## ABSTRACT

The habilitation thesis "CONTRIBUTIONS TO THE DEVELOPMENT OF PHARMACEUTICAL SYSTEMS FOR ENHANCING THE FUNCTIONAL PERFORMANCE OF BIOACTIVE COMPOUNDS" of Associate Professor Oana Karampelas, PhD, summarizes the main scientific, professional, and academic achievements obtained during the postdoctoral period in the field of Pharmaceutical Technology and Biopharmaceutics. The thesis is based on results published in scientific articles and aims to highlight contributions related to the design, optimization, and characterization of solid and liquid pharmaceutical systems intended to improve the biopharmaceutical performance and biological profile of active ingredients.

The first chapter, entitled "Scientific Activity", presents the main research directions developed during the postdoctoral period, structured around two major axes:

- ✓ **Biopharmaceutical optimization of solid pharmaceutical systems for modulating drug release and improving the physicochemical and biological characteristics of active ingredients**

This research direction brings together studies on the development of solid dosage forms, with emphasis on selecting the formulation system, the manufacturing method, and evaluating performance attributes. The studies addressed tablets, capsules, and pellets, aiming to increase the solubility, dissolution, and availability of active ingredients with challenging biopharmaceutical properties.

➢ Development, technological optimization, and in vitro evaluation of tablets containing inclusion complexes of rutoside with β-CD and HP-β-CD. The research aimed to obtain rutoside inclusion complexes and incorporate them into immediate-release tablets. The results showed that encapsulating rutoside in cyclodextrins improved its antioxidant activity and solubility, while the resulting tablets displayed appropriate pharmacotechnical characteristics: good mechanical strength, low friability, uniformity, and rapid disintegration.

➢ Technological design and antioxidant evaluation, using multiple methods, of innovative capsule formulations based on natural compounds. The study focused on formulating capsules containing complex mixtures of active ingredients, such as melatonin, biotin, coenzyme Q10, quercetin, and resveratrol. Preformulation studies

highlighted the decisive role of excipients in improving flowability, compressibility, particle size distribution, and mass uniformity. The selected formulation showed suitable pharmacotechnical properties and favorable behavior for the rapid release of the active compounds.

➢ Development of an innovative method to enhance the dissolution performance of rivaroxaban. Starting from the limitations associated with the use of cyclodextrins in solid dosage forms, the research proposed a method in which the liquid-state inclusion complex is sprayed onto cellulose pellets, which are subsequently encapsulated in hard gelatin capsules. The method is intended to improve the dissolution performance of rivaroxaban, a poorly soluble active ingredient, and offers a technological solution that is closer to industrial applicability.

Following this research direction, the thesis highlights the relationship between formulation, material properties, processing behavior, and final biopharmaceutical performance. The results support the idea that optimization of the pharmaceutical matrix can significantly modify the release, dissolution, and biological activity of active ingredients.

✓ **Design, physicochemical characterization, and evaluation of the biological profile of liquid dispersed systems based on active ingredients of natural origin**

The second research direction focuses on liquid and semisolid systems, specifically hydroalcoholic solutions and oil-in-water emulsions. These studies aimed to valorize active principles of plant origin, characterize their chemical composition, and evaluate the antioxidant, rheological, physicochemical, and biological properties of the formulations developed.

➢ Design and characterization of hydroalcoholic solutions. Within this subdirection, hydroalcoholic extractive solutions were obtained from plant materials such as Medicaginis herba, Trifolii pratense flores, Ginkgo bilobae folium, Myrtilli fructus, Cynosbati fructus, Ribes nigri fructus, Rubi idaei fructus, Rubi fruticosi fructus, and Fragariae moschatae fructus. Qualitative and quantitative analyses revealed bioactive compounds with antioxidant activity, including flavones, polyphenolic derivatives, tannins, anthocyanins, proanthocyanins, and ascorbic acid. The studies confirmed that the extraction method enables advanced solubilization of the compounds of interest and supports the antioxidant potential of the resulting preparations.

➢ Formulation and preparation of O/W emulsions based on oily extract of *Usnea barbata* in canola oil. This study addressed the formulation and rheological characterization of oil-in-water emulsions containing an oily extract of *Usnea barbata*. The emulsions were evaluated from physicochemical and biological perspectives, and the results suggested a reactive oxygen species-mediated anticancer potential, through DNA damage, cell cycle arrest, and induction of autophagy. The data obtained support the valorization of natural-origin extracts in dispersed pharmaceutical systems.

➢ Development and characterization of O/W photoprotective cosmetic formulations containing *Veronica* extracts. The study aimed to develop oil-in-water cosmetic formulations containing plant extracts and organic UV filters, and to evaluate their physicochemical, rheological, occlusive, antioxidant, and in vitro photoprotective properties. Formulations based on the Heliofeel® emulsifying system showed stability, homogeneity, pleasant sensory properties, and appropriate rheological behavior. The incorporation of *Veronica* extracts did not compromise formulation stability and was associated with increased antioxidant activity in formulations containing UV filters.

This research direction demonstrates the importance of an integrated approach to the development of liquid dispersed systems, in which the plant composition, formulation vehicle, and physicochemical profile must be correlated to obtain stable, effective products compatible with their intended use.

The two main research directions converge toward a common platform for pharmaceutical development, in which formulation becomes an essential tool for modulating release, increasing solubility, improving stability, and supporting the biological activity of active principles. The scientific activity is supported by ISI-indexed publications and interdisciplinary contributions in the fields of pharmaceutical technology, biopharmaceutics, pharmacognosy, and biological evaluation.

Regarding the development of academic, scientific, and professional activities, the directions presented may be continued by expanding formulation studies, optimizing characterization methods, developing innovative pharmaceutical systems, and strengthening interdisciplinary collaborations.

Overall, the habilitation thesis highlights a coherent postdoctoral activity focused on pharmaceutical and cosmetic formulations with applied value. The results presented support the candidate's ability to coordinate advanced research and contribute to the development of the field of Pharmacy.