Summary

This thesis investigated analytical and practical challenges of blood microsampling and the use of plasma protein adducts as biomarkers of exposure.

In the first part, a major limitation of dried blood microsampling was addressed: the hematocrit (Hct) effect. Non-destructive methods based on ultraviolet-visible and near-infrared spectroscopy were developed and validated for Hct determination in dried blood spots and volumetric absorptive microsampling (VAMS) samples. These methods were subsequently applied to evaluate the feasibility of self-sampling and to assess the impact of subtle modifications to VAMS tips on analytical results.

The second part focused on the interpretation of capillary blood microsampling results. A clinical validation study demonstrated that collection of capillary VAMS samples is a feasible alternative to conventional blood sampling for the quantification of paracetamol and its metabolites. In addition, several strategies enabled accurate conversion of capillary VAMS results to plasma-equivalent concentrations, allowing correct clinical interpretation.

In the final part, detection of human serum albumin (HSA) adducts was improved by reducing plasma matrix complexity. A generally applicable procedure based on polyclonal antibody-based peptide enrichment enabled detection of both *in vitro* and *in vivo* formed HSA adducts.

These results promote the application of microsampling and protein adductomics in research, clinical practice, and epidemiology.