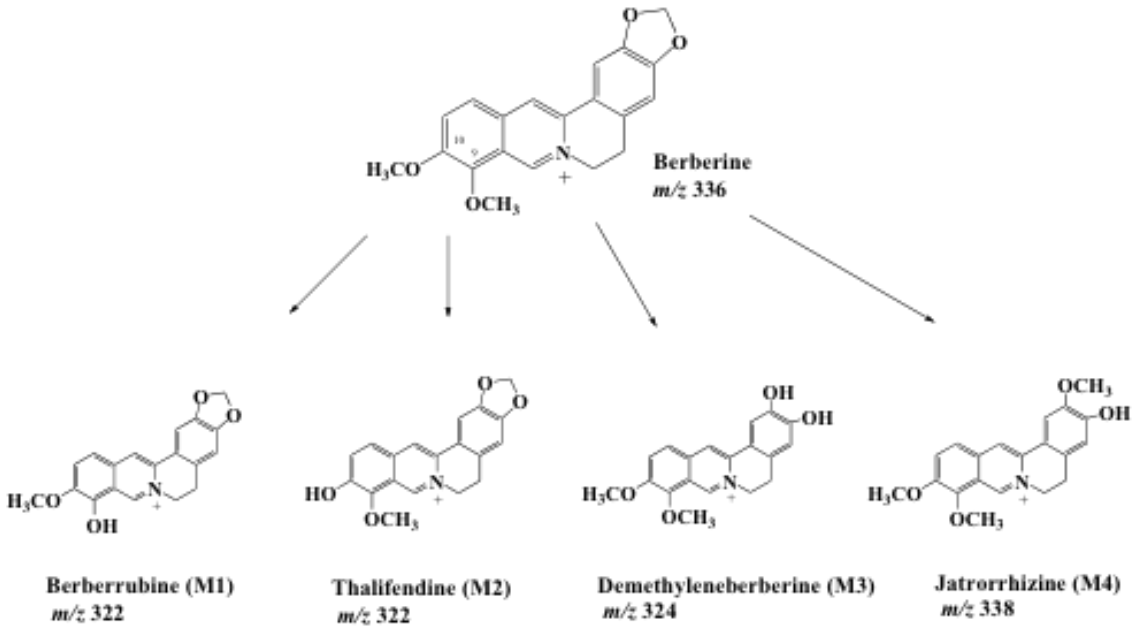
Berberine



Metabolism of berberine in rats

代謝実験
動物代謝　ラット
単一化合物　berberine

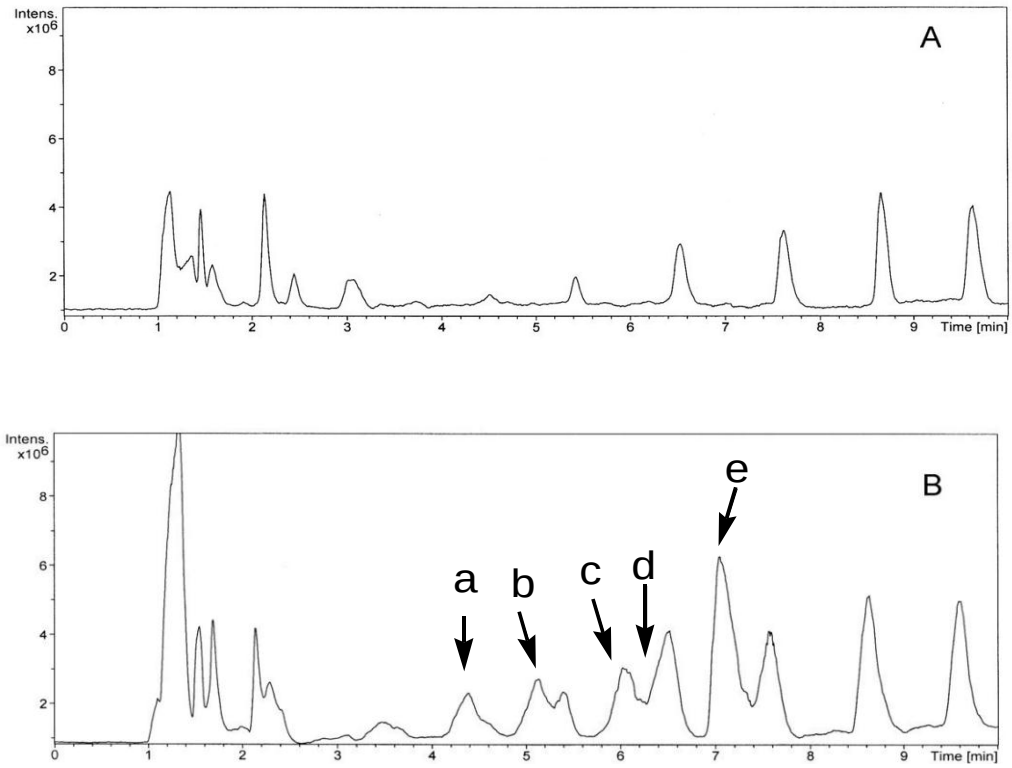


Fig. 1 Total ion current (TIC) chromatograms of rat plasma blank (A) and after oral administration of Ber (B).

The HPLC instrument was an Agilent 1100 system (Agilent Technologies., Waldbronn, Germany) comprising an Agilent 1100 series binary pump with a photodiode array detector and a series 7725i injector with a 20 μl loop. Data were acquired and intergrated using a ChemStation. The HPLC system was connected to an Esquire 3000^{plus} mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with an ESI source. All LC/MS-MS data were acquired using Esquire Control software and analyzed using software from by Bruker Daltonics. [Zuo *et al*., *Drug Metab. Dispos*., **34**, 2064-2072 (2006)]

