

PROFESIONAL OPINION

by Prof. Dr. **George Angelov Miloshev**,

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member of a Scientific jury for holding the academic position "Associate professor", according to a concourse announced by the Institute of Engineering Chemistry – BAS

1. Presentation of the candidate for participation in the concourse, the scientific specialty and the department for whose needs the concourse is announced.

The concourse is for the occupation of the academic position "Associate professor" in the field of higher education 4. Natural sciences, mathematics and informatics, professional direction 4.2. Chemical Sciences (Processes and Apparatus in Chemical and Biochemical Technology), announced in SG No. 65 of 28.07.2023. The concourse has been announced for the needs of the laboratory "Transfer processes in multiphase media" at the Institute of Engineering Chemistry - BAS.

The only candidate for the position is **Diana Ivanova Ivanova**, Assistant professor

2. The basis for writing this opinion is my participation in the scientific jury for the concourse, determined by order RD No. 15-467 of 25.09.2023 of the Director of the Institute of Engineering Chemistry.

3. Personal characteristics of the candidate.

Diana Ivanova Ivanova holds a Master's degree in "Chemistry" at the Faculty of Chemistry of the SU "KI. Ohridski" since 1988. She defended her dissertation on the topic "Design, synthesis and antitumor *in vitro* action of new retinoids and other physiologically active substances" and obtained the educational and scientific degree "Doctor" in the scientific specialty Code 010510 "Bioorganic chemistry, chemistry of natural and physiologically active substances" (Diploma No. 34828 of 17.01.2011).

Since 1988, Diana Ivanova has worked as a chemist and assistant successively at the Institute of Organic Chemistry - BAS, "Chemsab-Orbel" OOD, Sofia, and since 2021 she is the Ass. Prof. at the Institute of Engineering Chemistry - BAS.

Ass. Prof. Diana Ivanova has gained extensive experience as a scientist in the field of chemistry of biologically active substances and extracts. The repertoire of techniques and skills she has acquired over the years of her work in various scientific groups include techniques of organic synthesis of retinoids, cultivation of cell lines, the basic techniques of molecular and cellular biology.

3. General (quantitative and qualitative) evaluation of scientific research and research activity (based on the submitted documents).

The applicant meets the minimum national requirements under Art. 53, 54, 56 of the Regulations for the implementation of ZRASRB in scientific area 4 "Natural sciences, mathematics and informatics", Professional direction 4.2. Chemical Sciences, and the additional requirements defined in the Regulations for the development of the academic staff at the Institute of Engineering Chemistry.

- academic internship as "Assistant professor" at ICE: 2 years and 8 months;

- published scientific publications (outside the publications for the doctoral degree): 18 nos.; total number of publications: 22

The scientific production of the candidate is completely sufficient in volume and relevant in content to the announced competition.

4. Contributions from the scientific work of Ass. Prof. Dr. Diana Ivanova can be systematized as follows:

• Scientific and applied contributions:

The main scientific works presented for the concourse are devoted to the preparation of biologically active plant extracts. In particular, conditions for optimal extraction of antiproliferative substances from natural raw materials have been developed and supplemented.

First of all, a comparative analysis of the antiproliferative activity of extracts from multiple representatives of the foreign origin of the Juniper genus (*Juniperus* L., Cupressaceae) was made. The highest activity of the extracts of the species: *J. virginiana*, *J. sabina*, *J. chinensis*, *J. horizontalis*, the hybrid *J. × media*, incl. cultivars of *J. virginiana* ('Cinerascens', 'Glauca'), of *J. scopulorum*. In addition, a high antiproliferative activity was found for the leaf extract of the endemic representative *Juniperus sabina* var. *balkanensis* R. P. Adams & A. N. Tashev, distributed in the Balkan Peninsula and some regions in Italy.

Original results were obtained for a high antiproliferative/antitumour activity of the extracts of the mentioned species and it was shown that it is due to multiple substances (matairesinol, anhydropodorisol) which together with the previously identified lignans podophyllotoxin (PPT), deoxypodophyllotoxin, yatein and β -peltatin, show a combined action contributing to the high activity of the respective extracts.

The relevance and significance of the action of the studied extracts can be proved by the fact that they have proven their antitumour activity on more than 5 cancer cell lines, including NB-4, K-562, BV-173 and others. This unequivocally confirms the broad spectrum of activity of the respective extracts.

In second place (but not in importance) are the results that Ass. Prof. Diana Ivanova, in collaboration with her colleagues, received regarding the study of ecological conditions for the optimal production of the most active extracts from juniper leaves. Such are the experiments with species secreting an optimized content of the antitumor substance podophyllotoxin (PPT). As a result, Bulgarian and foreign juniper species with a high content of podophyllotoxin were successfully identified, which would have a potential application in pharmacy as an alternative natural source for the extraction of precursors for the industrial synthesis of antitumor substances.

• Scientific contributions:

Study of the mechanism of action of synthesized analogues of natural substances with optimized bioactivity.

In a series of experiments, the candidate has investigated the antiproliferative activity of synthesized analogs of retinoic acid (ATRA). Interest in retinoic acid is not accidental. It is justified because ATRA is a therapeutic agent with high activity in the treatment of a number of diseases, including some types of leukemia, psoriasis, etc. Retinoic acid is a ligand that binds to and activates the nuclear retinoid receptors RAR and RXR. The mechanism of antiproliferative activity of silicon analogs of polyaromatic retinoids (arotinoids) such as SR11237 and the antitumor substance Bexarotene (Targretin®) was investigated. As a result, increased activation of nuclear retinoid receptors (retinoid-X-receptors, RXR) was found with the silicon derivative of SR11237 compared to the parent carbon analog. It is becoming clear that the investigated retinoic acid analogs are effective activators of the nuclear retinoid

receptors (RXR) and represent potential model compounds for the design of new antitumor drugs.

6. Citation of the candidate in publications of other authors.

The candidate meets the minimum national requirements under Art. 53, 54, 56 of the Regulations for the implementation of ZRASRB in scientific area 4 "Natural sciences, mathematics and informatics", Professional direction 4.2. Chemical Sciences and the additional requirements defined in the Regulations for the development of the academic staff at the Institute of Engineering Chemistry.

7. Admitted weaknesses, critical remarks, recommendations.

I have no significant critical comments and recommendations for the candidate.

8. Summary evaluation - conclusion and opinion.

In conclusion, as a member of the scientific jury, determined by order of the Director of the Institute of Engineering Chemistry - BAS (No. 15-467/25.09.2023), I express the opinion that the candidate Ass. Prof. Diana Ivanova Ivanova, PhD, participating in a concourse for the academic position "Associate professor", announced in the Official Gazette, no. 65 of 28.07.2023 **meets the mandatory and specific conditions** and scientometric criteria for the academic position "Associate professor".

Signature:



19.11.2023

(Prof. Dr. G. Miloshev)