R E V I E W
by

Assoc. Prof. Dr. Radostina Kalinova, Institute of polymers, BAS
Member of the Academic Jury set to render a decision
on a procedure for the acquisition of Academic Degree "Doctor of Philosophy" (PhD)
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 and Polymer Materials")

Author: Eng. Selin Erdinch Kyuchyuk-Hyusein
Title: „Electrospun fibers with core-sheath architecture based on poly(ethylene oxide), a biodegradable aliphatic polyester and beeswax "
Thesis supervisors: Assoc. Prof. Dilyana Paneva, DSc and Prof. Iliya Rashkov, DSc, Corresponding Member of BAS

This Peer Review is prepared in response to Order № РД-09-125 of 01.10.2025

issued by the Director of the Institute of Polymers, Bulgarian Academy of Sciences, following the decision made by the Academic Jury that was held on 02.10.2025

The Review is in compliance with *Development of Academic Staff in the Republic of Bulgaria Act (DASRB)*, *the Rules for the Application of the Development of Academic Staff in the Republic of Bulgaria Act*, the *Rules of BAS* and with the *Rules set at the Institute of Polymers, Bulgarian Academy of Sciences, for applying the Act aforementioned*.

Biographical information about the candidate

Selin Erdinch Kyuchyuk-Hyusein graduated from the University of Chemical Technology and Metallurgy – Sofia, where in 2021 she obtained a Bachelor's degree in Technology of Glass, Ceramics, and Binders. In 2023, she earned a Master's degree in Chemical Engineering with a specialization in Fine Organic Synthesis. She joined the Institute of Polymers at the Bulgarian Academy of Sciences (BAS) in 2020 as a chemical technician, and in 2021 she was appointed to the position of chemist at the same institute. Since November 1, 2023, Selin Kyuchyuk-Hyusein has been enrolled as a PhD student in self-preparation form of education in the Laboratory of Biologically Active Polymers, within the Scientific Division "Polymeric Biomaterials" at the Institute of Polymers – BAS. By a decision of the Scientific Council of the Institute of Polymers – BAS dated September 4, 2025, she has been withdrawn with the right to defend her dissertation.

Assessment to meet the minimal criteria in accordance with the Rules for Granting Academic Degrees set at the Institute of Polymers, Bulgarian Academy of Sciences, (Application 1).

The presented report on the doctoral candidate's research activities demonstrates that she not only meets but significantly exceeds the minimum requirements for obtaining the educational and scientific degree "Doctor", in accordance with the Law for the Development of the Academic

Staff in the Republic of Bulgaria (LDASRB), its implementing regulations in the Republic of Bulgaria and the Bulgarian Academy of Sciences (BAS), as well as the Regulations of the Institute of Polymers – BAS (Appendix 1). Under indicator A, which carries 50 points, the doctoral candidate has fulfilled the requirement by submitting a dissertation thesis. Under indicator G, referring to the candidate's scientific publications, she has presented five papers published in peer-reviewed journals indexed in globally recognized databases such as Web of Science and Scopus. For this indicator, she has accumulated a total of 110 points, which substantially exceeds the minimum requirement of 30 points. The total number of points under Indicator D, which is not mandatory for the award of this educational degree, is 42 points, corresponding to 21 citations of her publications in the scientific literature.

Review of the Dissertation and Analysis of the Results

The dissertation comprises 148 pages and includes nine sections: an introduction, a review of the state of the art (26 pages), the aim and objectives of the dissertation, results and discussion (88 pages), an experimental section (12 pages), conclusions, contributions, a list of publications and conference communications, and a bibliography. The work is illustrated with 3 schemes, 70 figures, and 9 tables. A total of 123 references have been used, the majority of which were published after 2010.

The dissertation begins with a concise introduction, followed by a comprehensive literature review that thoroughly examines the types of devices used for obtaining fibers with complex architectures, as well as the variety of systems employed in fiber formation using a single-capillary nozzle. The main methods for physicochemical and mechanical characterization of fibrous materials are presented, along with the factors influencing their morphology. The final part of the literature review discusses biocompatible and/or biodegradable polymers such as polyethylene oxide, poly(L-lactide), poly(ε-caprolactone), poly(butylene succinate), poly(hydroxybutyrate), poly(D,L-lactide-co-glycolide), and poly(L-lactide-co-D,L-lactide), emphasizing their properties related to applications in medicine and pharmacy. Special attention is given to beeswax, its properties, and the production of electrospun materials containing beeswax. The review is written concisely and reflects the current state of research in the field developed within the dissertation.

The aim of the dissertation is clearly and precisely defined, and four main tasks have been formulated to achieve it successfully.

