

## REVIEW

from Prof. Iliana Ilieva Ionkova, DSc,  
Faculty of Pharmacy, Medical University-Sofia

Regarding: The announced competition for the academic position “Professor” in the field of higher education 4. “Life sciences, mathematics and informatics”, scientific direction 5.11. Biotechnology (Technology of biologically active substances), for the needs of the Department of Biotechnology, Laboratory of Metabolomics, announced in the State Gazette No 47 from 22.05.2020.

Reviewer: Professor Iliana Ilieva Ionkova, DSc, Head of Department of Pharmacognosy at the Faculty of Pharmacy, Medical University (MU)-Sofia.

Grounds for the review: Order No I-79/01.07.2020 of the Director of the Stephan Angeloff Institute of Microbiology – BAS (IMicB-BAS), Assoc. prof. Penka Petrova and Resolution of the first session of the Scientific Jury for reviewer assignment.

### GENERAL DATA

The announced competition is in the field of the higher education 4. “Life sciences, mathematics and informatics”, scientific direction 5.11. Biotechnology (Technology of biologically active substances) for the needs of the Department of Biotechnology, Laboratory of Metabolomics. **Assoc. prof. Milen Ivanov Georgiev, PhD**, Department of Biotechnology, Laboratory of Metabolomics is the only candidate, who has submitted documents for the competition call. Assoc. prof. Milen Georgiev has presented a complete set of the required documents, according to the Act for the Development of the Academic Staff in the Republic of Bulgaria and the Rules of IMicB-BAS. He is presenting exclusively well-prepared documentation to the Scientific Jury.

### CARRIER DEVELOPMENT OF THE CANDIDATE

The candidate graduated a MSc degree in Biotechnology, in 2001, at the University of Food Technologies, Plovdiv, Bulgaria. In 2006 he was awarded a PhD degree on a thesis of dissertation: “Possibilities to increase the rosmarinic acid yield in cell suspension culture of *Lavandula vera* MM”. Following the obtaining of prestige Marie Curie Postdoctoral Fellow, he was appointed as a postdoctoral researcher at the Institute of Food Technology and Bioprocess Engineering, Technical University of Dresden, Germany, for 2 years, between 2005 and 2007. Later on, from 2010 to 2012, he was selected as postdoctoral fellow at the Institute of Biology, Leiden University, the Netherlands, receiving the same fellowship for the second time. Subsequently, he was invited several times as a guest-researcher at both universities. Along with that he was an invited lecturer in over 20 countries (incl. USA, Germany, The Netherlands, China, Greece, Thailand, *etc.*), where he has hold above 50

lectures in the field of the announced competition. Since 2007 he has been appointed as a research fellow at the Stephan Angeloff Institute of Microbiology – BAS, since 2010 as an Assoc. professor, and currently he is a head of the Laboratory of Metabolomics (IMicB-BAS). In addition, he is a leading lecturer of a specialized course in Metabolomics for the MSc students at the Biological Faculty, Plovdiv University “Paisii Hilendarski”. During all the years, he is withstanding high level of proficiency – supervisor of three PhD students, one of which is approved to have the legal right for PhD defence, five diploma students and nine trainees from Bulgaria, Romania and Spain.

The current scientific investigations of the candidate are mainly orientated on the biosynthesis and the metabolic engineering of pharmaceutically-relevant plant-derived molecules and their sustainable biotechnological production. The research focus is on natural compounds with anti-inflammatory and anti-obesity activity. Assoc. prof. Georgiev has introduced for first time in Bulgaria the contemporary platform for metabolomics based on nuclear magnetic resonance (NMR).

Assoc. prof. Georgiev has established himself as an authoritative scientist at the IMicB-BAS since a long time. I will underline his merits as a researcher and lecturer further.

## **EVALUATION OF THE RESEARCH ACTIVITY**

### **1. Publication activity**

The research activity of the candidate as a whole is in the field of the announced competition call Biotechnology (Technology of biologically active substances). The total number of publications is over 130 with a **gross impact factor of 392.02**, which attracted more than 2500 citations. Following invitations, he has delivered reports in over 50 scientific conferences in 20 different countries. In the competition for professor he takes part with 57 publications, of which 54 in indexed journals (40 in Q1, 11 in Q2, 1 in Q3 and 2 in Q4) and 3 book chapters (different from the presented for the previous competitions for Associate professor and “Doctor of Philosophy” degree). In 26 of the publications, which represent 46% of the total number, Assoc. prof. Georgiev is a first or corresponding author and co-author in the remaining papers.