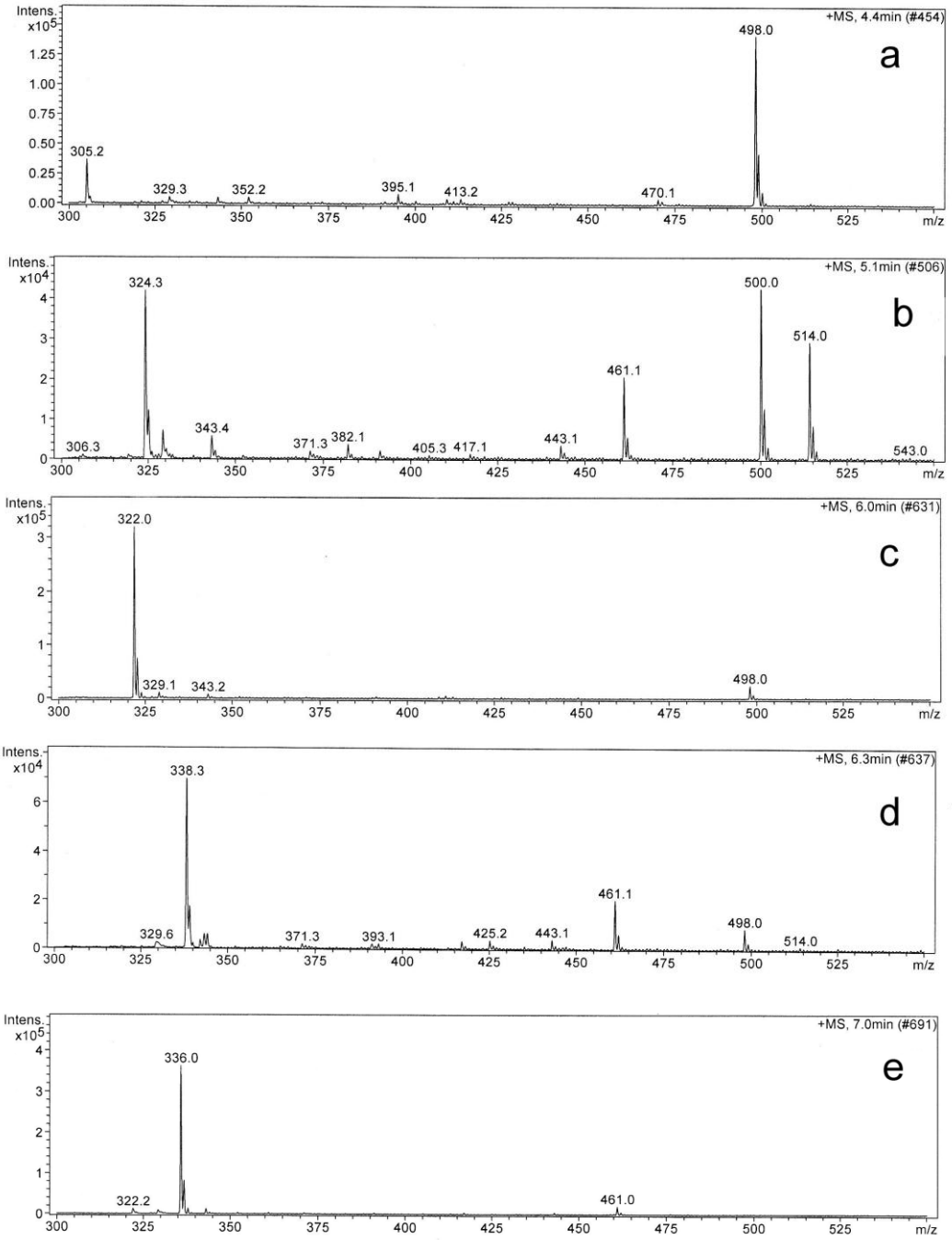


Fig. 2　MS spectra of TIC peaks in rat plasma after oral berberine administration. Ion peaks are located at t_R 4.4 (a), 5.1 (b), 6.0 (c), 6.3 (d) and 7.0 min (e). [Zuo *et al*., *Drug Metab. Dispos*., **34**, 2064-2072 (2006)]

