R E V I E W

on the competition for the occupation of the academic position **"Professor"** in Higher Education Area 4. "Natural Sciences, Mathematics and Informatics", Professional field 4.2 “Chemical Sciences” (Analitical chemistry) for the needs of the Faculty of Chemistry and Pharmacy at Sofia University “St. Kl. Ohridski", announced in the Bulgarian State Newspaper, vol. 57 from July 26, 2020

By Assoc. Prof. Dr. Mariya Ivanova, Faculty of Chemistry and Pharmacy at Sofia University “St. Kl. Ohridski", Member of a Scientific Jury, appointed by Order RD-38-56 from 30.07.2020 of the Rector of Sofia University, selected as a reviewer at the first meeting of the Scientific Jury on 04.09.2020.

Only one applicant has submitted documents for participation in the announced competition – **Assoc. Prof. Ivaila Nedialkova Pantcheva-Kadreva** (*Scopus Author ID 6506664875* **)**

APPLICATION DATA

Assoc. Prof. Dr. Ivaila Pantcheva – Kadreva presented all required documents in electronic form which are in accordance with the Act for the Development of the Academic Staff in the Republic of Bulgaria (ADASRB, ЗРАСРБ), the Regulations for the application of the ADASRB, the Regulations for the terms and conditions for acquiring academic degrees and occupying academic positions at Sofia University "St. Kliment Ohridski" and the Recommended criteria of the Faculty of Chemistry and Pharmacy for acquiring scientific degrees and occupying academic positions at SU in professional field “ Chemical Sciences ”, related to the procedure for occupying the academic position (AP) “Professor”. The submitted documentation (19 pieces) is precisely prepared and provides comprehensive information about the research and teaching activities of Assoc. Prof. Dr Pantcheva-Kadreva.

BIOGRAPHICAL DATA, EDUCATION AND PROFESSIONAL EXPERIENCE

The applicant Ivaila Pancheva was born on 12.05.1969 in Sofia, Bulgaria. She has graduated with Master’s degree in Chemistry (Inorganic and Analytical Chemistry), Sofia University “St Kliment Ohridski“ with excellent grades in 1993. In 2001, the High Attestation committee awarded her the educational and scientific degree "Doctor" (PhD) in the specialty

01.05.04. "Analitical chemistry" after a successful defense of her PhD thesis on the topic: "Coper (II) complexes with antihypertensive medicinal products". Ivaila Pantcheva-Kadreva has over 20 years of experience in the speciality at the Faculty of Chemistry and Pharmacy at the Sofia University "St. Kl. Ohridski ". Since 1997 she has held the positions of "Assistant" and Senior Assistant Professor (2006), and in 2011 she acquired the academic position of "Associate Professor" which she holds till now. During the period 2011-2019 Assoc. Prof. Pantcheva-Kadreva has held a management position as a Deputy Dean of the Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski" with the respective intensive administrative activities and responsibilities. Assoc. Prof. Pantcheva-Kadreva is a faculty coordinator for the Erasmus+ programme.

During the period 2012-2020 she completed 9 short-term specializations under Erasmus+ programme and EU Calipso+ project at the Seget University, Hungary – 4 and Arhus University, Danmark – 5, carrying out useful international scientific cooperation.

The applicant presented a list of participations in 10 scientific projects in the period 2011-2020: four of which are national, funded by the Scientific Research Fund at the Ministry of Education and Science, four are funded by Operational Programs of the European Structural Funds, two by FP-7 REGPORT, one of which is international (Materials Networking – TWINNING, Horizon 2020). Assoc. Prof. Dr. Pantcheva-Kadreva was a project manager of three projects, two of which are under Operational Programs of the European Structural Funds, which proves team management skills and good knowledge of the regulatory basis of the project management through the Operational Programmes.

The international scientific community has recognized the scientific competence of Assoc. Prof. Dr.Pantcheva-Kadreva and therefore she has been invited to join the editorial board of the prestigious scientific journal The Scientific World Journal (Inorganic Chemistry).

EVALUATION OF SCIENTIFIC AND TEACHING ACTIVITY

Assoc. Prof. Dr Pantcheva-Kadreva has presented a list of the full scientific publications for her entire creative period, a list and copies of scientific publications for the participation in this competition and a Habilitation work.

