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Dissertations-Kurzfassung

Development and Evaluation of a Closed Loop System for Transcutaneous Measurement of Acute Changes in Renal Function

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Glomerular filtration rate (GFR) is the most important measure of renal function. The renal marker FITC-S, whose concentration can be determined transcutaneously and independently from the plasma/urine samples, provides new possibilities to perform more precise GFR measurements and real-time GFR monitoring.

In this study a novel closed loop regulated constant infusion clearance (CIC) system is described and evaluated in experiments with different animal models. The conventional gold standard of GFR measurement, the CIC method was improved, so that the changes in GFR could be monitored in real-time.

Each advance towards this goal was validated:

1. A miniaturized device was developed, allowing the determination of GFR non-invasively in freely moving rats with no need for blood sampling and laboratory assays. The real-time collected marker fluorescence signal provides precise GFR bolus clearance assessment and important parameters for two-compartment modeling.

2. The pharmacokinetic process of FITC-S distribution and excretion was investigated by simulations of two-compartment modeling according to the parameters acquired from the bolus clearance results and phantom tests. This reveals the necessity of the steady-state monitoring during CIC procedures.

3. A closed loop regulated CIC system was developed so that the steady state condition could be reached and maintained independent of GFR level. The steady state condition can be monitored for hours during which GFR can be determined by a single blood sample.

The developed closed loop regulated CIC system allows real-time GFR monitoring. In animal models (*e.g.* renal ischemia and norepinephrine-induced hyperfiltration) the change of GFR can be detected in real-time, whereas a new steady state is reached within 20 min after renal ischemia. In long-term regulated CIC experiments, the measurement is valid as long as steady state can be maintained.

In conclusion the novel closed loop system could keep the steady state condition of the fluorescence marker FITC-S autonomously constant and the acute changes in GFR could be monitored in real-time. This is a powerful tool in the research of acute renal injury and it provides rapid evaluation of nephrotoxicity in early screening of drug candidates in pharmaceutical industry.