

multiple-dose, while there was no significant difference in the AUC of tacrolimus between them when the two drugs are administered with single-dose.

#### Conclusions

1. CYP3A5\*3 is an important factor affecting the tacrolimus pharmacokinetics.
2. Among the CYP3A5\*1/\*1 and CYP3A5\*1/\*3 subjects, amlodipine raises significantly the whole blood tacrolimus concentration.
3. Among the CYP3A5\*3/\*3 subjects, amlodipine raises the oral clearance of tacrolimus and decrease the blood tacrolimus concentration.

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### EFFECT OF AMLODIPINE ON THE PHARMACOKINETICS OF TACROLIMUS IN RELATION TO CYP3A5\*3 GENETIC POLYMORPHISM IN HEALTHY CHINESE SUBJECTS

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**Objectives** To investigate the effect of amlodipine on the pharmacokinetics of tacrolimus in relation to CYP3A5\*3 genetic polymorphism in healthy Chinese subjects.

#### Methods

1. A PCR-RFLP technique was used for CYP3A5\*3 genotyping.
2. HPLC-MS/MS methods were applied to determine the tacrolimus whole blood samples.
3. An open, randomised, three-period crossover clinical trial was used to investigate the effect of amlodipine on the pharmacokinetics of tacrolimus in healthy volunteers in relation to different CYP3A5\*3 genotypes.

#### Results

1. The oral clearance of tacrolimus in CYP3A5\*1/\*1 or CYP3A5\*1/\*3 group was significantly higher than that in CYP3A5\*3/\*3, the area under the concentration (AUC) of tacrolimus was less than that in the latter.
2. When tacrolimus and amlodipine were coadministered with single dose or multiple dose in CYP3A5\*1/\*1 or CYP3A5\*1/\*3 subjects, the AUC of tacrolimus in coadministration group was significantly higher than that in tacrolimus alone group.
3. For CYP3A5\*3/\*3 subjects, the AUC of tacrolimus in tacrolimus plus amlodipine group is significantly lower than that in tacrolimus alone group when the two drugs are administered with