Supplemental Data:

Mechanisms Underlying Differences in Systemic Exposure of Structurally Similar Active Metabolites: Comparison of Two Preclinical Hepatic Models

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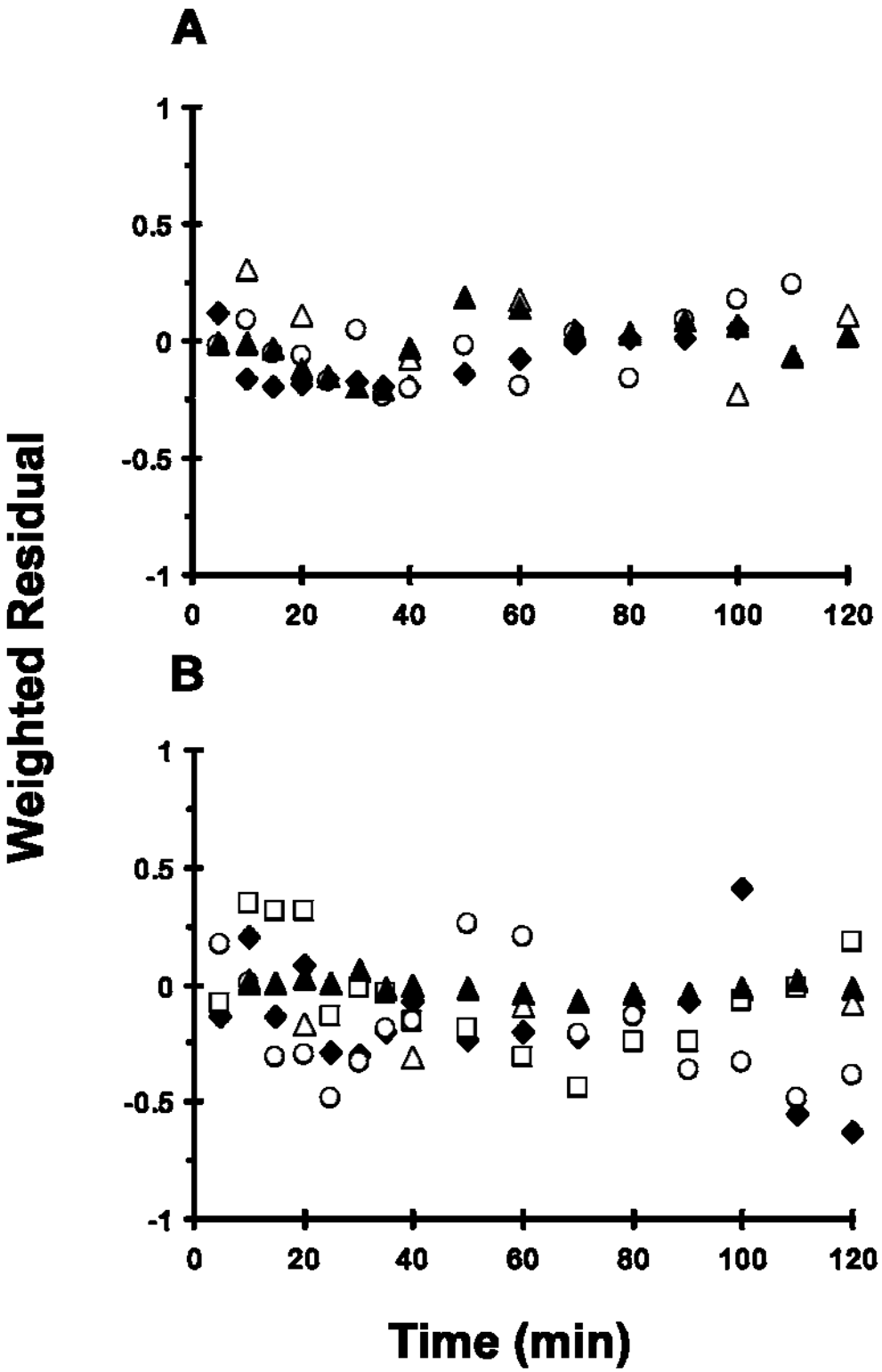
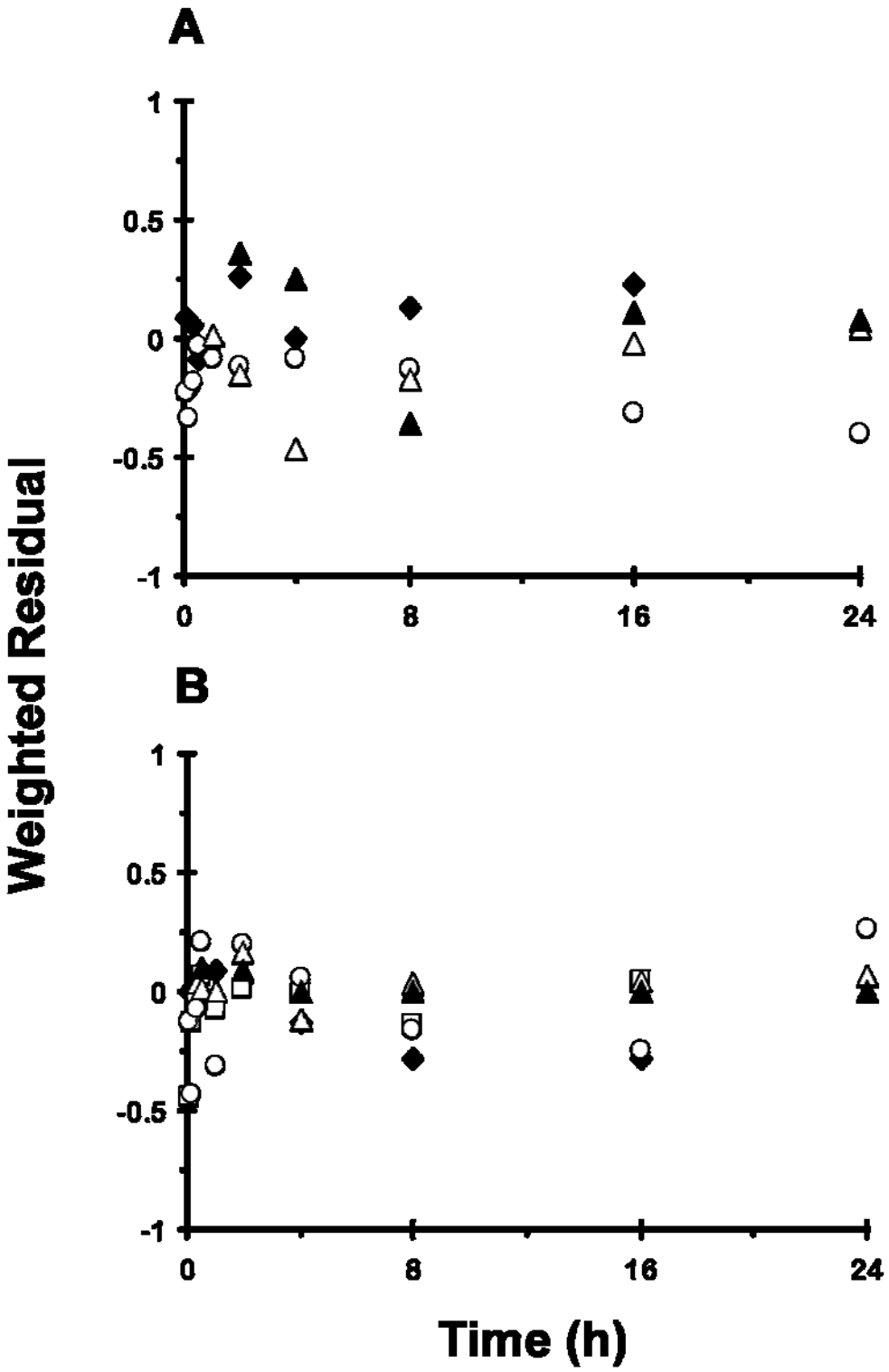
Legends for Figures

Supplemental Fig. S1. Plot of the weighted residual *vs.* time data from the computer-generated best fit of Model 1 to the rat isolated perfused liver data depicted in Fig. 3. Pafuramidine/metabolites (A) and CPD-0868/metabolites (B) are denoted as follows: ◆, prodrug in perfusate; □, M1 in perfusate; ○, M3 in perfusate; ▲, active metabolite in perfusate; △, active metabolite in liver. A weighting factor of $1/y^2$ was applied.

Supplemental Fig. S2. Plot of the weighted residual *vs.* time data from the computer-generated best fit of Model 1 to the rat sandwich-cultured hepatocyte data depicted in Fig. 5. Pafuramidine/metabolites (A) and CPD-0868/metabolites (B) are denoted as follows: ◆, prodrug in medium; □, M1 in medium; ○, M3 in medium; ▲, active metabolite in medium; △, active metabolite in hepatocytes. A weighting factor of $1/y^2$ was applied.



Supplemental Fig. S1



Supplemental Fig. S2