It is impressive that all 54 publications are published in prestige international journals with impact factor. These publications, published after his appointment as an Assoc. professor and not included in his doctoral thesis, have a **total impact factor of 247.1**. The candidate has participated 67 times in national and international scientific conferences, in 30 of which as an invited speaker (incl. as a plenary or key-note speaker). The presented scientific publications in the competition call are evidence for the scientific competence of the candidate, as well as, the broad scientific interests in the field of biotechnology of natural biologically active molecules. He is also a chair of the organizing committee of four International Conferences on Natural Product Utilization: from Plants to Pharmacy Shelf (ICNPU). He is also a member of the organizing committee of 13 scientific conferences.

Assoc. prof. Milen Georgiev is a scientist with a remarkable international activity, which is evident not only by his participation in scientific conferences, but also from the fact that he is desired partner in scientific projects – 12 projects, of which 5 international, 6 national and 1 business contract. The amount of the attracted funding from the projects coordinated by Assoc. prof. Milen Georgiev for the basic research organizations is nearly 7 million BGN.

He has been invited as a reviewer in more than 30 international scientific journals, as well as, as a reviewer of PhD thesis and of scientific projects at the University of Lorraine (France), Medical University Plovdiv, Medical University Sofia, University of Karachi (Pakistan), Indian Institute of Technology Madras (India), University Putra (Malaysia), IMiCB – BAS, *etc.*

## **2. Accomplishment of the requirements according to the relevant indexes**

In the Professor competition, Assoc. prof. Georgiev takes part with a total of 57 publications, of which 28 are classified in exponent B and 29 in exponent G.

EXPONENT B 4. Habilitation monograph includes 28 publications. Required minimum score – 100 points. Presented by the candidate – 639 points.

EXPONENT G 7. Research publications in journals, index in the international scientific databases (SCOPUS and WEB of SCIENCE), not included in the habilitation monograph – 21 in Q1 x 25 points = 525 points; 4 in Q2 x 20 points = 80 points; 1 in Q3 x 15 points = 15 points. Required minimum score – 200 points. Presented by the candidate – 665 points.

EXPONENT G 8. Published book chapter or shared monograph – 3 x 15 points = 45 points.

EXPONENT D. Citations. The candidate has submitted the impressive 2114 points from citations of his publications while the minimal required scores is 100 points.

EXPONENT E. Participation in national scientific or educational projects and attracted funding from projects coordinated by the candidate – 1604 points in total. Hereby, I would like to underline the contribution of the candidate with total amount of 6.771.477,69 BGN of attracted funding for the basic organizations.

**Total impact factor of the scientific publications included in the current competition – 247.1.**

The submitted publications in the professor competition call in exponents 4, 7, 8 and 9 notably exceed the requirements in the field of higher education 4. “Life sciences, mathematics and informatics”, scientific direction 5.11. Biotechnology. With minimal required score of **600** points, the candidate has accomplished a total of **5072** points.

## **3. Scientific recognition**

After analyzing the delivered set of documents, I could draw the conclusion that the main contributions of the candidate research production are highly appreciated within the

scientific community. The reflection of his scientific achievements on the progress of the science in his research field is unambiguous. The main results have been explicitly recognized from the scientists in the respective research area. According to the provided data, the results obtained from the research of the candidate after his appointment as Assoc. Professor are with strong international acknowledgment – 1057 citations of the publications included in the professor competition, predominantly by international authors, many of which are multiple citations of one publication, such as *Publication No 2*, in *Pharmacognosy: Fundamentals, Applications and Strategy* cited 27 times; *Publication No 23*, in *Journal of Experimental Botany*, 69(8): 1955-1966. – cited 12 times; *Publication No 24*, in *Critical Reviews in Food Science and Nutrition*, 58(4): 513-527 – cited 77 times, *etc.* Evaluation of these cited publications of Assoc. Prof. Georgiev reveals that regardless the journal of publication his research is of high interest for the scientific community, which is important indicator for quality of the scientific production. In this regard I have to notice the fact that his publications are cited over **2 500** times and the individual Hirsch index (*H-index*) is **31** (Google scholar) and **25** (Scopus).

