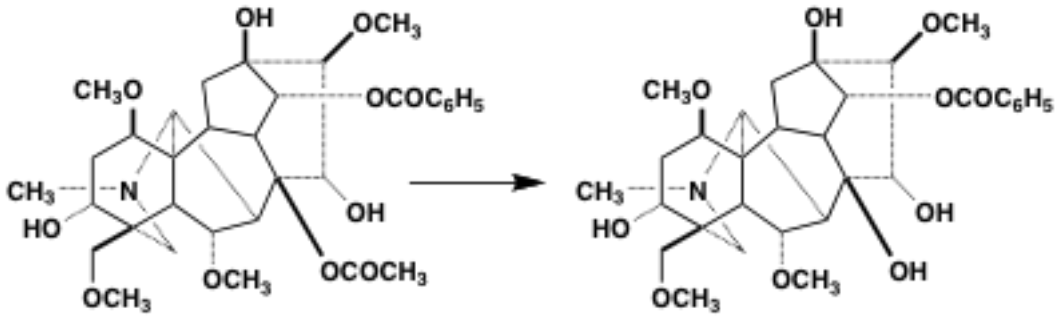
Benzoylmesaconine



Mesaconitine (1) **Benzoylmesaconine (2)**

代謝実験

動物代謝 ラット

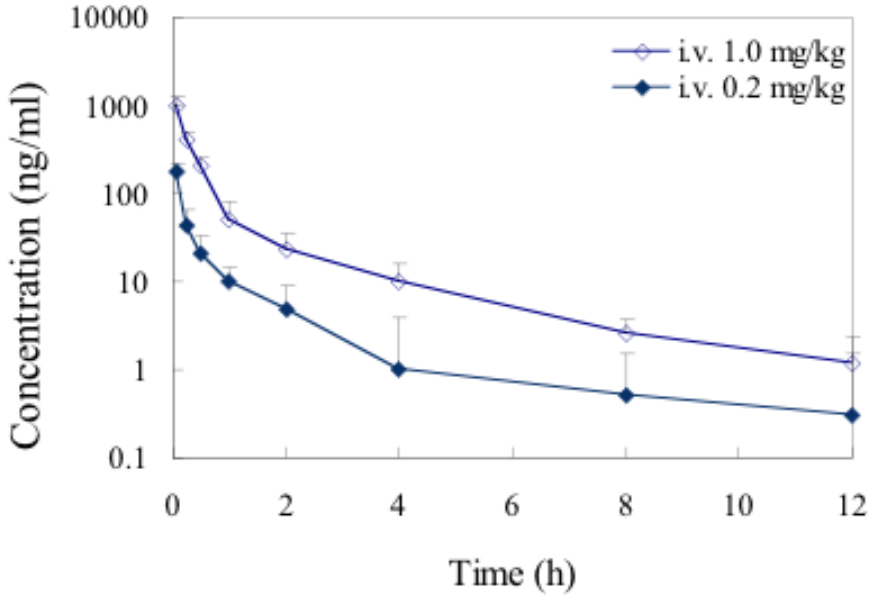


Fig. 1. Sera concentration–time curve of benzoylmesaconine (**2**) after i.v. administration in rats

Enzyme immunoassay for benzoylmesaconine (2)

The immunization protocol included primary inoculation of three female albino rabbits with DBAE-BSA (2 mg) conjugate in saline (2 ml) emulsified with the same volume of complete Freund's adjuvant. After two weeks, the rabbits were continued with booster injections at two weeks for 3 months and three weeks' interval for two months. The emulsion was prepared with 1.5 mg of the conjugate in saline (1.5 ml) and incomplete Freund's adjuvant (1.5 ml).

Samples or standard solutions (50 μl) containing various amounts of BM were incubated with an antiserum (50 μl) and a 10^3-fold diluted β-Gal conjugate (25 μl) at room temperature for 2 h. Ten-fold diluted goat anti-rabbit IgG (50 μl) and 100-fold diluted normal rabbit serum (20 μl) were then added to the reaction mixture. The mixture was left overnight at 4°C. After addition of buffer A (1 ml), the resulting mixture was centrifuged at 1100 × g for 20 min at 4℃ The supernatant was discarded, and the precipitates were washed with buffer A followed by incubation with 0.1 mM 4-methylumbelliferyl β-D-galactoside for 30 min at 30℃ The reaction was stopped by

the addition of 100 mM glycine-NaOH buffer, pH 10.3 (3 ml). The fluorescence intensity of a product (4-methylumbelliferone) was spectrofluorometrically measured at wavelengths of 365 nm (excitation) and 448 nm (emission). [Zuo *et al*., *J. Nat. Med*., **60**, 313-321 (2006)]

