



## STATEMENT

by **Assoc. Prof. Elisaveta Georgieva Apostolova, PharmD, PhD**

Department of Pharmacology, Toxicology and Pharmacotherapy,

Faculty of Pharmacy, Medical University - Plovdiv

regarding a Ph.D. thesis for awarding the educational and scientific degree 'doctor'

professional direction 4.3. "Biological Sciences",

Ph.D. program "Biophysics".

**Author:** Vera Nikolaeva Gledacheva

**Form of doctoral program:** independent preparation

**Department:** Medical Physics and Biophysics

**Topic:** Biological activity of novel molecules as papaverine analogues

**Scientific supervisors:**

Prof. Iliyana Stefanova-Kancheva, PhD - Medical University - Plovdiv

Prof. Stoyanka Atanasova, PhD - Plovdiv University "Paisiy Hilendarski"

**Scientific consultant :**

Chief Assist. Prof. Valeri Slavchev, PhD - Medical University – Plovdiv

### 1. General presentation of the procedure and the doctoral student

I received a set of materials on an electronic medium, which is in accordance with Art. 70 (1) of Section I. Acquisition of educational and scientific degree "DOCTOR" and scientific degree "DOCTOR OF SCIENCES" at MU-Plovdiv; Regulations of the MU-Plovdiv from 28.01.2021 and includes the following documents: application to the Rector of the MU-Plovdiv, curriculum vitae, copy of a higher education diploma, orders of enrollment and termination of the doctoral studies, a protocol for passing the exam "Doctoral minimum in the specialty", dissertation work, abstract, list and copies of scientific publications on the topic of the dissertation, list of participations in scientific forums, declaration of originality and authenticity of documents. The Ph.D. student has attached a list of 7 publications, of which 5 are full-text articles and 2 are abstracts from scientific conferences.

The documents meet the requirements of the regulations for starting a dissertation defense procedure.

Vera Nikolaeva Gledacheva graduated from Plovdiv University "Paisii Hilendarski" in 2008 with a bachelor's degree, majoring in physics engineering. In 2017, she graduated with a master's degree in the specialty of engineer-physicist in medical and radiation physics and technology. During the period 01.01.2010 - 31.01.2011, she worked as a junior inspector in the "Radiation Control" department of Regional Health Inspection in Plovdiv, and during the period 01.02.2011 - 31.08.2017, worked as a medical physicist in the "Imaging Diagnostics" department at St. George Hospital. Vera Gledacheva began her academic career on September 1, 2017, when she was appointed as an assistant at the Department of Medical Physics and Biophysics at the Department of Medical Physics and Biophysics at the Medical University of Plovdiv. She teaches practical exercises in medical physics and biophysics to students from the specialties of medicine, dentistry, and pharmacy in Bulgarian and English, prepares presentation materials, and participates in exam sessions. Assistant Gledacheva has participated in 5 courses to increase her qualification, she holds a certificate for English language proficiency level B2, issued by the University of Cambridge. It is impressive the large number of projects in which she participated - 6 scientific projects, two of which were financed partially by the European Union.

## **2. Relevance of the topic**

The current dissertation focuses on the study of the biological activity of newly synthesized compounds, which determines its relevance. The newly synthesized compounds have a structure similar to papaverine - an isoquinoline alkaloid with antispasmodic action, for which several side effects such as arterial hypotension, tachycardia, loss of appetite, drowsiness, dizziness, and potential liver toxicity have been established. Thus, the study of new compounds with similar effects and reduced or absent side effects is of significant scientific and scientific-applied importance.

## **3. Knowledge of the problem**

The literature review represents an in-depth study of the problem and lays the theoretical background for the experiments performed. It includes a detailed description of the methods for chemical synthesis of the main structures of the new compounds, data on the biological activity of isoquinoline derivatives, structure and innervation of the gastrointestinal muscles. The included analysis of factors, which can influence smooth muscle contraction and relaxation is of great practical importance and justifies the further selection of *ex vivo* biological effects study parameters. The diagrams and figures included show knowledge of the problem, and the summary of the literature review testifies to the doctoral student's abilities to evaluate creatively the literature material.