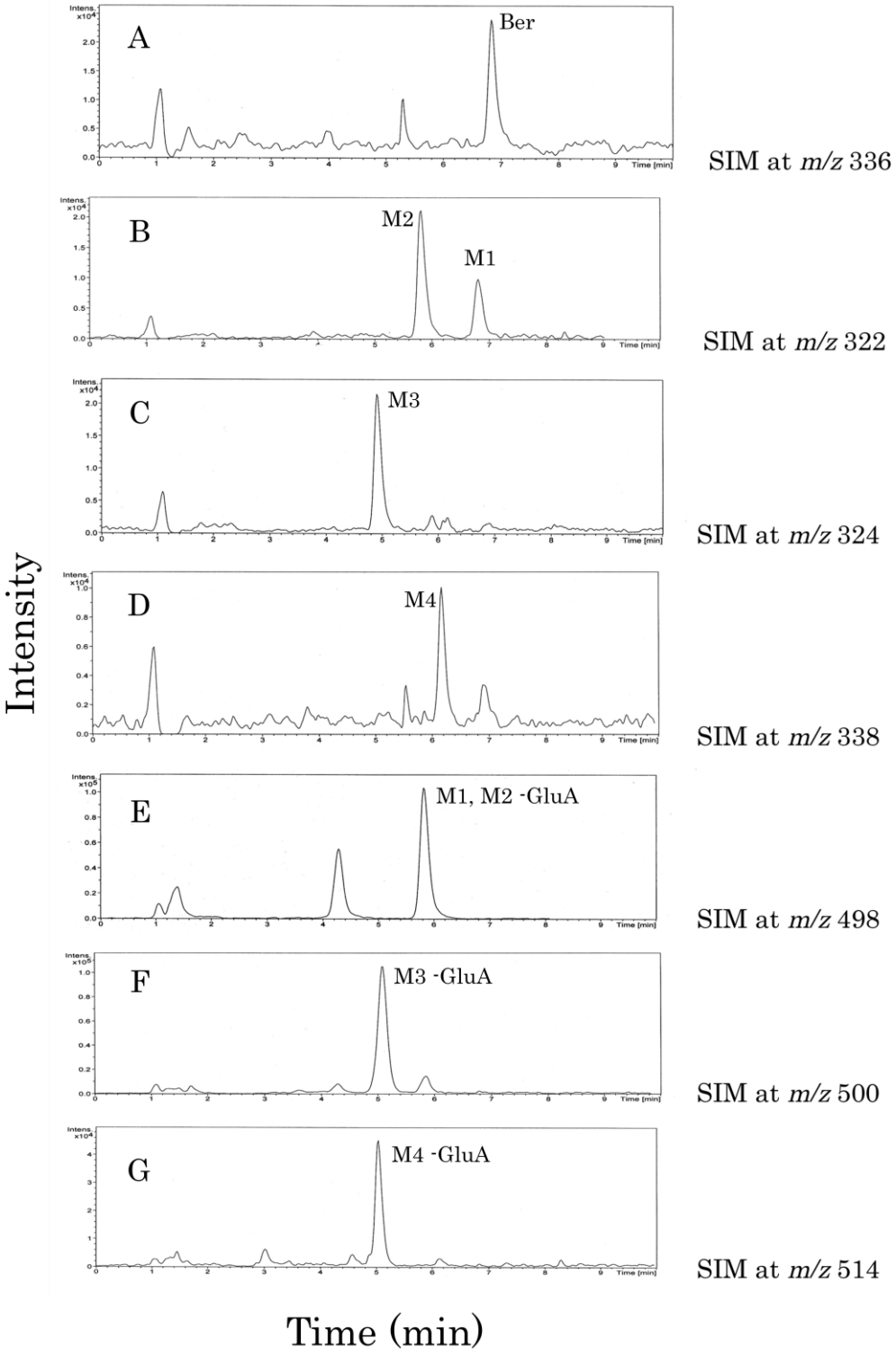

A
Ber
SIM at m/z 336
B
M2
M1
SIM at m/z 322
C
M3
SIM at m/z 324
D
M4
SIM at m/z 338
E
M1, M2 -GluA
SIM at m/z 498
F
M3 -GluA
SIM at m/z 500
G
M4 -GluA
SIM at m/z 514
Intensity
Time (min)

Fig. 3 SIM chromatograms of Ber at *m/z* 336 (A) and the metabolites at *m/z* 322 (B), 324 (C), 338 (D); glucouronide conjugates at *m/z* 498 (E), 500 (F) and 514 (G).
Ber, berberine; M1, berberrubine; M2, thalifendine: M3, demethyleneberberine; M4, jatrorrhizine.