#### **4. Analysis of the main contributions from the delivered set of publications**

In all publications and materials presented for the current competition is visible the implementation of a multidisciplinary approach.

Assoc. prof. Milen Georgiev, PhD has clearly defined profile of his research. The scientific achievements and contributions are in the field of plant biotechnology (Publications No 23, 28, 50, 53, 55), chemistry of natural compounds (incl. metabolomics and metabolite profiling) (Publications No 5, 12, 31, 33, 34, 38, 42, 43, 52) and pharmacology (Publications No 10, 15, 17, 19, 20, 21, 25, 27, 29, 32, 35, 37, 54, 56). The methodology of the research investigations, described in the aforementioned publications is relevant to the targeted goals and employs various phytochemical (incl. metabolomics and metabolite profiling), biotechnological and pharmacological approaches. Besides the exploited contemporary methods, development of new protocols, technologies and methods, along with adaptation of the existing methods to the specific research problems have been performed by Assoc. prof. Georgiev. The statistical data analysis and interpretation of the results have been done with complex and modern methods.

The presented publications for the current competition are 57 in total, of which 28 are included in the habilitation monograph. Special attention in this treatise is devoted to the plant biotechnology (a clade of jasmonate-responsive subgroup 4 MYB transcription factors, FtMYB13, FtMYB14, FtMYB15, and FtMYB16, which directly repress rutin biosynthesis in *Fagopyrum tataricum*, has been identified; stability of the genetically modified hairy root cultures from Tobacco, regarding the production of *t*-resveratrol and its derivatives, such as *t*-piceatannol and *t*-pterostilbene, has been established; high content of secologanin, epigallocatechin, caffeic and gallic acids, as well as, mitragynine were found by metabolic profiling of the *Mitragyna speciosa* leaves; an efficient protocol for the establishment of

transformed root culture of *Verbascum xanthophoeniceum* using ultrasound-assisted *Agrobacterium rhizogenes*-mediated transformation has been developed; process for phenylethanoid biosynthesis in a 3-L stirred tank reactor and a 1-L glass-column bioreactor operated with pulsed aeration has been designed, *etc.*).

With regards to the thematic area of chemistry of natural compounds (incl. metabolomics and metabolite profiling) an analytical platform for investigation of the phytochemical variety of *Rhodiola* species has been established, which permits the recognition of unique metabolites between different species and the identification of adulterated products; two new minor “Valeriana type” iridoid glycosides and three known flavonol glycosides were isolated from *Sambucus ebulus* leaves; *etc.* The contributions to the phytochemical research are mainly directed toward enrichment of the knowledge in the field: isolation and identification of secondary metabolites, many of which are new chemical entities. Contemporary phytochemical analytical techniques and isolation approaches are used for these identifications.

The pharmacological investigations concern the estimation of the anti-viral effect of plant extracts, the evaluation of the antineoplastic potential of an isoflavone, isolated from the fruits of *Cudrania tricuspidata* on breast cancer cell line and animal models, the anti-inflammatory activity of *Clinopodium vulgare* extract, the immunomodulatory and antidepressant effects of salidroside and curcumin, development of a method of plant-based synthesis of nano-materials (silver and gold) through ethanol extraction of *Melissa officinalis*, *etc.* These pharmacological studies provide completeness of the scientific contributions of the candidate. Integrative approach has been employed ubiquitously for the data analysis and interpretation.

Theory and experiment have been combined in a rational way in the publications, featured with pharmacological evaluation, which represent original, consolidated work within the field of biotechnology of the natural bioactive compounds.

**Fundamental contributions** could be summarized as follows:

- Establishment of new complex knowledge on a molecular level for the metabolite regulation of the plant secondary metabolism.
- Distinct scientific contribution is the proposed metabolomics platform (NMR, GC-MS and LC-MS) for complex analysis of the metabolite fingerprints in the cells as a result of different biochemical reactions and its application for quality and quantity control of complex pharmaceutical products and food supplements.
- Using contemporary phytochemical methods numerous biologically-active molecules have been isolated and identified.

**Applied contributions:**

- Establishment of anti-inflammatory, anti-viral, immunoregulatory activities and antineoplastic potential and their mechanisms of action of plant extracts and isolated pure compounds.

- Development of new approaches for obtaining new phytochemicals based on the “green” chemistry concept.

When summarizing the research activity and the published results what attracts attention is the significant presence of originality and the utilization of the proved concepts for future fundamental and applied research problems.

