English abstract

Drug substances that are poorly soluble in water are hampered in their oral bioavailability which is of great concern for pharmaceutical industry considering that the major fraction of new chemical entities exhibit poor aqueous solubility. Efforts are made in both academia and industry to create drug formulations that promote absorption of the active compound in a predictive manner. Yet, a poor mechanistic understanding of drug solubility/absorption interplays delays progress and formulation processes remain empirical.

The aim of this thesis was to establish a novel analytical approach, based on asymmetric flow field-flow fractionation (AF4) combined with static light scattering detected at multiple angles (MALLS), to characterize and follow phase-changes in bio-relevant media as well as to enable drug disposition assessment from polydisperse samples. The outcome of the project was envisaged to benefit both rational drug formulation designs and *in vitro* assays employing bio-relevant donor media in permeation studies.

The analytical setup was established and validated for dynamic colloidal structures present in bio-relevant media, with regards to their stability during analysis and the accuracy of obtained particle size-distributions. Phase-changes of polydisperse bio-relevant media could be followed in detail and was thus compared with the ultrastructure of real human intestinal fluids. Clear differences between widely used surrogates for intestinal fluids and real intestinal fluids were evident and are proposed to contribute to the poor *in vitro*/*in vivo*-correlations often found in bioavailability studies.

The ability of AF4/MALLS to separate individual colloidal phases in bio-relevant drug dissolution media with subsequent collection of fractions for off-line analysis, enables investigations important for a mechanistic understanding of drug solubility/permeability interplays. Such studies are expected to aid an understanding of drug disposition and correlations to bioavailability.