

## **OPINION**

by Prof. Dr. Rumen Pavlov Nikolov, MD

Faculty of Medicine, Department of Pharmacology and Toxicology,  
Medical University of Sofia

**Member of a scientific jury (order of the Rector of the MU - Varna "Prof. Dr. Paraskev Stoyanov" No. P-109-282/08.07.2022) in connection with the procedure for the defense of a dissertation work on the topic "PHARMACOLOGICAL STUDY OF THE EFFECTS OF ARONIA MELANOCARPA FRUIT JUICE IN AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME" by Dr. Mehmed Reizov Abtulov, PhD student of independent training at the Department of Pharmacology and Clinical Pharmacology and Therapy at the MF, MU - Varna in a doctoral program in pharmacology (including pharmacokinetics and chemotherapy), professional direction "7.1. Medicine" and field of higher education "7. Health care and sports". Scientific supervisor of the doctoral student: Prof. Dr. Stefka Valcheva-Kuzmanova, DSci.**

All documents in accordance with the requirements of the Regulations for the conditions and procedures for acquiring scientific degrees and holding academic positions at the Medical University - Varna were provided to me.

Dr. Mehmed Abtulov has successfully passed the required exams: doctoral minimum (pharmacology) and foreign language.

### **Biographical data**

Dr. Mehmed Reizov Abtulov completed his secondary education in 2011 in the city of Kubrat. He obtained a master's degree in medicine at the Faculty of Medicine of the Medical University - Varna in 2017. Since 2018, he has been an

assistant in The Department of Pharmacology and Clinical Pharmacology and Therapy at the Faculty of Medicine, MU - Varna. He serves as an administrative assistant in the department.

Dr. Abtulov is fluent in written and spoken English. Has very good computer skills with basic office programs and statistics.

### **Assessment of the submitted dissertation work**

#### **Structure of the dissertation**

Presented to me dissertation contains 159 pages and is illustrated with 30 figures and 27 tables. 407 literary sources are cited, of which 3 are in Cyrillic.

The scientific work is properly structured in the following sections: introduction - 2 pages, literature review - 40 pages, summary of literature data - 2 pages, goal and tasks - 1 page, materials and methods - 10 pages, results and discussion – 50 pages, conclusions – 4 pages, contributions – 2 pages, list of publications and participations related to the dissertation work – 2 pages and bibliography – 35 pages.

#### **Relevance of the dissertation topic**

The dissertation is written thoroughly, competently and comprehensively. The topic of the dissertation is dedicated to a current problem related to the study of the pharmacological effects of Aronia melanocarpa fruit juice on an experimental model of metabolic syndrome.

Metabolic syndrome is characterized by the presence of a group of risk factors specific to cardiovascular disease (abdominal obesity, high blood pressure - over 130/80 mm Hg, elevated fasting blood sugar levels, high triglyceride levels and low HDL cholesterol. Metabolic syndrome significantly increases the risk of developing type 2 diabetes, heart disease, stroke, or all three. Most people with metabolic syndrome develop insulin resistance.

The search for new therapeutic approaches in the treatment and prevention of metabolic syndrome is extremely important to reduce cardiovascular risk as well as the risk of type 2 diabetes mellitus. Aronia juice is a rich source of polyphenols, including anthocyanins, procyanidins, phenolic acids and flavonols (a class of flavonoids that have the 3-hydroxyflavone backbone). There is evidence in the literature for anti-inflammatory and insulin-sensitizing activity of the biologically active substances contained in chokeberry juice.

### **Literature review**

The literature review is competently written and includes contemporary sources related to the topic of this dissertation. In the first part of the literature review, a comprehensive characterization of the metabolic syndrome was made on the following issues: definition and criteria for diagnosis, epidemiological data, risk factors, pathogenesis, co-morbidities, treatment, and experimental models. The second part of the review presents the botanical and chemical characteristics of the plant *Aronia melanocarpa*, as well as the pharmacological effects of the polyphenols in the fruit juice of the plant.

