

by Prof. Rayko Dimitrov Peshev, Ph.D., D. of Science, Dept. "Epizootology and Infectious Diseases of Animals" in NDNIVMI, Sofia, according to the competition announced in State Gazette no. 60, dated 29.07.2022, to occupy an academic position "Docent" for the needs of the Institute of Microbiology of the Bulgarian Academy of Sciences, Sofia, Department of "Virusology", Laboratory "DNA viruses and oncolytic viruses", Professional direction 4.3 Biological sciences.

In connection with the competition announced by the Institute of Microbiology of the Bulgarian Academy of Sciences, Sofia for the needs of the Department of "Virusology", Laboratory "DNA Viruses and Oncolytic Viruses", Professional Direction 4.3 Biological Sciences, for the occupation of the academic position "Associate Professor", the documents were submitted by the only candidate, Assistant Professor Neli Milenova Vilhelmova-Ilieva, Ph.D. The documents required for the competition have been submitted, namely: curriculum vitae, diploma for ESD doctor, abstract of dissertation for ESD doctor, list and copies of publications according to indicators B and D from the table with minimum national requirements, list of the candidate's participation in scientific conferences, list of the citations, the candidate's participation in research projects, a certificate of fulfillment of the minimum national requirements according to the Law for development of scientific staff, a certificate of fulfillment of the additional requirements of the Institute of Microbiology of the BAS, a declaration of originality and credibility of the presented results in the scientific works.

Scientific publication activity

The dissertation work of Dr. Neli Vilhelmova is on the topic: Combined effect of ellagitannins and acyclovir on the replication of herpes simplex viruses and was defended in 2012. In the abstract, 3 titles of learned messages are presented, which have already been reviewed and used in the acquisition of the general educational and scientific degree "doctor".

In connection with the announced competition, 12 publications were presented, which were printed in journals with an impact factor and with reviewers. The results are distributed in the following directions: The anti-herpesvirus activity of tannins (ellagitannins and halotannins) was determined against sensitive and resistant to acyclovir - HSV-1 and HSV-2 strains (article no. 1). The ellagitannin(s)-ACV combination administered against ACV-resistant HSV-1 gave a much stronger synergistic effect compared to the effect observed against ACV-resistant HSV-2. Examination of the effects of the ellagitannin(s)-ACV combination on intact cell monolayers did not show any toxicity resulting from an interaction between the two substances. The results obtained from the study indicate the good polyphenolic potential of these plants as antiherpetic agents.

An extract of Canadian propolis was investigated for its effects on the replication and viability of extracellular HSV-1 virions (Article No 2). It was found to have a strong virucidal effect against HSV-1 and HSV-2 strains and to interfere with the adsorption of viruses.

Scientific Communication No. 3 reported data from the creation of two new photoactive dendrimers, which were compared with two monomeric naphthalimides, and it was found that dendrimers 3 and 4 in solutions completely inhibited the growth of Gram-positive bacteria after light treatment, while in Gram-negative bacteria, this effect is achieved only with dendrimer 4. Compounds 1-4 after application to cotton fabric and after photoactivation completely inactivate the growth of Gram-positive bacteria, and these

compounds can be used as agents for antibacterial photodynamics and therapy in the production of antibacterial textile. It has been found that substance 4 can act in at least two ways in the production of viruses, and substances with a similar structure can be developed as inhibitors of herpes infection.

The anti-herpesviral activity of rose essential oils and samples from their production was investigated in relation to HSV-1 replication and extracellular virion viability (article No. 4). Their influence on the stage of adsorption of the virus to the host cell and the protective effect they exert on healthy cells have been established. They have been shown to work synergistically when administered with ACV.

Scientific Communication No. 5 reports data from an in vitro study of the antineoplastic and antiviral potential and in vivo toxicity of twelve extracts of different polarity obtained from the herbaceous perennial plant *Geum urbanum* L. It was found that the ethyl acetate extract of aerial parts (EtOAc- AP) of the plant showed the strongest antineoplastic activity on bladder cancer cell lines by inducing apoptosis.

Post metabolites from different lactic acid bacterial strains used in the production of different dairy products were determined to have antiviral activity (Article No. 6). Their influence on the replicative cycle and viability of extracellular virions of fish (KHV) and human (HSV-1) herpes viruses was compared, and their influence on the stage of virus attachment to susceptible cells and the protective effect of post-metabolites on healthy cells before the herpes virus infection occurs were determined.

