

REVIEW

by Prof. Gergana Nenova, PhD, DSc,
Faculty of Public Health, Medical University “Prof. Dr. Paraskev Stoyanov” - Varna

About: Competition for an Associate Professor academic position, announced in State Gazette, issue 41/03.06.2022, for the Public Health Management (Medicinal Product Analysis) specialty, in the professional sphere 7.4. Public Health, in the field of higher education 7. Healthcare and Sports; for the needs of TS of Assistant Pharmacist, Medical College at the Medical University “Prof. Dr. Paraskev Stoyanov” - Varna.

1. Information about the procedure

By an ordinance № P-109-319/29.07.2022 of the Rector of the Medical University of Varna, I was appointed as a member of the Scientific Jury and tasked with preparing a review for the competition for the Associate Professor academic degree at Medical College, MU-Varna for the Public Health Management (Medicinal Product Analysis) specialty, in the professional sphere 7.4. Public Health, in the field of higher education 7. Healthcare and Sports.

The competition is announced in the State Gazette, issue 41/03.06.2022 and complies with the Law on the Development of Academic Staff in the Republic of Bulgaria (LDASRB) and the Regulations to the Law for the Development of Academic Staff (RLDAS) of MU-Varna. Based on the aforementioned legal documents, all procedure requirements for the announcement of the competition, the deadline for submission of documents, and the selection of a Scientific Jury have been met.

The sole candidate is Silviya Georgieva Mihaylova, PhD.

2. Short information about the career path and qualifications of the candidate

Silviya Mihaylova was born on 03.06.1978 in Varna. In 2003 she graduated from the Faculty of Pharmacy at the Medical University of Sofia, earning a Master’s degree in Pharmacy. In 2021 she acquired her specialty in Medicinal Product Analysis by Ordinance 1/2015 for the acquisition of specialty in the sphere of healthcare. In 2019 she gained her PhD at the Medical University of Varna with a dissertation titled *Synthesis and Biological Assessment of SMAC-NT Peptide Conjugates with Combined Antineoplastic and Analgesic Activity*. The professional competencies of Ch. assist. prof. Mihaylova are marked by depth and excellent teaching skills, which is a prerequisite to the high quality of her work as a researcher, lecturer, and practitioner. Ch. assist. prof. Mihaylova has good skills in English and Russian.

3. General compliance of the candidate with the requirements of RLDAS of MU-Varna

	Conditions based on art. 100 of RLDAS	Information about the candidate
1.	To have acquired PhD in the relevant scientific specialty	Yes—2019
2.	Requirements for a time period and teaching load of no less than 100 hours on average annually for 4 years	Yes, incl. above the quota 371 hours for the acad. yr. 2016/2017, 471 hours for the acad. yr. 2017/2018,

		423 hours for the acad. yr. 2018/2019, 363 hours for the acad. yr. 2019/2020, 511 hours for the acad. yr. 2020/2021
3.	To have presented a published monograph	Yes
4.	To have presented original scientific research publications	Yes—22

4. Characteristics of the monograph

The candidate presents a monograph (research work) titled *Peptides as Drugs. Application of Chemical Methods in the Synthesis and Optimization of Peptide Medicinal Products* with an ISBN 978-619-221-378-7, published and printed by Varna Medical University Press. The monograph is dedicated to the opportunities offered by peptide chemistry for synthesis and improvement of physicochemical properties leading to an increase in the biopharmaceutical and pharmacokinetic parameters of peptide molecules. On the basis of a SWOT analysis, the possibilities of the future development of these molecules as effective and safe medicinal products have been defined. The work was reviewed by three reviewers: Assoc. prof. Diana Dobрева, PhD; Assoc. prof. Velichka Andonova, PhD; and Assoc. prof. Emiliya Georgieva, PhD. The bibliography includes 268 sources. The monograph does not contain any advertisements.

5. Scientometric indicators and scientific contribution

Minimum required points by indicator groups for the Associate Professor academic degree according to LDASRB and RALDASRB

Indicator Groups	Content	Associate Professor RALDASRB (points)	Silviya Mihaylova
A	Indicator 1: Dissertation for the acquisition of a PhD degree	50	50
B	Indicators 3 or 4: Research work, i.e., monograph, presented in regard to a procedure for the acquisition of an academic degree	100	100
G	Total sum of the indicators from G5–9: Publications	200	230.50
D	Total sum of the indicators from D10–12: Citations	50	105

As it is seen from the inquiry made, the candidate covers the national criteria set for the Associate Professor academic degree.

