REVIEW

from

Prof. Lyubomir Todorov Vlaev, DSc

Subject. Natural Sciences, Mathematics and Informatics, professional field 4.2. Chemical Sciences, scientific specialty "Chemistry", promulgated in the State Gazette No. 43 of 17.05.2024 with a deadline of two months from the announcement and published on the website of the University "Prof. Dr. Assen Zlatarov" - Burgas for the needs of the same University.

Position of the person submitting the review: member of the scientific jury for election to the academic position of Professor.

Candidate for the academic position of "Professor": the only candidate in the announced competition is Assoc. Prof. Dr. Rumiana Zlatinova Yankova - Avramova, Dean of the "Faculty of Medicine" and member of the Department of Physiology, Pathophysiology, Chemistry and Biochemistry at University "Prof. Dr. Assen Zlatarov" – Burgas.

Grounds for the review: Order No. RD 235 of 15.07.2024 of the Rector of Prof. Dr. Assen Zlatarov University - Burgas.

I have known the candidate personally since she joined the Department of Inorganic Chemistry of the University and have followed her scientific development as colleagues in the same Faculty. I was a reviewer in her habilitation competition, in which another candidate participated. I have no joint publications and have no conflict of interest with the candidate in the current competition.

1. Data and analysis of the professional development of the canid.

In 1990 Rumiana Yankova - Avramova graduated as a chemical engineer in the specialty "Inorganic and electrochemical production" at the University "Prof. Dr. Assen Zlatarov" - Burgas. Later, at the same University, she acquired a Master's degree in Pedagogy. In 2015, at the University of Russe "Angel Kanchev", he acquired the degree of Doctor of Science, and in 2016 he acquired the scientific title of Associate Professor, scientific specialty and the code 01.05. 02 "Inorganic Chemistry" at the University "Prof. Dr. Assen Zlatarov,. in "Natural Sciences" - Burgas. She has been a secretary of the departmental council of the Department of Inorganic Chemistry, a member of the faculty council of the Faculty of Physiology, Pathophysiology, Chemistry and Biochemistry, a chairman of the Medical Faculty, a chairman of the COOPCO, a chairman of the NID, a head of the Department of Physiology, Pathophysiology, Chemistry and Biochemistry, a deputy dean of the Faculty of Medicine, and eventually a dean of the same at the University.

2. Evaluation of the candidate's research activity.

The documents submitted by Assoc. Prof. Dr. Rumiana Yankova-Avramova for participation in the current competition are in accordance with the requirements of the Regulations and reflect to the maximum extent her scientific research work during the period after her habilitation. The list of her

scientific publications does not include any that have been used for obtaining the degree of Doctor of Education and Science or the post of Associate Professor. The overall scientific production of Assoc. Prof. Dr. Rumyana Yankova-Avramova is in accordance with the subject of the course. From the attached documents on the candidate's scientific and teaching work at the University it can be seen that her scientific and teaching experience is 33 years (assistant, senior assistant, senior assistant, associate professor); she has published 8 textbooks (5 independent and 3 co-authored), 25 developed curricula; two successfully defended PhD students; eight defended diploma students; participation in one international scientific project, participation in one national scientific and one national educational project, participation in 13 internal university projects at the Research Institute of University "Prof. Dr. Assen Zlatarov" – Burgas (three of the projects he is the head).

She has participated in the establishment of a teaching laboratory in "Methodology and Technique of Chemical Demonstrations in Inorganic Chemistry" and in "Chemistry" of the specialty "Medicine". She has participated in 36 international and national scientific conferences, with a total of 119 scientific publications (of which: 57 in Scopus and Web of Science; 61 publications refereed and indexed in world literature and one monograph); Hirsch index, *h*-index = **14.**

The number of scientific publications, published in journals with impact factor (Web of Science) and impact rank (Scopus), accredited under the current competition for "professor" is 30 (8 of them are in quartile Q1; 7 in quartile Q2 and 15 in quartile Q3). The three journals with the highest impact factor in which the candidate has publications are Fuel, IF=8.035, Journal of Molecular Liquids with IF=6.633 and Spectroshimica Acta, Part A, Molecular and Biomolecular Spectroscopy with IF=4.400. In 14 publications Assoc. Jankova is the first and 12 is the second co-author. This is an indication of her leading role in ongoing research. A total of 150 citations have been noted on these publications to date, none of which are by Bulgarian authors. The highest number of citations to date (36) has been received by the publication Tankov I., R. Yankova, S. Genieva, M. Mitkova, D. Stratiev, J. Mol. Struc., 2017, 1139, 400-406. All this shows that the scientific publications of Assoc. Prof. Dr. Yankova have been noticed and appreciated by the scientific community, which is evidence of the relevance and importance of the candidate's scientific publications. According to the participant's own judgement, the main scientific contributions related solely to the thirty scientific papers submitted for the competition for professor can be structured in the following thematic areas:

