

**“VICTOR BABEȘ” UNIVERSITY OF MEDICINE  
AND PHARMACY FROM TIMIȘOARA**

**DOCTORAL SCHOOL**

**MEDICINE DOMAIN**



**INTERDISCIPLINARY APPROACH ON NATURAL AND  
SYNTHETIC COMPOUND DETECTION, BIOMARKER  
RESEARCH AND PHYTOTHERAPY: ADVANCING  
DIAGNOSTIC AND THERAPEUTIC APPROACHES**

**ABSTRACT**

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**Timișoara  
2024**



## ABSTRACT

The present thesis entitled **“INTERDISCIPLINARY APPROACH ON NATURAL AND SYNTHETIC COMPOUND DETECTION, BIOMARKER RESEARCH AND PHYTOTHERAPY: ADVANCING DIAGNOSTIC AND THERAPEUTIC APPROACHES”** highlights the scientific research followed during my career and reflects my academic and professional way. Advancement in the medical field is a multifaceted process that seeks to foster continuous knowledge acquisition, benefiting both academic and professional domains. The teaching profession demands unwavering dedication, passion, and a commitment to enhancing and maintaining the quality of work. Achieving excellence in this area requires ongoing personal development and sustained scientific research, driven by a continuous thirst for learning.

The scientific research is disposed in four directions of major importance at present, namely:

- innovative approaches to detect natural and synthetic compounds;
- the importance of biomarkers in the prognosis and evolution of cancerous and non-cancerous pathologies;
- a comprehensive examination of viral and infectious pathology;
- new insights concerning phytotherapy- pharmacotoxicological investigations.

Research activity is reflected in 13 publications as lead author, 10 as co-author, and other publications in the form of abstracts or posters. The quality of the publications is highlighted by the fact that the works are cited, thus the h-index calculated on Web of Science is 6.

The present thesis is organized into four chapters. The first one highlights scientific achievements. It is divided into 4 subchapters in which the previously mentioned research directions are addressed separately. Thus, in the first part, new methods and procedures are discussed to identify and quantify compounds.

Since benzodiazepines are commonly encountered in emergency rooms and toxicology laboratories, a variety of reliable and specific techniques have been developed for their identification and confirmation in the human body. These drugs are widely prescribed for treating anxiety and sleep disorders, serving as key psychoactive medications. Diazepam, a long-acting 1,4-benzodiazepine, is particularly popular due

to its relative safety and frequent use in the treatment of conditions such as stress, panic disorders, sleep disturbances, muscle spasms, alcohol withdrawal, and seizures. Following administration, diazepam undergoes demethylation, producing nordiazepam as its primary active metabolite. To predict the concentration profile of these substances in biological fluids, it is essential to follow modern toxicological analysis methods.

Phytotherapy has become a resource in medicine, for its prevention purpose, and also for its use in the treatment of different affections. The use of plants and herbs for the purpose of cure has become attractive all over the world in the last decades.

Medicinal plants, and also spontaneous or crop plants are used as empirical therapy. Some active biological compounds from plants present antimicrobial effects; their action mechanisms sometimes ensure a pathway to treat some infections determined by antibiotic-resistant microorganisms. Increased attention was focused on finding new “natural” sources due to the side effects caused by the administration of antibiotics as well as the resistance gained by many microbial strains.

Many plant species (spontaneous, cultured, medicinal) showed pharmaceutical and antimicrobial properties therefore testing the possible antimicrobial effects of different parts of plant extracts is recommended.

In addition to its antibacterial potential, its anticancer effects are being intensely studied. Chemical investigations of plant material are of great interest in medicine, because of their multiple potentials. Mistletoe (*Viscum album*), also known as iscor, helixor, isorel in European countries, is a semi-parasitic plant, that is regarded as an effective medication in treating cancer. Numerous studies regarding the identification of biological potential of the plant were reported so far. Antioxidant properties were assessed in different host plants proving the neuroprotective effect of the semi-parasitic plant. The antitumor effect was also evaluated in several carcinoma cell lines and the results evidenced cytotoxic, apoptosis-inducing, and immunostimulatory activity. Various clinical studies reported the improvement in survival and quality of life, after using mistletoe extracts, underling the ability of the plant to support conventional medicine.