Scientific publications

The full list of scientific publications of Assoc. Prof. Dr. Ivaila Pantcheva-Kadreva contains 53 scientific papers, 33(62.3%) of which are in referenced international journals and 19 are in a non-refereed in Scopus journals.

The total number of the applicant's **citations (until** 04.07.2020) is 336, 251 of which have been found in publications printed in refereed and indexed in Scopus editions. The Hirsch index (h-idex) of Assoc. Prof. Pantcheva-Kadreva, verified in the Scopus scientific information database without self-citations is 9 which indicates the high quality of work and the up-to-date tasks. Her scientific results are reported in 102 presentations at national and international forums, 43 of which are oral reports.

Assoc. Prof. Dr. Pantcheva-Kadreva participates in the competition for AP "Professor" with 22 original scientific publications. The publications were not included in the thesis for "Doctor" degree (2001) and in the list of publications for participation in the competition for AP "Associate Professor" (2011). The list of publications included 19 papers in **referenced journals** with impact factor and 3 chapters of three collective monographs (period 2011-2020). By quartiles (WoS and Scopus categorization) she has 2 (10.5%) publications in Q1 (first quartile), 6 (31.6%) publications in Q2 (second quartile), 7 (36.8%) publications in Q3 (third quartile) and 4 (21%) publications in Q4 (fourth quartile) journals.

Assoc.Prof. Dr. Pantcheva-Kadreva is a first and/or corresponding author in ten of these publications indicating the applicant's leadership role. Fourty citations were noted on the papers for the competition, 28 of which were in referenced and indexed in Scopus editions.

A total of 69 citations were included after she occupied the position "Associate Professor". The results of the research activities of Assoc.Prof. Dr. Pantcheva – Kadreva were reported in 16 national and 30 international scientific conferences in the form of 46 scientific communications (20 oral reports and 26 posters).

In regard to the fulfilment of the minimum national requirements for the academic position of "Professor" Assoc. Prof. Dr. Pantcheva-Kadreva has presented the following achievements: indicators group A – 50 points (required 50); indicators group C – 115 points (required 100); indicators group D – 251 points (required 220); indicators group E – 138 points (required 120).; indicators group F – 209 points (required 150) and indicators group G – 180 points (required 120). It is evident from the above summary that the applicant either fulfills or goes beyond the minimum national requirements in all groups of indicators. The overall scientific metrics are in compliance with the general requirements of ADASRB, the statutes for its application, and the additional recommendations of FCP.

A careful review of the materials submitted to me for review gives me a reason to claim that there is no evidence of plagiarism in the scientific works of Assoc. Prof. Dr Ivaila Pantcheva Kadreva and she fulfills the condition referred to in Article 29, Paragraph 1, Item 6

of the law. Additional basis for this statement is the publication of papers in reputable journals that monitor the plagiarism.

The Habilitation work of Assoc. Prof. Dr. Pantcheva-Kadreva on the topic: "The diversity in the properties of the natural antibiotic Monensin" fully meets the requirements in the Recommendations for the criteria for acquiring scientific degrees and occupying academic positions at Sofia University in professional field 4.2. “Chemical Sciences”. It has been prepared at a high scientific level and summarizes the applicant's research described in 6 publications, half of which are the research from the last 2 years. The candidate is the first author in 3 of the publications and a corresponding author of all publications, which shows the undisputed leading candidat’s role in the research work presented in these publications.

The Habilitation work is illustrated with 12 figures and presents studies on the properties of the polyether ionophorous antibiotic Monensin – a widely used natural antibiotic in vetirinary medicine for decades due to its coccidiostatic properties. In the last years, the scientific interest of Monensin is increasing with new experimental data for the potential use of polyether ionophores as antitumor agents, including against cultivated cell lines of human origin.

