PEER REVIEW

By Prof. Vassya Stefanova Bankova, DSci, Corresponding Member of the Bulgarian Academy of Sciences, Institute of Organic Chemistry with Centre of Phytochemistry (IOCCP), Bulgarian Academy of Sciences

of the documents submitted for participation in the competition for the occupation of the academic position 'Professor'
at the Institute of Organic Chemistry with Centre of Phytochemistry, BAS
in the Field of higher education 4.0. "Natural Sciences", Professional Field 4.2. "Chemical Sciences", scientific specialty *„Bioorganic Chemistry, Chemistry of Natural and Physiologically Active Substances"*

In the competition for the position of "Professor", announced in the State Newspaper, issue 43 of 31.05.2019 and on the web site of IOCCP - BAS, Assoc. Prof. Dr. Antoaneta Borisova Trendafilova-Savkova from IOCCP - BAS participates as the only candidate. The set of documents presented by Dr. Trendafilova-Savkova is in accordance with the Regulations for the Development of the Academic Staff of IOCCP, and meets the criteria of IOCCP-BAS for the academic position of "Professor". The candidate has submitted a total of 33 scientific publications not included in her PhD thesis and in the competition for the academic degree "Associated Professor", all of them related to the current competition. The distribution of scientific works by quartile is as follows: Q1 - 8, Q2 - 12, Q3 - 9, Q4 - 4.

Prof. Antoaneta Trendafilova was born in 1967 in Dupnitsa. She graduated in 1991 at the Faculty of Chemistry, Sofia University St. Cl. Ohridski "as a MSc with a specialty "Organic and Analytical Chemistry", after which she started work as a specialist chemist at IOCCP - BAS, with the research group of Assoc. Prof. Elena Tsankova, Department / Laboratory Chemistry of Natural Products. In 1997 she defended her PhD thesis on the topic "Sesquiterpene lactones in some Bulgarian medicinal plants of the genus Asteraceae" under the supervision of Assoc. Prof. Tsankova. At that time, the candidate was an Assistant Professor grade II, after defending her dissertation she was promoted to Assistant Professor grade I, and

Associate Professor. She specialized at the University of Siena, Italy, which is not reflected in the submitted CV.

Assoc. Prof. Trendafilova has presented for participation in the competition 33 scientific papers, all published in journals, indexed and referenced in the Web of Science and Scopus databases, including respected international journals such as *Phytochemistry*, *Phytochemistry Letters*, *Chemistry and Biodiversity*, *Journal of Ethnopharmacolgy*, etc. In 13 papers the candidate is the first author, in 11 - the second, and in 15 papers she is the author for correspondence. A list of 63 papers presented at international scientific forums was presented, three of which were oral. A total of 250 citations were noted (2010-2019), not included in her PhD thesis and the competitions for the academic degree of Associate Professor, with 42 publications cited, i.e. the average is about 6 citations per cited publication. The Hirsch index is 11 (Scopus).

In the period after becoming an Associate Professor, the candidate has participated in 21 projects, of which 4 are internationally funded, incl. one under Horizon 2020, and is the coordinator of two projects funded by the National Science Fund and two more bilateral projects supported by BAS. The successful leadership of research projects is a confirmation of the ability of Assoc. Prof. Trendafilova to organize and lead scientific research.

Along with the research work, Assoc. Prof. Trendafilova also carries out educational and pedagogical activity - insofar as the conditions at the BAS allow. She was a consultant to a PhD student with the University of Food Technologies - Plovdiv, supervisor of the MSc theses of two graduate students with the Faculty of Chemistry and Pharmacy, Sofia University "St. Cl. Ohridski", and one with the University of Chemical Technology and Metallurgy - Sofia, as well as two student trainees in Student Practice projects.

The main topic in the research work of Assoc. Prof. Trendafilova is the phytochemical study of medicinal plants and unexplored endemic species, aimed at discovering new biologically active substances, revealing chemotaxonomic correlations, developing methods for extraction and control of the amount of bioactive secondary plant metabolites. This interdisciplinary scientific field is up-to-date, modern and socially relevant, given the increasing interest in recent years, including commercial one, for natural substances as a basis for medicinal preparations. The candidate's attention is focused primarily on sesquiterpene lactones and components

of essential oils, as well as on the accompanying phenolic compounds, which is largely determined by the topics of the scientific group in which her scientific career has begun and developed.

Sesquiterpene lactones have valuable pharmacological properties, and the chemical diversity of their structures is a challenge for phytochemists. An essential part of the candidate's research - 12 publications - is devoted to the Asteraceae family, many of whose representatives biosynthesize sesquiterpenes. Well-known medicinal plants have been studied, such as *Artemisia alba* and *Inula* species (publications 30, 56, 64, 66, 69,73), Bulgarian and Balkan endemics - *Jurinea tzar-ferdinandii* (publication 75), *Centaurea davidovii* (publication 59), *Anthemis rumelica* (publication 35), and the Mongolian endemic *Asterothamnus centrali-asiaticus* (publication 53). As a result, the structures of 21 newly discovered natural sesquiterpenoid compounds - alcohols, acids and lactones - were established. It is worth noting publication 57, it describes the structure elucidation of 10 new compounds in *Artemisia alba* by the skillful application of NMR techniques. These results contribute to characterizing the structural diversity of sesquiterpenoids. A detailed study of both sesquiterpenes and phenolic compounds of *A. alba* (publication 74) contributes to the knowledge of intraspecific variability of this species. I also highly appreciate the characterization of the newly discovered naphthenol quinovozide in the Mongolian endemic, the first cembranolid glycoside in the plant world (publication 53).

