

## OPINION

regarding the acquisition of the academic position of "professor", in the field of higher education 4. Natural Sciences, professional field 4.3. Biological Sciences, scientific specialty "Biochemistry" - for the needs of the Section "Pathology" at IEMPAM- BAS

**Candidate:** Assoc. Prof. Ivan Angelov Iliev

**The opinion was prepared by:** Prof. Dr. Lyudmila Kabaivanova

The candidate Ivan Angelov Iliev graduated as a master with a degree in "Biochemistry" in 2005 at Sofia University "St. Kliment Ohridski", Faculty of Biology. In 2012, he successfully defended and acquired the ESD "doctor" with a dissertation on the topic "Research on the biological properties of natural and newly synthesized substances through *in vivo* and *in vitro* experiments" at IEMPAM-BAS. At the same Institute in 2018 - he won a competition for the Academic position of "associate professor" in the "Pathology" Section.

The upward career growth of Assoc. Prof. Iliev is the result of in-depth and active research activities in important scientific fields - cell biology, biochemistry and biophysics.

The topics he develops are also undeniably relevant, namely determining the biological activity of newly synthesized substances and natural products, studying their cytotoxicity, phototoxicity and antiproliferative activity in *in vitro* models and *in vivo* conditions for the purpose of safe and effective use in pharmacy and biomedicine.

The variety of methods applied in his scientific work is formed by cytological, biochemical, histological and microscopic methods.

The scientific activity of Assoc. Prof. Iliev can be highly assessed, based on his high scientometric indicators. He is an author/co-author in 119 publications for his scientific experience, which have been cited 415 times (h-index: 13). 257 citations were noted in the competition. He participated in the competition with 33 scientific publications. The results of the experimental work have been presented at 88 significant scientific forums. The candidate is an executor in 13 scientific research projects. He has one successfully defended doctoral student and seven graduate students.

In this competition, Ivan Iliev's publications are distributed as follows: by indicator A - Abstract for obtaining the educational and scientific degree "Doctor" - 1 pc. or 50 points; in List B there are 10 scientific publications (6xQ1; 1xQ2 and 3xQ3) or 215 points, and in List D - 23 scientific publications (9xQ1, 6xQ2, 5xQ3 and 3xQ4) or 481 points. A registered utility model is also included - 1 pc.

According to the submitted report on the fulfillment of the minimum requirements for the academic position of "professor" based on the Regulations for the Implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Bulgarian Academy of Sciences, it can be seen that the candidate fully meets all the requirements - he has submitted materials corresponding to 1450 points out of the required 640.

I cannot fail to note some important contributions reflected in the published scientific works of Assoc. Prof. Iliev:

1. For the first time in Bulgaria, the *in vitro* method for testing the safety of new chemical substances, the BALB 3T3 Neutral Red Uptake test, has been introduced and adapted to the LED - solar simulator Helios - iO, which will allow new compounds to be tested with the aim of preserving health and improving the quality of life of people.
2. 17 peptide analogues of BIM-23052 have been synthesized, which can specifically bind to the somatostatin receptor and modulate its activity, thus affecting the proliferation of certain types of tumor cells. These analogues with various chemical modifications lead to stability of the molecule in a biological environment, reduced toxicity and increased antiproliferative activity.
3. The biological activity of (KLAKLAK)<sub>2</sub>-NH<sub>2</sub> peptide analogues was studied and antimicrobial and antitumor activity was established, with the component responsible for the high biological activity and selectivity being the amino acid  $\beta$ -Ala in the structure of these peptides.
4. 7 FELL peptide analogues were studied and it was found that D-Phe at the first position in the molecule, combined with the two Leu residues at the third and fourth positions, are the best combination in terms of analgesic activity.

5. Substitution of lysine at positions 7 and 8 leads to better anticancer activity of 7 peptide analogues of Aurein 1.2, with the photosafety test showing reduced toxicity in some of the analogues studied and a complete lack of phototoxic effect.
6. Antitumor activity was established upon synthesis of 4 Temporin A peptide analogues modified at position 1 with Tyr or fluorinated Phe. Modifications performed at position 10 lead to the preparation of a compound with low cyto- and phototoxicity and very good antiproliferative activity against luminal type A breast cancer (MCF-7).
7. Novel pyrrole-based carbohydrazide (1) and hydrazones (1A–D) were synthesized, which showed a high selectivity index and very high antiproliferative activity, based on the ability to induce apoptosis and cause cell cycle arrest in S phase.
8. The biological activity of the natural product myosmin was studied and induction of a significant dose-dependent decrease in the viability and proliferative activity of erythroleukemic and hepatocellular carcinoma cells was found.
9. The main non-volatile compounds obtained from extracts of *Tanacetum vulgare* L. flowers have been studied, and a high antitumor effect on the MCF-7 cell line has been established.
10. The antioxidant and antitumor potential of the polyphenolic fraction of grape marc obtained from the vinification of a local Bulgarian grape variety Mavrud has been reported, and the sensitivity of the MCF-7 cell line to the studied extracts has been established.
11. The *in vitro* study of new combinations between the European mistletoe extract Iscador Qu and standard chemotherapeutic agents suggests the establishment of promising therapeutic protocols for breast cancer compared to traditional monotherapies.
12. The *in vitro* study of the antiproliferative activity of mono- and di-rhamnolipids (RL-1 and RL-2) in breast cancer (MCF-7 and MDA-MB-231), as well as the combination of rhamnolipids with Cisplatin, showed that both tested cancer lines showed sensitivity to treatment with RL and only in the triple negative cell line MDA-MB-231 was a synergistic effect of the combined treatment observed.
13. Nine hemocyanins and their subunits were studied for toxicity, antiproliferative and antitumor effects, under *in vitro* and *in vivo* conditions on 5 tumor cell lines, with

cytomorphological analysis revealing that the observed antitumor effects were associated with induction of apoptosis in tumor cells.

14. Biocompatible and biodegradable coatings have been designed for biofunctionalization of medical devices, allowing regulation of cell adhesion across the entire range between completely prevented and strongly stimulated cell adhesion, without systemic cytotoxicity.

Assoc. Prof. Ivan Iliev has undoubtedly proven himself as an established scientist and specialist. The modern concept of in-depth research of biologically active substances of importance for pharmacy and biomedicine, together with newly synthesized ones, as well as the combined effects of already well-studied compounds, under in vitro and in vivo conditions are carried out with the hope that their biological and medical applications will be widely used in the next decade with the most important common goal - improving the quality of life of people.

## CONCLUSION

Based on my familiarization with the submitted documents, scientometric data and works, with their undeniable significance, the scientific and applied contributions contained therein, as well as the active scientific research of the candidate, I find it reasonable to state that my opinion regarding the acquisition of the Academic position "Professor" in Professional Field 4.3. Biological Sciences, scientific specialty "Biochemistry" is positive.

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Sofia

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