Abstract

The oral mucosa is an attractive site for non-invasive drug delivery because of its accessibility and good patient compliance. The buccal and sublingual mucosae are non-keratinized and highly vascularized. Drugs absorbed through the oromucosal route avoid the harsh environment of the gastro-intestinal tract and by-pass hepatic first-pass metabolism, which is beneficial for drugs with low physiochemical stability. However, drug delivery by the oromucosal route is challenged by the risk of washout due to the salivary flow, and the epithelium lining the oral cavity comprises a significant barrier for drug absorption especially of hydrophilic drugs of high molecular weight.

In this work, three biocompatible drug delivery systems were developed and evaluated: i) a two-layered drug delivery system consisting of mucoadhesive chitosan/polyethylene oxide (PEO) nanofibers and a saliva-repelling backing film for oromucosal delivery of desmopressin; ii) a nanofiber-on-foam-on-film (NFF) drug delivery system for oromucosal delivery of desmopressin based on three layers i.e. mucoadhesive chitosan/PEO nanofibers, peptide-loaded porous foam, and a saliva-repelling backing film; and iii) electrospun α-lactalbumin/PEO nanofibers with a high protein content for the delivery of the small molecules ampicillin and nicotine. The morphology, mechanical properties, and disintegration in aqueous medium of the aforementioned drug delivery systems were assessed in vitro recognizing that these properties are important for their potential use as formulations for oromucosal application. The performance of the nanofibers in vitro were systematically investigated, which also elucidated a high level of tunability of the nanofiber-based systems. Strategies to improve drug absorption were evaluated, which included mucoadhesion, unidirectional, fast and controlled drug release to achieve a high concentration gradient across the mucosa. The permeation of drug released from the nanofiber-based drug delivery systems were benchmarked against marketed formulations for oromucosal administration.

This thesis highlights the benefits of electrospun nanofiber-based drug delivery systems for delivery of small molecules and therapeutic peptides, and discusses the technology in relation to current formulation strategies for oromucosal administration. The results of this project support that electrospun nanofiber-based drug delivery systems are indeed promising to overcome challenges associated with oromucosal drug delivery.