

**REPORT**

of dissertation for the acquisition of:

educational and scientific degree " <b>doctor</b> "	X
scientific degree " <b>Doctor of Science</b> "	
	the true is indicated by the sign "X"

**Author of the dissertation:**

		<b>Boryana</b>	<b>Biserova</b>	<b>Borisova</b>	<b>UCTM</b>
academic position	scientific degree	name	middle name	last name	workplace

**Topic of the dissertation:**

<b>Design and synthesis of phosphodiesterase inhibitors with dual activity</b>
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**Scientific area:**

<b>5</b>	<b>Technical sciences</b>
code	name

**Professional area:**

<b>5.11</b>	<b>Biotechnology</b>
code	name

**Scientific specialty:**

<b>Technology of biologically active substances</b>
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**The report was written by:**

<b>Prof.</b>	<b>PhD</b>	<b>Nelly</b>	<b>Vladova</b>	<b>Georgieva</b>	<b>UCTM</b>
academic position	scientific degree	name	middle name	last name	workplace

**1. Meeting the minimum requirements under the Regulations:**

A) The candidate meets the minimum requirements	20 points	X
B) The candidate doesn't meet the minimum requirements	0 points	
		one of the answers given is marked with the sign «X»

It is mandatory to fill in if answer B is marked. The publication activity of the candidate is analyzed. The response of the results achieved (quoted) is analyzed.

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Boryana Borisova has presented 4 articles published in refereed journals Web of Science and Scopus, which brings 30 points. The submitted documents are in compliance with the requirements of the Act for the Development of the Academic Staff in Republic of Bulgaria. She is the first author in all articles, which proves her leading role in the research conducted. The results of the scientific developments have been presented at a number of national and international scientific forums with reports and posters.

## 2. The relevance of the topic of the dissertation:

A) The topic is relevant and new (there are no known results on the topic by other authors)	8 points	X
B) The topic is relevant and results from other authors are known	6 points	
C) The topic is not relevant, but results from other authors are known	2 points	
D) The topic is not relevant and no results from other authors are known	1 point	
E) The topic does not correspond to the level of dissertation	0 points	
		one of the answers given is marked with the sign «X»

The evaluation of the relevance of the dissertation must be substantiated

The topic of this dissertation is aimed at the synthesis and creation of biologically active compounds used in the control of inflammatory processes. Inflammation as a complex pathological process cannot be effectively controlled by medications directed at only one target. Therefore, it is necessary to develop strategies for creating new drugs capable of simultaneously affecting multiple inflammatory processes and their accompanying conditions. The doctoral student's research is focused on the creation of new modified anti-inflammatory peptides and bioconjugates, with the aim of obtaining a synergistic effect on different pathways of the same pathophysiological process, such as inflammation. Therefore, I believe that the topic of the dissertation is relevant.

## 3. Type of research:

A) Theoretical	4 points	
B) Applied	4 points	
C) Theoretical with application elements	4 points	X
D) It does not correspond to the level of dissertation	0 points	
		one of the answers given is marked with the sign «X»

The level of research must be substantiated if answer D is marked.

In the course of the implementation of the experimental work on the dissertation by Boryana Borisova, it is clearly evident that she has acquired competence in terms of knowledge in the specific scientific field, skills in applying a complex methodological approach to solving the tasks set. She has mastered a variety of methodological approaches - methods for solid-phase peptide synthesis,

analytical techniques and approaches used in chemical research, as well as competence in analyzing and evaluating the obtained results. She has skills in working with scientific literature, analyzing and summarizing scientific information.

#### 4. Objectives of the research:

A) Realistic and of scientific and / or applied interest	8 points	X
B) Realistic, but not of scientific and / or applied interest	3 points	
C) Unattainable (unrealistic)	0 points	
		one of the answers given is marked with the sign «X»

Objectives must be specified. The type of the set objectives must be justified.

The goal of the dissertation and the experimental tasks related to its achievement are clearly formulated and realistic. The goals set are quite ambitious and are related to the molecular design of new structures with potential anti-inflammatory and analgesic activity. In this regard, the tasks naturally follow, namely: design, synthesis and characterization of new analogues of the tetrapeptide FELL (Phe-Glu-Leu-Leu), design, synthesis and characterization of new isothiazolone analogues possessing a -COOH group, design, synthesis and characterization of new pyridazine analogues possessing a -COOH group, determination of the biological activity of the synthesized peptides, as well as synthesis of bioconjugates between a pyrrole heterocycle and a peptide with potential analgesic activity.

#### 5. Contributions of the dissertation:

A) With lasting scientific and / or applied response, they form the basis for new research and applications	20 points	X
B) They are of significant scientific and / or applied interest, complete and / or summarize previous research	16 points	
C) They are of scientific and / or applied interest	12 points	
D) Lack of significant contributions	8 points	
E) Lack of contributions	0 points	
		one of the answers given is marked with the sign «X»

Contributions must be specified. The type of results achieved must be justified.

Based on the experimental work, 16 conclusions have been formulated, which logically follow from the obtained results. The contributions of the dissertation work are of a scientific and applied nature. The most important scientific contributions are: new reaction conditions were found for obtaining 4-chlorinated *S*-nonoxidized ITZ which is precursor for designing ITZ possessing acidic function, design, synthesis and characterization of 19 new analogs with general structure Phe-Glu-X<sub>3</sub>-X<sub>4</sub>, ameliorating reaction conditions described before in the Laboratory [185] for cross coupling reaction *via* Suzuki-Miyaura for obtaining 5-SO<sub>2</sub> ITZ with -COOH functional groups. Further applying these conditions in 4- and 5- SO ITZ series. 11 new ITZ analogs were synthesized and analyzed by <sup>1</sup>H

NMR, C13 NMR, MS, IR and melting point. 9 new (dihydro)pyridazinone derivatives bearing on position 2 indole moieties, were synthesized and analyzed by 1H NMR, C13 NMR, MS, IR and melting point. 6 new bioconjugates (4-pyrrole-peptide and 2-ITZ-peptides) were synthesized and characterized. Analgesic and anti-inflammatory properties of several peptides were studied and important structure-biological activity relationships were made.

## 6. Conclusion

A) The evaluation of the dissertation is <b>POSITIVE</b>	This evaluation is assigned to a total number of at least 40 points	60
B) The evaluation of the dissertation is <b>NEGATIVE</b>	This evaluation is assigned to a total number below 40 points	
		one of the answers given is marked with the sign "X"

To be filled in at the request of the member of the scientific jury

I positively evaluate the dissertation work developed by Boryana Borisova. The precisely conducted experiments, the good layout and illustration, as well as the thoroughly interpreted results give me reason to believe that during the doctoral studies, she has developed as a young scientist and researcher, possessing good knowledge in the field of synthesis of biologically active compounds. The presented dissertation work in terms of relevance, volume of research, achieved scientific contributions, as well as publication activity, fully meets the requirements of the law for acquiring the educational and scientific degree "Doctor". I consider it reasonable to propose **Boryana Biserova Borisova** to acquire the educational and scientific degree "Doctor" in the scientific specialty Technology of Biologically Active Substances.

<b>24.11.25</b>	The report was written by:	
date		signature