I. Preparation and characterization of new ionic liquids.

II. Analysis of surface phenomena occurring in heterogeneous ionic liquids.

III. Investigation of thermal decomposition kinetics of ionic liquids.

IV. Application of ionic liquids as effective catalysts for esterification.

V. Characterization of compounds for their application.

VI. Preparation and characterization of coordination compounds. Study of their reactivity.

I. Preparation and characterization of new ionic liquids

The majority of the research papers submitted to the competition focused on the preparation and characterization of new active and stable homogeneous and heterogeneous esterification catalysts. The following homogeneous catalysts were synthesized: pyridine hydrogen sulfate, pyridine dihydrogen phosphate, pyridine nitrate, 4-amino-1H-1,2,4-triazole nitrate, 2-amino-1,3-thiazole hydrogen sulfate monohydrate, imidazole hydrogen sulfate, imidazole hydrogen selenate [Publ. 4-7, 10, 13, 15, 16]. Various modern physicochemical methods such as X-ray structure and X-ray phase analysis, X-ray photoelectron spectroscopy, infrared spectroscopy, spectroscopy in the ultraviolet and visible regions, thermogravimetric analysis, differential scanning calorimetry, low-temperature nitrogen adsorption and adsorption porosimetry have been expediently used to characterize the obtained ionic liquids. The synthesized ionic liquids were also studied by quantum chemical methods of analysis. The results obtained have been interpreted adequately and thoroughly.

It has been found that the formation of hydrogen bonds between the organic cation and the inorganic anion is the reason why the structure of these compounds contains an additional distinct intramolecular cycle (besides the aromatic one) formed between the organic cation and the inorganic anion possessing aromatic character. Quantum chemical analysis showed that the reason for this was a significantly increased polarization of the chemical bonds involved in the formation of a cycle between the organic cation and the inorganic anion.

The main contributions in this thematic area are:

- New ionic liquids were synthesized: pyridine dihydrogen phosphate, imidazole hydrogensulfate, imidazole hydrogenselenate.
- The aromaticity of an inorganic anion in the structure of ionic liquids has been documented.
- Pyridine hydrogensulfate, pyridine dihydrogen phosphate and imidazole hydrogensulfate have been found to possess nonlinear optical properties.

II. Analysis of surface phenomena occurring in heterogeneous ionic liquids

Based on the synthesized ionic liquids, heterogeneous systems were obtained by using carriers with developed specific surface such as Al_2O_3 and rice husk ash. The ionic liquid-carrier interface surface phenomena were investigated for the following heterogeneous systems: pyridine hydrogen sulfate/α-Al_2O_3 [Refs. 9 and 14], pyridine hydrogen sulfate/rice husk ash [Refs. 9], 2-amino-1,3-thiazole hydrogensulfate sulfate monohydrate/α- Al_2O_3 [ref. 1], imidazole hydrogen sulfate/kappa- Al_2O_3, and 2-amino-1,3-thiazole hydrogensulfate sulfate monohydrate/kappa- Al_2O_3 [ref. 30]. Infrared and X-ray photoelectron spectroscopy as well as Density Functional Theory were used.

The main contributions in this thematic area are:

- The vibrational couplings of the synthesized ionic liquids and the resulting heterogeneous systems were investigated for the first time.
- The nature of the surface interactions in these heterogeneous systems as a function of the nature of the carrier is elucidated.
- The spatial arrangement of the immobilized active phase on the carrier surface in heterogeneous pyridine hydrogensulfate/α-Al2O3 systems has been determined.

