

SUMMARY OF THE THESIS

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The habilitation thesis entitled *“Contributions to the study of silver fluoroquinolones complexes and the development of capillary electrophoresis methods for the analysis of pharmaceutical substances”* represents a synthesis of the research activity carried out in the postdoctoral period (2013-2017). The most important research directions approached in this thesis have been the implicit continuation of the PhD study, respectively of the PhD dissertation entitled *“Research regarding the physicochemical characteristics of quinolone derivatives through optimised analytical methods”*, publicly defended in December 2012. The thesis is structured in several distinct parts, briefly presented below.

In the chapter dedicated to the scientific achievements the approached research directions are synthetically structured and described: new compounds with biological properties and therapeutic potentials and the development and optimisation of new methods of capillary electrophoresis with applicability in the pharmaceutical field.

The first part of the habilitation thesis comprises original studies focused on obtaining and characterising silver complexes with ligands from fluoroquinolone class. The coordination of a metal ion with an organic ligand (a compound with pharmacological activity) can often lead to compounds with superior biological effects compared to ligands. The selected ligands belonging to class of fluoroquinolones were norfloxacin, ofloxacin, and levofloxacin, and silver was the ion selected to obtain combinations with biological potential. Consequently, several combinations of silver complexes with the three selected ligands were obtained. In addition to the antibacterial activity on various bacterial species, antifungal activity has also been tested.

The research was financed by a internal grant after a successful application as an individual research project, won by competition in 2014. The results were published as full-text articles in three ISI indexed journals and in one BDI indexed journal and also presented at national and international scientific events.

The second direction of research was the continuation of the doctoral studies based on already accumulated experiences. Thus, I participated as first author, principal author or co-author in a series of researches that aimed the development of capillary electrophoresis techniques and testing their applicability in the pharmaceutical industry, and also the development of personal practical skills.

These studies were divided into two research directions: developmental and optimisation methods for the enantioseparation of therapeutically important chiral compounds; and developmental, optimisation and validation methods applicable in the pharmaceutical industry.

A current issue of the pharmaceutical industry is the production of drugs that contain active substances with stereochemical particularities, being marketed as racemic mixtures or as pure enantiomers which may present differences through their pharmacological effects. The current international trends supported by regulatory institutions, recommend the use of enantiomers which are the most beneficial from the therapeutical point of view. An economically cost-effective alternative for the enantioselective determination of chiral pharmaceutical substances is the capillary electrophoresis method that offers the possibility of optically active molecule enantiomers separation by using chiral selectors.

In this thesis, the analysed stereochemical compounds separated by capillary electrophoresis were from several different classes of therapeutically important drugs: proton pump inhibitors, beta-blockers, antidepressants, H1 antihistamines, diuretics, calcium channel blockers, and opioid analgesics.

The second part of the thesis presents the development, optimisation and validation of some capillary electrophoresis methods used for the determination of several types of important compounds used in therapy. These compounds were aromatase inhibitors, cephalosporin class antibiotics, antitubercular compounds, statins, and H1 antihistamines.

The postdoctoral research results have been consolidated through further research studies: projects (1

project –as director, 3 projects –as member), a series of publications (30 full-text articles - 20 articles in ISI WOS flow journals, 10 BDI articles indexed in international databases), and granted awards; the cumulative impact factor is 26.947, with 65 citations and Hirsch index=5.

The evolution and development career plan has several directions, namely teaching activity, increasing personal competitiveness and scientific research activity. The developmental objectives regarding the scientific activity are based on the continuation of the current research projects and capitalisation of results, but also the approach of some new research topics:

- the continuation of research studies regarding the synthesis and the study of biological properties of fluoroquinolone-metal complexes but also of other classes of compounds with chelating effect; testing of several types of metals, ligands and biological effects;

- the development of new sensitivity analysis methods; the development and validation of new techniques aiming the analysis of optically active pharmaceutical substances, as a result of these the reorientation of the pharmaceutical industry towards the stereochemical properties of drugs;

- further studies to deepen knowledge regarding the physicochemical properties of compounds presenting pharmaceutical interest and their interaction with receptors that need initiation in molecular modelling and computational design.

The planned activities related to the research directions are: publishing articles in the UEFISCDI yellow and red awarding area, the dissemination of scientific results at national and international scientific events, submitting successful grants/projects, participation in interdisciplinary and interuniversity projects, collaboration with economic agents, the study of new analytical techniques related to the research area or specialization in the already known techniques of analysis.

Other goals of the professional activity are: continuous search and development of new research directions correlated with the selection of new topics, the supervision of students doing research, encouraging participation at scientific manifestations, the application of other postgraduate forms of studies (master of science, doctorate) and scholarships; obtaining membership in editorial staff of specialized journals.

These objectives are permanent, and they contribute to the personal development at the academic level and consequently these will help to increase the quality of the educational performance that will lead to the training of valuable graduates and professionals in the pharmaceutical field.