Population pharmacokinetic model of sildenafil describing first-pass effect to its metabolite

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Although sildenafil is an old drug, its population PK has been rather neglected. This PK modeling was performed to investigate the PK characteristics of sildenafil (Viagra®) using data from several different comparative PK studies in healthy male Korean subjects. The major active metabolite (N-desmethyl sildenafil, NDS) was also modeled.

METHODS
Non-linear mixed effect analysis (NONMEM ver 7.2) was performed using a total of 6,130 observations (3,065 for each chemical entity) from 223 subjects (27.5 observations / subject) obtained after single 50-100 mg sildenafil citrate dose in 5 PK studies. The samples were collected just before and 0.17, 0.33, 0.5, 0.67, 0.83, 1, 1.25, 1.5, 1.75, 2, 3, 4, 6, 8, 12 and 24 hours after dosing. First-order conditional estimation method with interaction option was used for all applicable minimization process.

RESULTS
A two-compartment first-order elimination model was finally chosen for both sildenafil and NDS. The absorption of sildenafil and the first-pass metabolism to NDS were best with zero-order process. The population PK parameter estimates are summarized in the table.

CONCLUSION
The first pass effect model successfully described the time-concentration profile of sildenafil and its major metabolite in this population PK model.

REFERENCE