Clinical Pharmacokinetics

Prediction of Human Oral Plasma Concentration-Time Profiles Using Preclinical Data

Comparative Evaluation of Prediction Approaches in Early Pharmaceutical Discovery

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Supplemental Digital Content

This Supplemental Digital Content contains the information referred to in the full version of this article, which can be found at http://adisonline.com/pharmacokinetics

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Figure S-1. Predicted versus observed pharmacokinetic parameters for the Dedrick SA approach (grey dots) and the Dedrick Corr approach (black dots): (a) $t_{1/2}$; (b) MRT; (c) $C_{max}/C_{last}$; (d) $V_z/F$; (e) $C_{max}$; and (f) AUC$_\text{inf}$. The solid lines signify unity and the dashed lines signify 2-fold error between predicted and observed values. AUC$_\text{inf}$ = area under the plasma concentration-time curve from time zero to infinity;  $C_{last}$ = concentration at the last observed time point;  $C_{max}$ = maximum concentration;  Corr = with correction factors;  MRT = mean residence time;  SA = simple allometry;  $t_{1/2}$ = terminal elimination half-life;  $V_z/F$ = apparent terminal volume of distribution.
Figure S-2. Predicted versus observed pharmacokinetic parameters for the \( C_{ss} \)-MRT SA approach (grey dots), the \( C_{ss} \)-MRT Corr approach (black dots) and the \( C_{ss} \)-MRT Wajima approach (black crosses): (a) \( t_{1/2} \); (b) MRT; (c) \( C_{max} / C_{last} \); (d) \( V_z/F \); (e) \( C_{max} \); and (f) \( AUC_{inf} \). The solid lines signify unity and the dashed lines signify 2-fold error between predicted and observed values. \( AUC_{inf} \) = area under the plasma concentration-time curve from time zero to infinity; \( C_{last} \) = concentration at the last observed time point; \( C_{max} \) = maximum concentration; \( Corr \) = with correction factors; \( C_{ss} \) = steady-state plasma drug concentration; MRT = mean residence time; SA = simple allometry; \( t_{1/2} \) = terminal elimination half-life; \( V_z/F \) = apparent terminal volume of distribution.
Figure S-3. FE of (a) $t_{1/2}$; (b) MRT; (c) $C_{\text{max}}/C_{\text{last}}$; (d) $V_z/F$; (e) $C_{\text{max}}$; (f) $t_{\text{max}}$; and (g) $AUC_{\text{inf}}$; and (h) WFE of the profiles for the different approaches. The data are presented as geometric mean ± 95% CI. $AUC_{\text{inf}}$ = area under the plasma concentration-time curve from time zero to infinity; CI = confidence interval; $C_{\text{last}}$ = concentration at the last observed time point; $C_{\text{max}}$ = maximum concentration; Corr = with correction factors; $C_{\text{SS}}$ = steady-state plasma drug concentration; FE = fold error; MRT = mean residence time; SA = simple allometry; $t_{1/2}$ = terminal elimination half-life; $t_{\text{max}}$ = time to reach $C_{\text{max}}$; $V_z/F$ = apparent terminal volume of distribution; WFE = weighted FE; * p < 0.05 for the one-sided Wilcoxon rank sign test (Dedrick Corr vs Dedrick SA, and $C_{\text{SS}}$-MRT Corr vs $C_{\text{SS}}$-MRT SA).