

Abstract

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Title of Doctoral Thesis: Nanofibrous membranes as drug delivery systems

Nanofibres are material structures of unique properties that are well-useable in many exciting areas, including medical products. In the field of air filtration, different types of nanofibre filters are produced industrially. On the other hand, in the area of medicated nanofibres, there is still a major barrier for production, and hence the commercial use of nanofibres, especially due to the low weight and required content uniformity of the final products. Electrospinning technology is the most promising in this context, however, no results on the evaluation of nanofibrous products intended for the systemic administration of drugs obtained by certified manufacturing process have been published.

In this doctoral thesis the individual steps of the nanofibrous products production are described, experimentally evaluated in compliance with good manufacturing practice and documented with an emphasis on the validation procedures and thus on the desired repeatability of all steps leading to the production of the final product. Validation processes included the validation of the production of nanofibrous layers however also validation procedures of analytical methods especially content uniformity and dissolution which are determined by pharmacopeia allowing the release of the medicinal product for clinical evaluation. The produced products were also tested in *in vitro* permeation tests using fresh porcine sublingual membranes in order to verify the functionality of the proposed nanofibrous product.

The manufactured product was finally tested according to the rules of good clinical practice in a comparative study that examined the bioavailability of rizatriptan as the chosen drug from nanofibrous carrier to sublingual administration to healthy volunteers. The results of this thesis proved the utility of nanofibrous technology for the production of

single-dose drug forms. The clinical trial demonstrated its improved pharmacokinetic parameters compared to a therapeutically already marketed sublingual formulation of the lyophilized tablet.