

# CORRECTION TO “USE OF ISOLATED HEPATOCYTE PREPARATIONS FOR CYTOCHROME P450 INHIBITION STUDIES: COMPARISON WITH MICROSOMES FOR $K_i$ DETERMINATION”

While processing the proof corrections for the article above [Brown HS, Chadwick A, and Houston JB (2007) *Drug Metab Dispos* 35:2119–2126], several superscript symbols used in the body of Tables 2 and 3, respectively, were not updated to reflect changes made to the table footnotes that define these symbols. The corrected tables appear below.

The online version of this article has been corrected in departure from the print version.

The printers regret this error and apologize for any confusion or inconvenience it may have caused.

TABLE 2

*Kinetic parameters for metabolism of dextromethorphan, midazolam, phenytoin, and tolbutamide in rat liver microsomes and freshly isolated hepatocytes*

Data are expressed as the mean of  $n = 3$  (microsomes) and  $n = 4$  (hepatocytes)  $\pm$  S.D.

In Vitro System	Pathway	$V_{\max}$	$K_M$	$S_{50}$	Hill Coefficient	$K_{i,s}$	$CL_{int}$
		<i>nmol/min</i>	$\mu M$	$\mu M$	$n$	$\mu M$	$\mu l/min$
Microsomes	Dextrophan	$0.53 \pm 0.04^{a,b}$ $0.97 \pm 0.18^{a,c}$	$0.42 \pm 0.01^b$ $75 \pm 12^c$			$448 \pm 142$	$1246 \pm 86^{a,b}$ $13.4 \pm 4.6^{a,c}$
	3-Methoxymorphinan	$1.30^a$		65			$21.5 \pm 9.3^{a,d}$
	1-Hydroxymidazolam	$0.58 \pm 0.07^a$		$11 \pm 2$	$1.37 \pm 0.17$		$29 \pm 5^{a,d}$
	4-Hydroxymidazolam	$0.89 \pm 0.17^a$		$9 \pm 4$	$1.76 \pm 0.17$		$50 \pm 22^{a,d}$
	5-(4-Hydroxyphenyl)-5-Phenylhydantoin	$0.027 \pm 0.009^a$	$3.21 \pm 0.56$				$8.40 \pm 2.75^{a,b}$ $0.18 \pm 0.06^{a,c}$
	4-Hydroxytolbutamide <sup>e</sup>	$4.2^a$	710				$5.91^a$
	Dextrophan	$0.08 \pm 0.02^{b,f}$ $0.48 \pm 0.11^{c,f}$	$0.15 \pm 0.03^b$ $10 \pm 3.6^c$			$645 \pm 188$	$545 \pm 50^{b,f}$ $49 \pm 9^{c,f}$
Hepatocytes	3-Methoxymorphinan	$0.84^f$		25			$31.3 \pm 6.1^{c,f}$
	1-Hydroxymidazolam	$0.28 \pm 0.10^f$	$18 \pm 6$				$16 \pm 7^f$
	4-Hydroxymidazolam	$0.17 \pm 0.10^f$	$15 \pm 7$				$12 \pm 7^f$
	5-(4-Hydroxyphenyl)-5-Phenylhydantoin	$0.22 \pm 0.05^f$	$5.23 \pm 1.38$				$43.3 \pm 7.4^{b,f}$
	4-Hydroxytolbutamide <sup>e</sup>	$0.74^f$	650				$0.39 \pm 0.27^{c,f}$ $1.14^f$

<sup>a</sup> Values expressed per milligram protein.

<sup>b</sup> Data for the high-affinity, low-capacity site.

<sup>c</sup> Data for the low-affinity, high-capacity site.

<sup>d</sup>  $CL_{\max}$  (maximal clearance).

<sup>e</sup> Tolbutamide data taken from Ashforth et al. (1995).

<sup>f</sup> Values expressed per  $10^6$  cells.

TABLE 3

*In vitro inhibition data in rat microsomes and hepatocytes obtained for substrates and inhibitors of CYP2C9, CYP2D6, and CYP3A4*

In the present study microsomal values represent mean ( $n = 3$ )  $\pm$  S.D. and hepatocyte values represent mean ( $n = 4$ )  $\pm$  S.D.

P450 Inhibitor	Pathway	Unbound $K_i$ Values		Cell-to-Medium Ratio	Fraction Unbound in Incubation ( $f_{u,inc}$ )		$K_i$ Ratio <sup>a</sup>
		Microsomes	Hepatocytes		Microsomes	Hepatocytes	
		$\mu M$					
Miconazole	Hydroxy-tolbutamide	$0.22 \pm 0.06$	$0.22 \pm 0.08$	6000	$0.06^b$	$0.06^c$	1
Fluconazole	Hydroxy-tolbutamide	$29 \pm 0.4$	$16 \pm 1.0$	4.2	$1^b$	$0.99^c$	1.81
	1-Hydroxy midazolam	26	30				0.87
	4-Hydroxy midazolam	17.8	9				1.98
	Phenytoin	3.5	1.31				2.67
Ketoconazole	Hydroxy-tolbutamide	$0.88 \pm 0.30$	$0.44 \pm 0.10$	1200	$0.23^b$	$0.26^c$	2
	1-Hydroxy midazolam	0.08	1.19				0.07
	4-Hydroxy midazolam	0.05	0.04				1.25
	Phenytoin	0.19	0.28				0.68
Quinine	Dextrophan	$1.6 \pm 0.65^d$	$1.4 \pm 0.82^d$	$143^e$	$0.85^f$	$0.85^g$	1.14
	Dextrophan	$3.0 \pm 1.6^h$	$8.3 \pm 1.32^h$				0.36
	3-Methoxymorphinan	$5.7 \pm 2.6$	$6.2 \pm 2.13$				0.92
Fluoxetine	Dextrophan	$0.06 \pm 0.03^d$	$0.15 \pm 0.05^d$	$2010^e$	$0.51^f$	$0.28^g$	0.4
	Dextrophan	$0.97 \pm 0.47^h$	$0.58 \pm 0.22^h$				1.67
	3-Methoxymorphinan	$1.5 \pm 1.3$	$0.94 \pm 0.22$				1.60
Fluvoxamine	Dextrophan	$0.26 \pm 0.02^d$	$0.44 \pm 0.08^d$	$577^e$	$0.79^f$	$0.58^g$	0.59
	Dextrophan	$1.4 \pm 0.4^h$	$1.6 \pm 0.21^h$				0.88
	3-Methoxymorphinan	$3.3 \pm 1.38$	$0.99 \pm 0.27$				3.33

<sup>a</sup>  $K_i$  ratio is represented as microsomal  $K_i$ /hepatocyte  $K_i$ .

<sup>b</sup>  $f_{u,inc}$  determined at 0.5 mg/ml.

<sup>c</sup>  $f_{u,inc}$  determined at  $0.5 \times 10^6$  cells/ml.

<sup>d</sup> Inhibition data for the high-affinity, low-capacity dextrophan pathway.

<sup>e</sup> Taken from Hallifax and Houston (2007).

<sup>f</sup>  $f_{u,inc}$  determined at 0.1 mg/ml.

<sup>g</sup>  $f_{u,inc}$  determined at  $0.25 \times 10^6$  cells/ml.

<sup>h</sup> Inhibition data for the low-affinity, high-capacity dextrophan pathway.