

REVIEW

of the materials submitted for participation in a competition for the academic position "**professor**" in the field of Higher education 4. "Natural Sciences, Mathematics and Informatics", Professional field 4.2. "Chemical Sciences" (**Analytical Chemistry**), announced in State Gazette, issue 103 of 12.12.2023, for the needs of the Faculty of Chemistry and Pharmacy at Sofia University "St. Kliment Ohridski"

Reviewer: prof. Irina Karadjova, PhD, Faculty of Chemistry and Pharmacy at Sofia University "St. Kliment Ohridski"

The only candidate in the announced competition for the academic position (AP) "Professor" is **Assoc. Prof. Dr. Galina Gencheva-Kissovska** (SCOPUS Author ID 6506664875).

1. Brief biographical data

Assoc. Dr. Galina Georgieva Gencheva is admitted as a chemistry student at the Faculty of Chemistry of Sofia University "St. Kliment Ohridski", in specialty Inorganic and Analytical Chemistry in 1981. In 1986, she graduated from the Faculty of Chemistry with a master's degree after defending his diploma thesis on "Complex formation of creatinine with Pt(II) and Pd(II)" in the Department of "Analytical Chemistry". He obtained the scientific and educational degree "doctor" in 1993 with a doctoral thesis on the topic: "Complex formation of the bioligand creatinine with nickel, palladium and platinum in aqueous and organic media" in the specialty "Analytical Chemistry". The entire scientific career of Assoc. Dr. Galina Georgieva Gencheva took place in the Department of Analytical Chemistry, starting with her admission as a full-time doctoral student in 1988. Following the successful defense of her doctoral thesis, she acquired the academic positions from chemist, assistant to associate professor in 2004 in the "Analytical Chemistry" department of the FHF.

Prof. Galina Gencheva has a successful scientific career, which includes a total of 52 publications, 1 patent, one textbook for the 12th grade and one manual for solving problems in analytical chemistry.

She has an active project activity: she is the leader and member of several successfully completed projects at the National Scientific Fund. He is a participant in projects of FHF and she is the leader of 6 projects from the SU fund.

2. General characteristics of the received materials.

The materials presented by Assoc. Dr. Galina Gencheva to participate in the competition are very well structured, regardless of the technical errors noticed, mainly related to the accepted number of points for various journals. A distinction is indicated between the materials used for the habilitation in 2004 and the materials for the current competition. The careful organization of the attached materials allows one to easily conclude that all the formal requirements of Low for development of the academic staff in Republic of Bulgaria and the

regulations for its application and the recommended additional criteria for acquiring scientific degrees and occupying academic positions at Sofia University "St. Kl. Ohridski" for professional field 4.2 "Chemical Sciences" have been met. Associate professor Gencheva presented a list of scientific papers for her entire scientific career, with the selected publications presented to award the educational and scientific degree PhD, the materials presented to award the academic position of associate professor, and the materials selected for the current competition as well as additional materials that characterize her research interests and achievements.

She is the co-author of a total of 52 publications, of which 40 were published in journals included in SCOPUS/web of science data base. Prof. Gencheva is the author of a manual for solving problems in analytical chemistry and the textbook for 12th grade for profiled learning in chemistry. The number of observed citations of all scientific publications without self-citations is 284. h-index of the candidate, according to citations of all articles (Scopus, Web of Science, Google Scholar) without self-citations of the author and co-authors is 8.

A list of 21 publications were submitted for participation in the competition, all of them were published in journals with an impact factor or impact rank (Web of Science, SCOPUS). The articles distribution between quartiles is: in quartile Q1 - 6 publications, in quartile Q2 - 3 publications, in quartile Q3 - 2 publications and in quartile Q4 - 7 publications. In addition to the presented publications, one patent from 2011 is also included. In two of the presented publications Prof. Gencheva is the first author, and in 11 publications she is the corresponding author. 63 citations were found on the articles from the list of papers. (Scopus)

The habilitation thesis is based on the results of 4 publications.

The scientific results from research studies have been reported in more than 50 national and international forums, including 1 plenary report and 2 participations with sectional reports, according to the submitted reference.

Associate Professor Gencheva presents data on participation in projects funded by the Ministry of Education and Science and the National Research Institute and internal projects financed by the SU. She is a member of the team of one project and the head of two projects of FNI. She is the head of 6 projects from the SU fund.

All presented materials are related to the theme of the competition. On the basis of the declared publication activity, the candidate has attached a report on the fulfillment of the minimum national requirements and the additional recommended criteria of Faculty of chemistry and pharmacy for occupying the academic position "Professor" in the scientific field "Natural Sciences, Mathematics and Informatics", professional direction "Chemical Sciences". The distribution by indicators is as follows: indicator A - 50 points; indicator B - 100 points (recommended 100); indicator D - 247 points (recommended 220); indicator D - 128 points (recommended 120) and indicator E - 270 points (recommended 150), indicator G - 292 points (recommended 120). It is obvious that the scientometric data of Assoc. Prof. Dr. Gencheva meet and exceed the necessary minimum for all requirements.

