

Supplementary Material

Figure S1. Representative chromatograms of MBR (upper) and IS (lower) (a) stock solution of 0.01 $\mu\text{g/mL}$ MBR and IS; (b) drug-free mouse plasma; (c) mouse plasma standard of 1 $\mu\text{g/mL}$ MBR; (d) mouse plasma sample at 30 min after oral administration of 50 mg/kg MBR; (e) drug-free mouse urine; (f) mouse urine standard of 10 $\mu\text{g/mL}$ MBR; (g) mouse urine sample collected at 24 h after oral administration of 50 mg/kg MBR; (h) drug-free mouse GI; (i) mouse GI standard of 1 $\mu\text{g/mL}$ MBR; (j) mouse GI sample collected at 24 h after oral administration of 50 mg/kg MBR.

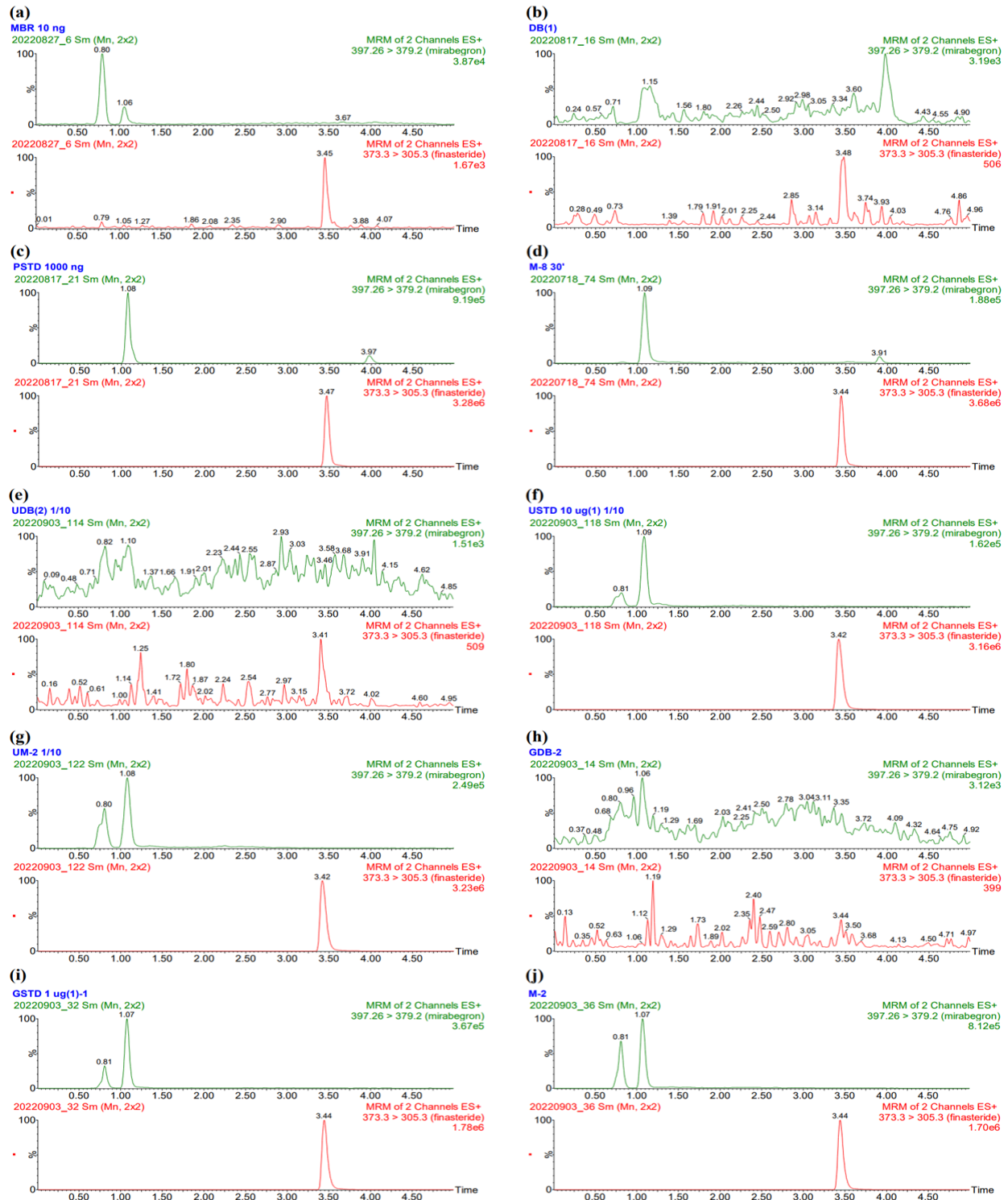


Table S1. Mean (\pm S.D.) concentrations and T/P ratios of MBR in plasma and various tissues at 0.5, 2, 4, 8, and 10 h after intravenous administration (5 mg/kg as MBR) and oral administration (50 mg/kg as MBR) of MBR or various formulations of MBR to mice. The units of MBR concentrations in plasma and tissues are presented in $\mu\text{g/mL}$ and $\mu\text{g/g}$ tissue, respectively.

