

Background & Aims

Recently, growing attention has emerged for microsampling techniques as alternative to dried blood samples (DBS) for therapeutic drug monitoring (TDM). Volumetric Absorptive Microsampling (VAMS), called Mitra® (Neoteryx), are devices consisting of porous absorbent tips that allow collection of few blood volumes (~10 µl) overcoming the hematocrit effect (1). So far, Mitra® have been used in several pharmacokinetic studies (2-5). Here, we have compared plasma concentrations of three antifungal agents (Voriconazole, Posaconazole and Isavuconazole) to dried plasma spot (DPS) and Mitra®.

50 samples of plasma, DPS and Mitra® were obtained from pediatric patients hospitalized in our Centre. Mitra® were collected by dipping tips into whole blood before centrifugation for plasma recovery. Antifungal concentrations were measured by using a validated LC-MS/MS kit (MassTox® Antimycotic Drugs/EXTENDED) provided by Chromsystems (Chromsystems Instruments & Chemicals), on a Waters XEVO® TQ-S micro Triple Quadrupole Mass Spectrometry.

Methods



DPS, dried plasma spot

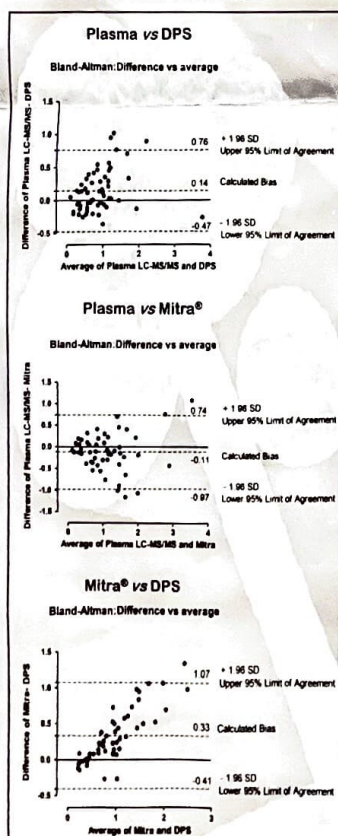


Mitra® micro-sampling device

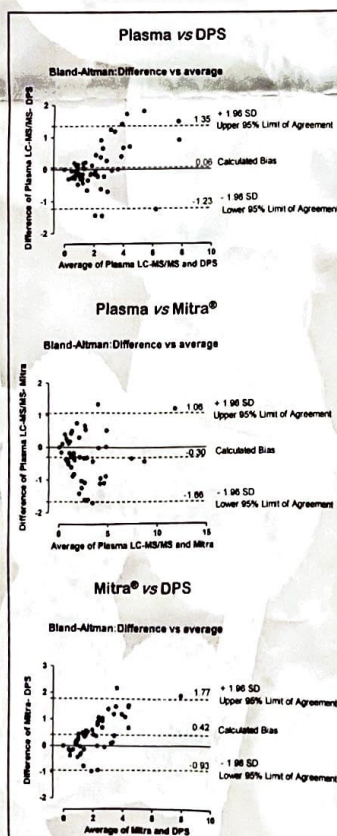


XEVO® TQ-S micro Triple Quadrupole Mass Spectrometry

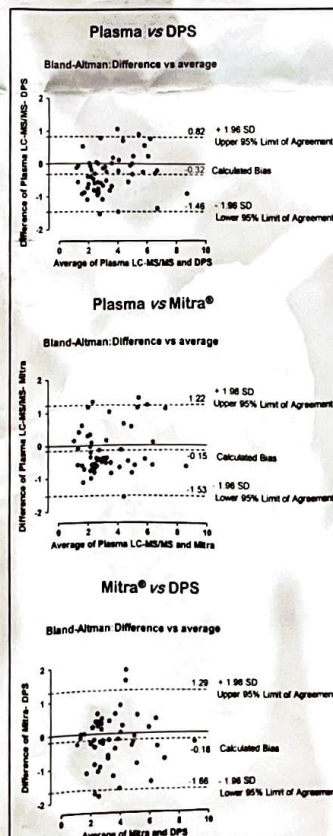
POSACONAZOLE



VORICONAZOLE



ISAVUCONAZOLE



Results

A positive correlation was found for Posaconazole plasma vs DPS (Spearman $r=0.82$, $p<0.001$). Bland-Altman test gave a bias of 0.14. A similar result was obtained for Posaconazole plasma vs Mitra® (Spearman $r=0.84$, $p<0.001$) while bias was -0.11. Correlation of Voriconazole plasma vs DPS produced a Spearman r of 0.94 ($p<0.001$) and a bias of 0.06. A positive correlation was observed for Voriconazole Mitra® ($r=0.91$, $p<0.001$) with a bias of -0.30. Isavuconazole correlations gave for DPS $r=0.93$ ($p<0.001$) and Mitra® $r=0.88$ ($p<0.001$). A bias of -0.32 and -0.15 were observed for DPS and Mitra®, respectively.

Conclusions

Our results demonstrate that DPS and Mitra® could be used as alternative to CVC (central venous catheter) blood drawing for TDM of antifungal agents. However, Mitra® do not require plasma recovery and could be suitable for pediatric and neonatal settings where compliance, ethical and physiological concerns limit large volumes drawing. Further studies are needed to confirm these results by collecting blood with Mitra® after finger or heel prick.

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2) Sciberras D, Otoul C, Lurquin F, Smeraglia J, Lappert A, De Bruyn S, Jaap van Lier J. A pharmacokinetic study of rasiprodil oral suspension in healthy adults comparing conventional venous blood sampling with two microsampling techniques. *Pharmacol Res Perspect.* 2019 Jan 28;7(1):e00459. doi: 10.1002/prp2.459. PMID: 30705758; PMCID: PMC6349788.
3) Schulz JD, Neodo A, Coulbaly JT, Kaiser J. Pharmacokinetics of Albendazole, Albendazole Sulfonate, and Albendazole Sulfonate Determined from Plasma, Blood, Dried-Blood Spots, and Mitra Samples of Hookworm-Infected Adolescents. *Antimicrob Agents Chemother.* 2019 Mar 27;63(4):e02489-18. doi: 10.1128/AAC.02489-18. PMID: 30745388; PMCID: PMC6437472.
4) Velghe, S., Stove, C.P. Volumetric absorptive microsampling as an alternative tool for therapeutic drug monitoring of first-generation anti-epileptic drugs. *Anal Bioanal Chem* 410, 2331–2341 (2018).
5) D'Urso A, Rudge J, Patsalos PN, de Grazia U. Volumetric Absorptive Microsampling: A New Sampling Tool for Therapeutic Drug Monitoring of Antiepileptic Drugs. *Ther Drug Monit.* 2019 Oct;41(5):681–692. doi: 10.1097/FTD.0000000000000652. PMID: 31095069.