Bioequivalence of Two Misoprostol Tablets in Healthy Chinese Volunteers: A Single-Dose, Single-Blind, Two-Period, Double Crossover Study

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Objective: To assess the bioequivalence of a new generic formulation of misoprostol 0.2 mg tablets (test) and the available branded tablet (reference) for the requirement of state regulatory criteria and the marketing of the test product in China. Methods: A randomized-sequence, 2-period crossover study was conducted in 20 female healthy Chinese volunteers in the fasted state. Blood samples were collected at baseline and 0.083, 0.17, 0.25, 0.33, 0.5, 0.75, 1, 1.25, 1.5, 2, 3, 4 and 6 hours after a single oral dose of 0.6 mg misoprostol test or reference, followed by a 7-day washout period. Misoprostol acid was determined by an HPLC-MS/MS method. Drug and Statistics-2.0 was used to calculate the pharmacokinetics parameters and assess the bioequivalence of the two formulations. Results: The main pharmacokinetics parameters misoprostol acid for test and reference were as follows: $t_{1/2}$ was (0.680±0.371) h and (0.650±0.264) h; $T_{\text{max}}$ was (0.415±0.087) h and (0.399±0.097) h; $C_{\text{max}}$ was (1.941±0.417) ng/mL and (2.047±0.397) ng/mL; AUC$_{0-1}$ was (1.535±0.419) ng·h/mL and (1.652±0.400) ng·h/mL; and the AUC$_{0-\infty}$ was (1.576±0.465) ng·h/mL and (1.686±0.396) ng·h/mL. The bioavailabilities of test, calculated with AUC$_{0-1}$ and AUC$_{0-\infty}$, were 92.65%±17.31%, and 93.61%±18.97%, respectively. No significant differences in pharmacokinetic parameters were found between preparations, treatments and periods. Conclusions: Misoprostol is quickly metabolized to misoprostol acid after oral administration and the metabolite can be used to evaluate the bioequivalence of misoprostol tablets. Misoprostol test and reference were met the requirement of US and China regulatory criterion, and two preparations were bioequivalent.