REVIEW

of the materials submitted for the **competition for the academic position of „Associate Professor"** in the Faculty of Chemistry and Pharmacy, St. Kliment Ohridski University of Sofia in Higher education professional field 4.2. Chemical Sciences (Radiochemistry)
from **Prof. DSc Dimitar Stefanov Todorovsky**, pensioner, former professor in the Faculty of Chemistry and Pharmacy, St. Kliment Ohridski University of Sofia

1. Administrative remarks

Announcement of the Competition*:* Darzhaven vestnik (State Gazette) No 103/10.12.2021.
Rector's order for the constitution of the Scientific jury: РД-38-61/24.01.2022.
Appointment of D. Todorovsky as a reviewer: Protocol No 1/21.02.2022 of the Scientific jury.
Candidate in the competition: **Dr. Boyan Rumenov Todorov**, Chief Assist. Prof. in the Department of Analytical Chemistry of the Faculty of Chemistry and Pharmacy, St. Kliment Ohridski University of Sofia; Author ID (SCOPUS): 55682578600.

2. Brief biographical data for the candidate

Mr. Boyan Todorov was born in 1978.

Education. He is graduated as a Master of Science in Inorganic and Analytical Chemistry at the Faculty of Chemistry, St. Kliment Ohridski University of Sofia in 2001. In 2009 he defended PhD dissertation on the „Determination and evaluation of the distribution of radionuclides (^{137}Cs, ^{60}Co and ^{241}Am) in the environment" under the supervision of Prof. DSc Rumiana Djingova.

Professional experience*:* 2002 – 2004: Institute of Nuclear Research and Nuclear Energy of the Bulgarian Academy of Sciences. Since 2007: Assist. Prof., since 2010 - Chief Assist. Prof. in Laboratory „Trace analysis: ICP techniques and radioanalytical methods", Department of Analytical Chemistry, Faculty of Chemistry and Pharmacy, Sofia University.

Specializations: University of Luxembourg (2006, 2 months), Max-Planck-Institut für Polymerforschung, Mainz (2014, 2015, 2016, 1 month each), University of Helsinki (2011, 1 year, postdoc position; 2014, 2015, 2018, 1 month each), Univ. de Barcelona (2019, 1 month).

3. General description of the deposited materials

Deposited materials are available on the Elearn electronic platform of the University of Sofia; they are mentioned in Dr. Todorov' application for the participation in the competition and consist of the files numbering as follow: 1.CV, 2,3. Diplomaя for MSc and for PhD, 5-7. Documents for the taken academic positions, 10A, 10B. Lists of all publications of the candidate and of those presented for the competion, 11. Titles of the candidate's dissertation, projects, reports at scientific forums and diploma works performed under his guidance and bibliographic description of his scientific publications, 12. Check-up for the fulfillment of the minimal national requirements according to the Act for the Development of the Academic Staff in Republic of Bulgaria, 13. Lists of citations of the publications presented in the completion, 14. The author's reference for the scientific contributions in the papers, presented in the competition, 15. Certificate for the teaching activities of the candidate, 16. List of publications presented in the competition divided into the indicators „В" and „Г" and copies of the publications, 17. Abstracts of presented publications, 18. Scan of the announcement of the competition published in State Gazette. By the request of the Scientific jury, the candidate presented Author's summary of his dissertation, proving that papers included in the dissertation are not presented in the competition.

The fulfillment of the official minimal requirements for the acquiring the academic position of „Associate Professor" (according to both the national law and the specific recommendations of the Faculty of Chemistry and Pharmacy) is seen in the following Table.

Publication activity, participation in scientific projects. Dr. Todorov is author of 23 publications, incl. 21 in journals with impact-factor. The total impact factor of the journals with his publications is 31. It has been observed 61 independent citations. His h-index is 5.

Dr. Todorov participates in the competition with:

- 20 *scientific papers* published in the period 2010-2021. Their distribution between the ranks

Table. Fulfillment of the official minimal requirements for the acquiring the academic position „Associate Professor"and some scientometric data for the published papers

Indicator	A	B			Г						Д	Ж
Scores												
National requirements	50	100			200						50	-
Faculty recommendations	50	100			220						70	70
Dr. B. Todorov	50	102			228						74[1]	230
Journal rank		Q1	Q2	Q4	Q1	Q2	Q3	Q4	-	Book chapter[2]		
Number of publications		2	2	1	1	4	4	4	1	1		

[1]The candidate presents a list of 41 citations but 4 of them are self-citations.
[2] Published by J. Wiley & Sons.

of the journals is shown on the above Table. Most of the papers are published in specialized journals including highly appreciated Separation and Purification Technflogy, Europ. J. Medicinal Chemistry, Applied Radiation and Isotopes, Applied Geochemistry,

- list of titles of *11 reports* (including 3 oral) on scientific forums (2018-2021) (without bibliographic description and abstracts); lists of titles (without detailed description) of 10 *scientific projects* (2008-2019) (he is a leading scientist in two of them), some of them financed by the Bulgarian National Science Fund, European program and the IAEA.

