

**"VICTOR BABEȘ" UNIVERSITY OF
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DOCTORAL SCHOOL
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HABILITATION THESIS

CONTRIBUTIONS TO THE PHYSICO-CHEMICAL STUDY AND CHARACTERIZATION OF THE BIOLOGICAL PROPERTIES OF SOME NATURAL AND SYNTHETIC DRUGS

A B S T R A C T

Assoc. Prof. TRANDAFIRESCU CRISTINA-MARIA, PhD
Department II
Discipline of Pharmaceutical Chemistry

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ABSTRACT

The habilitation thesis CONTRIBUTIONS TO THE PHYSICO-CHEMICAL STUDY AND CHARACTERIZATION OF THE BIOLOGICAL PROPERTIES OF SOME NATURAL AND SYNTHETIC DRUGS presents the results of the scientific research activity carried out after obtaining the title of Doctor of Pharmacy, in 2008, under the leadership of Professor Gyéresi Árpád, professor at the Discipline of Pharmaceutical Chemistry at the University of Medicine and Pharmacy in Tirgu Mures, Faculty of Pharmacy. The thesis also presents my academic and professional path, as well as the plan for the development of the academic and professional career, for the benefit of obtaining the certificate of habilitation.

The postdoctoral scientific research activity naturally continued the research direction approached in the case of doctoral studies, in the field of cyclodextrins and extended to interconnected fields.

The first direction of research aimed at optimizing the physico-chemical and biological properties of some pharmaceutical substances and natural bioactive compounds, by using cyclodextrins and nanostructures, as carrier molecules. Molecular encapsulation by means of cyclodextrins and nanoparticles is a relevant research direction in the field of pharmaceutical sciences, due to the potential of these supramolecular structures to improve the physico-chemical and biological properties of drugs. In addition, the study of these new structures provides important information for obtaining modern pharmaceutical formulations with multiple advantages over conventional ones.

Binary systems of some pharmaceutical substances and natural bioactive compounds with natural and semisynthetic cyclodextrins have been prepared, and characterized by simple and easily reproducible laboratory methods. The solid-state interaction between the guest and the cyclodextrin was characterized by the use of thermal and spectral methods of analysis. The geometry of presumptive inclusion complexe has been evaluated by molecular modeling studies. The characterization of the interaction in solution between guest and cyclodextrin was achieved by phase solubility studies and by solubility profile studies. The biological activity of the drug

included in the supramolecular system was determined by *in vitro* and *in vivo* tests on models of cell lines/on experimental animals.

Polyurethane-based nanoparticles, loaded with natural or synthetic active substances were synthesized and were physico-chemical characterized. Polyurethane nanoparticles are biocompatible and may act as carriers for drugs, thus enabling and enhancing their biological activity. The synthesis of polyurethane particles was done using interfacial polycondensation technique, with recognized utility in the field of nanotechnology. The nanoparticles were analyzed in terms of particle size, surface charge, and homogeneity. Spectral and thermal analyses were used to investigate the encapsulation process. The nanoparticles were further subjected to *in vitro* analyses in order to assess their pharmacologic and toxicologic profile.

The second research direction is dedicated on different studies realized in the pharmaceutical field, aiming to contribute to the physico-chemical and biological characterization of synthetic and natural compounds with biologic activity. In this context, the following research was done: studies on the solid-state thermal behavior of drugs, studies on the compatibility between drugs and pharmaceutical excipients, evaluation of biologic activity of natural compounds.

The postdoctoral research activity resulted in the publication of 36 scientific articles in ISI journals, of which four articles published in journals classified in quartile Q1 and three articles published in journals classified in quartile Q2. The cumulative impact factor of these articles is 27.707. Citations of these articles prompted a Hirsch index of 10. The recognition of the scientific research activity was achieved through the awarding of some articles and through the activity of reviewing the scientific articles at journals such as *Molecules* (IF = 4.927) and *Pharmaceutics* (IF = 6.525), as well as through the invitation received this year, to be a guest editor at a special issue within the journal *Pharmaceutics*.

