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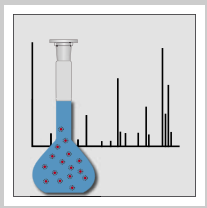

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A Novel Tube-based Format for Dried Blood Spots Integrating Sample Collection and Sample Preparation

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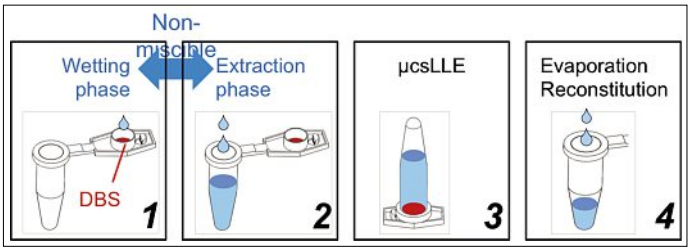
Dried blood spots (DBS) are a convenient way to collect and to store small-volume blood samples. Typically, after finger pricking, a few droplets of blood are deposited onto dedicated paper cards and allowed to dry. The benefits rely especially in an easy and cheap sample storage (under ambient conditions) and shipment (in a standard envelope) and in reduced biohazard risks. DBS have been applied recently to the quantitation of drugs and metabolites for therapeutic drug monitoring and drug development. Whereas modern bioanalytics relies on the handling of liquid samples (*e.g.* in tubes) for liquid chromatography–mass spectrometry (LC–MS) analysis, DBS cards represent a sample format in the solid state, thus less compatible with the usual bioanalytical workflow. The standard approach is to punch a small DBS disk from the paper card into a tube, and analytes are extracted with the addition of an appropriate solvent.

To retain all the inherent advantages of DBS and to better match the sample collection format with the sample handling/preparation format, an alternative tube-based format was introduced, whose design consists in a tube with a paper disk immobilized in the lid for sample collection. The extraction can be then performed directly in the device by adding the extraction solvent into the tube (solid–liquid extraction, SLE).



DBS tube-based format and micro cellulose-supported liquid-liquid extraction (µcsLLE).

In addition, a new sample preparation strategy specific to this format can be used, namely micro cellulose-supported liquid–liquid extraction (µcsLLE). Its concept consists in the wetting of the paper disk in the lid with an aqueous-based solvent (wetting phase), while a non-miscible, organic extraction solvent is added in the tube (extraction phase). After closing the tube, the sample is extracted under sonication upside-down. Then the extraction phase containing the analytes is easily separated from the paper patch by simply opening the tube. The extracts have shown to contain fewer endogenous blood interferences (especially phospholipids) and to generate fewer matrix effects. **Finally, this integrated device has been demonstrated as a suitable format for quantitative analysis in dried plasma and blood spots.**

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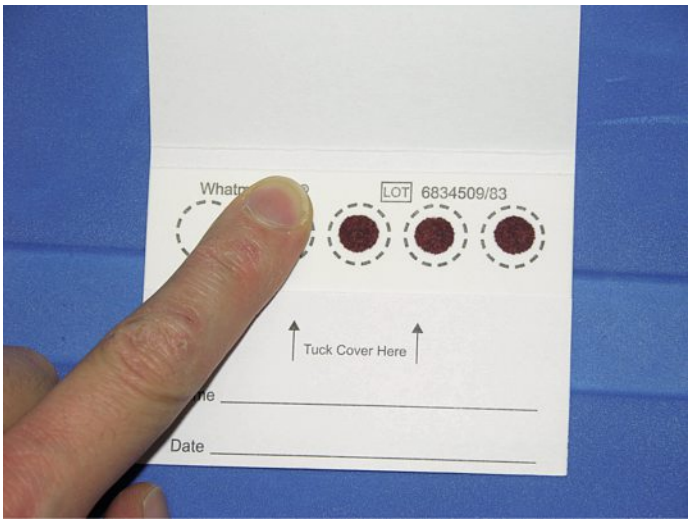
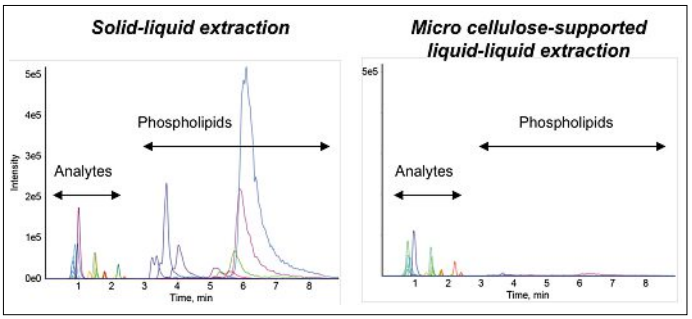
Reference

M. Wagner, E. Varesio, G. Hopfgartner, priority application number EP 11153161.2 (filed on Feb 3rd, **2011**, European Patent Office).



DBS in the card format.



LC-MS analysis illustrating analyte extraction from DBS in the tube format and concomitant sample clean-up (phospholipid removal). Analytes consisted of 18 representative substances (amphetamines, cocaine and metabolites, benzodiazepines, tricyclic antidepressants and antiretroviral drugs).

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