REVIEW

by Emilia Mitkova Mihaylova, PhD

Professor - Agricultural University - Plovdiv

of a dissertation for the award of the educational and scientific degree "PhD"

field of higher education: **4. Natural sciences, mathematics and informatics**

professional field **4.1. Physical sciences**

doctoral program **Electrical, magnetic and optical properties of condensed matter**

Author: Aleksandar Vasilev Grigorov

Topic: Modified multilayer structures for immobilization of biologically active molecules

Scientific supervisor: Assoc. Prof. Dr. Asya Petrova Viraneva, University of Plovdiv "Paisii Hilendarski"

1. General presentation of the procedure and the PhD student

By order № РД-22-2563/16.12.2025 of the Rector of Plovdiv University (PU) "Paisii Hilendarski" I have been appointed as a member of the scientific jury to provide a procedure for the defense of a dissertation entitled "Modified multilayer structures for immobilization of biologically active molecules" for awarding the educational and scientific degree "PhD" in the field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.1. Physical Sciences and doctoral programme "Condensed Matter Physics". The author of the dissertation is Aleksandar Vasilev Grigorov - PhD student in fulltime education at the Department of Physics at PU with scientific supervisor Assoc. Prof. Dr. Asya Petrova Viraneva, University of Plovdiv "Paisii Hilendarski.

The set of paper materials submitted by the PhD student includes the following documents: Application to the Rector of PU for the opening of the dissertation procedure; CV in European for-

mat; minutes of the departmental council related to the reporting of the readiness for the opening of the procedure and the preliminary discussion of the dissertation; opinion from the scientific supervisors; dissertation; abstract in Bulgarian and English; list of scientific publications on the topic of the dissertation; copies of scientific publications; declaration of the authenticity and reliability of the attached documents; statement of compliance with the minimum national requirements. The doctoral candidate has attached copies of 4 papers on the subject of the dissertation, published in reputable journals.

All materials presented are in accordance with Article 36 (1) of the Regulations for Development of the Academic Staff of the University of Plovdiv.

2. Brief biographical data of the doctoral student

- From September 2021 - until now – Assistant, Plovdiv University "Paisii Hilendarski";
- 2020 – 2024 – Researcher, Plovdiv University "Paisii Hilendarski";
- Higher education OKS Master in PN 4.1 Physical Sciences -– diploma No. 1-6-F of July 19, 2018, Plovdiv University "Paisiy Hilendarski"
- Participation in 6 research projects;Participation in 7 scientific conferences;
- Scientific publications – total number - more than 9.

The doctoral student Dr. Aleksandar Vasilev Grigorov has significant scientific experience in connection with the dissertation submitted for the award of the educational and scientific degree "PhD" on the topic "Modified multilayer structures for immobilization of biologically active molecules".

3. Relevance of the topic and appropriateness of the set goals and tasks

Controlled release is the individual delivery of biologically active substances (e.g. drugs, proteins, fertilizers, nutrients, etc.) at an effective level in response to time and various stimuli, such as pH, temperature, enzymes, UV light, magnetic fields, and others.

Controlled release finds application in fields such as medicine – for pharmaceutical applications, cosmetics, pesticides, agriculture and food science.

The relevance of the problem developed in the dissertation work in scientific and scientific-applied terms is determined by the fact that conventional systems for the release of pharmaceutical drugs (напр. таблетки, капсули и др.), very quickly after application to the body, they release the biologically active substances contained in them, which results in a sharp increase in the concentra-

tion of the drug in the bloodstream and a rapid decrease in a short period of time. Multiple dosing may be required to maintain drug concentrations within the effective range. Such fluctuations in plasma drug levels may be toxic and/or result in reduced drug efficacy.

Compared to conventional delivery systems for biologically active substances, controlled release systems provide many advantages such as maximum drug efficacy, minimal side effects, and reduced drug accumulation during chronic dosing. However, they are also associated with several disadvantages, including possible toxicity or lack of biocompatibility of the polymer carriers used, undesirable degradation products, difficulty in dose modification, poor systemic availability. These problems determine the relevance of the problem developed in the dissertation work in both scientific and applied terms.

One of the new and developing methods for immobilization of biologically active molecules is the creation of multilayer structures in which various biologically active substances can be incorporated. A main direction of research on multilayer structures for medical applications in recent years has been the creation of fully biodegradable and biocompatible multilayer structures from various polyelectrolyte materials, in which various biologically active substances can be immobilized. Therefore, the main goal and specific tasks developed in the dissertation are very relevant.

4. Understanding the problem

A significant number of scientific publications (over 200 cited literature sources) were used in the development of the dissertation. The doctoral student demonstrates in-depth knowledge of existing scientific publications in the field of multilayer structures for immobilization of biologically active substances.

