OPINION

From Assoc. Prof. Velichka Yordanova Andonova, Ph.D., Head of the Department of Pharmaceutical Technologies, Faculty of Pharmacy, Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, member of the scientific jury according to Order No. R-109-229/26.07.2024 of the Rector of the Medical University of Varna

Subject: *Competition for the academic position of "Associate Professor" in the field of "Technology of Dosage Forms and Biopharmacy," professional field 7.3. "Pharmacy," area of higher education 7. "Healthcare and Sport," announced in the State Gazette, issue 45/28.05.2024, for the needs of the Faculty of Pharmacy, Department of Pharmaceutical Technologies.*

By Order No. R-109-229/26.07.2024 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna (MU – Varna), I have been appointed a member of the Scientific Jury (SJ), and according to Protocol No. 1 from the first meeting of the SJ, I am assigned to prepare a statement regarding the procedure for occupying the academic position of "Associate Professor" in the field of "Technology of Dosage Forms and Biopharmacy." The only candidate in the competition is Ch. Assist. Prof. Viliana Eduardova Gugleva, Ph.D. The competition procedure has been followed, and the candidate's documents comply with the requirements of the Development of Academic Staff in the Republic of Bulgaria Act, the regulation for implementation of this Act, and the Regulations on Academic Staff Development at Medical University Prof. Dr. Paraskev Stoyanov – Varna, including the established criteria for occupying the academic position of "Associate Professor."

Short Biography and Professional Development

Ch. Assist. Prof. Viliana Eduardova Gugleva was born in 1987 in Varna. In 2011, she obtained a Master's degree in the regulated profession "Pharmacy" with a professional qualification "Master Pharmacist" from the Faculty of Pharmacy at the Medical University – Sofia. From 2020 to 2021, she was a doctoral student in independent study form at the Faculty of Pharmacy at the Medical University – Sofia, working on the dissertation topic "Design and characterization of doxycycline hyclate-loaded niosomes for ophthalmic application." In 2017, she acquired a specialization in "Technology of Medicines with Biopharmacy" under Ordinance No. 1/22.01.2015. In 2022, she completed a course on "Safety Assessment of Cosmetic Products" at Sofia University "St. Kliment Ohridski" and obtained additional qualification as a "Safety Assessor of Cosmetic Products."

From 2012 to 2021, she served as an assistant professor in the field of "Technology of Dosage Forms and Biopharmacy," Department of Pharmaceutical Sciences (until 2014) / Department of Pharmaceutical Technologies (from 2014 to present), Faculty of Pharmacy, MU – Varna. From 2021 to present, she is an Ch. Assist. Prof. in the same field and department. Ch. Assist. Prof. Viliana Gugleva has over 12 years of academic experience in the professional field of "Pharmacy."

She is responsible for quality in the Department of Pharmaceutical Technologies (from 2021 to present) and course leader for first-year students in the unregulated profession "Cosmetology" (from 2022 to present). In September 2023, she was invited to be a guest editor for the scientific journal *Pharmaceutics*. She is a member of the American Chemical Society (ACS), Academy of Pharmaceutical Sciences (APS), Bulgarian Scientific Society of Pharmacy (BSPhS), and the Union of Scientists – Varna. She is proficient in English, German, and Russian.

Teaching Activities

Ch. Assist. Prof. Viliana Gugleva began her teaching career as an assistant professor in the Department of Pharmaceutical Sciences (until 2014) / Department of Pharmaceutical Technologies (from 2014 to present) at the Faculty of Pharmacy at MU-Varna in 2012, where she conducted practical exercises in "Technology of Dosage Forms I and II," Biopharmacy and Pharmacokinetics, and elective course "Technology of Medicinal-Cosmetic Products" for Pharmacy students. In the master's program in "Cosmetology," she is involved in practical exercises in subjects such as "Technology of Cosmetic Product Manufacturing," "Quality and Properties of Raw Materials in Cosmetics," "Innovative Carriers in Cosmetics," "Good Laboratory and Manufacturing Practice and Quality Assurance of Cosmetic Products." Over the last five academic years, her total teaching load averages 422.8 hours per year against a norm of 360 hours, with a departmental resolution assigning a total of 99 lecture hours for the same subjects.