The literature reference shows that the doctoral student is thoroughly familiar with the issues related to the dissertation work, incl., and the latest studies in this direction.

### **Purpose and tasks of the study**

The purpose of the study is precisely and clearly formulated. The tasks for its implementation are well defined, specific and correspond to the set goal.

The objective was to investigate and summarize the pharmacological effects of *Aronia melanocarpa* fruit juice administered orally in rats with an experimental model of metabolic syndrome induced by a high-fat, high-fructose diet.

To achieve this goal, Dr. Abtulov has set himself 2 main experimental tasks, which are well formulated and specified in sub-points and exactly correspond to the set goal.

## **Materials and methods**

The experimental studies were carried out on male Wistar rats. An experimental model of metabolic syndrome by 10-week administration of a high-fat, high-fructose diet and a model of acute inflammation induced by carrageenan injection were established.

The methodical approach is modern and sufficient to fulfill the set goals and tasks. The study used behavioral tests (open field test, social interaction test, object recognition test, forced swimming test), biochemical methods (e.g. oral glucose tolerance test, triglyceride determination, serum activity of superoxide dismutase and glutathione peroxidase), histology, immunohistochemistry and statistical methods.

## **Results**

The results of the conducted experimental studies are in-depth and illustrated in detail.

Own data obtained in a model of metabolic syndrome in rats show the development of visceral obesity and manifestations of anxiety. Biochemical changes are characterized by increased serum levels of glucose and triglycerides, as well as an increase in serum superoxide dismutase activity. Histopathological changes are expressed in hypertrophy of adipocytes, inflammatory and degenerative changes of the liver, degenerative changes of cardiomyocytes and disorders of the vascular endothelium. Immunohistochemical studies confirmed a process of apoptosis of adipose tissue, as well as processes of inflammation and apoptosis in the liver.

Oral administration of Aronia melanocarpa fruit juice at three different doses (2.5 ml/kg, 5.0 ml/kg, and 10 ml/kg) resulted in the improvement of a significant proportion of behavioral, biochemical, histopathological and immunohistochemical disorders associated with metabolic syndrome.

Aronia melanocarpa fruit juice administration reduces hind paw edema in a rat carrageenan model of acute inflammation.

### **Conclusions and scientific contributions**

The main conclusions reached by the doctoral student are 2 and represent a logical sequence of the in-depth and competent analysis of the obtained results.

The contributions in the dissertation work are 7, and all the contributions formulated by the doctoral student are original. Scientific contributions are significant theoretical and methodological value, as well as potential clinical-applied importance in the prevention and treatment of metabolic syndrome.

### **Scientometric indicators related to the dissertation work**

In connection with his dissertation, Dr. Mehmed Abtulov has submitted a list of 4 publications, 1 of which is in a journal with IF. He is the first author in all the publications presented.

Dr. Abtulov has presented a list of 4 participations in congresses and conferences. Participated as a researcher in 1 scientific project related to the topic of the dissertation work.

### **Doctoral Thesis**

The thesis of the dissertation contains 78 pages, 26 figures and 22 tables. The attached abstract adequately reflects the main content of the dissertation and the results obtained.

**Recommendations and critical remarks:** I recommend the doctoral student to continue her publication activity.

### **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 on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB and the Regulations of the MU - Varna "Prof. Dr. Paraskev Stoyanov". The presented materials and dissertation results fully correspond to the specific requirements adopted in connection with the Regulations of the Ministry of Education - Varna for the application of the ZRASRB.

I believe that the presented dissertation work is well designed, impressing the use of a wide range of adequately selected experimental methods and excellent performance of the set goals and tasks, confirmed by the results obtained. Based on the detailed positive aspects of the dissertation presented to me for review, I strongly recommend to the respected members of the scientific jury to vote positively for awarding the educational and scientific degree "Doctor" in the doctoral program in pharmacology (incl. pharmacokinetics and chemotherapy) to Dr. Mehmed Reizov Abtulov.

24.08.2022

Prepared the review:

/Prof. Dr. Rumen Nikolov, MD/