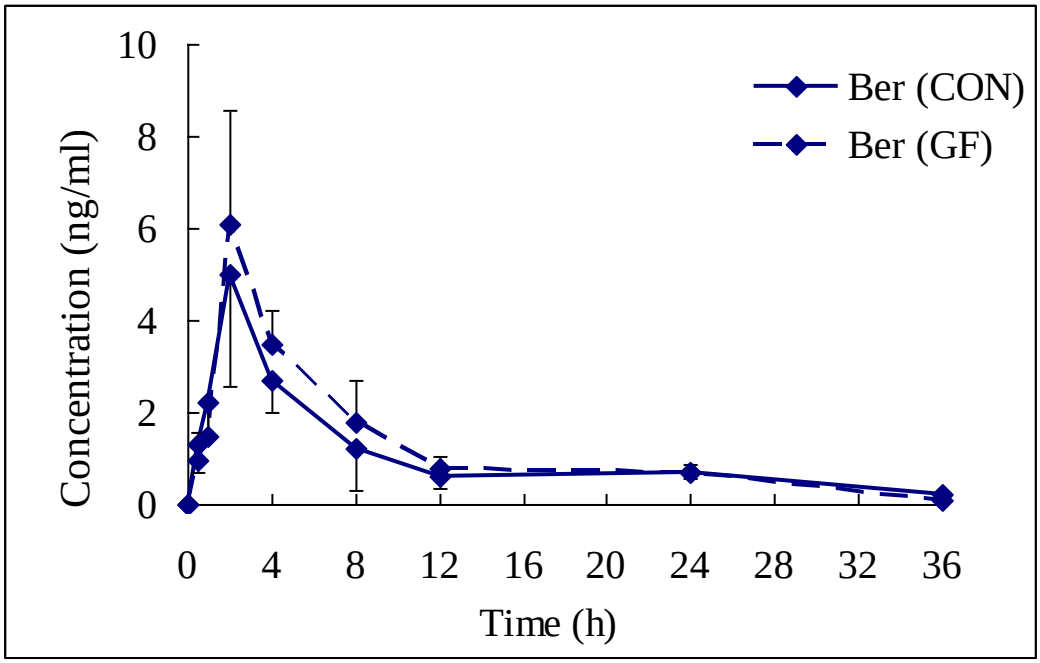
