

## Review

on the materials submitted for participation in a competition for occupation of the academic position of "professor" in the field of higher education 4. "Natural sciences, mathematics and informatics", professional direction 4.2. "Chemical Sciences" (Analytical Chemistry), announced in SG No. 103 of 12.12.2023 for the needs of the Faculty of Chemistry and Pharmacy at Sofia University "St. Kl. Ohridski"

Reviewer: Natasha Trendafilova, Prof. Dr., IGIC-BAS

The only candidate in the current competition for occupation of the academic position of "professor" is **Assoc. Prof. Dr. Galina Georgieva Gencheva - Kisiovska**, *ORCID: 0000-0003-1696-1589, Scopus Author ID: 6701758294*.

Assoc. Prof. Dr. Gencheva has presented all the necessary documents indicated in the Law for Development of the Academic Staff in the Republic of Bulgaria (LDASRB) and the Regulations on its Implementation. The documents are in accordance with the Regulations for the terms and conditions for acquiring scientific degrees and holding academic positions at Sofia University "St. Kl. Ohridski", as well as with the Recommended criteria of the Faculty of Chemistry and Pharmacy. Assoc. Prof. Dr. Gencheva fulfills, and in some indicators ("Г", "Д", "Е" and "Ж") even exceeds the minimum national requirements under Art. 2b of LDASRB and those of the Faculty of Chemistry and Pharmacy when occupying the academic position of "professor" in professional direction 4.2. "Chemical Sciences".

Assoc. Prof. Dr. Galina Gencheva graduated from the Faculty of Chemistry of Sofia University in 1986, after successfully defending a diploma thesis on "Complexation of creatinine with Pt(II) and Pd(II)", with the qualification "Master of Chemistry" and specialization in inorganic and analytical chemistry. From 1988 to 1992, Galina Gencheva was a full-time PhD student in the Department of Analytical Chemistry of the Faculty of Chemistry at Sofia University. In 1993, under the supervision of Prof. Dr. Sci. P. R. Bonchev and Prof. Dr. Sci. M. Y. Mitewa, she defended her PhD thesis on the topic: "Complex formation of the bioligand creatinine with nickel, palladium and platinum in aqueous and organic media", as a result of which, she received the educational and scientific degree "doctor" (PhD). Her scientific career continued at the Faculty of Chemistry of Sofia University, where she successively held the positions of assistant (1992), senior assistant (1996) and principal assistant (1997). In 1997, she was awarded the 3rd prize at the International Competition for Young Scientists on the topic: "Instrumental methods of analysis in bioinorganic and environmental chemistry", organized by the International Institute in Zittau, Germany and the company "Perkin Elmer". After successfully participating in a competition in 2004, Dr. Gencheva was elected as an "associate professor" at the Faculty of Chemistry of the Sofia University in the scientific specialty of Analytical Chemistry.

Galina Gencheva carried out a number of successful and fruitful specializations at Saarland University, Saarbrücken, Germany (1997 – 2012, 2016) and at the Institute of General and Inorganic Chemistry, University of Münster, Germany (2003, DAAD), where she conducted scientific research on the synthesis, structure and the antitumor activity of platinum complexes of tertiary amine ligands. The design and testing of new antitumor drugs of metal ions with different

bioligands is the main topic of her research and scientific projects she leads: four - funded by the Scientific Research Fund at Sofia University and two - funded by the Scientific Research Fund at the Ministry of Education and Science. She also participated in other projects as a performer.

The teaching activity of Assoc. Prof. Dr. Gencheva is an integral part of her scientific activity and includes eight courses in the field of Analytical chemistry for various bachelor's and master's programs: Modern applications of molecular spectroscopy in chemical analysis (2022, 2023), Analytical chemistry and instrumental methods 1<sup>st</sup> part (2021), Instrumental methods – 2<sup>nd</sup> part (2009), Methods of the vibrational spectroscopy (2010), Modern methods of the molecular spectroscopy (2010), Electrochemical methods of analysis (2010), Complex compounds in Analytical chemistry (2004), Analytical chemistry 1<sup>st</sup> and 2<sup>nd</sup> part (2006 – 2009).

Assoc. Prof. Dr. Gencheva works very intensively with students, graduates and PhD students from the Faculty of Chemistry of Sofia University. She was the supervisor of nine successfully defended diploma theses after 2012 (Bachelor – five and Master – four). Under her supervision, two PhD students are successfully defended and of one she was a consultant.