III. Investigation of thermal decomposition kinetics of ionic liquids

The thermal behavior of: pyridine hydrogensulfate [refs. 2 and 9], 4-amino-1H-1,2,4-triazole nitrate, pyridine dihydrogen phosphate [ref. 2], pyridine nitrate [refs. 2 and 12], pyridine hydrogensulfate/α-Al_2O_3, and pyridine hydrogensulfate/rice husk ash [ref. 9] in inert media was investigated. A combination of experimental (TGA, DSC) and quantum chemical approaches was used to investigate the thermal stability of the above samples. It was found that the nature and degree of intramolecular interactions significantly influence the thermal behaviour.

Non-isothermal thermogravimetry and the Friedman (FD) and Kissinger-Akahira-Sunose (KAS) computational procedures were used to calculate the values of activation energy, E_A, and the preexponential factor, A, in the Arrhenius equation for the thermal decomposition of the ionic liquid pyridine nitrate. The influence of the carrier on the thermal behavior of ionic liquids was investigated in the cases of pyridine hydrogensulfate/α- Al_2O_3 and pyridine hydrogensulfate/rice husk ash [ref. 9].

The main contributions in this thematic area are:

- The thermal behavior of the ionic liquids pyridine hydrogen sulfate, pyridine dihydrogen phosphate, pyridine nitrate, and the heterogeneous systems (pyridine hydrogen sulfate/α- Al_2O_3 and pyridine hydrogen sulfate/rice husk ash) based on them was investigated for the first time.
- The melting and decomposition mechanisms of the samples were determined as a function of the degree of intramolecular hydrogen bonding and the nature of the carrier.
- The kinetics of thermal decomposition of pyridine nitrate was investigated for the first time

IV. Application of ionic liquids as effective catalysts for esterification

Seeking a practical application, the catalytic activity of the synthesized ionic liquids was investigated in the processes of producing butyl acetate and methyl oleate (biodiesel). Based on the presented mechanisms of the esterification process, mathematical models were derived to study the kinetics and thermodynamics of the preparation of the target products. The results of these studies have been described in a number of publications [1, 6-9, 11 and 29].

The main contributions in this thematic area are:

- The mechanism of preparation of butyl acetate by formation of an active complex involving ionic liquid pyridine hydrogensulfate as a catalyst is presented.
- On the basis of detailed kinetic and thermodynamic analysis, the optimum conditions for the preparation of butyl acetate and methyl oleate in the presence of pyridine hydrogensulfate, 4-amino-1H-1,2,4-triazole nitrate and pyridine nitrate have been established.

V. Characterisation of compounds for the purpose of their application

In the field of medicine, quinoxalins are an essential part of various structures that exhibit biological activity related to antimicrobial, anticancer, antituberculosis, and anti-inflammatory activity. Since the practical application of quinoxaline derivatives strictly depends on their structural and electronic properties, the structure-property relationship has been investigated at the molecular level. The results

obtained in this thematic area have been reported in publications [17-19, 21, 26-28]. To date, publication [17] has been cited 19 times.

The main contributions in this thematic area are:

- A new derivative of quinoxaline-2,3-dione, namely 1,4-dialyl-6-chloroquinoxaline-2,3(1H,4H)-dione has been synthesized and its reactivity has been investigated.
- A complete theoretical study of carvone and linalool has been made. Theoretical calculations were used to interpret the difference in antimicrobial and antioxidant activity of the compounds.
- A new synthetic block-co-polymer, homogeneous PDMS-b-PAA (polydimethylsiloxane-block-polyacrylic acid) with different chain lengths of PAA was designed. The resulting PDMS-b-PAA surfaces exhibit improved characteristics (morphology and very good stability, uniform in width and continuous fibers) and favor the attachment and proliferation of epithelial cells). The obtained polymeric nonwoven surfaces based on PDMS-b-PAA are biocompatible. The biocompatibility of the electrospun nonwoven surfaces was influenced by the roughness (homogeneity of fibers) and charge (presence of COOH groups and length of charged polymer chains).

VI. Preparation and characterization of coordination compounds. Study of their reactivity

The following coordination compounds have been characterized experimentally and theoretically (Density Functional Theory): Dioxo-molybdenum(VI) complex with glycylglycine; bis(2-aminothiazole)dibromozinc(II); bis(2-aminobenzothiazole-N)dichlorocobalt(II); [Pt(3-amino-1,2,4-triazole)2Cl_2] and bis(benzimidazole)silver(I) nitrate [publications 19,20,22-25]. The intra- and intermolecular interactions have been studied by Bader's theory and Hirschfeld's surface, respectively.

