

R E V I E W

Referring to the competition for **ASSOCIATE PROFESSOR** in professional field 4.2.
Chemical Sciences (Processes and Apparatus in Chemical and Biochemical Technology)

announced in DV No. 65 from 28.07.2023, page 49

with candidate **Diana Ivanova Ivanova, Ph.D., Assistant Professor at the Institute of Chemical Engineering – Bulgarian Academy of Sciences (IChE–BAS)**

Reviewer: Konstantza Atanassova Tonova, Ph.D., Associate Professor at IChE–BAS

1. Biographical data about the candidate. Scientific interests. Participation in projects

Diana Ivanova Ivanova graduated from the Faculty of Chemistry at the Sofia University “St. Kliment Ohridski” in 1988. She worked in three institutes of the BAS, IOCCF (1988-2002), IBEI (2012-2015) and IChE, from 2016 to now, where from 01.2021 she holds the position of “assistant professor”. She was a doctoral student at the IOCCF, successively in full-time and part-time form during the period 1992–1997. In 2010, she obtained a Doctoral degree in “Bioorganic Chemistry, Chemistry of Natural and Physiologically Active Substances”, after defending a dissertation on the topic “Design, synthesis and in vitro antitumor activity of new retinoids and other physiologically active substances”. The Ph.D. study was developed under the European project “Anticancer retinoids” QLK3-CT2002-02029 and other programs. A good impression on me is made by the long-term specializations and scholarships under international agreements, of which Assistant Professor Ivanova was a beneficiary in France (2002–2007), Spain (2003–2004) and Russia (1989–1993). In this regard, the candidate continues to create and work in international cooperation, as evidenced by the recently completed “Erasmus+” Program Agreement between BAS and the Medical University of Lublin, Poland, as well as the ongoing project to access the plant species collection of Harvard University in Boston, USA.

The biographical data outlined in this way also trace the path along which the candidate's scientific interests in the field of natural substances with medical application in oncology were formed and developed. They received their most recent development as a result of the work under contract DN 07/25 with the Bulgarian Science Fund on the topic “Complex analysis of antitumor metabolites of unstudied species from the Bulgarian flora and certified foreign hybrids of the genus *Juniperus L.* (Cupressaceae) through modern research technologies”. As it will become clear later, Assistant Professor Ivanova has a leading role in

the publications of this project and they represent a significant part of the asset in support of her habilitation.

2. Science indicators about the publications presented

2.1. Implementation of the science indicators acc. to the Regulations on the terms and conditions for the acquisition of scientific degrees and for the occupation of academic positions at the Bulgarian Academy of Sciences

Science indicators for the articles presented in the competition are summarized and grouped into the three required categories, as follows Table 1. Associate Professor – Group B, index 4, Table 2. Associate Professor – Group G, index 7 and Table 3. Ph.D. – Group G, index 7.

Table 1. Associate professor – Group B, index 4.

Publications acc. to the order in the List of Scientific Contributions of the candidate.

no	Publication	Number of authors	A place in the order of authors	Q, acc. to year of publ. and database	Number of points
1.	<i>Molecules, 2021</i>	10	1* [#]	Q1 (SJR)	25
2.	<i>Plants, 2023</i>	9	1* [#]	Q1 (SJR)	25
3.	<i>Organometallics, 2005</i>	10	8	Q1 (SJR)	25
4.	<i>ChemMedChem, 2009</i>	12	5	Q1 (SJR)	25

* – corresponding author of the publication;

– leading contribution in the research and publication.

Associate professor – Group B, index 4

Total: 100 points

Minimum threshold: 100 points

Table 2. Associate professor – Group G, indicator 7.

Publications acc. to the order in the List of Scientific Contributions of the candidate.

no	Publication	Number of authors	A place in the order of authors	Q, acc. to year of publ. and database	Number of points
5.	<i>Tetrahedron, 1996</i>	3	1*	Q1 (SJR)	25
6.	<i>Tetrahedron Letters, 1999</i>	4	1*	Q1 (SJR)	25
7.	<i>ChemMedChem, 2011</i>	3	1	Q1 (SJR)	25
8.	<i>Arch. Toxicol., 2013</i>	4	1	Q1 (SJR)	25

9.	<i>J. Indian Chem. Soc., 2003</i>	5	1*	Q4 (SJR)	12
10.	<i>Archiv der Pharmazie, 1991</i>	2	2	Q2 (SJR)	20
11.	<i>Breast Cancer Res. Treat., 2019</i>	6	1	Q1 (SJR)	25
12.	<i>Bulg. Chem. Commun., 2018a</i>	12	1*,#	Q4 (SJR, only)	10
13.	<i>Bulg. Chem. Commun., 2018b</i>	6	1*,#	Q4 (SJR, only)	10
14.	<i>Appl. Sci., 2020</i>	8	3 [#]	Q2 (WoS) _	20
15.	<i>Bulg. Chem. Commun., 2020</i>	11	1*,#	Q4 (SJR, only)	10
16.	<i>Curr. Iss. Pharm. Med. Sci., 2023</i>	8	1*	Q3 (WoS)	15
17.	<i>J. Pharm. Res., 2018</i>	3	3*	–	–

* – corresponding author of the publication;

– leading contribution in the research and publication.

