Simple micro-extraction procedures have been used in our laboratory for the analysis of lipophilic drugs and metabolites in plasma for many years [1]. A large excess of solvent is often unnecessary. Butyl acetate [2] and methyl tert-butyl ether (MTBE) [3] give efficient extraction of many drugs and metabolites from plasma at an appropriate pH, and form the upper layer thus simplifying extract removal. These solvents are cheap, available with high purity, and do not interfere in NPD, ECD, or MS. HPLC eluents that use a high proportion of an organic component [4] also allow MTBE extracts to be analysed directly (MTBE has a relatively low UV cutoff, 215 nm). Unlike some other ethers, MTBE does not form peroxides at ambient temperature and thus stabilisers are unnecessary.

A well defined LLE system is robust and cost-effective. Appropriate repeating dispensers are used for solvent and reagent additions. Use of clear glass test-tubes (60 x 5 mm i.d., Dreyer tubes) rather than plastic tubes as extraction vessels simplifies extract removal via a syringe or fine-tipped plastic Pasteur pipette and minimises the risk of contamination with the aqueous phase. Of the mixing methods available, vortex-mixing is the quickest and the most efficient method for relatively small volumes (50-200 µL) and is safe if performed in a fume hood or safety cabinet. Use of an appropriate centrifuge with sealed rotors can give relatively small volumes (50-200 µL) and is safe if not form peroxides at ambient temperature and thus stabilisers are unnecessary.

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