

REVIEW

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Subject: Procedure for a competition for an academic position "ASSOCIATE PROFESSOR" in the field of higher education 5. "Technical Sciences", professional field 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. 12 from 12.02.2021

Reviewer: Prof. Iliana Ilieva Ionkova, Head of the Department of Pharmacognosy at the Faculty of Pharmacy, MU-Sofia.

Grounds for the review: Order № I-31/29.03.2021 of the Director of the Institute of Microbiology – BAS, Prof. Dr. Penka Petrova, and Decision of the first meeting of the Scientific Jury for selection of reviewers.

GENERAL DATA

The announced competition is in the field of higher education 5. "Technical Sciences", professional field 5.11. Biotechnology (Technology of biologically active substances) for the needs of the Department of "Biotechnology", Laboratory of Metabolomics. For participation in the competition, documents have been submitted by a single candidate, **chief assistant professor Dr. Andrey Stoyanov Marchev**, Department of Biotechnology, Laboratory of Metabolomics. According to the procedure chief assist. prof. Dr. Andrey Marchev has presented all required documents and materials, according to the requirements of the Law and Regulations of IMicB-BAS on the terms and conditions for obtaining a scientific degree and for holding academic positions. He presents to the Scientific Jury strictly prepared documentation.

CAREER DEVELOPMENT OF THE CANDIDATE

The candidate graduated in Biotechnology at the University of Food Technology, Plovdiv, Bulgaria in 2006. In 2014 he defended his dissertation for a doctorate on "Biologically active substances from rare Bulgarian Salvia species and their in vitro cultures." He specialized for 3 months (2010 - 2011) at the Institute of Food Technology and Bioprocessor Engineering, Technical University of Dresden, Germany and later at the same University in 2015 and 2017. In 2015 he specialized in the Laboratoire de Biologie Moléculaire et Cellulaire du Cancer (LBMCC), Luxembourg, and in 2017 at the Jacqui Wood Cancer Center, University of Dundee, Dundee, Scotland.

At the Stephan Angeloff Institute of Microbiology – BAS, Dr. Marchev has established himself as an authoritative scientist. He is an invited reviewer of scientific articles in prestigious international journals such as Phytochemical analysis; Cellular and Molecular Life

Sciences, Phytochemical Analysis; Phytomedicine; Biotechnology Letters; Biomolecules; Molecules; Biology; Clean Technology; Foods; Forests; Marine Drugs; Industrial Crops and Products; Food Frontiers; Frontiers in Pharmacology; Aging; African Journal of Biotechnology; African Journal of Plant Science; Zeitschrift für Naturforschung C and others. In 2016 he reviewed a dissertation "In vitro propagation and ex situ conservation of the western-Mediterranean endemic species *Lapiedra martinezii* Lag. (Amaryllidaceae) "at the University of Alicante, Spain.

He has won a number of scientific awards: in 2016 Dr. Marchev was nominated for the Pythagoras Award of the Ministry of Education and Science in the category "Young Scientist". In 2017 he received an award for excellent project management under the joint program "Supporting Young Scientists" at the initiative of MES and BAS, awards for best poster at international congresses in 2010, 2012, 2016, 2018 and others. He is a member of the organizing committees of international congresses, the Union of Scientists in Bulgaria and the Bulgarian Phytochemical Society, and since 2017 he is a member of the board of the latter.

Since 2012 he has been elected as an assistant professor at the Stephan Angeloff Institute of Microbiology - BAS, and since 2015 - a chief assistant professor, where he currently works.

His research is mainly focused on the biosynthesis and metabolic manipulation of the biosynthesis of biologically active molecules of plant origin and their sustainable biotechnological production. The main focus of research is natural molecules with anti-inflammatory action, antitumor and cytoprotective activity of secondary metabolites of plant origin, as well as the application of different approaches to metabolic engineering.

EVALUATION OF RESEARCH ACTIVITY

1. Publishing activity

The overall research activity of the candidate is in the field of the announced competition Biotechnologies (Technology of biologically active substances). The total number of publications of the candidate during the whole scientific career is 49 scientific publications with a total **Impact Factor 86.83**. Of these, 43 are represented in the current competition for associate professor and 6 outside the current competition, which are presented for obtaining the educational and scientific degree "Doctor". Dr. Marchev is a participant in 2 international and 10 national projects (in 3 of them as a leader). From the list of 43 scientific papers, one is a utility model, 4 are book chapters, 27 publications in refereed and indexed journals (13 in Q1, 6 in Q2, 3 in Q3 and 1 in Q4) with a total impact factor of 83.18 and 11 in journals without an impact factor. In 17 of the presented scientific works chief assist.prof. Dr. Marchev is a leading or author of correspondence. Publications № 8, 9, 10, 11, 14, 15, 19, 20, 21 and 22 are included in indicator B. Publications № 2, 3, 4, 5, 6, 7, 12, 13, 16, 17, 18, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42

and 43 are included in indicator Г. Publication № 1 is included in indicator E. The list contains 219 citations and H-index 9(9 articles cited 9 times).

