A microfluidic platform for the rapid determination of distribution coefficients by gravity assisted droplet-based liquid-liquid extraction

The determination of pharmacokinetic properties of drugs, such as the distribution coefficient, $D$, is a crucial measurement in pharmaceutical research. Surprisingly, the conventional (gold standard) technique used for $D$ measurements, the shake-flask method, is antiquated and unsuitable for the testing of valuable and scarce drug candidates. Herein we present a simple microfluidic platform for the determination of distribution coefficients using droplet-based liquid-liquid extraction. For simplicity, this platform makes use of gravity to enable phase separation for analysis and is 48 times faster and uses 99% less reagents than performing an equivalent measurement using the shake-flask method. Furthermore, the $D$ measurements achieved in our platform are in good agreement with literature values measured using traditional shake-flask techniques. Since $D$ is affected by volume ratios, we use the apparent acid dissociation constant, $pK'$, as a proxy for inter-system comparison. Our platform determines a $pK'$ value of 7.24 ± 0.15, compared to 7.25 ± 0.58 for the shake-flask method in our hands and 7.21 for the shake-flask method in literature. Devices are fabricated using injection moulding, the batch-wise fabrication time is less than 2 minutes per device (at a cost of 1 USD per device) and the inter-device reproducibility is high.

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