The research results are systematized, analyzed, and discussed in four chapters included in the section "Results and Discussion." The first chapter focuses on the preparation of composite fibrous materials based on polyethylene oxide (PEO) and beeswax (BW) by electrospinning

homogeneous solutions of the two components in chloroform. The formation of fibers with a core–sheath architecture was confirmed by contact angle measurements, X-ray photoelectron spectroscopy (XPS), transmission electron microscopy (TEM), and selective extraction of PEO and BW (in water and hexane, respectively). It was demonstrated that the model drug 5-nitro-8-hydroxyquinoline (NQ) can be incorporated into the fibrous materials due to its solubility in chloroform—a solvent common to all three components of the mixture. The second chapter presents an advancement of the system through the incorporation of the biocompatible and biodegradable polymer poly(L-lactide) (PLA) into the PEO/BW spinning solution. TEM analyses revealed that the fibers possess a core–double-sheath architecture, and XPS analyses combined with selective extraction of PEO and BW showed that the fiber core is composed of PEO, the inner shell of PLA, and the outer shell of BW. The results also confirm the concept that, through single-step electrospinning, the PEO/PLA/BW mats can incorporate a model drug compound such as NQ. The third chapter focuses on validating the proposed method for obtaining fibers with a core–double-sheath architecture by substituting PLA with other biodegradable aliphatic polyesters such as poly(ε-caprolactone) (PCL), poly(lactide-co-glycolide) (PLGA), poly(butylene succinate) (PBS), and poly(3-hydroxybutyrate) (PHB). It was shown that electrospinning homogeneous solutions of the PEO/polyester/BW system leads to the formation of such fibers. The influence of the molar mass ratio between the polyester and PEO on the composition of the core and inner sheath of the fibers was investigated. It was found that, at lower polyester molar mass, clearly separated layers are formed—a PEO core, an inner polyester sheath, and an outer BW sheath—whereas higher molecular weights result in partial mixing of the components. For the first time, sequential selective extraction of the sheaths using hexane and tetrahydrofuran was applied. The mechanical properties of the fibers were found to depend on the type of polyester used. Using hydrophilic ZnO and hydrophobic ZnO(Si), the possibility of targeted deposition of substances in the fiber core or sheaths, respectively, was demonstrated. In mats composed of PEO/BW, PEO/PCL/BW, and PEO/PLA/BW, NQ was again incorporated, and monitoring of the release profile revealed that, in the initial stages, the drug release depends on both the fiber architecture and the nature of the polyester. The fourth chapter is devoted to the study of the antibacterial, antifungal, and anticancer activity of the fibrous materials based on PEO/BW, PEO/PLA/BW, and PEO/PCL/BW containing NQ and 5-chloro-7-iodo-8-hydroxyquinoline (CQ). It was shown that fibers containing NQ, regardless of their structure, exhibit antibacterial and antifungal activity, while mats composed of PEO/BW/NQ also demonstrate selective anticancer activity, making them potentially applicable in wound healing and oncotherapy. In terms of applications in bio-agriculture, it was established for the first time that fibers containing NQ and CQ exhibit antimicrobial activity against both phytopathogens and beneficial microorganisms.

The experimental part of the dissertation, presented over 12 pages, provides detailed information on the solvents, reagents, and materials used, as well as on the biological tests and the methods applied for the physicochemical characterization of the obtained fibrous materials.

The conclusions drawn at the end of the dissertation are precisely formulated and fully consistent with the obtained results.

The Dissertation abstract accurately and comprehensively reflects the content of the dissertation. It includes the results of the conducted research, the conclusions derived from them, and the formulated scientific contributions.

Characterization and Evaluation of the Contributions of the Dissertation

The main contributions of the dissertation are of fundamental scientific significance, while also possessing potential scientific and practical applicability, which may be utilized in future research and further practical implementation. The original scientific contributions of the dissertation can be summarized as follows:

- For the first time, a novel approach for obtaining fibers with core–sheath and core–double-sheath architecture has been developed and experimentally confirmed through electrospinning of homogeneous solutions, without the use of a coaxial device.
- The universality of the proposed approach for producing fibers with core–double-sheath architecture has been demonstrated for a wide range of biodegradable and biocompatible polymers.
- A correlation between the molecular weight of the components and the fiber morphology has been established. It has been proven that the composition of the outer sheath in the core–double-sheath fibers does not depend on the molar mass ratio of the polymers, whereas the composition of the core and inner sheath does depend on this ratio.
- By applying various analytical techniques (SEM, TEM, XPS) and a systematic method of selective extraction of individual components, the structure of the obtained fibers has been confirmed.
- It has been demonstrated that the newly developed fibrous materials can serve as carriers of biologically active substances (NQ, CQ). The conducted in vitro screening revealed their potential applications in medicine and bio-agriculture.
- It has been shown that hydrophilic and hydrophobic biologically active compounds can be selectively deposited during the electrospinning process.

