CONTRIBUTION TO THE DEVELOPMENT OF POLYMER-BASED PHARMACEUTICAL DOSAGE FORMS

Throughout the years, the main focus of the research activity was the applicability of different types of carboxyvinyl polymer, commercially available as Carbopols. Given the fact that the PhD thesis focused mostly on development of cutanous gel formulations, based on two traditional (Carbopol 940 and Carbopol 980) and one newly developed carboxyvinyl-type polymer (Ultrez 10), further research was conducted to enlarge to applicable polymers (for ex. by using Ultrez 21) for hydrogel formation, but also to incorporate different pharmaceutical active ingredients. Comparative *in vitro* dissolution test were performed in order to quantify the released active ingredient from the hydrogels. Numerous active pharmaceutical ingredients were incorporated in different gel bases, formulated with carboxyvinyl-type polimers, but also, by employing other polymers, such as methylcellulose or carboxymethylcellulose.

The first part of the habilitation thesis presents the results of these research activities, in a chronological order. Beginning with 2004, comparative rheological studies were performed in order to evaluate a novel member of the carboxyvinyl-type polymer class, namely Ultrez 21. In another study, several ecogel formulations were evaluated in order to find a suitable dosage form to be used in medical investigations.

In the following years, several active substances were incorporated in these hydrogels, such as: hydrocortisone acetate, bifonazole, acyclovir, dexpanthenol, aceclofenac, meloxicam, benzocaine. These studies aim to investigate drug-loadability and release characteristics of the prepared hydrogels.

When preparing the hydrogels, the primordial scope was to increase the bioavailability of the active ingredients from the topical preparations, in order to enhance their applicability. During the timespan of several years, a certain experience has developed regarding the development and applicability of these hydrogels, which was reflected by the appearance of several scientific publications. In 2008, a study was published about acyclovir-loaded hydrogels, which summarizes the efforts undertaken to improve these preparations by increasing the quantity of active released from the gels. In 2014 and 2015 two other articles appear in ISI listed journals (Tropical Journal of Pharmaceutical Research and Studia UBB Chemia) containing rheological and *in vitro* release data for some the hydrogels prepared.

The second part of the research focused on another type of pharmaceutical dosage form, namely, sustained-release tablets, using the same carboxyvinyl-type polymers among other polymers in order to create hydrophilic matrixes. Some of the results obtained regarding the study of retard pentoxyfiline formulations with hydrophile, lypophile and inert matrixes were included in a PhD thesis and also appeared as scientific publications in the journals Farmacia and Clujul Medical, but also as abstracts in international scientific conferences.

Development of sustained-release formulations was realized using two separate approaches: using carboxyvinyl-type polymers and using other polymer types such as: polymethacrylates (Eudragit), ethylcellulose and hydroxipropylmethylcellulose. Using these polymers, several retard formulation were developed, incorporating active ingredients such as: theophylline, ascorbic acid, tramadol and aceclofenac (the prolonged release of the actives was achieved by using carboxyvinyl polymers), sodium diclofenac, indapamide, tramadol and captopril (prolonged release was achieved by using other

polymers). In some of the cases, compatibility studies were also conducted between the active and excipients employed results of these studies being disseminated in an ISI listed journal (Journal of Thermal Analysis and Calorimetry, 2011). For sustained-release formulation, dissolution studies are crucial and there is an obvious need for validated method to determine the quantity of the released active ingredient. The development and validation process of analytical methods suitable for these determinations were published in different journals (Studia UBB Chemia, Pharmaceutical Development and Technology).

The abovementioned sustained-release formulations were results of several trials and numerous variables were changed in the development process (quantity and quality of excipient, technological characteristics – compression force, mixing order etc). This approach proved to be lengthy and time consuming and was replaced by the use of experimental designs. Results regarding the development of an optimal formulation with two active substances – enalapril maleate and indapamide – were published in a ISI listed journal (Acta Pharmaceutica, 2016).

In a similar manner, an orodispersible formulation was developed using the SeDeM and SeDeM-ODT models, which were employed to characterize both the active substance and the superdisintegrant excipient (Ludiflash). Results of the study appeared in the journal Acta Pharmaceutica in 2017.

Over the past few years, my research was mainly focused on the use of nanotechnology, namely, different polymer-based (polyvinyl-alcohol, polycaprolactone) nanofibers produced by electrospinning. Results of these studies were published in top ranked journals (Journal of Pharmaceutical and Biomedical Analysis).

Regarding the professional and academic realizations, these were materialized in teaching activities (theoretical and practical courses), elaboration of didactic material (theoretical and practical course books), diploma thesis supervising, coordinating student research groups, participating in comissions for the elaboration of subjects for different exams (final exam. residential exam), coordinating the activities of the Drugs Industry discipline, member in faculty board - prodean (2009-2012), responsible for the accreditation of the Medical Biotechnology masters course (2013).

Plans for the professional, scientific and academic development include the following: on the didactic level – continuous improvement of the theoretical and practical courses at the Drugs Industry discipline for the 5th year students, improving students' awareness of biotechnology and pharmaceutical technology by introducing novel theoretical courses and elaborating adequate course books to support this process. On the scientific level future plans include continuously improving the research staff at the Discipline, but also to collaborate with other faculty members by elaborating multidisciplinary research projects. Dissemination of research results in high-end journals and at national and international conferences is also primordial. Future research directions will include preparation and characterization of nanofibrous scaffolds and analytical method development, all joint together in a quality by design environment. On the academic level, the main focus will be on implication in different institutional activities (institutional accreditation, accreditation of study programs) and establishing different channels for collaborations with prestigious European universities.