Supplemental Data

Article title: Evaluation of in vitro models for assessment of human intestinal metabolism in drug discovery

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Supplementary tables

Supplementary Table 1. Measured $f_{u,inc}$ values of test compounds using human intestinal microsomes (n = 15), permeabilized enterocytes (n = 32), and intestinal mucosa (n = 8) and their respective observed *in vivo* f_g value. The $f_{u,inc}$ values were measured at 10 µM of the substrate after 4 h of equilibration with the RED device.

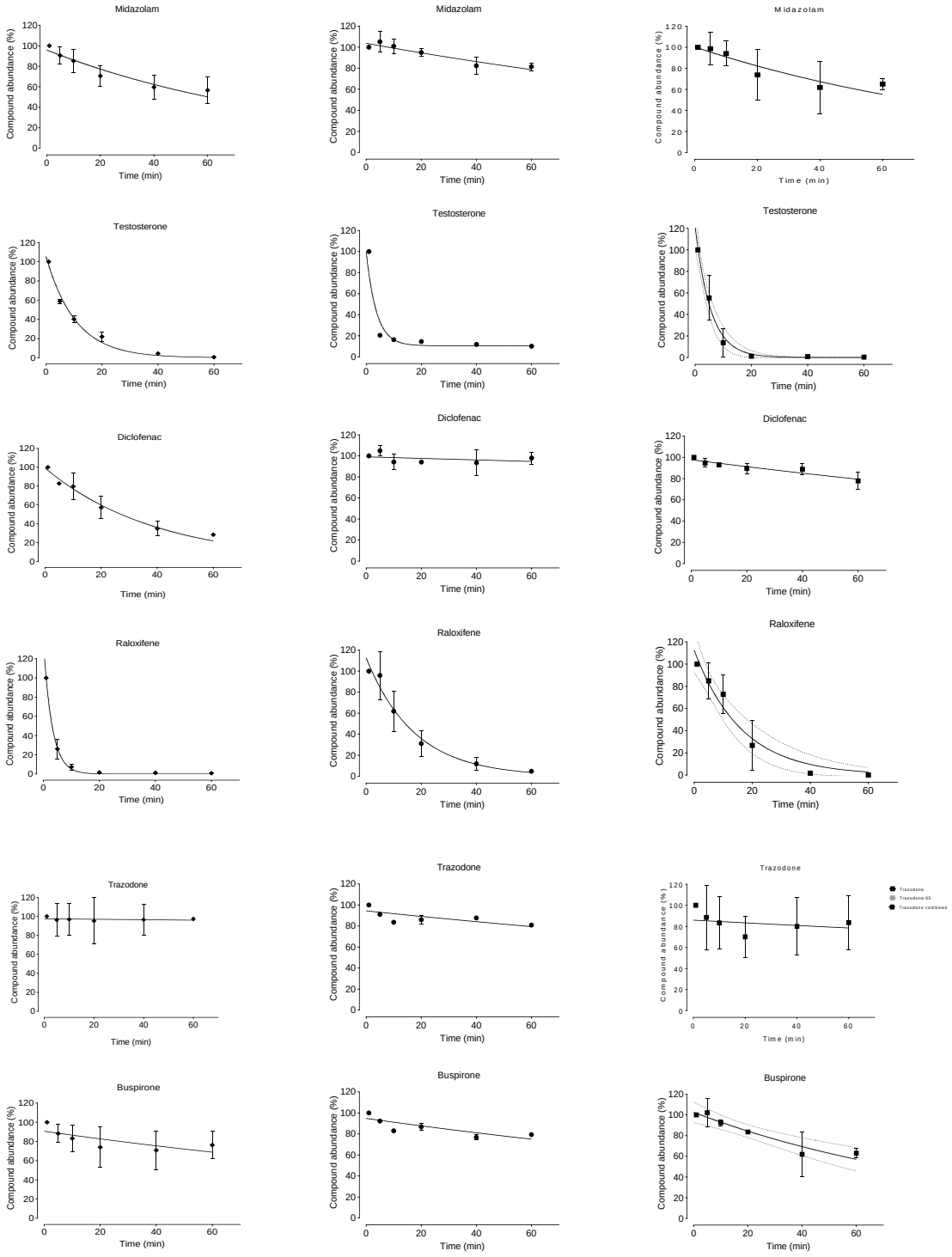
Test compound	Observed human f_g value	$f_{u,inc}$ values measured by RED device			
		Intestinal microsomes	Permeabilized enterocytes	Cryopreserved mucosa	Mean
Dabigatran-etexilate	0.05	NM[2]	1.00	NM[2]	1.00
Raloxifene	0.05	0.15	0.21	0.26	0.21
Testosterone	0.05	0.74	1.00	NM[2]	0.87
Lovastatin	0.07	0.25	0.25	NM[2]	0.25
Nisoldipine	0.11	0.24	0.18	0.42	0.28
Buspirone	0.18	0.80	0.93	NM[2]	0.87
Rifabutin	0.21	0.49	0.48	0.67	0.55
Saquinavir	0.28	0.17	0.11	NM[2]	0.14
Simvastatin	0.29	NM[2]	0.48	NM[2]	0.48
Atorvastatin	0.40	NM[2]	0.69	NM[2]	0.69
Terfenadine	0.40	NM[2]	0.05	NM[2]	0.05
Felodipine	0.42	0.07	0.03	0.00	0.03
Cyclosporin	0.48	0.02	0.01	0.05	0.03
Midazolam	0.55	0.74	0.74	0.71	0.73
Cisapride	0.57	0.54	0.57	NM[2]	0.56
Ramipril	0.59	NM[2]	1.00	NM[2]	1.00
Verapamil	0.60	0.69	0.54	NM[2]	0.62
Sildenafil	0.62	NM[2]	1.00	NM[2]	1.00
Nifedipine	0.71	NM[2]	0.88	NM[2]	0.88
Diclofenac	0.78	0.88	0.91	1.00	0.93
Methadone	0.78	NM[2]	0.80	NM[2]	0.80
Zolpidem	0.79	NM[2]	0.92	NM[2]	0.92
Trazodone	0.83	NM[2]	0.85	NM[2]	0.85
Repaglinide	0.89	NM[2]	0.56	NM[2]	0.56
Quinidine	0.91	NM[2]	1.00	NM[2]	1.00
Indinavir	0.93	0.82	0.70	NM[2]	0.76
Alprazolam	0.94	0.93	0.91	0.96	0.93
Enalapril	0.97	NM[2]	0.74	NM[2]	0.74
Benzydamine	0.98	NM[2]	0.54	NM[2]	0.54
Carbazeran	1.00	NM[2]	1.00	NM[2]	1.00
S-Mephenytoin	1.00	NM[2]	0.95	NM[2]	0.95
Terbutaline	NA[1]	NM[2]	1.00	NM[2]	1.00