Parameter	Intravenous	Oral			
	MBR	MBR	MBR-EFA	MBR-NDA	MBR-PG
0.5 h					
Plasma	0.0635 \pm 0.0127	0.0633 \pm 0.0361	0.313 \pm 0.180	0.135 \pm 0.0198	0.0589 \pm 0.0126
Liver	2.53 \pm 0.462 (41.8 \pm 14.1)	7.47 \pm 4.97 (131 \pm 59.8)	9.33 \pm 2.66 (34.5 \pm 14.7)	13.9 \pm 2.84 (102 \pm 8.36)	12.9 \pm 8.10 (219 \pm 112)
Kidney	2.67 \pm 0.231 (42.8 \pm 6.16)	9.20 \pm 4.61 (154 \pm 34.7)	14.7 \pm 2.57 (58.9 \pm 31.4)	18.0 \pm 11.2 (128 \pm 65.0)	10.3 \pm 10.7 (209 \pm 255)
Small intestine	N.D. (N.C.)	72.5 \pm 52.3 (1353 \pm 863)	135 \pm 52.5 (464 \pm 89.0)	372 \pm 286 (2901 \pm 2539)	127 \pm 69.8 (2434 \pm 1920)
Large intestine	4.00 \pm 1.70 (70.4 \pm 26.4)	6.67 \pm 4.41 (191 \pm 244)	11.7 \pm 8.10 (35.9 \pm 4.23)	22.8 \pm 13.1 (166 \pm 78.3)	12.4 \pm 8.65 (242 \pm 221)
Stomach	3.60 \pm 0.400 (58.0 \pm 11.2)	76.8 \pm 36.3 (2066 \pm 2394)	92.4 \pm 46.4 (412 \pm 304)	37.3 \pm 20.6 (296 \pm 201)	68.6 \pm 78.9 (1066 \pm 1242)
Lung	6.40 \pm 0.400 (103 \pm 18.4)	9.33 \pm 2.89 (174 \pm 70.3)	13.9 \pm 5.46 (47.7 \pm 12.7)	53.3 \pm 39.6 (424 \pm 368)	2.53 \pm 1.29 (48.0 \pm 36.2)
Heart	3.33 \pm 0.611 (54.5 \pm 16.8)	8.40 \pm 4.21 (141 \pm 24.4)	7.73 \pm 3.78 (25.9 \pm 4.21)	17.6 \pm 5.66 (125 \pm 53.7)	6.40 \pm 5.09 (133 \pm 129)
Brain	0.138 \pm 0.0195 (2.13 \pm 0.246)	0.312 \pm 0.0516 (7.50 \pm 6.88)	0.508 \pm 0.435 (2.03 \pm 1.64)	1.12 \pm 0.891 (8.31 \pm 6.76)	0.983 \pm 0.721 (19.3 \pm 18.5)
Fat	0.102 \pm 0.0600 (1.84 \pm 1.17)	0.564 \pm 0.862 (22.5 \pm 37.5)	0.354 \pm 0.318 (1.86 \pm 2.39)	0.859 \pm 1.00 (6.57 \pm 7.45)	0.191 \pm 0.0223 (3.42 \pm 1.19)
2 h					
Plasma	0.0135 \pm 0.0400	0.0182 \pm 0.0024	0.187 \pm 0.0421	0.0667 \pm 0.0367	0.0490 \pm 0.0297
Liver*	1.60 \pm 0.400 (128 \pm 54.2)	2.53 \pm 0.611 (139 \pm 25.1)	15.6 \pm 8.03 (84.4 \pm 41.3)	25.2 \pm 4.21 (488 \pm 331)	16.9 \pm 6.21 (380 \pm 117)
Kidney**	N.D. (N.C.)	N.D. (N.C.)	20.8 \pm 6.73 (115 \pm 49.0)	14.8 \pm 1.06 (172 \pm 32.4)	18.8 \pm 10.4 (324 \pm 34.1)
Small intestine	N.D. (N.C.)	66.9 \pm 24.8 (3864 \pm 2031)	321 \pm 283 (1635 \pm 1479)	221 \pm 292 (6923 \pm 10961)	276 \pm 196 (5344 \pm 1378)
Large intestine	N.D. (N.C.)	3.87 \pm 1.89 (226 \pm 144)	118 \pm 110 (560 \pm 489)	42.1 \pm 23.1 (932 \pm 815)	83.6 \pm 86.4 (2029 \pm 2417)
Stomach	2.53 \pm 0.231 (200 \pm 68.3)	32.9 \pm 23.1 (1959 \pm 1639)	66.7 \pm 49.6 (327 \pm 195)	28.6 \pm 3.11 (730 \pm 496)	38.2 \pm 9.33 (691 \pm 212)
Lung	4.67 \pm 1.97 (356 \pm 171)	4.40 \pm 0.693 (242 \pm 8.89)	18.7 \pm 17.9 (96.4 \pm 93.9)	23.1 \pm 10.6 (441 \pm 332)	7.73 \pm 7.55 (133 \pm 77.7)
Heart	1.07 \pm 0.611 (75.3 \pm 32.4)	2.27 \pm 0.611 (129 \pm 51.0)	7.80 \pm 4.24 (40.4 \pm 9.91)	10.0 \pm 2.26 (264 \pm 203)	7.87 \pm 1.15 (191 \pm 79.3)
Brain	0.0936 \pm 0.0187 (6.82 \pm 1.29)	0.375 \pm 0.359 (20.1 \pm 18.4)	0.370 \pm 0.282 (2.03 \pm 1.48)	0.953 \pm 0.507 (22.0 \pm 24.3)	0.821 \pm 0.611 (25.9 \pm 26.7)
Fat	0.150 \pm 0.0803 (9.59 \pm 2.62)	0.166 \pm 0.0335 (9.44 \pm 3.27)	0.252 \pm 0.130 (1.29 \pm 0.410)	N.D. (N.C.)	N.D. (N.C.)
4 h					
Plasma	0.00907 \pm 0.00231	0.0348 \pm 0.00356	0.115 \pm 0.0451	0.106 \pm 0.0361	0.0612 \pm 0.0283
Liver	0.800 \pm 0.0001	3.47 \pm 0.462	15.2 \pm 7.73	22.1 \pm 13.1	17.1 \pm 4.60