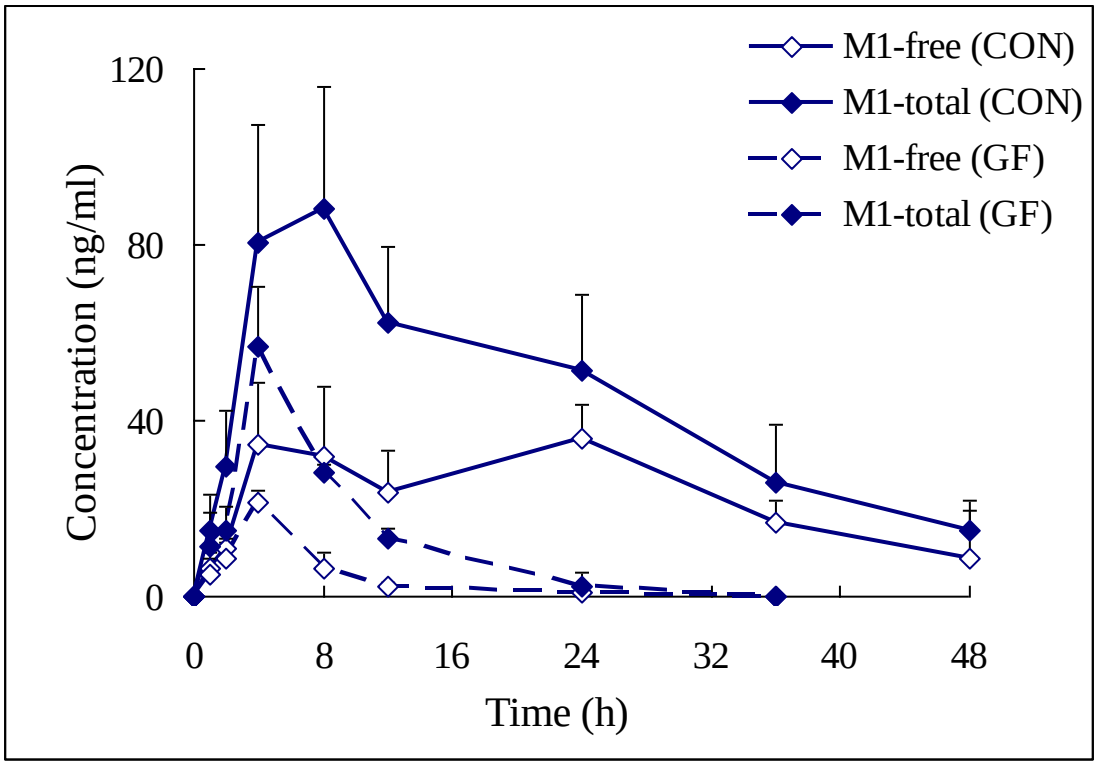
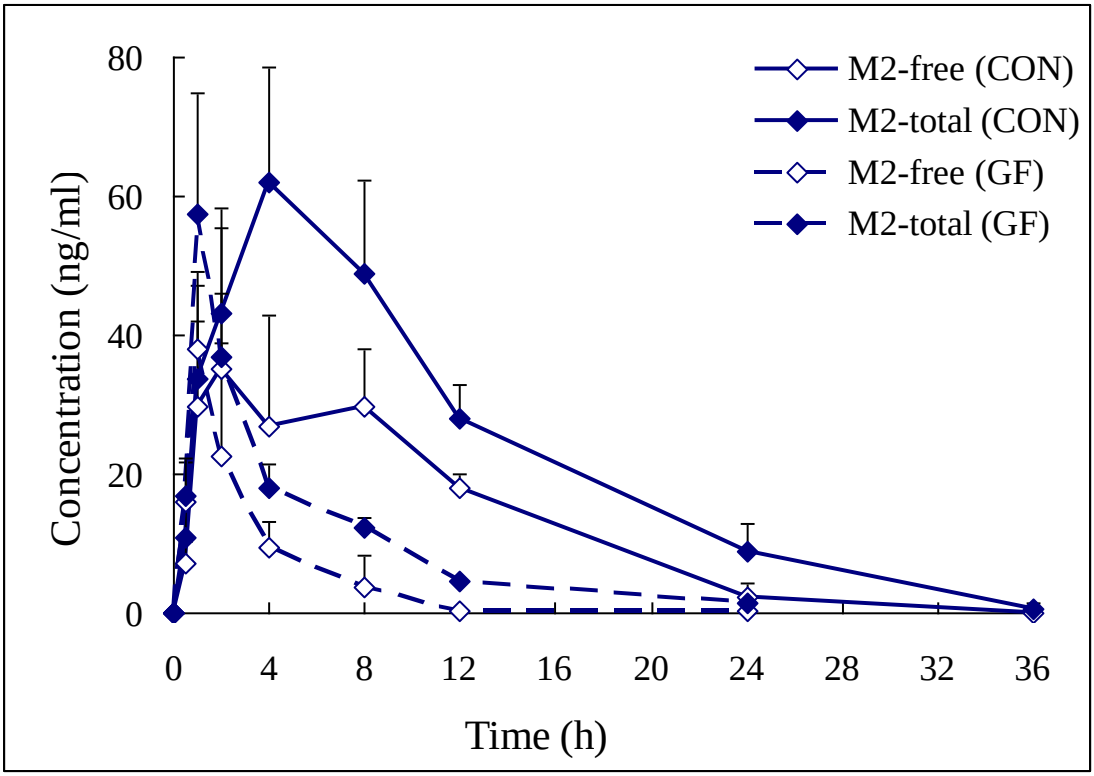
