UNIVERSITATEA DE MEDICINĂ ŞI FARMACIE
„CAROL DAVILA” BUCUREŞTI
ŞCOALA DOCTORALĂ
DOMENIUL FARMACIE

DEZVOLTAREA ȘI EVALUAREA UNOR PREPARATE FARMACEUTICE SOLIDE ȘI SEMISOLIDE

REZUMATUL TEZEI DE ABILITARE

CANDIDAT:
Conf. Univ. Dr. Mitu Mirela Adriana
Disciplina Tehnologie farmaceutică și Biofarmacie
Facultatea de Farmacie
Universitatea de Medicină și Farmacie "Carol Davila", București

2024

ABSTRACT

The habilitation thesis entitled "The Development and the Evaluation of Solid and Semisolid Pharmaceutical Preparations" comprises an important part of my academic achievements realized after obtaining the Ph.D. title, in 2011. It is organized into four main chapters, according to my achieved scientific, educational, and professional activities.

The first chapter presents my scientific achievements in three main research directions based on the most relevant publications.

The first research direction is dedicated to the development and evaluation of hydrophilic semi-solid pharmaceutical preparations with topical action.

The first study in this direction of research focused on the development and control of semi-solid pharmaceutical forms for topical administration, having as active pharmaceutical ingredient ciclopirox olamine, naftifine hydrochloride, or terbinafine hydrochloride, in a concentration of 1%. Thus, the experimental plan aimed at the following objectives:
1) Development of new semisolid topical pharmaceutical formulations, which include the three antifungals in 1% concentration, solubilized in semisolid matrices with obvious structural differences, induced by different concentrations and combinations of hydrophilic macromolecular agents; 2) In vitro release study; 3) Evaluation and modeling of the rheological properties of the developed drug formulations.

The next study in this direction addressed the development of topical hydrophilic semi-solid pharmaceutical forms with the active ingredient betamethasone or dexamethasone in a concentration of 0.1%. The experimental plan aimed at 1) The development of new topical semi-solid pharmaceutical formulations by inclusion of active pharmaceutical ingredients in the semi-solid matrix in three possible situations: as such, lyophilized inclusion complex of dexamethasone and betamethasone in β-cyclodextrin and hydroxypropyl-β-cyclodextrin and physical mixtures of dexamethasone or betamethasone – cyclodextrins; 2) In vitro release study.

The research carried out in this direction resulted in 4 ISI-indexed articles, 3 studies communicated and published in summary in journals and the volumes of scientific events, and two published patent applications.

The second research direction presents studies for the development and evaluation of solid pharmaceutical preparations containing inclusion complexes in cyclodextrins obtained by direct compression.

This part presents pre-formulation and formulation studies for chewable tablets with carbamazepine-β-cyclodextrin inclusion complex, orodispersible tablets containing: captopril-β-CD inclusion complex, nimodipine (nimodipine-HP-β-CD and nimodipine-Me-β-CD), amlodipine (amlodipine-HP-β-CD and amlodipine-Me-β-CD), nifedipine (nifedipine-HP-β-CD and nifedipine-Me-β-CD), and fast-release tablets with simvastatin inclusion complexes (simvastatin-β-CD, simvastatin-HP-β-CD and simvastatin-Me-β-CD).

The objectives of the studies are:

1) Incorporating inclusion complexes of various active pharmaceutical ingredients into cyclodextrins in tablets together with modern excipients to ensure stability and increase the dissolution rate of the active ingredient, using the direct compression preparation method;

2) Evaluation of the obtained tablets: organoleptic control, dimensions (diameter and height), mass uniformity, mechanical strength, friability, in vitro disaggregation capacity, and in vitro dissolution rate of active drug release.

The obtained results demonstrate the beneficial influence of the inclusion of the active drug in the cavity of cyclodextrins on the dissolution profiles of chewable, orodispersible, or fast-release tablets. At the same time, the excipients selected for the formulation of the tablets allowed their manufacture by the direct compression method, the final product presenting appropriate characteristics and an excellent disintegration time.

The research carried out in this direction resulted in 6 ISI-indexed articles, and in all of them I was the main author, and 2 communicated studies were published in journals or volumes of scientific events (one was awarded by the Romanian Pharmaceutical Society, 2016).

The third direction of research shows the development and evaluation of solid pharmaceutical forms, mucoadhesive oral films. The studies provide data on the formulation, the obtaining, and the results of the specific quality control performed on oral mucoadhesive films based on Usnea barbata (L.) extracts. The research carried out in this direction resulted in 2 ISI-indexed articles, and all of them I was the main author.

The second chapter describes my academic achievements in the field of Pharmaceutical Technology and Biopharmacy, which include the teaching activities for the students of the Faculty of Pharmacy in the I, III, IV, and V years, and my involvement in the scientific and practical activities of the students. coordination of undergraduate theses, organization and support of courses for first-year residents in the General Pharmacy specialization, and tutorial activities for students and residents. I have participated, as a co-author, in the development of several specialized books addressed both to students and residents, as well as to professionals

in pharmaceutical practice. Some of the published books have been awarded at various pharmaceutical events.

The third chapter is dedicated to my professional concerns in the pharmaceutical community. We have developed and supported a postgraduate course with annual frequency, addressed to graduates of the faculty of pharmacy, regardless of the field in which they work, and even the university environment, as well as doctors, chemists, or biologists. During the activity, I participated in the scientific and organizing committees of several national congresses and conferences and gave several oral presentations of great interest to the entire pharmaceutical community. The professional pharmaceutical activity plan also included the publication of scientific articles addressed to pharmacy and medical professionals, with whom we want to strengthen an interdisciplinary relationship.

The fourth chapter presents my future university career plans, following the three main fields of activity: educational (good teaching for future pharmacists and training/consolidation of the necessary knowledge in medical science), professional (maintaining a close link between the academic pharmaceutical environment and the pharmaceutical environment in the community) and scientific (adaptation, organization and framing of Romanian pharmaceutical research in the current international context).

The scientific research I am considering further in my career will continue the research directions of the Pharmaceutical Technology and Biopharmacy Discipline and will also address innovative topics involving my participation in multidisciplinary research teams. To this end, I will conduct studies in the field of expertise and new challenges in my work:

• Formulation studies, and experimental drug design studies, the objectives of which are to establish the influence of critical parameters and the impact of process parameters on the quality conditions and the variability of the release of the product;

• Development and evaluation of new, innovative pharmaceutic or cosmetic products with active ingredients included in various cyclodextrins;

•Formulation and preparation of new micro- and nano-encapsulated pharmaceutical forms;

• Use of new manufacturing technologies. Studies for drug capsules loaded with pellets obtained by new technologies;

• Use of 3D printing technology in obtaining pharmaceutical forms.