The entrance door in different fields especially medicine is given by the significance of plants that are used as crude extract for their active principles. Components with important biological activity, in general, are extended and

characterized by high-performance analytical techniques such as liquid chromatography and gas chromatography-tandem mass spectrometry.

In addition to therapeutic solutions, knowledge of the specific signs of various pathologies is essential. Thus, biomarkers are measurable indicators of biological processes, pathological conditions, or responses to therapeutic interventions. In medical research and clinical practice, they play a critical role in understanding disease mechanisms, predicting outcomes, and tailoring treatments. For both cancerous and non-cancerous pathologies, biomarkers have transformed how diseases are diagnosed, monitored, and managed.

When about oral health, periodontal tissue is constituted of epithelial and conjunctive cell populations capable of generating defense mechanisms against pathogens or foreign bodies in the oral cavity. The cellular response consists of the synthesis of local and systemic pro-inflammatory molecules, such as cytokines and chemokines.

Concerning gastrointestinal disorders, laparoscopic cholecystectomy can be defined nowadays as the gold standard for the treatment of patients with symptomatic gallstones. 6.5 % of men and 10.5 % of women are affected by gallbladder stone disease. 1 – 4% of these patients will develop gallstone-related complications each year, first and foremost acute cholecystitis. Early cholecystectomy was considered superior to open delayed cholecystectomy in the pre-laparoscopic era, because of shortened hospitalization and recovery time, without an increase of postoperative morbidity and/or mortality

In the cancer field, breast cancer is one of the most encountered forms. Breast imaging plays a key role in detecting and monitoring breast tumors. Before obtaining additional imaging, breast cancer may progress with ineffective treatment. In some situations, imaging fails to show progression at an early stage. Biomarkers, especially serum biomarkers, can provide additional insight or even detect disease progression or response to treatment before imaging can. Although the primary diagnostic techniques for early breast cancer include imaging, ultrasound, and pathology, these methods are subject to variability because of subjective factors, for example, the medical practice experience and the current state of technological advancements. Tissue expression biomarkers in breast cancer, such as estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2, are extensively used as tumor-specific markers to guide breast cancer therapy.

Cardiac diseases are another health challenge that results in an increased percentage of fatal cases. Peripheral arterial disease incidence has increased significantly in the last few years. Most patients are asymptomatic for long periods, but at least 10% will progress toward chronic limb-threatening ischemia or will present per primam in this stage of the disease. The modifiable risk factors for these disorders are smoking, diabetes mellitus, arterial hypertension, chronic kidney disease, sedentary lifestyle, and obesity. Despite the best medical treatment and the progress made in correcting the risk factors, chronic limb-threatening ischemia is still associated with higher morbidity and mortality.

Chronic limb-threatening ischemia guidelines published in 2019 proposed that the definition of these should include a broader spectrum and a more heterogenous group of patients, with different ischemia degrees and a higher major amputation risk. Inflammation plays a key role in Peripheral arterial disease and chronic limb-threatening ischemia, but its mediators are not clearly defined. The role of inflammatory biomarkers in the atherosclerotic process has been extensively analyzed, both in experimental and clinical studies. Although inflammatory mediators such as IL-6, TNF- $\alpha$ , and C-reactive protein were identified as predictors for major cardiovascular events, randomized studies demonstrated opposite results, which justifies a more thorough analysis of these markers in chronic limb-threatening ischemia.

Another alarming problem of the actual medicine is infections. The examination of viral and infectious pathologies involves a multidisciplinary approach, combining clinical assessment, laboratory diagnostics, and advanced imaging techniques. These methods aim to identify the causative pathogens, assess disease severity, and guide effective treatment strategies.

The second chapter describes the academic achievement. My academic career in the university environment started in 2016 at the University of Medicine and Pharmacy “Victor Babes” Timisoara (UMFT), at the Pharmacology Discipline, Department of Biochemistry and Pharmacology. In addition to the work carried out with students at the medical faculty, I was involved in various postgraduate courses.

During my teaching career, I coordinated 18 bachelor's theses, both from general medicine and dentistry faculties.

