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Abstract - Master Thesis Project, the Pharmacy Programme

Optimization of a microdialysis method using urea as a marker of vasoconstrictor-induced changes in dermal blood flow

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Early drug development work results in drug candidates where the pharmacokinetics and pharmacodynamics of the drug in humans are unknown. The drug industry is in need of techniques such as microdialysis, that can show the effect and the potency of a drug candidate at an early stage early in the drug development.
The aim of this microdialysis study was to obtain dose-response relationships between ascending doses of vasoactive drugs (eg. Noradrenaline and Vasopressin) and blood flow, measured as urea concentration differences in the dialysate in a human skin model.

8 healthy volunteers participated in the trial. CMA 70 Brain Microdialysis catheters were used throughout the study. Dialysate samples were analysed for urea, as well as for the metabolic markers glucose and lactate. Local skin perfusion was assessed in parallel by measuring urea concentrations in dialysate and by polarized light spectroscopy imaging (TiVi).

Significant dose dependent responses were found for glucose and lactate. The blood flow response measured as a urea change was only found to be significant for Vasopressin. There was a good correlation between TiVi measurements and the concentration of urea in the dialysate.

The results indicate that in this microdialysis model *in vivo* in humans, there is a dose-dependent change in the recovery of urea, glucose and lacatate during microdialysis of vasoconstricting drugs. These findings support that the model described appears relevant for early dose effect experiments in humans and reflects the state of the local microvasculature in the skin.