REVIEW

on the competition for the academic position "Professor"
in professional field 4.2. Chemical sciences, specialty "Processes and apparatus in chemical and biochemical technology" for the needs of the laboratory "Biochemical engineering" at the Institute of Chemical Engineering of Bulgarian Academy of Sciences (IChE-BAS),

announced in SG No 67 from 04.08.2023 г.

with candidate Assoc. Prof. Dr. Daniela Ilieva Batovska

Reviewer Prof. Dr. Daniela Boyanova Dzhonova- Atanasova

1. Brief scientific biography of the candidate and area of scientific interests

Assoc. Prof. Dr. Daniela Baovska completed higher education in 1992. at the Chemical Faculty, SU „St. K. Ohridski" as a chemist specialized in organic and analytical chemistry. In 2001 she defended a PhD thesis at the Institute of Organic Chemistry with a Center for Phytochemistry (IOCCP)-BAS on the topic "Synthesis and biological activity of sterol derivatives", in the scientific specialty "Bioorganic chemistry, chemistry of natural and physiologically active substances" and received the educational and scientific degree "Doctor". In 1991-1992 she worked as a chemist at the Department of Clinical Pharmacology and Therapy, MU. In the period from 1992 to 2017, she worked at (IOCCP)-BAS, successively in the positions of chemist and Assistant Professor, and from 2010 - Senior Researcher II deg., equivalent to the academic position "Assoc. Prof". In the period 2017-2023, she carried out scientific research and development activities in the position of chemist at RLG 2016 Ltd. From 01.08.2023, she was appointed to the position of chemist at IChE-BAS. In the period 2002-2004 Dr. Batovska participated in two one-year postdoctoral programs at two universities in Japan.

2. General characteristics of scientific and applied research

The scientific and applied research activity of the candidate is in intensively developing fields in the chemistry of natural products, as follows:

- Synthesis of biologically active compounds and investigation on their biological activity.

- Analysis of medicinal plants and their products

- Phytochemical studies (publications in the competition for “Assoc. Prof.)

She has published the results of this activity in a total of 64 publications in prestigious international publications, widely cited in the world databases with over 1400 citations, according to information from Scopus. She is a co-author of an invention registered as a patent in the United States.

The candidate is the co-supervisor of one successfully defended PhD student in India and is the coordinator of two international projects in cooperation with Germany and India.

3. Overall assessment of the presented materials

A total list of 64 publications is presented in the competition materials. From them, 22 publications are presented for the present competition, which include 19 articles in journals with quatiles, 1 book chapter and 1 patent. The rest of the publications from the general list are outside of this competition and are related to the PhD thesis and the competition for "Assoc. Prof.", but they participate in covering the condition for the total number of articles according to the rules of IChE-BAS.

By all indicators, the requirements are met and exceeded, both those of the law and the regulations of BAS, as well as those of the regulations of ICHE

Out of 22 publications in the competition, the candidate has 19 articles in journals with quartiles, and this is accepted as one of the criteria for the quality of the publications. The distribution by quarters is as follows: 3 articles in the highest category Q1 (16%), 9 in Q2 (47%), 5 in Q3 (26%), 2 in Q4 (11%). Impressive is the significant share of articles with quartiles Q1 and Q2, which shows the high quality of these publications, due to the high requirements of the journals and their reviewers. I rate highly the availability of 3 articles in Q1 and 9 in Q2, which make up nearly 2/3 of publications with quarters. Only 1 publication in a journal, outside the world databases, is presented, which does not carry points, but contributes to the fulfillment of the requirements of IChE for the number of publications in the competition.

As a general characteristic of the publication activity, it can be said that the candidate has publications in the 4 important categories: journal articles, book chapters, conference proceedings and patents. Predominant are articles in prestigious international periodicals, indexed inworld databases.

