
AUTOMATED PROCESSING OF WHOLE BLOOD SAMPLES FOR LC-MS/MS ANALYSIS OF SMALL MOLECULES

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LC-MS analysis of drugs, xenobiotics and endogenous small molecules in dried blood spots (DBS) instead of blood plasma or serum specimens becomes increasingly attractive in pharmaceutical and clinical-chemical analysis. A prominent example is the screening of newborns for inborn metabolic disorders. This approach, however, has significant drawbacks such as multiple, mainly manual sample handling steps, semiquantitative results, poor reproducibility, dependence on hematocrit and risk of infection. Recently, we described a method which allows – for the first time – a fully automated in-line processing of whole blood [1].

Thereby, anticoagulated whole blood sample is mixed and injected into and pumped through a heated stainless-steel LC-capillary. This heat-shock treatment causes the disintegration of cellular blood components such as erythrocytes. The resulting microvesicles do not sediment and do not clog conventional LC-tubings and column sealings. Thus, the so called cell-disintegrated blood (CDB) can be further processed on-line by, for example Solid Phase Extraction (SPE). In addition, our method also allows – for the first time – on-line SPE of the supernatant (e.g. plasma) of the same – but sedimented – blood sample.

We set-up and investigated such a SPE-LC-MS/MS platform for the analysis of model compounds bound predominantly to plasma proteins (antimycotics) and erythrocytes (immunosuppressants) respectively. We could demonstrate that the results obtained with our fully automated method compare very good with established procedures relying on manually performed blood/plasma protein precipitation (MeOH/ZnSO₄) step prior to SPE.

[1] R. Morello, J. Milojkovic, K.-S. Boos, *Therap. Drug Monit.* **2007**, *29*, 5005

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