFD and the development of oxidative stress, chronic low-grade inflammation, and endothelial dysfunction has been demonstrated. Intake of an HFD leads to morphometric and pathomorphological changes in the wall of the left ventricle, expressed as thickening of the left ventricular wall.

The applied contributions are of importance for the development of effective therapeutic methods for the prevention, diagnosis, and treatment of obesity.

The results of the dissertation have been published in three articles printed in *Varna Medical Forum*. In addition, four communications with published abstracts have been presented at international scientific forums and one at a national forum in Bulgaria.

Conclusion:

The dissertation thesis submitted for review contains significant scientific and practical contributions and meets the qualitative and quantitative criteria set out in the Regulations for the Development of the Academic Staff of the Medical University of Varna, in accordance with the Law on the Development of the Academic Staff in the Republic of Bulgaria. In view of the

well-conducted scientific research, the in-depth analysis of the obtained results, the overall presentation of the work, and the scientific publications on which it is based, I firmly recommend that the honorable members of the Scientific Jury vote in favor of awarding the scientific degree "Doctor" to Dr. Diyana Asparuhova Kyuchukova.

As a member of the jury, I declare that my vote will be positive.

29.01.2026

Pleven

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

Prof. Anelia Dimitrova, MD, PhD