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Bioequivalence Evaluation of two Tablet Formulations of Isosorbide 5-Mononitrate after Single Oral Administration in Healthy Volunteers

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OBJECTIVE

The objective of this study was to compare the bioavailability of a generic isosorbide 5-mononitrate 20 mg tablet (Monosordil® as the test preparation) with a commercially available 20 mg tablet (Isomon® as the reference preparation) in healthy volunteers, under fasting conditions.

METHODS

The study design was an open-label, randomized, single dose, two treatment, two period, two sequence cross-over design to 14 healthy volunteers with a washout period of seven days, under fasting conditions. Serial blood samples were collected prior to each administration and at 17 points within 36 hours after dosing. Plasma concentrations of isosorbide 5-mononitrate were measured by a validated Gas Chromatographic assay. The pharmacokinetic parameters used to assess the bioequivalence of the two preparations were $AUC_{0-\infty}$ and AUC_{0-t} for the extent of absorption and C_{MAX} and T_{max} for the rate of absorption. Statistical comparisons of $AUC_{0-\infty}$, AUC_{0-t}, and C_{max} data, after logarithmic transformation were evaluated by two-way repeated-measures analysis of variance (ANOVA) and differences of T_{MAX} were performed nonparametrically. This study was conducted according to the principles of the revised World Medical Association Declaration of Helsinki and the corresponding recommendations of Good Clinical Practice and Good Laboratory Practice.

RESULTS

The parametric 90% confidence intervals of the geometric mean values of the test/reference ratios were 92.4% to 104.0% (point estimate; 98.0%) for $AUC_{0-\infty}$, 93.3% to 105.0% (point estimate: 99.0%) for AUC_{0-t}, and 864.4% to 107.8% (point estimate; 96.5%) for C_{max} within the acceptance criteria for bioequivalence (80-125%). No statistically significant difference was found for T_{max} elimination half-life and MRT values.

CONCLUSION

In accordance with the European Union requirements it is concluded that the test and reference isosorbide 5-mononitrate preparations are bioequivalent for both the extent and the rate of absorption and it can be assumed that they are therapeutically equivalent and exchangeable in clinical practice.