The author's reference is comprehensive and detailed, containing introduction to the problem and clearly presenting the scientific contributions in papers submitted in the competition including those included in indicator "B".

4. Scientific activity

The main part of the scientific activity of Dr. Todorov is in the area of the ***development and application of radiochemical methods for synthesis and analysis***. From the point of view of the objects of study, the investigations can be divided into three fields: 1. Analysis of radionuclides and toxic contaminants in environmental and food samples. 2. Preparation of potential radiopharmaceuticals and related problems. 3. Archeometry.

The **main results** are summarized in the following text.

4.1. Analysis of radionuclides and toxic contaminants in environmental and food samples

Few ***important characteristics*** of these works should be mentioned:

- Various types of objects are investigated - soils of different type, plants, sediments, waters.
- The behavior of natural (U, Th) and technogenic (^{60}Co, ^{137}Cs and, mainly, ^{241}Am) isotopes, toxic metals and pesticides are studied. The choice of ^{241}Am as a representative of the transuranium elements is felicitous due to it's (and of his decay isotopes) long half-live and high radiotoxicity and, in the same time, presence of suitable for investigations gamma-line. The ^{60}Co and ^{137}Cs are most important and commonly studied nuclides in radioecology.
- The works are not limited to determination of contaminants in the object but deal with some important problems – transfer factors of radionuclides from soil to plants, their bioavailability and bioaccumulation of toxic elements.
- Along with gamma spectrometry, a few other analytical methods are applied.
- The works are detailed and comprehensive with clearly expressed interdisciplinary elements; when appropriate, conclusions important for the practice are derived.

Few directions of these works can be distinguished:

4.1.1. Development of analytical methods

- ✓ The applicant performs few investigations on the ***methods for extraction of Am***
  - ***The advantage of the method proposed in [1g[1]]*** is that it ensures determination of the

[1] The numbers follow numbering in the list of publications, presented by the applicant for participation in competition; with „v" and „g" papers included in indicator „B", resp. „Г" are noted.

bioavailable Am (with a yield of 92%) instead of its total content. Accounting for the facts that americium presents in the environmental in very low concentrations and its bioavailable form is Am^{3+}, the authors study the Am complexes with fluorinated β-diketons as a specific reagent for Am, suitable for extraction from water. The optimal reaction conditions for the complex formation at pH near to the neutral (the Am^{3+} exists at such acidity) are found.

- ***Further development of the method is reported in [4g].*** A two-stage procedure is proposed, appropriate for field sampling because the two stages of the extraction scheme may be separated in time – the complexing agent *tris*- β-diketon is added to the water (fresh or salty) in the moment of sampling and the extraction can be done lately. ***This way of work permits long preservation of Am^{3+} in the sample before analysis.***
- The very low contents of ^{241}Am and other anthropogenic radionuclides in surface waters (one to two orders of magnitude lower than those of natural radionuclides) forces researchers to search for more effective methods for concentration. ***Probably the study [5v] is the first attempt for selective extraction recovery of ^{241}Am from environmental samples applying ionic liquids.*** Using octylimidazolium saccharinate the authors establishe conditions (buffer, presence of complexing agent, etc.) permitting reproducible concentration and separation of ^{241}Am from ^{137}Cs and ^{60}Co (separation factors 298 and 447, resp.). A hypothesis is proposed that the existence (at the analytical conditions applied) of more complex forms of Am than of Cs and Co favors its interactions with the ionic liquid and contributes to its higher extraction yield.

✓ The optimization of the instrument parameters in a laser ablation-ICP-MS method gives the possibility for simultaneous determination of 30 micro and macro elements in soils and sediments samples. ***The main novelty in the work [8g] is the developed procedure for homogeneous sample pellets preparation.*** Certified reference materials (distributed by IAEA in form of powder) have been used for optimizing and validation of samples preparation.