### **SIGNIFICANCE OF THE CONTRIBUTIONS FOR SCIENCE AND PRAXIS**

The publications include theoretical conclusions – models and experimental methodologies. Notably important for the future research are the original research contributions: for instance, for the first time in Bulgaria a design of glass-column bioreactor with pulsed aeration, suitable for hosting Devil’s claw cell suspension culture, has been proposed; a complex model for in-depth analysis of the reproductive systems is proposed among others. Further, a vision and directions for future research of the candidate are presented, linked to the main areas of his research accomplishments.

The outline directions of the research interests of Assoc. prof. Georgiev harmonize on one hand systematic scientific production and on the other hand consistent ambition towards implementation of applied results into practise.

### **CRITICAL COMMENTS AND RECOMMENDATIONS**

- Expanding of the pharmacological investigations with regard to justification of the potential application of the obtained fundamental findings into practise is essential.
- Particular recommendation to the candidate is to focus his future activities towards the establishment of scientific school and specialized direction in the area of his high scientific achievements.

### **ASSESSMENT OF THE CANDIDATE**

Assoc. prof. Georgiev, for many years, has well-established reputation as a scientist and a lecturer. I give high assessment of the work of the candidate with young specialists – trainees, MSc and PhD students.

Assoc. prof. Milen Georgiev is scientist with impressive international scientific activity. He serves as an associate editor of the journals *Phytomedicine*, *Food and Chemical Toxicology* and *Food Frontiers*, and is also a member of the editorial boards of *Biotechnology Letters*, *Chinese Medicine* and *Molecules*. Along with that, he is a co-founder and a member of the executive board of the Center of Excellence of Plant Systems Biology and Biotechnology in Plovdiv.

As a scientist, Assoc. prof. Georgiev shows broad spectrum of interests and high competence in the field of phytochemistry and biotechnology of natural compounds. The presentation of his original results on national and international conferences is constantly excellent. He is a solicited partner in scientific projects. His loyalty and will for scientific and methodological advice and assistance are remarkable.

The only candidate in the current professor's competition call – Assoc. prof. Georgiev is a leading specialist in the field of Biotechnology of natural compounds with significant fundamental and applied contributions, substantial research production and teaching experience.

### **EXPERT ACTIVITY**

Assoc. prof. Milen Georgiev holds three Pythagoras awards (currently the only scientist in Bulgaria awarded three times), Marin Drinov award of BAS for young scientists and a Diploma for excellent achievements from the Executive Board of BAS.

He is a member of the scientific committees for Doctor of Philosophy degree, member of the committee for the appointment for the academic position “associate professor”, member of the Scientific Board of the IMicB-BAS, member of the editorial boards of the journals Biotechnology Letters (Springer), Chinese Medicine (Springer) and Molecules (MDPI), co-founder and member of the Executive Board of the Bulgarian Phytochemical Society, former chairman of the Pythagoras awards committee, member of the Executive Board of the Center of Excellence of Plant Systems Biology and Biotechnology, guest-editor for Biotechnology Advances (Elsevier), Food Chemistry (Elsevier), Phytochemistry Reviews (Springer) and Food and Chemical Toxicology (Elsevier), reviewer and expert for the European Commission, the Austrian, Polish, Romanian and Latvian National Science Funds, *etc.*

### **CONCLUSION**

Assoc. prof. M. Georgiev, as the only candidate in the competition call for PROFESSOR, announced for the needs of the Department of Biotechnology, Laboratory of Metabolomics, decisively takes part with impressive and more than sufficient scientific and applied contributions, as well as, with comprehensive research, teaching and expert experience. Assuredly, he meets all the criteria according to the Act for the Development of the Academic Staff in the Republic of Bulgaria and the Rules of IMicB-BAS to take the academic position “Professor”. Assoc. prof. Georgiev is accomplished specialist in the field of Biotechnology of biologically active substances. He has convincing original scientific and applied contributions in his publications. Within his comprehensive research, he has achieved harmonization between the academic teacher and the scientist.

Based on the scientific achievements and personal merits of the candidate, I found reasonable to propose to the Scientific Jury **my positive evaluation** for **Assoc. prof. Milen Ivanov Georgiev** to attain the academic position PROFESSOR.

25.08.2020

Reviewer: .....

Prof. Iliana Ilieva Ionkova, DSc