Review

by Prof. Dr. Strahil Berkov

Institute of Biodiversity and Ecosystem Research at the Bulgarian Academy of Sciences (IBER-BAS)

of the materials submitted for participation in the competition to hold the academic position of 'associate professor' at the Institute of Organic Chemistry with the Center for Phytochemistry (IOCCP), BAS in the field of chemical sciences and professional direction “Bioorganic chemistry, chemistry of natural and physiologically active substances” announced in the State Gazette, no. 102 of 08.12.2023 and on the website of the IOCCP, BAS.

1. Summary of the received materials

Only one candidate, Dr. Tsvetelina Emilova Doncheva, has submitted documents for participation in the announced competition.

The set of documents presented by Dr. Tsvetelina Doncheva is in accordance with the Rules for the Development of the Academic Staff of the IOCCP, and meets the criteria of the IOCCP-BAS for occupying the academic position of "associate professor".

Dr. Tsvetelina Doncheva has submitted a total of 19 scientific papers and a list of 14 scientific research projects, in which she participated. 19 scientific papers, published after her PhD dissertation and 14 scientific research projects are accepted for review. Scientific works included in the PhD dissertation and those outside the competition's issues are not reviewed. The distribution of the presented scientific articles in the quartiles according to the Scimago Journal Rank (SJR) metric for Scopus refereed scientific journals is as follows: two publications fall in Q1, seven in Q2, seven in Q3 and two in Q4.

2. General information on the applicant's career development

Tsvetelina Doncheva obtained a master's degree with a specialization in "Biotechnologies" from the University of Chemical Technology and Metallurgy - Sofia in 1998. From 1999 to 2010, she worked as a chemist at IOCCP, BAS. In 2010, he defended his PhD dissertation on the topic "Alkaloid composition of species from the Datureae tribe" and held the position of chief assistant at the same institute. Dr. Doncheva is the author of 29 scientific papers, 22 of which are in peer-reviewed journals. She participated in 9 international (as coordinator of 3 of them) and 5 national projects. She is a member of the collective of a utility model registered in 2023. She has reviewed articles in prestigious international journals such as *Natural Product Research*, *Chemistry and Biodiversity*, *Molecules*, *BMC Chemistry* and *Scientific Reports*. Dr. Doncheva is a member of the Bulgarian Phytochemical Association and the Union of Chemists in Bulgaria.

3. General description of the activity of the candidate

Evaluation of the candidate's scientific and applied activity

Nineteen publications are reviewed in the current competition, of which 18 are in journals with an impact factor and 1 is in a book published abroad. Dr. Doncheva has published in prestigious scientific journals such as *Natural Product Communications*, *Natural Product Research*, *PloS ONE*, *Biochemical Systematics and Ecology*, *Diversity*, etc. The candidate is first author in 11 out of 19 publications. The scientific results have been presented in 7 international and 4 national scientific forums.

Considering the criteria for minimum requirements of IOCCP for holding the academic position of 'associate professor', Dr. Doncheva has 100 points according to indicator B (with a minimum of 100 points), 234 points according to indicator D (with a minimum of 220 points), 300 points according to indicator D (with a minimum of 70 points) and h7 according to indicator G (with a minimum of h≥5).

Assessment of educational and pedagogical activity

From the presented CV, it is evident that Dr. Doncheva was the supervisor of two graduate students and a consultant of one foreign doctoral student.

Contributions (scientific and applied) and citations

The contributions presented for the competition are mainly of a scientific nature and summarized in three fields:

• Investigation of the composition, structure and biological activity of secondary metabolites isolated from hitherto unexplored, rare and/or endemic plant species and organisms.

• Comparative analysis of the alkaloid composition of plants of the genus *Fumaria*, *Glaucium*, *Coridalis* and *Hypecoum* and derivation of taxonomic and chemotypic relationships.

• Determination of the alkaloid composition of *in vitro* cultivated and *ex vitro* adapted endemic plants.

Of the six publications presented (B1 – B6) according to indicator B of the criteria for minimum requirements of IOCCP-BAS for occupying the academic position of 'associate professor', two have been published in journals with Q2 and four in journals with Q3. Dr. Doncheva is first author in five of the articles and corresponding author in the sixth article.

Considering the first field of contributions, as the most essential contribution I would highlight the structural identification with spectral methods (^{1}H and ^{13}C NMR, ^{1}H-^{1}H COSY, ^{1}H -^{13}C HSQC, ^{1}H -^{13}C HMBC, NOESY, UV, IR and MS) of 3 new for science natural compounds, leptopyrin [G8] and leptofumarin [B2] from *Leptopyrum fumarioides* and hypepontin [G5] from *Hypecoum ponticum*. Leptofumarin is a novel dimeric aporphine-benzylisoquinoline type alkaloid linked by two ether bridges. Leptopyrine is the first example of a dimeric

alkaloid containing a benzyltetrahydroisoquinoline moiety linked to 3,4-dihydroisoquinoline. *L. fumarioides* (the only representative in the genus *Leptopyrum*, Ranunculaceae) and *H. ponticum* (a Balkan endemic) were studied for the first time. Dr. Doncheva is the lead author in publications G5 and G8 and the corresponding author in publication B2, which is indicative of her contribution to the isolation and identification of the above-mentioned new alkaloids.

