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Bioequivalence Study of two Atenolol / Chlorothalidone Fixed Combination Formulations

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INTRODUCTION

Atenolol is a selective (1-adrenoceptor antagonist and is well established as treatment for mild to moderate hypertension and stable angina pectoris. Chlorthalidone is a widely used diuretic which has been co-administered with atenolol for the treatment of hypertension.

The objective of this study was to evaluate the bioequivalence of a fixed combination (doses 100 mg atenolol and 25 mg chlorthalidone) in two different tablet formulations, a new formulation, Apress (100+25 mg and the innovators product Tenoretic (100+25 mg).

MATERIAL AND METHODS

The study was a two-way cross-over design, carried out in 12 healthy volunteers, dosed in the fasted state and the wash-out period was one week.

The plasma samples were collected up to 24 hours postdose. The determination of atenolol and chlorothalidone was performed by a validated new HPLC method.

Pharmacokinetic parameters for the atenolol and chlorothalidone were obtained using an independent pharmacokinetic analysis model.

RESULTS

Statistical analysis of the data showed that there were no significant differences between the two formulations: (R: innovator product), (T: the new formulation) with respect to $AUC_{0\rightarrow\infty}$, R=1355.53 ng(h/mL, T=1327.11 ng(h/mL and 1.02 T/R with 90% confidence interval 0.85, 1.21 T/R. Cmax: R=187.89 ng/mL; T=188.33 ng/mL and 1.015T/R and 90% confidence interval 0.91, 1.13 T/R, Tmax: R=1.50(0.56h; and T=1.61(0.49h and; 90% conf. int:-0.214, 0.425(T-R).

CONCLUSIONS

This study was conducted to evaluate the bioequivalence of Apress((100+25) mg/tablet (test formulation) to Tenoretic((100+25) mg/tablet (reference formulation).

The statistical analysis revealed that the 90% confidence intervals for the difference between the test and reference formulations of AUC_{∞}, AUC_t and Cmax parameters lie within the acceptance range for bioequivalence (0.80, 1.25). The non-parametric tests for Tmax indicated that there is no significant difference ($p \leq 0.005$) between the two formulations.

Hence these two formulations are bioequivalent with respect to both the rate and extent of availability of atenolol and chlorthalidone.