

제 목 : Decreased oral bioavailability of cyclosporin A at second administration in human

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Method : Sandimmune Neoral[®] and Neoplanta[®] capsules were administered to twenty four healthy Korean male subjects at a cyclosporin A (CsA) dose of 175 mg in a 2 x 2 crossover investigation with a two-week wash-out phase. Concentrations of CsA in blood were measured by RIA method for over a period of 48 h.

Result : The two formulations were found bioequivalent, but analysis of variance (ANOVA) indicated that there is a significant ($p < 0.01$) period effect in AUC_{0-LAST} (area under the blood concentration above assay limit of quantification-time curve) and C_{max} (maximum blood concentration) between the administrations. Paired t-test revealed 6 and 9% decreases in AUC_{0-LAST} and C_{max} , respectively at the second administration. This period effect on the pharmacokinetics of CsA may be relevant for the patients who need consecutive administration of the drug. A number of mechanisms, such as induction of the enzymes responsible for metabolism of the drug in the gut wall and/or liver and modulation of P-glycoprotein upon the consecutive dosing, appear consistent with the change, and needs experimental proof.