

## STATEMENT

from Prof. DSc Sonia Varbanova Ilieva,

Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski"

on a dissertation for awarding the educational and scientific degree "Doctor"

in Professional field 4.2. Chemical Sciences (Polymers)

**Author:** Denitsa Valerieva Nikolova

**Topic of the dissertation:** *Smart polymeric materials for modified release of timolol maleate in the eyes*

**Supervisors:** Assoc. Prof. Dr. Elena Vassileva and Assoc. Prof. Dr. Lachezar Christov

The author of the dissertation is Denitsa Valerieva Nikolova – a full-time PhD student in the laboratory "Structure and properties of polymers", Department of pharmaceutical and applied organic chemistry, Faculty of Chemistry and Pharmacy, enrolled by order No РД-20-242/ 28.01.2019. The supervisors are Assoc. Prof. Dr Elena Vassileva and Assoc. Prof. Dr Lachezar Christov. Denitsa Nikolova was unenrolled with the right of defense on February 1, 2022. She has successfully passed the specialty exam and the English language exam.

D. Nikolova graduated with a Master of Chemistry - Polymers at the Faculty of Chemistry and Pharmacy, Sofia University in 2018 and after that, she was enrolled as a full-time doctoral student. During her PhD, she worked as a chemist/researcher at the Institute of Polymers, BAS. She completed a one-year specialization at the Leibniz Institute for Polymer Research (Dresden, Germany), funded by the German Environmental Protection Organization, and three short-term specializations abroad. The PhD student participated with posters and scientific reports at 10 national and international scientific conferences/seminars held in Bulgaria. She participated in the work on 7 national scientific projects.

The materials presented by Denitsa Nikolova meet all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria and the relevant regulations for its implementation, and meet the criteria for obtaining the scientific and educational degree "Doctor". For the period 2019-2023, D. Nikolova has 4 publications in reputed international journals with impact factor. Research within the framework of the dissertation is included in two publications: *Polymer International*, IF 3.213, quartile Q1 и *Gels*, IF 4.432, quartile Q1. Therefore, the minimum criteria for the Doctoral degree are met and exceeded: the doctoral student has achieved 50 points (according to the indicator  $\Gamma$  30 points are required).

The dissertation work is devoted to the development of appropriate drug carriers for the drug timolol maleate, which would ensure a higher concentration/bioavailability of the drug in the human eye. The subject of the dissertation is topical and especially interesting from a scientific point of view because solving problems related to the bioavailability of the active substance is a pharmaceutical challenge. The zwitterionic polymer poly(sulfobetaine methacrylate) was investigated as a "smart" polymer with the potential to develop nano/micro carriers for timolol maleate. The dissertation work (118 pages) consists of 3 main parts – Literature review (38 pages), Experimental part (12 pages), Results and discussion (41 pages). The main conclusions are clearly formulated at the end of the dissertation. The scientific contributions of the research are presented in the extended abstract.

Nanoparticles of linear and cross-linked poly(sulfobetaine methacrylate) were synthesized (for the first time) and their properties - morphology, hydrodynamic diameter, etc. - were characterized. In view of the potential application, the efficiency and capacity of drug loading and the release profile of the drug substance thymol maleate from the PSBM particles were investigated. It was found that “cross-linked nanoparticles” of poly(sulfobetaine methacrylate) showed a more suitable release profile for ocular application compared to “linear nanoparticles”.

Copolymer hydrogels of poly(sulfobetaine methacrylate-co-vinyl pyrrolidone) cross-linked with poly(ethylene glycol) diacrylate were synthesized (for the first time) and investigated as potential drug-delivery soft contact lenses for eyes. An in-depth analysis of the studied characteristics of the copolymer hydrogels - swelling, elasticity, transparency, loading capacity and efficiency, and drug release profile - was made. The newly synthesized copolymer hydrogels were found to have a very good potential as drug delivery systems for timolol maleate in the form of soft contact lenses for eyes with the added advantage of blocking harmful UV-B rays.

It is clear from the conducted scientific research, from the conclusions drawn, as well as from the publications, that the work has an innovative character with a high potential for the application of the synthesized and characterized new polymeric materials.

The conducted research and the published results have fundamental scientific contributions, which can be formulated as proving with new means of significant new aspects of existing scientific fields, problems, theories, hypotheses, and obtaining new facts. The obtained results have a high potential for practical application.

The presented dissertation work and the extended abstract are written very accurately and precisely. I believe that the results achieved are largely the personal work of the doctoral student and she has made a major contribution to the dissertation publications. Her overall performance testifies to excellent chemical training, persistence,

consistency, and purposefulness in work. For the scientific research included in the dissertation, D. Nikolova was awarded the "Outstanding Young Scientist in the Field of Polymers" prize in the name of Prof. Ivan Shopov for 2023.

### **CONCLUSION**

According to the submitted materials and scientific papers, the above analysis of their importance and scientific contributions, as well as my personal opinion, I confidently give my **positive assessment** and vote '**yes**' for awarding the educational and scientific degree "**Doctor**" to **Denitsa Valerieva Nikolova**, in the professional field **4.2. Chemical Sciences (Polymers)**.

18/05/2023

Reviewer:

*Prof. Sonia Ilieva*