## SCIENTIFIC REVIEW BY

## PROF. DR. MILA VLASKOVSKA MD, PHD, DSC, CORRESPONDING MEMBER OF BAS DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY, FACULTY OF MEDICINE, MEDICAL UNIVERSITY OF SOFIA

Member of the scientific jury for a competition for an academic position "Associate Professor" (published in SG, ed. 61/23.07.2021), approved with order  $N_{\rm P}$  P-109-396/20.09.2021 by the Rector, in the field of higher education 7. "Healthcare and sport", professional field 7.1. "Medicine", scientific specialty "Pharmacology (incl. Pharmacokinetics and Chemotherapy)" – one, for the needs of Department of Pharmacology and Clinical Pharmacology and Therapeutics, Faculty of Medicine, Medical University of Varna

Documents for the competition were submitted by a single candidate – Dr. Silvia Gancheva Marinova, MD, PhD

#### Biographical data and career development/profile

Dr. Silvia Gancheva was born in 1982 in the town of Silistra. She completed her secondary education in 2001. In 2007 she graduated as a "master" in medicine at MU "Prof. Dr. Paraskev Stoyanov", Varna. Dr. Silvia Gancheva acquired a specialty in "Pharmacology" in 2017. In 2018 she successfully defended her dissertation, entitled "Effects of Vitamin K in an experimental model of metabolic syndrome", and acquired an educational and scientific degree "Doctor" in the scientific specialty "Pharmacology (incl. Pharmacokinetics and Chemotherapy)".

I know Dr. Gancheva as an excellent combination of diligence, creativity and modesty. She is exceptionally active in scientific research and teaching with a talent for team work.

#### **Teaching activity**

Dr. Silvia Gancheva has 13 years of teaching experience in Medical University of Varna. She was appointed to the position "Assistant Professor" at the Pharmacology Department soon after her graduation – in February 2008. In 2019, after acquiring the educational and scientific degree "Doctor" in the specialty "Pharmacology (incl. Pharmacokinetics and Chemotherapy)" she was appointed to the academic position "Chief Assistant Professor". From 2018 until now Dr. Gancheva has implemented the functions of administrative assistant of the Department of Pharmacology and Clinical Pharmacology and Therapeutics.

The teaching activity of Dr. Silvia Gancheva includes leading of disciplines "Pharmacology" for medicine and dental medicine students and "Clinical Pharmacology" for medicine students. Dr. Gancheva teaches also students from the English language education program of the Medical University of Varna. The reference for the teaching activity of the candidate shows that the average academic activity of Dr. Silvia Gancheva in the last 5 years is more than 560 hours per year, thus indicating her high commitment to the educational process.

As an assistant professor at the Pharmacology Department, Dr. Gancheva is a co-author of four training manuals published by MU Varna. Three of them are pharmacology workbooks for conduction of practical seminars intended for medicine, dental medicine and pharmacy students. The fourth manual includes collection of sample tests aiming to facilitate the students' self-study.

Dr. Gancheva is accepted as a teacher with high authority by her colleagues and she is highly appreciated by the students.

#### Scientific activity

Dr. Silvia Gancheva has an extensive publishing activity. She is an author of 1 monograph and a co-author of 4 training manuals, 17 articles and 5 full-text reports. Her research is presented at numerous international scientific forums. Ten of the abstracts that she co-authored are published in supplements of international journals with impact factor.

Dr. Silvia Gancheva participates in 5 research projects funded by the Science Fund of Medical University of Varna. She is a coordinator and a financial and administrative manager of 2 of them. Most of these projects are focused on the hormonal role of vitamin K-dependent protein osteocalcin in the regulation of energy metabolism.

Dr. Silvia Gancheva attends the current competition with a total of 20 scientific publications as follows:

• Monograph entitled: "Kochia scoparia – the health benefits of a "common" plant", which is presented as a main habilitation thesis – 139 pages;

• 10 publications and reports, published in scientific journals, referenced and indexed in world-famous databases of scientific information (Scopus и Web of Science) according to the Academic Reference for compliance of minimal requirements;

• 6 publications in unreferred journals with scientific review

• 3 full-text publications in scientific journals and collections that are not included in the evidence for compliance of minimal requirements for academic position "Associate Professor".

