R E V I E W

by **Snezhanka Metodieva Bakalova, PhD,**

Associate Professor at the Institute of Organic Chemistry with Centre of Phytochemistry of the Bulgarian Academy of Sciences (IOCCP - BAS), member of the Scientific Jury, Order of the Director of IOCCP – BAS No РД-09-125/23.06.2025

On the documents deposited for participation in the competition for the academic position of “professor”

In the professional area 4.2. Chemical Sciences, scientific specialty 01.05.10 Bioorganic chemistry, chemistry of natural and physiologically active compounds

1. General presentation of received documents

The competition for the academic position “Professor” at the IOCCP - BAS has been announced by the State Gazette, rel. 40 of 16.05.2025 and on the internet page of IOCCP – BAS. Documents for participation in the competition have been submitted by a single candidate, Associate professor Doctor of chemical sciences Vanya Nikolova Mantareva, IOCCP – BAS

The deposited set of documents by Vanya Nikolova Mantareva corresponds to the Regulation of development of the academic personnel of IOCCP as well as to the criteria of IOCCP – BAS for occupying the academic position of “professor”. A review of these papers shows that the competition procedure is regular, and the documents follow the requirements of the Law of Development of the Academic Staff in the Republic of Bulgaria. The set is also in accord with the regulations of academic staff development of BAS and the criteria of IOCCP – BAS awarding the position of “professor”. Included are: scientific curriculum vitae; checklist of minimal requirements of the Regulations for the implementation of the same Law of IOCC-BAS for the scientific degrees and positions; diplomas for acquiring the educational and scientific degree of "doctor" (PhD), scientific degree DrSc, and for awarding the academic position of Associate professor; Abstract of the PhD thesis; Abstract of the DrSc thesis; Extended habilitation reference for scientific contributions in Bulgarian and

English; full list of scientific publications; a list and copies of the publications for the competition equivalent to habilitation thesis by group of indicators B; a list and copies of the publications articipating in the competition by group of indicators D; a list of conference participations with certificates; a list of citations; a list of participations in research projects.

The applicant Vanya Nikolova Mantareva has supplied a list of 90 scientific articles for her scientific carreer. In the present competition she participates with 26 papers and a published book on the basis of the DrSc thesis. Five publications are equivalent to habilitation thesis (group C), and 19 papers participating by group of indicators D. A publication with impact factor from databases other than Scopus or Web of Science, but no quartil is in each of groups C and D. The distribution of papers over quartils is Q1: 5 papers; Q2: 7 papers; Q4: 3 papers. All of the 26 papers correspond to the theme of this competition and have not been deposited for other competitions or procedures entered by this candidate. Therefore, all of these are accepted and will be taken into account for the final evaluation. A list of 9 research projectis is deposited as well. There is no data on implemented methodologies.

2. Brief biographic data

Vanya Mantareva graduated Higher Chemical Technology Institute (now University of Chemical Technology and Metallurgy), Sofia with a master degree in chemical engineering in 1991. Since 1991 she was affiliated to the IOCCP-BAS in the field of bioorganic chemistry. In 1998 she defended successfully a PhD thesis. She graduated as PhD in 1998. In the period 1999 – 2003 she was on grants at the Universities of Bremen, Louisville, Kentucky, and Autonoma de Madrid. She worked thereafter at the IOCCP-BAS in the area of bioorganic and analytical chemistry. In 2021 she obtained the scientific degree of Doctor of Chemical Sciences from the IOCCP – BAS. She is fluent in English, and uses Russian and German as well.

Vanya Mantareva has competence and experience in the mentorship of student graduates and a PhD student. She is capable in the coordination and the expertise with colleagues of other natural science branches. Also has the expertise to coordinate projects as lead scientist and partner in projects of other colleagues in natural sciences.

3. General characteristic of applicant activities. Evaluation of scientific activity

The main area of scientific activity of the candidate is PDT (PhotoDynamic Therapy) used in mainly in medicine and ecology. PDT comprises cascade photophysical and subsequent photochemical processes at selected optimal conditions as results of appropriate irradiation of a photosensitive compound. PDT is now developing rapidly in the direction of its three components: photosensitizers, light sources and oxygen saturation of the medium.