4.1.2. Radionuclides and heavy metals in soil, plants and sediments

✓ Dr. Todorov takes part in ***a series of extensive, detailed and carefully interpreted investigations*** of the behavior of ^{241}Am, ^{137}Cs and ^{60}Co in soils.

- *The effect on the geochemical fractionation* of ^{241}Am in soils [1v], its migration rate and availability, time to reach equilibrium in the soil [2v] of the following factors is investigated: (i) soil type; mainly Fluvisol and Cambisol but other types [2v] are also studied, (ii) environmental temperature - sharp drop (-18 ^{o}C [1a]) or sharp increase [6g], (iii) soil drought, (iv) time of storage (1-5 months [1v] or 3 years [6g]) after the contamination). The possibilities of *few extraction schemes* for ^{241}Am recovery are evaluated and most appropriate is chosen followed by gamma-spectrometry.

- As a result of the investigations, the *water solubility of Am, its association with organic matter, binding/sorbing to the soil carbonates or associated with* Fe/Mn *oxyhydroxides* are established. The drought or sharp freezing enhances the spreading and bioavailability of Am from Fluvisol (with low pH and cation exchanging capacity and sand content). The opposite effect is found for clay-containing Cambisol soil [1v]. The time after contamination when highest migration and availability of ^{241}Am in soils are observed is established [2v].

- It is shown that a sharp temperature increase or deep freezing for one month leads to *different changes in the fractionation of the ^{241}Am, ^{137}Cs and ^{60}Co* in Fluvisol soil stored for three years after its contamination [6g].

- The respond (*migration and potential bioavailability*) of ^{60}Co and ^{137}Cs on cooling, freezing and drought of Fluvisol and Cambisol soils is rather different. A high migration and potential bioavailability of ^{60}Co is observed only in Fluvisol soil [7g].
- *The transfer factor of ^{241}Am in the soil-plant chain* is find out from the analysis of three crops of planted grass [2v]. The conditioning at 40 ºC caused increased *bioaccumulation* of the ^{241}Am, ^{137}Cs and ^{60}Co in grass [6g]. The established double increase of exchangeable ^{137}Cs under some circumstances is registered in [7g].

The mentioned effects are explained with the influence of the sharp variation in the temperature and soil humidity on the organic compounds in the soil, its pH, aggregation, etc.

The results of these works contribute toward a better assessment of the risk of the radioactive contamination and especially of the enhanced migration of radionuclides, their transfer in the food chain and bioaccumulation.

✓ Because of its location (Struma river, below highly industrialized town of Pernik), Pchelina Reservoir sediments are very interesting object for investigation of the in-time dynamic technogenic contribution to the environmental pollution. ***The paper [15g] is one of the very small numbers and, probably, the most careful and extensive research of these sediments.*** The paper presents a very large amount of analytical results processed by a variety of methods of the statistical analysis leading to calculation of enrichment factors (distinguishing anthropogenic pollution from the natural content of elements in the sediment) followed by ecotoxicity assessment (revealing low toxicity of the investigated surface sediments). *The measurement of γ-activity of* ^{137}Cs (which genesis is related to 1986-Chernobil wreck) *permits the average sedimentation rate to be determined.*

✓ ICP-MS is used to determine ***U and Th content in soil and plants from Buhovo mining area***. Precautions are taken to eliminate factors which could interfere with the precision of the analysis. The concentrations of the elements in the soils and U/Th ratio prove U contamination. *The sampled plants exhibit increased concentrations of Th and especially of U,* the values depend on type and part of the plant. Season variations in U- and Th- forms are established [3g].

4.1.3. Analysis of toxic metals and pesticides

- The content (14 ng/g – 18 μg/g) of Cd, Co, Cr, Cu, Mn, Ni, Pb and Zn in two apple varieties is determined by ICP-MS method. A sequential analytical procedure applied permits fractioning of the studied elements as water-soluble, polyphenol-bound and included in lignin. ***An attention is paid to bioaccessibility of metals.*** The *in vitro* procedure includes gastric and intestinal digestions, carried out at simulated human conditions leading to data for the respective metal absorption. Accounting for the high bioaccessability (about 70%) of Cu, Zn and Cd, a special attention to the problem in Cd-polluted areas is recommended [11g].
- ***The potential of HPLC-DAD for determination of pesticides in surface water*** (after extraction with dichlormethane) as an alternative to gas chromatography is shown [13g]. The accuracy and precision, limits of detection and quantification, linearity and range of applicability of the proposed method for every one of the studied pesticides are established. Their stability in water (for 6 months) is studied at room temperature and in climate chamber.

