### UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE "CAROL DAVILA" BUCUREȘTI ȘCOALA DOCTORALĂ DOMENIUL MEDICINĂ

## ENHANCING QUALITY OF LIFE THROUGH RESEARCH ON PRECISION MEDICINE ACROSS DIFFERENT LIFE STAGES. INTEGRATED EVALUATIONS AND ADVANCED THERAPEUTICAL INTERVENTIONS FOR ACUTE AND CHRONIC CONDITIONS

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#### ABSTRACT

The habilitation thesis entitled "Enhancing Quality of Life through Research on Precision Medicine Across Different Life Stages. Integrated Evaluations and Advanced Therapeutical Interventions for Acute and Chronic Conditions" was elaborated following the recommendations of the National Council for Attestation of University Degrees, Diplomas and Certificates and the CSUD regulations of the "Carol Davila" University of Medicine and Pharmacy in Bucharest regarding the obtaining of the habilitation certificate; it consists of a brief display of the evolution of my career from a professional, academic and scientific point of view.

The habilitation thesis is structured into four sections;

- The first chapter presents the leading scientific achievements after the Ph.D. research and thesis;
- The second chapter highlights the academic achievements;
- In the third chapter, the professional achievements are presented;
- The last chapter presents the plans regarding the evolution and development of the professional, scientific, and academic profiles.

In the chapter "Professional Achievements," I presented my entire academic and professional career during my over 25 years of activity within the Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy Bucharest, Romania (EU). I went through all the stages of academic education, starting from the professor assistant status, which I obtained through a contest. During this period, numerous exams were passed to obtain academic titles and degrees specific to the medical doctor profession, which is a resident specialist. In 2005, I defended my Ph.D. thesis in Medical Sciences. Professional training has been the core of my formation, and I have a multidisciplinary educational path adapted to the nature of the subjects taught.

Thus, I graduated with the Anesthesia and Intensive Care specialty, the Geriatry and Gerontology medical specialty, the Age Management specialty, and numerous clinical competencies in the field of Emergency medicine, First aid, Toxicology, Pain management and also Nutrigenetic, Nutrigenomics, and numerous sub-specializations in the field; the professional training was performed in the country at the Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, or abroad at International Universities and Professional associations.

In the chapter entitled "Academic Achievements," regarding the didactic activity, I have been involved in teaching the fourth-to sixth-year students of the Faculty of medicine, residents of Anesthesia and Intensive Care specialty, Emergency medicine, Toxicology, and recently the Geriatric and Gerontology medical specialty specialties, and medical residents. The didactic activity was not only focused on teaching but also on motivating and supporting medicine students, medicine residents, and students in different scientific activities, sustaining the presentation of their results within scientific events, scientific papers, and their bachelor's thesis. I also participated as a co-author in improving the didactic materials and published two books in the field specific to the teaching subjects.

In the third chapter, entitled "Scientific Achievements," I have detailed the main research directions sustained by the most important publications, as follows:

Innovative therapeutic systems using new technologies. This direction comprises studies regarding the pre-formulation and formulation of pharmacologically active agents of synthetic and natural origin in the form of final products with particular delivery systems (slow release, nanocapsules). We have shown that optimal pharmacokinetics must be ensured for a valuable pharmacodynamic active substance to head the pharmacological targets optimally and exert the therapeutic role. The dynamic in time and through the passage by the body's internal (end external) barriers are particular for each substance from the millions of molecules.

Lipid nanoencapsulation of natural active molecules (curcumin, diosgenin, hesperidin) and derivatives (oleoyl ethanolamide, oleamides) - by having an increased biodisponibility due to the rapid passage of the cellular barriers - showed enhanced therapeutic potential in the treatment of obesity and age-related states (menopause). This research direction is sustained by eight ISI-quoted scientific papers, three patents, and more than five research projects. One research project was being conducted under a scientific research grant.

#### Studies on Anesthesia and Intensive Care specialty

The first specialty areas, toxicology, clinical pharmacology, anesthesia, and intensive care, were the main priorities in early medical practice. During a period of 20 years, I have dedicated my professional, academic, and scientific activity to in-depth learning and top-ranked practice in the area. I have focused the research activity on increasing the safety profile in ICU & and anesthesiology patients, increasing performance and skills in anesthesia and intensive care—advanced management in critical situations. To establish drug susceptibility models, the control of superinfections and nosocomial infections in intensive care units was evaluated in a

retrospective joint research with the "Marius Nasta" Institute of Pulmonary Medicine (MNIPM), Bucharest, Romanians. For this purpose, we evaluated all antibiograms of ESKAPE pathogens isolated from respiratory samples from adult patients hospitalized between 2010-2015 at MNIPM. We analyzed 2859 isolates (61% of the 4683 ESKAPE isolates).

