"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY
BUCHAREST
DOCTORAL SCHOOL
PHARMACY

INTERDISCIPLINARY APPROACHES IN DEVELOPING PHARMACEUTICAL SYSTEMS FOR PRECISION THERAPY

SUMMARY OF THE HABILITATION THESIS

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The habilitation thesis, titled ***"Interdisciplinary Approaches in Developing Pharmaceutical Systems for Precision Therapy,"*** comprises three sections in accordance with national guidelines. The work presents the key outcomes of my professional, academic, and research activities since the completion of my doctoral thesis in 2010. Additionally, it outlines my vision for advancing my academic and research career, particularly in response to the increasing demand for innovative and tailored therapeutic solutions in precision medicine.

In the chapter titled *"Professional and Academic Achievements,"* I detailed my academic and professional journey spanning 18 years at the Faculty of Pharmacy, "Carol Davila" University of Medicine and Pharmacy in Bucharest. In 2006, I secured the role of Junior Assistant in the Department of Physical and Colloidal Chemistry through a competitive process. I was promoted to Assistant Professor in 2008, advanced to Senior Assistant in 2015, and became an Associate Professor in 2019, a position I currently hold. Following graduation, I pursued a residency in Pharmaceutical Laboratory specialization alongside my doctoral studies. In 2010, I earned my Ph.D. in Pharmacy with a thesis titled "*Bioanalytical and Pharmacokinetic Particularities in the Bioequivalence Evaluation of Drugs with Active Metabolites*," under the mentorship of Prof. Dr. Constantin Mircioiu.

In addition to my academic appointments, I pursued advanced training to broaden my expertise in pharmaceutical sciences. From 2016 to 2018, I completed a Master's degree in *Biotechnologies for the Pharmaceutical Industry* at the Faculty of Biotechnologies, University of Agronomic Sciences and Veterinary Medicine in Bucharest, Romania, equipping myself with specialized skills relevant to emerging technologies in drug development.

I also actively contribute to the academic community by teaching and coordinating courses in several key areas. I lead the "*Bioequivalence Studies"* course in the Master's program *Clinical Studies Monitoring and Analysis* and the "*GMP and GLP Standards"* course within the *Biotechnologies for the Pharmaceutical Industry* program at USAMV Bucharest. In addition, I oversee the "*Technology Transfer and Validation"* module for industry residents and teach within the "*Physical and Colloidal Chemistry"* department, supporting the training of future professionals in pharmaceutical sciences and biotechnology.

I currently hold the position of Head of the Research, Development, and Innovation Department at "Carol Davila" University of Medicine and Pharmacy.

The second chapter, titled *"Scientific Achievements"* outlines my main areas of expertise in terms of key scientific contributions obtained after defending my doctoral thesis.

Study of the in-vitro release kinetics of active compounds from solid, semisolid and nanoparticulate formulations. This includes developing a mechanistic understanding of the release mechanisms through detailed mathematical modeling, providing insights into how formulation characteristics influence drug release profiles and guiding the design of more effective pharmaceutical delivery systems. In recognition of the contributions in this area, one of my main papers, namely *"Mathematical Modeling of Release Kinetics from Supramolecular Drug Delivery Systems, Pharmaceutics, 2019; 11(3): 140, doi:*

10.3390/pharmaceutics11030140., was granted the "Pharmaceutics 2021 Best Paper Award" (https://www.mdpi.com/journal/pharmaceutics/awards/1381). The paper attempts an insight into the phenomenological and mathematical aspects that describe how drugs are released from different supramolecular delivery systems, with special emphasis on polymeric matrices and micro- and nano-particulate formulations. Understanding the phenomenology behind the drug release mechanism allows predictions on how the experimental parameters will impact the drug release rate, and therefore impact the pharmaceutical product quality.

