

STATEMENT

To certify the educational and scientific degree “Doctor”

by: Assoc. Prof. Dr Valentina Kostadinova Broshtilova-Nikolova, MD
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Scientific filed 7. Healthcare and sports

Professional division 7.1 Medicine

PhD program: “Dermatology and Venereology”

Subject: *“Investigations on hemostatic parameters of erysipelas”*

Author: Dr Tsveta Ivanova Kalinova

PhD form: attending

Department: Infectious diseases, parasitology and dermatovenereology
Medical University “Prof. Dr Paraskev Stoyanov”, Varna, Bulgaria

Scientific Supervisor: Prof. Dr Sonya Stoyanova Marina-Kirova, MD

According to the Order of the Rector of MU-Varna, No P-109-323/ 30.07.2021, based on the Decision No 1 / 04.08.2021 of the Scientific Jury, I herein, present my official assessment of the theoretical and practical merits of the PhD thesis of Dr Tsveta Ivanova Kalinova.

General presentation of the applicant and PhD thesis

The presented set of documents fully meets the legal requirements of the Academic Staff Development Act of the Republic of Bulgaria and the Rules for the Academic Staff Development of the Varna Medical University to certify the education and scientific degree “Doctor”.

1. Applicant personal information

Dr Tsveta Ivanova Kalinova obtained her Master Degree in Medicine at the Medical University of Varna in 2017 with honours. In 2018 she is enrolled in the Dermatology and Venereology PhD attending program at the Department of Infectious diseases, parasitology and dermato-venereology at her alma mater. Dr Kalinova dedicates all her energy and knowledge to the educational and scientific activity of the Department, both as an assistant professor and researcher. She co-authors 7 papers in international journals and more than 20 original publications in Bulgarian language, one of which a textbook for medical and dental students. Dr Kalinova speaks Russian and English languages. She is a member of the Bulgarian Dermatological Society and European Academy of Dermatology and Venereology.

2. Evaluation of applicant's personal and professional qualification

Dr Tsveta Kalinova is a highly qualified medical specialist with specific interest in the field of clinical dermatology. She has been trained specifically in Dermatopathology, Dermoscopy and emerging therapeutic modalities of inflammatory dermatoses. Dr Kalinova is fluent in foreign languages and computer science. Her communication skills and team work capability are highly valued by her colleagues and patients.

3. Evaluation of the theoretical and practical aspects of the PhD thesis

The PhD thesis consists of 99 standard pages; contains 18 tables and 7 figures. It has 3 applications. The literature sources are 85 in number, 24 of which are in Cyrillic and 61 – in Latin alphabet. It contains high-quality, informative color illustrations.

The structure follows the accepted requirements: Review of literature; Materials and Methods; Results; and Discussion sections.

The **Introduction** reveals the social impact of the streptococcal dermo-hypodermatitis and its main complications: chronic-persistent clinical course and secondary lymphedema. The **Review of literature** highlights further details, depicting the specificity of dermatological manifestations, seasonal findings, broadly accepted methods of therapeutic prophylaxis. The modern concept of “intracellular reservoirs” of latent forms of pathogenic beta-hemolytic strains to perpetuate the endogenic bacteremia, is widely discussed. The hypothesis that anticoagulation therapy can induce hematological spreading of the latent strains, and cause an acute inflammatory relapse, is suspected.

Based on this up-to-date review, the PhD thesis **Objective** arises. The applicant hypothesizes whether hemostatic changes in the setting of acute bacterial streptococcal infection occur and how they can influence the course of the disease. Additionally, the level of serum procalcitonin is correlated to the severity of the skin infection.

Eight main **Tasks** are settled to prove the Objective. In my opinion, Task 2.2.1, 2.2.2 and 2.2.4 do not strictly address the theoretical background and have no clinico-pathological correlation. However, they reflect the modern epidemiology, demographic features and clinical specificity of the investigated entity and give some interesting, although unrelated to the main subject of the PhD thesis, data.

The **Materials and Methods** section clearly presents the investigational tools and methodology. The statistical analyses are reliable, and well established, serving as a solid pre-requisite for the research authenticity.

