OPINION

by Assoc. Prof. Paraskev Todorov Nedyalkov, PhD - Faculty of Pharmacy at Medical University – Sofia

Regarding the materials submitted for application in a competition to hold the academic position of "**Associate Professor**" at **the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences (IOCCP-BAS),** by field of higher education 4. Natural sciences, professional direction 4.2. Chemical Sciences, scientific specialty "Bioorganic chemistry, the chemistry of natural and physiologically active substances"

The competition for Associate Professor was announced in the State Gazette, no. 102 of 08.12.2023, and on the Internet page of IOCCP-BAS. Chief Assis. Prof. Tsvetelina Emilova Doncheva, Ph.D. from the Laboratory "Chemistry of Natural Substances" at the Institute of Organic Chemistry with Center of Phytochemistry, Bulgarian Academy of Sciences was the only applicant who participated in this competition.

1. General evaluation of the procedure and the applicant

Only one applicant, Ch. Assist. Prof. Tsvetelina Emilova Doncheva, Ph.D., from the "Chemistry of Natural Substances" laboratory at the Institute of Organic Chemistry with the Center for Phytochemistry, Bulgarian Academy of Sciences, participated in the competition. The set of paper and electronic materials presented by Dr. Tsvetelina Doncheva was by the Regulations for the Development of the Academic Staff of the IOCCP, and meets the criteria of the IOCCP-BAS for occupying the academic position "associate professor".

The applicant Tsvetelina Doncheva, Ph.D. has attached a total of 18 scientific publications and one book chapter. All the attached 19 scientific works are outside the dissertation for the acquisition of the Ph.D. and are on the thematic of the competition. The distribution of scientific works by the relevant Q factors is as follows: Q1 – 2 pcs. (Indicator C – 0; Indicator D – 2); Q2 – 7 pcs. (C – 2; D – 5); Q3 – 7 pcs. (C – 4; D – 3); and Q4 – 2 pcs. (C – 0; D – 2). In indicator C (habilitation thesis - monograph), a total of 6 publications are given, in which the candidate is the first author in 5 of them and the corresponding author in 3. The total number of points for this indicator is 100 (out of the required 100 points), which corresponds to the required minimum number of points. In indicator D, the candidate applied 13 works, 12 of which were published in journals with an impact factor. The total number of points according to indicator D, which forms the candidate's work, is 234 out of the required 220 points. Dr. Doncheva presented two lists of citations: 1) a list of citations of the referenced (Web of Science or Scopus) works participating in this competition; 2). a list of citations of all works published in refereed and non-refereed journals that have not been submitted in other competitions for holding academic positions and acquiring scientific degrees of the candidate. According to the rules of the IOCCP-BAS, she has excluded the self-citations of all authors participating in the relevant publications. According to the first list (indicator E) 300 points are obtained (150 citations × 2 points), and according to the second list, a total of 400 points (200 citations × 2 points) are calculated. The minimum requirements of the rules of the IOCCP-BAS under indicator E for occupying the academic position "associate professor" is 70 points. According to both presented lists, the candidate repeatedly exceeds the required minimum under criterion E. A SCOPUS reference shows that

after excluding self-citations the h-index Dr. Doncheva's is 7, which meets the minimum requirements (Hirsh-index not less than 5). The documents presented as evidence cover all the mandatory indicators for holding the academic position of "associate professor". I have checked thoroughly and I found no instances of overlapping content, missing documentation, or missing full-text content.

Tsvetelina Emilova Doncheva graduated from the University of Chemical Technology and Metallurgy - Sofia in 1998 with a master's degree in biotechnology. In 2010, she defended her dissertation on the topic "Alkaloid composition of species from the tribe *Datureae*" and received a Ph.D. from the National Academy of Sciences in the specialty "Bioorganic chemistry, chemistry of natural and physiologically active substances". On 04.05.2011 she was appointed as the chief assistant at the Institute of Organic Chemistry with the Phytochemistry Center - BAS.

2. General characteristics of the applicant's activity

The interdisciplinary research presented by Ch. Assist. Prof. Tsvetelina Doncheva for this competition has resulted in her scientific works, with contributions that can be summarized in the following topics:1). Investigation of the composition, structure and biological activity of secondary metabolites isolated from hitherto unexplored, rare and/or endemic species; 2). Comparative analysis of the alkaloid composition of plants from the Papaveraceae family (genera *Fumaria*, *Glaucium*, *Coridalis,* and *Hypecoum*) and derivation of taxonomic and chemotypic relationships; 3). Determination of the alkaloid composition of *in vitro* cultivated and *ex vitro* adapted endemic plant species.

The researches in the first direction are published in the attached papers with numbers B2, B3, Г2, Г5, Г6, Г8, Г9, Г10, Г11, Г12 and Г13. In 4 of these publications Ch. Assist. Prof. Doncheva is the first author, and in 8 she is the second, which is indicative of her significant contribution to conducting the research and writing the articles. The essence of these works is primarily related to establishing the chemical composition of plant species belonging to the genera *Leptopyrum*, *Hypecoum*, *Papaver*, *Pandanus*, *Thalictrum*, and *Gentiana,* and also to clarifying the chemical structure of the natural compounds isolated from them. In this topic, the GC-MS analysis of the skin secretion of the endemic species of newt *Triturus ivanbureschi* was carried out, based on which cholest-5-en-3-ol was identified as the main component.

