

**”VICTOR BABEȘ” UNIVERSITY OF  
MEDICINE AND PHARMACY FROM TIMIȘOARA  
DOCTORAL SCHOOL  
MEDICINE DOMAIN**



**OPTIMIZATION OF PHARMACOTHERAPY  
AND NEW THERAPEUTIC SOLUTIONS IN  
PATHOLOGIES WITH INFLAMMATORY COMPONENT**

**ABSTRACT**

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The present habilitation thesis entitled "Optimization of pharmacotherapy and new therapeutic solutions in pathologies with inflammatory component" briefly presents the research activity of the undersigned carried out after obtaining the PhD scientific title, in 2017.

The first chapter of the present thesis groups the scientific achievements, namely the main research directions developed, the research projects carried out and the results of the scientific activity. The main research direction was initiated during the doctoral studies and was subsequently extended throughout the academic career. This direction aimed to assess endothelial function and, implicitly, the degree of endothelial dysfunction, both by classical ultrasound assessment methods (IMT – intima-media thickness, FMD – flow-mediated vasodilation) and by analysis of biochemical markers quantified from venous blood samples, from classical inflammatory ones (fibrinogen, highly sensitive C-reactive protein) to less studied markers which included pentraxin-3 - a marker of acute inflammation produced locally by several cells including endothelial cells, soluble endoglin - a marker of fibrogenesis involved in tone, homeostasis and vascular remodeling, and thrombospondin-1 - a marker involved in regulation of endothelial cell adhesion, cell migration, apoptosis and angiogenesis. The studies focused on hypertensive patients with endothelial dysfunction on various antihypertensive therapeutic strategies. The aim was to identify medicines/substances that can better reverse vascular lesions, in addition to decreasing blood pressure values, to prevent cardiovascular complications that may occur. We also aimed to find non-invasive biomarkers, easy to quantify in current medical practice, that would highlight vascular endothelial lesions and local homeostasis impairment as accurately and early as possible, and also assess the efficacy of the pharmacological therapy implemented. Thus, the pleiotropic properties of two antihypertensive molecules (perindopril and candesartan) were evaluated both in retrospective, observational studies (chronic treatment administered as monotherapy, over a treatment period of > 1 year), compared with other classes of antihypertensive drugs (beta-blockers, calcium channel blockers, diuretics), and in dynamic, prospective, observational studies over a period of 1 year, with patients evaluated at baseline and after 1 year of treatment. Less studied markers (pentraxin-3, soluble endoglin and thrombospondin-1), also implicated in vascular homeostasis, were included in the study and quantified at different times of treatment or under different therapeutic regimens and correlated with classical methods of endothelial function analysis. The scientific results obtained have been disseminated both in the form of

publications in the ISI stream and through communications at prestigious national and international conferences.

In the context of the studies implemented during the doctoral internship on endothelial function, I participated in studies carried out in collaboration with the Department of Psychiatry of the Faculty of Medicine of Timisoara. Thus, my scientific activity also focused on the relationship between cardiovascular complications, psychiatric diseases and pharmacological treatment implemented in various contexts: evaluation of (1) cardiovascular risk factors in patients with psychiatric pathology under antipsychotic treatment; (2) degree of endothelial inflammation in the first psychotic episode of schizophrenia and after 6 months of treatment; and (3) long-term risks of cardiovascular disorders in patients under treatment with long-acting antipsychotics. The commonality between these studies is the quantification of inflammation and endothelial dysfunction correlated with the existence of other cardiovascular risk factors. Furthermore, these studies have highlighted the need for early identification of cardiovascular risk factors in all patients with psychiatric pathology in order to improve their quality of life and reduce complications - including cardiovascular morbidity and mortality.

Over the years, I have paid particular attention to the management of pharmacotherapy in elderly population (patients over 65 years old), an extremely frail category of patients. Initially, three years after completing my undergraduate studies, in 2013, I completed one-year master's program on the topic "Pharmacotherapy management in the elderly", and in 2017 I completed a three-month internship in Belgium in the geriatrics department under the supervision of Prof. Anne Spinewine, Prof. Paul Tulkens and Prof. Olivia Dalleur at the Université Catholique de Louvain, in Brussels. In this context, upon my return to Romania, I conducted several research projects on inappropriate prescribing and prescribing habits of chronically administered drugs in the elderly population in Romania, both in rural and urban settings. The aim of the research was to determine to what extent the prescribing of medicines is in line with international recommendations, in particular with European and American guidelines on rational and optimal pharmacotherapy in older adults - the largest consumer of medicines. The results revealed not only inappropriate prescribing practices, including problems with choice of medicines, overuse and underuse of certain medicines, but also differences in optimal pharmacotherapy between rural and urban settings.

Since 2018, I have been collaborating with Prof. Corina Danciu in aspects regarding phytochemical characterization and evaluation of *in vivo* and/or *in vitro* pharmacological actions (antioxidant, antiproliferative, anti/pro-apoptotic, antimicrobial) of various types of extracts, fruit juices or essential oils. A particular topic that interested me was combating resistance to "classical" antimicrobials, by finding new substances/active principles with antimicrobial properties that can either be therapeutic alternatives or can be used as complementary substances to enhance the antimicrobial effect of a classical agent. Combating antimicrobial resistance (AMR) is among the ten global health problems identified by the World Health Organization (WHO) in 2021. While AMR is a natural occurring process, the inappropriate use of antibiotics in different situations and legislative gaps have led to the extremely rapid progression of this process. As a result, AMR has now become an extremely serious global threat, affecting both humans and animals, and as a consequence, the entire ecosystem. Thus, the implementation of effective prophylactic measures, as well as finding more potent and non-toxic antimicrobial agents, is imperative in the current context.

