REVIEW

by Prof. Stefan Dimitrov Nikolov, DSc.
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Subject: **Procedure for selection of "Associate Professor" in the scientific specialty "Pharmaceutical Chemistry and Pharmacognosy"**, announced in SG, issue 105 of 11.12.2020 for the needs of the Department of Pharmacy at the Medical College of the University "Prof. Dr. Asen Zlatarov ", Burgas,

General data

The announced competition is in the field of higher education 7. "Health and Sports", in professional field 7.3. Pharmacy and scientific specialty "Pharmaceutical Chemistry and Pharmacognosy". For participation in the competition, documents have been submitted by a single candidate, Ch. Assistant Prof. MPharm. Stefan Vanev Harkov, PhD. Pursuant to Art. 57 (2) of PPZRASRB and Art. 70 (2) of PURPNSZAD at the University "Prof. Dr. Asen Zlatarov "- Burgas, with order № RD-28 / 05.02.2021 of the Rector of the University" Prof. Dr. Asen Zlatarov "- Burgas and a decision of the absentee meeting of the Scientific Jury coordinated by the Director of the Ministry of Culture and the Head of the Department, I have been appointed as a reviewer under the procedure of the above competition.

I declare that I do not have a conflict of interest with the candidate in the competition, I have not been the scientific supervisor of the candidate's doctoral dissertation and I have no co-authorship in the scientific papers presented at the competition.

Professional Development

Ch. Assistant Professor Harkov graduated with a master's degree in the regulated professions "Pharmacy" in 2010 at the Lviv National Medical University "Danilo Halitsky" in Lviv, Ukraine. He defended his master's thesis at the Department of Pharmacognosy and Pharmaceutical Botany. In the same year he was accepted and began training in full-time doctoral studies for a period of 4 years at the Lviv National Medical University "Danilo Halitsky". In 2014 he successfully defended his dissertation on "Synthesis and biological activity of thiazolidine derivatives with 2-oxo-1,3-dihydroindole fragment in the molecule" and acquired "PhD" in Pharmaceutical Chemistry and Pharmacognosy, which is recognized accordingly in Bulgaria - Certificate № 120/10. 01.2020 and the candidate is included in the NACID register. After returning to Bulgaria he worked as a master of pharmacy and manager of pharmacies in Burgas. Since 2016, after a competition, he has held the academic position of "Assistant" in Pharmaceutical Chemistry at the Department of Pharmacy of the Medical College. Since 2018 he has been a senior assistant, and since January 2020 - Deputy Director of the Medical College. The CV attached to the competition documents provides information on foreign language proficiency - self-assessment for levels of comprehension, conversation and writing in Polish, Russian and English, as well as computer skills and competencies.

Description and analysis of the submitted materials in the competition

In the competition documents Ch. Assistant Professor Harkov attaches a list of 26 publications. The list is consistent, without systematization by topics, sections and subsections.

This is done in the Author's reference, in which there are two sections: on "Pharmacognosy" and on "Pharmaceutical Chemistry". In the Author's reference the candidate divides the publications into: "Scientific publications in publications, referenced and indexed in world-famous databases with scientific information (SCOPUS) - 16 issues" and "Scientific publications in non-refereed journals with scientific review - 10 issues". It would be more correct for the candidate, in the submitted documentation, to make a more detailed analysis of his scientific production. Indicate with the number of publications which are on pharmacognosy, which are on pharmaceutical chemistry, which are related to clinical trials, which are in other fields, which are review articles, with which publications the "PhD" in Pharmaceutical Chemistry and Pharmacognosy acquires, as these publications were once reviewed and are now dropped. In this regard, the Abstract of the dissertation should be attached to the documents and it should be below № 1. The lack of numbers of scientific papers to correspond to the numbers in the list, which lacks even a title, significantly complicates the work of reviewer.

From the review of publications 4 refer to pharmacognosy (papers №№ 1, 2, 3 and 5), scientific reviews are 5 (papers №№ 4, 6, 12, 14 and 19). In the Author's reference of the scientific works of the candidate there are data for only 15 publications, of which the above-mentioned works in the section pharmacognosy are 3 (№№ 1, 2, 3). The Pharmaceutical Chemistry section describes and provides data for 12 publications (№№ 10, 11, 12, 13, 14, 17, 18, 19, 22, 24, 25 and 26). The candidate in the Author's reference could make a self-assessment of a very important moment for participation in a competition, these are the scientific contributions and their nature. Instead of applying abstracts to the publications, he had to analyze all his scientific production and highlight the scientific contributions and indicate the publications with the numbers they contain and highlight which ones are of scientific-theoretical, scientific-applied or confirmatory nature.