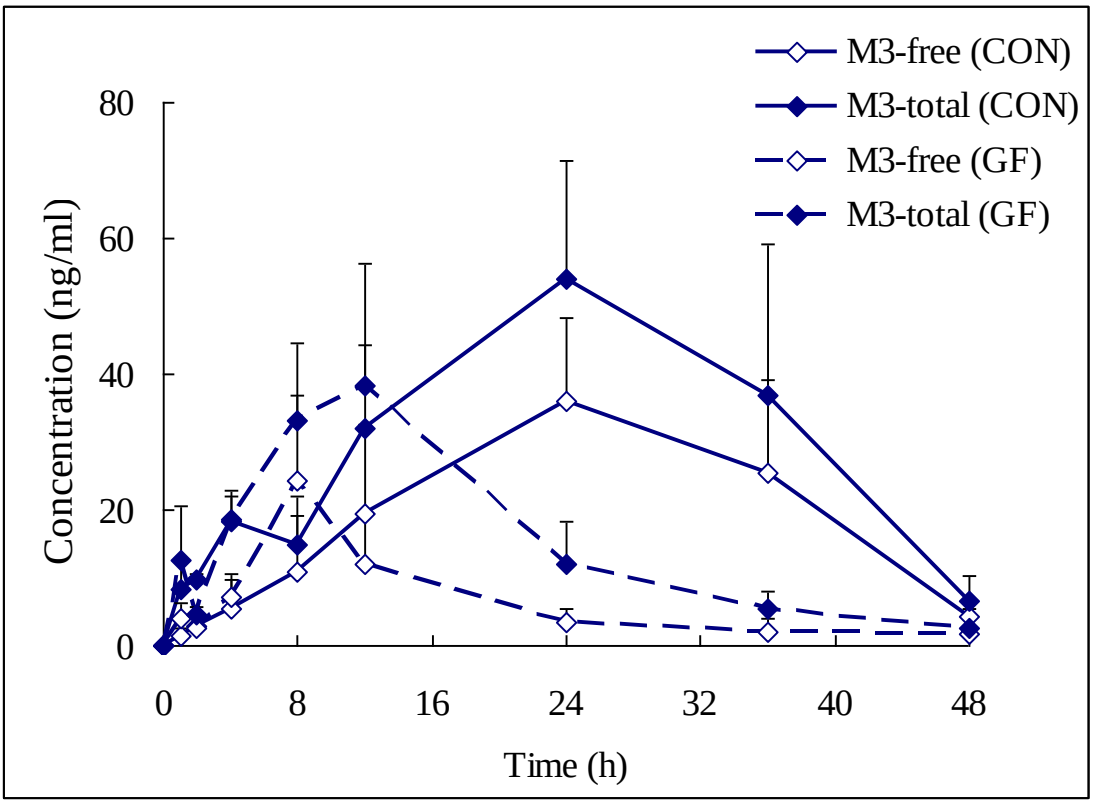