	(88.2 ± 28.1)	(100 ± 5.94)	(129 ± 24.6)	(194 ± 63.0)	(321 ± 173)
Kidney*	N.D.	3.00 ± 1.41	19.7 ± 5.40	27.7 ± 14.8	25.7 ± 4.81
	(N.C.)	(92.7 ± 49.1)	(180 ± 47.6)	(263 ± 112)	(465 ± 148)
Small intestine	N.D.	91.6 ± 12.1	187 ± 139	375 ± 284	246 ± 127
	(N.C.)	(2651 ± 436)	(1813 ± 1748)	(3991 ± 2865)	(4203 ± 1830)
Large intestine	N.D.	4.40 ± 1.20	241 ± 201	144 ± 102	187 ± 170
	(N.C.)	(125 ± 21.9)	(2405 ± 2588)	(1736 ± 1698)	(2566 ± 1602)
Stomach	N.D.	10.1 ± 1.85	45.0 ± 52.9	68.2 ± 60.2	34.7 ± 15.4
	(N.C.)	(290 ± 34.9)	(288 ± 293)	(917 ± 1035)	(695 ± 432)
Lung	2.13 ± 0.611	3.47 ± 1.29	21.2 ± 23.2	20.6 ± 4.24	12.7 ± 3.45
	(234 ± 16.0)	(103 ± 45.6)	(138 ± 124)	(168 ± 57.6)	(234 ± 112)
Heart	0.533 ± 0.231	2.53 ± 1.01	17.8 ± 13.3	53.6 ± 61.7	9.33 ± 2.84
	(57.3 ± 9.90)	(75.3 ± 36.9)	(126 ± 52.5)	(504 ± 502)	(169 ± 61.3)
Brain*	N.D.	0.147 ± 0.0710	1.21 ± 0.0322	1.67 ± 0.210	0.664 ± 0.237
	(N.C.)	(4.10 ± 2.26)	(10.1 ± 4.21)	(16.7 ± 4.26)	(14.0 ± 10.4)
Fat	0.0718 ± 0.0433	0.0652 ± 0.0173	0.353 ± 0.000849	0.366 ± 0.250	0.387 ± 0.326
	(9.10 ± 5.00)	(1.85 ± 0.337)	(2.93 ± 1.15)	(4.43 ± 4.39)	(10.6 ± 11.4)

