

OPINION

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Regarding

a dissertation submitted for the award of the scientific degree “Doctor”
by Dr. Diyana Asparuhova Kyuchukova,
Assistant Professor at the Department of Physiology and Pathophysiology,
on the topic:

“INVESTIGATION OF THE RELATIONSHIP BETWEEN OBESITY AND CARDIOVASCULAR DAMAGE IN AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME”

Pursuant to Order No. P-109-520, Varna, dated 16.12.2025, issued by the Rector of the Medical University “Prof. Dr. Paraskev Stoyanov”, Varna, I was elected as a member of the Scientific Jury, and on the basis of Protocol No. 1/29.12.2025 of the Department Council of the Department of Physiology and Pathophysiology, I was designated to prepare the present opinion.

The dissertation submitted to me for review comprises a total of 170 pages and is illustrated with 74 figures and 5 tables. A total of 445 literature sources are cited, of which 1 is in Cyrillic and 444 in Latin script.

The dissertation includes the following sections: Introduction – 2 pages; Aim and Objectives of the Dissertation – 1 page; Materials and Methods – 9 pages; Original Results and Discussion – 64 pages; Conclusion – 1 page; Conclusions – 2 pages; Contributions – 2 pages; Publications and Communications Related to the Dissertation – 1 page.

I consider the distribution of content across the sections to be appropriate in volume for a dissertation submitted for defense. The initial presentation of the abbreviations used facilitates reading, and the acknowledgements expressed at the end to those who assisted in the preparation of the dissertation are commendable.

In the Introduction, Dr. Kyuchukova convincingly directs our attention to obesity, an undoubtedly extremely important problem of the present century. She notes that the prevalence of this disease has escalated rapidly over the past 60 years and that, according to WHO data for 2022, 2.5 billion adults (aged 18 years and over) were overweight, of whom 890

million were living with obesity, while at the same time contemporary treatment methods remain insufficiently effective. Despite numerous studies on risk factors such as genetic predisposition, lifestyle, and dietary habits, there is still inconclusive evidence regarding causative factors and consequences, particularly with respect to subsequent cardiovascular diseases. This precisely guides the author toward the stated aim—to investigate the relationship between obesity and cardiovascular damage, as well as to evaluate the effect of antioxidant administration in a fructose-induced experimental model. The aim is formulated precisely and clearly; I would personally omit the word “investigation,” since the entire work undoubtedly constitutes an investigation.

The six objectives are formulated sequentially, with a progressively deeper elucidation of the expected changes in mechanisms and, most importantly, with potential protective effects aimed at preventing the development of cardiovascular disorders.

In the Materials and Methods section, the author employs a fructose-induced experimental model that has also been tested in other studies within the teaching sector of pathophysiology. This lends reliability and allows for further development and comparison with other types of research. The application of analytical methods—zoo-metric, biochemical and clinical-laboratory, immunological, and morphological—enables a comprehensive evaluation of the investigated and expected changes in the experimental model. Statistical analysis has been performed correctly in accordance with the requirements of descriptive and analytical methods. It is noteworthy that a relatively small number of rats (18 animals) was used, which is also commendable, given that in many studies authors resort to a large number of experimental animals to achieve statistical significance. In this case, the approach is sufficiently economical while remaining adequately informative.

Dr. Kyuchukova presents the results in the sequence of the stated objectives. After each obtained result, she provides a discussion, referring both to relevant literature sources and to her own reasoning. The figures and tables presented further and illustratively substantiate the discussions conducted. In most works of this type, authors separate results and discussion into distinct chapters. One of the strengths of this dissertation is that here, elegantly, each result is immediately followed by its corresponding discussion, which makes the material more accessible and comprehensible to the reader. I deliberately refrain from commenting on each individual result and discussion. The data are so rich that they could be interpreted at length. The author has done this thoroughly and with insight. On this basis, she formulates her conclusion, namely that high fructose intake significantly increases the risk of developing various metabolic changes such as hyperglycemia, dyslipidemia, chronic low-grade inflammation, oxidative stress, and insulin resistance, referring to the relevant pathophysiological mechanisms. As a possibility, Dr. Kyuchukova emphasizes that, albeit with a

certain degree of speculation, the intake of S-AME is capable of reducing systemic oxidative stress and improving adipose tissue dysfunction, thereby reducing the risk of developing endothelial dysfunction and various cardiovascular disorders.

The conclusions reached by the author correspond to the results and discussions presented and reinforce the impression that the stated objectives have been fulfilled. Some of them—for example, 2 and 3; 4 and 5; 6, 7, and 8; 9 through 12—could potentially be combined, but Dr. Kyuchukova has likely presented them in this manner in order to draw greater attention to each of the investigated parameters.

The original contributions of Dr. Kyuchukova, five in number, are clearly and appropriately stated. I would personally position contribution 1.5 immediately after 1.1, although the order is not of substantial importance. Contributions 1.2, 1.3, and 1.4 represent the “cherry on the cake.” They provide grounds for reflection and for potential further studies by both experimental researchers and practicing clinicians.

The confirmatory nature of the contributions demonstrates that the author is well acquainted with global experience in this field and, to her credit, does not claim these contributions as entirely novel discoveries. As for the applied contributions, I am confident that they will find practical implementation for anyone who becomes acquainted with this scientific work.

The publications and communications related to the dissertation are sufficient and comply with the requirements for this defense.

My final evaluation and conclusion of this opinion is that Dr. Diyana Asparuhova Kyuchukova should be awarded the scientific degree “Doctor.” I also propose that the other members of the Scientific Jury join me in this positive and objective assessment.

Prepared the opinion

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