WRITTEN OPINION

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(Internal member of Scientific jury, according to order №RD-109-292/05.09.2024 of Prof. Dr. Dimitar Raikov, PhD, DSc - Rector of Medical University "Prof. Dr. Paraskev Stoyanov"-Varna)

Subject: Competition for the academic position of "Associate Professor" in the specialty "Toxicology", professional field 7.3. Pharmacy, field of higher education 7. Healthcare and sports- one position for the Department of "Pharmacology, Toxicology and Pharmacotherapy ", Faculty of Pharmacy, published in SG, no. 57 of 05.07.2024

Only one candidate took part in the announced competition for the occupation of the academic position of "ASSOCIATE PROFESSOR" - chief assistant professor Nadezhda Rumenova Karkkeselyan, MScPharm, PhD, from the Department of "Pharmacology, Toxicology and Pharmacotherapy" at the Faculty of Pharmacy, Medical University - Varna, for whose needs it has been announced.

The submitted set of materials on electronic carrier is **in full compliance** with the legal requirements and Art. 138 of the current Regulations for the development of the academic staff at MU-Varna (last revision 21.11.2022) as the evidence presented are not repeated with the submitted and evaluated ones when acquiring the educational and scientific degree "doctor" and occupying the academic position "chief assistant professor".

All administrative deadlines for the competition have been met.

Candidate's career profile

Chief assist. prof. N. Karkkeselyan was born in 1987 in the city of Varna. She completed her secondary education at the First language school with "Foreign language profile with German", Varna. She graduated with higher pharmaceutical education from the Faculty of Pharmacy at MU-Plovdiv in 2011 and obtained a **master's degree in Pharmacy** (diploma series МУПІ-09 № 008379 dated 08.03.2012).

Since 2013, she has been successively a part-time assistant professor, a full-time assistant professor and chief assistant professor at the Faculty of Pharmacy at the Medical University of Varna, where she is currently working in this position.

In 2018, N. Karkkeselyan defended a dissertation in the scientific specialty "Toxicology" on the topic "Pharmacotherapeutic Study, Potential Side and Toxic Effects of Cardioactive Drugs in the Treatment of Hospitalized Patients with Chronic Heart Failure " and acquired the **educational and scientific degree "Doctor"** (diploma No. 316/21.12.2018).

Increasing her qualification, chief. assist. prof. N. Karkkeselyan acquired a **specialty in "Toxicology and toxicological analysis"** in February 2020 (certificate No. 4326/2020) and to date she has also successfully completed the individual training plan for the specialty "Hospital Pharmacy" and is about to take the state exam.

The above clearly indicates that Nadezhda Rumenova Karkkeselyan fully meets the requirements of Art. 125 of the current Regulations for the development of the academic staff at MU-Varna for the occupation of the academic position "associate professor":

- she has acquired a master's degree and a doctoral degree in the same specialty (7.3. "Pharmacy") for which the competition is announced;

- she held the academic position "assistant professor" and subsequently "chief assistant professor" at MU-Varna for more than five years;

- she has a recognized specialty in the health care system (such is regulated in Ordinance No. 1 of 22.01.2015 on acquiring a specialty in the health care system) in the same specialty of the competition.

Teaching and learning activity

Chief assist. prof. Nadezhda Karkkeselyan conducts practical exercises and seminars as well as participates in conducting the semester exams in the academic disciplines:

- "Pharmacology" for 3/4 year students, specialty "Pharmacy";
- "Toxicology" for 4th year students, specialty "Pharmacy";

According to the regulated possibility in the regulations of MU-Varna, she also conducts lectures on Toxicology to students of the 4th year, EQD "Master" majoring in "Pharmacy". She is also a leading lecturer on the disciplines "Pharmacology" and "Toxicology" for assistant pharmacists at the Medical College of the MU-Varna.

The academic workload of chief assist. prof. N. Karkkeselyan is **328** hours, calculated arithmetically for 5 academic years, with a requirement of 100 hours from MU-Varna for admission to the competition for "associate professor". She is a co-author of 5 textbooks with theses and tests on the disciplines she teaches. A monograph in the field of toxicology has also been published.