Fig. 4 Plasma concentration-time courses of after oral administration of berberine (Ber) (40 mg·kg^{-1}) in conventional (CON) and pseudo germ-free (GF) rats. [Zuo *et al*., *Drug Metab. Dispos*., **34**, 2064-2072 (2006)]


M1-free (CON)
M1-total (CON)
M1-free (GF)
M1-total (GF)
Concentration (ng/ml)
120
80
40
0
0
8
16
24
32
40
48
Time (h)


M2-free (CON)
M2-total (CON)
M2-free (GF)
M2-total (GF)
Concentration (ng/ml)
80
60
40
20
0
0
4
8
12
16
20
24
28
32
36
Time (h)



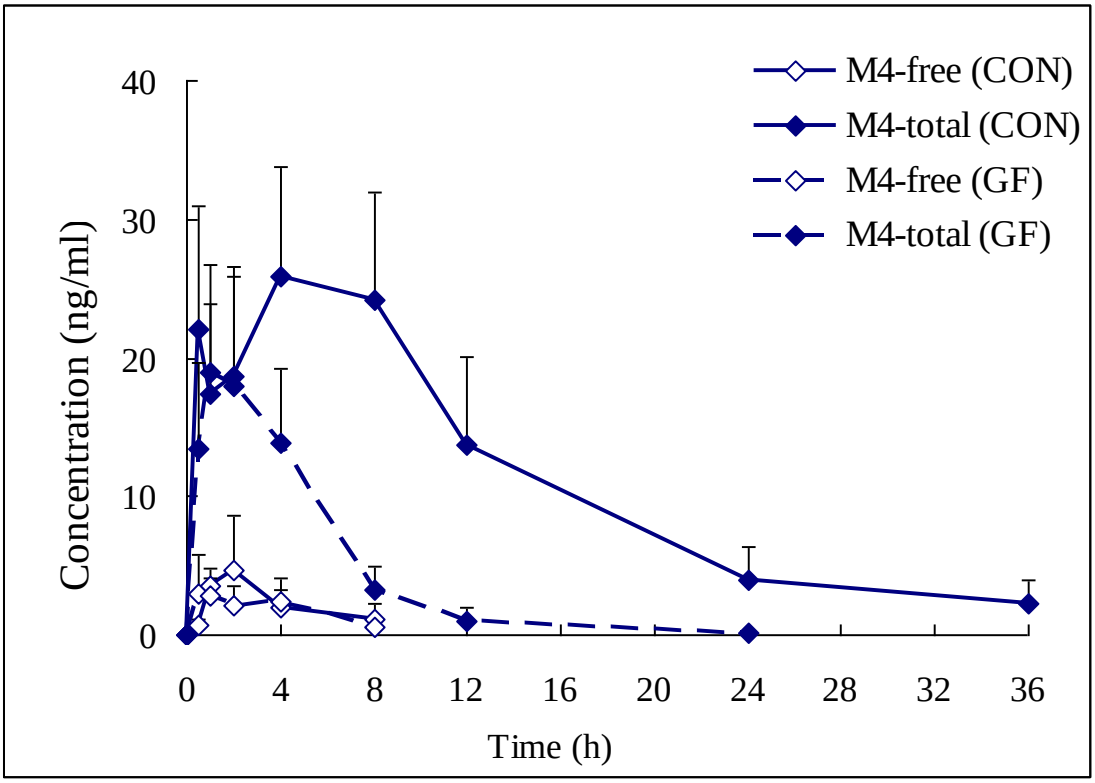


Fig. 5. Plasma concentration-time courses of free and total metabolites after oral

administration of berberine (40 mg·kg^{-1}) in conventional (CON) and pseudo germ-free (GF) rats. [Zuo *et al*., *Drug Metab. Dispos*., **34**, 2064-2072 (2006)]

Table 1 Pharmacokinetic parameters of berberine (Ber) and its metabolites (total contents) in conventional (CON) and pseudo germ-free (GF) rats after administration of 40 mg·kg^{-1} oral berberine.

	Pharmacokinetic parameters			
	$AUC_{0\text{-limt}}$ (ng·h·ml^{-1})	$T_{1/2}$ (h)	*MRT* (h)	*MAT* (h)