P. aeruginosa was the most common pathogen, while Enterococcus spp. and Enterobacter spp. were virtually absent. The antibiotic profile of P. aeruginosa isolates showed more resistance in the intensive care unit (ICU)/surgery, probably as a result of antibiotic pressure. A. baumannii, although less common (and the only pathogen more common in the surgery department), had an even more resistant profile to almost all antibiotics except Colistin. Methicillin-resistant S. aureus (MRSA) accounted for about 60% of all isolates, more in the intensive care/surgery ward. K. pneumoniae shows less resistance and more stability when analyzing the antibiogram model in medical wards. The main conclusion was that interventional programs comprising appropriate antibiotic management and active surveillance had to be implemented to mitigate the antibiotic profile. Further research should focus on a more detailed characterization of the molecular mechanisms leading to the high resistance, which is detailed here. This study adds to the literature reporting Romania's antibiotic resistance spectrum for these highly resistant pathogens. Furthermore, we investigated advanced materials to reduce bacterial contamination. We have analyzed the potential of silver fabric impregnation of medical tissues in critically ill patients in control of bacterial contamination. The importance of using silver textiles and linen bandages in medical practice is emphasized by the need derived from the legislation in force in Romania (harmonized in 2006 with EU standards), by increasing civil liability in case of medical malpractice accusations issued as a result of damages caused by patients with nosocomial infection.

This research direction is sustained by four ISI-quoted scientific papers, two BDI, one patent, seven research projects, one national basic and advanced life support national program, one industrial design patent, numerous courses and trainings for healthcare professionals, and two published books.

# Studies on the Geriatry and Gerontology medical specialty. Studies on nutrition and metabolic profiling

During the last years, I have emphasized my research activity on clinical and pharmacological aspects regarding geriatrics and gerontology medical specialty. Studies on nutrition and metabolic profiling, metabolic diseases, and especially metabolic syndrome, pathologies with a high prevalence in European society and globally, according to the call of the World Health Organization to health specialists. We have developed epidemiological studies in the inter-university and interdisciplinary, integrated team, together with the reputed Universities of Medicine and Pharmacy "Iuliu Haţieganu", Cluj Napoca, and the Faculty of Psychology, "Babes Boyai" the University of Cluj Napoca regarding nutrition and lifestyle epidemiological studies and Metabolism Disease Research Institute and their outstanding research teams.

We have analyzed the eating and drinking profiles of medical students, IT workers, and certain diabetes mellitus patients; as the prevalence of eating disorders (anorexia, bulimia) starts at early childhood ages, we prepared the terrain for evaluation of the diagnostic tools and patient profile in the area of eating disorders, together with top researchers from Romania and USA. This research direction is open and will be developed. Current results were published in ISI-indexed papers in Q1 ranking.

The present research direction materialized with over seven conferences on the topic, coordinator of two sections of the international congress, two participations in editorial teams on the research direction, a national grant, an international grant, and two ISI papers, of which one in Q1, a special issue on the topic "Nutrigenetic, Nutrigenomic & Nutriepigenetic Approaches in Age Management Interventions.

The fourth chapter delineates "Strategic Plans for the Advancement of Academic, Scientific, and Professional Endeavors." This segment integrates pedagogical activities and scientific investigation to uphold premier educational standards. There is a concerted emphasis on the continual enhancement of didactic operations, which involves the modernization of theoretical and practical aspects pertinent to the subjects taught and fostering skill development through active participation in scientific inquiry among emerging doctors.

Future initiatives will revisit the previously outlined scientific trajectories that yielded substantial outcomes and explore ancillary research avenues. The primary goals are cultivating partnerships within critical domains—spanning academic, professional, and real life—to conceptualize innovative products and advance new technologies under established research directives. Additional objectives include securing funding via prospective projects, promulgating study findings through publications in high-impact journals, and submitting protective patent applications.

Both academic and scientific pursuits are intrinsically linked to professional activities, focusing on dynamic participation in the socio-professional facets characteristic of the healthcare sector. I am committed to leveraging resources to enhance and mentor emerging scholars within my field of research, uphold meticulous scholarly standards, feed and encourage creativity, maintain the rigorous working style for scientific and academic prestige, and contribute to the scientific and academic reputation of the University of Medicine and Pharmacy "Carol Davila".