Evaluation of the Doctoral Candidate's Publications Related to the Dissertation

The results of the dissertation have been published in five scientific papers in renowned international journals: Macromolecular Bioscience (IF2022 = 4.6, Q1), Polymers (IF2022 = 5.0,

Q1), Journal of Applied Polymer Science (IF2024 = 2.8, Q2), Materials (IF2023 = 3.1, IF2024 = 3.2, Q1) – two publications. In all these publications, the doctoral candidate is the first author. The relevance of the research topic and the high quality of the obtained results are further evidenced by the 21 citations of these five papers indexed in the Web of Science and Scopus databases. All publications were issued between 2022 and 2024. On the topic of the dissertation, the candidate has also presented three oral reports and two poster communications at national and international scientific conferences. During these participations, Selin Kyuchuk-Hyusein received distinctions for her scientific achievements, including the Best Presentation Award at the Thirteenth Poster Session "Young Scientists in the World of Polymers," organized by the Institute of Polymers, Bulgarian Academy of Sciences (2022), and the Bulgarian Academy of Sciences Award "Acad. Ivan Evstratiev Geshov" for young scientists under 30 years of age (2023).

Critical Remarks and Comments

I have several remarks regarding the dissertation, which do not affect the essence or reliability of the scientific results but refer to certain stylistic and technical inaccuracies in the text.

1. Reading the section "Review of the State of the Art" is somewhat hindered due to:
- inconsistencies between the numbering of figures in the main text and in the figure captions;
- inconsistent citation formatting – in some places references are indicated by numbers and author names, while in others only by names;
- simultaneous use of Bulgarian and English versions of the same terms, for example:
- p. 12 – "homogeneous blend solutions" and "хомогенни смесени разтвори";
- p. 13 – "difference in solubility parameter" and "параметър на разтворимост ";
- p. 13 – "core–sheath structures," while in the rest of the dissertation the Bulgarian equivalent " структури тип сърцевина–обвивка" is used.

2. In the review section, after point 3.4, there is a technical error in the numbering – the next subsection is labeled as 1.4 instead of 3.5.
3. The review section ends with conclusions from the preface, although such a section ("Preface") is missing from the dissertation.

Questions to the Doctoral Candidate

1. Have XPS analyses been performed to determine the surface composition of the fibers after each stage of selective extraction of the individual components in any of the studied architectures?

2. Has a quantitative (gravimetric) and qualitative evaluation (by IR and NMR spectroscopy) of the dry residue after evaporation of hexane or water during the selective extraction been conducted?
3. How can the selectivity of the PEO/BW/NQ mats toward cancer cells be explained, considering that 5-nitro-8-hydroxyquinoline (NQ) itself exhibits such selectivity? If an additional effect of the mats is observed, what is its possible origin?

Conclusion

Based on the analysis presented above, it can be concluded that the dissertation of Selin Erdinch Kyuchuk-Hyusein represents a serious, comprehensive, and independent scientific investigation. The doctoral candidate demonstrates excellent theoretical preparation, strong experimental skills, and a high capacity for critical analysis and interpretation of the obtained results. In the course of developing the dissertation, the candidate has successfully mastered and applied the electrospinning method for producing micro- and nanofibrous polymer materials with controlled morphology and structure. A wide range of modern analytical techniques has been employed for the characterization of the synthesized materials. The application of these methods has enabled an in-depth investigation of the physicochemical properties, morphology, and thermal stability of the obtained fibrous materials.

The dissertation and the accompanying materials submitted by Selin Erdinch Kyuchyuk-Hyusein fully meet the requirements for the award of the educational and scientific degree “Doctor”, in accordance with the Law for the Development of the Academic Staff in the Republic of Bulgaria, its Regulations for Implementation, as well as the Regulation of the Bulgarian Academy of Sciences and the Institute of Polymers – BAS. All the above, together with my personal impressions, give me full confidence to express my positive evaluation and recommend to the respected members of the Scientific Jury to award Selin Erdinch Kyuchyuk-Hyusein the scientific degree "Doctor” in the professional field 4.2 – Chemical Sciences, specialty “Polymers and Polymeric Materials.

Date: 13/11/2025

Reviewer:

Assoc. Prof. Dr. Radostina Kalinova, Member of the Academic Jury