Based on the literature data and on the previous own results for Monensin in terms of coordination properties that allow complexation with metal ions to a higher degree of oxidation and seeking answers to the open questions regarding the complexes and biological action of Monensin (acidic and sodium form) Assoc. Prof. Dr. Pantcheva-Kadreva has carried out a series of logically justified experiments in solution and solid state. A new approach has been used to characterize Monensin complexes with monovalent (Li+, Na+, K+, Rb+, Cs+, Ag+ и EtN+), divalent (Co2+, Mn2+, Mg2+, Ca2+, Ni2+, Zn2+, Cd2+) и trivalent (La3+ и Nd3+) metal ions **in solution**, based on the method of **circular dichroism (CD) and synchrotron radiation circular dichroism (SRCD)**. In addition quantum-chemical models have been applied - computational modelling based on the density functional theory (DFT) and continuum solvent model, time-dependent density functional theory (TDDFT) etc. A series of biological tests were performed to assess the ability of the ligand and the corresponding complexes to affect the viability of bacterial strains and cell lines. On the basis of the in-depth research work described in these publications, fundamental scientific results have been obtained with the possibility of practical application.

Main scientific and scientific-applied achievements of the applicant

The information provided on the research activities of Assoc. Prof. Dr. Ivayla Pantcheva-Kadreva is prepared competently and fully reflects the contributions of the candidate. The main contributions can be summarized in the following two directions:

1. **(Bio)Coordination chemistry;**
2. **Bioanalitical chemistry**

The research work of Assoc. Prof. Dr. Ivayla Pantcheva-Kadreva in the **first direction** (publications № 1-4, 6,8,9, 11,13,17-22) has fundamental nature. In general, the original contributions can be summarized as follows:

- The ability of a series of natural biologically active substances to complex in a solution and solid phase has been evaluated. The studies in a solution have high scientific value because such investigations have not been carried out before and they play a key role in interpreting the results (especially biological ones). Representatives of this group are polyether ionophorous antibiotics Salinomicin, Monensin and macrolide antibiotic Tylosin as well as acetylcholinesterase (enzyme, the activity of which is blocked by the action of phosphorus organic compounds but can be recovered through the use of appropriate reactivators). **For the first time** in the literature it is reported the preparation and structure elucidation of new complexes with mono-, di- and trivalent metal ions in solution using precisely selected modern spectral techniques- IR, ESI-MS, FAB-MS, EPR, SRCD, quantum-chemical models have been applied in addition. The application of the **SRCD method** to characterize the ability of Monensin to interact with metal ions in different degrees of oxidation **in solution is a novelty** in the field.

- **It has been found** that the inclusion of a metal ion in the structure of complexes, in most cases, **significantly enhances the effect of biological activity** of free (uncordined) natural antibiotic. This conclusion is based on a series of *in vitro* experiments to assess the antitumor, antibacterial and acute toxic ability of the structurally characterized complexes of natural antibiotics Monenzin, Salinomycin and Tylosin.

- Some of the newly obtained complexes have a promising **antitumor effect** – these results were obtained on the basis of a series of *in vitro* experiments using a large number of cell lines of human and animal origin. For example, the antitumor eficacy of Monensic acid and its complexes with biometals (II) ions (Mg, Ca, Mn, Co, Ni, Zn) was evaluated against cultured human cell lines established from glioblastoma multiforme, cancers of the lung, breast, uterine cervix and liver, as well as against cultured permanent cell lines originated from virus-induced transplantable tumors in chicken (hepatoma) and in rat (sarcoma). The complexes of Monensic acid with La3+ and Nd3+ ions have been tested against cell lines from breast cancer

and transplantable sarcoma in rad. It has been established that all complexes significantly reduce the viability and proliferation of treated cells in a time-and-concentration-dependent manner with metal (II)/(III) complexes being more effective than the non-coordinated ligand.

- **The second direction** (publication No 5, 7, 10, 12, 14-16) is mainly scientifically applied with a significant contribution to medical practice. The most important results can be summarized as follows:

- The toxic subunit – **phospolipase A (sPLA2)** of the hydrodimeric neurotoxin Vipoxin, isolated from the Bulgarian long-nosed viper *Vipera ammodytes meridionalis*) **is characterized**. The effect of Ca2+ ions and some related divalent metal ions (Mg, Sr, Ba, Cd) on hydrolysis of natural and artificial substrates catalyzed by sPLA2 and the effect of sPLA2 on hemolysis, morphology of erythrocytes and platelet aggregation were investigated.

