Development and Characterization of
Drug Delivery Systems for
Oral and Intravaginal Applications

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PhD Thesis
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To my loved ones

To my family,

To my friends,

To my girlfriend

“Everyone sees what you appear to be, few experience what you really are.”

- Niccolò di Bernardo dei Machiavelli -
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Preface

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Abstract

Drug delivery systems are important medical tools that can effectively improve therapeutic outcomes. Establishing new drug delivery systems, to enhance the effectiveness of active pharmaceutical ingredients, is extremely important. It is moreover essential to consider the benefits of using a specific material for providing the drug delivery system with desired properties taking into account the route of administration that has to be used. Among the various routes of administration, the oral one is the preferred by the patients and with the highest compliance. Oral drug delivery is however limited by physiological barriers that determine a reduction in bioavailability. Nowadays, oral administration is performed using tablets and capsules. The interest towards new oral drug delivery systems based on micro-fabricated devices is, however, increasing.

Within the frame of this PhD project, microcontainers were deployed as an alternative oral drug delivery system. Microcontainers have been extensively studied in the past years, some question have, however, yet to be answered.

As a first goal of the PhD project, the addition of a water soluble sacrificial layer, included during the microcontainers fabrication, has been explored to improve the handling of the microcontainers. The compatibility of this layer with the loading and coating of microcontainers was also assessed. The resulting formulation has been tested in vivo and ex vivo. The effect of tuning the loading method in terms of different release profiles was also assessed. Finally, the 3D distribution of the active pharmaceutical ingredients within the microcontainers was visualized by Raman spectroscopy, evaluating the effect of changing the microcontainers sizes.

A second goal of the PhD project was to develop an intravaginal drug delivery system able to exploit the intravaginal environment for improving the retention time of the formulation. To reach this objective, an AL and CH mucoadhesive and biocompatible membrane was fabricated and tested in vitro. The membrane demonstrated to possess good mechanical properties and to slowly degrade in a simulated vaginal medium, remaining intact for up to one month.
The third goal of the PhD project involved the fabrication of polymeric nanoparticles. Polymeric nanoparticles have been extensively studied and used for several applications by many research groups. The focus of this study was to evaluate the possibility of using an ultrasonic spray coater as a novel technique for continuously producing polymeric nanoparticles in a controlled fashion. In this work, the parameters controlling the ultrasonic spray coater were also modulated to elucidate their influence upon the nanoparticles size distribution.

I dette PhD projekt testes mikrocontainere som et alternativt oral drug delivery system. Mikrocontainere er blevet udførligt beskrevet de seneste år, men der er stadig ubesvarede spørgsmål.


Dernæst var målet at udvikle et intravaginalt drug delivery system, i stand til at udnytte det intravaginale miljø og derigennem forbedre retentionstiden for formuleringen. En alginat og chitosan mucoadhesive og biokompatibel membran blev derfor fabriket og testet in vitro. Membranen demonstrerede gode mekaniske egenskaber samt en langsomm edbrydning i et simuleret vaginalt miljø, varende op mod en måned.