Associate professor – Group G , index 7

Total: 222 points

Minimum threshold: 220 points

Table 3. Ph.D. – Group G, index 7.

no	Publication	Number of authors	A place in the order of authors	Q, acc. to year of publ. and database	Number of points
18.	<i>Bioorg. Med. Chem., 2002</i>	5	1	Q1 (SJR)	25
19.	<i>Bioorg. Med. Chem. Lett., 2004</i>	7	1	Q1 (WoS)	25
20.	<i>ChemBioChem, 2007</i>	13	4	Q1 (SJR)	25
21.	<i>Antiviral Therapy, 2008</i>	12	6	Q1 (SJR)	25

Ph.D. – Group G, index 7

Total: 100 points

Minimum threshold: 30 points

It can be seen that the works presented cover and exceed the required minimum thresholds in the categories “Associate Professor – Group G” and “Ph.D. – Group G”, acc. to the Regulations of the BAS. In addition, a check through the world's recognized databases of scientific information shows that the citing articles are as follows, without self-citations: 169,

acc. to Scopus and 172, acc. to Web of Science, which values repeatedly exceed the required minimum of 30 citations in the Regulations of the BAS ("Associate Professor – Group D"). Until now, according to WoS, 132 articles cite works of Assist. Prof. Ivanova outside those included in her Ph.D. dissertation.

2.2. Implementation of the scientific indicators acc. to the Methodology for the promotion of scientists at the Institute of Chemical Engineering/ 23.11.2022

A reference to the fulfillment of the requirements for occupying the academic position "associate professor" at the IChE–BAS is given in Table 4.

Table 4. Associate Professor - Requirements IChE–BAS.

no	Minimum requirements for "Associate Professor" Methodology for the promotion of scientists at IChE–BAS	Minimal requirements IChE–BAS	Assist. Prof. Diana Ivanova, PhD
1.	<i>Number of publications other than those presented for the acquisition of Ph.D.</i>	15	17
2.	<i>Number of publications, of which in refereed journals</i>	20 15	21 21
3.	<i>Number of publications under item 2, which are in scientific journals with IF/SJR</i>	5	20
4.	<i>Number of citations noticed</i>	20	169 (Scopus) no self-citations
5.	<i>Recommended h–index</i>	4	8 (Scopus) self-citations excluded

It can be seen that the specific requirements of IChE–BAS have been met, and the indicators related to the quality of scientific production, such as publications indexed in the world-recognized scientific databases and citations, have been exceeded several times. I especially note *the h–index* of Assist. Prof. Ivanova, who is 8, according to Scopus, excluding all self-citations. At IChE–BAS, 8 is the recommended h–index in a competition for the position of "Professor".

3. Basic scientific and scientific-applied contributions of the candidate

The scientific interest and publications of Assist. Prof. Diana Ivanova are in the field of natural substances with medical application in oncology. The earlier publications on the list constitute a group of studies related to the synthesis, pharmacological characterization and

study of the action mechanism of analogues of the natural substances retinal and retinoic acid (the latter being a therapeutic agent for the treatment of leukemia). Regarding retinoic acid, analogues with reduced toxicity (*Publ. 3, Table 1*) or with increased activity (*Publ. 4, Table 1*) were obtained and studied. They represent potential model compounds for the design of new antitumor drugs. Regarding retinal analogs, new pigments with potential application in biotechnology have been obtained. They can be used as artificial photoreceptors, generating an electrical signal upon light irradiation (*Publ. 5, 6, Table 2*). This group of studies also includes *Publs. 7–10 and 17 of Table 2*. Of the 9 articles cited so far, 6 of them were published in journals of category Q1, and in 6 Assist. Prof. Ivanova is the first and/or corresponding author, which is a certificate for the high scientific level of the studies and for the leading contribution of the candidate in them. One publication from 2019 (*Publ. 11, Table 2*) stands out here, in which the candidate has a major role in elucidating the mechanism of activity of combinations of new classes of cytostatics, namely antimetabolites and aromatase inhibitors. *The contribution of Assist. Prof. Ivanova in the cited publications shows the wide and deep set of knowledge and skills she has accumulated over the years in the field of chemistry of natural substances, methods for optimizing their bioactivity, high-tech concepts for structural characterization and pharmacological testing.*

