J. Pharm. Pharmacol. 1998, 50 (Supplement): 116

Determination of carbamazepine in plasma, urine and formulations by HPLC

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The aim of the present study was to develop and validate an HPLC method for the determination of concentration of carbamazepine (CBZ) in plasma and urine samples in presence of metabolites, as well as in formulations. The Waters chromatographic system consisting of two 510 pumps, 717 autosampler, 486 tunable UV/VIS detector and Nova Pak C18 column was used. Potassium phosphate buffer (0.01M, pH-7.0)-acetonitrile-methanol (11:5:3 v/v) was used as the mobile phase and detection wavelength was 214 nm. The drug contents were estimated using this method in marketed formulations and also *in vivo* studies were performed in Sprague Dawley rats to estimate the drug contents in the plasma samples. Spiked human urine was used for drug analysis. Naloxone was used as an internal standard (IS) for plasma samples whereas, ibuprofen was used as IS for formulations. An attempt was also made to use the autoanalyzer (Schiapparelli Ace™) to quantify the CBZ concentrations in the presence of its metabolites in rat plasma. After checking the stability of stock solutions, selectivity, sensitivity, accuracy and precision of the proposed method, Calibration graphs were constructed for CBZ in pure solutions, as well as in plasma and urine. The calibration curve was linear in the concentration range of 4-20 μg/ml for pure drug, 1-12 μg/ml for plasma and 2-20 μg/ml for urine. The correlation coefficients were always > 0.990. The method was successfully applied to three different solid dosage forms available in the local market, as well as to plasma and urine samples. The concentrations obtained by autoanalyzer were always, 2-3 μg, less than that of obtained by HPLC. One of the reasons for observing lower concentrations of CBZ may be due to rat plasma, as the autoanalyzer is always calibrated with respect to human plasma. CBZ analysis by autoanalyzer (Ace™ kit) in any other biological matrix other than human serum is yet to be established. However, when pure CBZ was simultaneously analyzed by HPLC and autoanalyzer, there were no significant differences found. The present assay is sensitive and operationally simple to use to quantify CBZ in presence of metabolites. It requires a one step extraction procedure and a chromatography run time is less than 15 min. for biological samples, where as for drug analysis in the formulations the run time was about 10 min. The method is found to be sensitive to at least 400 ng/ml of CBZ.

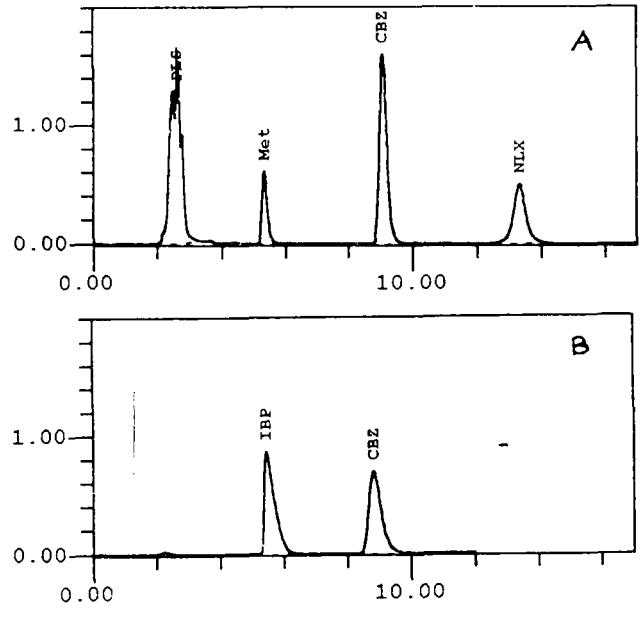

Figure 1. Chromatogram showing baseline separations of Carbamazepine (CBZ) and Naloxone (NLX) in the preseence of its metabolite: *in-vivo* studies [A]; CBZ and Ibuprofen (IBP) [B].