CHROMATOGRAPHIC ANALYSIS OF LISINOPRIL, HYDROCHLOROTHIAZIDE AND THEIR IMPURITIES IN TABLETS

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Evaluation of impurity level in pharmaceutical dosage forms is a very important in pharmaceutical analysis. Usually, concentration of impurities in dosage forms is on very low level, so the method for their analysis must be enough sensitive and selective. In this paper, lisinopril dihidrat (L) and its impurity diketopiperazine (DKP), hydrochlorothiazide (HTZ) and its two impurities (chlorothiazide (CHTZ) and disulfamamide (DSA) were analysed employing a reverse–phase High–performance Liquid Chromatographic method (RP–HPLC) with UV detection. Till now, authors didn't found any published articles regarding analysis L and HTZ in mixture, only particular compounds or mixture with some drugs were investigated [1–4]. The chromatographic system Hewlett Packard 1100 was used. Acceptable chromatographic behavior of the investigated mixture was achieved on Zorbax Extend C–18 column (150 x 4.6 mm, 5 µm particle size). Detection was performed at 215 nm. The critical pairs in separation were L and DSA, DSA and CHTZ. Comparing to other four compounds which were eluted in 5 min., under the same chromatographic conditions DKP, was retained for almost 40 min. Each changes in composition of the mobile phase did not gave possibility for isocratic elution, so gradient elution was established. Mobile phase was acetonitrile–water phase (12:88 v/v for A pump and 50:50 v/v for B pump). Water phase was consisted of 50 mM/L potassium dyhidrogenhosphat pH 5.0. As internal standard (IS) cilazapril was choses. Under this conditions, retention times were 2.39 min. (L), 4.54 min. (DSA), 5.19 min. (CHTZ), 6.51 min. (HTZ), 15.46 min. (IS) and 19.50 min. (DKP). The developed method was then subjected to method validation, e.g. selectivity, linearity, precision, accuracy, limit of quantification (LOQ) and limit of detection (LOD) was determined.