**REVIEW**

by Prof. Sevdalina Hristova Turmanova, PhD

Member of the Academic Jury set to render a decision

on the competition for filling the academic position of a Professor

in the Professional Field **4.2.** Chemical Sciences according to the Classifier of the Areas of Higher Education and the Professional Fields

(Scientific Specialty “Polymers”)

announced in SG, issue 24/ 17.03.2023

This Review is prepared in response to Order № RD-38-162/ 06.04.2023 issued by the Rector of the Sofia University „St. Kliment Ohridski“*.*

The Review is in compliance with Development of Academic Staff in the Republic of Bulgaria Act (DASRBА), the Rules for the Application of the Development of Academic Staff in the Republic of Bulgaria Act, and with the Rules set at the SU "St. Kliment Ohridski, for applying the Act aforementioned.

1. **Professional development**

Associate Professor Elena Dimitrova Vasileva graduated in 1995. as a master's degree in the Faculty of Chemistry of the Sofia University "St. Kliment Ohridski", and later in 2000 successfully defends a thesis,which grants her the scientific degree “Doctor”. The candidate's academic career began in 2003 as an assistant, successively occupying the positions of senior assistant in 2004 and chief. assistant in 2005 From 11.01.2008 until now he holds the position of associate professor at the Faculty of Chemistry and Pharmacy of the SU "St. Kliment Ohridski". Assoc. Prof. Vasileva is a renowned university lecturer in the field of “Polymers” which is taught as a part of the following majors: "Computer Chemistry", "Engineering Chemistry and Modern Materials", "Chemistry and Informatics", "Ecochemistry", "Nuclear Chemistry" at the Faculty of Chemistry and Pharmacy, SU "St. Kliment Ohridski". She is a lecturer in elective courses "Modern Biomedical Applications of Polymers" and "Film-Forming Polymers" at the Faculty of Chemistry and Pharmacy of SU "St. Kl. Ohridski. From 1997 to 2002, the candidate gained professional experience successively at the Institute of Structure of Matter, Higher Council for Scientific Research, Madrid, Spain; Center for Polymer Research, School of Chemistry, University of Cincinnati, USA; Institute of Composite Materials at the University of Kaiserslautern, Germany; Faculty of Process and Materials Engineering Chemistry, University of Palermo, Italy.

1. **Assessment of the scientific and research accomplishments**

According to Art. 2b and Art. 29 of DASRBА, the candidates for the academic position "professor" for a scientific field 4.2. Chemical sciences must meet minimum requirements for their scientific activity. The documents presented by Associate Professor Dr. Elena Vasileva in relation to the announced competition define her as a researcher with clearly expressed scientific orientations in the professional direction and the scientific specialty of the competition procedure. She participated in the competition with 15 scientific publications, 10 of which were published in the last 5 years. These publications do not repeat the publications presented for the acquisition of the educational and scientific degree "doctor" and the position "associate professor". 14 scientific publications are printed in specialized editions that are referenced and indexed in world-renowned databases of scientific information (*Web of Science and Scopus*), falling into quartiles from Q1 to Q3 according to the grouping of scientific journals. Dr. Vasileva also participated in the competition with 1 chapter from a book by the renowned publishing house *Wiley-VCH GmbH*. According to data from *Scopus*, the publications presented for the competition were cited a total of 68 times. It is noteworthy that the publications are cited in reviews, in book chapters and in publications that are referenced and indexed in the world-renowned scientific information databases *Web of Science* and *Scopus*. The combined impact factor of these articles is 51.96, the average impact factor per article is 3.46, and the average citation rate per article is 4.5. For participation in the competition, Assoc. Prof. Vasileva also presents a habilitation thesis on the topic "Polyzwitterions and materials based on them with application in medicine and pharmacy".