The publications that are presented by the candidate for participation in the competition are published in different Bulgarian and international scientific journals and collections in the field of clinical medicine, experimental pharmacology, neuropsychopharmacology, and others. According to the Academic Reference, seven of the publications, presented by the candidate for participation in the current competition, have an impact factor with a total value of 25.119.

Dr. Silvia Gancheva is a first author of 7 and a second author of 4 of the presented for the competition publications. In her self-assessment, the candidate has divided the points for each submitted scientific publication in proportion to the number of co-authors, and the candidate's points by groups of indicators that I approve are as follows:

## Indicator A - 50 pts, Indicator C - 100 pts, Indicator D - 215.48 pts.

My complex evaluation for the submitted monography and scientific publications is very positive. The presented publications can be summarized in the following main research directions:

#### 1. Vitamin K and osteocalcin

This direction is presented by 8 publications and reports. Five of them are published in referred and indexed journals and three of them have an impact factor. The publications consider the role of vitamin K and vitamin K-dependent protein osteocalcin in the regulation of energy metabolism. Most of the publications present original experimental studies held on intact rats and rats subjected to a model of metabolic syndrome. An experimental model of subclinical vitamin K deficiency is verified. The model is consequently utilized for exploring the hypothesized endocrine activity of

Uncarboxylated osteocalcin. The publications demonstrate that the pharmacologically induced changes of uncarboxylated osteocalcin levels are associated with opposite changes in the energy metabolism, behavior and cognition of experimental animals, thus indicating the hormonal role of this vitamin K-dependent protein in the rat organism. One of the publications in the direction presents a cross-sectional clinical study, which confirms the regulatory role of osteocalcin on carbohydrate

metabolism. The clinical study shows, however, that most probably the carboxylation of the protein is not essential for its endocrine activity in humans.

In general, my assessment of the research on this problem is high. The candidate is one of the first to present results in this direction, which has provoked regulatory discussions in the EMA in recent years.

## 2. Drug interactions

The problem of potential drug interactions to which different groups of patients are subjected is considered in 4 publications and reports. Two of them are published in referenced and indexed journals, and one of the reports has an impact factor. The studies in this direction are extremely important from a practical point of view, as they show that the rate of potential drug interactions leading to a risk for patients' health is high and additional attention needs to be paid for minimizing them.

#### 3. Pharmacological effects of Kochia scoparia

This direction is presented by the habilitation thesis – the monograph "Kochia scoparia – the health benefits of a "common" plant", edited by Assoc. Prof. Dr. Maria Zhelyazkova-Savova, MD, PhD, as well as two publications in a referenced and indexed scientific journal with impact factor. The monograph reviews in details the botanical characteristics of the plant, the content of biologically active substances in its fruits and seeds, and their various pharmacological effects. The monograph includes original experimental studies on the effects of aquaeous infusion from kochia seeds in young healthy rats and in animals with diet-induced metabolic syndrome.

The results from the experiments show that Kochia scoparia seeds possess high biological activity in an easy to prepare and consume form. They could be a useful tool in the prevention and/or adjunctive therapy of socially important diseases, such as metabolic syndrome, type 2 diabetes, non-alcoholic fatty liver disease, anxiety-depressive disorders, and cognitive impairment. The monograph is written very intelligently and includes a wealth of scientific information that proves the conclusions about the usefulness of the plant.

# 4. Effects of biologically active substances of natural origin in different experimental models.

This direction includes 4 full-text publications, 1 of which is published in a journal with impact factor. All articles report results from original experimental studies. Two of them are focused on the beneficial effects of biologically active substances (eugenol and gallic acid) in a rat model of inflammatory bowel disease. The significance of the research stems from the high prevalence and severity of these diseases in humans, necessitating the search for additional low-toxicity agents for their treatment. One of the presented studies demonstrates the effects of Aronia melanocarpa fruit juice on acute inflammation in rats with diet-induced metabolic syndrome, thus confirming and enriching the already available data on pronounced anti-inflammatory activity of the plant.

