Micro-device integrated platforms for Point-Of-Care Therapeutic Drug Monitoring

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Therapeutic Drug Monitoring (TDM) allows personalized treatment for diseases where continuous control of drug dosage is required in order to avoid adverse effects. Currently, this process is demanding for the patient, costly and time consuming. For this reason, single-step whole blood tests are desirable as they eliminate analytical errors arising from the complex process of sample preparation (i.e. transportation of the sample, centrifugation, dilution, extraction).To address this issue, we introduce the ability of paper-like membranes to run quantitatively clinical chemistry using Fluorescence Polarization Immunoassay (FPIA) as tool for direct quantification of small molecules in whole blood. Even though paper is extensively used in diagnostic tests[1], the direct quantification of small drugs combined with sample preparation is still limited. Moreover, optical techniques, especially Fluorescence Polarization (FP) have not been associated with paper mainly due to the intrinsic fluorescent background. In our case, the feasibility of such measurement, directly within paper is given by using a near infrared-fluorescent (NIR) labeling, which has low interference with whole blood sample and with the paper itself while the competition was investigated within the reservoirs created by the paper-based microstructures. Our approach showed good analytical performance for Tobramycin a small molecule antibiotic, with a limit of detection and limit of quantification of 0.2 and 0.6 µg/mL, respectively. To further test the assay with reduced and simplified sample pre-processing for Tobramycin, a miniaturized FP analytical demonstrator was designed. The measurements were performed within glass capillaries with a 300 µm diameter while preserving the analytical performance (Fig. 1).

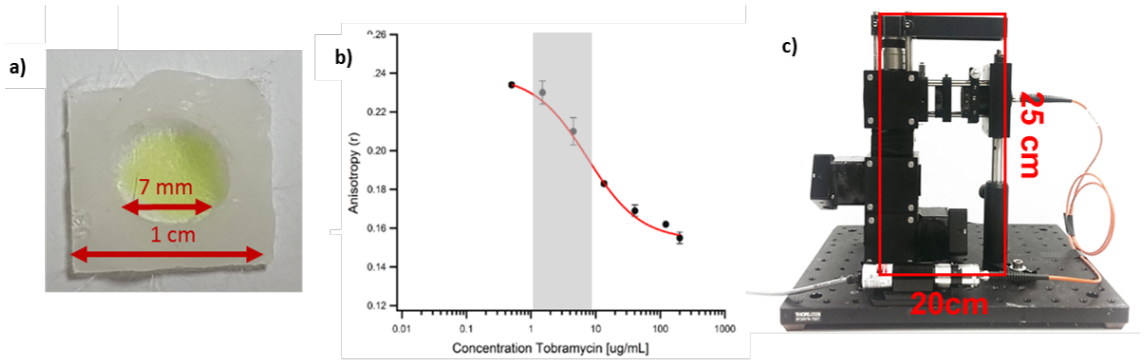

Fig. 1: Whole blood filtration and quantification of Tobramycin through FPIA: a) the design of paper-based microchamber for drug analysis; b) FPIA dose-response curves within paper were performed during three consecutive days: Tobramycin quantification in whole blood showed good stability and reproducibility between measurements with a mean Coefficient of Variation (CV) of 30%; c) a miniaturized optical analytical device for drug quantification.

(1) Yetisen, A. K.; Akram, M. S.; Lowe, C. R. *Lab Chip* **2013**, *13* (12), 2210–2251.