

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



ADVANCED ANALYTICAL METHODS: FROM BASIC RESEARCH TO BIOMEDICAL APPLICATIONS

ABSTRACT

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The habilitation thesis entitled "Advanced analytical methods: from basic research to biomedical applications" includes the principal scientific, academic and professional contributions that I made after obtaining the scientific title of PhD at the University of Medicine and Pharmacy "Carol Davila" in Bucharest, under the supervision of Prof. Leon Zagrean, as well as outlining the path forward for my professional, scientific and academic career.

The habilitation thesis fully complies with the guidelines for the preparation of the habilitation thesis, published by the National Council for the Accreditation of University Degrees, Diplomas and Certificates in Romania, and was written according to the Guidelines for the elaboration and writing of the habilitation thesis of the University of Medicine and Pharmacy "Victor Babes" in Timișoara, being organized in 3 sections:

- I. scientific, professional and academic personal achievements;
- II. personal career development plans;
- III. bibliographical references associated with the content of the first two sections.

The thesis is structured in four chapters, dedicated to the first two sections, followed by the bibliographical references.

Chapter 1 of the thesis contains the main scientific activities and achievements (research areas, research projects, scientific and research activity outputs), carried out after earning my PhD, in the Biochemistry Discipline and in other research laboratories in the country, with which I collaborated in the research activities undertaken: The Mass Spectrometry Laboratory of the National Institute of Research and Development for Electrochemistry and Condensed Matter (INCEMC) of Timișoara, the Genomic Medicine Centre of UMF "Victor Babeș" of Timișoara, the Centre for Organic and Organometallic Supramolecular Chemistry of the University "Babeș-Bolyai" of Cluj-Napoca, the Institute of Chemistry "Coriolan Dragulescu" of the Romanian Academy, and the Department of Pharmaceutical Sciences, Faculty of Pharmacy, "Vasile Goldiș" Western University of Arad.

The first chapter is organized into 3 subchapters:

1.1. Scientific research areas, which describe the central studies and research activities in which I have been involved or which I have coordinated, after earning my PhD. I grouped these, in turn, into 4 sub-subchapters:

1.1.1 Lipidomics: the use of mass spectrometry-based methodologies in glycolipid analysis. I present studies dedicated to the assessment of glycosphingolipid profile in the normal and pathological human brain (secondary tumors/brain metastases) by implementing and optimizing extraction and purification procedures of the obtained

mixtures, followed by mass spectrometry (MS) analysis using matrix-assisted laser desorption/ionization (MALDI) ionization and nanoESI, respectively, with robot infusion and time-of-flight (TOF) and ion trap (IT) analyzers. This part also presents extensive literature studies dedicated to analyzing gangliosides and acid glycosphingolipids by mass spectrometry coupled with different separation methods and carried out by chip-based nanoESI infusion into MS.

1.1.2 Gliomics: use of mass spectrometry-based methodologies in the analysis of glycosaminoglycans, glycans from various natural extracts, functionalized polysaccharides, and some modified monosaccharides. The use of mass spectrometry and characteristic mass-energy profiles for the identification of isomers of some acetalized monosaccharides and for the identification and structural characterization by mass spectrometry of both a neutral polysaccharide obtained from the extract of *Fomes fomentarius*, a non-edible fungus which presents significant medical properties, and a synthetic one obtained by reductive amination, is described. Mass spectrometric exploration of chondroitin- and dermatan sulfates, proteoglycans of particular importance in the extracellular matrix, is mentioned. Extraction and purification procedures are described, and fragmentation techniques are used to make their detailed structural analysis possible.

1.1.3 Analysis by mass spectrometry and other analytical methods of various drugs, cosmetics, natural extracts, and synthetic compounds. In this sub-subchapter, the behavior of riboflavin, epinephrine, chloramphenicol, metronidazole, and dipyrindamole under EI MS conditions is investigated utilizing quantum chemical calculations. The cardioprotective effect of trimetazidine, a metabolic modulator against myocardial ischaemia and the antioxidant properties of various extracts of *Fomes fomentarius* are highlighted in the experimental data obtained in two other studies. Moreover, the structural investigation by multi-stage mass spectrometry (MS^n) of trisilanolisobutyl-POSS, an important precursor for biocompatible materials and drug delivery systems and an extensive study carried out on the analysis of cosmetic ingredients by different methodologies based on mass spectrometry and hyphenated methods are also described.

1.1.4. Research into molecular and systems neuroscience. In this sub-subchapter, the examination of brain electrical activity under the influence of different auditory stimuli is described, through the development of characteristic mathematical models for alpha, beta, delta and theta rhythms, and the potential therapeutic modalities of targeting cell signaling pathways involved in stroke pathology are explored.

1.2 Scientific research projects

In this sub-chapter, we briefly present nationally-funded research projects in which we participated - a participating member in a Collaborative Applied Research Projects (PN-II-PT-PCCA) type project, project director in a PD type post-doctoral project, and an international mobility grant.

