Stability-indicating RP-LC method for determination of azilsartan medoxomil and chlorthalidone in pharmaceutical dosage forms: application to degradation kinetics

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Abstract

A RP-LC method was developed and validated for simultaneous determination of the active components, azilsartan medoxomil (AZL) and chlorthalidone (CLT), in their novel antihypertensive combined recipe. The chromatographic separation was achieved on an Eclipse XDB-C18 (4.6ĭ150 mm, 5 εm) column using a mobile phase consisting of methanol/potassium hydrogen phosphate buffer (pH 8, 0.05 M) (40:60, v/v) in isocratic mode. The flow rate was maintained at 0.8 mL minī1 at ambient temperature. Detection was carried out at 210 nm. The method was validated according to the ICH guidelines. Linearity, accuracy, and precision were satisfactory over the concentration range of 5.0ï50.0 and 2.5ï25.0 εg mLī1 for AZL and CLT, respectively (r 2=0.9999). LODs for AZL and CLT were 0.90 and 0.32 εg mLī1, whereas LOQs were 2.72 and 0.98 εg mLī1, respectively. Both drugs were subjected to forced degradation studies under hydrolysis (neutral, acidic, and alkaline), oxidative, and photolytic extensive stress conditions. The proposed method is stability indicating by the resolution of the investigated drugs from their degradation products. Moreover, the kinetics of the acidic degradation of AZL as well as the kinetics of the alkaline degradation of CLT were investigated. Arrhenius plots were constructed and the apparent first-order rate constants, half-life times, shelf-life times, and the activation energies of the degradation processes were calculated. The method was successfully applied for the determination of the studied drugs simultaneously in their coformulated tablet. The developed method is specific and stability indicating for the quality control and routine analysis of the cited medications in their pharmaceutical preparations

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