REVIEW

by Prof. Dr. Rumen Pavlov Nikolov, MD

Department of Pharmacology and Toxicology, Medical Faculty, MU – Sofia

Member of a scientific jury (order of the Rector of the MU - Varna "Prof. Dr. Paraskev Stoyanov" No. P-109-46/14.02.2024) in connection with the procedure for the defense of dissertation work on the topic "PHARMACOLOGICAL STUDY OF THE EFFECTS OF FRUIT JUICE FROM CHAENOMELES MAULEI IN AN EXPERIMENTAL MODEL OF METABOLIC SYNDROME" by Dr. Klementina Moncheva Moneva-Marinova, a full-time doctoral student at the Department of Pharmacology and Clinical Pharmacology and Therapy at the Faculty of Medicine, Medical University - 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 under the requirements of the Regulations for the conditions and procedures for acquiring scientific degrees and holding academic positions at the MU - Varna were provided to me.

Dr. Klementina Moneva-Marinova has successfully passed the required exams: doctoral minimum (pharmacology) and foreign language.

Biographical data

Dr. Clementina Moneva-Marinova was born on 10.11.1993 in Stara Zagora. He finished his secondary education in 2012 in Stara Zagora. She obtained a master's degree in medicine at the Faculty of Medicine of the Medical University - Varna in 2018. Since 2018, he has been an assistant in the Department of Pharmacology and Clinical Pharmacology and Therapy at the Faculty of Medicine, Medical University - Varna.

Dr. Moneva-Marinova is fluent in written and spoken English and German. Has very good computer skills with basic office programs and statistics.

Dr. Clementina Moneva-Marinova is a member of the Bulgarian Society of Pharmacology and Clinical Pharmacology and Therapy and the European Association of Clinical Pharmacology and Therapy.

Assessment of the submitted dissertation work

Structure of the dissertation

The presented dissertation contains 123 pages and is illustrated with 30 figures and 13 tables. 187 literary sources are cited.

The scientific work is properly structured in the following sections: introduction - 2 pages, literature review - 27 pages, goal and tasks - 2 pages, materials and methods - 7 pages, results and discussion - 50 pages, conclusions - 3 pages, contributions – 2 pages, list of publications and participations related to the dissertation work – 2 pages, and bibliography – 15 pages.

Relevance of the dissertation topic

The dissertation is written thoroughly, competently and comprehensively. The topic of the dissertation work is dedicated to an actual problem related to the study of the pharmacological effects of Chaenomeles maulei fruit juice on an experimental model of metabolic syndrome.

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.

Metabolic syndrome is characterized by the presence of a group of risk factors that are 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.

The fruit juice of Chaenomeles maulei, called the Japanese quince or Maule's quince, is rich in polyphenolic substances, among which the concentration of procyanidin oligomers is the highest, followed by phenolic acids (vanillic, caffeic, chlorogenic, neochlorogenic, p-coumaric, ellagic, ferulic and 4-dihydroxy-benzoic) and flavonoids (epicatechin, catechin, quercetin-3-β-glucoside, quercetin, rutin, naringin, kaempferol and myricetin). The sour taste of the juice and its low pH are due to the high content of organic acids (malic, quinic, citric, ascorbic, and oxalic). Carbohydrates are represented by glucose, fructose, galactose, xylose, rhamnose and arabinose.

Modern in vivo and in vitro studies show that the fruits of Chaenomeles maulei have hepatoprotective effects, antioxidant action, anti-inflammatory properties, and antimicrobial and neuroprotective effects. The antioxidant activity of Japanese quince fruit juice may be due to the high content of polyphenols.

In addition, Japanese quince fruit juice can stimulate the growth of beneficial intestinal microflora and contribute to the regulation of body weight.

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, epidemiological data, pathogenesis, pathogenesis and pathophysiology, and experimental models. The second part of the review presents the botanical and chemical characteristics of the plant Chaenomeles maulei, as well as the biological activity of the fruit juice from the plant.

The literature review 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 precise and formulated. The tasks for its implementation are well defined, specific, and correspond to the set goal.

The objective was to investigate the pharmacological effects of Chaenomeles maulei 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. Moneva-Marinova has set herself 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 was established by a 10-week administration of a high-fat, high-fructose diet.

The methodical approach is modern and sufficient to fulfill the set goals and tasks. The study used behavioral tests (open field test, cross-maze test, social interaction test, object recognition test, forced swimming test), biochemical methods (e.g. determination of glucose levels by oral glucose tolerance test test, determination of total cholesterol and triglycerides, determination of serum superoxide dismutase activity), histological studies, spectrophotometric study, determination of adipose tissue indices and statistical methods.

Results

5The results of the conducted experimental studies are in-depth and illustrated in great detail.

The obtained data in a model of metabolic syndrome in rats show the development of visceral obesity, insulin resistance and 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.

Oral administration of Chaenomeles maulei fruit juice at three different doses (2.5 ml/kg, 5 ml/kg, and 10 ml/kg) resulted in amelioration of a significant proportion of behavioral, biochemical and histopathological changes associated with metabolic syndrome.

Conclusions and Scientific Contributions

The main conclusions reached by the doctoral student are 3, which 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 of the contributions formulated by the doctoral student are original. The scientific contributions have significant theoretical and methodological value, as well as potential clinical application in the prevention and treatment of metabolic syndrome.

Scientometric indicators related to the dissertation work

In connection with her dissertation work, Dr. Klementina Moncheva Moneva-Marinova has presented a list of 4 publications, 1 of which is in a journal with IF. She is first author on all publications presented.

Dr. Moneva-Marinova has presented a list of 2 participations in scientific forums.

Doctoral thesis

The doctoral thesis contains 79 pages, 26 figures and 13 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 on the topic of the dissertation.

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 Medical University - 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 esteemed 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. Clementina Moncheva Moneva-Marinova.

15.03.2024

Prepared the review:
/Prof. Dr. Rumen Nikolov, MD/