8 h

Plasma	N.D.	0.0272 ± 0.0389	0.0710 ± 0.0250	0.0858 ± 0.0490	0.0879 ± 0.0212
Liver	N.D.	3.47 ± 1.80	6.80 ± 0.556	6.27 ± 1.01	6.40 ± 1.70
	(N.C.)	(50.7 ± 17.0)	(120 ± 29.4)	(93.2 ± 54.9)	(66.3 ± 2.29)
Kidney	N.D.	2.80 ± 1.13	19.3 ± 5.52	11.9 ± 2.34	14.1 ± 3.89
	(N.C.)	(32.5 ± 19.9)	(280 ± 49.7)	(196 ± 164)	(166 ± 56.9)
Small intestine	N.D.	87.7 ± 34.1	16.4 ± 10.2	12.9 ± 4.64	59.7 ± 49.3
	(N.C.)	(1627 ± 1357)	(251 ± 148)	(172 ± 59.1)	(706 ± 634)
Large intestine	N.D.	38.5 ± 43.8	45.3 ± 28.6	48.0 ± 29.0	102 ± 127
	(N.C.)	(1028 ± 1549)	(691 ± 477)	(798 ± 779)	(1228 ± 1606)
Stomach	N.D.	9.87 ± 2.41	17.6 ± 9.06	8.53 ± 3.84	18.4 ± 11.7
	(N.C.)	(165 ± 78.4)	(250 ± 110)	(110 ± 34.4)	(227 ± 182)
Lung	1.33 ± 0.611	4.00 ± 0.800	7.07 ± 7.49	10.9 ± 3.63	7.07 ± 4.09
	(N.C.)	(67.4 ± 33.5)	(97.6 ± 102)	(148 ± 54.6)	(82.8 ± 55.1)
Heart	8.00 ± 4.53	2.13 ± 0.833	3.60 ± 0.566	3.07 ± 0.611	3.80 ± 0.283
	(N.C.)	(32.4 ± 8.92)	(60.8 ± 38.6)	(52.7 ± 48.0)	(50.4 ± 7.90)
Brain	N.D.	0.135 ± 0.00446	0.174 ± 0.0274	0.195 ± 0.145	0.402 ± 0.334
	(N.C.)	(2.42 ± 1.59)	(2.68 ± 1.15)	(2.44 ± 1.31)	(5.24 ± 5.03)
Fat	0.104 ± 0.0339	0.341 ± 0.178	N.D.	N.D.	0.192 ± 0.0624
	(N.C.)	(5.63 ± 1.87)	(N.C.)	(N.C.)	(2.21 ± 0.726)

10 h

Plasma**	N.D.	0.0674 ± 0.0282	N.D.	0.0314 ± 0.0290	0.0160 ± 0.00453
Liver	N.D.	2.93 ± 1.29	N.D.	N.D.	N.D.
	(N.C.)	(43.5 ± 3.18)	(N.C.)	(N.C.)	(N.C.)
Kidney	N.D.	3.20 ± 0.0001	4.40 ± 2.26	3.80 ± 3.11	3.20 ± 1.13
	(N.C.)	(42.9 ± 14.7)	(N.C.)	(131 ± 22.0)	(219 ± 133)
Small intestine	N.D.	15.2 ± 11.3	N.D.	7.60 ± 2.83	7.20 ± 2.83
	(N.C.)	(201 ± 49.5)	(N.C.)	(349 ± 232)	(443 ± 51.6)
Large intestine	N.D.	12.5 ± 5.00	8.80 ± 0.566	30.0 ± 18.7	24.0 ± 21.5
	(N.C.)	(205 ± 119)	N.D.	(2144 ± 2574)	(1760 ± 1841)
Stomach	N.D.	5.87 ± 3.26	2.20 ± 0.849	21.0 ± 25.2	3.60 ± 0.566
	(N.C.)	(84.5 ± 12.2)	N.D.	(521 ± 321)	(240 ± 103)

Lung	2.00 ± 0.001 (N.C.)	7.33 ± 1.40 (125 ± 68.2)	5.00 ± 0.849 (N.C.)	10.4 ± 0.001 (577 ± 533)	5.80 ± 1.41 (391 ± 199)
Heart	4.80 ± 2.26 (N.C.)	1.07 ± 0.462 (19.4 ± 15.3)	N.D. (N.C.)	N.D. (N.C.)	N.D. (N.C.)
Brain	N.D. (N.C.)	N.D. (N.C.)	N.D. (N.C.)	0.126 ± 0.0325 (6.17 ± 4.66)	0.132 ± 0.0359 (8.94 ± 4.77)
Fat	0.0871 ± 0.0139 (N.C.)	N.D. (N.C.)	N.D. (N.C.)	N.D. (N.C.)	N.D. (N.C.)

*MBR-NDA and MBR-PG mice were significantly different ($p < 0.05$) from MBR mice.

**MBR-EFA and MBR-PG mice were significantly different ($p < 0.05$) from MBR mice.

*MBR-NDA mice was significantly different ($p < 0.05$) from MBR mice.