

ABSTRACT

I elaborated the present *Habilitation Thesis* in the field of *Physics* with the title: **"Integrative Physical Methods Applied in Medicine"** and it illustrates the most important achievements of my professional, academic and scientific activity since obtaining the first title of *Doctor in Physics* (2000), followed by the defense of my second PhD Thesis in Medicine, for which I obtained the title *Doctor in Medicine* (2012), and until now (2024).

Under the scientific coordination of Prof. Univ. Dr. Doc. Mircea Sanduloviciu from the Faculty of Physics of the "Al.I.Cuza" University in Iași, I obtained the scientific title of Doctor of Physics based on MEN Order No. 3774/10.V.2000 for defending my PhD Thesis with the title: "Self-organization phenomena and their role in the production of instabilities".

For the second PhD Thesis, under the supervision of Prof. Univ. Dr. Rodica Marieta Chiriac from the University of Medicine and Pharmacy "Grigore T. Popa" Iași, I obtained the title of Doctor of Medicine, with the thesis entitled "Contributions to the Therapy of Chronic Pain in Juvenile Arthritis through Physical Means and Alternative Medicine", in basis of MECTS Order No. 5743/12.09.2012.

I mention that my entire training and activity was multidisciplinary, centered on the essential objective of making my own contributions to the implementation of physical principles and methods in medicine, with predilection in medical recovery.

The connection between physics and medicine has been strongly realized in my career due to a wide palette of knowledge, a thorough training and my great desire to introduce and apply new discoveries from physics to the complex universe of medicine in order to find innovative solutions and multiple treatment techniques for increasingly frequent and aggressive diseases, with unsatisfactory responses to conventional treatments, in an attempt to put into practice new devices and techniques, such as laser photobiomodulation in order to improve, to trigger remission, or even cure some conditions.

For this essential objective, I have carried out scientific collaborations with domestic and foreign specialists in various fields of physics and, scientific and clinical research, with a broad vision, critical thinking in the choice of options and solutions, as well as creative imagination, for the use of medical devices, especially lasers in physiotherapy and medical recovery, in a multidisciplinary approach through integrative and individualized treatment programs.

All my professional development reflects the very strong connection between physics applications in medical practice and scientific research, carried out with great passion and energy.

Integratively applied physical methods in medical recovery are an extremely active field that have stimulated change and progress, especially in recent years, in the era of COVID-19, triggered a series of accelerated discoveries in medical research and nanomedicine.

My complex training in Physical Therapy, being also a graduate of this Specialization as a second Faculty at UAIC, my Master's degree in Prophylactic Nutritional Education,

together with the fundamental knowledge of physics, self-organization in the structures of the living world, as well as the applications of lasers, paved the way for me to addresses many in-depth and innovative research topics in integrative applied physics in medicine.

This Habilitation Thesis is organized into three main sections, meeting all the norms and principles proposed and approved by CNATDCU.

Section I is an overview structured in three subsections, illustrating my professional, academic and scientific achievements.

Section II summarizes personal postdoctoral scientific achievements, being organized into **three main chapters**:

Chapter I of **Section II** is entitled "*Applications of Photobiomodulation in Rheumatic Pathology, Chronic Pain and Pharmacovigilance. Personal Scientific Achievements*" and comprises eight sub-chapters in which my main scientific researches in this field are presented, regarding the benefits of low-power laser therapy in early-onset rheumatoid arthritis and juvenile spondylarthropathies, tracking the effects of this treatment modality according to power and energy (W or J), energy density (J/cm^2), repetition rate (Hz), wavelength (nm), pulse duration, beam diameter, treatment time, number of sessions administered and possible side effects.

In the cases of child patients with moderate and severe forms of juvenile idiopathic arthritis, who did not respond to conventional therapy, I was asked to participate in the application and monitoring of an innovative technique, introduced for the first time in our country, regarding the administration of intravenous laser photobiomodulation, particularly in cases whose evolution was unfavorable to the administration of disease-modifying drugs, including the biologic agents Enbrel and Tocilizumab, the only pharmaceuticals approved at that time for children, but to which some patients did not respond adequately.

Since the method of intravenous laser application is an invasive technique, which most children are afraid of (even though we used topical analgesic products before the administration of intravenous photobiomodulation), we implemented new devices created recently for sublingual administration, starting from the idea and the anatomical reality of the fact that at the level of the oral cavity and especially in the sublingual area, there is an abundant superficial blood circulation, through which the laser radiation can be very easily absorbed.

For a better understanding of laser photobiomodulation, I engaged in the in-depth study and modeling of molecular and cellular mechanisms of arthritis in children and adults to provide new insights into applied photobiomodulation.

Other aspects of my research related to the implications of photobiomodulation during SARS-CoV-2 infection in systemic juvenile idiopathic arthritis, biomarkers that could be used in cases of systemic disease with fulminant evolution, macrophage activation syndrome and their importance in COVID era.