She has supervised two graduates in the field of "Cosmetology," who successfully defended their theses in 2024 with excellent grades.

According to the information available on the website of the Medical University of Varna, the University Publishing House indicates that Ch. Assist. Prof. Viliana Gugleva has participated in the preparation and publication of "Test Questions for Self-Preparation in Technology of Dosage Forms for Pharmacy Students. Part I," published by the Medical

University of Varna, ISBN: 978-619-221-259-9, and "Test Questions for Self-Preparation in Technology of Dosage Forms for Pharmacy Students. Part II," published by the Medical University of Varna, ISBN: 978-619-221-264-3. She has also been involved in the authorship of four published workbooks for practical exercises in drug form technology, which are also published by the Medical University of Varna.

Based on the information regarding the teaching activities of Ch. Assist. Prof. Viliana Gugleva, she can be unequivocally classified as a well-established and continuously developing educator who fully meets the requirements of the Development of Academic Staff in the Republic of Bulgaria Act, the regulation for implementation of this Act, and the Regulations on Academic Staff Development at Medical University Prof. Dr. Paraskev Stoyanov – Varna for occupying the academic position of "Associate Professor."

Scientific Activity

In the competition for the academic position of "Associate Professor," Ch. Assist. Prof. Viliana Gugleva participated with a total of 16 scientific works, excluding those presented for obtaining the academic title "Doctor," 1 habilitation work – a monograph – and an additional full-text publication in a scientific journal indexed in the global databases WoS and Scopus, exceeding the minimum scientometric requirements for occupying the position of "Associate Professor," namely:

- Habilitation work – a monograph entitled "Contemporary Trends and Perspectives in the Design of Vesicular Systems: A Focus on Niosomes," published by the Medical University of Varna in 2024, ISBN: 978-619-221-498-2, comprising 129 pages **(indicator B3 – 100 points)**.

- 12 scientific publications in peer-reviewed journals indexed in renowned scientific databases (WoS and Scopus: 179.56 points), 3 in non-peer-reviewed journals or published in edited collective volumes (35 points), and 1 published chapter from a collective monograph (15 points). In the published full-text scientific publications in journals and proceedings, Ch. Assist. Prof. Viliana Gugleva is the first author in 8 of them, second author in 7, and subsequent author in 1. The total score for **indicators G5-G9 is 229.56 points**, exceeding the required minimum of 200 points. Beyond the minimum scientometric requirements for the position of "Associate Professor," Ch. Assist. Prof. Viliana Gugleva presents another full-text publication in a scientific journal indexed in the renowned global databases (WoS and Scopus), which brings her 6.66 points. The publications are in reputable

scientific journals with a **high impact factor – totaling 41.947**, and together with the publications for the academic title "Doctor," the overall impact factor of her scientific output is **52.667**.

- Citations of the publications by Ch. Assist. Prof. Viliana Gugleva exceed the minimum requirements for the position of "Associate Professor" – 6 are presented under indicator **D10 (90 points, with a requirement of 50 points)**. A check of Ch. Assist. Prof. Gugleva's profile **on Google Scholar reveals 523 citations with an h-index of 11**, while in **Scopus, there are 279 citations with an h-index of 8** (as of October 4, 2024), which is indicative of the significance of the candidate's scientific works.

Ch. Assist. Prof. Viliana Gugleva has participated in 2 national scientific projects, namely:

- Funding Organization: Ministry of Education and Science, Scientific Research Fund, Project Number: № КП-06-Н43/3 from November 30, 2020. Topic: "Design and Characterization of Conventional and Modified Niosomes and Hybrid Stimuli-Responsive In Situ Gel-Forming Drug Forms for Effective Drug Delivery." Project Leader: Prof. Denitsa Bogomilova Momekova, PhD; Duration: 3 years until December 2023.

