

**To Assoc. Prof. Lyuben Zagorchev, DSc,
Chairman of the Scientific Jury,
determined by Order № RD 38-543/18.09.2023
of Prof. Anastas Gerdjikov, DSc
Rector of the Sofia University
„St. Kliment Ohridski”**

STANDPOINT

on the procedure for obtaining the academic position "Associate Professor" in professional Direction 4.3 Biological Sciences (Virology – Molecular Virology), announced in the Bulgarian State Gazette No 65 from 28.07.2023 for the needs of the Sofia University "St. Kliment Ohridski", Faculty of Biology

This standpoint was prepared by Prof. Neli Stoyanova Korsun, MD, DSc,
a member of the scientific jury

Specialty: Virology

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<p>The standpoint was compiled following the requirements of the Law on the development of the academic staff in the Republic of Bulgaria (LDASRB) and Section III / Section IV of the Rules of LDASRB - Terms and Conditions for Obtaining the Academic Position "Associate Professor"</p>

I declare that I have no joint publications or participation in scientific forums and projects with the candidate.

I. Description of the presented materials

I received all the materials for the competition by e-mail. The candidate Assistant Professor Kalina Shishkova has submitted a curriculum vitae, a diploma for higher education, a diploma for the educational and scientific degree "doctor", a document for the academic position "Assistant Professor", a list of publications, participation in conferences and projects, a sample reference for the fulfillment of the minimum national requirements for the relevant scientific field and the additional requirements of SU "St. Kliment Ohridski" with the necessary proofs attached, reference to the citations, reference to the original scientific contributions with the relevant proofs attached, scientific works submitted for participation in the competition, summaries of the publications, copy of the announcement in the "State Gazette", reference to academic employment, for scientific guidance of graduates, etc.

II. General characteristics of the activity

Scientific production and publication activity

For participation in the current competition Assist. Prof. Kalina Shishkova presents a total of 21 full-text publications in scientific publications, referenced and indexed in world-famous databases with scientific information (Scopus and Web of Science), 4 publications in journals without IF or SJR-factor and 5 scientific articles published in full text in proceedings of international and national scientific forums. A total of four publications are in Q1 issues, six in Q2 issues, six in Q3 issues, and five in Q4 issues. Among the publications presented, 18 are in journals with an impact factor with a total impact factor of 32,885. In the listed publications Assist. Prof. K. Shishkova is the first author in 4 (13%). The publications submitted for the competition do not repeat those submitted for the acquisition of the educational and scientific degree "doctor". She has participated in 31 international scientific forums, of which 8 are held abroad, and in 14 national scientific forums.

The candidate presents a total of 137 citations. Of these, 102 citations are in publications referenced and indexed in world-renowned scientific information databases (Scopus and Web of Science). The H-index of Assist. Prof. K. Shishkova in Scopus is 6. The citations in the world databases show the significance of the scientific topics developed by the candidate and the recognition of the international academic community. Assist. Prof. K. Shishkova has participated in 20 research projects financed by SU "St. Kl. Ohridski" and the Ministry of Education.

III. Compliance of the applicant with the minimum national requirements contained in the Regulations for the implementation of the LDASRB - Section III. Conditions and procedure for occupying the academic position "Associate Professor" (amended and supplemented, SG No. 15 of 19.02.2019; Field 4. Natural sciences, mathematics, and informatics; Professional direction 4.3. Biological sciences) and in the Regulations for the conditions and the procedure for obtaining scientific degrees and for holding academic positions at the SU "St. Kliment Ohridski"

Table 1. Number of points by indicators

A group of metrics	Indicators	Number of points according to Regulations for the implementation of the LDASRB	Number of points based on the evidence presented
A	1. Dissertation work for the educational and scientific degree "Doctor"	50	50
B	4. Habilitation work - scientific publications in journals that are referenced and indexed in world-famous databases with scientific information (Web of Science and Scopus)	25 for publ. in Q1 20 for publ. in Q2 15 for publ. in Q3 12 for publ. in Q4 10 for publ. in edition with SJR without IF	50 (2 x 25) 20 (1 x 20) 30 (2 x 15) Total: 100
Г	7. Scientific publication in journals that are referenced and indexed in world-renowned databases of scientific information (Web of Science and Scopus), outside the habilitation work	25 for publ. in Q1 20 for publ. in Q2 15 for publ. in Q3 12 for publ. in Q4 10 for publ. in edition with SJR without IF	50 (2 x 25) 100 (5 x 20) 60 (4 x 15) 48 (4 x 12) Total: 258
Д	11. Citations in scientific publications, monographs, collective volumes, and patents, referenced and indexed in world-renowned databases of scientific information (Web of Science and Scopus)	2	60 (30 x 2) Total: 60
	Total points		468

Table 2. Minimum required points by groups of indicators for occupying the academic position "Associate Professor" and number of points based on presented evidence

A group of metrics	Content	Minimum points required according to Regulations for the implementation of the LDASRB	Number of points based on the evidence presented
A	Indicator 1	50	50
B	Indicators 3 or 4	100	100
Г	A sum of indicators from 5 to 10	200	258
Д	A sum of points in indicator 11	50	60
E	A sum of the indicators from 12 to the end	-	-
	Total points	400	468

It is clear from the tables above that the evidence for the separate groups of requirements from the two Regulations significantly exceeds the required number of points.