As a member of PRINTO (Paediatric Rheumatology International Trials Organisation), an international organization of clinical trials in Pediatric Rheumatology established in 1996, which initially included 14 European countries, and later expanded to 95 countries worldwide, I collaborated in several research grants, among which EPOCA and PharmaChild, as an affiliate of the Pediatric Rheumatology Study Center RO01 in Iasi, Romania, where I conducted

investigations into pharmacovigilance and multidimensional assessment of arthritis in children and adolescents.

Chapter II of **Section II**, entitled "*Scientific Research and Laser Applications in Viral Infections and Cancer. Innovative Approaches in Nanomedicine*" is structured in nine sub-chapters and focuses on personal studies on light as a healing modality in the COVID-19 pandemic; research conducted on physical devices used in integrative photomedicine in the COVID era; the interrelation between infection, dysbiosis and inflammation; aspects of long COVID status, and the involvement of mitochondrial dysfunction; physical and molecular mechanisms of autoimmunity in pandemic; controversies and challenges regarding the use of probiotics, photobiomodulation and disease management. Other personal scientific research published and presented in this chapter concerns curcumin - as a natural photosensitizer and laser applications in chronic viral hepatitis and hepatocellular carcinoma; nanotechnologies with curcumin applied in photodynamic cancer therapy, as well as integrative synergistic physical applications in photodynamic, photothermal and photoimmune therapy of hepatocellular carcinoma.

Chapter III of **Section II** presents studies and contributions regarding the regenerative applications of photobiomodulation in sports medicine, as well as in neurodegenerative diseases, being organized in two subchapters. The scientific works presented in this chapter, along with other published works in Chapters I and II, were carried out in collaboration with Professor Dr. Gerhard Litscher, Director of the Biomedical Engineering Research Unit in Anesthesia and Intensive Care Medicine, of the Research Unit for Complementary and Integrative Laser Medicine and of the Traditional Chinese Medicine Research Center, Medical University of Graz, Austria. We researched the literature on the effects of photobiomodulation by individual laser diodes or clusters, LEDs or arrangements of both, different adaptable devices, optimal wavelengths, optimal time of application - before or after exercise, and at what exact time interval compared to physical activity; optimal parameters (power density, fluence, modulation frequency); the number of points for each muscle to increase sports performance. Given the biphasic dose response in therapy, a research issue has been how much energy needs to be delivered precisely by photobiomodulation so that too much irradiation and inhibition of physiological processes does not result.

The last subchapter presents intranasal, transcranial, pulsed transcranial, intracerebral transcatheter, transcutaneous radial artery *laser stimulation* as potential cognitive enhancement treatments in various neurodegenerative pathologies. Transcranial PBM in the picosecond range could be used to overcome the blood-brain barrier, and together with the latest nanotechnologies, nanomedicines and the state-of-the-art breakthroughs in their delivery systems, be applied in Alzheimer's disease therapy.

Section III entitled "*Future directions in professional, academic and scientific research activities*" presents the development plan of my future career in terms of professional, didactic and scientific activities.

In the professional development plan, I propose to continue my training and improve my activity through internships and new training courses in the country and abroad, completing the other professional degrees and obtaining new certificates and competencies.

The academic development plan includes the conception and put into practice of new postgraduate courses, the design and publication of materials for master's and PhD students, as

well as their active involvement in activities to promote the applications of physics in physical therapy and medical recovery. The development of original academic projects, the organization of scientific meetings for the dissemination of the latest information in the field, exchanges of experience with national and international academic cooperation, facilitating access to Erasmus-type academic programs and others, are future projects for master's students and PhD students.

Future directions in scientific activity include the involvement of master's and PhD students in scientific exploration activities and the development of integrative physical methods applied in medical fields, to highlight their role and importance in supporting the general health of our country's population, participation in scientific workshops, symposia, national and international conferences and congresses, with successful scientific papers.

I will contribute together with my master's and PhD students to the development of modern physical therapy and medical recovery centers, where they can practice their specialty successfully and at new standards, through the innovative use of physics in the regenerative nanomedicine, laser photobiomodulation, as well as other advanced nanotechnologies in integrative medical rehabilitation, for individualized patient management.

The last section entitled *References* includes the in-text citations that support the data in this Habilitation Thesis.

My international scientific visibility is reflected by:

Clarivate Web of Science Publications: 41;

Clarivate Web of Science H-index: 10;

Clarivate Web of Science Times cited without self-citations: 281;

Scopus H-index: 10;

Scopus citations: 330;

Google Scholar H-index: 13;

Google Scholar citations: 646.

Member of 4 grants, of which 1 (one) national and 3 (three) internationals.

Director of an international grant.

This Habilitation Thesis highlights my main professional, academic and scientific development, as well as the recognition I have acquired since the defense of my PhD Thesis in the field of Physics until now.

11.11.2024

Conf. Dr. LAURA-MARINELA AILIOAIE