From the above-mentioned scientific activity of Assoc. Prof. Vasileva it becomes clear that she meets the minimum requirement of 760 points and even exceeds it as the total number of points in the groups of indicators, mandatory for holding the academic position "Professor" is 1181. The requirement under indicator A(1) for having the educational and scientific degree "Doctor" is fulfilled and carries 50 points. According to indicator C (3-4), the candidate presents 5 publications - two with rank Q1 and three with rank Q2 with a total of 110 points, at a mandatory minimum of 100 points. Group D (5-10) includes various indicators for which the participant in the competition has presented 11 scientific publications. Publications are distributed by journal rank as follows: 5 issues with Q1, 4 issues with Q2, 1 issue with Q3, 4 issues with Q4 and one monographic chapter in a book. The sum of points according to indicators of group D (5-10) is 245, with a mandatory minimum of 220, and according to indicator D (11), the candidate has 136 points, with a required minimum of 120. According to indicators of group E (12-20), the candidate for the position of "Professor" there are 380 points, and she has presented a list of 11 participations in research and applied projects, all successfully completed, as well as co-supervision of two PhD students. The projects have both national and European funding. According to indicators from group G (21-25), the candidate presents 270 points, out of a set minimum of 150. A list certifying the management of 11 graduates is presented. The scientific works of the only candidate in the competition - Assoc. Prof. Elena Vasileva are very well reflected in the world scientific space, with an *h*-factor of 13.

Assoc. Prof. Elena Vasileva meets the requirements, according to the Development of Academic Staff in the Republic of Bulgaria Act (DASRBА), the Rules for the Application of the Development of Academic Staff in the Republic of Bulgaria Act, the Rules for the Application of the Development of Academic Staff in SU "St. Kliment Ohridski" and has the right to participate in this competition.

1. **Main contributions, analysis and evaluation of the candidate's scientific and scientific-applied contributions and relevance of the topic**

The main scientific contributions of the presented publications are in accordance with the professional field for which the competition was announced. The scientific publications show consistency in a relevant and problematic interdisciplinary field, with the application of chemical and instrumental methods to solve various problems, having a fundamental and medical nature. The well-planned and targeted scientific research on the topic "Polymer materials with application in medicine", enriched with new methods and performed at a high methodical level, can be summarized with contributions in three important directions:

***Contributions related to the preparation of polyzwitterionic hydrogels and their biomedical applications as materials for chronic wound dressings (No. 8, 9, 13) and for modified drug release (No. 16).***

The application of polyzwitterionic networks (poly(sulfobetaine methacrylate) (PSB) and poly(carboxybetaine methacrylate) (PCB) as innovative materials for making dressings for chronic wounds was shown for the first time in articles (No 8, 9). New hydrogels were developed, obtained using cross-linking agents with ethylene glycol monomer units, demonstrating high anti-biofilm activity against the most common bacterium in chronic wounds, *S. aureus*. Their anti-biofilm activity, together with their non-adhesive properties to tissues make them non-adhesive to the wound, and hence excellent candidates as dressing materials for chronic wounds. PSB hydrogels were found to possess "intelligent" behavior (No. 8) related to the linear dependence of the degree of swelling in water on temperature in the range 20-70°C. The antipolyelectrolyte behavior the salt and pH sensitivity of the polyzwitterions were studied in detail, as well as their strong ability to bind water - ∼40%, which could be determined as the main reason for their ultralow non-specific protein adsorption.

The non-cytotoxicity and biocompatibility of the hydrogels were proved *in vitro* and *in vivo*. Thus, the study demonstrated the PSB hydrogels’ advantages as dressing materials for chronic wound healing, namely: (i) high ability to absorb wound exudate; (ii) high ability to bind water; (iii) good control on the enzymes concentration in the chronic wounds through absorption (iv) without inhibiting their activity; (v) antibiofilm activity against common for the chronic wounds bacteria; (vi) non-cytotoxicity and (vii) *in vivo* proved very good tolerance by the surrounding tissues.