- Oral fluid (OF) for forensic toxicology purposes is characterized. Many biochemical parameters have been determined (α-amylase, createnin, AST, ALT, CK, Urea и ect.). For the first time, **biochemical markers/criteria for identification** (electrophoretic profile and a-amylase activity) and **for dilution/concentration** (createnin concentration) of oral fluid have been proposed. The storage conditions of OF (temperature, period, stabilizers) were also assessed, which is of great importance in the OF'using as an alternative biological specimen of the blood that can provide an estimation of exposure to drugs of abuse. Another important contribution in this direction is the development and optimization of the technique of **dried oral fluid spot** (oral fluid on filter paper), which allows easy transportation and storage on the one hand, and on the other hand – eliminates the enzymatic and hydrolysis degradation of analytes and the influence of matrix. **An optimized protocol for extracting drugs from OF** and the corresponding dried spot has been proposed, and the applicability and reliability of the results have been demonstrated by oral fluid samples of subjects who have recently used illicit drugs. This is an undisputable important contribution to the clinical practice for the purposes of forensic toxicology.

- The **effect of anesthetics and psychoactive substances** in clinical cases with fatal outcome by analysis of the biological fluids and tissues with advanced analytical techniques such as gas chromatography-mass spectrometry (GC-MS), nuclear magnetic resonance (NMR) and high performance liquid chromatography – diode array/fluorescent detector. This is an undisputable contribution to achieving accurate expertise in cases with not quite clear etiology of death.

Teaching activity

Assoc. Prof. Dr. Pantcheva-Kadreva is a highly respected university lecturer. Her teaching activity is related to the preparation and conduct of three mandatory lecture courses in the Bachelor's Degree and Master's Degree: Analitical chemistry for students of Biological Faculty at SU "Kliment Ohridski" – "Biology" and "Ecology and Environmental Protection"; Analytical chemistry (1th and 2nd part) for students in the Biological Faculty at SU, in the specialty „Bilogy and Chemistry"; for students in the Faculty of Chemistry and Pharmacy at SU, in the specialty „Pharmacy" in Bulgarian and in English. In recent years, she has a classroom employment of about 480 hours per school year. A proof of the quality of teaching and organization of the learning process of Assoc.Prof. Pantcheva- Kadreva is the high score of her students.

Assoc.Prof. Ivaila Pantcheva is a **scientific advisor or co-adviser of** a total of 9 graduated and a 2 PhD students. During the period 2012-2020 she supervised 2 PhD thesis's (supervisor and co-supervisor) 6 diploma works (supervised 3 and co-supervised another 3) which were successfully defended. It needs to be noted that 3 of her diploma students were from abroad, namely from the Faculty of Chemistry and the Faculty of Pharmacy and Food Sciences, University of Barcelona. At present, she is a scientific advisor of the PhD student (Radoslava Stamboliiska, Part-time studies). By all means this data shows the high quality standard of the teaching activites of applicant.

CONCLUSION

The publications presented by the applicant are on the topic of the competition and represent original scientific achievements with significant contribution to biocordination and bioanalytical chemistry. Analyzing the applicant's scientific achievements, the relevance and perspective of the topics, active participation in research projects, active teaching, administrative and peer review activities and her personal qualities and skills, I think Dr Pantcheva-Kadreva meets all requirements of the Act for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the application of the ADASRB, the Regulations for the terms and conditions for acquiring academic degrees and occupying academic positions of the Sofia University "St. Kliment Ohridski" and the Recommendations on the criteria for acquiring scientific degrees and occupying academic positions at the Sofia University for the professional field" Chemical Sciences", related to the procedure for occupying the academic position " Professor ". On the basis of the above, **I strongly**

recommend to the Honorable Scientific Jury to propose to the Faculty Council of the Faculty of Chemistry and Pharmacy at the Sofia University to **award to Associate Professor Doctor Ivaila Pantcheva Kadreva** the academic position of **"Professor"** in the field of higher education 4. Natural sciences, mathematics and informatics, professional field 4.2. Chemical Sciences (Analitical Chemistry).

Octomber 14, 2020

Reviewer:

/Assoc.Prof. Dr Mariya Ivanova/