IR spectroscopy goes to the hospital: Progress in reagent-free blood analysis and haemodialysis monitoring

Andreas Roth, Fabian Dornuf, Oliver Klein and Werner Mäntele

Institut für Biophysik, Goethe-Universität Frankfurt am Main
Max-von-Laue-Straße 1, D-60438 Frankfurt am Main

In clinical routine, analysis of body fluids is performed either by automated laboratory analysis using chemical and biochemical reagents or, in point-of care situations, by test kits. Either analysis bears disadvantages such as unnecessary time delays, imprecise measurements or high costs. Over the past years, we have been developing infrared spectroscopic techniques using either FT-IR spectroscopy or IR spectroscopy with fixed-frequency or widely tuneable quantum cascade IR lasers (QCL). We use attenuated total reflection (ATR) spectroscopy because of the easy accessibility of the sample interface and the easy handling of samples in clinical routine. In particular, new miniature ATR units with ZnS or ZnSe internal reflection elements (IRE) have been developed, either for small (some µl) sample volumes (such as a blood droplet) or as special high-flow® cells for haemodialysis. As a basis for calibration, we use clinical reference analysis with optimized methods. Multivariate methods are used to determine quantitatively the concentrations of body fluid constituents from the IR spectra [1].

In blood analysis, our present data base including >1.500 full blood and blood plasma samples reliably allows to analyze small (approx. 5-10 µl) full blood samples. A combination of the ATR cell with an ultrasound device allows *in situ* haemolysis and thus prevents the sedimentation of cells on the horizontal IRE. At present, the concentration of glucose, urea, triglycerides, cholesterol and of total protein as well as haemoglobin, albumin and immunoglobulin can be quantitatively analyzed, all of them (except immunoglobulin) at clinically sufficient precision. We report tests of this *point-of-care* analysis under clinical conditions.

In haemodialysis, no control of detoxification is presently available although highly desirable. An *online clearance measurement* is regularly required to validate the efficiency of hemodialysis for each patient. Furthermore, unstable haemodialysis patients need precise supervision of potential loss of blood constituents or medication. We have thus developed an FT-IR based haemodialysis monitoring system based on a novel high-flow® ATR cell which is connected downstream of the haemodialysis filter. During a 4 hour haemodialysis session, up to 180 l of dialysis liquid are used which contains electrolytes and buffer solutions as well as a base level of glucose. A calibration model was established from samples taken from the dialysis liquid near the flow ATR cell and analyzed by calibrated chemical analysis. This model was developed to tolerate fluctuations in buffer concentrations and was optimized for the quantitative determination of urea as the lead substance, as well as glucose, lactate and creatinine, all at a precision only limited by the chemical reference analysis [2].

We report here the first reagent-free, real-time and in-line monitoring of haemodialysis patients by FT-IR spectroscopy. Tests with haemodialysis patients demonstrate that detoxification can be clearly monitored, and that dialysis times based on detoxification monitoring can be adapted to the individual patient, thus resulting in shorter dialysis sessions and more efficient use of dialysis machines. Furthermore, these experiments demonstrate that a wide control of the patient physiological parameters is possible with this method, which leads to an enhancement of patient safety.

References

[1] G. Hosafci, O. Klein, G. Oremek and W. Mäntele, *Anal. Bioanal. Chem.* 387, 1815-1822 (2007)
[2] A. Roth, F. Dornuf, O. Klein, D. Schneditz and W. Mäntele (2011) *Anal. Bioanal. Chem., submitted*