

Characteristics of new TDM assays, described in literature, based on dried blood spot methods

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We have published a review article about TDM assays based on the dried blood spot method (DBS), earlier in June 2009 [1]. Now we present an update of TDM assays based on DBS methods, which have been recently published.

<i>Medicine</i>	<i>Analytical technique/Limit of quantitation (LOQ) /assay range</i>	<i>Patient sampling (A = drop of blood directly on paper; B = blood sample pipetted on paper); Extraction of reference standards</i>	<i>Analytical validation</i>	<i>Clinical validation</i>	<i>Stability of dried blood spot</i>
Actinomycine D, Damen C et al 2009 ²	HPLC-MS/MS, LOQ : NR, assay range suitable	Method A; 40 µl whole blood pipetted on Whatman 903 paper, a 0.25 inch punch. Extraction with 0.1 ml acetonitrile/methanol/water 1:1:1. Recovery: 80%	Analytical validation adequate. Interassay precision 6.8-12%. Accuracy 92-106%. Ion suppression observed.	No clinical validation of actinomycin	Dried blood spots stable 3 months at room temperature and at 40-45°C.
Canrenone, Suyagh M et al 2010 ³	HPLC-MS/MS, LOQ : 25 ng/ml, assay range suitable	Method A; 30 µl of whole blood pipetted onto a Guthrie card, 6-mm Ø punch; extraction with 2 ml methanol. Recovery 82.9-114.2 %	Analytical validation adequate; inter-assay precision 3.46-7.78% and accuracy 92.5-104.8%. No ion suppression	Limited clinical validation by application of the method to 160 DBS samples of 37 neonates	No deterioration was found with DBS quality samples at RT for one month.

			measured.		
Cyclosporin, Wilhelm A et al 2009 ⁴	HPLC-MS/MS ; LOQ 25 µg/l, assay range suitable	Method A; 50 µl of whole blood pipetted on Whatman 903 paper. 8 Ø punch; extraction with 300 µl methanol/water 1:1; recovery 97%	Analytical validation adequate; Inter-assay precision 2.9-15%; accuracy 88-101%. No ion suppression measured.	No clinical validation	Spiked DBS reference standards were stable for 17 days at RT and 45 days at 4°C.
Fluoxetine + norfluoxetine, Deglon J et al ⁵	GLS-MS/MS; LOQ: 1 ng/ml. assay range suitable	Method B; 10 µl whole blood pipetted on STS 105355097. Whole spot punched out. Derivatisation with pentafluoropropionacidanhydride. Recovery: 60-89%.	Analytical validation adequate. Inter-assay precision 4.6-11.9% and accuracy 96.2-111.2 %. No ion suppression measured.	Limited clinical validation. Concentration time curve of one volunteer.	Good stability during 20 days from -20°C up to +40°C.
Metronidazol, Suyagh M et al 2010 ⁶	HPLC-UV; LOQ: 1.8 µg/ml. Assay range suitable	Patient method A; 30 µl whole blood pipetted on S&S 903. Extraction with 1 ml water. Recovery 78-80%	Analytical validation adequate. Inter-assay precision 1.4-3.1%. Accuracy 98.7-104%	Limited clinical validation. Method used in pharmacokinetic study. Results not shown.	Spiked DBS samples were stable for 28 days at -20°C.
Mycophenolic acid, Wilhelm A et al 2009 ⁷	HPLC-UV, LOQ: 0.74 mg/l. Assay range suitable	Patient method A. 50 µl whole blood pipetted on Whatman 903. Extraction with 0.25 ml methanol. Recovery 95.2%	Analytical validation adequate. Inter-assay-precision 4.9-7%; Accuracy 88.8-102.3%	No clinical validation	Spiked DBS reference and quality standards were stable for 26 days at 4°C.

Paroxetine, Deglon J et al 2010 ⁵	See fluoxetine, LOQ 20 ng/ml				
Reboxetine, Deglon J et al 2010 ⁵	See fluoxetine. LOQ 20 ng/ml				
Vincristine, Damen C et al 2009 ²	See actinomycine	Recovery about 100%	Inter-assay precision 9.4- 15.4%. Accuracy 102.6-108%		

HPLC, high performance liquid chromatograph; HPLC-MS, high performance liquid chromatography-mass spectrometry; HPLC-MS/MS, high performance liquid chromatography –tandem-mass spectrometry; LOQ, Limit of Quantitation; VC, variation coefficient.

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