It is impressive that most publications are papers in prestigious international journals with an impact factor. These articles with IF, published after the dissertation for a doctor have a **total impact factor of 83.18**. He has participated many times in national and international scientific forums, for which he was awarded. The presented scientific papers are proof of the high scientific competence of the candidate and of a wide range of scientific interests in the field of biotechnology of natural biologically active substances.

2.Fulfillment of the requirements by indicators

The total number of publications included by Dr. Marchev in the competition for associate professor is 43, of which 10 by indicator B, 32 by indicator Г and 1 by indicator E.

INDICATOR A. Dissertation for educational and scientific degree "Doctor", Dr. Marchev has 50 points out of the required 50.

INDICATOR B 4. Habilitation work - scientific publications (not less than 10) in publications that are referenced and indexed in world-famous databases of scientific information. Minimum required number of points 100 - the candidate submits - 102.74 points.

Sum of INDICATOR Г: Minimum number of points 200 - presented 202.70, formed as follows:

INDICATOR Г 7. Scientific publications in journals that are referenced and indexed in world-famous databases with scientific information (SCOPUS and WEB of SCIENCE), 17 publications with a total number of 149.18 points.

INDICATOR Г 8. Scientific publication in unreferenced journals with scientific review or in edited collective volumes, 11 publications with a total number of 41.86 points.

INDICATOR Г 9. Published chapter of a collective monograph, 4 book chapters with a total of 11.66 points.

INDICATOR E. Citations or reviews in scientific journals, referenced and indexed in world-famous databases with scientific information or in monographs and collective volumes - with a minimum required 50 points, the candidate has submitted a total of 219 points (219 citations x 10 points).

Sum of INDICATOR E - 216 points are presented, although such are not required in a competition for associate professor.

INDICATOR E 18 - Participation in a national scientific or educational project 70 points.

INDICATOR E 19 - Participation in an international scientific or educational project 40 points.

INDICATOR E 20 - Guidance of a national scientific or educational project 60 points.

INDICATOR E 22 - Raised funds for projects led by the applicant 6 points.

INDICATOR E 26 - Recognized application for utility model, patent or copyright certificate 40 points.

GENERAL IF of the publications in the competition–83.18.

The papers presented in the competition for associate professor on indicators 4, 7, 8 and 9 significantly exceed the requirements in the field of "Technical Sciences", professional field 5.11. Biotechnology. With a minimum required score of **400** in the competition for a associate professor in the specified field, the candidate has covered **2 761.44**.

3. Reverberation—from the data I have, I can conclude that the main results of the research activities of the candidate have found a significant positive response among the college of specialists in the field. The reflection of the publications in science is undoubtedly - a total of 219 citations of his works. The main results have found a significant positive response among the foreign college of specialists in the field. According to the presented reference, the results described in the scientific papers after his appointment as a chief assist. prof. and PhD have a strong international recognition - 81 citations of articles in the competition for associate professor, mainly in articles by foreign authors and the personal Hirsch index (h index) is 9.

4. Analytical characteristics of more significant scientific contributions

All proposed for review papers and other materials are in the field of competition and have a multidisciplinary focus.

Chief assist. prof. Dr. Andrey Marchev has a clearly defined profile of his research activities. According to the presented author's report, the scientific contributions from the overall research activity are summarized in 3 main areas: in the field of plant biotechnology (Publications № 22), chemistry of natural molecules (including metabolomics and metabolic profiling based on nuclear magnetic resonance) and high performance liquid chromatography) (Publications № 9, 14 and 20) and pharmacology (Publications № 8, 10, 11, 15, 19 and 21).The scientific publications in the competition for associate professor unite several from the mentioned scientific fields. The research methodology described in the publications is adequate to the set goals. It includes a number of phytochemical (including metabolomics and metabolic profiling), biotechnological and pharmacological studies. In addition to the applied modern methods, new methods have been developed, and where necessary, together with the team in which he works, existing methods have been successfully adapted for specific purposes. Modern methods for statistical processing, analysis and interpretation of the results are used.

The publications submitted for participation in the competition are a total of 43. Research is aimed mainly at enriching existing knowledge in the field: isolation and identification of secondary metabolites, establishment of new sources of active compounds

in vitro, pharmacological study of purified extracts, fractions and isolated pure substances. Particular attention is paid to plant biotechnologies (initiation of plant in vitro systems, optimization of cultivation conditions and metabolic manipulation of secondary metabolism). A utility model has been developed that relates to the composition of the nutrient medium for in vitro propagation of the plant *Haberlea rhodopensis* Friv. (Orpheus flower) for the needs of the pharmaceutical industry. Effective protocols have been developed for initiating transformed root cultures from rare Bulgarian plant species, such as *Verbascum eriophorum* and *V. nigrum*, by applying genetic transformation with *Agrobacterium rhizogenes* and ultrasound treatment. Initiation of transgenic tobacco root cultures for biosynthesis of t-resveratrol and its derivatives has been performed.