Pharmacokinetics and In Vitro-In Vivo Correlation Models. Following the completion of my Ph.D., pharmacokinetics and pharmacokinetic variability have remained central points to my research activity. I have concentrated on study of the absorption, distribution, metabolism, and excretion of drug compounds and their active metabolites on both healthy and diseased populations. Another significant focus of my work has been examining the effects of food intake and other sources of pharmacokinetic variability, evaluating their influence on drug efficacy. To enhance the predictability of in vivo drug behavior from in vitro data, I develop and apply in vitro-in vivo correlation (IVIVC) models, supporting the design of precision therapies tailored to individual patient needs. My postdoctoral research (2014-2015), *In Silico, In Vitro, and In Vivo Investigations into Reducing Pharmacokinetic Variability and Treatment Resistance in Antiplatelet Drugs,* further honed my expertise in this critical area.

Development and Optimization of Innovative Pharmaceutical Formulations with Enhanced Biopharmaceutical Profile. My scientific work is deeply rooted in the application of advanced modeling, simulation, and optimization techniques in pharmaceutical technology. I focus on enhancing solubility through various physico-chemical methods such as cosolvency, eutectic solvents, and solid dispersions, as well as through nano-encapsulation strategies involving synthetic and natural bioactive compounds in ultradeformable liposomal systems, nanolipid carriers, and microemulsions. For formulation optimization, I employed a systematic approach based on Quality by Design (QbD) principles, utilizing Design of Experiments (DoE) techniques.

Chromatographic Method Development and Validation. Rooted in my early experience within a GLP environment, I have pursued scientific research in chromatographic method development and validation, evolving from HPLC-UV to more advanced mass spectrometry methods (LC-MS/MS), and more recently, high-resolution techniques such as HPLC-QTOF/MS. I employed systematic approaches, including Analytical Quality by Design (AQbD), to optimize and validate liquid chromatographic methods (HPLC-DAD, HPLC-QTOF/MS, HPLC-MS/MS) for analyzing bioactive compounds in biological and pharmaceutical media. These methods are essential in drug development, pharmacokinetic studies, and therapeutic drug monitoring, with further applications in metabolomics and pharmacogenomics, supporting advancements in precision therapies.

Valorization of Therapeutic Potentials of Natural Compounds. My research explores the therapeutic potential of plant-derived compounds, focusing on their chemical "fingerprinting" using advanced analytical methods, optimizing the phytochemical profile

of natural extracts through systematic approaches, and integrating natural compounds into innovative formulations with experimentally demonstrated biological activity.

Throughout my career, I have contributed to 37 national research grants (within PNCDI II and III frameworks, with 4 as Partner Responsible) and 7 international projects, including 3 within the Horizon2020 and 1 within Horizon Europe framework. My scientific output includes 69 ISI-indexed papers (H-index of 16 in WoS). I have also co-authored 8 books and book chapters, submitted 6 patent applications, and presented over 100 scientific papers at conferences. I have received 11 international awards, underscoring my contributions to pharmaceutical science.

The last section of the thesis contains my future objectives for developing teaching and scientific activities within the educational mission of the Carol Davila University of Medicine and Pharmacy. It presents some of the research directions I intend to pursue, plans for developing interdisciplinary collaborations, and the objectives and measures for conducting teaching activities.

In conclusion, my academic, educational, and research activities will continue to uphold high standards, aligned with both my guiding principles and the qualitative and ethical standards outlined in the Charter and Strategic Plan of "Carol Davila" University of Medicine and Pharmacy. Future scientific endeavors will build on established research directions where I have already achieved significant results, while also aligning with the National Strategy for Research, Development, and Innovation and the Horizon Europe Framework. The main new research direction, connected to previous interests, focuses on the applications of high-resolution mass spectrometry in metabolomics, aiming to enhance untargeted screening capabilities and the identification of biomarkers associated with disease diagnosis, progression, and treatment response. This approach aims to maintain a balanced integration of scientific research with other academic responsibilities, driving performance, competitiveness, and cross-discipline compatibility to support meaningful contributions to European scientific research and technological innovation in the pharmaceutical field.