

## Correction to: “PBPK Modeling to Unravel Nonlinear Pharmacokinetics of Verapamil to Estimate the Fractional Clearance for Verapamil N-Demethylation in the Recirculating Rat Liver Preparation”

In the above article [Qi Joy Yang, Luqin Si, Hui Tang, Helle H. Sveigaard, Edwin C. Y. Chow, and K. Sandy Pang (2015) *Drug Metab Dispos* 43:631-645], the authors would like to make the below corrections.

1. In the *Introduction* (page 631, right column, first paragraph, line 2): “Mehvar et al., 1994” should be “Mehvar and Reynolds, 1996”.
2. In the *Introduction* (page 632, left column, second paragraph): “To this end, Mehvar et al. (1994) estimated the extent of formation of norverapamil from verapamil in the perfused rat liver preparation and examined removal of verapamil from plasma, but had not addressed the occurrence of sequential metabolism of formed norverapamil (Pang and Gillette, 1979) nor did they account for verapamil partitioning into RBCs.” should be “To this end, Mehvar et al. (1994) estimated the extent of formation of norverapamil from verapamil in the perfused rat liver preparation and examined removal of verapamil from plasma.”
3. In *Discussion* (page 637, right column, second paragraph): “However, our reported average unbound fraction of verapamil in the blood perfusate ( $f_B^{VER}$ ) was higher (0.45 versus 0.19), and the total intrinsic hepatic clearance of verapamil ( $CL_{int,tot}^{VER}$ ) was lower (16 versus 50–130 ml/min) compared with those reported by Mehvar et al. (1994).” should be “However, our reported average unbound fraction of verapamil in the blood perfusate ( $f_B^{VER}$ ) was higher (0.45 for racemic-VER versus 0.12 for S-VER and 0.22 for R-VER) (Mehvar et al., 1994), and the total intrinsic hepatic clearance of verapamil ( $CL_{int,tot}^{VER}$ ), lower (30 ml/min versus about 1475 ml/min for S- and R-VER), compared with those reported by Mehvar et al. (1994); the product,  $f_B^{VER} CL_{int,tot}^{VER}$ , was also smaller (16 ml/min vs. 234 to 491 ml/min).” (Pang and Yang, 2015).
4. In *Discussion* (page 640, left column, first paragraph): “The  $h_{mi}^{VER \rightarrow NOR}$  value (0.12) from Mehvar et al. (1994) was much underestimated due to their failure to account for sequential metabolism. The  $h_{mi}^{VER \rightarrow NOR}$  value (0.23) based on lowest-dose data under the assumption of linear kinetics (Table 2) was closer to the  $h_{mi}^{VER \rightarrow NOR}$  value (0.31) based on the ratio of the formation intrinsic clearance, normalized to the summed intrinsic clearances using fitted  $V_{max}$  and  $K_m$  values for metabolism and biliary excretion (Table 5).” should be “The  $h_{mi}^{VER \rightarrow NOR}$  value (0.19 - 0.23) from Mehvar et al. (1994) was similar to the value based on the lowest dose (0.23) estimated by AUC comparisons assuming linear kinetics. This value, however, remained an underestimation due to prevailing nonlinearity in metabolism, compared the value obtained upon comparison of the formation intrinsic clearance normalized to the total intrinsic clearance (0.31) (Yang et al., 2015).”

The Full Text article is corrected with the issue of this erratum.

The authors apologize for any inconvenience this may have caused.

### References

- Mehvar R, Reynolds JM, Robinson MA, and Longstreth JA (1994) Enantioselective kinetics of verapamil and norverapamil in isolated perfused rat livers. *Pharm Res* 11:1815–1819.
- Mehvar R and Reynolds J (1996) Reversal of stereoselectivity in the hepatic availability of verapamil in isolated perfused rat livers. Role of protein binding. *Drug Metab Dispos* 24:1088–1094.
- Pang KS and Yang QJ (2015) Letter in Response to Rebuttal from Resa Mehvar: Fractional clearance for verapamil N-demethylation in the isolated rat liver preparation. *Drug Metab Dispos* 43:1058–1059.
- Yang QJ, Si L, Tang H, Sveigaard HH, Chow ECY, and Pang KS (2015) PBPK modeling to unravel nonlinear pharmacokinetics of verapamil to estimate the fractional clearance for verapamil N-demethylation in the recirculating rat liver preparation. *Drug Metab Dispos* 43:631–645.