The candidate works mainly in the area of photosensitizers which should absorb light in the range between visible and near infrared. This is characteristic for compounds with sufficiently extended conjugated structure. This scientific area has initially started in Bulgaria in a laboratory of the IOCCP – BAS parallel to other world scientific labs in the 80^{th} years of the last XX century. The result of these first scientific efforts has been a patent for a porphyrine compound for clinical applications of tumor PDT in Bulgaria. Further years saw continued development of a new generation of photosensitizers on the basis of phthalocyanine and naphthalocyanine derivatives which meet the requiredments of photodynamic methods applicable in biomedicine. The candidate started her work in IOCCP – BAS in 1991 in this very laboratory and continues its developing today.

Nowadays PDT is rapidly developing for problems related to its three components: photosensitizer, light sources and radiation transfer, and approaches to oxygen saturation of the media. Therefore PDT is persistently in the focus of scientific challenges, due to low specificity of effects of photosensitization products processes and also due to the urgent need for different mechanism of action for the rapidly varying reality of increasing drug resistance. The PDT method is accepted as effective modern therapy, without alternatives in urgent life-threatening situations.

The direction of syntheses of novel photosensitizers includes the development of novel structures based on the porphyrine cycle, generalized as porphyrinoid compounds, as well as other photoactive compounds with structures differing from porphyrin. All these are considered second and third generation photosensitizers. Phthalocyanines are considered porphyrinoid compounds with the so called flexible structures for chemical modifications and unique photo- and physicochemical properties and unlimited potential for diverse applications. Importantly, this scientific topic has been introduced first in a laboratory of IOCCP along with world scientific centers at the early 80's of the 20-th century, and the first studies led to the patent of a porphyrine compound for clinical application in tumor PDT in this country. The following years saw

continued work on a novel generation of photosensitizers based on phthalocyanine and naphthalocyanine derivatives, aiming to cover the requirements for a photodynamic method applicable in biomedicine.

4. Scientific contributions and Citations

The habilitation report is clear and finely structured. The papers supplied for the competition belong to four scientific topics: 1. Novel phthalocyanine complexes as photosensitizers for PDT. Synthesis and photo-properties; 2. Natural photosensitizers – cobalamine and anthraquinone derivatives; 3. Conjugates of phthalocyanine complexes with proteins and enzymes; 4. PDT with phthalocyanines for socially significant maladies – antimicrobial PDT, PD inactivation of viruses, tumor PDT.

The latter research of Dr. Mantareva deals with the third generation of photosensitizers for PDT. The new photosensitizers being developed for the PDT method are based on the ring molecule of phthalocyanine with possible peripheral, non-peripheral, and axial functional substituents. Various phthalocyanine metal complexes have been synthesized; with best effect in the PDT experiments are those of lutetium, palladium and gallium, studied in comparison to zinc complexes of the same ligands. Functional substituents have been cationic and biologically active, and receptor oriented, as well as specific for pathogenic microorganisms or tumor cells. This part of candidates' studies has the most weight among the deposited materials according to quartiles (Q1 and Q2) of the respective publications. The candidate is first and corresponding author of six of these publications.

The common feature of candidate's work is the development of PDT for potential novel medicinal applications. Studies of cobalamine applications to PDT are related to the reduction of phthalocyanine sensitizer toxicity in the dark, as well as of its phototoxicity. The effect is positive and improves selectivity, beneficial for its further application. The candidate is first and corresponding author of both papers on this topic. One of these has a quartile of Q1, ant the other has SJR.

The properties of natural plant anthraquinones as cures in tumor chemotherapy are well known. Their studies as natural photosensitizers are at a starting stage. The candidate coauthors a review paper in this direction.

Physical conjugates of a phthalocyanine sensitizer with protein (collagen hydrolysate) and an enzyme (alpha-chymothripsin) are stable and useful transport means to the target cells. Two of the deposited Q1 papers in these directions have the candidate as the first and corresponding author, and a third has SJR.

