

ABSTRACT

The habilitation thesis entitled *Development of new drug administration systems. Pharmacotechnical formulation and characterisation* presents a synthesis of the research, professional and academic activity following the defence of the doctoral thesis in 2001, entitled *Contributions to the pharmaceutical forms with controlled release*. It approached only a category of the multitude of systems that can respond to such release of the active drug, idest microspheres.

The research directions addressed in the seven chapters of this habilitation thesis have as a starting point the results obtained from previous research activities materialised in scientific publications.

The first direction in post-doctoral research was to apply the previously gained experience. Thus, the formulation of oral microparticulate therapeutic products with prolonged or controlled release was approached. The preparations developed in the form of microspheres based on a natural biocompatible polymer were proposed for active drugs whose pharmacokinetic properties justify the processing in slow-release preparations. Microspheres with nifedipine, metoprolol, tramadol, etc. were developed for their subsequent conditioning in capsules or compressed tablets, depending on the desired release profiles. Studies were conducted to obtain microparticulate pellet products targeting metoprolol and carbamazepine as active drugs. An important role in the characterisation of these microsystems was the elucidation of the kinetic mechanism of release of the active drug.

Given that in many situations a rapid effect is desired or the use of mild medicinal products is necessary, another way of research was the development of accelerated release formulations of orodispersible tablets. The correlation of the formulation and technological parameters with the characteristics of the obtained products was made and the mathematical models describing the release mechanisms were established. These experimental studies were conducted in a research project entitled *Developing new drug formulations for paediatric therapy and the in vitro assessment of their performance*, a project in which loratadine was explored as an active drug associated with superdegenerants without lactose and its

derivatives. Other orodispersible products with nevirapine, clopidogrel, etc. were proposed, in which, apart from the formulation and pharmaco-technical characterisation, the compatibility between active principles and excipients, as well as their stability were studied.

The administration of systemically effective drugs is mostly oral, but the rectal route is an excellent alternative because of the benefits it has. The development of anticonvulsant preparations for paediatric use was explored in an interdisciplinary research. The study protocol had as a starting point the formulation of rectal preparations and their characterisation and was concluded by determining the bioavailability of the active drugs of the preparation in preclinical *in vivo* studies, aspects presented in the third chapter of the thesis.

The transepidermal absorption of active drugs is widely studied, seeking alternative solutions for products that cannot be administered orally or which have side effects. Chapter four presents the results of research into the formulation of non-steroidal anti-inflammatory drugs (meloxicam, tenoxicam, indometacin) in polymeric matrix type transdermal therapeutic systems. Studies of the diffusion of the active drug were performed both through the synthetic membrane as well as the biological one.

Although systemic effect drugs occupy the largest share on the pharmaceutical market and in therapy, the approach of products with local effect should not be neglected, which is why developing products for mucosal and skin administration was performed. In both cases, hydrogel type preparations were proposed due to their advantages of efficiency and compliance. Within an interdisciplinary collaboration, preparations for the treatment of parodontopathies were developed and analysed. The research into formulation and preparation was completed by clinical trials. Drug formulations were also proposed and analysed, dexpanthenol being one of the substances studied in such preparations.

The development of a new drug cannot be achieved unless modern methods and techniques of analysis are used. Thus, in the quantitative determination of the drugs in the developed products analytical methods such as NIR spectroscopy or capillary electrophoresis were also used, the studies being presented in the next chapter.

The approach of thermal analysis in the development of a new drug is mandatory in the preformulation stage, when checking for incompatibilities between the components of a product and conducting stability studies. This is why these methods of analysis were

approached in numerous formulation studies without which the development and optimisation of a product cannot be complete.

Subsequent research plans are outlined in three main directions, but not limited to these. The aim is to expand studies of the development of orodispersible products with new active drugs and to develop methods of their study that reproduce the physiological conditions at the site of administration as accurately as possible. Another approach is to prepare these products by freeze drying. The second direction of research is the continuation of studies on the preparation of transdermal therapeutical systems, but also the realisation of biofilms with cutaneous or mucosal administration, with extended release or with rapid dissolution. The third research direction is the subject of collaboration with dermatologists and consists of the development of methods for the preparation of drug liposomes as vectors for transport through the skin, mucosa, and tissues for therapeutic and diagnostic purposes.

The professional and academic activity is highlighted by the presentation of the main achievements: the publication of 13 books and book chapters addressed to students, pharmacists, and other professionals in the field, supervision of 77 bachelor's and master's dissertations, participation in numerous congresses, coordinating the Cosmetology and Dermofarmacy master's programme, engaging in various activities for the benefit of the academic community. In the future, the teaching activity will be continuously improved through content and by approaching a student-based learning process by developing new teaching materials, all these in order to train professionals with the necessary skills to quickly integrate into a diverse labourmarket.