As a significant contribution, I would also highlight the reporting for the first time of 23 alkaloids in plants from the genera *Leptopyrum, Hypecoum, Papaver, Pandanus* and *Thalictrum* [B2, B3, D5, D6, D8 and D10].

It should also be noted the first study on the alkaloid composition of the Bulgarian endemic *Papaver degenii* from the family Papaveraceae, from which 14 alkaloids were isolated and identified and Dr. Doncheva is the lead author [B3].

Regarding the second field of contributions, I would highlight the study on the alkaloid composition of plants from the genera *Fumaria, Glaucium, Coridalis* and *Hypecoum*, in which 86 alkaloids were reported for the first time in the respective species out of a total of 246 identified compounds.

The establishment of chemotypes in *Glaucium flavum* is a contribution with scientific and applied significance [B6], where Dr. Doncheva is the lead author. The yellow poppy is a raw material for obtaining the alkaloid glaucine, from which Sopharma AD produces a number of pharmaceutical preparations sold on our and the international market. Establishing populations with high glaucine content is a key for future selection of high-yielding genotypes to optimize production.

Also, a team of authors led by Dr. Doncheva studied various species of the genus *Fumaria* and established two new chemotypes for the genus with predominant spirobenzylisoquinoline and protopine alkaloids in the alkaloid mixtures [B1].

From a taxonomic point of view, the study on *Corydalis slivenensis* and *C. solida* (Papaveraceae) is of interest, where significant differences in the alkaloid composition were found [B5]. *C. slivenesis* is a Bulgarian endemic with not yet fully clarified taxonomic status and considered by some authors to be a variety or subspecies of *C. solida*.

In a similar study, it was found that *Hypecoum ponticum*, which some authors consider as a synonym of *H. procumbens*, is well separated from *H. procumbens* and *H. imberbe* due to the presence of a large number of quaternary isoquinoline alkaloids [G4]. Dr. Doncheva is the lead author of the above-mentioned two studies.

Dr. Doncheva's ability to identify alkaloids in plant samples by GC-MS allowed her to make contributions in the field of alkaloid composition in *in vitro* cultivated and *ex vitro* adapted endemic plants. The candidate studied for the first time the quantitative and qualitative alkaloid composition in *in vitro* cultures and *ex vitro* adapted plants of the endemic *Papaver degenii* [G3 and G7], where she found a significantly higher alkaloid content in the *in vitro* cultures compared to the wild ones. Dr. Doncheva is the lead author in one of the two articles with contributions in this field.

The articles proposed for review have been cited 150 times (without self-citations) in journals referenced and indexed in world-famous databases (WoS and Scopus), which is indicative of the interest and significance of the research conducted by the candidate.

As a summary, the scientific articles and the response from the international scientific community undoubtedly show that Dr. Tsvetelina Doncheva is a well-established scientist, recognized internationally, who has significantly contributed to the enrichment of our knowledge on the chemical diversity of biologically active substances (alkaloids in particular) in rare and endemic plants from the Bulgarian flora, as well as in foreign species. Her skills of a classic phytochemist to isolate and identify natural substances with spectral methods, as well as to identify those in complex mixtures with chromatographic methods, are very valuable for the continuation of the traditions and development of the phytochemistry and the alkaloid chemistry, in particular, in our country.

4. Evaluation of the candidate's personal contribution

The personal contribution and merits of Dr. Doncheva in the experimental work, processing and interpretation of the results and preparation of the publications is undoubted, evident from the fact that she is the first author in 11 of the 19 scientific papers submitted for review in this competition.

5. Critical remarks and recommendations

As a critical note, I would point out that the wording of the contributions could be structured more clearly and concisely.

6. Personal impressions

I have known Dr. Tsvetelina Doncheva for more than 20 years as a serious, erudite and responsible colleague with a desire to work in the field of alkaloid chemistry. These qualities are important for the successful development of this scientific field in our country.

CONCLUSION

The documents and materials presented by Dr. Tsvetelina Doncheva meet 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 in the Bulgarian Academy of Sciences and the Regulations of the IOCCP-BAS.

The candidate has submitted a sufficient number of scientific articles published after her PhD thesis defense. The candidate's works contain original scientific and applied contributions that have received international recognition and have been published in journals issued by

international academic publishing houses. The scientific qualification of Dr. Tsvetelina Doncheva is beyond doubt.

The scientific results achieved by Dr. Tsvetelina Doncheva fully correspond to the specific requirements of the Regulations of the IOCCP-BAS for the application of LDASRB.

After reviewing the documents and scientific papers presented in the competition, analyzing their scientific and applied significance, I find it reasonable to give my positive assessment and to recommend the Scientific Jury to prepare a report-proposal to the Scientific Council of IOCCP-BAS for the election of Dr. Tsvetelina Doncheva as an associate professor at IOCCP-BAS in the field of Bioorganic chemistry, chemistry of natural and physiologically active substances.

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Prof. Dr. Strahil Berkov