ABSTRACT OF DOCTORAL THESIS DEMISLI SOTIRIA

Abstract

The main goal of the present thesis was the development of novel biocompatible nanodispersions to be used as carriers for diverse lipophilic bioactive compounds. The purpose of these systems was the effective delivery of the encapsulated substances while providing alternative routes of administration, other than the oral which is the most commonly used. Two different nanodispersions were developed namely, oil-in-water nanoemulsions and nanoemulsion-filled hydrogels. These systems were used as carriers for the encapsulation and delivery of various lipophilic substances with pharmacological interest.

Initially, the structure of the developed systems was elucidated in order to reveal possible differences and determine the localization of the encapsulated compounds. It was also essential to investigate whether the nanoemulsions' structure was affected after its incorporation into the hydrogel matrix. In order to obtain the structural characterization of the formulated nanocarriers Dynamic Light Scattering (DLS), Electron Paramagnetic Resonance Spectroscopy (EPR), Confocal Fluorescence Microscopy (CFM), Cryo-Electron Microscopy (Cryo-EM) and Small-angle X-ray Scattering (SAXS) were performed. The investigation was carried out for both systems in the absence and presence of bioactive compounds. Regarding the nanoemulsions, the structural study revealed that the localization of the encapsulated compounds was dependent on their structure and had an effect on the size of the nanodroplets and the surfactant monolayer. Nevertheless, no significant changes in the structure of the nanoemulsion were observed after its incorporation into the hydrogel.

In order to evaluate the suitability of the formulated nanodispersions to act as delivery vehicles of bioactive compounds different *in vitro* methods were implemented for their biological evaluation. The cytotoxic effect of both nanocarriers in the absence and presence of the encapsulated molecules was assessed through a cell viability assay using the cell lines RPMI 2650 and WS1 as models of the human nasal epithelium and skin, respectively. Subsequently, *in vitro* permeation study through Franz difussions cells and tape stripping experiments were conducted indicating that the nanoemulsion-filled hydrogels could be more effective for the delivery of bioactives through the skin since it demonstrated increased penetration and improved release profiles compared to the bioactive released from the nanoemulsions.

Consequently, the proposed nanodispersions could be promising candidates as carriers for the effective delivery of various substances of pharmacological interest through the skin providing increased efficacy as well as the possibility of alternative delivery routes.