[1] – Insufficient amount of information in the literature to calculate f_g

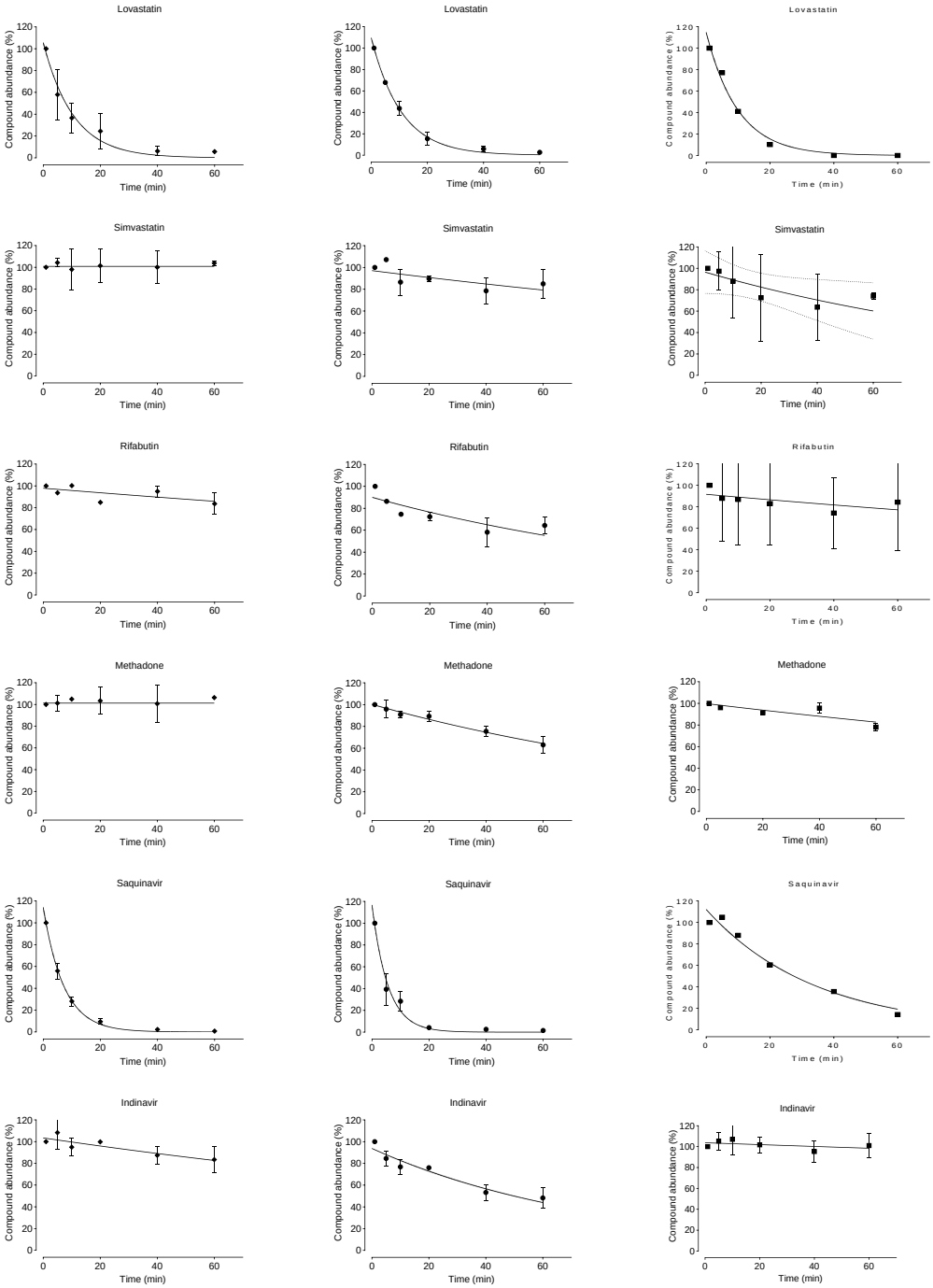
[2] – $f_{u,inc}$ not measured. As the $f_{u,inc}$ was similar across all three models, the $f_{u,inc}$ for all compounds was determined in permeabilized enterocytes and applied across all three models

