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The effect of cilostazol on the pharmacokinetics of simvastatin in healthy Korean volunteers: *In vitro* time dependent inactivation of cilostazol and its active metabolite, OPC-13015

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Cilostazol is a phosphodiesterase III inhibitor with antiplatelet activity and mainly metabolized to 3,4-dehydrocilostazol (OPC-13015) and 4'-trans-hydroxycilostazol (OPC-13213) via CYP3A4/5 and CYP2C19. Our previous IC50 shift assay revealed that both cilostazol and OPC-13015 were CYP3A time-dependent inhibitors *in vitro* and inhibitory effect on CYP3A4 in humans was further investigated. In this study, a randomized, open-label, multiple-dose, parallel study was conducted with 7 healthy Korean subjects and all subjects received the single oral dose of 40 mg simvastatin, a CYP3A4 probe substrate, on day 1. From day 2 to 7, the subjects were given 100 mg cilostazol 2 times per day with 12 hours interval. On day 8, the subjects received the single oral dose of 40 mg simvastatin on day 1 and 8 were measured using LC-MS/MS for pharmacokinetic assessment. AUC and  $C_{max}$  ratio of simvastatin concentration in human plasma on Day 1 and Day 8 were 3.56 and 4.3, respectively, suggesting that cilostazol is a moderate inhibitor of CYP3A4. In conclusion, inhibitory effects of cilostazol and OPC-13015 on CYP3A4 *in vitro* were in line with clinical study and it is expected that significant drug-drug interaction between other CYP3A4 substrates and cilostazol may be possible.

## Biography

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