“CAROL DAVILA” UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST, ROMANIA

DOCTORAL SCHOOL

DOMAIN OF STUDY MEDICINE

HABILITATION THESIS ABSTRACT

BIOCHEMISTRY OF ACUTE AND CHRONIC DISEASES

CANDIDATE:

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Abstract

The present habilitation thesis entitled “Biochemistry of acute and chronic diseases” reviews the author’s most important scientific, professional and academic results obtained subsequently to the PhD (2003), as well as the perspectives for future scientific and professional development. The thesis includes four main parts.

In the first part I present my research work in different fields such as: oxidative stress, aging, obesity, diabetes mellitus, ocular diseases, thyroid diseases etc. My professional development started with the field of oxidative stress while my doctoral thesis, entitled "Redox systems in senile cataract - systemic aspects", is based on the serum determinations of some antioxidants in senile cataract. As lead author I have published 5 BDI articles on senile cataract and diabetic cataract, pointing out that in diabetic cataract local, ocular and systemic oxidative stress are all much more pronounced.

Although the research project on senescence had a small budget and a short duration, the research team I was part of, managed to publish a minireview on the oxidative stress mechanisms of senescence (145 citation). Part of the results of a Viasan project about chronic renal failure was published in J. Nephrology (30 citations). In the period 2003-2005, I participated as a member of an international mobility research project focused on diabetic foot patients. Together with prof. dr. Mohora Maria, I laid the foundations of this project. In this project we have demonstrated that the diabetic patients from Bucharest had a better antioxidant serum status in comparison with the patients from Anvers, with the same disease. We wrote articles (3 ISI and 10 BDI) about type 2 diabetes mellitus and its underlying microvascular and macrovascular complications and we managed to highlight the relations of diabetes with obesity (27 citations), with oxidative and carbonyl stress (41 citations), with inflammation and with advanced glycation processes (58 citations). Having experience in the study of diabetes, in 2011, we were involved in a national project in which more than 100 patients with type 2 diabetes were statistically processed. We demonstrated that the inflammation parameters were correlated with those of insulin resistance and with anthropometric parameters.

Based on three databases with overweight and obese children obtained from hospitals and from ambulatory medicine we wrote 6 ISI and 3 BDI articles. We have demonstrated the importance of some supplemments (Omega-3 fatty acids, associated with low doses of antioxidant vitamins or Sea Buckthorn pulp oil) in improving the metabolic profile. The

intake of these supplemments improved the lipid and the mineral profile, reduced the insulin resistance and thus the number of children with fatty liver or with preatherosclerotic has decreased. As lead author I wrote a chapter on childhood dyslipidemia and the beneficial effects of Sea Buckthorn supplemment in the international book “Lipoproteins from bench to bedside”, 2015 and an article in ISRN Oxidative Medicine, 2013.

In the experimental studies we have evaluated the metabolic effects of a high caloric/high fat diet in NMRI mice, in young and old Wistar rats and in pregnant female Wistar rats. In the obese NMRI mice, the metabolic imbalances were revealed by the presence of dyslipidemia, dysglicemia, as well as the presence of fatty liver and fatty pancreas. The treatment either with Sea Buckthorn (pulp oil or fresh fruit) or with Omega-3 fatty acids, reversed the histopathological aspects of the liver and pancreas almost to normal and decreased the lipid peroxidation in these tissues.

By using Wistar rats on obesogenic diet, our research team compared the effects of some Supplements: fish oil, Nigella sativa or Sea buckthorn oil. The best neuroprotective effect was noticed in fish oil, the best renal and placenta protector was Sea buckthorn fruit and a relative cardio protective effect was provided by Nigella sativa oil.

Having at our disposal the biobase of the faculty and the Polylactic-co-glycolic acid nanoparticles (PLGA-NPs) loaded with vitamin E or lutein, our research studies focused on nanomedicine. PLGA-NPs are FDA-approved biodegradable polymers with multiple applications in medicine, serving as a drug vector and they have a minimal risk of toxicity. We were the first researchers who have demonstrated that PLGA-NPs loaded with vitamin E can show promising results in reducing the side effects induced by glucocorticosteroids, by reducing the amount of visceral fat and cholesterolemia. Also we have demonstrated Lutein-loaded PLGA-NPs associated with oral Prednisone treatment markedly decreased drug-induced ocular side effects.

The second part of this thesis includes my professional achievements. Since March 1993 I have been carrying out an intensive teaching activity at the Department of Biochemistry of the "Carol Davila" University of Medicine and Pharmacy at the English module, at the Romanian module, for the first, second and third year students. The promotion steps were university assistant (1996), lecturer (2007) and from 2017 associate professor. I have published as coauthor 14 books on medical biochemistry and chemistry for students. For another 5 books for students, entitled Clinical Biochemistry, I wrote half of the total number of pages and I laid the foundations for this new speciality. I have

coordinated more than 50 bachelor theses since 2017. I have participated at many national and international students congresses as assessor, I have prepared workshops for summer schools, for medical educational days. I have been occasional reviewer for at least 28 medical or biochemistry journals listed on the international data bases.

The third part of this thesis follows my professional path. In 1992, I graduated from the "Carol Davila" University of Medicine and Pharmacy, with the mark 9.24 and received the title of medical doctor.

I received the title of specialist in General Medicine in 1996, with mark 8.98. I had been working at the emergency unit of The Emergency Universitary Hospital for 5 years (2001-2005) and I received the certification in pre-hospital emergencies with mark 10 and the certificate in general abdominal ultrasound with mark 9. In 2003 I obtained a governmental research grant in Anvers for two months and in 2012-2013 I was a member of a research POSDRU project (POSDRU/89/1.5/S/60746). For one year, 2017-2018 I was the director of the project entitled "Algorithm for estimating the severity of fatty pancreas in obese children", financed by SC Chiajna Medical Center SRL. In 2012, I was UEFISCDI evaluator and in December 2022 I have obtained the GRADE OF MERIT for five years. Since 2003, I have, as author and coauthor, 20 ISI articles, 38 BDI articles, 14 award-winning posters, 2 award-winning books, 3.47 citations per item and a Hirsch index Web of Science 7, Hirsch index Scopus 9.

The fourth part of this thesis includes the strategies envisaged for my future professional and scientific development. In my double qualification, as doctor and teacher I will improve the future books on clinical medicine and I will write about medical analyzes for emergency clinical cases. My research activity will be focused on gestational diabetes, obesity sarcopenia, aging diseases and on the supplemments with beneficial effects in metabolic syndrome. Because we already have significant results on algorithms and on medical alerts (2 BDI articles) will apply for Machine Learning and Deep Learning algorithms in medicine.