Supplementary figures

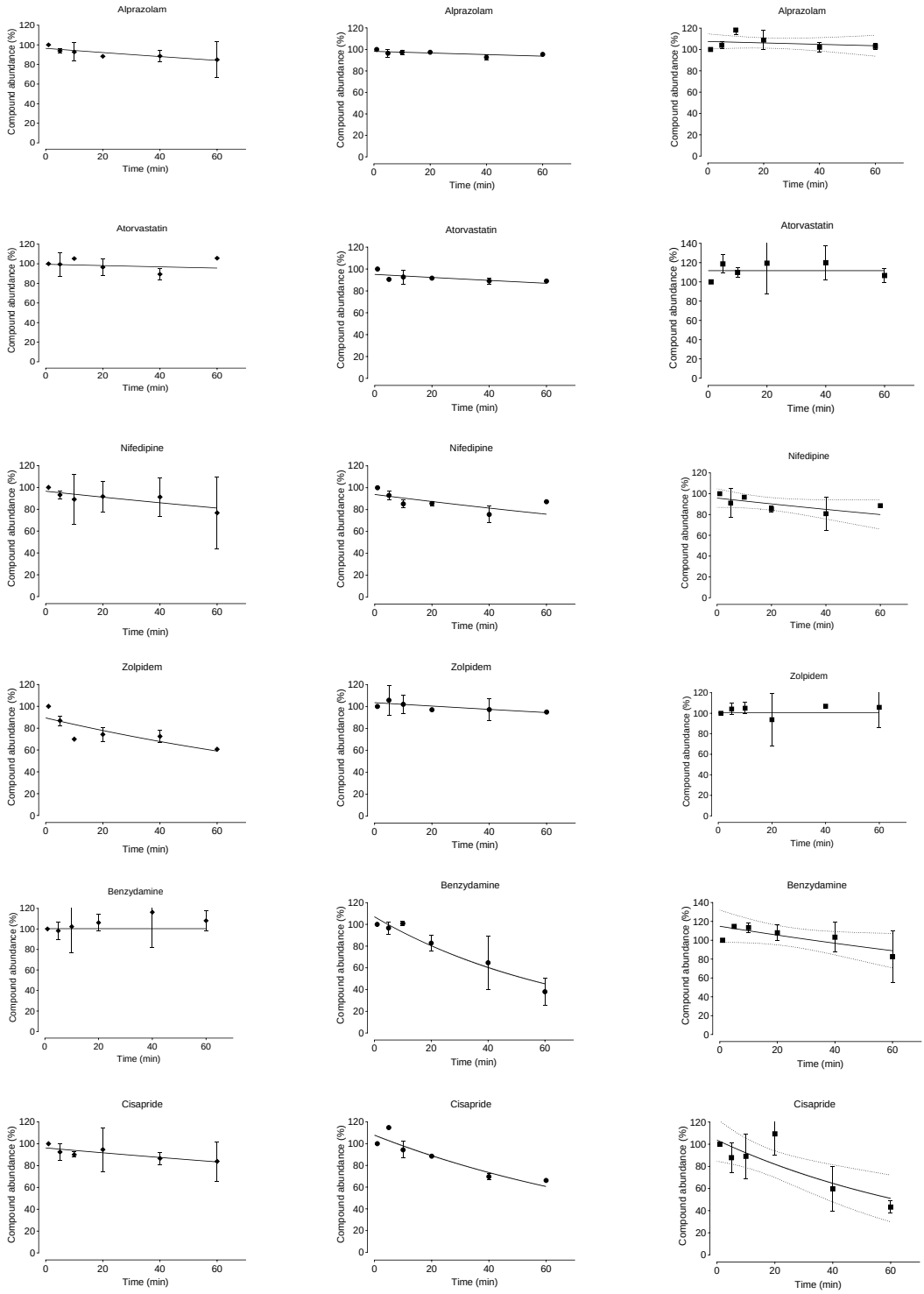
Supplementary Fig. 1. CL_{int} measurements for midazolam, testosterone, diclofenac, raloxifene, trazodone, and buspirone in human intestinal microsomes (♦), permeabilized enterocytes (●), and mucosa (■), respectively.