Summarizing the educational and teaching activities of Nadezhda Rumenova Karkkeselyan, I can categorically define her as a well-established and continuously developing tutor who fully meets the requirements of LDASRB, RILDASRB and the Regulations for the Development of the Academic Staff at MU-Varna for occupying the academic position "associate professor":

- ***she conducts practical exercises and seminars as well as participates in conducting the semester exams in the disciplines "Pharmacology" and "Toxicology";***
- ***conducts lectures to students in the disciplines "Pharmacology" and "Toxicology";***
- ***she has an arithmetic average of 328 teaching hours for 5 academic years;***
- ***she is a co-author of 5 textbooks with theses and tests on the disciplines she teaches.***

Scientific research activity

Chief assist. prof. N. Karkkeselyan presents **18 original articles in scientific journals** that are not conected to the dissertation work. Of these, **8** are in refereed and indexed scientific journals in world databases with scientific information - Scopus and Web of Science. Of the presented publications, 7 are in journals with an «impact factor» (JCR). **The total "impact**

factor" of the journals in which the candidate has publications is 11,827. The candidate also has **9** articles that have been published in non-refereed peer-reviewed journals.

A search of the available databases reveals the following citations:

- in Scopus – 42;
- in Web of Science – 41;
- in Google Scholar – 76;
- in ResearchGate – 54.

Most of the citations are in leading journals, referenced and indexed in world-renowned databases of scientific information.

Chief assist. prof. Nadezhda Karkkeselyan has **33** participattions in **scientific forums and conferences**, of which **4 are international** and 29 **are national.**

The candidate is an author of the **monograph** "Drug interactions in patients with cardiovascular disease", published in 2024 (ISBN 978-619-221-492-0), with two reviewers. In the presented habilitation thesis, it is considered how awareness can be raised about the potential clinically significant adverse drug interactions of the major groups of medications for CVD therapy (arterial hypertension, arrhythmias, ischemic heart disease and heart failure). A current topic related to patient safety in the use of drugs is highlighted. By definition, a drug interaction is considered clinically significant when it is associated with safety concerns due to toxicity or loss of efficacy that require the attention of healthcare professionals and/or systems involved in the drug therapy process. Original results of the candidate and author studies in the field of adverse drug interactions in patients with CVD are also presented.

Chief assist. prof. Nadezhda Karkkeselyan has participated in **3 research projects** (financed by the "Science" fund of MU-Varna).

In the last 5 years, the research work of chief assist. prof. N. Karkkeselyan is mainly in the field of the scientific specialty " Toxicology ". Her main contributions, reflected in scientific publications, represent a significant contribution to pharmaceutical science and practice and can be summarized as follows:

<u>Scientific and theoretical contributions</u>

- PHARMACOTHERAPEUTIC AND TOXICOLOGICAL STUDIES - scientific publications are focused on new pharmacotherapeutic approaches and toxicological aspects of drug therapy in patients with heart failure and diabetes. The risks of hyperkalemia in patients with heart failure and new possibilities for influencing it are discussed. In two of the presented articles, the information regarding the use of SGLT2 inhibitors in the treatment of heart failure and the incretin mimetic drugs therapy with their benefits and risks is studied and summarized.
- RESEARCH OF NATURAL SUBSTANCES AND PROBIOTICS - In the indicated chapter of the book, a comprehensive review of information on probiotics is made with an emphasis on new challenges in scientific research related to their application.
- PHARMACOTHERAPEUTIC AND TOXICOLOGICAL STUDIES These publications are provided for the acquisition of educational and scientific degree

"Doctor" and are focused on the study of hospitalized patients with chronic heart failure - demographic characteristics, comorbidities, pharmacotherapy, including its toxicological aspects.

- MARINE MEDICINE, THERAPY AND TOXICOLOGY - Two of the articles analyze and summarize information on bioactive substances of marine origin. Two marine toxins - saxitoxin and tetrodotoxin, clinical picture of intoxications with them, as well as their potential pharmacological application are examined. Information on currently registered medicinal products derived from marine organisms has also been studied and summarized, providing an opportunity for a comprehensive view of the development of marine pharmacology. The remaining two articles are related to an overview of the available clinical possibilities of modern thalassotherapy, a rapidly developing part of health tourism worldwide, including in a coastal country like Bulgaria. and also the legal regulation concerning the medical equipment of the ships.