In the field of chemistry of natural molecules (including metabolomics and metabolic profiling) an analytical platform based on magnetic resonance spectroscopy and high performance liquid chromatography has been developed to study metabolic variations in medicinal plants, applied to study the difference in phytochemical composition of different species of *Rhodiola*, to discriminate the unique metabolites between them and the identification of adulterated products. Its application in the study of the authenticity and quality of commercial products from medicinal plants are a clear scientific and applied contribution. Phytochemical research is mainly aimed at enriching existing knowledge in the field: isolation and identification of secondary metabolites. Modern phytochemical methods and approaches have been used for their identification.

Impressive is the work of the candidate in the field of pharmacological research, which gives a completion of his research. They relate to the study of the anti-inflammatory, immunomodulatory and antiviral activity of plant extracts and isolated compounds. Myconoside and calceolarioside E, biotechnologically derived from *H. rhodopensis*, have been shown to stimulate the activity of the transcription factor Nrf2, thereby revealing their potential for regulating pathological processes associated with oxidative stress and cellular homeostasis. *Veronica austriaca* extract, whose main metabolite is arbutin, has been shown to stimulate the survival of neutrophils isolated from the bone marrow of mice. *R. rosea* extract and isolated compounds modulate TNF-related apoptosis-inducing ligand (TRAIL) which is an innovative approach to overcome apoptosis resistance in some autoimmune and cancerous diseases. A standardized *Rhodiola* extract has a positive effect on training, recognition functions and memory in both healthy and rats with scopolamine-induced memory impairment. Aqueous extract of *Nepeta nuda* ssp. *nuda* L. exhibits antiherpes activity against Human Alpha Herpes (HHV) virus type 1, strain F (ACV-sensitive) and HHV type 2, strain DD (ACV-resistant). The aqueous extract of *N. nuda* is thought to affect both the early phases (absorption) and the late manifestations (replication) of HHV infection.

The publications successfully combine theory and experiment, accompanied by pharmacological evaluations, which is an original, integral work in the field of biotechnology of natural active substances.

Contributions of a priority scientific research can be summarized as follows:

- Significant scientific contributions to the proposed metabolic platform (magnetic resonance spectroscopy and high performance liquid chromatography) for complex analysis of medicinal plants and its application for qualitative and quantitative control of complex pharmaceuticals and food additives.
- A number of biologically active molecules have been isolated and identified through modern phytochemical methods and approaches.

Contributions with a priority scientific and applied research:

- Anti-inflammatory, antiviral, immunoregulatory activity of a number of extracts and isolated molecules has been investigated in order to determine the applicability of the achieved theoretical results in practice.
- Methods for obtaining new sources of biologically active substances based on genetic transformations for initiating transformed root cultures of rare Bulgarian plant species, preserving the flora of Bulgaria, have been developed.

SIGNIFICANCE OF THE CONTRIBUTIONS TO SCIENCE AND PRACTICE

In the overall research activity and the published results, significant original scientific results stand out, representing substantiated and proven regularities for solving many scientific and scientific-applied problems.

Visions for future research work of the candidate related to his main achievements in the field are also presented. One of the most interesting views is the application of "omics" approaches, especially metabolomics to study the effect of plant extracts and pure molecules on signaling pathways associated with the regulation of various diseases, as well as the definition of disease-specific metabolic markers in in vitro and in vivo models.

Thus outlined areas of creative work of chief assist. prof. Dr. Andrey Marchev harmoniously combine on the one hand systematic effective research, and on the other - a consistent effort to achieve the necessary results for practice.

ASSESSMENT OF THE CANDIDATE

Chiefassist. prof. Andrey Marchev has established himself as an authoritative scientist and lecturer. He is a scientist with outstanding research activity and international activity - he is a member of the organizing committees of 3 and has 25 participations in international conferences. As a scientist he has a wide range of interests and high competence in the field of phytochemistry and biotechnology of natural compounds. He has always presented excellent research results at all international and national forums, for which he has received a number of awards.

The only candidate in the competition - chief assist. prof. Andrey Marchev in the field of Biotechnology of natural compounds is presented in the competition with significant scientific products, citations and scientific contributions. I assume that a great role in this

regard was played by the head of the unit in which the candidate was built - Prof. Milen Georgiev, a scientist with world renown and exceptional research activity.

CONCLUSION

The only candidate in the competition for **Associate Professor**, announced for the needs of the Department of Biotechnology, Laboratory of Metabolomics, chief assist. prof. Dr. Andrey Marchev participated in the competition convincingly with sufficient scientific and applied activity, as well as his overall research. Undoubtedly, he fully meets the criteria of the Law and the Regulations of IMicB-BAS for acquiring the scientific degree "Associate Professor". He has proven recognized scientific and applied contributions in the publications. With his overall activity he has managed to harmoniously combine the university lecturer with the researcher.

Due to the achievements and qualities of the candidate in the competition, I offer to the Scientific Jury my **positive** assessment of the award of the **chief assist. prof. Dr. Andrey Stoyanov Marchev** to the scientific degree of **ASSOCIATE PROFESSOR**.

15.06.2021

Prepared the review:

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