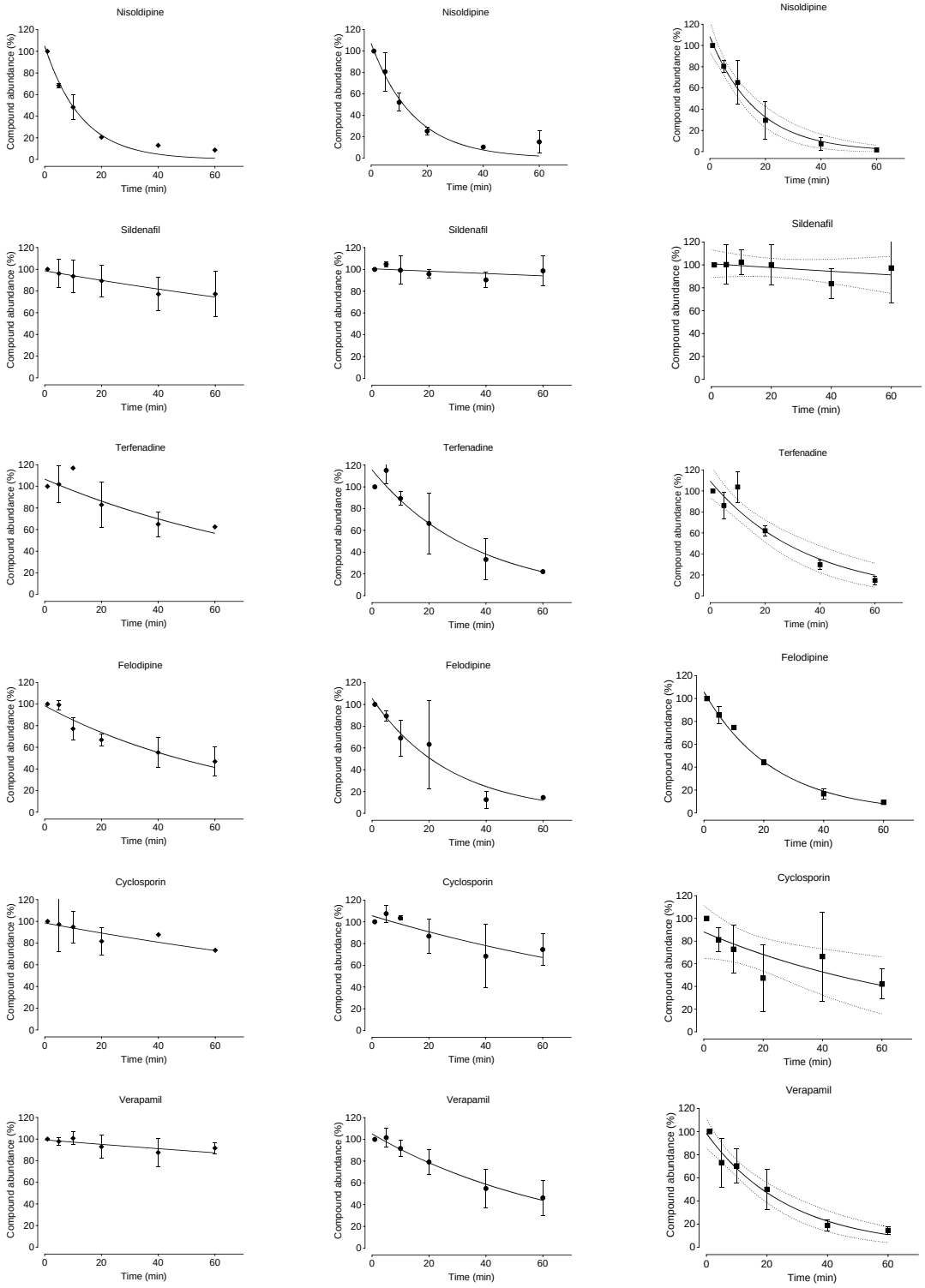
Supplementary Fig. 2. CL_{int} measurements for lovastatin, simvastatin, rifabutin, methadone, saquinavir, and indinavir in human intestinal microsomes (♦), permeabilized enterocytes (●), and mucosa (■), respectively.



