

WRITTEN STATEMENT

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*(Internal member of the Scientific Jury, approved by Order No. P-109-337/09.08.2021 of the
Rector of MU-Varna)*

**Subject: Procedure for the defence of a dissertation for obtaining educational and scientific degree
"Doctor", FHE 7. Healthcare and sports, PF 7.3. Pharmacy, in the doctoral program "Toxicology".**

Topic of the dissertation:

" CHARACTERISTICS OF ACUTE MEDICINAL POISONING CASES IN VARNA
DISTRICT OVER A 30-YEAR PERIOD"

Author of the dissertation:

STANISLAVA ANGELOVA GEORGIEVA, MPharm - PhD student in full-time education at the
Medical University of Varna.

Supervisors:

Prof. Dr. Petko Marinov, MD, Ph.D. and Prof. Antoaneta Tsvetkova, Ph.D.

Significance of the topic: Poisoning is a significant public health problem worldwide. According to WHO data, in 2016 more than 1,206,000 people died as a result of accidental poisoning. The majority of these deaths occur in low- and middle-income countries. The causes of poisoning are many: human error, industrial, intentional and accidental. The problem is exacerbated over time as more and more new drugs and chemicals are developed and produced on a huge scale with each passing day. The most common toxic agents worldwide are pesticides, drugs (sedatives, painkillers, antidepressants, etc.), chemicals (acids and copper sulfate), alcohol, plant toxins, and household preparations. There are significant differences in patterns of poisoning between different countries. In developed countries, the annual prevalence of accidental or deliberate poisoning in humans varies between 0.2 - 9.3 exposures to poisoning per 1,000 people and continues to increase annually worldwide as their reporting and registration increases.

Relevance of the developed topic: The dissertation work of Stanislava Georgieva is dedicated to the study of the characteristics of acute drug poisoning in the Varna region for a 30-year period in Bulgaria. After reviewing numerous scientific publications on the problem, the current data provided by the author unequivocally prove that the developed topic is in one direction, which in the last decade has been developing extremely actively in scientific terms. The doctoral student

manages to trace the historical development, classification and specific aspects of drug poisoning and to draw important conclusions and recommendations in practical terms. I also appreciate this part of the review, which describes the general principles for the treatment of acute poisoning. At present, there are very few such comprehensive studies and in this respect the topic of the dissertation is undoubtedly very relevant.

The implementation of various studies and analyzes related to drug poisoning may be key to making management decisions to increase the role of the pharmacist in the control and prevention.

Structure of the dissertation: The dissertation work of Stanislava Georgieva is very well formed and structured in terms of its main parts. It starts with an introduction and contains a total of 5 separate chapters:

- Literature review;
- Methodology (purpose, object, methods, research time and inclusion criteria);
- Results
- Discussion of the results;
- Conclusions, conclusions, contributions;

Bibliography and appendices follow. The dissertation covers a total of 160 standard typewritten pages, including 25 figures and 21 tables. 260 literary sources are cited, of which only 4 are in Bulgarian.

The literature review contains a sufficient amount of summarized and analyzed material, which reflects a lot of data and information about research on the topic so far. It is systematically presented and reveals a very good knowledge of the subject related to drug poisoning and justifies the choice of the author for its topic. the role of the pharmacist in the control, etc. The review itself ends with the presentation of a very interesting idea-proposal for the establishment of a Coordination Center for Poisoning for the countries of the Black Sea region.

The main goal of the dissertation is to study, analyze and derive the main characteristics and epidemiology of acute drug poisoning in Varna region, registered in KILOT at MMA-MHAT Varna for the period 1991-2020 to improve measures for their prevention. The doctoral student has no formulated scientific hypotheses on which to base her research.

The tasks, 8 in total, arise from the set goal. They are formulated precisely, they are selected precisely, they are logically justified, and their solution allows them to correctly achieve the defined goal.

The object of the study are 6977 patients with AMI, admitted for treatment in the Clinic for intensive treatment of acute poisoning and toxicallergies of the Hospital at the Military Medical Academy in Varna for period 1991 – 2020.

The research methods used are classic and are selected in view of its specifics:

- General research methods
- Content analysis
- Documentary method
- Statistical methods
- Database analysis
- Image recognition, data classification and natural language processing (NLP) technologies

The overall design of the study is evidence of the in-depth knowledge and mastery of the doctoral student of modern methodological approaches in toxicology and informatics.