To the critical remarks of the Author's reference can be added the lack of information about the publications in which the scientific papers have been published. It is not clear which 16 scientific publications are printed in publications, referenced and indexed in world-famous databases of scientific information. I accept the data for 11 of these publications, which are indicated in the signed declaration for the number of points by indicators in the field of the competition. There are no data on the candidate's participation in scientific forums with reports and their publication in relevant publications.

The attached document for "Reference to the citations in which the candidate's publication is cited" is also subject to serious critical remarks. This reference should contain the name of the publication and where (authors, name of the publication and journal) it is cited. The information on Scopus on which the report is prepared must also contain the authors, the publication and the number of citations. In the attached reference this is done only for one publication № 22, which is cited 4 times, or the candidate participates in the competition with only 4 citations !?

From the analysis of the candidate's scientific production, the observed jump in research and publication in the last three years, during which 15 of the entire scientific production have been published, is also impressive. For the past 2020 alone, 9 works have been published. Pharmacognosy is an experimental science and I consider it real and normal as a result of the scientific work of a researcher in this specialty to be able to prepare and publish about 2-3 publications in one year.

From the review of the scientific production, I can competently take a stand and accept for review publications №№ 1, 2, 3, 5, related to the specialty pharmacognosy.

Assessment of the most significant scientific contributions

Of the above-mentioned peer-reviewed publications, the first three relate to pharmacognostic studies of the genus **Geum L**. The first publication № 1, which is entirely printed in English, studies the anatomical structure of the rhizome and root of **Geum urbanum. L.** The goal is set correctly, as these studies are very useful for the microscopic identification of the plant substance. The publication printed a color figure of microscopic sections of the studied objects, from which nothing is understood, as there are no signs and no text at all. Some conclusions have been made regarding the secondary structure of the root and rhizome, the location of the periderm in the cortex of the organs, the conclusions that the cortical part lacks facial sclerenchyma (mechanical fibers) and the presence of calcium oxalate crystals only in the rhizome are of diagnostic importance. . It has also been established, without pointing to the figure, that the wood sclerenchyma of the primary xylem consists of thick-walled fibers.

Morphological and anatomical studies were performed on the fruit, the bark of younger twigs and pomegranate leaves. They are reflected in publication № 5 of the list, which is also in English only and without any comment on it in the author's reference. The publication contains 2 color figures of microscopic sections of a fruit and a leaf, marked only with titles. Morphological examination refers to the macroscopic description of the leaves, their shape, size, texture and other features. The same is done for the fruit, adding the organoleptic characteristics, smell and taste and the characteristic arrangement of the pomegranate fruit in the fruit in nests separated by a light fleshy membrane with a smooth surface and light yellow color. Microscopic examination of the leaves revealed that the upper epidermis consisted of thick-walled, almost square cells, and the cells of the lower epidermis were polygonal with slightly curved thickened membranes. The stomata are numerous elliptical with 3 to 5 accompanying cells located mainly on the lower epidermis. In the same examinations of the fetus it was found that the cells of the epidermis of the exocarp are unevenly thickened, lie stepwise in different planes, another 2-3 rows of collenchyma, mesocarp composed of loose parenchyma, single crystals of calcium oxalate and groups of scleroids.

The second publication № 2 from the list is also in English only and refers to the phytochemical study of the genus **Geum L.** For this article there are only 3 lines of commentary in Bulgarian in the Author's reference. It is determined only: "The purpose of this article is to make a comparative phytochemical study of extracts from the various organs of the genus Geum, including aboveground and underground organs. For this purpose, fresh and dried parts of the studied representatives were used. The analysis of the publication shows that of the 8 species of the genus "Geum" distributed in the Bulgarian flora, two species of the genus - Geum urbanum and Geum montanum - were studied phytochemically.

Aqueous alcoholic and acidified aqueous extract of the leaves and underground organs of Geum urbanum and Geum montanum were phytochemically examined for the presence of main groups of biologically active substances. Tannins (hydrolyzed and condensed), flavonoids and small amounts of anthocyanins and coumarins have been qualitatively proven. Quantitative determinations of polyphenols from the groups of tannins and flavonoids were also performed, and a higher content was found in all studied organs of the two groups of compounds in Geum montanum. Tannins are determined titrimetrically and flavonoids spectrometrically. The results are reflected in two tables in the publication. In both studied types, the presence of rutin and quercetin was proved by thin layer chromatography. In conclusion from the conducted phytochemical studies reflected in this publication, it is concluded that the results are promising

for further study of pharmacological activity and the development of new herbal medicines from these raw materials.