Five of the presented by Assoc. Prof. Trendafilova publications are dedicated to the study of other poorly studied plant species, as well as unexplored endangered and endemic plants. This type of phytochemical research has a great potential for obtaining valuable fundamental and applied scientific results, for the discovery of new biologically active substances with important therapeutic effect and potential drug candidates. The phenolic components of three species of *Alchemilla* (publications 36, 40 and 65), three species of *Heracleum* (publication 79), *and Arum palaestinum* from Jordan (publication 68) were studied, and the chemical analysis was combined with bioactivity tests. Radical scavenging (publication 36), antitumor and antiviral activity (publication 68), acetylcholinesterase inhibition (publication 79) have been found.

Another significant group of publications relates to the analysis of essential oils by gas chromatography and gas chromatography-mass spectrometry. Essential oil profiles of aromatic and medicinal plants and *in vitro* grown plants - 9 species of the

Asteraceae (publications 44, 52, 67, 76), Lamiaceae (publications 48, 50, 49, 80) and Apiaceae families (publications 42 and 51). Over 200 individual components have been identified, chemotaxonomic dependencies and correlations between chemical composition and environmental conditions have been identified, and the impact of growth regulators on the accumulation of certain components in *in vitro* grown plants has been evaluated. I would like to emphasize here the contributions to the chemical profiling of the popular Mountain Tea *Sideritis scardica* - significant variability in chemical composition and correlation between the essential oil profile and environmental conditions were found for both wild and cultivated *S. scardica* (publications 48 and 50). The candidate's in-depth knowledge of this species has also allowed her to co-author a review article, published in the respected *Journal of Ethnopharmacolgy* (publication 55), which has received 30 citations since 2014.

An important aspect of modern phytochemistry is the development of reliable, accurate and reproducible methods for determining the content of bioactive secondary metabolites in plant material and their adequate application for the purposes of quality control of extracts, for studying the influence of environmental factors, for assessment of the effectiveness of extraction and cultivation, for revealing composition-activity relationships and chemotaxonomic correlations. Eight of the publications presented by Dr. Trendafilova are dedicated to the quantification of biologically active substances in medicinal plants - sesquiterpene lactones in *Arnica montana* (publication 62), phenolics, flavonoids and one sesquiterpene lactone in *Centaurea davidovii* (work 59), total phenolics and flavonoids in *Artemisia alba* (publication 72), *Inula britannica* (publication 64) and *I. oculus-christi* (publication 66), total phenolics and tannins in 3 species of the genus *Alchemilla* (publications 47 and 54). The methods of quantitative analysis are appropriately selected according to the nature of the compounds analyzed - gas chromatography, high performance liquid chromatography, spectrophotometry. The method developed for the quantification of furanocoumarins in 4 *Heracleum* species using NMR spectroscopy is worthy of appreciation (publication 79). This group of contributions has the potential for practical application.

Another scientific contribution is worth noting – publication 30, describing the application and optimization of innovative ultrasound-assisted extraction of bioactive sesquiterpene lactones from *Inula helenium*, which aroused the interest of many foreign authors and received 29 citations.

The scientific contributions of Assoc. Prof. Trendafilova can be characterized as a novelty for science - proving with new means of significant new sides of already existing scientific fields, and enriching the existing knowledge. The international and national recognition of the applicant's qualities is confirmed by the number of independent citations (over 250), as well as the fact that she is the coordinator of two bilateral international projects supported by BAS - with Turkey and Serbia, and of two projects funded by the National Science Fund.

I personally know Assoc. Prof. Antoaneta Trendafilova and was able to follow her progress from a young inquisitive chemist to a highly skilled, inventive, thorough and self-critical researcher with a sense of the current issues in phytochemistry and a worthy heir to the traditions of the Institute of Organic Chemistry with Centre of Phytochemistry in terpenoid chemistry and essential oils. Therefore, I am convinced that the results and contributions to the research presented are largely her own.

I have no substantial critical remarks on the scientific publications presented by Assoc. Prof. Trendafilova. As for the submitted documents on the competition, I have to note one discrepancy: on the presented cover page of Victoria Genova's MSc Thesis as scientific supervisor was noted Assoc. Prof. Milka Todorova, not Assoc. Prof. Trendafilova.

In the Report for Scientific Contributions, the candidate presented the prospects for her research work in the next 5 years, as she intends to develop her research in the directions in which she has successfully worked so far with the inclusion of new aspects and innovative approaches for the extraction and structural characterization of bioactive secondary metabolites from medicinal and aromatic plants. These perspectives are closely related to the projects in which IOCCP participates under the Horizon 2020 program and the Center of Competence, funded by the Operational Program Science and Education for Intelligent Growth, in which Assoc. Prof. Trendafilova is an important participant.

CONCLUSION

The published research papers presented by Assoc. Prof. Trendafilova contain significant and original scientific and applied contributions in the field of phytochemistry, which meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the implementation of this Law and the corresponding Regulations of IOCCP - BAS. The

volume and undoubtedly high quality of the scientific contributions reflected in the materials presented, as well as the overall activity of the candidate as an internationally recognized scientist in the field of terpenoid chemistry and essential oil chemistry, give me a deep conviction to give my positive opinion and to recommend to the Honorable Scientific Jury to prepare a report-proposal to the Scientific Board of IOCCP-BAS for the promotion of Assoc. Prof. Dr. Antoaneta Trendafilova-Savkova in the academic position "Professor" in the professional field 4.2. Chemical Sciences, scientific specialty "Bioorganic chemistry, chemistry of natural and physiologically active substances".

August 2019, Sofia

Reviewer: —

Vassya Bankova