Assoc. Prof. Dr. Batovska was appointed the academic position of "Assoc. Prof" 13 years ago. Since then she has 22 publications, which makes almost 2 publications per year, with outstanding activity in 2023, when there are 5 publications. Quantitatively, I rate this performance as significant.

The candidate has a teaching activity as a part-time teacher at SWU "Neofit Rilski" Blagoevgrad in the period 2009-2010. This, together with the supervision of the foreign PhD student and 2 international projects, completes the general picture of her activity, which can be characterized by the presence of a complex of scientific research, scientific-organizational and teaching activity.

4. Basic scientific and applied scientific contributions

I accept all the scientific and applied contributions, presented in the author's reference, the most important of them are as follows.

4.1. Habilitation work - synthesis of chalcones and research on their biological activity - 6 publications

Most of the publications presented in the competition examine and solve problems related to the design and synthesis of pharmacologically active chalcones. This topic is the basis of the presented 6 publications, equivalent to the habilitation work (№1 - №6), and reveal different sides of the potential of these compounds.

- 16 chalcones were synthesized in high yields, purified and characterized. The structure-activity relationship is revealed, which contributes to the knowledge of the design of the chalcones of this type (publication №2).

- For the first time, chalcones were synthesized through an enzyme-catalyzed reaction with very high stereoselectivity. Such a "green" approach to the synthesis of these compounds is of great interest, due to their important applications as formula ingredients in the pharmaceutical, food and cosmetic industries. (publication №3).

- Synthesis of chalcones with antimalarial activity – the interest in the subject arises after the establishment of such activity for "licochalcone A" exclusively obtained from Chinese licorice. Chalcones with high antimicrobial activity have been synthesized, purified and structurally characterized. At the same time, they exhibit negligible toxicity in relation to human cells and are not mutagenic (publication №4). Three lead compounds have been released. It is shown that they cause a significant violation of all parasitic membranes, including those of the nucleus, mitochondria and food vacuole (publication №5). In addition, conclusions are made for multiple mechanisms of action for these chalcons. Unfortunately, in vivo pharmacokinetic study showed a serious limitation of the therapeutic efficacy of the three chalcones against tropical malaria. (publication No. 6).

4.2. Contributions outside the habilitation work on the topic of chalcone synthesis and the study of their biological activity - 4 publications

- The interaction of 6 of the chalcones with peroxide radicals was investigated through a highly sensitive chemiluminescence method. The absolute rate constants of the reaction were measured and the stoichiometric coefficients of inhibition were obtained. The study of the mechanism of antioxidant action of the chalcones showed that they also exhibit a prooxidant effect (publication №7).

- Synthesis of chalcones as a means of combating cancer diseases with developed resistance to anticancer drugs. Chalcones have been synthesized as a means of treating human bladder cancer with multiple drug resistance. A concentration-dependent cytotoxic effect was obtained. Based on 3 previously established leader structures, 15 chalcones were synthesized and evaluated for reversibility of multidrug resistance in mouse lymphoma cells (publication №8). In the model of combined chemotherapy, it is shown that one of the most active compounds exhibits an additive effect when interacting with the anticancer drug doxorubicin.

- Synthesis of chalcones with antimalarial activity – overall, the results show that chalcones are promising antimalarial agents. At the same time, in an in vivo model for the study of tropical malaria in humans, all three of the most promising chalcones significantly reduced parasitemia levels on the fifth and eighth day after infection, and were found to modulate the immune response of infected mice (publication №14). In an in vivo model of mice with induced cerebral malaria, chalcones showed a significant reduction in the percentage of parasitemia on the 10th day after infection (publication №19).

4.3. Adaptation of spectrophotometric methods for determination of antiradical activity in microscale - 3 publications

Spectrophotometric methods have been adapted for determining antiradical activity against highly reactive oxygen- and nitrogen-containing particles present in living systems. Some of the adapted methods are applied to determine the activity of methanolic extracts of biologically active substances from aerial and root parts of in vitro cultivated medicinal plants (publication №9) and synthetic biologically active compounds (publication №11) (publication №12).