PDT may be used to inactivate pathogenic bacteria, which is very important in the current drug resistence situation. Inactivation of viruses is also an area of use of PDT. Studies in this direction are carried out by the candidate in collaboration with colleagues of the Institute of microbiology of BAS.,

The articles of the candidate in group C deal simultaneously with results of the four topics discussed so far, which gives a multidisciplinary character as well. In total, the candidate is first and corresponding author of 11 of the deposited papers, which is an argument for significant personal contribution. The papers where contributions are declared show that the candidate participates in conceptualization, sometimes alone, as well also in the methodology.

Eight papers (full text conference reports) in collaboration with Russian universities have the candidate participating with synthesized by her compounds, as well as with ideas for their application in tumor PDT. The candidate has a long year collaboration with Prof. Mahmut Durmus of the Gebze Technical University Turkiye. She also has a science collaboration with China since 2024.

The candidate participates in 4 projects with the National Science Fund, and is the coordinator of one of these (КП-06-Н29/11, 2018-2022 г.) She is on good terms with prominent scientists and may count on their advice and expertise (Prof Dieter Woerle, Uni Bremen).

The articles of the candidate have accumulated 249 citations since 2022. 21 of these are of 4 publications of the past century. Cited publications after 2002 are 40, and are authored by large international groups. This is an argument in favor of significant attention to these works, which have accumulated 241 citations so far. In total, there are 249 citations since 2022, without self-citations. The H-index is 17. Titles of the citations are methodological, as well as with direct medical application, and show broad international popularity.

No data are given on applied activities of the candidate. The personal contribution to the deposited publications is hard to evaluate, due to the participation of many coauthors. A separation might be possible knowing the personal attitudes of every author. In the case of V. Mantareva, the attitude is well defined to the potential medicinal applications and defines the personal contribution as well.

General requirement group points accumulated by the candidate are:

Criteria	Minimum required for professor of the IOCCP-BAS	Points of the candidate
A	50	50
B	-	100
C	100	115
D	250	296
E	200	498
F	150	359
G (H – factor)	≥ 10	17

Numerical characteristics of the candidate are better than the requirements of the applied Regulations for the implementation of the LAPDRB as well as those of IOCCP-BAS everywhere possible, with criteria E and F overcame by more than twice. The H-factor 17 is significantly higher than the required 10.

5. Critical remarks and recommendations

Future application and usefulness of scientific contributions of the candidate are out of doubt. As far as these contributions are related to medicine, they may be expected to have immediate and lasting success should good sensibiizator(s) for PDT be found.

6. Personal impressions

I have been coordinating a project with Vanya Mantareva as participant. Works quickly and precisely, always discussing the arising problems. Actively takes part in the discussions with colleagues, having her own ideas and suggestions as well.

CONCLUSION

The documents and materials presented by Assoc. Prof. Vanya Nikolova Mantareva fully comply with all the requirements of the Law of Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the implementation of the same Law and the specific requirements in view of the corresponding Regulations in BAS and the IOCCP - BAS.

The candidate in this competition has presented a sufficient number of scientific papers which have not been used in the competitions for acquiring the PhD, the scientific degree of Doctor of Sciences and for the academic position “Associate professor”. The candidate has internationally recognized original scientific contributions, a representative part of them being published in journals of international academic publishers.

After reviewing the materials and scientific works presented in the competition, analysis of their significance and the scientific contributions contained in them, I confidently give my positive assessment of the candidate and recommend the members of the Scientific Jury to submit a report-suggestion to the Scientific Council of the IOCCP-BAS to award Vanya Nikolova Mantareva with the academic position of “professor” at the IOCCP – BAS in the professional area 4.2. Chemical Sciences, scientific specialty Bioorganic chemistry, chemistry of natural and physiologically active compounds.

Sofia, September 20, 2025 Reviewer: ……..

Assoc. professor Dr. Snezhanka Bakalova