These studies by Dr. Vasileva are one of the first in the scientific literature and clearly demonstrate the valuable applicability of polymers possessing zwitterionic functionality. An excellent summary review of this scientific contribution to the application of polyzwitterion-based materials for wound dressings has been published as a monographic chapter in a book (No. 13). For the first time, copolymer networks based on sulfobetine methacrylate (SB), vinyl pyrrolidone (VP) and poly(ethylene glycol) diacrylate (PEGDA) were synthesized and studied for modified drug release (No. 16). The obtained three copolymer networks with different compositions, as well as pure PSB hydrogel, were investigated as precursors for the preparation of soft contact lenses. The latter can be used to release the medicinal substance timolol maleate (TM) in the visual organ. The influence of the composition of the copolymer networks on the loading capacity with TM drug units was studied. PSB/PVP copolymer networks were found to be suitable for fabricating soft contact lenses due to their light transmission and providing modified TM release in the patient's eyes.

***Contributions related to the preparation of interpenetrating polymer networks (IPNs)*** ***for the creation of functional polymer materials (No. 2, 3, 4, 5, 6, 14, 15).***

The main scientific contributions in this direction refer to the creation of interpenetrating polymer networks suitable for modeling drug delivery systems (No. 3, 5, 6, 14), as matrices for the creation of polymer composites (No. 15) and as "smart" biomaterials (No. 4). Two interpenetrating polymeric networks based on poly(acrylic acid)/polyacrylamide and poly(methacrylic acid)/polyacrylamide were synthesized and used as carriers for sustained release of verapamil hydrochloride (VPM). The interaction of the drug substance with the polymer networks through both ionic and hydrogen bonds has been demonstrated, showing that the ratio between the two polymer components in the networks affects the release profile of VPM. The functionality of the components and the density of the network, which determines their ability to swell, affects both the loading efficiency and the VPM release profiles. It is reasonably concluded that the appropriate choice of components and their composition in networks can be used to control structure and properties, and hence their characteristics as drug delivery systems.

Suitable conditions were found for the application of interpenetrating polymer networks of polyacrylic acid and polyacrylamide as matrices, in which polymer composites (No 4) are formed by *in situ* precipitation of calcium phosphates. This innovative research by Prof. Vasileva, in which interpenetrating polymer networks are used as matrices for the precipitation of calcium phosphates, is an attempt to follow the natural process of biomineralization and will probably be another scientific niche of her future research. As a particularly valuable contribution, I consider the first synthesized interpenetrating network of PSB and PCB, based on the specific properties of polyzwitterions, which has the ability to respond simultaneously to three "biological" external stimuli - temperature, pH and salt concentration (article No. 15). This research demonstrates the potential and flexibility of this approach as a method for creating smart materials. In addition to its "smart" properties, the IPNs PCB/PSB hydrogel exhibits anti-biofilm activity against common bacteria such as *P. Aeruginosa*, *A. Baumanii and K. Pneumoniae*, is non-cytotoxic and has very good *in vivo* biocompatibility. The latter makes it a unique smart material that can find many applications in medicine, pharmacy, for smart sensor materials, etc. In a scientific publication (No. 2), the interactions between the polymer components forming interpenetrating polymer networks are characterized. The results indicate that due to the strong hydrogen bonds in them, the IPNs hydrogels of poly(2-acrylamido-2-methyl-1-propanesulfonic acid) and polyacrylamide possess significant strength and mechanical properties.

***Contributions devoted to the study by different approaches of the preparation of polymer particles of different size, shape and structure. The results are summarized in scientific works (No. 1, 7, 10, 11, 12).***

Part of the research in the scientific production presented by the candidate, Assoc. Prof. Vasileva, is related to the successive production of protein capsules by ultrasonic (sonochemical) (No. 1, 10), as well as chemical and physical crosslinking of polyzwitterions, described in a publication (No. 12). For the first time, the application of an ultrasonic (sonochemical) method for the production of protein micro- and nanoparticles has been demonstrated. The potential of gelatin capsules as carriers for medicinal substances -*α*-tocopherol and acetylsalicylic acid has been studied in detail. In a critical review (No. 1) the advantages and disadvantages of the sonochemical method for obtaining other protein particles are described. Polyzwitterionic particles obtained by chemical and physical cross-linking (No. 12) were also synthesized and characterized in detail from the point of view of their "intelligent" behavior when the temperature changes. Physically cross-linked PSBs were found to have a smaller hydrodynamic diameter and lower zeta potential in the ophthalmic temperature range compared to chemically cross-linked ones. The latter leads to higher TM load efficiency in them (about 30%).