Assoc. Prof. Dr. Gencheva has internationally recognized and proven expertise in the field of inorganic, analytical and pharmaceutical chemistry, which is why she was invited as a reviewer for a number of scientific journals: Crystals, Pharmaceutics, Inorganics, International Journal of Molecular Science, Molbank, Bulgarian Chemical Communication, Magnetochemistry. She was a guest editor of the Bulgarian Chemical Communications, Vol. 49, Special Issue A, Proceedings of the VI<sup>th</sup> National Crystallographic Symposium, Sofia, October 5-7, 2016, *Research on the Design of New Metal-Based Antitumor Drugs, Pharmaceutics*. She is a member of the Bulgarian Crystallographic Society.

The total number of scientific publications of Assoc. Prof. Dr. Gencheva is 52. Of these, 40 are in refereed international and bulgarian journals (Scopus-38, Web of Science-2), and 12 are in collections with an editor and publisher, and non-refereed journals and collections. The total number of observed citations (without self-citations) in Scopus is 284. The Hirsch index (without self-citations) is 9. The candidate is a co-author of a Textbook and a Study Guide.

In the current competition for the academic position of "professor", Assoc. Prof. Dr. Gencheva participate with 21 scientific publications and one patent. Six of the publications are in journals of the category Q1, 4 – Q2, 2 – Q3, 4 - Q4, 3 - Q4 (SJR), 1 scientific article is in a Proceedings with editor, and 1 is in a journal, indexed after 2012. In 11 of the publications, Dr. Gencheva is the corresponding author, and in 2, she is the first author. 63 citations (Scopus) were found on the articles for participation in the present competition. Assoc. Prof. Dr. Gencheva participated in a team that registered a patent, protected in 2011. The results of her scientific research have been presented at more than 50 national and international scientific forums, symposia and conferences with posters and reports.

The Habilitation thesis of Dr. Gencheva is on the topic: "Instrumental methods for determining molecular structure - application in modeling of non-classical antitumor drugs." It is based on 4 scientific publications, all in journals of category Q1, with which she fulfilled the minimum requirements for "Group B" indicators. The Habilitation thesis summarizes the accumulated

experience, results and conclusions of Dr. Gencheva's research on the subject. The idea of the innovative approach in designing the structure of metal complexes with a "non-classical" structure and the potential for their application as antitumor drugs is presented. It contains an informative overview of the instrumental methods used for the structural studies and spectroscopic characterization of the new complexes, as well as the analytical procedures used to specify the conditions for directed synthesis of the objects, for the study of chemical, biochemical or physiological processes, for analysis of foods and objects from the environment. The topic and content of the Habilitation thesis are in full agreement with the topic of the current competition - Analytical Chemistry.

### *Original scientific contributions*

Three new stable mononuclear complexes of Pt(III) with hematoporphyrin IX have been designed, synthesized and characterized for the first time. The complexes showed promising antitumor activity, comparable to that of cisplatin (*pubs. 3, 4, 10*).

An original reaction scheme was proposed for the preparation and isolation of two new complexes of Pd(III) with hematoporphyrin IX (*pubs. 11, 16*).

Complex and inovative procedure was applied to obtain stable monomeric paramagnetic complex of Au(II) with hematoporphyrin in a pseudo-octahedral environment (*pubs. 1, 6*).

Two octahedral complexes of Pt(IV) with the ligand *taci* (1,3,5-triamino-1,3,5-trideoxy-cis-inositol), possessing a "non-classical" cytostatic structure were isolated and structurally characterized: *fac*-[Pt(*taci*)<sub>3</sub>]I and *bis*-[Pt(*taci*)<sub>2</sub>](CO<sub>3</sub>)<sub>2</sub> (*pubs. 20, 21, 22*). The selection of the starting compound for Pt(IV) and the specification of the reaction conditions for its preparation are innovative contributions of the research and they deserve special attention.

Comprehensive biological tests of hematoporphyrin IX complexes with metal ions in intermediate oxidation states: Pt(III), Pd(III), Au(II) and Pt(IV) have been performed (*pubs. 3, 6, 10, 11, 12, 16, 21*). Promising pharmacological properties have been found for the complex of Pt(III) with hematoporphyrin, the dinuclear complex of Pd(III) with hematoporphyrin, and the complex of Pt(IV) with *taci*. The complexes have shown efficacy against certain cell lines, which made them candidates for specific therapies.

