

PHYSICO-CHEMICAL AND BIOLOGICAL STUDIES OF BIOACTIVE SUBSTANCES WITH OPTIMIZED BIOAVAILABILITY AND THERAPEUTIC POTENTIAL

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THESIS SUMMARY

This habilitation thesis summarizes the main data enabling the scientific, professional and academic achievements during the postdoctoral period, in order to prove the qualifications required for habilitation degree. The main scientific papers were accomplished in several scientific areas in the field of Pharmacy; all publications resulting from research are sound proofs of its originality and relevance, being accepted by important impact factor journals, as shown in the list of papers. The main professional and academic achievements are presented in chapter I.1, having as landmark an activity of over 15 years in university education.

The scientific achievements represent an important part of the habilitation thesis and are divided in three main chapters: *Synthesis and physico-chemical evaluation of inclusion complexes of biologically active substances with hydrophilic cyclodextrins*; *Synthesis and physico-chemical analysis of polyurethane microparticles acting as drug carriers* and *Contributions to the physico-chemical study of drugs and their interactions with active / auxiliary associated compounds*. The scientific achievements materialized in over 90 full-text scientific publications – 53 listed on ISI

Web of Science and numerous participations in national and international congresses. According to Web of Science, h-index = 10; total citations without self-citations are 160 and the number of citing articles, without self-citations, is 116; average citations per article: 3,79. I am author and co-author of 7 scientific books and first author of one patent application.

The main line of research consisted in the preparation of inclusion complexes with semisynthetic hydrophilic cyclodextrins, research that continues the studies that began during my PhD thesis defended in 2007. Molecules included inside the cyclodextrin cavity are natural compounds, pentacyclic triterpenes, with a plethora of pharmacologic activities, mainly antiproliferative; all compounds exhibit a very low water solubility which causes poor bioavailability accompanied by the impossibility of parenteral administration. The inclusion in cyclodextrins represents a possibility to increase aqueous solubility and hence to optimize the pharmacokinetic properties of the guest-molecule. Inclusion complexes were prepared by using well established methods and were subsequently analyzed by spectroscopic and thermal techniques, X-ray diffraction, electronic microscopy, etc. The research expanded interdisciplinary by *in vitro* tests, on tumor cell lines, using the inclusion complexes of pentacyclic triterpenes against the active principles as such.

The *in vivo* testing on animal models completed the exhaustive characterization of inclusion complexes, emphasizing a significant increase of the biological activity as a result of cyclodextrin embedding.

Another line of research consisted in the synthesis of polyurethane polymeric microparticles; polyurethanes are bio- and hemocompatible products currently used in the medical and pharmaceutical field. Polyurethane synthesis involves a reaction of polyaddition between diols and diisocyanates; microparticle' size and stability can be influenced by various factors such as: isocyanate type, stirring speed, presence/type of surfactant/emulsifier, pH. Scanning electron microscopy, thermal analysis and Zeta potential determination were used in order to physico-chemically characterize the polyurethane microparticles. Subsequently, the microparticles were subjected to *in vitro/in vivo* tests for the assessment of their pharmacological and toxicological potential.

The physico-chemical study of drugs as well as their interaction with auxiliary compounds represents an important issue in medicinal chemistry. The third part of the scientific research introduced by this habilitation thesis is centered on various studies in the field: synthesis and analysis of metallic complexes of ambazone, structure-toxicity studies in the azo-derivatives series, physico-chemical studies of drug-excipient interaction, co-crystallization studies, synthesis and analysis of the antibacterial activity of triazolic derivatives.

I was a member in 10 research projects in the above mentioned areas of research, among which: 4 international projects (1 project manager – 674/2013), 5 national projects and 1 internal project – Partnership UMFT (partner manager). I am currently mentor in a postdoctoral project in the pharmaceutical field. Most of the research projects focused on the use of natural principles as antitumor compounds, included or not-included inside cyclodextrins. Following the international visibility gained as result of publications arising from the research work, I was recruited as author of two book chapters by an international publisher (2014) and I am currently involved in the publication of another two books in the same field.

During 2007-2015 I attended numerous national, but mostly international, scientific manifestations: European Conference on Cyclodextrins, International Cyclodextrin Symposium, Eurotox, DKMT, Timmedica, National Congress of Pharmacy, etc.). The acknowledgement of the scientific achievements materialized in national awarding of several publications (2011-2014) as well as in the invitation as scientific reviewer by distinguished journals: *Int J Pharm*, *Nat Prod Res*, *Pl Foods Hum Nutr*, *J Ther Anal Cal*, *Eur Pol J*, *Drug Dev Ind Pharm*, *J of Surf Det*, *Lett Drug Des & Discov*, *Mini Rev Org Chem*, *Chem Eng Res Des*, *Bull Chem Soc Japan*, *Pharm Dev Technol*, *Biomaterials*.

The thesis concludes with a chapter on future prospects in teaching and scientific career followed by the bibliography of each chapter / subchapter. From the teaching perspective, I intend to continue upgrading the activity of Pharmaceutical Chemistry discipline according to the most recent discoveries at international level as well as the publication of courses and practical guides for students in Pharmacy. In the scientific domain, I will continue to submit project proposals at national, European and international level in order to be able to develop and deepen the research activity as well as the material basis necessary to achieve this goal.

The main aspects of my future scientific activity will consist in: semisynthetic modulation of pentacyclic triterpenes, nanoformulations including cyclodextrin complexing of ester derivatives of triterpenes, physico-chemical and biological analysis of final compounds and products.

My entire activity, both teaching and scientific, was and will be focused on excellence, through high standards in all fields of activity.