4. Impact and contribution section analysis

The PhD thesis has a provocative and modern concept. The number of investigated subjects, however, together with the hemostatic parameters, is insufficient to drive statistically reliable conclusions and reasonable outcome. This shortcut, in my opinion, comes from the bad research design and not properly verified inclusion and exclusion criteria.

The applicant confirms well-known demographic and co-morbid features of the diseases. However, the high percentage of male subjects with chronic venous insufficiency (84% to 15,8% female) is rising suspicion on the correct recruitment and proper enrollment of research objects. The preponderance of subjects on retarded

form of penicillin prophylaxis further confirms this observation, proving the improper enrollment of chronic erysipelas patients in the cohort of acute ones.

The analyzed hemostatic parameters do not constellate specific laboratory findings in the erysipelas patients. The only significantly verified trend is the elevated levels of serum acute inflammatory proteins- a well-known and widely accepted finding. No correlation is found between the basic hemostatic parameters and severity of the dermal-hypodermal streptococcal infection. Probably, a broader spectrum of hemostatic parameters is needed to identify some other trend. This requires future investigations on a larger cohort of patients in close collaboration with multidisciplinary team of clinical pathologist, angiologist, infectious disease specialist and vascular surgeon.

Furthermore, there is no clinical data on the specific group of anticoagulants and their use as a therapeutic modality to cope with the acute episodes of erysipelas. This makes original Contribution 4 as well as the diagnostic-therapeutic algorithm inconsistent and unreliable.

More precise and critical analysis of the literature sources, accumulation of larger clinical and laboratory data, and closer contact with multidisciplinary team of renowned specialists is highly advisable to clarify the theoretical concept and confirm the task force achievements.

5. Scientific publications related to the PhD thesis

The applicant presents 5 publications:

In international journals:

1. Kalinova Ts, Velevska Y, Márina S. Hemostasis in erysipelas - modern concepts. Scripta Scientifica Medica. 2019; 51(3): 7-11.

In Bulgarian journals:

2. Kalinova t, Marina S. Erysipelas and deep venous thrombosis – the role of procalcitonine. Medical Magazine. 2019; 68(8): 44-47 (in Bulgarian).

3. Kalinova T, Marina S. Modern concepts on the hemostasis changes in erysipelas. Dermatol Venereol 2020; 58(4): 9-14 (in Bulgarian).

4. Kalinova T, Yungareva I, Marina S. Intercellular persistence of *Streptococcus pyogenes* – a reason for recurrent erysipelas? Dermatol Venereol 2020; 1: 14-19 (in Bulgarian).

5. Kalinova T, Yungareva I, Marina S. Pathophysiological role of hemostatic changes in erysipelas.. MedInfo. 2020; 11: 106-111 (in Bulgarian).

6. Abstract

The Abstract fully meets the requirements of the Act, and objectively present the theoretical background, tasks, and results. It confirms the scientific contributions of the PhD thesis and reflects the most important impact of the research.

7. Conclusions

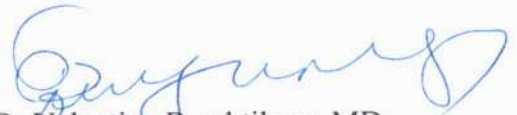
Despite the significant critical remarks and the above-stated controversial aspects, I consider the theoretical and practical grounds of PhD thesis presented enough to satisfactory meet the legal requirements of the Academic Staff Development Act of the Republic of Bulgaria and the Rules for the Academic Staff Development of the Varna Medical University to certify the education and scientific degree "Doctor". The research contains authentic contributions with original and applicable nature. The applicant demonstrates deductive approach, criticism, and analytic abilities, which merit the standards of PhD educational program.

I herein express my positive assessment of the PhD thesis, recommending to the honorable members of the scientific jury to vote positively and certify the PhD degree in Dermatology and Venereology to Dr Tsveta Kalinova.

Date: Aug 30th 2021

Sofia

Signature:



Assoc. Prof. Dr Valentina Broshtilova, MD

Valentina Broshtilova