The results obtained are presented clearly and well structured for each aspect of the study, accompanied by numerous figures and tables. They clearly outline the current situation for acute drug intoxications, and numerous comparisons have been made. The percentages of poisoning with various drugs have been studied in detail, including all acute drug intoxications. All drug groups with toxic potential were analyzed in detail and the risks to human health were identified. Among the more important results obtained by the doctoral student, I would highlight the original study for economic evaluation of drug poisoning in Bulgaria.

During the discussion, the doctoral student appropriately summarized the data and results of each aspect of his research. Specific conclusions from the study have been formulated, which are important for the development of the regulation and treatment of acute drug intoxications in our country. The obtained results are original and reliable, supported by a large analyzed and summarized scientific material.

Conclusions. The scientific results obtained in the dissertation are systematized in formulated conclusions, in accordance with the collected and analyzed data. It is reasonable to say that the most common etiological causes of acute drug poisoning are benzodiazepines, followed by combined drug intoxications, cardiovascular, sedative-hypnotics and neuroleptics. I also support the statement that there is a decreasing trend of AMI towards the increase of the gross domestic product per capita for the indicated period. The cost of managing acute drug poisoning decreases as the number of cases decreases, despite the increase in the value of the clinical pathway. Independent intoxications with benzodiazepines, neuroleptics, anticonvulsants, cardiovascular, opiates did not significantly change their frequency and relative share during the period under review. The incidence of mixed drug intoxications is significantly increased. The amount and type of drugs used in combined intoxications are different, usually taking 2-9 medicines, OTC and dietary supplements for different therapeutic purposes.

I accept all other conclusions that objectively reflect the results obtained by the doctoral student.

Contributions to the dissertation

- *For the first time, a description of acute drug poisoning in the Varna region for a period of 30 years (1991-2020) was made and a statistical analysis was prepared in terms of demographic and etiological indicators, on the basis of which measures can be taken to improve and optimize of medical care for the population, as well as the development of effective preventive measures, as well as those for rehabilitation, aimed at reducing the impact of toxic factors as a cause of preventable morbidity and mortality.*
- *The typical toxicodromes in drug poisoning and treatment methods are summarized. A specific emergency form and selection of therapeutically effective dosage forms can be proposed and developed in any modern treatment center, as well as advanced training of pharmacists in order to assess and prevent cases of poisoning or refer intentional cases of poisoning to a psychologist or psychiatrist, specific educational programs.*
- *For the first time, an approach has been developed and a platform for anonymization of clinical data of patients compliant with the EU regulation on personal data protection (GDPR) has been proposed and an approach for analysis and prerequisites for implementation of a software application for visualization of clinical data has been proposed. data in mobile devices.*
- *For the first time, an approach for training a model and classifiers for patient documents containing text in natural language has been proposed, which has the ability to assess the possible risk of combined drug intoxication and an algorithm for building a mobile application with trained models has been proposed. classifiers to a poisoning coordination center of international and national importance.*
- *For the first time, the roles of pharmacists as consultants in poisoning, data annotation and assessment of toxicity risk models are presented, and additional training of pharmacists and pharmacy students is needed on prevention and prevention of suicide trials with medicinal products.*

Abstract and publications. The abstract is prepared according to the requirements of the Regulations for the development of the academic staff of the Medical University of Varna and correctly reflects the results obtained and the scientific contributions of the dissertation.

Four publications in scientific journals related to the dissertation and 3 participations in scientific conferences with a poster were presented. In almost all of them the doctoral student is the first author, which is an indisputable proof of his personal participation in the development, discussion and presentation of the obtained results.

Conclusion. I positively evaluate the dissertation work of Stanislava Georgieva and I believe that in terms of content and scientific contributions it fully meets the requirements of ZRAS in the Republic of Bulgaria and the Regulations for the development of the academic staff of MU-Varna. The good methodological preparation, the in-depth theoretical knowledge and the accumulated practical experience of the doctoral student in the field of Toxicology are an excellent prerequisite for his future successful development as a scientist. All this gives me reason to convincingly recommend to the members of the respected Scientific Jury to award **STANISLAVA ANGELOVA GEORGIEVA** the educational and scientific degree "**Doctor**".

Varna

November 11, 2021

Member of the Scientific Jury:.....

(Assoc. prof. Evgeni Evgeniev Grigorov, MScPharm, PhD)

By signing here, I declare that I am not related to the doctoral student, and that I have no private interest that could affect the impartial and objective implementation of the opinion in the current procedure for acquiring ESD "Doctor".