Article No. 7 reflects an in vitro study of the biological potential of the waste water obtained after the distillation of four Bulgarian oil-bearing roses. The antioxidant effect of wastewater and a weak antiproliferative effect against *Staphylococcus aureus* were established. None of the effluents had activity against Gram-negative bacteria or a bactericidal or antifungal effect. The authors conclude that the four types of Bulgarian oil roses and their wastewater have promising antioxidant and antiherpesviral effects.

Paper No. 8 reported data on the antibacterial potential of *G. glabra* and *H. perforatum* extracts on various bacteria and found them to be more effective against Gram-positive bacteria than Gram-negative bacteria. Almost all tested extracts inhibited the extracellular virions of the enveloped viruses tested (HSV-1 and HCov-OC-43) to a greater extent than the non-enveloped viruses (PV-1 and HAdV-5). They inhibit the viral adsorption step (HSV-1) in the host cell (MDBK) and show a protective effect on healthy cells (MDBK) before being subjected to HSV-1 viral invasion.

The data from chelate complexes of acyclovir with various metals are reflected in scientific communication No. 9. The cytotoxicity of the complexes was established, and the most effective in suppressing HSV-1 and HSV-2 was the zinc chelate complex with ACV.

In article No. 10, changes in oxidative stress parameters are determined in MDBK cells infected with herpes simplex virus-1. A significant increase (more than 3-fold) in lipid peroxidation was found in MDBK cells infected with herpes virus compared to control cells. As a result of viral invasion, a reduced level of intracellular total glutathione was found in the infected cells by 24% and a threefold increase in the activity of the investigated antioxidant enzymes.

According to Scientific paper No. 11, rose essential oils and extracts have therapeutic properties - such as respiratory antiseptics, anti-inflammatory agents, mucolytics, expectorants, decongestants, and antioxidants - that can act as symptomatic prophylactics and medications and thus alleviate patients' conditions. during severe illnesses.

Scientific Communication No. 12 reported data from studies of the anti-herpes virus 1 activity of specially selected groups of tannins and found that different series of ellagitannins showed significantly stronger activity against HSV-1 replication than that of gallotannin.

Fulfillment of minimum national requirements

According to the report on the minimum national requirements, according to indicator A - 1, the candidate has 50 points, according to indicator B - 2 articles in Q 1 - 100 points, according to indicator D - sum of indicators from 5 to 10 of articles in Q 1 has 100 points, articles in Q 2 there are 60 points, articles in Q 3 there are 30 points, articles in Q 4 there are 36 points or all – 226 points. According to the minimum requirements for this indicator, Vilhelmova must have 200 points, and she exceeds this number. Four chapters from published books representing 60 points are presented. 30 quotes are presented, which carry 60 points. Or, in total, these indicators bring 396 points.

Fulfillment of the additional requirements of the Institute of Microbiology

According to the Institute of Microbiology supplementary criteria - 21 scientific communications are presented in journals with an impact factor, SGR, chapters of monographs - 1, in proceedings of international forums, published in full text - 2, or a total of 24 scientific communications. 120 citations are presented with an impact factor of 36,295 from the cited publications and 46,154 for the entire scientific career. Her H index is 6. The candidate participated in 4 scientific research projects financed by a scientific research fund. She participated in the execution of two contracts with Bulgarian companies and 2 contracts with foreign companies. There are 7 reviews written in scientific journals, referenced and indexed in WoS/Scopus and 3 issues in other international and academic publications, for which there is written evidence. He has lectured in microbiology, parasitology and virology at the Southwestern University, Blagoevgrad, certified by an official note for the 25 lectures and 5 exercises held. She participated in 32 scientific forums, as an author and co-author of scientific communications and presentations

Conclusion

The scientific - research and applied achievements presented to me by the assistant professor Dr. Neli Milenova Vilhelmova-Ilieva, and the results achieved in the field of virology give me reason to conclude that she meets the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the Regulations for its Application at the Institute of Microbiology of the BAS. The scientific metrics and indicators are high and meet the requirements for acquiring the academic position "Associate Professor". This allows me to recommend to the members of the Scientific Jury and to the members of the Scientific Council of the Institute of Microbiology of the Bulgarian Academy of Sciences, Sofia, to vote positively for awarding the academic position of "Docent" to the head assistant. Dr. Neli Milenova Vilhelmova - Ilieva in professional direction 4.3 Biological Sciences.

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Sofia

Wrote the opinion:
(prof. Rayko Peshev, PhD)

На основание
чл. 2 от ЗЗЛД