4.2. Preparation of potential radiopharmaceuticals and related problems

- *Synthesis is realized of radiotracers for in vivo non-invasive imaging investigations of the role of prolyl oligopeptidase* (POP is associated with neurvous systeme diseases). Two novel bifunctional POP-specific ^{123}I-labeled pyrrolidines are synthesized of which 4-(4-[^{123}I]iodophenyl)butanoyl-L-prolyl-2(S)-cyanopyrrolidine is used for POP labeling. The authors perform a ***rather extensive and tough but fruitful chemical and radiochemical work.*** *A known organic synthesis method is adapted for work at specific radiochemical conditions* (micro concentrations and volumes, high radioactivity, automatic laboratory set-up) thus achieving product with high radiochemical yield (87 ± 4%), radiochemical purity >99% and specific activity of 456±98 GBq/μmol. Further on, the performance of the synthesized product is evaluated in mice by *ex vivo* biodistribution studies and SPECT imaging [5g].
- *A variation of a method for photoisomerization of cis- to trans-cyclooctene is developed* [12g]. The work can be indirectly associated to this group of papers as far as the *trans*-isomer is a much more advantageous precursor for a reaction for biomolecules radiolabeling performed at physiological conditions. The authors derive a theoretical model of the thermodynamic equilibrium in the used system and on this base ***develop a procedure much easier to be performed, achieving 3- to 5-fold higher yield*** of the *trans*-product than procedures proposed in the literature.
- *Optimized procedure for recycling of irradiated ^{18}O-enriched water is proposed.* The problem is economically important due to the high cost of the enriched water and great amount of the water wasted from ^{18}F-labeling of glucose derivates used in positron emission tomography. ***The main advantage*** of the 3-step procedure proposed in [4v] is that radionuclides, contained in the water, are discharged in the first processing step thus reducing the radiation burden of the personal. An

interesting approach is applied to set free water from organic pollutants by its inclusion in Na_2SO_4 crystalohydrate. *The quality of the so recycled* [^{18}O]H_2O *is comparable to commercially available product achieving by means of conventional set-up with minimal losses of* ^{18}*O-enrichment and mass* along with enormous reduction of the radioactive waste.

- *The contribution to the identification of the ecological effect of radiopharmaceutical residual (organic part of the radiopharmaceuticals) is made.* The paper [10g] is an example of applying of the quantitative structure-properties relationship methods in the radioecological studies. ***The authors' approach differs from the proposed prognostic models***; the latter account only for the chemical form of radioisotope, neglecting the non-radioactive part. The authors deal with great number of bifunctional forms - parts of the modern radiopharmaceuticals, able to provide „click reaction". The application of cluster and principal component analysis enable the identification of the effect of residuals for which experimental values are not yet available.

- The review [3v] reflects the fast development of the theranostic copper radiopharmaceuticals investigations. It is based on 196 literature sources and ***has the ambition „to facilitate the mutual understanding between all different specialists working on this multidisciplinary field". To my opinion this aim is achieved.*** The review contains detailed data on (i) Production and properties of the copper radioisotopes, which meet the requirements of nuclear medicine (^{60,61,62,64,67}Cu) and which cost remains, so far, a limiting factor for their applications. (ii) Design and synthesis of copper radiopharmaceuticals (development of copper bifunctional chelators, very complete **s**ummary of the biological /*in vitro, in vivo/* studies). (iii) The medical uses and trends in theranostic application.

- The review [14g], based on 85 literature sources, considers the production of ***superparamagnetic iron oxide nanoparticles*** (incl. both conventional and recently developed procedures) and their application for anticancer drug delivery and as contrast enhancement in magnetic resonance imagining for biomedical investigations. The role of the surface properties, aqueous stability, etc. related to their teranostic applications is considered. Factors affecting resolution and sensitivity, incl. the size and the colloidal stability are reviled. Toxicological effects, comparison with the popular Gd-based contrast agent are also covered in the review.

4.3. Archeometry. X-ray fluorescent analysis application.

The results reported in the presented two papers are interesting from both archeological and chemical points of view. To my opinion ***the work [9g] is a model of the organization of an archeometric study***. (i) It is the first investigation of the gold objects found in the Great Sveshtari tumulus (district of Razgrad). (ii) The authors account for one of the major difficulties of the handheld ED-XRF instruments – lack of the suitable calibration materials. That is why they prepare (with the financial support of the IAEA) series of gold standard. One of the standards is validated by three foreign laboratories. (iii) The detailed description of the objects and great amount of analysis are done. (iv) Cluster analysis of the results is performed. (v) The interpretation of the results from archeological point of view is extensive and thorough. Based on precise determination of the composition of an ingot found in Black sea, the rather serious mistake in earlier reported dating of the find is shown [2g]. A very high content of gold (22.4 – 23.8 carats) is found in jewelry from Great Sveshtari. The results permit *some hypothesis* for raw materials source and for manufacturing technology of the investigated Thracians artifacts to be proposed [9g].

