

POSITION

by Prof. Dr. Slavina Kirilova Surcheva, MD
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Concerning: Dissertation for the award of the degree of "Doctor of Science" in Higher Education "7. Health and sports "in the professional field" 7.3. Pharmacy, specialty "Pharmacology (including pharmacokinetics and chemotherapy)"

Topic: Identification, analysis and evaluation of pharmacokinetic and pharmacodynamic drug interactions.

Author: Assoc. Prof. Kaloyan Dobrinov Georgiev. M.Sc., Master of Pharmacy

The dissertation was discussed, approved and proposed for defense of the Departmental Council in the Department of Pharmacology, Toxicology and Pharmacotherapy, Faculty of Pharmacy, Medical University Varna.

The thesis defense materials are submitted on time and meet the requirements.

The dissertation is presented on 320 pages, illustrated with 77 figures and 78 tables. The references include 441 sources.

The topic of the thesis is contemporary and up-to-date. The identification, analysis and evaluation of pharmacokinetic and pharmacodynamic drug interactions has been presented in the light of both preclinical developments and clinical practice. The role and place of computer technologies in the preclinical and clinical stages of the introduction of new drugs is presented. Computer technologies also provide an opportunity to assess the risk of drug interactions in specific patient groups. In this regard, the assessment of the risk of polypharmacy in different categories of patients (e.g. adults) is at the heart of optimizing therapy.

The literature review thoroughly analyzes the problem and substantiates the goals of scientific development - study, analysis and evaluation of drug interactions at the pharmacokinetic and pharmacodynamic level through the application of approved software platforms (in silico) - the study of isolated plant fractions and new synthetic oligopeptide molecules; detection and analysis of pharmacokinetic and pharmacodynamic interactions in clinical practice. Eleven tasks have been adequately formulated that methodologically meet the set goals.

The correctly described results are richly illustrated. The original results are presented in 11 publications, two of which are in IF journals. The Academic Citation Reference reports 33 citations.

I accept the formulated conclusions and contributions of the dissertation, which can generally be presented as:

- Isolated methylxanthine fractions from Bancha leaf and Puer tea are characterized pharmacokinetically and pharmacodynamically for the first time;

- New pharmacokinetic characteristics have been added with respect to newly synthesized oligopeptides, endomorphin-2 analogues and RGD;
- Isolated fractions (polysaccharide, pectin-free and total extract) of *L.barbarum* (Goji berry) have been characterized pharmacokinetically and pharmacodynamically for the first time;
- For the first time, the medical documentation of patients with heart failure for a two-year period (2014-2015) was processed to investigate drug-drug interactions between standard therapy received and drug with low therapeutic width;

The abstract reflects the structure and content of the dissertation and complies with the LDAS of the Republic of Bulgaria and the regulations for its implementation.

I have no significant criticisms of the thesis.

I believe that the dissertation work of Assoc. Prof. Kaloyan Georgiev on "Identification, analysis and evaluation of pharmacokinetic and pharmacodynamic drug interactions" is an own and current work with scientific contributions and practical focus. The dissertation fulfills all the criteria for awarding the degree of Doctor of Science and this gives me a reason for positive assessment.

In conclusion, I recommend to the Honorable Members of the Scientific Jury to award the Scientific Degree "Doctor of Science" to Assoc. Prof. Kaloyan Dobrinov Georgiev, Ph.D. for his dissertation.

17.02.2020

Sofia

Member of the scientific jury:



/ prof. Dr. Surcheva /