General characteristics of the research activity and personal contribution of the candidate. Scientific contributions

All publications of the candidate in the competition are collective. Assoc. Prof. Gencheva is the head of the Teaching and Research Laboratory of Molecular Spectroscopy for

Structural Analysis and successfully builds up on the achievements of the laboratory in the field of coordination chemistry.

Assoc. prof. Gencheva's research interests are in the field of:

- Synthesis, structure and characterization of coordination compounds, designed as new drugs, mainly cytostatic;
- Development of a methodological approach to determine molecular structure and quantitative composition of complexes based on the application of a set of instrumental methods (UV/Vis, IR, Raman, EPR, NMR, X-ray structural analysis of single crystal samples);
- Evaluation of spectral characteristics and reactivity of ligands and the associated complexes by quantum-chemical modeling.

Prof. Gencheva realized a successful research idea - from very good knowledge and characterization of the structure of coordination compounds to a new task - targeted synthesis of complexes with predictive properties as cytostatic, their subsequent structural characterization and evaluation of their antitumor effectiveness to a conclusion about the effect of structure of the complex on the mechanism of action and efficacy of the medicinal action. Prof. Gencheva managed to achieve largely positive results for this task by using data from:

□ A wide range of instrumental methods for determining molecular structure of a coordination compound and studying complex equilibria in solution. To obtain reliable results, Associate Professor Gencheva applied combinations of data obtained by: Nuclear Magnetic Resonance (NMR), one-dimensional and two-dimensional techniques (in ranges for ^1H and ^{13}C nuclei), Solid phase NMR in ^{13}C and ^{15}N - nuclei ranges; Electron Paramagnetic Resonance; Infrared Spectroscopy; Raman spectroscopy; Electron absorption spectroscopy (UV/Vis); X-ray photoelectron spectroscopy; Single crystal X-ray diffraction; Thermal analysis (Thermogravimetry and Differential Scanning Calorimetry (DSC); Magnetic measurements. The conclusions were made by studying 20 new complex compounds - a series of complexation equilibria and the redox processes running in parallel to the complexation were followed. The structure of the synthesized complexes was established and described in solid phase and solution.

□ Research has been conducted and molecular, electronic structure and properties of purposefully selected organic ligands have been demonstrated. Based on the obtained results, a theoretical approach for evaluating the complex-forming ability of organic ligands is proposed. In addition, as a result of the obtained data, a relationship between the spectral characteristics of the ligands and their complexation abilities was deduced. In my opinion this a major achievement because in general ligand complexation is evaluated by experimental data and predictions are rarely possible.

□ Methods were developed and biological studies were carried out to evaluate the mechanism of the antitumor activity of the obtained complexes.

Targeted studies with preselected ligands and metal ions ensuring controlled interaction between them have been carried out and essential conclusions reached for understanding the process of antitumor action of new complex compounds of platinum, palladium and gold and the effect of structure of the complex on drug effectiveness. Complexes of Pt(III), Pd (III) and Au(II) with hematoporphyrin IX and complexes of Pt(IV) with 1,3,5-triamino-1,3,5-trideoxy-*cis*-inositol (taci, all-*cis*-2,4,6-triaminocyclohexane-1,3,5-triol were synthesized and characterized in terms of composition and structure in solution and solid state. The biological

studies performed show that the metalloporphyrin complex of Pt(III) and the dinuclear complex of Pd (III) are characterized by a different mechanism of action against cancer cells than cisplatin and that this mechanism correlates with cytotoxicity. New complexes of Pt(IV) with taci are characterized by alternative pharmacologic properties and are able to overcome the inactivation mechanisms of cisplatin. In addition complexation of hematoporphyrin IX with essential elements Cu(II), Fe(II) and Fe(III) was studied and conclusions are drawn for the structure of complexes synthesized.

The methodology for a directed complexation process after selection of a suitable ligand has been demonstrated with tertiary phosphine oxides functionalized with a primary amino group and Pd(II) and tertiary phosphine oxides functionalized with a secondary amino group and Cu(II).

Within the scope of the research on the application of nanomaterials in the treatment of various cancer cells, pegylation of nanographene oxide (nGO-PEG) has been investigated as an approach to increase its effectiveness. Nanomaterial characterization, confirmation of pegylation and subsequent modifications as well as evaluation of their physicochemical properties are essential requirements. Reliable conclusions in this direction were obtained using the methods of vibrational spectroscopy, and the obtained results were interpreted by Assoc. prof. Gencheva.