The cytotoxicity of the platinum(II) complex with 3-amino-1,2,4-triazole was evaluated using 2 types of eukaryotic cells: the MDCK II renal epithelial cell line and the A549 cancer alveolar cell line. The results of this study showed the high cytotoxic effect of [Pt(3-amino-1,2,4-triazole)2Cl2], especially on cancer cells. Pt(II) complex is a promising nanomaterial for various biomedical applications, including anticancer therapy [ref. 22].

The antibacterial effect of silver(I) complex with benzimidazole was evaluated against Gram-negative E. coli ATCC25922 and Gram-positive Staphylococcus aureus ATCC 25923 and compared with that of silver nitrate and platinum(II) complex with 3-amino-1,2,4-triazole [ref. 25]. Gram-positive S. aureus showed higher susceptibility than E. coli, known for their efflux pumps used to protect metal ions and antibiotics. The silver complex did not inhibit the fungus Candida lusitaniae grown in Sabouraud's dextrose medium. The cytotoxic activity of the complex was tested against two cell line types: cancer (A549) and non-cancerous eukaryotic cell (MDCK). All tested concentrations of silver(I) complex were toxic to the cancer cell line and had no effect on normal cells up to 5 μg/ml.

The main contributions in this thematic area are:

- The cytotoxicity of platinum(II) complex with 3-amino-1,2,4-triazole was evaluated and found to be a suitable nanomaterial for various biomedical applications, including anticancer therapy.
- The antibacterial effect of silver(I) complex with benzimidazole was evaluated against Gram-negative E. coli ATCC25922 and Gram-positive Staphylococcus aureus ATCC 25923.

3. Opinions, recommendations and comments

Having got acquainted in detail with the scientific production of Assoc. Prof. Dr. Rumyana Yankova, I believe that her scientific research has been conducted at a modern level using a number of appropriate modern physicochemical methods of analysis, quantum-chemical models and computational procedures using established mathematical apparatus. The interpretation of the results obtained has been adequately carried out, and appropriate scientifically sound conclusions and inferences have been drawn. This is also confirmed by the good publication activity of the candidate in specialized scientific journals and the citations obtained thereon. Four certificates from the editors of the scientific journals Journal of Physics and Chemistry of Solids, Journal of Molecular Structure, Journal of Molecular Liquids and Molecules, Crystals, Materials, Polymers have been presented, which confirm that Assoc. Rumiana Yankova has been a reviewer of scientific publications published in their journals. This is an international recognition of the scientific community for the recognition of Assoc. Prof. Dr. Rumyana Yankova in the scientific world.

Nevertheless, I have the following remark to the candidate and one recommendation for her future scientific work.

- I am surprised that in the list of 30 scientific publications submitted for the competition, there is not a single work related to or derived from the work of the two successfully defended PhD students. The condition required by the Regulations of having a minimum of two PhD holders is not an end in itself, but a condition for successful future reproduction and growth of the scientific staff in the Universities in our country.

- In reference [9], it was noted that rice husk ash (RHA) was used as a support for the immobilized catalysts, which is not accurate enough. Thermal destruction of rice husk in an oxidizing medium produces so-called "white" ash (WRHA) and in an inert medium "black" ash (BRHA), respectively. The former is almost pure amorphous SiO_2, the surface of which is polar, and the latter is amorphous SiO_2, the surface of which is incorporated with amorphous carbon, and the surface of the product is therefore non-polar. These differences determine the specificity of the interaction of the modifier with the surface of the carrier, which is why studies are usually conducted with both types of carriers.

4. Conclusion

The materials submitted for the competition and the contributions of Assoc. Prof. Dr. Rumiana Yankova-Avramova show that her scientific metrics meet and significantly exceed the requirements for the academic position of "professor" set forth in the Academic Staff Development Act in the Republic of Bulgaria and the Regulations for its implementation. On the basis of all the above, I have formed an unquestionably positive assessment of the candidate, and I can confidently recommend the Scientific Jury to propose to the FS of the "Faculty of Medicine" at the University "Prof. Dr. Assen Zlatarov" - Burgas to elect Assoc. Prof. Dr. Rumiana Zlatinova Yankova-Avramova to the academic position of "Professor", in the field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.2. Chemical Sciences, scientific specialty "Chemistry".

Date:
20.08. 2024 г.

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/ Prof. Lyubomir Todorov Vlaev, DSc /