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Bioequivalence Study of two Captopril / Hydrochlorothiazide Fixed Combination Formulations

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INTRODUCTION

Captopril is a potent and specific ACE inhibitor and has been extensively used for the treatment of hypertension. However, co-administration of captopril with the diuretic hydrochlorothiazide enhances the anti-hypertensive effect of captopril and has been proved clinically effective for the treatment of hypertension.

The objective of this study was to evaluate the bioequivalence of a fixed combination (doses 50mg captopril and 25mg hydrochlorothiazide) in two different tablet formulations, a new formulation Zidepril® 50+25mg and the innovators product Superace(r) 50+25mg.

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 the free captopril and hydrochlorothiazide was performed by a validated new HPLC method.

Pharmacokinetic parameters for the free captopril and hydrochlorothiazide were derived using model independent pharmacokinetic analysis.

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 $AUC_{0-\infty}$: R=410.38 ng(h/mL; T=396.30 ng(h/mL and T/R =0.966 and 90% confidence intervals 0.929, 1.005 T/R; Tmax: R=0.6783±0.1732 h and T=0.7117±0.1781 h, 90% confidence intervals: -0.010, $0.100(T-R)^3$; Cmax: R=264.95 ng/mL; T=268.13 ng/mL and 90% confidence intervals 0.984, 1.039T/R.

CONCLUSIONS

This study was conducted to evaluate the bioequivalence of Zidepril((50/25) mg/tab (test formulation) to Superace((50/25) mg/tab (reference formulation).

The statistical analysis revealed that the 90% confidence intervals for the ratio of AUC_∞, AUC_t and Cmax values for the test relative to the reference formulations were completely lie within the acceptance range (0.80, 1.25); hence these two formulations are bioequivalent with respect to both the rate and extent of availability of captopril and hydrochlorothiazide.

Additionally, comparison of Tmax by non-parametric tests showed that the difference of the values of the two formulations also lie within the 90% interval of confidence for both components.

Apart from one incidence of mild headache and one incident of hypotension the dosage of 50 mg captopril + 25mg hydrochlorothiazide was safe and well tolerated.