

REVIEW

from Prof. DSc Sonia Varbanova Ilieva,

Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski"
of the materials submitted for the competition for the academic position of **'Professor'**
in the **Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski"**,
higher education professional field **4.2. Chemical Sciences (Analytical chemistry)**

In the competition for the academic position 'professor' announced in the State Gazette, issue 57/26.06.2020, **Assoc. Prof. Dr. Ivayla Nedyalkova Pantcheva-Kadreva** from the Faculty of Chemistry and Pharmacy, Sofia University is the only candidate.

General presentation of the materials deposited

The materials submitted by Assoc. Prof. Ivayla Pantcheva **meet all the requirements** of the Law for the Development of the Academic Staff in the Republic of Bulgaria and the relevant regulations for its implementation (including those of Sofia University and Faculty of Chemistry and Pharmacy). The applicant meets and exceeds the criteria (minimum requirements) of the Faculty of Chemistry and Pharmacy for the academic position "Professor".

Associate Professor Pantcheva has published a total of 52 scientific papers (33 in peer reviewed journals, 19 in international journals without impact factor, 350 citations, h index 9) and for the participation in this competition she has submitted **19 publications in scientific journals and 3 papers in conference proceedings**, which do not repeat the ones presented in other competitions for occupying academic positions and obtaining scientific degrees. Submitted publications are distributed among the relevant Q factors as follows: 2 - Q1; 6 - Q2; 7 - Q3; 4 - Q4.

The candidate has submitted a **habilitation thesis** "Diversity in the properties of the natural antibiotic Monensin" and a **report for the scientific contributions** of the research work. The main scientific contributions of Assoc. Prof. Pantcheva are discussed in the report in a concise and clear manner. The presentation of the scientific results in the habilitation thesis is accompanied by a brief discussion of the place of the relevant developments in a given scientific field as a whole and their contribution in solving specific problems in the field.

Brief biographical information

I. Pantcheva graduated as a Master of Sciences in Inorganic and Analytical Chemistry at the Faculty of Chemistry, Sofia University "St. Kl. Ohridski" in 1993. In 2001 she defended her doctoral thesis on the topic "*Copper II complexes with antihypertensive drugs*". Then she continued her scientific work at the Faculty, Department of Analytical Chemistry as an assistant (until 2006) and subsequently chief assistant (2006-2011). Since 2011 she has held the academic position of Assistant Professor in the same laboratory. Therefore, the professional and scientific experience gained is fully linked to the announced competition.

Assoc. Prof. Pantcheva has specialized in foreign research groups - Tokyo Institute of Technology and Okayama University, Japan, Szeged University, Hungary, Aarhus University, Denmark. She has

participated in a number of national / international scientific congresses conferences and research / educational projects. Her teaching activity is rich and diverse and is expressed in the management of graduates, postgraduates and doctoral students, as well as in regular teaching activities in the Faculty.

General characterisation of the applicant's scientific activities

The applicant's overall scientific activity is in the field of analytical chemistry that is completely in line with the announced competition. Scientific publications submitted for participating in the competition reflect the work of Assoc. Prof. Pantcheva in two **main scientific areas: biocoordination and bioanalytical chemistry.**

In the field of biocoordination chemistry, the work of Assoc. Prof. Pantcheva is dedicated to the study of complexes of natural biologically active substances: polyether ionophore antibiotics Salinomycin and Monensin, Salinomycin sodium and Monensin sodium, acetylcholinesterase reactivators – Obidoxime and oxime containing ACE reactivators. Short-time and long-term experiments have been performed to study the biological activity of the natural antibiotics metal complexes. The complexes studied were found to be cytotoxic in human tumor cell lines. The conducted research has contributed to the knowledge expansion in the field of coordination chemistry of polyether ionophores, and at the same time new approaches and methods for analysing their properties have been established and further developed. A number of spectral techniques (IR, ESI-MS, FAB-MS, EPR, (SR)CD) and computer modeling based on density functional theory (DFT) were used in the work. The obtained results have led to new insights into coordination chemistry of natural antibiotics and new fundamental understandings of the properties of this class of compounds. Bulgaria is one of the few countries - producers of polyether ionophores (Monensin and Salinomycin) and part of the research in this field resulted from the close cooperation with Biovet-Peshtera, where one of the graduates of Assoc. Prof. Pantcheva (chemist Petar Dorkov) started his work experience.

In the field of bioanalytical chemistry, the main contributions of the scientific work of Assoc. Prof. Pantcheva are related to (i) studies of the properties and biochemical activity of the enzyme phospholipase A2, isolated from the neurotoxin Vipoxin, isolated from the Bulgarian viper; (ii) the oral fluids as an object to study in forensic toxicology; (iii) anaesthetics and psychoactive substances - propofol, synthetic cannabinoids.