The coordination properties of a number of phosphine oxides have been elucidated: series of (aminoalkyloxymethyl)dimethylphosphine oxides with respect to Pd(II) (*pub. 2*), of bis((dimethylphosphinyl)methyl)amine with respect to Cu(II) (*pub. 15*), and of tertiary phosphine oxides (from theoretical studies) (*pub. 8*). Contribution is the crystal structure determination of Pd(II) and Cu(II) complexes.

The interactions of Cu(II), Fe(II) and Fe(III) with hematoporphyrin IX in different environments have been elucidated. The resulting metal complexes, which are suitable model systems for studying biological processes, have been characterized in solid phase and solution by means of IR, EPR, NMR and UV/Vis spectroscopies (*pubs. 4, 5, 9*).

The vibrational spectroscopy methods (IR and Raman) have been successfully applied to the study of graphene materials (*pubs. 19, 18*).

By means of FTIR spectroscopy, the ability of two biomaterials from the group of essential oil plants, to retain Cu(II) ions from aqueous solutions (*Mentha spicata* L. (MS) and *Ruta graveolens* L. (RG)) was investigated (*pub. 17*). The complexation processes of Cu(II) with the surface functional groups were studied and it was shown that they are not responsible for the retention of Cu(II) on the surface.

A new, and fourth, polymorph of a ruthenium complex has been demonstrated: dichloridotetrakis(dimethylsulfoxide)ruthenium(II) (*pub. 7*).

The crystal structure of a new squaric acid derivative, 3-methylpyridazinium hydrogensquarate, has been determined. The compound was characterized in solution by UV/Vis spectroscopy and in the solid state by FTIR spectroscopy (*pub. 14*).

The crystal structure of 3-(2-(diphenylphosphorothioyl)phenyl)-4-oxo-1-phenyl-3,4-dihydroquinazolin-1-ium perchlorate has been determined (*pub. 13*).

### *Summary*

The described scientific contributions and results in the research of Assoc. Prof. Dr. Gencheva are the result of in-depth wide-spectrum experiments dedicated to the design and study of the properties of a large number of coordination compounds and ligands, which are the basis of medicinal preparations and new materials. Of particular note is her pioneering research aimed at the design and proof of new coordination compounds with antitumor activity, including those with a "non-classical" structure. The research scheme includes design, directed synthesis, analytical, structural and spectroscopic studies in solution and solid phase and biological tests of Pt(III), Pd(III), Au(II), Pt(IV) complexes with hematoporphyrin and *taci* bioligands. As a result of very precise studies of the complexation processes in solution, for the first time compounds possessing predetermined biological properties have been successfully synthesized. The proof of the new compounds and the determination of their structure were carried out convincingly with appropriate instrumental methods and analytical techniques in solution and solid phase: UV/Vis, infrared and Raman spectroscopies, single crystal X-ray diffraction, electron paramagnetic resonance, nuclear magnetic resonance, electrochemical methods and magnetic measurements. Assoc. Prof. Dr. Gencheva's leading role in these studies is indisputable. It should be noted that she has a deep knowledge and very skillfully applies the methods listed above for structural, analytical and spectroscopic characterization of the newly synthesized compounds. These skills, combined with innovative thinking and strategy, help her to conduct cutting-edge scientific research, which she has initiated and systematically conducted over the years. A distinctive and very positive feature of her research is that it has a clear and specific goal, has been carried out systematically and extremely thoroughly, and in all cases has led to the production of the target compounds with the desired applied properties.

### *Conclusion*

Assoc. Prof. Dr. Galina Gencheva is an in-depth researcher and expert in the field of designing, synthesizing and proving new formulas metal-organic complexes with potential antitumor properties, incl. "non-classical" structures. She has undisputable scientific qualifications and potential to perform and lead valuable scientific research in the field of biocoordination and analytical chemistry. After the analysis of the materials, presented for the present competition: scientific publications, Habilitation thesis, data on teaching and expert activity, scientific projects and scientific forums participation, I find it reasonable to give my positive assessment by voting "yes" for the election of Assoc. Prof. Dr. Galina Gencheva to the academic position of "professor" in the Faculty of Chemistry and Pharmacy at Sofia University "St. Kl. Ohridski" in Professional direction 4.2. "Chemical Sciences", scientific specialty - Analytical Chemistry.

Sofia, 29.03.2024

Reviewer:

(Natasha Trendafilova, Prof. PhD)