

Iasi University of Life Sciences

HABILITATION THESIS

**Evaluation of new therapeutic means through
experimental pharmacology studies**

Assoc. prof. Valentin Năstasă

IAȘI - 2022

CONTENTS

Abstract (in Romanian)	5
Abstract (in English)	8
Section I – Scientific, professional and academic achievements	11
Chapter I – Scientific achievements	12
1.1. Anesthesia and pain control during surgery	13
1.2. Nanomedicine: <i>in vitro</i> and <i>in vivo</i> testing of nanoconjugate complexes and nanomaterials with biological effects: antitumoral, antimicrobial, antioxidant, antiparasitics and bone matrix regenerators	19
1.2.1. Drug design and antitumor effect	19
1.2.2. Drug design and antimicrobial effect	26
1.2.3. Nanoconjugates and nanomaterials with antimicrobial, anti-inflammatory and antiparasitic effect	35
1.2.3.1. Inclusion complexes (carrier molecules)	35
1.2.3.2. . Nanoparticles and Nanomaterials with therapeutic potential	53
1.3. Antibiotic sensitivity assessment and resistance detection	62
1.3.1. Resistance to quinolones (fluoroquinolones)	62
1.3.2. Resistance to azoles and echinocandins	64
1.4. Alternative solutions to fight infections	74
1.4.1. Plasma activated water (paw): antimicrobial effect and toxicity	74
1.4.2. Immunoglobulin y: antimicrobial effect and immunological profile	91
Chapter II – Professional achievements	99
2.1. Professional lifelong learning	100
2.1.1. Postgraduate courses	100
2.1.2. International scientific meetings	104
2.2. Involvement in continuing medical education projects	105
2.3. Active member of professional societies	106
2.3.1. National societies	106
2.3.2. International societies	107
2.4. Reviewer for journals, projects and scientific meetings	108
Chapter III – Academic achievements	109
3.1. Teaching activity	109

3.2. Publishing activity	109
3.3. Other activities	111
Section II – Long term plans for evolution and career development	113
Chapter IV – Scientific career	114
Chapter V – Professional career	117
Chapter VI – Academic career	118
Section III – References	119

ABSTRACT

The habilitation thesis entitled "Evaluation of new therapeutic means through experimental pharmacology studies" represents the synthesis of my scientific activity. The thesis describes the main research directions and the results obtained, representing a necessary base for the authorization to coordinate doctoral students. According to the criteria recommended and approved by CNATDCU, the habilitation thesis is structured in 3 sections, as follows: Section I presents the scientific, professional and academic achievements. Section II career development and Section III - references.

After earning the PhD degree I have conducted studies in experimental pharmacology, this studies were focused on the following domains: anesthesiology, pharmacology, mycology and microbiology. In addition to contributing to the development of new anesthetic associations whose structure includes a central opioid, we have also contributed to the development and testing of nanoconjugates with antimicrobial, antioxidant activities and biocompatible materials for biomedical applications. Specifically, we tested various structures with applications in the controlled release of active agents involved in bone regeneration and cancer treatment.

This habilitation thesis presents a synthesis of the results published in over 33 scientific papers published in prestigious journals abroad, listed ISI (Q1 and Q2), on the above mentioned topics, with a cumulative impact factor of 86.006 and 113 articles indexed in international databases or presented at national and international conferences and symposia. So far, the scientific contribution totals, according to Google Scholar, a total of 329 citations and a Hirsch index of 11 (Web of Science and Scopus iH = 10). I also participated as a project manager and partner manager in 4 research projects and as a team member in another 13.

Section I

In the field of scientific research, the following thematic domains were addressed:

- Anesthesia and pain control during the surgery;
- Nanomedicine: in vitro and in vivo testing of nanoconjugates and nanomaterials complexes with biological effects: antitumor, antimicrobial, antioxidant, antiparasitic and bone matrix regenerator;
- Evaluation of antibiotic susceptibility and resistance detection;

- Alternative solutions to fight infections (non-thermal plasma activated water and Immunoglobulin Y).

This first direction of research is a continuation of the research included in the doctoral thesis and emphasized on the use of a group of substances with special regimen (opioid analgesics). The research was carried out between 2004-2008, being financially supported by CNCSIS through an IDEI project (Influence of general injectable anesthesia on hemodynamic function and variables of acid-base balance in dogs. CNCSIS Code 689, no. 27671). The next research direction, carried out in collaboration with teams from the Petru Poni Institute of Macromolecular Chemistry and UMF Gr.T. Popa from Iași refers to the chemical modification of a known drug, the design of new target-based molecules (cellular inhibitors, nanoparticles), combinatorial synthesis, complexation with carrier molecules (cyclodextrins, polymers), *in silica* design in order to discover new agents for the treatment of cancer and various infectious (fungal, parasitic and even tuberculosis). Testing the resistance to fluoroquinolones was done on clinical isolates of *Mycoplasma hominis* and *Ureaplasma urealyticum* from a group of women investigated for infertility. Another topic, that is ongoing, is represented by the applications of non-thermal plasma activated water (PAW) and hyperimmune egg in medicine and their characterization.

I also improved my knowledge by completing continuing medical education courses organized in Sweden, Austria, Romania by various universities and pharmaceutical companies (Charles River) or professional associations (International Society of Antimicrobial Chemotherapy). I have participated in international scientific events, as a member of the organizing and scientific committee of national and international conferences (Balkan Fungus, 2018). Since 2012, I have participated as a lecturer in the National System of Continuing Education (SNEC), organized by to the General Association of Veterinarians in Romania and the College of Veterinarians.

I am an active member of 8 national (6) and international (2) professional societies.

Within the Faculty of Veterinary Medicine in Iași, I worked as a junior assistant between 1993-1996, then assistant professor 1996-2001, lecturer between 2001-2005 and associate professor since 2005, all positions were obtained through competition. During these years I taught Pharmacology and Pharmacy (course and practical works) to the students involved in both Romanian and English programs. In 2012-2013, I worked at the Apollonia University of Iași, as a head of the discipline of Experimental Medicine and Research Methodology, course and practical works in the specialization of Dentistry.

I have written and published 14 monographs and manuals for students, doctoral students and veterinarians.

Section II

I mainly intend to continue my research dedicated to testing nanoconjugates and nanomaterials with biological effects - pharmacodynamics, but I will also address new areas such as the mechanisms of antimicrobials - microorganisms interaction or the possibilities of using non-thermal plasma activated water (PAW) in vivo and food safety and the prevention of infectious diseases (decontaminant). Being involved in the interdisciplinary collaboration with various teams (P. Poni, UMF Gr. T. Popa, Faculty of Chemistry in Vienna) I will continue the studies and I will help to clarify the role of new molecules in cancer therapy (LS-80) and of bone and skin regeneration. I also propose the regular publication of textbooks for students, doctoral students and veterinarians (anti-infective therapy and pain management in experimental animals).

Section III

It includes the list of references that used for this thesis and also the articles included in this synthesis.