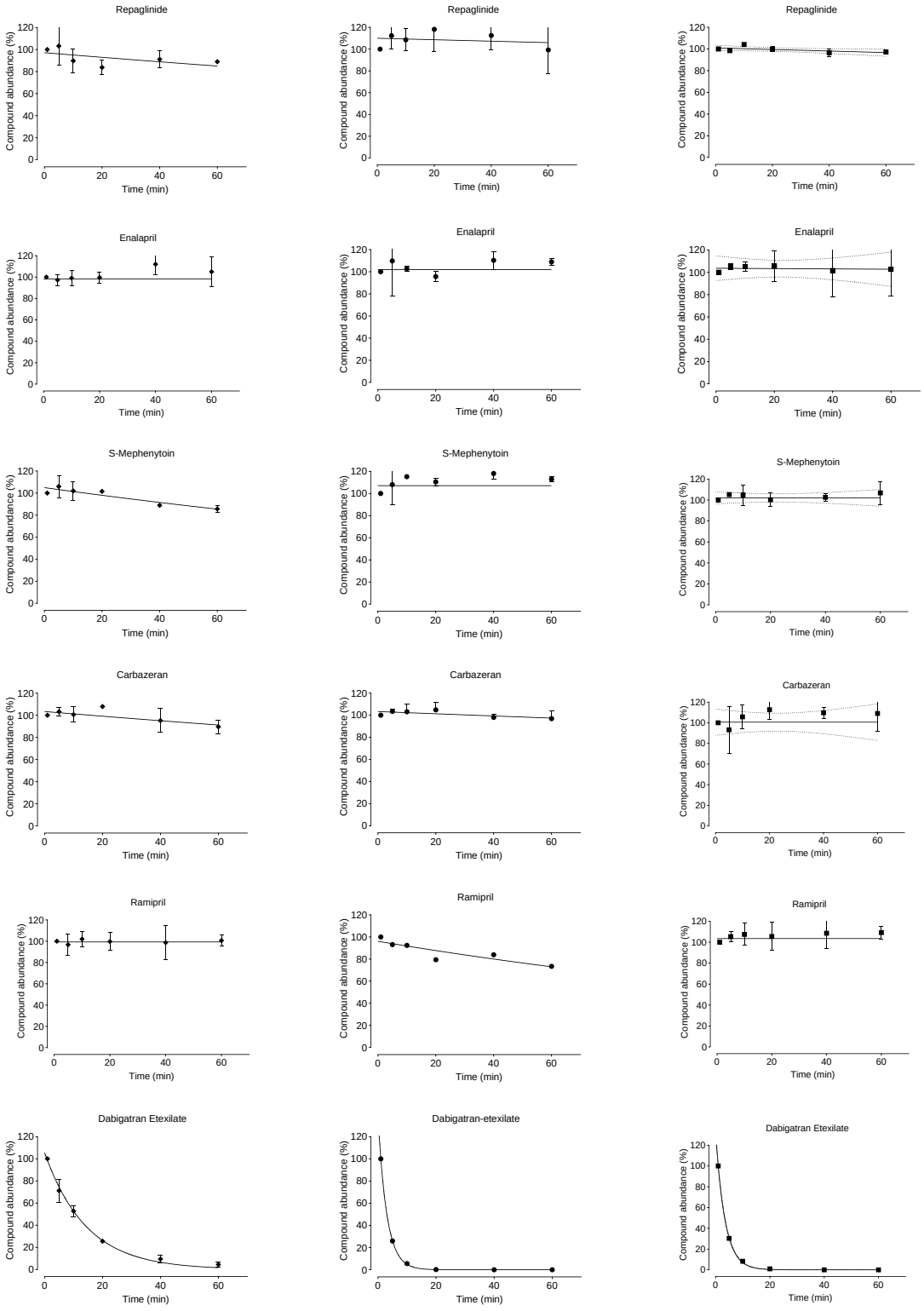
Supplementary Fig. 3. CL_{int} measurements for alprazolam, atorvastatin, nifedipine, zolpidem, benzydamine, and cisapride in human intestinal microsomes (♦), permeabilized enterocytes (●), and mucosa (■), respectively.