1.3. Scientific and research results

The 2 invited book chapters in the series "Methods in Molecular Biology (Springer Protocols)", published by Humana Press, are mentioned. They are dedicated to glycomics analysis using electrospray ionization mass spectrometry-based methodologies.

The post-doctoral scientific articles are presented, a list that includes 10 articles published in ISI-indexed journals with impact factor as main author (first/last author, corresponding author), and one article published in an ISI indexed journal without impact factor in the current year as first author, 6 articles published in ISI indexed international journals with impact factor as co-author, and 3 in journals indexed in international databases (BDI). Abstracts published in ISI journals with impact factor (1) and those published in BDI journals/conference abstract volumes with ISSN/ ISBN (12) are also mentioned.

The elements of recognition of scientific and research activity mention the Hirsch index of 12 and the 380 ISI citations according to the Web of Science Core Collection, a Hirsch index of 13 and 411 ISI citations according to Scopus, and a Hirsch index of 13 and 517 ISI and BDI citations according to Google Academic. The following are briefly presented: membership in professional-scientific structures, activity as reviewer for articles in ISI and BDI listed journals, activity as Guest editor for an ISI indexed journal (*Molecules*, IF of 4.6), activity as CNCSIS expert evaluator for the Partnerships program - PCCA type, 2013 competition, national awards, including the I. G. Murgulescu Prize of the Romanian Academy for Chemistry.

Chapter 2 presents my academic activity and achievements during my teaching career, making mention of: the full course of my academic career, from university preparator and doctoral student, to Assistant Professor, Lecturer and finally Associate Professor; teaching Biochemistry courses in Romanian (the Faculty of Medicine and the Faculty of Pharmacy), Chemistry, Biochemistry and Biochemistry of the Oral Cavity in English (the Faculty of Dentistry) and Biochemistry laboratories in Romanian (the Faculty of Medicine, Faculty of Dentistry and Faculty of Pharmacy, the College of Dental Technology and Dental Prophylaxis Assistance as well as General Nursing) and in English (the Faculty of Medicine and the Faculty of Dentistry); my work in developing and revizing teaching materials in Chemistry and Biochemistry for students of the Faculties of Medicine and

Pharmacy; my mentoring of students in their undergraduate work and their didactic volunteer work; my participation in university admission, bachelor and residency examinations, and as committee member in department position contest examinations.

Chapter 3 presents my post-doctoral professional activity and the achievements that support my constant concern to improve teaching, medical, scientific and research activities: I participated in a training internship in the field of analytical biochemistry in the Discipline of Medical Chemistry and Biochemistry of the University of Zagreb of Croatia, I took part in training courses in the field of analytical chemistry and biochemistry, and in molecular medicine (both organized at UMF "Victor Babes" Timisoara), and by accessing various dedicated online platforms, I completed the master program "Formulation and evaluation of dermato-cosmetic products" in the Faculty of Pharmacy of UMF "Victor Babeş" Timișoara. I have also continued my training in the field of Laboratory Medicine by working in a private laboratory.

Currently, I am involved in a multidisciplinary project (ROGEN), coordinated by UMF „Carol Davila" Bucharest in which six Universities of Medicine and Pharmacy from across the country, as well as other research institutes and universities, are taking place. This project aims to create a Romanian reference genome and to identify representative genomic characteristics for the Romanian population in the case of rare diseases, through multOMICS functional studies.

Chapter 4 presents the plans for the evolution and development of my academic career. I aim to increase my professional level for teaching, professional, and research activity, and to bring it into harmony, as much as possible, with the latest developments in all fields.

At the didactic level, I desire to support and to participate in the development of new course materials for first-year students of the English teaching sections of the Faculties of Medicine and Dentistry, to update the existing ones, to improve the use of didactic methods by training the students in the discussion of the topics presented, by presenting clinical cases correlated with the biochemical parameters taught, and by guiding them in the use of medical language and the adoption of appropriate medical conduct.

Regarding scientific and research activity, I will support students' undergraduate research activity and scientific volunteer activities (VADA program) and promote the importance of their involvement in doctoral studies to improve their professional prospects. I will participate in national and international competitions to win new research projects, attract funding, and contribute to the development of an integrated bioanalytical and omics research group in our university. I also aim to develop national and international

collaborations, both academically in the Biochemistry department, and scientifically through collaborations with research institutes and universities at home and abroad in the research areas of my interest. Through my scientific and research activity, I intend to constantly contribute to increasing the visibility of UMF "Victor Babes" Timisoara by publishing articles in ISI journals with high impact factor, and by combining teaching with scientific and research activity I want to contribute to the evolution and development of the educational and scientific process in our university.

The final part of the thesis presents the bibliographical references mentioned in the thesis, associated with the contents of the first two sections.

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