Scientific activity and scientific contribution

The candidate, Silviya Georgieva Mihaylova, has presented a total of 29 scientific publications. Of them, for review for the current competition are 23: a monograph—1, and articles in scientific journals and periodicals—22, with the contribution being distributed as follows:

1. Sole author—1 (monograph)

2. First author—2 publications, or 9%
3. Second authors—8 publications, or 36%
4. Third and subsequent author—12 publications, or 52%

Five of the publications, in one of which the candidate is first author and in two—a second author, are featured in scientific publications, which are peer-reviewed and indexed in famous international databases with scientific information. The number of publications from peer-reviewed and non-indexed in famous international databases journals is 16. Outside the materials presented in order to cover the minimum requirements for the acquisition of the Associate Professor academic degree, the candidate presents one full-text publication available in Varna Medical Forum.

The scientific publications are distributed into the following fields:

1. Food and nutrition
2. Oncology and rare diseases
3. Prevention, disease management and health system management
4. Peptide chemistry

The studies in the **first field** are related to terminological introduction, research, and presentation of the *functional food* concept. The Academy of Nutrition and Dietetics (USA) defines functional foods as each potentially healthy food or food ingredient, which may provide benefits for health outside the traditional nutritional components it contains. Based on detailed research, the role of food in prevention, treatment, and rehabilitation of various diseases is shown, with a focus on those with a high disease burden for society. The main chemical characteristics of various medicinal plants used successfully in pharmacy and medicine are determined. Several groups of medicinal plants are analyzed in the context of complementary and alternative medicine. The indications for their application in severe socially significant diseases are reviewed and additional benefits for the patient from their inclusion in the conventional therapy are shown. The epidemiological and social aspects of food and nutrition are studied. The role of functional foods in the prevention and treatment of hepatic, socially significant oncological, and infectious diseases is presented (G.8.5; G.8.8; G.8.10; G.8.11).

The scope of the **second field** is focused on the epidemiology of neoplastic diseases, the need of developing efficient approaches and means for timely diagnostics and adequate treatment. Personalized medicine and the accent on the efficiency and safety in the current regulatory environment require for the therapeutic agents to possess high flexibility, specificity, and safety.

The molecular characteristics and potential of short peptides and peptide mimetics as new therapeutic opportunities and control of the oncological pain are researched.

The interest in the therapeutic effects of the RGD and NT(8-13) analogs (e.g., antineoplastic, analgesic, etc.) is increasing exponentially, but still little is known about the pharmacokinetics of these peptides. In the presented scientific research, the pharmacokinetic behavior and the possible drug interactions in which RGD and NT(8-13) can be engaged are studied. The impact of these sequences on the activity of the most common enzyme, cytochrome P450 CYP3A4, responsible for the majority of drug interactions, is researched.

Drugs used to manage strong pain are with a pronounced affinity to opioid receptors. According to the new multitarget approaches, analgesics must interact with different receptors participating in the transmission and modulation of pain. The analgesic activity of newly synthesized neurotensin analogs is studied and a central mechanism for realization of an analgesic effect, independent of opioid pathways, is established.

The place of mycotherapy and fungotherapy in patients with oncological diseases is examined. The benefits of beta-glucans (heterogeneous group of polysaccharides) on the immune system and their synergic activity in combination with chemo- and/or radiation therapy are indicated (G.7.3; G.7.4; G.8.8; G.8.9; G.8.11, publication related to the dissertation).

The scientific publications from the **third field** are focused on encouraging the maintenance of good health and disease prevention, as well as the provision of economically efficient health service. All of Silviya Mihaylova's publications are led by the scientific conviction that the concentration of more resources towards the strategies for health promotion and disease prevention is the most important part in the aim to decrease the impact of risk factors. A research focus is established—quality care for chronic non-infectious socially significant diseases.

Medicinal products are important for the modern society, both for the improvement of public health and for the economic growth. The main focus of the effective drug therapy is the satisfaction of society's needs of quality, affordable, proven in therapeutic practice, and cost-effective medicinal products. Chronic diseases are the main reason for decreased length and quality of life.

Current problems of modern healthcare are presented, namely how the healthcare system is influenced by the new health technologies and measures to provide patients with access to them are defined—by developing suitable mechanisms. The possibilities of new technologies to change the disease course in patients with chronic diseases are studied. The advantages of peptide drugs over small-molecule drugs and biotechnological proteins are shown, as well as different methods for peptide modifications with the aim of increasing the metabolic stability, bioavailability, and pharmacokinetic properties of peptides.

