

## Comparison of Pharmacokinetics and Pharmacodynamics of Ticlopidine between Administration of a Combined Formulation of Ticlopidine/Ginkgo Extract, and Coadministration of Ticlopidine and Ginkgo Extract

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**Background:** The antiplatelet agent ticlopidine has often been used in combination with ginkgo extract. The aim of this study was to evaluate the pharmacokinetic and pharmacodynamic characteristics of ticlopidine in a ticlopidine/ginkgo extract combined formulation, compared with coadministration of a ticlopidine tablet with a ginkgo extract tablet.

**Methods:** A randomized, open-label, two-treatment, two-way crossover study was conducted in 24 healthy male subjects. Subjects were evenly allocated into two sequence groups. In one period, a ticlopidine 250 mg / ginkgo extract 80 mg combined formulation was taken orally, and in the other period, ticlopidine 250 mg and ginkgo extract 80 mg were co-administered. A seven-day wash-out separated the two periods. Serial blood sampling and bleeding time measurements were performed till 48 hours after drug administration during each period. Plasma concentrations of ticlopidine were analyzed by liquid chromatography-tandem mass spectrometry. Pharmacokinetic parameters were calculated by noncompartmental methods.

**Results:** The geometric mean ratio of ticlopidine area under the curve of combined formulation to coadministration was 1.04 (90% confidence interval 0.96-1.13) and that of peak plasma concentration was 1.09 (0.96-1.23). The ratio of maximal change of bleeding time to baseline was  $43.5 \pm 44.0\%$  (mean  $\pm$  standard deviation) after combined formulation administration and  $43.0 \pm 50.0\%$  after coadministration. There was no statistically significant difference between two treatment groups in the ratio of maximal change of bleeding time to baseline ( $P = 0.974$ ).

**Conclusions:** Administration of a combined formulation of ticlopidine / ginkgo extract and coadministration of ticlopidine and ginkgo extract showed similar pharmacokinetic and pharmacodynamic characteristics regarding ticlopidine.