- Funding Organization: Medical University of Varna, Science Fund "Project № 23011: Classical 2D and Modern 3D ALI Cell Models for Investigating the Antimicrobial and Cytotoxic Properties of New Therapeutic Agents and Nano-structured Drug Carriers," led by Ch. Assist. Prof. Nadezhda Antonova Ivanova, PhD; Duration: 3 years until December 2026.

She has participated in a total of 22 scientific forums, 5 of which are international and 5 are national with international participation.

Overall Assessment of Candidate's Compliance with Mandatory Conditions and Quantitative Criteria and Scientometric Indicators According to the Development of Academic Staff in the Republic of Bulgaria Act, the regulation for implementation of this Act, and the Regulations on Academic Staff Development at Medical University Prof. Dr. Paraskev Stoyanov – Varna and the Established Criteria for the Academic Position of "Associate Professor"

Ch. Assist. Prof. Viliana Eduardova Gugleva provides evidence of meeting the mandatory conditions and quantitative criteria and scientometric indicators according to the Development of Academic Staff in the Republic of Bulgaria Act, the regulation for implementation of this Act, and the Regulations on Academic Staff Development at Medical

University Prof. Dr. Paraskev Stoyanov – Varna and the established criteria for the academic position of "Associate Professor" in the area 7. "Healthcare and Sport," professional field 7.3. Pharmacy. It is evident that the total score across the indicator groups for the candidate is 469.56 points, with a required minimum of 400 according to the Regulations on Academic Staff Development at Medical University Prof. Dr. Paraskev Stoyanov – Varna.

Ch. Assist. Prof. Viliana Eduardova Gugleva fulfills the mandatory conditions and significantly exceeds the minimum national requirements and those of the Regulations on Academic Staff Development at Medical University Prof. Dr. Paraskev Stoyanov – Varna for the academic position of "Associate Professor" in the area 7. "Healthcare and Sport," professional field 7.3. Pharmacy.

Assessment of Scientific Contributions

The research activity of Ch. Assist. Prof. Viliana Gugleva primarily focuses on nanoscale drug delivery systems, mainly of vesicular type. Her main achievements and contributions, as reflected in her scientific publications, have a distinct scientific and applied character and represent a significant contribution to pharmaceutical science and practice. They correspond to the theme of the announced competition in professional field 7.3 "Pharmacy" and can be summarized as follows:

- pH-sensitive niosomes based on hexadecyl-poly(acrylic acid) copolymers have been developed, and their potential for loading with a hydrophilic model substance and the hydrophobic curcumin has been investigated, optimizing their physicochemical properties. *In vitro* studies on tumor cell lines have shown higher cytotoxic and apoptogenic activity compared to free curcumin.

- The results obtained from studies involving non-ionic surfactants (Span 20, Span 60, Span 80, Span 60, and Tween 60) niosomes are original. Promising results were achieved regarding the high loading efficiency with cannabidiol and the favorable physicochemical characteristics, which would allow the application of these carriers for a systemic drug product.

- Original contributions include the development of sterically stabilized niosomes with cannabidiol. Novel amphiphilic linear or star-shaped (3- and 4-arm) copolymers based on polyglycidol and poly(ε-caprolactone) were used. Controlled release of cannabidiol and steric stabilization in physiological conditions were achieved. The vesicles

retained the antineoplastic activity of cannabidiol and exhibited higher apoptogenic properties compared to the free substance.

- Original contributions also stem from the studies on the potential use of vesicular systems – ethosomes and transferosomes – loaded with curcumin as a drug delivery platform for dermal application. Hybrid systems based on bigels and nanostructured lipid carriers were developed. Their rheological characteristics were investigated and assessed using various mathematical models. The bigel based on hydrogel: oleogel (80:20) was identified as the most suitable carrier for dermal application, which may have practical implications for the effective treatment of dermatological diseases.

- The results from the investigation of the lyophilization processes of algae from the Black Sea concerning protein content may have practical significance for pharmaceutical technology, particularly for their use as suitable emulsifiers in emulsion and colloidal systems.

