OPINION

by Asya Petrova Viraneva, PhD

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University of Plovdiv "Paisii Hilendarski"

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

by: field of higher education: 4. *Natural sciences, mathematics and informatics*, professional field 4.1. *Physical sciences*, doctoral program "Condensed Matter Physics"

Author: Sofia Boyanova Milenkova

Topic: Biopolymeric Micro- and Nanoparticles as a Delivery System for Benzydamine

Scientific supervisors: Prof. Maria Marudova-Zsivanovits, PhD, Plovdiv University "Paisii Hilendarski", and Assoc. Prof. Bisera Pilicheva, PhD, Medical University - Plovdiv.

1. General presentation of the procedure and the PhD student

By order No РД-21-1447 /12.07.2024 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 "Biopolymeric Micro- and Nanoparticles as a Delivery System for Benzydamine" 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 Sofia Boyanova Milenkova - PhD student in full-time education at the Department of Physics at PU with scientific supervisors Prof. Maria Marudova-Zsivanovits, PhD from Plovdiv University "Paisii Hilendarski" and Assoc. Prof. Bisera Pilicheva, PhD from Medical University of Plovdiv.

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 format; 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 3

copies of her publications on the subject of the dissertation, 2 of which are with impact factor and 1 is with SJR factor in the Scopus database.

All materials presented are in accordance with Article 36 (1) of the Regulations for Development of the Academic Staff of the University of Plovdiv. All of them have been prepared diligently and correctly.

Sofia Boyanova Milenkova completed her higher education in 2018 at University of Plovdiv, Paisii Hilendarski, Bachelor degree Engineering Physics. From 2018 to 2019, she graduated Master's degree at University of Plovdiv, in a specialty Condensed Matter Physics. In 2021, Sofia Milenkova started working as a researcher in the Biopolymers and New Materials section at PU. Since 2024 to now, she has been working as an Assistant Professor at the Department of Physics, Faculty of physics and technology.

I know Sofia Boyanova Milenkova personally and I have excellent impressions of her as a teacher and a researcher.

2. Relevance of the topic

In recent years, the construction of new functional structures based on various biocompatible and biodegradable polymers with controlled properties in the micro- and nanoscale range, capable of immobilizing biologically active substances and releasing them in a prolonged manner, is of significant interest from both a fundamental and an applied point of view, because of their applications in biotechnology, tissue engineering, medicine, pharmacy and food technology. The influence of the polymer micro- and nano-sized particles in pharmacy in the preparation of various drug delivery systems is significant. These types of structures allow an individual approach tailored to the needs of the therapy and the selected active substance.

In the presented dissertation work, polymeric micro- and nano-sized particles based on two natural hydrocolloids (chitosan and casein) have been developed, optimized and characterized. Their potential application as a drug delivery platform for the controlled release of benzydamine hydrochloride with improved efficacy of the medicinal substance and increased yield was established.

3. Knowledge of the problem

The PhD student Sofia Milenkova is presented an in-depth analysis of the scientific literature. From the list and analysis of the cited references, it can be concluded that the PhD student has understood the current state and development trends of the problems, solved in the

dissertation work. The list of cited references contains 162 publications, all of which are in English. Most of the cited sources are articles in journals indexed in Scopus and Web of Science databases. Most of the cited sources were published in the last 5 years (36 %), which indicates the existence of a thorough analysis of the current state of the problem.

4. Research methodology

In the dissertation work presented polymer micro- and nano-sized chitosan and casein-based particles are developed, optimized and characterized. The structures are obtained by two different methods - ionotropic gelation and the spray drying, which are described in details. To characterize the polymer structures obtained, the PhD student is correctly selected and used different methods as atomic force microscopy, scanning electron microscopy, UV-vis spectroscopy, fourier transform infrared spectroscopy, differential scanning calorimetry. The potential application of the structures obtained as a drug delivery platform for benzydamine hydrochloride with controlled release was also established. For a better description and understanding of the drug release process from the polymer matrix, various mathematical models have been described and used (first-order model, Higuchi model, Korsmeyer-Peppas model, and Weibull model). In order to establish the release profile of the drug substance from the polymer structures, a couple of model particles were selected for each type of system, with which an in vitro release test was conducted.

5. Characteristics and evaluation of the thesis and contributions

The total volume of the dissertation work is 159 standard pages and it contains 49 figures, 13 tables, 9 formulas and 162 cited references. It consists of an introduction that justifies the relevance of the work, four chapters, a description of contributions, conclusions and a literature review. List of the publications, scientific conferences and mobilities of the PhD student are also presented.

The PhD student Sofia Milenkova has conducted a large number of experimental studies. The experimental results obtained are presented visually through figures and tables and a thorough analysis is made. Based on this, 5 scientific and scientific-applied contributions were realized, which emphasize the scientific-applied value of the dissertation work. For the first time, benzydamine hydrochloride-loaded casein particles using the ionotropic gelation method and the spray drying method under acidic conditions were developed.

6. Evaluation of the publications and the personal contribution of the PhD student

The PhD student Sofia Milenkova presents a list of 3 publications on the topics of dissertation. Two of the papers are in the journals with impact factor (IF): Materials with IF=3.4, indexed in the Scopus/Web of Science database and quartile Q2, and Gels with IF = 4.6, indexed in the Scopus/Web of Science database and Q1. The third publication is in the Journal of Physics: Conference Series, indexed in the Scopus database with SJR = 0.18.

All papers presented are co-authored, as in two of the publications the PhD student is the first author. This undoubtedly shows the importance of her personal contribution. 3 citations were noticed for one of the papers.

The PhD student Sofia Milenkova participated in 5 International scientific conferences and she conducted two mobilities, which led to an increase in knowledge and experience in the relevant scientific field.

Through the scientific publications presented the PhD student achieved 55 points out of the minimum required 30. This leads me to conclude that the necessary publicity for the research in her dissertation work has been secured. The number and quality of publications meet the minimum criteria and correspond to the minimum requirements of the PU and the Faculty of Physics and technology for the acquisition of a PhD.

7. Abstract

The Abstract is presented in Bulgarian and English. It consists of 32 pages, including contributions and publications related to the dissertation work. The abstract faithfully reflects the content of the dissertation in a shorter form. The abstract is prepared according to the requirements and it is in accordance with the dissertation work.

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

Taking into account the actuality of the topic, I would recommend to the PhD student to continue her research in this area by using, for example, other drug substances, as well as to acquire new methods for obtaining polymer structures.

CONCLUSION

After reading extensively the disertation and publications of the PhD student Sofia Milenkova, I am convinced that the results achieved of the conducted research, were obtained entirely with her participation. With the dissertation presented, the PhD student demonstrates

in-depth her theoretical knowledge, professional skills and opportunities to conduct research and solve scientific problems.

The dissertation of Sofia Milenkova contains scientific and scientific-applied results, which 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 University of Plovdiv “Paisii Hilendarski”.

Due to the above, I confidently give my **positive assessment** of the conducted research, represented by the peer-reviewed dissertation work, abstract, achieved results and contributions, and I propose to the scientific jury to award the educational and scientific degree **"PhD"** to Sofia Boyanova Milenkova in the field of higher education: 4. Natural sciences, Mathematics and Informatics, professional field 4.1. Physical Sciences, Doctoral programme “Condensed Matter Physics”.

05.09.2024 Prepared the opinion:.....

(Assoc. Prof. Asya Viraneva)