Scientific and applied contributions

- STUDY ON POTENTIAL DRUG INTERACTIONS - the scientific publications present author's data from studies on potential drug interactions of patients hospitalized in the Internal Medicine Clinic of St. Marina University Hospital - Varna. In the articles, the patients were selected according to different criteria – diagnosis of heart failure, age and medications taken. Interactions with drugs with a narrow therapeutic index that could have particularly dangerous consequences were specifically explored, with one article focusing specifically on cardiac glycosides. Another of the papers presented focuses on pharmacokinetic drug interactions, which are believed to be more difficult to predict. The observed results have a contribution to practice, as they increase the awareness of potential interactions with the simultaneous intake of certain drugs. These interactions could be avoided, but this requires a specific approach - the use of appropriate software or a clinical pharmacist with experience in the field of drug interactions to make the necessary expert conclusions for a given pharmacotherapy.
- STUDY OF NATURAL SUBSTANCES AND PROBIOTICS - publications present author's data from various experimental studies. They are focused on the study of the biological activity and organoprotective effects of natural substances (mainly plant extracts) and probiotics, as well as on the study of the qualitative and quantitative composition of plant extracts. The observed results have a contribution to practice as they indicate the occurrence of potential interactions when the studied extracts are taken simultaneously with drugs. This requires that the mentioned extracts be taken with caution. Several experiments have focused on investigating the organoprotective effects of plant extracts in experimental animals. The antioxidant activity of Bulgarian probiotic cultures in rats was also investigated. The developed experimental models (for cardiotoxicity, nephrotoxicity and hepatotoxicity) can be applied in the study of the biological effects of other herbal and medicinal substances. The results of the conducted experiments with laboratory animals can serve as a basis for future studies of the organoprotective effects of the studied extracts in humans, as well as for their application as preventive agents.

A significant part of the candidate's scientific work is focused on investigating potential drug interactions. A strong impression is made by the well-summarized data on the available information on major drug interactions in the therapy of patients with cardiovascular disease. Important and clinically relevant interactions that could be encountered in the treatment of patients with arterial hypertension, arrhythmias, ischemic heart disease and heart failure are thoroughly discussed. These are reviewed in detail with mechanisms, clinical implications and recommendations for risk reduction. Drug interactions are divided according to their mechanism into pharmacokinetic and pharmacodynamic. However, an analysis of the data reveals that this division is indicative for many of the examples reviewed, as they cannot be fully assigned to one or the other group. The candidate skillfully proves his thesis that drug interactions are often complex and occur at several levels. This testifies to the specialization and improvement of the candidate in the field of toxicology.

Summary

The scientific indicators of chief assist. prof. Nadezhda Karkkeselyan exceed the minimum national requirements specified in RILDASRB and Appendix No. 1 of the Regulations for the Development of the Academic Staff at MU-Varna for occupying the academic position "associate professor" in professional direction 7.3. "Pharmacy" - with a minimum score of **400**, the candidate has collected **522,47** points.

The values of the main groups of indicators are presented in the table:

Group of indicators	**RILDASRB**	***Regulations for the Development of the Academic Staff at MU-Varna***	**Chief assist. prof. Nadezhda Karkkeselyan**
А	50	*50*	50
В	100	*100*	100
Г	200	*200*	212,47
Д	50	*50*	160
Total points	**400**	***400***	**522,47**

Summarizing the results of the research work and the scientific indicators of chief assist. prof. Nadezhda Karkkeselyan, PhD, it can be categorically concluded that they demonstrate her significant achievements in the field of pharmacology and fully satisfy the requirements of the RILDASRB and the Regulations for the development of the academic staff of the MU-Varna for occupying the academic position "associate professor ":

- ***She has 18 scientific publications, 7 of them in journals with an "impact factor" (JCR);***
- ***42 citations (Scopus) and 41 citations (Web of Science) in foreign scientific journals are found;***
- ***She has participated in 3 scientific research projects.***

CONCLUSION

As a result of everything stated above, I firmly believe that chief assist. prof. Nadezhda Rumenova Karkkeselyan, PhD fully meets the conditions under Art. 24 of LDASRB, art. 53 of the RILDASRB and Art. 125 of the Regulations for the Development of the Academic Staff of MU-Varna, as well as the minimum national requirements laid down in Art. 24, para. 2 and Art. 2b, para. 2 and 3 of LDASRB, as well as the Regulations for its application for the occupation of the academic position "ASSOCIATE PROFESSOR".

Everything stated so far gives me grounds to vote positively and fully convinced to suggest to the honorable Scientific Jury to choose CHIEF ASSIST. PROF. NADEZHDA RUMENOVA KARKKESELYAN, MScPharm, PhD for the academic position "Associate Professor" in the specialty "Toxicology", professional field 7.3. Pharmacy, field of higher education 7. Healthcare care and sports for the Department of "Pharmacology, Toxicology and Pharmacotherapy", Faculty of Pharmacy at MU-Varna.

Varna
29 October 2024.

Member of the scientific jury:

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

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(Prof. Evgeni Evgeniev Grigorov, PhD)

By signing here, I declare that I am not a person related to the candidate, and that I have no private interest that could affect the impartial and objective implementation of giving an opinion in this competition for the academic position of "Associate Professor".