- The findings related to determining the antioxidant activity of extracts from the flowers of *Sambucus nigra* L., collected from four different regions in Bulgaria, have both scientific and applied significance. It has been established that the accumulation of secondary metabolites enhancing antioxidant potential is significantly influenced by geographical conditions.

- Contributions to pharmacy service functionality are reflected in the results of a survey among pharmacists and medical professionals in Varna regarding the application of extemporaneous forms in medical practice. An analysis of doctors' perceptions of extemporaneous and magistral prescriptions was conducted. Doctors still prefer extemporaneous prescriptions, as they meet the need for a personalized approach to specific patients. Particularly important among extemporaneous prescriptions are those intended for the treatment of dermatological diseases, as well as in some cases for pediatric prescriptions. Extemporaneous forms can serve as a good alternative when certain commercial products are unavailable on the market.

- The obtained pH-sensitive niosomes loaded with curcumin exhibit suitable physicochemical parameters and pH-dependent drug release. The demonstrated increased cytotoxic and apoptogenic activity during testing makes the resulting carriers potential candidates for translation into clinical practice in the treatment of bladder carcinoma and cutaneous T-cell lymphoma.

- Modified niosomes loaded with cannabidiol show controlled release, optimal physicochemical characteristics, and steric stabilization. Their biopharmaceutical characteristics in physiologically relevant conditions and enhanced apoptogenic effects make them potentially applicable in the treatment of oncological diseases.

- The developed ethosomes with curcumin, characterized by their physicochemical and biopharmaceutical properties and more pronounced anti-proliferative activity compared to the free substance, may be applied as a potential therapeutic option for cutaneous T-cell lymphoma.

Assessment of the Monographic Work

The monographic work of Ch. Assist. Prof. Viliana Gugleva titled "Contemporary Trends and Perspectives in the Design of Vesicular Systems: Focus on Niosomes" is structured into six chapters, each presenting different aspects of the design and trends in the development of vesicular systems, particularly niosomes. Niosomes are among the current and intensively studied drug delivery systems, finding widespread application in various fields such as nanomedicine, theranostics, and the cosmetic industry. In recent years, there has been particular interest in the possibility of structural modification through various targeting ligands, antibodies, or other fragments that mediate selective interactions with specific receptors and improve the internalization of nanocarriers. Like other vesicular systems, niosomes are often combined with various carriers, developing so-called hybrid drug delivery platforms. They are most frequently incorporated into *in situ* gel-forming systems and semi-solid forms to achieve prolonged contact time, mucoadhesion, as well as a reduced number of doses or dose reduction. The combination of niosomes with inorganic nanoparticles is also of interest, as they exhibit enhanced antitumor activity and can be successfully used as agents in theranostics. The application of Quality by Design (QbD) principles in the design of niosomes, conducting long-term toxicity studies, and standardized regulatory requirements are essential aspects for the subsequent translation of niosomes into clinical practice, leveraging their advantages and potential.

I believe that the scientific works of Ch. Assist. Prof. Viliana Eduardova Gugleva possess contemporary scientific-applied merits and provide an original contribution in the field relevant to the announced competition for the academic position of "Associate Professor" in the specialty of "Technology of Dosage Forms and Biopharmacy."

CONCLUSION

Based on the materials provided to me for the competition, as well as my personal impressions of Ch. Assist. Prof. Viliana Eduardova Gugleva, I am convinced that she fully meets the requirements of the Development of Academic Staff in the Republic of Bulgaria Act, the regulation for implementation of this Act, and the Regulations on Academic Staff Development at Medical University Prof. Dr. Paraskev Stoyanov – Varna, along with the established criteria for occupying the academic position of "Associate Professor."

Considering the above, I confidently give my positive assessment and recommend that the members of the scientific jury vote positively for the appointment of Ch. Assist. Prof. Viliana Eduardova Gugleva, Ph.D. to the academic position of "Associate Professor" in the area 7. "Healthcare and Sport," professional field 7.3. Pharmacy.

07.10.2024
Varna

Prepared by: .....
(Assoc. Prof. Velichka Andonova, PhD)