5. Research Methodology

The selected materials and methods for preparation, modification and characterization of polyelectrolyte multilayer films allow the preparation of modified multilayer structures for immobilization of biologically active molecules.

The selected methods for characterizing the properties of the obtained multilayer films are also appropriate, as the research methodology allows achieving the set goal and solving the specific practical tasks.

6. Characteristics and evaluation of the dissertation work

The dissertation contains 165 pages, of which 138 pages are the main text.

A seven-chapter structure has been chosen, with the first chapter presenting an introduction and an overview of the problems on the topic of the dissertation. In the introductory chapter, the author justifies the relevance of the topic. The second chapter reviews scientific publications on selected materials and methods for preparing, modifying and characterizing polyelectrolyte multilayer films, immobilization of biologically active substances in multilayer structures, controlled release of various biologically active substances from multilayer films and influence of the electret effect in delivery systems for biologically active substances..

The third chapter formulates the main goals and objectives of the dissertation work.

The fourth and fifth chapters contain the main part of the scientific research.

The fourth chapter describes the experimental work carried out by the doctoral student to obtain polymer films, modify the surface of the obtained films by the corona discharge method and by a chemical method. The fourth chapter also describes the methods used to characterize the obtained modified polymer films. The preparation of polyelectrolyte multilayer films by the layer-by-layer deposition method using an automated layer preparation system operating in immersion mode at a uniform speed is also described. An enzymological method used to determine the activity of the enzymes immobilized in the multilayer films is also described, as well as a method for studying the release of medicinal substances from the obtained multilayer films. The fourth chapter concludes with a description of 3 mathematical models used to describe the process of drug release from various modified polymer matrices.

Chapter Five presents the results of all the research presented in the dissertation. They are structured into three groups according to the method of modification of the polymer films used. In the discussion of the presented results, the author shows a deep knowledge of the problem and a purposeful analysis. Chapter six lists the author's conclusions, drawn on the basis of all the work done in developing the dissertation.

Chapter seven is concluding and contains the author's main contributions.

My opinion is that the presented research, on which the contributions of the dissertation are built, is credible.

7. Contributions and significance of the development for science and practice

According to the doctoral student, his main contributions to the dissertation research are six, which will not be retold here, as they are available in the dissertation and in the abstract to it. I acknowledge the contributions formulated by the doctoral student, and I generally characterize them as significant scientific and applied contributions in the field of developing new substrates for mul-

tilayer structures based on modified composite films of polylactic acid and polyepsilon caprolactone, enabling control of the amount and rate of release of biologically active substances immobilized in the multilayer structures.

8. Assessment of publications on the dissertation work

The doctoral student has co-authored four articles that have been published in reputable scientific journals. In two of the publications submitted, the doctoral student participated in conducting the research, processing the experimental data, and writing the articles in English. Data on the doctoral student's participation in the other two publications are not available. The publications presented are directly related to the topic of the dissertation.

9. Personal involvement of the doctoral student

I define the dissertation research as developed personally by the author. I have not found any plagiarism in the described scientific research.

10. Abstract

The abstract of the dissertation meets the requirements for obtaining the degree "PhD". It is 32 pages long and contains a brief presentation of the entire dissertation research. The main theoretical and applied results achieved are described. The contributions of the author are highlighted in his opinion.

11. Critical remarks and recommendations

I have no critical remarks or recommendations.

12. Personal impressions

I do not know Alexander Vassilev Grigorov and I have no personal impressions of him.

13. Recommendations for future use of the dissertation contributions and results

I recommend future use of the contributions of the dissertation research in practice for specific medical applications.

CONCLUSION

According to the provided documents, doctoral student Aleksandar Vasilev Grigorov meets the minimum national requirements for acquiring the educational and scientific degree "PhD" in the professional field of Physical Sciences.

The dissertation contains scientific and applied scientific results that represent an original contribution to science, and fully meets the requirements of the Law for the development of the Academic Staff of the Republic of Bulgaria, the Regulations for its implementation and the Regulations for the conditions and procedure for the acquisition of scientific degrees at Univerandsity of Plovdiv “Paisii Hilendarski”. The dissertation shows that the doctoral student Alexander Vassilev Grigorov possesses in-depth theoretical knowledge and professional skills in the scientific specialty of Physics, demonstrating qualities and skills for independently conducting scientific research.

In view of the above, I confidently give my positive assessment of the research conducted, presented by the above-reviewed dissertation, abstract, achieved results and contributions and I propose to the esteemed scientific jury to award the educational and scientific degree of "PhD" to Alexander Vassilev Grigorov in the field of higher education: 4. Natural sciences, Mathematics and Informatics, professional field 4.1. Physical Sciences, Doctoral programme “ **Electrical, magnetic and optical properties of condensed matter** ”.

Date: 4.2. 2026 Reviewer: .....

Prof. Dr. Emilia Mihaylova