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ABSTRACT

A specific and sensitive capillary liquid chromatography-ultraviolet detection (cap-LC-UV) method in combination with a micro-extraction by packed sorbent (MEPS) sample clean-up procedure has been developed and validated for the simultaneous analysis of chlorpromazine, olanzapine and their flavin-containing monooxygenase (FMO) mediated N-oxides in rat brain microdialysates. Chromatographic separation was obtained on an Acclaim Pepmap RP C18 column with an ID of 300 µm. An injection volume of 20 µL was used to inject the largely aqueous samples and was shown to have no influence on the obtained peak shape of the compounds of interest. Optimal conditions for MEPS extraction were obtained on a mixed-mode M1 (80% C8, 20% SCX) cartridge after diluting microdialysate samples with phosphate buffer pH 2.5 (1:3 v/v). The method was validated and lower limits of quantification (LLOQ) were determined at 0.5 nM for all compounds. Linearity was demonstrated between the LLOQ and 1 µM for all compounds (R^2 > 0.995). MEPS recoveries were between 92 and 98%, with intra- and interday variabilities below 15%. The applicability of the developed method was successfully demonstrated by analysing rat brain microdialysates. The capillary LC-UV method in combination with MEPS sample treatment provides a simple, sensitive method to quantify all compounds of interest in 45 min and can be applied for routine therapeutic monitoring and pharmacokinetic studies of olanzapine, chlorpromazine and their respective N-oxides.

Keywords: Olanzapine; Chlorpromazine; FMO; Capillary LC; microdialysis; MEPS