This expertise naturally leads to the second group of research, the subject of the current competition, in which the fundamental base is upgraded with scientific-applied and engineering research on the extraction of bioactive substances, more specifically on the optimization of extraction conditions for the isolation of substances with antiproliferative and antioxidant activity from medicinal plants. Developments in this area began when Assist. Prof. Ivanova arrived at the IChE–BAS in 2016 and with the launch in the same year of two scientific projects, in which Assist. Prof. Ivanova undoubtedly has a leading role. These scientific projects are dedicated to the study of bioactive metabolites from unstudied species and hybrids, mainly from the genus *Juniperus* L., but also from the genus *Rhodiola*, as well as the chemical engineering study of the extraction conditions for obtaining plant extracts with high bioactivity and optimized content of bioactive substances. This group of studies covers 7 of publications (*1, 2, Table 1; 12–16, Table 2*). The scientific and scientific-applied contributions here refer more specifically to:

- Investigation of the optimal conditions for the extraction of the active substance podophyllotoxin from Juniper leaves by different extraction methods, classic solid-liquid extraction, high-pressure extraction conducted in a conventional extractor or in supercritical fluid conditions. The study reveals the advantage of accelerated extraction at

moderately high pressure as a technique applicable on an industrial scale for the preparation of the particular concentrated extract (*Publ. 1, 2, Table 1; Publ. 12, Table 2*).

- In addition to the antiproliferative activity, the antioxidant properties of extracts from multiple plant species from the genera *Juniperus* L. and *Rhodiola* have been investigated. The antioxidant properties would have an additive effect for the protection of healthy cells during chemotherapy. The extraction conditions were optimized, two substances with powerful antioxidant properties were identified and quantified (*Publ. 13, Table 2*).
- Comparative study of the antioxidant properties of extracts from multiple plant species of the genus *Juniperus* L. from different habitats. The most active species were identified and their polyphenolic profile was investigated. A correlation of the composition with the antioxidant activity was established, as well as the relationship with their properties to form metal chelates or enzyme-inhibiting complexes (*Publ. 14, 15, Table 2*).
- Comparative study of the antimicrobial properties of methanol extracts from the leaves of seven species of the genus *Juniperus* L., incl. a hitherto unexplored endemic species, together with a phytochemical analysis for the content of total flavonoids and phenolic acids. Important information was obtained regarding the sensitivity of Gram-positive bacteria and yeasts to the extracts, which is also the basis for future research on the relationship between antimicrobial activity and phytochemical composition (*Publ. 16, Table 2*).

In the mentioned publications (with the exception of one) Assist. Prof. Ivanova is the first and corresponding author, and the reference given in the articles on the distribution of contributions unequivocally testifies to her leading participation (including in the article in which she is the 3rd author) in the following activities:

- conceptualization of the study,
- methodology and experimental work,
- material provision of the study,
- writing the text of the article,
- preparing the illustrative material,
- administration of one of the funding projects.

4. Critical notes and recommendations

In general, I believe that the candidate did not organize and distribute the evidentiary material well, acc. to the Regulations of the BAS, which also led to poor organization and

dispersal in the List of Scientific Contributions. What is more, this List is missing comments for **Publs. 7–10, acc. to Table 2**. These are articles in which Diana Ivanova is the first author and they should be of great importance in her contributions. There is also a lack of written, at least in general terms, own vision for the future developments of the subject, as I am convinced that Assist. Prof. Ivanova has such perspective.

5. Personal impressions of the candidate

I met Diana Ivanova in 2016, when she joined the Laboratory “Transfer Processes in Multiphase Media” of IChE–BAS, of which I am a part. We have not worked together on tasks and projects, but from my contacts with her in the laboratories of the Institute, I got the impression that she is consistent, persistent, dedicated person and uncompromising scientist towards the quality of the execution of the experimental work. I personally value the latter very much and believe that she would also contribute to the high scientific level of developments at IChE–BAS in the future.

C O N C L U S I O N

Based on the indisputable scientific quality of this candidacy, which convinced me that Assist. Prof. Diana Ivanova is already an established scientist-leader who would contribute a lot to the development of the ever-current topic related to the study of natural substances and the processes for their isolation or synthesis, with a focus on their medical application, *I recommend the Honorable Scientific Jury to approve the candidacy of Assistant Professor PhD Diana Ivanova Ivanova for the academic position “Associate Professor” in the professional field 4.2. Chemical Sciences (Processes and Apparatus in Chemical and Biochemical Technology)* at the Laboratory “Transfer Processes in Multiphase Media” of the Institute of Chemical Engineering – Bulgarian Academy of Sciences.

Date: 15.11.2023

Reviewer: 

/Assoc. Prof. Konstantza Tonova, PhD/