The second topic in the research activity of Dr. Doncheva is represented in the attached publications with numbers B1, B4, B5, B6, Г1, and Г4. In five of these articles, the applicant is the first author, implying her primary role in conducting the research published in them. Using various spectral techniques (GC-MS, NMR) and comparing with authentic samples, 246 alkaloids were identified in species of the plant genera *Glaucium, Fumaria, Coridalis, Alkanna,* and *Hypecoum*, with 86 of these compounds reported for the first time in the respective species. The change in the alkaloid composition of species from the genera *Glaucium* and *Fumaria* was monitored depending on the geographical location of the populations, based on which conclusions were drawn regarding the existing Bulgarian chemotypes. The results of the comparative analysis of the alkaloid composition of the species of the genera *Coridalis, Alkanna,* and *Hypecoum* are examined from a chemotaxonomic point of view to clarify the taxonomic status of some Bulgarian endemic species, such as *C. slivenesis, A. primuliflora, A. stribrnyi, A. graeca,* and *H. ponticum*.

Only two publications (Г2 and Г7) are classified as Ch. Associate Professor Doncheva's third topic of research. In the first document, she is listed as the primary author while in the second document, she is listed as the secondary author. Both articles are related to *in vitro* cultivated and

ex vitro adapted endemic species *Papaver degenii* (Urum. & Jav.) Kuzmanov. A significant increase in alkaloid content (5- to 6-fold) was found in the *in vitro* cultivated and *ex vitro* adapted plants (aerial parts and roots) compared to the wild ones. The main alkaloid in all analyzed samples is amurensine, a promising candidate for the development of future medicinal products intended for the treatment of neurodegenerative diseases. It was found that its content in the total alkaloid mixture was 63.4% and 88.1% in the *in vitro* cultures and in the aerial parts of the *ex vitro* adapted plants, respectively. The successful application of biotechnological approaches has enabled the utilization of rare and endangered species without harming their wild populations.

Along with the presented evidentiary material covering the mandatory requisites of the documentation, Ch. Assist Prof. Doncheva has attached evidence (summaries and title pages of books with summaries) for her participation in 11 poster and oral presentations at international and national scientific forums. In addition, Dr. Doncheva presented a list of 6 international and 5 national projects in which she is a participant and 3 of which she is the lead researcher. She has prepared numerous anonymous reviews of manuscripts submitted for publication in renowned journals (Natural Product Research, Chemistry and Biodiversity, Molecules, BMC Chemistry, Scientific Reports, Bulgarian Chemical Communications) in the field of this competition. In addition, she participated in the development of a utility model, was the scientific supervisor of two master theses, and was a scientific advisor to one Ph.D. student.

The testimony provided by Dr. Tsvetelina Doncheva confirms my initial impressions of her. She is highly focused on her scientific interests, particularly concerning the isolation, structural characterization, and qualitative and quantitative analysis of alkaloids. However, this does not prevent her from displaying scientific curiosity towards other subjects, such as triterpenes in *Gentiana cruciata*, pertaining to the chemistry of natural and physiologically active substances.

3. Critical remarks and recommendations

In her habilitation thesis, Dr. Tsvetelina Doncheva outlines her plans for future work, which includes the continuation of her current research. As a main recommendation, I would suggest that the applicant expand her scientific interest to include other groups of biologically active substances.

CONCLUSION

The documents and materials presented by Ch. Assist. Prof. Tsvetelina Emilova Doncheva, Ph.D. met all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of the LDASRB, the Regulations for the Implementation of the LDASRB of the Bulgarian Academy of Sciences and the Regulations of the IOCCP-BAS.

The applicant in this competition has submitted a sufficient number of scientific works published after the materials used in her Ph.D. thesis. The applicant's original scientific and applied contributions have been internationally recognized with numerous citations. A representative part of her work has been published in journals with an impact factor and in book chapters published by international academic publishers. The scientific qualification of Ch. Assist. Prof. Doncheva's in the field of chemistry of natural and physiologically active substances is undoubted.

The achievements of Ch. Assist. Prof. Tsvetelina Emilova Doncheva, Ph.D. in her research activity fully correspond to the specific requirements of the Regulations of the IOCCP-BAS for the application of LDASRB.

After reviewing the materials and scientific works presented in this competition, and analyzing their significance, scientific-applied contributions, and applied contributions, I strongly recommend that the Scientific Jury prepare a report-proposal to the Scientific Council of IOCCP-BAS for the appointment of Ch. Assist. Prof. Tsvetelina Emilova Doncheva, Ph.D. to the academic position of "associate professor" at IOCCP -BAS in professional direction 4.2, Chemical Sciences, scientific specialty "Bioorganic Chemistry, Chemistry of Natural and Physiologically Active Substances".

April 10, 2024

Reviewer: .....

/Assoc. Prof. Paraskev Nedialkov, Ph.D./