The formation of polyelectrolyte complexes from chitosan (Chi) and alginate (Alg) particles whose shape and morphology was varied by the concentration of the starting components is another interesting study and is the first attempt to apply Chi/Alg polyelectrolyte complex for modified release of diclofenac sodium (No. 11). A polyelectrolyte complex with a composition of chitosan : alginate 1:1 was determined as the most successful system for controlled diclofenac sodium release. This complex provides about 87% diclofenac sodium loading efficiency and its almost linear release in the first 8 h, and about 90% release within 24 h. This proves the potential of the obtained fibrillar complexes of chitosan and alginate аnd makes these materials appropriate as vehicles for controlled diclofenac sodium release diclofenac sodium.

I consider the preparation of polymer particles with an anisotropic shape, based on a new "*bottom-up*" method, known for low-molecular substances and transformed by her to obtain polymer particles, described in (No. 7) as an important scientific contribution of the candidate Assoc. Prof. Vasileva. Polymer composite particles have been obtained and studied by incorporating e.g. magnetic nanoparticles in the monomer drops, and by adding a cross-linking agent in the same drops, stable polymer-composite particles were obtained. In her habilitation thesis, candidate Assoc. Prof. Vasileva describes the development of new polymer materials based on polyzwitterions. Another addition to her overall contribution is the successfully deduced derived relationship between the zwitterionic nature of the monomeric units and the resulting properties of the polyzwitterions, which make them "smart" polymeric materials and determine the possibility of their application for dressings for chronic wounds and for modified drug release.

Long-term systematic self-development, accumulated knowledge and experience make the candidate's acquisition of the status of professor a logical and natural next stage in professional development. My arguments are supported by the promising scientific topic, significant in terms of volume and quality of scientific production, which found a noticeable echo in the literary space, and the essential scientific contributions of Prof. Vasileva. The only candidate Prof. Elena Vasileva is a winner of prestigious awards, of an individual Marie Curie scholarship, she is an evaluator in the National Science Fund of the Ministry of Education, Culture, Science and Technology, in the Belgian Research Fund, in the 7th Framework Program of the EU, in the Agency for Science, Innovation and Technology in Lithuania. She is a member of the Union of Chemists in Bulgaria, the International Union of Pure and Applied Chemistry (IUPAC) and the Association of Marie Curie Fellows. She is a reviewer in prestigious specialized journals and participates in scientific juries for awarding scientific degrees.

1. **Opinions, notes and recommendations**

I have no objections regarding the design and presentation of the contest materials. They are prepared according to the requirements of the law and the regulations for its implementation without technical omissions. All required documents are extremely precisely arranged and structured, which is a necessary condition for good readability and analysis. I have no critical comments on the publications submitted for participation in the contest. My impressions of the professional qualities of . Dr. Elena Vasileva are excellent. I would add that she also participated as a member of the Temporary Scientific Expert Committee on Chemical Sciences at the National Science Fund in 2021. I am convinced of her personal contribution to the obtained scientific results in the relevant publications and the development of the subject on which she works.

1. **Conclusion**

In accordance with the above, I clearly state that the mentioned research activity identifies Assoc. Dr. Elena Dimitrova Vasileva as a serious and ambitious scientist who meets the requirements laid down in the Regulations for the conditions and procedure for acquiring scientific degrees and holding academic positions at SU "St. Kliment Ohridski". The results achieved convincingly demonstrate the applicant's competence and research experience. Acquaintance with the presented competition materials and scientific publications, the analysis of their relevance, significance and contribution are grounds for recommending to the honorable members of the Academic Jury to support the election of Dr. Elena Vasileva at the Academic position of a Professor in the professional field 4.2. Chemical Sciences (Polymers) at the Sofia University „St. Kliment Ohridski”

**Date: 07.07.23 Reviewer:**

**Prof. Sevdalina Turmanova, PhD Member of the Academic Jury**