In order to update and improve the study material for students, I participated as author/co-author in writing the following books/chapters:

- V. Dumitrașcu, Daliborca Vlad, Corina Flangea, Ioana Malița, Simona Șipoș, Beatrice Barac, C. Vlad, Adelina Chevereșan, Ioana Ana, D. Ana. Pharmacology Course for General Medicine Students, vol. I, Second Edition, revised, "Victor Babes" Publishing House, Timisoara, 2024, ISBN 978-606-786-363-8; ISBN vol. I 978-606-786-363-5.
- Adelina Chevereșan, C. Vlad, Daliborca Vlad, Ioana Malița, Corina Flangea, Beatrice Barac, Simona Șipoș, Ioana Ana, Dorin Ana, V. Dumitrașcu (coordinator). Pharmacology Course for Dental Medicine Students, "Victor Babes" Publishing House, Timisoara, 2024, ISBN 978-606-786-380-2.
- V. Dumitrașcu, Daliborca Vlad, Corina Flangea, Ioana Malița, Simona Șipoș, Beatrice Barac, C. Vlad, Adelina Chevereșan, Ioana Ana, D. Ana. Pharmacology Course for General Medicine Students, vol. I, "Victor Babes" Publishing House, Timisoara, 2018, ISBN 978-606-786-093-1; ISBN vol. I 978-606-786-094-8
- V. Dumitrașcu, Daliborca Vlad, Corina Flangea, Ioana Malița, Simona Șipoș, Adelina Chevereșan, Beatrice Barac, C. Vlad, Ioana Ana, D. Ana. Pharmacology Course for General Medicine Students, vol. II, "Victor Babes" Publishing House, Timisoara, 2018, ISBN 978-606-786-093-1; ISBN vol. II 978-606-786-098-6
- Adelina Chevereșan, C. Vlad, Ioana Malița, Daliborca Vlad, Beatrice Barac, Corina Flangea, Simona Șipoș, Ioana Ana, Ioana Ana, V. Dumitrașcu (coordinator). Notions of Pharmacology for Dental Medicine, Mirton Publishing House, Timisoara, 2018, ISBN 978-973-52-1796-9.
- Ioana Malița, Daliborca Vlad, Corina Flangea, Simona Șipoș, D. Ana, C. Vlad, Beatrice Barac, Adelina Chevereșan, Ioana Ana, V. Dumitrașcu (coordinator). Pharmacology Course for General Medical Assistance, Victor Babes Publishing House, Timisoara, 2017, ISBN 978-606-786-035-1.
- V. Dumitrașcu, Marinela Popovici, Beatrice Barac, Daliborca Vlad, Ioana Malița, Adelina Chevereșan, Corina Flangea, D. Ana, Simona Șipoș, Ioana Ana, C. Vlad. Pharmacology Course 10th Edition, "Victor Babes" Publishing House, Timisoara, 2015, ISBN 978-606-8456-79-9.

- V. Dumitrașcu, Rodica Cîncă, Marinela Popovici, Beatrice Barac, Daliborca Vlad, Ioana Malița, Adelina Chevereșan, Corina Flangea, D. Ana, Simona Șipoș, Ioana Ana, C. Vlad. Pharmacology Course 9th Edition, Vest Publishing House, Timisoara, 2014, ISBN 978-973-36-0620-8.

In addition, I organized the study support for practical work in dental medicine: C. Vlad, Adelina Chevereșan, Daliborca Vlad, Ioana Malița, Corina Flangea, Simona Șipoș, Beatrice Barac, Ioana Ana, D. Ana, V. Dumitrașcu (coordinator). Practical Applications of Pharmacology for Dental Medicine, Vest Publishing House, Timisoara, 2017, ISBN 978-973-36-0708-3.

Out of passion for scientific research and improving the teaching process, I participated in the creation of a new course, in a previously undeveloped direction: Vlad Daliborca Cristina, Dumitrașcu Victor, Dema Alis, Popescu Roxana, Vlad Cristian Sebastian, Flangea Corina, Nica Cristian, Pantea Stelian, Danko Nikolic, Tomislav Jovanovic, Cobec Ionut. Molecular analysis guide in the diagnosis and treatment of breast and colon cancer. StudIS Publishing House, Iași, 2020, ISBN 978-606-48-0502-7.

