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Carbamazepine, lamotrigine, levetiracetam and valproic acid in dried blood spots with liquid chromatography tandem mass spectrometry; method development and validation.

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Highlights

- An LC-MS/MS dried blood spot method for common antiepileptic drugs was validated.
- 96-well format, automatic punching and barcode reading for improved workflow.
- The method is accurate in a hematocrit range of 0.35 to 0.50 L/L.
- Unknown blood volumes between 15 and 50 µL can be measured with bias within ±10%.
- Stability tests showed that DBS shipping and storage for these drugs were robust.

Abstract:

Monitoring of antiepileptic drugs in children with epilepsy require multiple visits at a clinic for blood collection. Dried blood spot sampling is an alternative way of collection, performed at home by self-collection and can save time and costs for patients and family members. The aim was to develop and validate an LC-MS/MS dried blood spot method for carbamazepine, lamotrigine, levetiracetam and valproic acid with the requirements of using standard equipment and material in a routine laboratory setting.

Whatman-903 filter paper was utilized, and discs were punched into a 96 well plate with an automated puncher and barcode reading. Extraction with methanol/water solution including internal standards on an orbital shaker was followed by a vacuum centrifuge step and reconstitution in mobile phase. Bioanalytical validation was performed according to guidelines from European Medicines Agency and additional dried blood spot specific validation.