The main object under consideration in the presented **habilitation work** is the polyether ionophore antibiotic Monensin. This veterinary antibiotic is practically inapplicable in humans due to its acute cardiotoxicity. It has been found that the biological activity of Monensin is influenced by the presence of a number of metal ions. Studies have been performed on the complexing ability of Monensin acid against a number of metal cations in varying degrees of oxidation. The possibility of the formation of new neutral polynuclear complex species, which show increased biological activity, has initiated studies of the antibacterial and antitumor activity of the newly obtained complexes. The results show that all compounds are toxic against targeted cell lines, including resistant ones, as well as the activity concentration range is quite similar. In most cases, the new coordination compounds have increased biological activity compared to the free (uncoordinated) antibiotic.

Structural studies of the complexation of Monensin with mono-, two- and three-charged metal ions in solution have been performed by applying spectra of circular dichroism (CD), circular dichroism with synchrotron radiation (SRCD), quantum chemical calculations using (TD)DFT approaches. The biological (antitumor) activity of Monensin acid and its complexes with some ions of biometals (Mg, Ca, Co, Mn, Ni, Zn) has been studied. All compounds have been found to significantly reduce the proliferation of treated cells (cultured human cell lines) and a dependence on treatment time and concentration exists. The metal complexes are more effective than the uncoordinated ligand Monensin acid.

It is evident from the publications presented that Assoc. Prof. Pantcheva has established fruitful **collaboration** with colleagues from the Faculty; Bulgarian teams from the Faculty of Pharmacy, Medical University, Sofia; MMA (Military Medical Academy); IOCCP and IEMPAM, BAS, Biovet/Huvepharma - Peshtera; foreign research groups from Japan, Hungary, Czech Republic.

I would like to emphasize the **interdisciplinary nature of the scientific work** of Assoc. Prof. I. Pantcheva that is confirmed by the above discussion and the published scientific developments. The focus of the research has been on the structure and complexation of natural antibiotics with metal ions. This is confirmed by the fact that the habilitation report reflects studies of Monensin coordination complexes. But at the same time, as already mentioned above, the work of Assoc. Prof. Pantcheva includes research on biological activity (*in vitro*, *in vivo*), developments of new and improved methodologies for structural characterization and analysis, theoretical quantum chemical calculations, including by establishing scientific collaboration with colleagues in Bulgaria and abroad. In my opinion, this is the strongest proof for the continuous scientific growth of I. Pantcheva, and therefore the professor position is a natural result in her scientific career.

I. Pantcheva is the leading/corresponding author in 12 out of 22 scientific works submitted for the competition. The average impact factor of the publications is 1.27, ranging from 0.242 (Bulg. Chem. Commun.) to 3.067 (RSC Advances).

The research carried out and the published results have **scientific as well as applied contributions** in the relevant fields of science. These contributions can be formulated as: substantiations of significant new sides of already existing scientific fields, problems, theories, hypotheses by means of new methods and approaches; creating new methodologies for analysis; getting new facts. These contributions are corroborated by reputable international scientific journals in which the articles have been published, as well as by **citations** in the scientific literature. The total number of citations (Scopus) is 350, 69 of which are on the publications submitted for this competition. Therefore, the research work of Assoc. Prof. Pantcheva is in extremely topical areas of scientific knowledge, with issues that are widely recognized in the scientific community, and the results achieved have high impact scientific contributions. The scientific results are disseminated through 116 participations in national and international scientific forums, including 45 oral presentations.

For the period 2012-2020 Assoc. Prof. Pantcheva participated in 10 national and 2 international scientific/educational projects, being the leader of 3 research projects. I would like to highlight the project in the framework of the Operational Programme Science and Education for Smart Growth, implemented

under the leadership of Assoc. Prof. Pantcheva and to emphasize the competence, exceptional responsiveness and collegiate approach of Ivayla that were highly appreciated by all participants.

The educational and pedagogical activity of the candidate is extremely replete and diverse. Since becoming an associate professor (2011), I. Pantcheva has been a lecturer in Analytical Chemistry for students of two specialties, Bachelor degree, Faculty of Biology, Sofia University and for Master degree students in Pharmacy in our Faculty, including lectures in English for foreign students with an annual teaching load of 240 lecture hours. For the period 2012-2020 she was the supervisor of 6 diploma works, 3 of which for foreign students from the University of Barcelona, and 2 dissertations. It should be mentioned that after the successful defence of theses and dissertations, Assoc. Prof. Pantcheva continues to actively work with graduated colleagues that is expressed in fruitful scientific collaborations, resulting in the published scientific articles.

CONCLUSION

According to the submitted materials and scientific papers, the above analysis of their importance and scientific contributions, as well as my personal opinion about the candidate as a highly erudite scientist, I am convinced in my **positive assessment** and firmly recommend to the Scientific Jury to prepare a report-proposal to the Faculty Council for the selection of **Assoc. Prof. Dr. Ivayla Nedyalkova Pantcheva-Kadreva**, for the academic position of '**Professor**' in the professional field **4.2. Chemical Sciences (Analytical Chemistry)** at the Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski".

08.10.2020 г.

Reviewer:

Prof. Sonia Ilieva