#### 4. Research methodology

The formulated tasks correspond to the set aim. The chosen research methodology allows achieving the aim and obtaining an adequate answer to the tasks solved in the dissertation work. The experimental settings are illustrated with figures that are the author's contribution of the doctoral student.

#### 5. Characterization and evaluation of the dissertation work and contributions

The dissertation is written on 146 standard pages and contains an introduction – 2 pages, literature review – 30 pages, aim and tasks – 1 page, material and methods – 16 pages, results and discussion – 70 pages, conclusions – 1 page, contributions - 1 page, publications – 3 pages, and bibliography - 16 pages. The results are presented in 18 tables and illustrated with 46 figures. The literature review includes 211 sources in English, of which 23 are from the last 5 years.

The **literature review** demonstrates knowledge of the literature and provides a theoretical background for the chosen research methods. **The aim** is clearly formulated, and **the tasks** are logically related to the set aim. The "**Materials and Methods**" section contains a detailed description of the experimental settings and they are appropriately selected according to the tasks set. The statistical methods guarantee a correct assessment of the confidence of the obtained experimental data. **The results** are supported by data from chemical analysis of the newly synthesized compounds, the spectra are analyzed and the chemical structures of the compounds are presented, as well as other data from *in silico* analyses. The choice of experimental models is well justified. The figures contain real records of changes in the contractile activity of smooth muscle preparations and are a prerequisite for the credibility and originality of the obtained results. The results are appropriately interpreted and substantiated with changes in intracellular signaling pathways. A comparison was made between the obtained *ex vivo* and *in vitro* results with the results of the *in silico* analysis. **The conclusions** are supported by the obtained results and fully meet the set tasks and objectives. Six **contributions** of scientific and scientific-practical importance have been formulated. Of great applied importance is the development of a complex of modeling methods, combining *in silico*, *ex vivo*, *in vitro*, and *in vivo* methods, allowing unifying the screening of newly synthesized isoquinolines. One of the newly synthesized compounds has been identified as particularly promising and suitable for future research as a medicinal molecule.

#### 6. Evaluation of the publications and personal contribution of the doctoral student

A list of 7 publications related to the dissertation is presented, of which 5 are full-text articles and 2 are abstracts in scientific conference proceedings. Two of the full-text articles are in journals referenced in the Scopus and Web of Science databases (one is in a journal with an impact factor). Assistant Professor Gledacheva is the first author in six of the seven publications. The doctoral student has participated in 8 scientific forums abroad and 4 in Bulgaria on the subject of

the dissertation work. The scientific production of the doctoral student fully covers the quantitative criteria specified in the Regulations of the MU - Plovdiv.

Based on the presented declaration of originality and credibility and my personal impressions of the doctoral student, I believe that she participated in the conduct of the experiments described in the dissertation, and the obtained results and formulated conclusions, and contributions are her personal merit.

## 7. Abstract

The submitted abstract contains 53 pages and meets the requirements of the regulations for its preparation. It includes a description of the materials and methods used, and reflects the main results, conclusions and contributions of the dissertation work.

## 8. Critical remarks and recommendations

I have no critical remarks about the doctoral student. I recommend her to increase her publication activity in refereed journals.

## CONCLUSION

The dissertation **contains scientific, scientific-applied, and applied results**, which represent an **original contribution** to science and **meet all the requirements** of the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of LDASRB and the Regulations of the MU - Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements included in the Regulations of the Ministry of Education - Plovdiv for the application of the LDASRB.

The dissertation shows that the doctoral student Vera Nikolaeva Gledacheva possesses in-depth theoretical knowledge and professional skills in the scientific specialty "Biophysics", demonstrating qualities and skills for independent conduction of scientific research.

Due to the above, **I confidently give my positive assessment** of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results, and contributions, and I propose to the honorable scientific jury **to award** the educational and scientific degree "doctor" to Vera Nikolaeva Gledacheva in a doctoral program in biophysics.

20.02.2024

Prepared by:



Залчено на основание  
Чл.5 §1, 6."В" Регламент (ЕО)2016/679

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