I participated as a member in four research projects, together with professors from the university.

The second chapter is dedicated to academic achievements, in which I mentioned my academic path, the main responsibilities, the administrative and managerial activities carried out as a member of the Faculty of Pharmacy Council since June 2012 and as Vice-Dean since May 2016. In the postdoctoral period I participated in the elaboration of three books for the course and two books of

practical works, edited nationally, as well as in the elaboration of two chapter in scientific work, edited internationally. I participated, as a member of the committee, in the organization and conduct of the admission and bachelor's exams of the study programs of the Faculty of Pharmacy.

I participated, as a member of the examination committee, in the competitions for filling the vacant teaching and research positions, organized by the "Victor Babeș" University of Medicine and Pharmacy in Timisoara. I participated, as an external scientific reviewer, in the defense of two doctoral theses in the Field of Pharmacy held by University of Medicine and Pharmacy, Sciences and Technology „George Emil Palade” from Tîrgu Mureș.

Chapter three presents my professional activity. I am a graduate of the Pharmacy Specialization within the Faculty of Medicine of the University of Medicine and Pharmacy in Timisoara, licensee of the "Carol Davila" University of Medicine and Pharmacy in Bucharest, class of 1992-1997.

I completed my doctoral studies under the leadership of Professor Gyéresi Árpád, from the discipline of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Medicine and Pharmacy of Tîrgu Mures, in the period 2002-2008. My professional path, after graduating from the faculty, followed the stages of my professional development: trainee pharmacist (1998), resident pharmacist (1999), specialist pharmacist (2002), pharmacist in the second specialty in Clinical laboratory (2019), primary pharmacist in General Pharmacy (2021).

The last chapter presents the academic career development plan, in terms of teaching, research and professional activity. In terms of teaching, the elaboration of course books and practical works for students is a permanent task, in accordance with the scientific development and the needs of practicing the profession, along with the enrichment of the offer of optional courses offered by the discipline.

In terms of scientific activity, I propose to continue the research directions, in collaboration with teachers and researchers, to establish collaborations for increasing the chances of participation in the realization and development of research projects. On a professional level, I will seek to participate in professional development activities, in order to guide my activity in accordance with the news in the field.

At the end of the thesis are presented the bibliographic references, as well as the list of the ten *in extenso* articles, that are representative of this thesis.

LIST OF 10 REPRESENTATIVE SCIENTIFIC PAPERS

1. Prodea Alexandra, Mioc Alexandra, Banciu Christian, **Trandafirescu Cristina** (corresponding author), Milan Andreea, Racoviceanu Roxana, Ghiulai Roxana, Mioc Marius, Șoica Codruța: The role of cyclodextrins in the design and development of triterpene-based therapeutic agents, *International Journal of Molecular Sciences* 2022; vol. 23: article no 736, IF 6.208
<https://www.mdpi.com/1422-0067/23/2/736>
2. Minda Daliana, Mioc Alexandra, Banciu Christian, Șoica Codruța, Racoviceanu Roxana, Mioc Marius, Macașoi Ioana, Avram Ștefana, Voicu Adrian, Motoc Andrei, **Trandafirescu Cristina**: Cyclodextrin dispersion of mebendazole and flubendazole improves in vitro antiproliferative activity, *Processes* 2021; vol. 9: article no 2185, IF 3.352
<https://www.mdpi.com/2227-9717/9/12/2185>
3. Soica Codruta, Voicu Mirela, Ghiulai Roxana, Dehelean Cristina, Racoviceanu Roxana, **Trandafirescu Cristina**, Rosca Oana-Janina, Nistor Gabriela, Mioc Marius, Mioc Alexandra: Natural Compounds in sex hormone-dependent cancers: The role of triterpenes as therapeutic agents, *Frontiers in endocrinology* 2021; vol. 11, article no. 612396, IF 6.055
<https://www.frontiersin.org/articles/10.3389/fendo.2020.612396/full>
4. Sbarcea Laura, Tanase Ionut-Mihai, Ledeti Adriana, Circioban Denisa, Vlase Gabriela, Barvinschi Paul, Miclau Marinela, Varut Renata-Maria, **Trandafirescu Cristina**, Ledeti Ionut: Encapsulation of risperidone by methylated beta-cyclodextrins: physicochemical and molecular modeling studies, *Molecules* 2020; vol. 25: article no. 5694, IF 2020: 4,412
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5. Racoviceanu Roxana, **Trandafirescu Cristina** (autor cu contributie egala cu primul autor), Voicu Mirela, Ghiulai Roxana, Borcan Florin, Dehelean Cristina, Watz Claudia, Aigner Zoltan, Ambrus Rita, Coricovac Dorina Elena, Circioban Denisa, Mioc Alexandra, Szuhaneck Camelia Alexandrina, Șoica Codruța: Solid polymeric nanoparticles of albendazole: Synthesis, physico-chemical characterization and biological activity, *Molecules* 2020; vol. 25: article no 5130, IF 2020: 4,412 <https://www.mdpi.com/1420-3049/25/21/5130>

