THESIS ABSTRACT

This habilitation thesis presents the most important postdoctoral activity achievements of the author, the scientific, professional and academic activity, highlighting the perspectives of career development in the final chapter.

The scientific research followed four main directions: drug analysis; applications of HPLC technique in bioanalysis; physico-chemical characterization of plant extracts; structural analysis of new compounds and preliminary research of their biological activity.

Drug analysis is a mainstream research domain, the generic drug market is under constant development and requires drug manufacturers to develop their own generic products based on research and development.

The author's personal research on drug analysis was focused on studying chemically related impurities. The results were mostly obtained through a national grant won by competition. Degradation studies in stress conditions on drug solution indicated the influence of pH, oxidative environment and UV light as important stress factors for the studied model molecules, simvastatin, captopril, spironolactone degradation following simple or complex kinetics. The developed HPLC methods can indicate the stability and profile the chemically related impurities.

The profiling of chemically related impurities has been corroborated with preformulation and the development of new pharmaceutical forms. Simple formulations which can be produced in pharmacy have been developed, captopril oral solution for pediatric use and spironolactone external solution in the treatment of alopecia.

In order to improve the stability of some medicinal substances, the chemical derivatisation was studied. Therefore, the captopril stabilization study by interacting with p-bromophenacyl bromide demonstrated that the reaction kinetics is better described by a logarithmic function and can be used as a chemical derivatization reaction for captopril determination in pharmaceutical products, respectively, from biological samples by HPLC.

The author had contributions in developing new pharmaceutical forms (tablets, gels, creams) with various active substances (clindamycin, adapalene, fosinopril, ondansetron etc.) by monitoring the concentration of active ingredients in the final product or in release/dissolution studies by optimized quality control HPLC methods.

Another subject in the field of chromatographic pharmaceutical analysis was chiral separation by HPLC, the most important result being related to the possible correlation of the chromatographic discrimination capacity of the chiral protein columns with the drug substances mechanism of action. In this regard, the ovomucoid columns seem to differentiate selective beta-blockers (without enantiomeric

chromatographic resolution) from non-selective (with separable chromatographic enantiomers).

Besides chromatographic methods, research in pharmaceutical analysis was performed by spectral and thermal methods, among them FT-IR impurities studies could be considered as premises for introduction of rapid quality tests of raw materials in case of drug substances with low chemical stability.

Bioanalysis by HPLC methods was another research direction. Various HPLC methods with classical detection have been developed and applied in clinical or non-clinical studies to determine the bioequivalence of generic products, in pharmacokinetic interaction and pharmacological screening studies. Methods have been developed to determine the concentrations in biological samples with specificity, accuracy and precision, in a short analysis time and performing as simple as possible sample preparation methods, some of the developed methods are considered as "high-throughput" methods.

Currently considered a gold technique in bioassay, the LC-MS/MS technique has been used to monitor pharmacotherapy, laboratory diagnosis or pharmacokinetic studies. The objectives of each study have influenced the methodology of extraction and optimization of analyte detection, bioanalytical determinations were performed with easy sample preparation procedures and very short analysis times by judicious selection of ionization and detection parameters. Based on the performed clinical and non-clinical studies, the following have been demonstrated: in patients with chronic kidney disease, it is necessary to reduce ciprofloxacin doses without changing the dosing interval in order to avoid adverse effects, even in patients in an early stage of disease; monitoring drug therapy by LC-MS/MS methods reduces the variability of measured response compared to immunological methods; olanzapine has a limited transfer to breast milk in sheep, confirming a benefit/risk ratio in favour of olanzapine use during breast-feeding.

Other applications in instrumental analysis consisted of spectral and chromatographic determinations in synthesis studies of new heterocyclic compounds with potential biological activity and qualitative characterization of plant extracts also with therapeutic potential.

After achieving the Ph.D. title, the author published 5 books, 7 book chapters and numerous articles, 45 of which are articles in ISI Web of Science Core Collection, 24 as main author, with index h = 9 in the same database. The author was involved in 13 research grants and institutional development projects won through national or university internal competitions (3 coordinated as a director, of which 1 grant was won through national competition) and 5 research contracts directly assigned by private companies (2 coordinated as a director).

Regarding the didactic activity, the author was the course coordinator of physical chemistry, pharmaceutical calculations, pharmaceutical scientific research

methodology for pharmacy specialization, drug analysis, elements of organic chemistry, elements of physical chemistry for pharmacy assistance, cosmetic product analysis for medical cosmetics, analytical separatology for the master program.

The career development plan is focused on continuing the research directions previously developed but also to access new themes in research projects: standardization of LC-MS/MS screening methods for biomarkers involved in cardiovascular, endocrine and neurodegenerative diseases; the study of drugs protein binding. The main goals for the didactic activity will be updating courses and developing interactive textbooks, introducing new courses for master and doctoral students, developing scientific books in pharmaceutical analysis and continuing to involve in the academic life of the university.