Regarding my capacity to coordinate research activities (including here the capacity to manage teams), to mentor students, residents and/or PhD students, I was the director of two research projects, with funding obtained through a competitive process: a. PII-C4-TC-2016/16441-09 - Role of perindopril and candesartan in hypertensive patients with endothelial dysfunction and b. 5DOC/1425/03.02.2020 - A comprehensive *in vitro* and *in vivo* evaluation of *Aronia melanocarpa* (Michx.) Elliot standardized bio juice on blood pressure levels and endothelial damage. A prospective study. I was also a member of the research team in two other projects won through a competitive process.

Since 2017 I have coordinated 30 undergraduate papers with students of the Faculty of Pharmacy of UMFVBT, Romanian and French sections and in 2022 I became the coordinator of the Clinical Pharmacy residency program in Timisoara. I am also a member of three PhD student mentoring committees at "Victor Babes" University of Medicine and Pharmacy of Timisoara (UMFVBT), Romania, and since May 2023, I am a member of the Education Committee of the European Society of Clinical Pharmacy, with clinical pharmacy colleagues from around the world, in recognition of my teaching, research and clinical work.

To date, I have published 51 articles (BDI or ISI) as lead author or co-author, with more than 60% of them as lead author (cumulative IF = 75,966). The published articles quantify a number of 434 citations, with a calculated h-index of 10 (as of 21 October 2023).

The second chapter of the habilitation thesis presents the academic achievements. My teaching career started in 2010, immediately after graduating from the Faculty of Pharmacy in Timisoara, initially on an hourly basis, in the Discipline of Pharmacology - Clinical Pharmacy. During the summer of 2013 I took up the position of Assistant Professor in the same discipline, working with students in the 3rd, 4th and 5th year of study, for both the Romanian and French series, in the practical works of Pharmacology and Clinical Pharmacy. In the summer of 2020 I was promoted by competition to the position of head of works (lecturer) and since February 2021 I occupy the position of Associate Professor in the Discipline of Clinical Pharmacy, Communication in Pharmacy, Pharmaceutical care. I have always had the student at the center of my educational concerns, for which I have tried to continuously improve myself to remain up to date with clinical pharmacy standards, both in Romania (psychopedagogy module) and abroad with two clinical internships in Europe. I always encourage dialogue, creativity, initiative and involvement of students and residents in the educational process. In my work, I place great emphasis on the development of practical skills necessary for the clinical pharmacist, without which he or she would not be able to carry out his or her work. Moreover, since entering academia, I have continued my work as a pharmacist, both in community and hospital pharmacy. Thus, through my professional experience, both in community and hospital pharmacy, I develop authentic, real-life examples of clinical situations that require the involvement of the clinical pharmacist, so that the aspects taught and discussed are in line with current clinical practice and with the requirements of the actual pharmaceutical field.

The third chapter is dedicated to my professional work. Immediately after graduation (2010 promotion), I opted for a 2-year Master's degree in Medical Biostatistics at the University of Bucharest, while also working as a pharmacist manager in a community pharmacy in Timisoara. Two years after completing my undergraduate studies, I attended the master's program "Pharmacotherapy management in the elderly" at UMFVBT, and in January 2013 I became a resident in Clinical pharmacy program in Timisoara. From October 2011 to October 2016 I attended doctoral studies at UMFVBT, Medicine field, under the supervision of Prof. Univ. Mirela Tomescu. After my PhD, I completed a training period at the Université Catholique de Louvain, Brussels, Belgium, from March 2017 to

June 2017, in the field of Clinical Pharmacy. At the beginning of 2020 I attended another theoretical and practical internship at Erasmus University Medical Center, Rotterdam, The Netherlands, in Personalized Medicine, under the supervision of Prof. Peter van der Speak, in the Department of Medical Bioinformatics. I became a primary pharmacist in the summer of 2021. During the same period I was also hired as a clinical pharmacist at Ineu City Hospital.

The last chapter details the development perspectives of my academic career on five main directions: (I) educational process; (II) scientific activity; (III) national and international collaborations; (IV) clinical integration and (V) continuing professional education. In order to improve the educational process I aim to: periodically update the course material and practical works according to the latest research in the field and on the basis of the latest therapeutic guidelines available, as it is known that therapeutic strategies are constantly developing and changing and these aspects must be made known to the student pharmacist; develop support teaching materials in dual format (printed and electronic); present the most important web resources that can assist pharmacists in their professional activities; harmonize the curriculum in line with international standards; increase the active involvement of students in the educational process and stimulate the collaborations between students/residents/doctoral students by organising courses, workshops and student circles that will address various topics, tailored to their needs; as well as facilitating the implementation of clinical internships with students in the 5th year for clinical pharmacy on the wards of medical units. In terms of scientific activity, I propose to continue the current research directions; to develop a multidisciplinary, national and international research team and to attract funding by accessing grants. In order to keep abreast of the latest information in the field and to open new doors for fruitful internal and external collaborations, I aim to participate annually in at least one national and one international congress in the field of Clinical pharmacy.