Drug interchangeability of generic and brand products of fixed dose combination tablets of sofosbuvir and ledipasvir (400/90 mg): Employment of reference scaled average bioequivalence study on healthy egyptian volunteers

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Abstract

Background and Objectives

The purpose of this study was to apply the reference-scaled average bioequivalence (RSABE) approach to evaluate the bioequivalence and to investigate the pharmacokinetic properties of two formulations of fixed dose combination (FDC) tablet of sofosbuvir (SOF) and ledipasvir (LED) (400/90 mg) in 36 healthy Egyptian volunteers.

Methods

The study was performed in single-dose, randomized-sequence, open-label, reference-replicated, 3-period crossover design (RTR, TRR, RRT), with a washout period of 2 weeks. A rapid and simple LCïMS/MS method was developed and validated for the simultaneous estimation of SOF and LED using eplerenone as an internal standard (IS).

Results

The results showed that the 90% confidence intervals (CIs) for natural log-transformed ratios of Cmax, AUClast and AUCÐ of SOF (89.95ï115.31, 98.77ï109.75 and 98.79ï109.75) were within the RSABE acceptance limits. The 90% CIs for natural log-transformed ratios of Cmax and AUClast of LED (87.33ï115.15 and 83.82ï112.26) were within the FDA bioequivalence limits (80.00ï125.00). In addition, the in vitro dissolution study was done and both formulations released > 85% of drug within 15 min in the proposed dissolution medium.

Conclusions

In conclusion, bioequivalence between the two fixed-dose combination products was demonstrated for both active ingredients.

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