The habilitation work is based on 4 publications, all in journals in the Q1 quartile and is dedicated to the main direction in the scientific research of Assoc. Prof. Gencheva: studies on the possibilities and application of a suitable group of instrumental methods for structural characterization of purposely synthesized new compounds for example, new metal complexes designed as antitumor drugs. The target synthesis includes control of the preparation methods with an idea of prediction of the physicochemical properties and medicinal effect of the obtained complexes.

The presented and implemented idea is based on prerequisites guaranteeing certain cytostatic properties to realize targeted synthesis of complexes with predicted high drug effectiveness. The research ends with *in vitro* experiments, which confirm the accepted premises for a high efficiency of antitumor action and show the possible relationship between the effect of the structure of the complex on the efficacy of the medicinal action. The logical conclusion follows that optimization of many factors is necessary to reach the correct drug formulation, which include not only the appropriate choice of metal ion and ligand, but also the appropriately constructed coordination polyhedron and appropriate coordination of the selected ligand.

The significant role of assoc. prof. Gencheva in the commented researches is unquestionable. In the presented statement of contributions, there is a detailed description of her leading role in publications related to the areas in which she works and is leading author. At the same time, in a number of publications with other lead authors, she is an important member of the team in the design of experiments and interpretation of results. As the head of the Laboratory of Molecular Spectroscopy for Structural Analysis, she continues the traditions in the development of the laboratory by introducing new ideas in all directions.

Scientific contributions can be characterized as new scientific results such as an approach and methodology for studying the structure of complexes and establishing the structure of newly synthesized complexes; approach and methodology for the directed synthesis of

complexes with ligands with antitumor activity and the evaluation of the effect of the structure of the complex on drug effectiveness. Scientific contributions can also be interpreted as results with good practical application and potential ultimate realization.

The reference for the contribution nature of Dr. Gencheva's scientific works is comprehensive and very correctly outlines her own contributions, which gives me reason to conclude that the candidate's personal contribution to the presented research is undoubted and significant.

4. Reflection in literature

Assoc. Prof. Gencheva-Kissovsy has presented a list of citations of the works with which she participated in the competition and the general conclusion is that the research she conducts and publishes has found a serious response in the literature. Publications related to hematoporphyrin IX complexation are cited by authors in specialized journals. Also of interest are the results obtained for pegylated graphene oxide and its effectiveness against cancer cells.

5. Pedagogical activity

Assoc. prof. Gencheva has a rich pedagogical activity. Within her career at Faculty of chemistry and pharmacy, she has taught almost all required courses related to analytical chemistry over a period of time. She compiled the curriculum of the Analytical Chemistry course for the specialty Ecochemistry and the Analytical Chemistry with Instrumental Methods of Analysis course for the specialty Chemistry and English. She developed the curriculum of a mandatory course on Instrumental Methods 2 and elective courses on Methods of Vibrational Spectroscopy and Methods of infrared and Raman Spectroscopy.

He is the main lecturer on the methods of molecular spectroscopy (obligatory course Modern methods of molecular spectroscopy) in the master's program "Modern Spectral and Chromatographic Methods for Analysis" of the Faculty of Chemistry and Pharmacy of SU "St. Kliment Ohridski" and lecturer of the course Modern Applications of Molecular Spectroscopy in Chemical Analysis for the Master's Degree "Smart Analytics"

She was the supervisor of two successfully defended doctoral students and a consultant to one successfully defended doctoral student. She was the supervisor of a number of bachelor's and master's theses.

6. Critical Notes

I have no fundamental critical remarks about the research from the publications of Assoc. Prof. Gencheva

CONCLUSION

Associate Professor Dr. G. Gencheva participated in the competition with a set of materials that fulfills the requirements for awarding the academic position "Professor" at the Faculty of chemistry and pharmacy in the professional direction "Chemical Sciences". The presented documents show that Prof. Gencheva is a leading researcher with his own vision and original idea that empirical studies can lead to more substantial conclusions and possibilities for predictions about the effectiveness of coordination compounds as antitumor agents. She succeeds in combining theoretical approaches with experimental results to solve complex tasks

such as ligand activity in a controlled complexation process. A review of the publications shows that she successfully builds on the achievements in the field of coordination compound research and the development of the methodology in molecular spectroscopy methods carried out by the Laboratory of Molecular Spectroscopy. In this aspect, based on the current and prospective scientific topics, the quantity and quality of scientific works, the response in the literature, scientific contributions, leadership and participation in scientific projects, I strongly recommend the Scientific Council of the Faculty of chemistry and pharmacy to vote positively for the awarding of the academic position "Professor" in professional direction 4.2. Chemical sciences, scientific specialty "Analytical chemistry" of associate professor Dr. G. Gencheva-Kissovsky.

Sofia, 19.04.2024

Reviewer: