REVIEW

by prof. Ivayla Nedialkova Pantcheva-Kadreva,PhD
on a competition for acquiring the academic position "associate professor",
Field of higher education 4. Natural sciences, mathematics and informatics,
professional field: 4.2. Chemical Sciences (Radiochemistry)
for the needs of the Department of Analytical Chemistry at the Faculty of Chemistry and Pharmacy at Sofia University "St. Kliment Ohridski"

The only candidate participating in the competition for an acquiring the academic position "assoc. prof.", announced in theSate Gazette (issue 103 of 10.12.2021), is a chief assist. prof. Boyan Rumenov Todorov, PhD, from the Department of Analytical Chemistry at the Faculty of Chemistry and Pharmacy at Sofia University "St. Kliment Ohridski". According to the running normative requirements, Dr. Todorov has presented all the necessary information, incl. that requested by the Scientific Jury at its first meeting, in electronic form.

1. Brief introduction of the candidate

Education: Boyan Todorov completed his secondary education in 1996 at the School of natural sciences and mathematics - Vratsa, and in 2001 he graduated as a MSc in Chemistry at Sofia University "St. Kliment Ohridski", Faculty of Chemistry, successfully defending a Diploma thesis. In the period from 2003 to 2007 B. Todorov was a PhD student at Sofia University "St. Kliment Ohridski" (Department of Analytical Chemistry) under the supervision of prof. R. Djingova, DSc. In 2009 he acquired the educational and scientific degree "PhD" with a defense of a PhD Thesis entitled "Determination and evaluation of the environmental distribution of radionuclides (^{137}Cs, ^{60}Co and ^{241}Am)".

Work experience: In the period 2002-2004 B. Todorov worked at the Institute for Nuclear Research and Nuclear Energy at the Bulgarian Academy of Sciences. Since 2007 he has held the positions of "assist. prof." (2007), "seniour assist. prof." (2008) and "chief assist. prof." (2010) at the Department of Analytical Chemistry - Faculty of Chemistry and Pharmacy at Sofia University "St. Kliment Ohridski". The main activities he performs, beyond those related to his research work, include conducting lecture courses and practical classes in the BSc program "Nuclear Chemistry" at FCP-SU. The average annual study engagement of Boyan Todorov during the last 5 years amounts to 537 hours with a requirement of 360 hours for the teaching activities at Sofia University "St. Kliment Ohridski".

2. Research activity of the candidate

Publication activity: Ch. assist. prof. Boyan Todorov published totally 23 scientific papers (20 - referenced and indexed in the Scopus database; 69 citations without self-citations of all co-authors; Hirsch index 5).

Scholarships: Since 2006 Boyan Todorov has been conducting a long-term and a number of short-term scholarships at the Universities of Helsinki (Finland), Luxembourg (Luxembourg), Barcelona (Spain) and the Max Planck Institute (Germany). It should be noted that some of the publications are co-authored by colleagues from these scientific organizations, which confirms the establishment and development of a fruitful international cooperation.

Project activity: Ch. assist. prof. Dr. Boyan Todorov is a member of the research teams of 11 research projects, and is a leader of two of them, funded by NIS at Sofia University "St. Kliment Ohridski" and the National Research Fund of the Ministry of Education and Science.

Dissemination of the results: The candidate presented running results of his research in 12 scientific events (3 oral and 8 poster contributions). The submitted report does not include details about the conferences held and in this sense the contribution of B. Todorov cannot be assessed.

Supervision: Dr. B. Todorov has supervised 17 students who successfully defended their Diploma Thesis (2 – BSc, Nuclear Chemistry, 12 – MSc, Nuclear Chemistry, 3 - MSc Radiochemistry).

3. Evaluation of the documents submitted for participation in the competition for acquiring the position "assoc. prof."

Dr. Boyan Todorov presents 20 scientific publications - 18 in refereed and indexed journals, 1 book chapter and 1 paper in a journal without IF (SJR). According to the current criteria the publications are distributed as follows: 3 (Q1), 6 (Q2), 4 (Q3) and 5 (Q4) with an impact factor ranging from 0.2 to 7.3 . The total number of citations to these articles is 44.

The habilitation thesis (indicator C) is based on 5 publications, the remaining 15 scientific contributions in full text are included in Indicator D. A significant number of these research papers belongs to the chemistry of radioactive elements, with an emphasis on the properties of particular isotopes and the potential application of radiopharmaceuticals. In addition, the candidate shown an interest in the analysis of toxic substances possessing various properties and archaeometric studies.

3.1. Analysis of man-made and natural radionuclides

In the field of radionuclides B. Todorov thoroughly studied the properties of ^{241}Am, using a number of procedures for its determination in various samples - soils, plants and water.

The comparative analysis of several extraction schemes applied to five soil types shows that the most effective for americium extraction is the one developed by the National Institute of Standards and Technology (NIST). This procedure was used to establish a relationship between the soil properties (cation exchange capacity) and the total amount of the element extracted (publication 2a). The same approach was later applied for the analysis of the natural radionuclides U and Th and their soil/plant transfer (publication 3b). The climatic parameters "temperature" and "humidity" were studied on two soil types to evaluate their influence on the geochemical fractionation of ^{241}Am and its geochemical forms depending on the soil characteristics. The soil-to-plant transfer coefficient of the isotope was determined at various temperature conditions, allowing an assessment of the radioecological behaviour of the systems studied (publications 1a, 6b). The latter study was extended towards two additional radionuclides, namely ^{137}Cs and ^{60}Co (publications 6b, 7b). Dr. Todorov moves from the analysis of americium in soils to its determination in natural aqua systems, where he faces a significant challenge – an extremely low concentration of the element and an absence of suitable radioanalytical methods for its direct determination. Given the shortcomings of the classical concentration methods such as evaporation or precipitation, B. Todorov focuses on the search for a specific reagent that can selectively bind americium, preserving its bioavailable form (Am^{3+}). This approach has been successful implemented by a series of fluorinated β-diketones that form Am^{3+}-based complex compounds under acidic conditions close to those of natural aquatic systems and allow its determination after a subsequent extraction procedure (publications 1b, 4b). The use of specific reagents and solvents also possesses some disadvantages – an expensive analysis, it is necessary to take into account the harmfulness / aggressiveness of some of the organic reagents, in many cases the procedures are multi-stage, energy-consuming, etc. Despite the positive results regarding the americium complexes, B. Todorov continues his research looking for softer and more favorable conditions to concentrate the element in aqueous sources. This aim was achieved using an ionic liquid and developing a simple procedure for extraction and concentration of ^{241}Am, where a significant separation coefficient of the element from the isotopes of ^{137}Cs and ^{60}Co was in addition achieved. Last but not least, the regeneration of the ionic liquid reported allows its multiple use and reduces the analysis cost (publication 5b).

3.2. Compounds with (potential) clinical application

Dr. Todorov's interests in the field of radiochemistry include the advantages of recent science developments for the preparation of new biologically active compounds which can be applied in nuclear medicine. The candidate has focused his efforts on the synthesis of bifunctional compounds (a component of radiopharmaceuticals), which are able to interact both

with a specific target biomolecule and with a radioisotope (therapeutic or diagnostic). To date, the most successful strategy to obtain such bifunctional compounds is their stereospecific synthesis, with the most promising being the reaction between tetrazine- and *trans*-cyclooctane-containing molecules. The isolation of *trans*-cyclooctene derivatives is accompanied by low yields, but based on a theoretical model B. Todorov developed a successful experimental procedure for photochemical isomerization of silver complexes of *cis*-cyclooctene derivatives to their corresponding *trans*-isomers. As a result, a fivefold yield was realized accompanied by the use of a simple experimental setup (publication 12b). The candidate was also involved in the synthesis of other bifunctional compounds (publication 5b), which specifically bind the enzyme polyoligopeptidase (biomolecule) and iodine radioisotopes. Unlike the classical organic synthesis, the radiochemical synthesis requires strictly predefined conditions for the production of labeled compounds with high radiochemical yield and purity. Overcoming the difficulties (working with microquantities, limited time, purification, automated synthesis), two new ^{123}I-labeled bifunctional indicators were synthesized and studied to confirm the potential properties of endopeptidase as a biomarker for an *in vivo* research.