Main directions in scientific activity

The scientific production of Assist. Prof. Kalina Shishkova is focused on researching the antiviral activity of many natural products and synthetic compounds, various aspects of medical virology, and also researching the antiherpes effect of physical factors. The scientific contributions of the candidate are presented in detail in the academic report. Of these, I will highlight contributions of an original and scientific-applied nature, divided into 4 directions:

Scientific contributions of Assist. Prof. Kalina Shishkova:

Screening of natural products for antiviral activity

1. An inhibitory and inactivating effects of the methanolic and aqueous extracts of plants from the *Lamiaceae* family - *Lamium album L.* and *Leonorus cardiaca L.* are established against herpes simplex virus strains 1 and 2, as well as against the acyclovir-resistant strain DD of HSV-2.
2. Antiviral activity of extracts obtained from the Bulgarian medicinal plants is established - Common dogwood (*Teucrium chamaedrys L.*), Catnip (*Nepeta nuda L.*), Mountain wormwood (*Artemisia chamaemelifolia Vill.*), and *Astragalus glycyphyllos L.* The results of research on the antiviral activity of Bulgarian medicinal plants from the last three decades are summarized. The effect of various extracts obtained from in vitro propagated plants is investigated. Phytochemical composition and its influence on specific stages of the virus life cycle are discussed in a review article. The review includes the following families: *Amaryllidaceae*, *Fabaceae*, *Geraniaceae*, *Lamiaceae*, *Onagraceae*, *Ranunculaceae*, *Rosaceae*, *Crophulariaceae*, and *Rhodophyta*.
3. For the first time, the antiviral effects of hemocyanins isolated from the Black Sea rapine (*Rapana hemocyanin*) and representatives of the genus Mollusca, Eriphia verrucose (hEv), mucus from *Helix aspersa* (Ha) and structural subunit α -HaH of hemocyanin from *H. aspersa* (sHa) versus BHC-1 replication are established.
4. The antiherpetic activity of secondary metabolites isolated from Lactic Acid Bacteria isolated from fermented products is investigated. For two of the five strains tested - *Lactobacillus delbrueckii* subsp. *Bulgaricus* KZM 2-11-3 and *Lactiplantibacillus plantarum* KC 5-12 are found to have strong activity against HHV-2 with a selectivity index (SI) above 45.

Investigation of new synthetic compounds for the presence of anti-herpes effect

1. The biological (antioxidant and antiviral) activity of new thiazole hydroxycinnamic acid amides containing TFA, an ethyl ester of valine-4-carboxylic acid is investigated. The

newly synthesized compounds are tested against the *in vitro* replication of influenza virus A (H3N2) and human herpesvirus 1 and 2.

2. New esters of acyclovir with peptidomimetics are synthesized and their antiviral activity on the replication of herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) is evaluated *in vitro*.
3. Esters of the antiherpes drugs ganciclovir and penciclovir with bile acids (cholic, chenodeoxycholic, and deoxycholic) and amino acid esters of acyclovir are synthesized. Their *in vitro* antiviral activity against herpes simplex viruses type 1 and type 2 (HSV-1, HSV-2) is determined. The analyses showed that the modified analogs of ACV and PCV are less active than the generic agents against HSV-1 and HSV-2.
4. A human coronavirus 229E (HCoV-229E) study is conducted to evaluate the *in vitro* efficacy of some analogs of the ion channel inhibitors amantadine and rimantadine. Derivative substance A4 shows higher antiviral activity compared to Amantadine. The molecular structures of the newly synthesized compounds are investigated using single-crystal X-ray analysis. Molecular docking studies show that two of the investigated compounds 2A and 4A have promising binding affinity.

Medical virology

1. The studies of the Torque Teno viruses, which were started during the development of the dissertation work, have been continued. The presence of these viruses has been demonstrated in samples from blood donors, patients with registered viral hepatitis, primary brain tumors, respiratory diseases, transplanted kidneys, and patients with unknown etiology. The phylogenetic analysis of Torque Teno viruses shows that most Bulgarian sequences are genetically related, highly correlated, and fall into one cluster. They most likely have a common ancestor.
2. In a study of patients with periodontitis, a connection between the bacteria causing the disease and high-risk human papillomaviruses (HPV) is established. The most common HPV genotype that gives a positive result for bacteria associated with the development of periodontitis is HPV58.

Investigating the impact of physical factors on the replication and extracellular virions of HSV-1

The antiviral and virucidal effects of surface-wave gas-discharge plasma-treated nutrient medium and distilled water are investigated. When studying the virucidal effect of a plasma-treated virus suspension diluted 1:2 with sterile water, which was treated for 300 s at a wave power of 13 W, a decrease in the titer of the virus sample is observed by 1.67 log₁₀ compared to the control.

Teaching activity

Assist. Prof. K. Shishkova has been a teacher at the Faculty of Biology of the "St. Kl. Ohridski" from 2002 to the present moment. She gives lectures to students for the acquisition of Bachelor's

and Master's degrees. She conducts practical exercises and educational practices, she is the academic supervisor of 7 graduates for the acquisition of the Master's degree and 2 graduates for the Bachelor's degree. She is the co-author of the Practical Guide to Virology.

CONCLUSION

The materials presented by Assist. Prof. Kalina Shishkova for this competition significantly exceed the requirements for holding the academic position "Associate Professor", contained in the Regulations for the Implementation of the ZRASRB and "Regulations on the terms and conditions for obtaining scientific degrees and holding academic positions at Sofia University "St. Kliment Ohridski". The scientific achievements, professional competence, and significant teaching activity of Assist. Prof. Kalina Shishkova gives me a reason to strongly support her candidacy and to recommend the respected scientific jury to award Assist. Prof. Kalina Shishkova, the academic position " Associate Professor" in the field of higher education 4. Natural sciences, mathematics, informatics; professional direction 4.3. Biological Sciences (Virology).

06 November 2023 г.

Member of the scientific jury:

/Prof. Neli Korsun, MD, DSc/