Phytochemical studies are also contained in work № 5. Studies of aqueous alcoholic and acidified aqueous extract of the fruit, the bark of younger twigs and pomegranate leaves have been performed. Tannins have been proven in all studied sites by the well-known conventional methods of sedimentation and color reactions.

Studies on the genus **'Geum'** continue in publication № 3 of the list, which describes studies on the antimicrobial activity of a tincture derived from the rhizomes and roots of Geum urbanum. The tincture is obtained by maceration with 40% ethanol and is characterized in terms of odor, moisture, relative density, qualitative and quantitative content of tannins. Microbiological studies were performed on three dilutions of the tincture. As a result of these studies, the tincture was shown to inhibit the growth of both gram-positive - Staphylococcus aureus, Bacillus cereus, Bacillus subtilis, and gram-negative bacteria - Escherichia coli, Pseudomonas aeruginosa, Salmonella enterica serovar abony. The best inhibitory action is registered in the undiluted tincture, which can be used in medical practice for the treatment of diseases caused by these microorganisms.

From the analysis of the achieved contributions from the scientific and scientific-applied activity of Ch. Assistant Professor Dr. Harkov, reflected in the peer-reviewed scientific papers (section Pharmacognosy) it is seen that there are no scientific-theoretical contributions. There are scientific - applied and confirmatory contributions, but they are difficult to find in the publications, which are without a clear experimental part, separated from the results, with long summaries, repeated with the introductions, very short discussion, illustrations, not showing the important things from the text. Significant scientific contributions are achieved after in-depth experimental work with appropriate materials and methods, competent discussion and discussion of the results obtained.

I hope that is not the case in the rest of the candidate's scientific output relating to the Pharmaceutical Chemistry section. From the author's reference, as well as from the publications themselves, it can be seen that in this production there are definitely scientific and theoretical contributions related to the synthesis of new compounds including thiazolidine, pyrazoline and isatin fragments - works № № 10, 11, 13, 17, 18, 22, 24 and 26.

The synthesized novel compounds were tested for antitumor, antiviral and antioxidant activity in vitro. An in silico study and COMPARE analysis of the groups for potentially antitumor and antiviral agents were performed, on the basis of which to build hypotheses about the mechanism of action and formulate proposals for targeted synthesis of new drug molecules. In №18, the novel thiazolo [4,5-b] pyridine derivatives were tested on carrageenan-induced rat edema and showed a strong anti-inflammatory effect that exceeded that of diclofenac. The newly synthesized compounds were tested for their in vivo toxicity. I believe that the results of the research reflected in these publications have a certain scientific-theoretical and scientific-applied character.

I also hope that the other reviewer, who is a specialist in the field of pharmaceutical chemistry and organic synthesis, will analyze and give an objective assessment of these scientific papers.

Reflection of scientific publications in the literature

The response of scientific publications in the literature is judged mainly by the scientometric data from the impact factor of the journals in which the scientific papers are

published and by the observed citations. The reviewer receives these data from the "Reference for citations", which is prepared by the candidate and must be attached to the competition documents. Above, in the review in the section "Description and analysis of the submitted materials in the competition" critical remarks were made about the method of preparation of the report and the information contained in it. According to the reference, only work № 22 was cited 4 times, without indicating the authors, publications and magazines where the citations were found. The same section of the review noted the lack of information about the impact factor of the journals in which the scientific papers were published. For these reasons, I cannot judge the response of the candidate's scientific publications in the literature. It is obvious that the citations are more in number, as the attached Declaration for the number of points by indicators in Area 7 indicates 60 points.

Educational activity

Three of the documents in the competition are related to the educational activity of the candidate. The first is a Certificate signed by the Rector of the University "Prof. Dr. Asen Zlatarov" for the date of the beginning of the teaching activity as an assistant in the Medical College Burgas, which is from 26.09.2016. From 14.02.2018 and till now he is the Chief assistant professor. The candidate applies a "Reference for teaching activities", which contains three sections: a list of curricula; teaching and learning activities. The report shows the participation in the development of 5 curricula, three of which are in Pharmaceutical Chemistry, in Internship and in Undergraduate Internship for the specialty "Assistant. Pharmacist "for Bachelor's degree, regular training and two curricula in Chemistry of Medicinal Products and in Phytotherapy and Cosmetology for Bachelor's degree, regular training in Chemistry of Cosmetics and Surfactants. The reference for the teaching activity shows that the candidate has taken part in the teaching of three of the most important pharmaceutical disciplines - pharmaceutical chemistry, pharmacognosy and technology of drugs with biopharmacy, as well as the management of the internship and undergraduate internship in the specialty "Assistant Pharmacist "for the Professional Bachelor's degree. The teaching activity of the candidate consists of giving lectures, conducting practical exercises and teaching practice, conducting practical exams with students and regular participation as a member of examination commissions in semester and state exams. The candidate is seriously engaged in these educational activities and the study load for each school year is almost twice as much as the norm. This is documented by the attached Reference for work load, signed by Deputy rector for academic work of the university. I have direct observations on the teaching work of Ch. Assistant Professor Dr. Harkov and I give a positive assessment of this activity. I am convinced that the candidate is fully responsible for this most important activity for the requested academic position of "Associate Professor" in the field of higher education.