Ber (CON)	37.1±10.2	2.39±1.2	10.52±2.3	1.09±0.7
Ber (GF)	43.9±8.9	2.61±1.4	9.56±1.6	1.28±0.6
M1 (CON)	2168.1±567.4	16.26±4.2	18.53±3.2	1.93±0.6
M1 (GF)	253.2±124.5[b]	9.53±3.2[a]	10.9±2.4[a]	1.71±0.8
M2 (CON)	651.1±164.3	4.08±2.6	9.61±4.7	0.65±0.4
M2 (GF)	144.3±93.2[a]	1.16±1.0[a]	2.68±1.5[a]	0.35±0.2
M3 (CON)	1523.7±448.9	7.96±2.7	24.39±6.3	4.33±3.2
M3 (GF)	655.9±204.3[a]	8.57±3.9	15.20±4.8[a]	6.76±2.4
M4 (CON)	397.0±67.4	8.66±3.3	10.33±3.1	1.69±1.1
M4 (GF)	110.9±32.1[a]	2.57±1.1[a]	4.06±1.7[a]	0.78±0.3

[a] $p< 0.05$, [b] $p< 0.01$ compared with conventional rats; Data are expressed as means±S.D. (n = 4). Ber, berberine; M1, berberrubine; M2, thalifendine: M3, demethyleneberberine; M4, jatrorrhizine. [Zuo *et al*., *Drug Metab. Dispos*., **34**, 2064-2072 (2006)]

参考文献

1) Zuo F., Nakamura N. and Hattori M.: Pharmacokinetics of berberine and its main metabolites in conventional and pseudo germ-free rats determined by liquid chromatography/ion trap mass spectrometry. *Drug Metab. Dispos*., **34**, 2064-2072 (2006).