6. Circioban Denisa, Ledeti Ionuț, Suta Lenuta-Maria, Vlas Gabriela, Ledeti Adriana, Vlas Titus, Varut Renata, Sbarcea Laura, **Trandafirescu Cristina**, Dehelean, Cristina: Instrumental analysis and molecular modelling of inclusion complexes containig artesunate, *Journal of Thermal Analysis and Calorimetry* 2020; vol. 142: pag. 1951-1961, IF 2020: 4,626 <https://link-springer-com.am.e-nformation.ro/article/10.1007/s10973-020-09975-3>

7. **Trandafirescu Cristina**, Ledeti Ionuț, Șoica Codruța, Ledeti Adriana, Vlas Gabriela, Borcan Florin, Dehelean Cristina, Coricovac Dorina, Racoviceanu Roxana, Aigner Zoltan: Albendazole-cyclodextrins binary systems. Thermal and spectral investigation on drug-excipient interaction, *Journal of Thermal Analysis and Calorimetry* 2019, vol. 138, issue 5, IF 2019: 2,731 <https://link-springer-com.am.e-nformation.ro/article/10.1007/s10973-019-08326-1>

8. **Trandafirescu Cristina**, Șoica Codruța, Ledeti Adriana, Borcan Florin, Șuta Lenuța-Maria, Murariu Marius, Dehelean Cristina, Ionescu Daniela, Ledeti Ionuț: Preformulation studies for albendazole. A DSC and FTIR analysis of binary mixtures with excipients, *Rev Chimie* 2016, vol. 67: 463-467, IF 2016: 1,232 <https://www-webofscience-com.am.e-nformation.ro/wos/woscc/full-record/WOS:000375364800016>

9. Ledeti Ionuț, Vlas Gabriela, Vlas Titus, Murariu Marius, **Trandafirescu Cristina** (autor corespondent), Șoica Codruța, Șuta Lenuța Maria, Dehelean Cristina, Ledeti Adriana: Non-isothermal isoconversional kinetic study regarding the degradation of albendazole, *Rev Chimie* 2016, vol. 67: 549-552, IF 2016:

1,232 <https://www-webofscience-com.am.e-nformation.ro/wos/woscc/full-record/WOS:000375364800034>

10. Danciu Corina, Vlaia Lavinia, Fetea Florinela, Hăncianu Monica, Coricovac Dorina, Ciurlea Sorina, Șoica Codruța, Marincu Iosif, Vlaia Vicențiu, Dehelean Cristina, **Trandafirescu Cristina**: Evaluation of phenolic profile, antioxidant and anticancer potential of two main representants of Zingiberaceae family against B164A5 murine melanoma cells, *Biological Research* 2015, vol. 48, no. 1, IF 2015: 1,328 <https://biolres.biomedcentral.com/articles/10.1186/0717-6287-48-1>