Abstract

In the drug development field, many of the new chemical entities (NCE) exhibit high lipophilicity and poor aqueous solubility, which result in difficulties for oral administration. Low aqueous solubility can be overcome by a good formulation design. An appropriate design could potentially result in a drug formulation which is suitable for oral administration. Lipid based formulations (LBF) is a promising approach to formulate poorly water soluble drugs (PWSD). LBF have shown to increase drug solubility, *in vitro*. However, a corresponding increase in oral bioavailability was not always found *in vivo*. Therefore, it is of great importance to understand LBF in terms of lipid digestion, drug release and drug absorption *in vitro*.

The aim of this thesis was to study and validate Permeapad®, a new biomimetic barrier, as an *in vitro* tool to study permeability of drug compounds and enabling formulations, e.g. LBF. This would include the setup of an *in vitro* lipolysis/permeation model, which comprises of lipid digestion and a drug absorption step.

The properties of the biomimetic barrier and its resistance against relevant surfactants and solvents, commonly used in enabling formulations, was studied and validated. Results showed the barrier to be resistant towards the studied surfactants, even in the highest concentration. The barrier was also shown to be resistant to biomimetic media, such as fasted/fed simulated intestinal fluids (FaSSIF/FeSSIF), which makes the barrier a good *in vitro* permeability model to study the effect of enabling formulations of PWSD.

The effect of pH and different concentrations, on permeation of different drugs was also studied in both the biomimetic barrier and caco-2 cells, and results showed that the apparent permeability coefficient (P_{app}) may not be concentration independent, as previously suggested.

An *in vitro* model which combines lipid digestion and drug permeation in a simultaneous way was proposed and developed in this thesis. The barrier was validated in relation to pancreatic enzymes and different LBF. Results showed that drug permeability of LBF may be increased up to 50x when combining lipid digestion with a permeation step, compared to drug permeability of the non-digested formulations. These findings indicate the importance of adding an absorptive step in lipolysis studies of LBF. The development of an *in vitro* model combing lipolysis and drug permeation is of high relevance and an important step towards the predictability of LBF bioavailability.