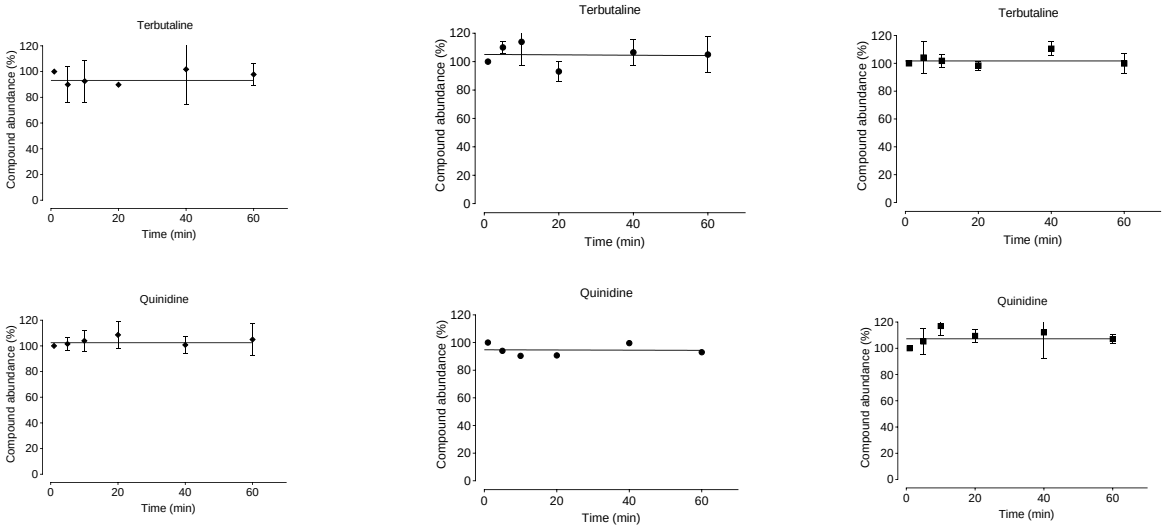
Supplementary Fig. 4. CL_{int} measurements for nisoldipine, sildenafil, terfenadine, felodipine, cyclosporin, and verapamil in human intestinal microsomes (♦), permeabilized enterocytes (●), and mucosa (■), respectively.



Supplementary Fig. 5. CL_{int} measurements for repaglinide, enalapril, s-mephenytoin, carbazeran, ramipril, and dabigatran etexilate in human intestinal microsomes (♦), permeabilized enterocytes (●), and mucosa (■), respectively.



Supplementary Fig. 6. CL_{int} measurements for terbutaline and quinidine in human intestinal microsomes (♦), permeabilized enterocytes (●), and mucosa (■), respectively.



Supplementary Fig. 7. Examples of biotransformation pathway analysis *via* the QuanQual approach (LC-HRMS).