The third chapter focused on my professional activity. My passion for the medical field appeared at a young age when I decided to continue my studies at the sanitary high school in Timisoara (from 1988 to 1992). For the next three years, I studied at "Hyperion" Dental College Timișoara. I took the bachelor's exam at UMF "Gr.T.Popa" from Iași. Later, I continued my studies at the University of Oradea, Faculty of Medicine and Pharmacy, specializing in dentistry.

To strengthen my knowledge in the medical field, I completed a Master's Degree Studies at the University of Medicine and Pharmacy „Victor Babeș” Timișoara, at the study program „Social and health services management”. My passion for continuous research encouraged me to participate continuously in various courses. In 2015 I completed my doctoral studies in the field of medicine, supporting the work entitled „Comparative pharmacological and clinical evaluation of nonsteroidal anti-inflammatory drug (NSAID) therapy in patients with chronic periodontal disease” coordinated by my scientific supervisor, Prof. Univ. PhD. Dumitrascu Victor, UMFT (Series J, No. 0016104; 104/23.02.2016).

I participated in more than 30 national and international scientific events. Moreover, I coordinate the project (as project director) OPORTUN - Opportunities for inclusion and increasing access to higher medical education through early intervention



for disadvantaged groups. Education and Employment Programme 2021-2027 Programme reference number: CCI 2021RO05SFPR001 Call no. PEO/291/PEO\_P6/OP4/ESO4.6/PEO\_A40 MySMIS2021+ code: 323275. I'm also part of an international team, within the project „The study of the biologically active compounds from the *Momordica Charantia* and *Viscum Album* extracts in order to establish the antitumor therapy” PN II Bilateral Capacities Hungary 677/2013. In addition, I am a member of the national teams for:

1. T-FDI-2023-0459 - Integrated approach to quality higher medical education based on the promotion of equity and social inclusion. PROMEDSOC 2023.
2. T-FDI-2024-0487 – Equity, diversity, and inclusion in medical education. MedDEI 2024.

My managerial skills are also developed due to the fact that I have been coordinating SC Dentissimo Dental Care SRL since 2008, where I apply theoretical knowledge, combining it with practical skills. Moreover, I have been the President of the Romanian Dentists' Employers' Association for 2 years, and this allows me to be in continuous contact with qualified specialists, to share professional experiences, and to collaborate in order to improve the quality of the medical process.

The main academic perspective emphasizes the role of education in producing competent healthcare professionals. Our daily aim is to design and deliver curricula that integrate foundational knowledge with clinical application. For this reason, I want to:

- update the curriculum with current needs and the latest discoveries in the field of pharmacology. Medical education must adapt to advances in science and technology while maintaining a focus on health care.
- ameliorate pedagogical strategies: to ensure effective medical education it is essential to employ a range of teaching methods, including problem-based learning, simulation, and interprofessional education. These methods foster critical thinking, collaboration, and real-world problem-solving.
- maintain lifelong learning: given the rapid evolution of medical knowledge, it is important to instill a commitment to lifelong learning among students, emphasizing continuous professional development.
- ensure mentorship: to support young specialists, I propose to serve as a mentor, guiding students and residents in career development, research endeavors, and ethical decision-making.

From a scientific standpoint, medicine is rooted in evidence-based practice and research. It is essential to contribute to the advancement of medical science through exploration, innovation, and application of new knowledge. This perspective involves:

- Research and Discovery: conducting basic, translational, and clinical research to uncover new mechanisms of disease, therapies, and diagnostic tools.
- Collaborating with multidisciplinary teams to integrate pharmacology, technology, and public health insights.
- Exploring advancements in medical technology, such as artificial intelligence, telemedicine, and genomics.

This dual focus ensures that graduates not only possess robust medical knowledge but are also prepared to contribute to the field's growth. Professors serve as catalysts for innovation, bridging the gap between theory and practice to advance both medical education and patient care. To disseminate the results, I propose to publish data in prestigious specialized journals with impact factors. This will allow us, in addition to increasing the image of both the discipline and the university, possible future collaborations in order to complete the level of knowledge in the field of pharmacology.

In short, academic and scientific perspectives in medicine are deeply interconnected. Teaching ensures that medicine continues to evolve in response to the needs of patients and society. Thus, I aim to contribute to improving the level of health through active involvement in the teaching and scientific process.