The diet-induced rat model of metabolic syndrome is additionally utilized in another experiment studying the effects of anethole on liver aminotransferases. The study indicates that anethole, which is widely used in food industry, is able to impair liver function in diet-induced obesity. This potential side effect of anethole has not been reported previously.

#### Citations

Dr. Silvia Gancheva covers the normative requirements for citation of scientific publications. According to the Academic Reference, the candidate has submitted a list of 4 citations in referenced and indexed scientific journals for covering of the minimal requirements for academic position "Associate Professor" (60 pts according to the Academic Reference), and an additional list of scientific citations (150 pts according to the Academic Reference), which undoubtedly reflects the international recognition of the candidate's scientific production.

My complex assessment of the scientific publications submitted by Dr. Silvia Gancheva is positive. As seen in the detailed statement, she is highly committed to her teaching and scientific research activities.

The scientific publications of the candidate and their citations meet the requirements for academic position "Associate Professor".

I have no critical remarks about the candidate. My recommendation is to continue with the same unceasing enthusiasm to train not only students, but from the view of the new position - specialists and younger colleagues, so as to keep the image of the Department of Pharmacology and Clinical Pharmacology and Therapeutics of a young, hardworking and creative team as I have known it in recent years.

## Overall assessment of the candidate's accordance regarding the mandatory requirements and quantitative criteria and science-metric indicators according to the Regulation for oc-cupation of academic positions of assoc.professorin Medical University of Varna

Field of higher education 7. "Healthcare and sport", professional field 7.1. "Medicine", scientific specialty "Pharmacology (incl. Pharmacokinetics and Chemotherapy)" for the needs of Department of Pharmacology and Clinical Pharmacology and Therapeutics, Faculty of Medicine, Medical University of Varna

Main pa- rameters	content	Assoc. Prof	Dr. Silvia Gancheva
А	Indicator 1	50	50
В	Indicator 2	-	
С	Indicators 3 or 4	100	100
D	Sum of indicators 5 to 9	200	215.48: 204 (in the main list) + 11.48 (in the additional list)
E	Sum of indicators 10 to 12	50	$\frac{210:}{60 \text{ (in the main list)} +}$ 150 (in the additional list)
F	Sum of indicators 13 to the last	-	

# Table 1. Minimum required points for groups of indicators for scientific degrees and academic positions

# **CONCLUSION**

Dr. Silvia Gancheva Marinova, MD, PhD **meets** and even exceeds the mandatory and specific requirements, specified in the Law for Development of the Academic Staff in the Republic of Bulgaria and the Regulation for its application in the Medical University of Varna, for occupation of academic position "Associate Professor".

The documents for participation in the competition submitted by the candidate show that Dr. Silvia Gancheva, MD, PhD fully meets the requirements for holding the academic position "Associate Professor" according to the Law for Development of the Academic Staff in the Republic of Bulgaria and the Regulation for its application in the Medical University of Varna. The scientific publications and the indicators of scientific activity meet the quantitative and qualitative criteria for occupation of the academic position "Associate Professor". They indicate the long-standing commitment to the education of students in medicine, dental medicine and pharmacy and research in the field of pharmacology, with a skillful combination of fundamental and practical research.

Based on my personal impressions, I can confidently say that the candidate has the necessary qualifications for pedagogical and research competence.

In view of the above, I confidently give my positive assessment to Dr. Silvia Gancheva, MD, PhD in the competition and I offer the esteemed Members of the Scientific Jury to award Dr. Silvia Gancheva, MD, PhD the academic position of "Associate Professor" in the field of higher education 7. "Healthcare and sport", professional field 7.1. "Medicine", scientific specialty "Pharmacology (incl. Pharmacokinetics and Chemotherapy)"

> Reviewer: Prof. Dr. Mila Vlaskovska, MD, PhD, DSc, Corresponding Member of BAS

Sofia, 01.12.2021