The use of radiolabeled compounds recently is an indisputable and they are already routinely applied for diagnostic and therapeutic purposes. After the elimination from the organism, however, they release into the environment and can cause a longer-lasting adverse effect depending on the radioisotope used. There are no experimental data on the biodegradation of most radiopharmaceuticals, so B. Todorov applied a chemometric approach to evaluate the properties of a series of tetrazine and cyclooctene derivatives that can be used as a bifunctional component in the radiopharmaceutic molecule. The study shows, that the values of certain physicochemical parameters could be used to assess the ecological effect of the radioisotope-containing organic residues (publication 10b). Dr. Todorov considers also an another environmental aspect of the radiopharmaceutics application, namely - the recycling of enriched ^{18}O water required for the preparation of ^{18}F-fluorodeoxyglucose used in positron emission tomography studies. Applying a simple chemical technique and using common reagents/equipment, B. Todorov develops a three-step procedure by which the enriched water can be recycled and reused (publication 4a).

The candidate is a co-author of two reviews, which deal with the trends in the use of Cu- and Fe-containing substances for human medicine purposes. In publication 5a, the candidate summarizes the properties of five copper radioisotopes with medical application. An attention is paid to the design and development of chelating agents and nanomaterials with potential use in tumor therapy, emphasizing the role of ^{64}Cu in the development of radioteranostics. In publication 14b B. Todorov discusses the properties of supermagnetic iron oxide nanoparticles, which possess a promising potential in the cancer diagnosis and treatment.

3.3. Non-radioactive materials

Apart from the intensive scientific activities in the field of radiochemistry, Dr. B. Todorov is also interested in the analysis of toxic substances and archaeometric research. The objects studied are food, water, soil and archaeological finds; analytes include metals and organic compounds; and the methods used were chromatography (publication 13b), inductively coupled plasma mass spectrometry (publications 8b, 11b, 14b) and X-ray fluorescence analysis (publications 2b, 9b). Among these studies the outstanding ones are the development of two reference materials (soil pellets and an alloy resembling the native gold) and the correct dating of an ingot found in the seabed near Kaliakra.

4. Concluding remarks

The review on the research activity of Dr. Boyan Todorov reveals that his interests are primarily directed to the chemistry of radioactive elements and in this sense the holding the position of "associate professor" in Radiochemistry is logical and consistent with the candidate competencies. Boyan Todorov uses a wide range of methods for analysis and characterization of samples of different origin and, accordingly, containing various target compounds. In addition, he successfully applies the organic and radiochemical synthesis methods. The latter is especially important to emphasize due to the possibility of obtaining new multifunctional compounds, incl. radiolabeled, with application in theranostics.

The following findings among the candidate contributions are impressive:

- extraction of technogenic americium from natural waters by appropriate ligands or ionic liquids;
- preparation of *trans*-cyclooctene derivatives for a stereoselective synthesis of bifunctional compounds;
- synthesis of new radiolabeled indicators of the enzyme polyoligopeptidase;
- recycling of enriched ^{18}O water;
- development of reference materials used in mass spectrometry and X-ray fluorescence analysis.

Boyan Todorov is the first and/or corresponding author in 30% of the scientific papers submitted for a review. Given the diverse nature of his research and the wide range of objects to be analyzed, I think this is a good indicator. From the point of view of the current requirements for acquiring the position of "associate professor", the scientific production and the involvement of Boyan Todorov in teaching / mentor activities meet the requirements set out in the national regulations and those of Sofia University "St. Kliment Ohridski", incl. the recommended criteria of FCP-SU. The significant number of successful graduates (17) which the candidate supervised must be mentioned. Recently, Dr. Todorov is a scientific leader of a

research project funded by the National Science Fund, which confirms his ability to plan and conduct an independent scientific research.

The numerical indicators for acquiring the position of "associate professor" are in accordance with the national minimum and recommended criteria of FCP-SU in the professional field 4.2. Chemical sciences:

Group	Indicator	Points	Required points
A	1	50	50
C	4	102	100
D	7, 8	228	220
E	11	82	70
G	21, 23, 25	230	70

Shortcomings: The author did not include a comment in his summary regarding publication 14b according to the submitted list of scientific papers for participation in the competition. The submitted documents also contain some technical errors, which correction would improve the quality of the peer-reviewed papers. These remarks do not misjudge the quality of the candidate's achievements and do not call into question his competence in the field of the radiochemical analysis.

In conclusion, the scientific contributions of Dr. Boyan Rumenov Todorov to the chemistry of radioactive elements and his teaching activity and knowledge in the same field, give me a reason to strongly support his election as an "associate professor" in the professional field 4.2. Chemical Sciences (Radiochemistry) for the needs of the Faculty of Chemistry and Pharmacy at Sofia University "St. Kliment Ohridski".

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