Basic scientific contributions

1. *Contribution to the evaluation of the risk from technogemic and natural rdionuclides and heavy metals contamination of soils, sediments, waters, plants*, incl. (i) Development of extraction methods for determination of bioavailable Am in waters. (ii) Established behavior (migration, availability) of ^{241}Am, ^{137}Cs and ^{60}Co in soils and sediments as a function of number of factors. (iii) Assessment of the potential transfer of radioactive contaminant and toxic metals in the food chain. (iv) Evaluation of radioactive contamination in specific area.

2. Development, optimization and application of radiochemical/chemical/chemometric methods in the field of radiopharmaceuticals and related problems, incl. methods for (i) Radiochemical synthesis of new bifunctional ^{123}I- labeled compounds, successfully applied for *in vivo*

imaging of prolyl oligopeptidase. (ii) Optimized method for recycling of irradiated ^{18}O-enriched water. (iii) Preparation of a precursor for biomolecule labelling reactions. (iv) Assessment of the organic part of radiopharmaceuticals in terms of their environmental impact.

The published comprehensive and detail reviews contribute to the better understanding of the present status and trends of development of radiocopper-labeled radiopharmaceuticals and of superparamagnetic iron oxide nanoparticles preparation and theranostic applications.

3. *Well-grounded hypothesis for dating and manufacturing of archeological artifacts are derived* from the results of the performed precise analysis.

Citations. Nine of the papers presented for the competition have 37 citations. Citing papers are published in highly ranked specialized journals in the fields of radio-, geo-, inorganic, coordination and medicinal chemistry, ecology and nuclear medicine.

Evaluating citation rate of the Dr. Todorov' papers, one has to take in account that 7 of the presented 20 papers are published in 2020 and 2021 and more citation could be expected.

Personal contribution. The average number of co-authors of the presented papers is 4.1 which can be expected for interdisciplinary works. Dr. Todorov is 1-st or 2-nd author in 80% of the papers and his personal contribution is clearly expressed.

5. Teaching activity

The pedagogical activity of Dr. Todorov is impressive. In recent 5 years he has an average total employment of 643, incl. classroom of 537 academic hours which significantly exceeds the load required by the University regulations. He is giving lectures in few compulsory courses for bachelor students in Nuclear Chemistry: Ionizing radiation measurement (30 acad. hours), Radioanalytical chemistry (30 acad. hours), Radioecology (15 acad. hours), as well as Environmental radioactivity (30 acad. hours) for the master program of Radiochemistry and Radioecology. Dr. Todorov is giving tuition in seminars and laboratory practice for the above mention and few other courses.

In the period 2010-2019, 17 diploma works have been performed under the supervision of Dr. Todorov, all of them in the field of radiochemistry.

The rich and diverse pedagogical activity of Dr. Todorov is reflected in his rather high value of the indicator „Ж". It has to be mentioned that the real value of this indicator is even higher because the applicant' participation in scientific projects is not fully taken into account.

Conclusion

The materials provided for the competition satisfy the requirements of the national law and of the recommended criteria of the Faculty of Chemistry and Pharmacy. They approve Dr. Todorov as a qualified scientist and university teacher in the field of radiochemistry.

His scientific activity is mainly in the field of radiochemistry but most of his works are with clearly expressed interdisciplinary elements with contribution to the synthetic and analytical radiochemistry and the radioecology.

I know Dr. Todorov since his student years and I have some contact with him up to 2010. He is an enthusiastic and promising young scientist and I believe that his promotion will be useful for both his academic carrier and the further developing of the radiochemical investigations in the Faculty.

Taking in mind the scientific and teaching activities of Dr. Todorov as well as my personal opinion I recommend to the Scientific jury ***to propose to the Faculty Council Chief Assist. Prof. Dr. Boyan Rumenov Todorov to be elected for the academic position of Assoc. Professor*** in the Professional field 4.2. Chemical Sciences, scientific field Radiochemistry at the Faculty of Chemistry and Pharmacy, St. Klment Ohridski University of Sofia.

24.3.2022

Reviewer:
D. Todorovsky