The knowledge and skills of pharmacists are used for analysis and assessment of the effects of macrolevel decisions, which have an impact on the patients in the field of pharmacy as part of healthcare. The concept of Pharmaceutical Care of the International Pharmaceutical Federation (FIP) is confirmed. Part of the presented publications prove that pharmaceutical care can decrease both the number of errors and the expenditures resulting from them.

A critical factor in the treatment of individual patients is the pharmacoeconomic aspect—increased morbidity of the population, prolonged hospitalization, high treatment costs, etc. The development of new integrative approaches and the application of instruments for the assessment of safety, efficiency, quality, impact on public health, or drug efficacy will facilitate the regulatory decision-making (G.7.1; G.7.2; G.7.5; G.8.1; G.8.3; G.8.4; G.8.6; G.8.7; G.8.10; G.8.12; G.8.13; G.8.14; G.8.15; G.8.16).

In the **fourth field**—Peptide Chemistry, the main contribution consists of increasing the knowledge about the therapeutic effects, which can be achieved through the different synthetic processes and which are related to specific modifications in the structure of peptides. The conducted situational analysis forms a strategic vision for the key role of peptides as an economically effective and safe alternative to modern small-molecule drugs. The publications present the achievements of peptide chemistry in the synthesis and improvement of the physicochemical properties leading to an increase of the biopharmaceutical and pharmacokinetic parameters of peptide molecules. Part of the studies is related to design, synthesis, and characterization of new peptides by which the scope of knowledge in the sphere of peptide chemistry is expanded.

By experiments in the field of the fundamental chemistry are discovered those changes and substitutes in peptide molecules which increase their stability and improve their pharmacological effect. Newly synthesized peptides are studied for analgesic and cytotoxic activity with the aim of potentially

including them in the therapy of neoplastic diseases. The obtained results and experience will potentiate subsequent, upgrading fundamental research.

Peptide drugs have three main limitations, which hinder their therapeutic efficiency: in vivo instability, poor oral adsorption, and membrane impermeability. There is detailed study of the methods of improvement of the metabolic stability of peptide drugs.

In a systematized way are presented the various classes of antimicrobial peptides (AMPs), which are found in nature and represent an important part of the innate immune defense of plants, insects, and mammals (incl. humans). Outlined are their potential therapeutic advantages when counteracting antimicrobial drug resistance (G.7.1; G.7.3; G.7.4; G.8.2; G.8.9; G.8.10, publications related to the dissertation).

Citations. The candidate has presented a transcript from the library of the Medical University of Varna containing 13 citations of which 1 is from scientific journals, which are peer-reviewed and indexed in international databases, 6—in monographs and collective volumes with peer review, and 6—in non-indexed journals with peer review. Autocitations are excluded. Based on the transcript, the impact factor of Ch. assist. prof. Silviya Mihaylova, PhD is 4.162. The citations bring a total of 105 points to Silviya Mihaylova with the minimum national requirement for this indicator being 50 points.

Scientific activity. Silviya Mihaylova is part of 5 scientific research projects, has participated in 10 scientific forums with proceedings and in 5 poster sessions of which 2 being international.

In conclusion, the complex assessment of the scientometric indicators and scientific contribution I believe that those of a practical and applicable character predominate over the ones of theoretical and methodological character. I think that the field of Peptide Chemistry has the potential of further development and can be a subject of the future scientific research and practical activity of the candidate.

6. Teaching activity

Up to 13.06.2022 Silviya Mihaylova has 16 years, 10 months and 11 days of **experience in her specialty** with her **teaching experience** being 8 years, 7 months and 15 days. Since 2013 until now, she has achieved the needed teaching load and even exceeds it in the last five years. **The teaching load** of Ch. assist. prof. Silviya Mihaylova includes classes in Pharmaceutical Chemistry, Homeopathy, practice, and pre-graduate internship.

Conclusion

Based on covering the minimum national requirements indicated in the Regulations to the Application of the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations of MU-Varna, the established contribution of the scientific activity of the candidate and her teaching experience I suggest that the estimated members of the Scientific Jury vote positively and propose to the Rector of MU-Varna that **Silviya Georgieva Mihaylova obtain the Associate Professor academic degree** in the Public Health Management (Medicinal Product Analysis) specialty, in the professional sphere 7.4. Public Health, in the field of higher education 7. Healthcare and Sports for the needs of TS of Assistant Pharmacist, Medical College at Medical University of Varna.



Prof. Gergana Nenova, PhD, DSc

October 2022