Critical notes

A number of critical remarks were made above in the qualitative and quantitative analysis of the scientific works, as well as for the entire research and publication activities of the candidate. Summarizing all the critical remarks, I make the conclusion to evaluate the unsatisfactorily presented scientific activity of the candidate, reflected in the works, which I review in the section Pharmacognosy. The reason for this is the small number of publications, the lack of significant scientific contributions, citations, incorrectly written publications and more. All scientific papers in the Pharmacognosy section were published in 2020. I define this fact as a campaign in research and publishing and chasing the necessary number of scientific papers required by the regulations

for participation in the competition for associate professor. With great reservations, due to the lower requirements, I remain with the journal Knowledge - International Journal, which publishes all of the peer-reviewed scientific papers.

This negative assessment is objective, not malicious, it is partial and refers only to the Pharmacognosy section and to the research activity. The aim is also to provoke and motivate the candidate, if he has decided to build a scientific career and develop in the field of Pharmacognosy, it should be borne in mind that a lot of knowledge and work is needed, as it is one of the most labor-intensive pharmaceutical disciplines and scientific base, for which he can use some of his own research laboratories at the Medical College and the base of buildings and numerous, well-equipped chemical laboratories of the University. To this I will add that in the future there are prerequisites for the development of the candidate in the field of Pharmacognosy. As a student he defended his master's thesis in the Department of Pharmacognosy and Pharmaceutical Botany. In college he teaches Pharmacognosy, masters many morphological-anatomical and phytochemical scientific methods used in Pharmacognosy.

The full assessment of everything else that is presented and required for the award of an Associate Professor will be reflected in the conclusion of the review.

Personal impressions

I know Ch. Assistant Professor Dr. Harkov since his admission as an assistant at the Medical College in Burgas in 2016. I have been impressed ever since with the desire to work at the college, accompanied by perseverance in performing the tasks and above all great diligence. He was everywhere, from the design of curricula to their implementation in the teaching of the most important pharmaceutical disciplines. As I shared above, I am satisfied with the joint study work with the candidate in teaching these disciplines at the Medical College in Burgas. I can confidently say that he is an erudite teacher, with extensive and in-depth knowledge and pedagogical skills in presenting the teaching material, is demanding of students and deservedly enjoys the respect and authority of colleagues and all students. During the last year of the pandemic, and even before that, Harkov was the connection of all students from all courses in the specialty "Assistant. pharmacist "with the teachers - local and newcomers. His participation in the establishment of the laboratory of Technology of drugs with Biopharmacy and its equipment with materials, reagents, relevant equipment, etc. is active. Along with the busy teaching work, he perfectly handles the administrative work in the Department of Pharmacy. He is the secretary of the department council, collects information, prepares meetings, makes requests for everything necessary for the department, etc. As Deputy director of the college is also doing well in this administrative position. Especially useful for the department will be Harkov in the coming period, when the accreditation of the specialty "Asistant pharmacists" will be held at the Medical College - Burgas.

Conclusion

Assessing the overall scientific activity, which highlights scientific contributions, echo in the scientific literature and coverage of the minimum national requirements of ZRASRB and scientometric indicators of the Regulations on the terms and conditions for obtaining scientific degrees and holding academic positions at the University "Prof. Dr. Asen Zlatarov "- Burgas (PURPNSZAD) and taking into account the high evaluation of the educational activity, which is important for the requested academic position, I make the following conclusion: **I recommend** the members of the Scientific Jury to choose Ch. Assistant Professor MPharm. Stefan Vanev Harkov,

PhD for Associate Professor, in professional field 7.3, "Pharmacy", in the scientific specialty "Pharmaceutical Chemistry and Pharmacognosy".

Sofia
23rd of March 2021

Reviewer:

/prof. Stefan Nikolov, DSc/