Validated stability-indicating chromatographic methods for the determination of chlordiazepoxide and clidinium bromide in the presence of its alkali-induced degradation product.

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Abstract

Accurate, simple and selective stability-indicating reversed phase HPLC and TLC-densitometric methods with UV detection have been developed and validated for simultaneous determination of chlordiazepoxide (CDZ) and clidinium bromide (CDB) in the presence of its alkali-induced degradation product (DEG). Successful separation of the drugs from the degradation product was achieved. For the RP-HPLC method, the stationary phase was ACE-126-2546 AQ C-18 (250 Ĭ 4.6 mm i.d., 5µm particle size) column at 25 ÁC, in an isocratic mode, using mobile phase containing a mixture of 25 mM ammonium acetate (pH 5.4): acetonitrile in the ratio of (20:80, v/v), at the flow rate of 1.0 mL min−1 and UV detection was performed at 222 nm. The retention times were (4.13 Ñ 0.01) and (8.5 Ñ 0.01) min for CDZ and CDB, respectively. For the TLC-densitometric method, the separation was performed using a stationary phase of precoated Silica Gel G/UV254 and mobile phase composed of a mixture of ethyl acetate: methanol: ammonia (8:3:1, v/v/v) and scanned at 222 nm. The R f values were (0.79 Ñ 0.02) and (0.11 Ñ 0.01) for CDZ and CDB, respectively. The linearity graphs for CDZ and CDB, respectively, were found to be linear over (0.5–40) µg mL−1 and (2–45) µg mL−1 with mean percentage recoveries (99.69 Ñ 0.836) and (99.28 Ñ 1.838) for RP-HPLC method and (1–14) µg band−1 and (0.5–10) µg band−1 with mean percentage recoveries (100.00 Ñ 0.782) and (100.19 Ñ 1.010) for TLC-densitometric method. A comparative study of different analytical validation parameters such as accuracy, precision, specificity and robustness were conducted. The obtained results were statistically compared with those of the official and reported methods; using Studentôs t test, F test and one-way ANOVA, showing no significant difference with high accuracy and good precision. The proposed RP-HPLC method was also used to study the kinetics of the alkaline hydrolysis of clidinium bromide that was found to follow pseudo-first order kinetics. The t 1/2 was 8.5729 min while k (the degradation rate constant) was 0.0808353 min−1.

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