4.4. Analysis of medicinal plants and products from them - 6 publications

A study has been conducted on the chemical composition of fresh juice obtained from the list of the succulent plant *xGraptoveria* (Crassulaceae) (publication No. 10), used in natural medicine for the treatment of conjunctivitis. The main groups of organic compounds are identified by gas chromatography/mass spectrometry (GH/MS) analysis. It is assumed that *xGraptoveria* exhibits activity against conjunctivitis through a synergistic effect on various chemical compounds, most likely alkylamines and mainly hydroxycarboxylic, aliphatic and aromatic carboxylic acids. Hydroethanolic extract from *Potentilla reptans* was obtained and divided into fractions with different polarities (publication №13). Given the data from natural medicine of extract application of the plant to relieve mastitis, the fractions were tested for antibacterial activity against 3 strains of *S. aureus*. The results showed bacteriostatic activity, with the n-hexane fraction being the most active. The chemical composition of the essential oil of *Lavandula angustifolia* (lavender) was investigated by means of GH/MS analysis (publication №17). 44

components are identified, which serve to evaluate the quality of the oil. The data are compared with the descriptions in the literature for samples of lavender essential oil from different habitats in the country. Bulgarian lavender oil has been shown to meet European standards in terms of its main components. Data published in the scientific literature on *Gentianaceae* (gentian) as a means of pain control (publication №15) and wound treatment (publication №16) have been summarized. Data have been collected on the secondary metabolites of gentians growing in the Bulgarian mountains (publication №18), which will facilitate the finding of compounds that are possibly involved in the attraction, oviposition deterrence, and feeding of various insect orders.

There is no doubt that the contributions are results of the candidate's individual efforts in equal cooperation with the co-authors.

The scientific topics are significant and promising for the continuation of research in this field during the upcoming work of the candidate on the topic of the competition in the next 5 years.

5. Reflection of scientific publications in Bulgarian and foreign literature

The citation of publications reflected in world databases is an important criterion for evaluating their quality, their significance and usage by the scientific community. The number of citations in the world databases of the candidate's publications is impressive, reaching over 1400 citations for the entire publication period (30 years) and 383 citations of the publications presented in the present competition, which many times exceeds the requirements for this indicator. According to the reference from Scopus, the candidate has and H-index of 14 (recommended 8).

6. Critical notes and recommendations

There is some difficulty in tracking the compliance of the publication list from the minimum requirements fulfillment with the general publication list.

7. Personal impressions of the candidate

I have known Assoc. Prof. Batovska from several months since she joined IChE. My impression is of a sociable person who successfully adapts and integrates into a new environment and has dedication and professionalism as a researcher and scientist.

CONCLUSION

In general, the research activity of Assoc. Prof. Batovska is characterized by the presence of scientific, scientific-applied and real applied and innovative contributions. They lead to the synthesis of new biologically active compounds, by analogy with the structure of biologically active substances of plant

origin, with a proven significant effect for the treatment of a number of serious diseases such as malaria and tumor diseases. New valuable knowledge about the chemical composition of plant products and their associated qualities and mechanism of action for medical purposes has been obtained. The activity of the candidate is valuable and leads to useful results.

The minimum requirements of the Law for Development of the Academic Staff, also these of the Bulgarian Academy of Sciences and the Institute of Chemical Engineering have been met and exceeded.

Based on the careful examination of the presented scientific works, their significance for science and bioengineering practice and the contributions in them, I propose Assoc. Prof. Batovska to acquire the academic position of "Professor" in professional field 4.2. Chemical Sciences, specialty "Processes and Apparatus in Chemical and Biochemical Technology" at IChE-BAS.

13.11.2023 г.

Sofia

Reviewer: [redacted]

/Prof. Dr. Daniela Dzhonova-Atanasova/