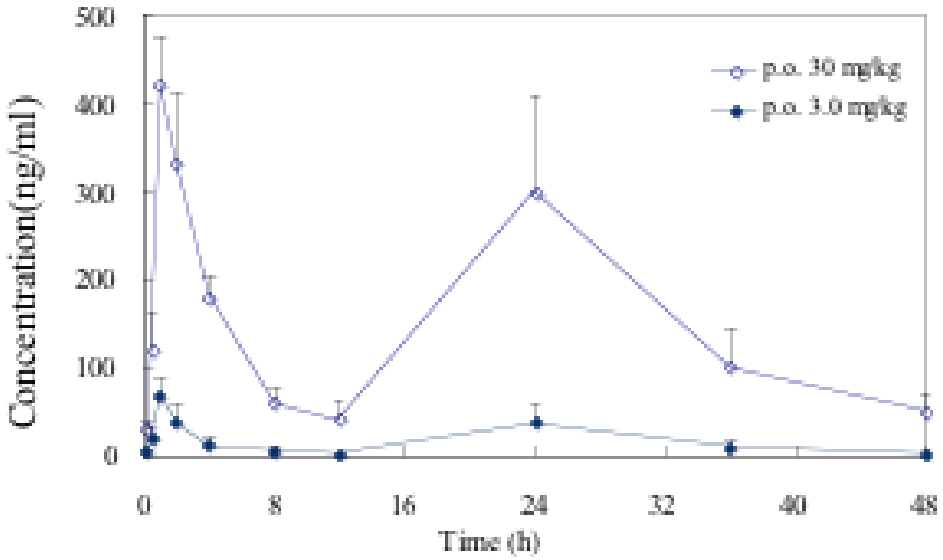


Fig. 2. Sera concentration–time curve of benzoylmesaconine (**2**) after oral administration in rats [Zuo *et al*., *J. Nat. Med*., **60**, 313-321 (2006)]

Table 1. Pharmacokinetic parameters of benzoylmesaconine (**2**) after i.v. administration in rats

	Dosage (mg/kg)	
	1.0	0.2
A (ng/ml)	1169.2±320.1	128.12±13.4
α (1/h)	3.89±0.67	2.83±0.54
B (ng/ml)	47.7±10.33	4.65±0.83
β (1/h)	0.33±0.02	0.26±0.01
$T_{1/2(\alpha)}$ (h)	0.18±0.04	0.25±0.10
$T_{1/2(\beta)}$ (h)	2.12±0.53	2.78±0.48
Vc (l/kg)	0.82±0.04	1.53±0.27
Vd (l/kg)	3.13±0.76	14.1±4.61
Cl (ml/h kg)	1.03±0.34	3.69±0.47
$AUC_{0\text{-}12}$ (ng h/ml)	969.4±103.5	54.2±12.4
MRT (h)	3.03±0.34	4.01±0.26

Each value represents the mean±S.D. of four rats.

A, B: Experiential parameters (intercept)

α: Apparent first order hybrid rate constant for the distribution

β: Apparent first order hybrid rate constant describing the elimination

$T_{1/2(\alpha)}$: Half-life of distribution phase

$T_{1/2(\beta)}$: Half-life of elimination phase

Vc : Apparent volume of distribution in the central compartment

Vd : Apparent volume of distribution

Cl : Total body clearance

AUC : Area under the serum concentration-time curve

MRT : Mean residence time

[Zuo *et al*., *J. Nat. Med.*, **60**, 313-321 (2006)]

Table 2. Pharmacokinetic parameters of benzoylmesaconine (**2**) after oral administration in rats

	Dosage (mg/kg)	
	30	3.0
C_{max} (ng/ml)	477.4±134.6	77.64±21.34
T_{max} (h)	1.31±0.56	1.08±0.31
K_a (1/h)	1.84±0.59	1.94±0.40
AUC_{0-48} (ng h/ml)	7209.6±2104.6	769.1±238.5
MRT (h)	22.1±1.2	21.3±0.8

Each value represents the mean±S.D. of six rats.

C_{max} : Maximum serum concentration

T_{max} : Time taken to reach to maximum serum concentration

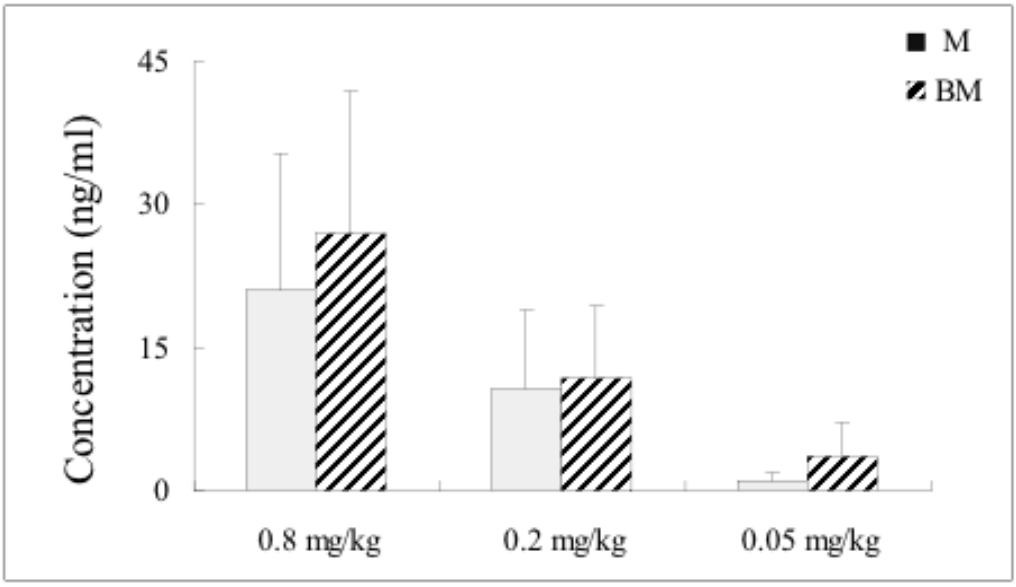
K_a : Absorption rate constant

AUC : Area under the serum concentration-time curve

MRT : Mean residence time

[Zuo *et al*., *J. Nat. Med.*, **60**, 313-321 (2006)]

I



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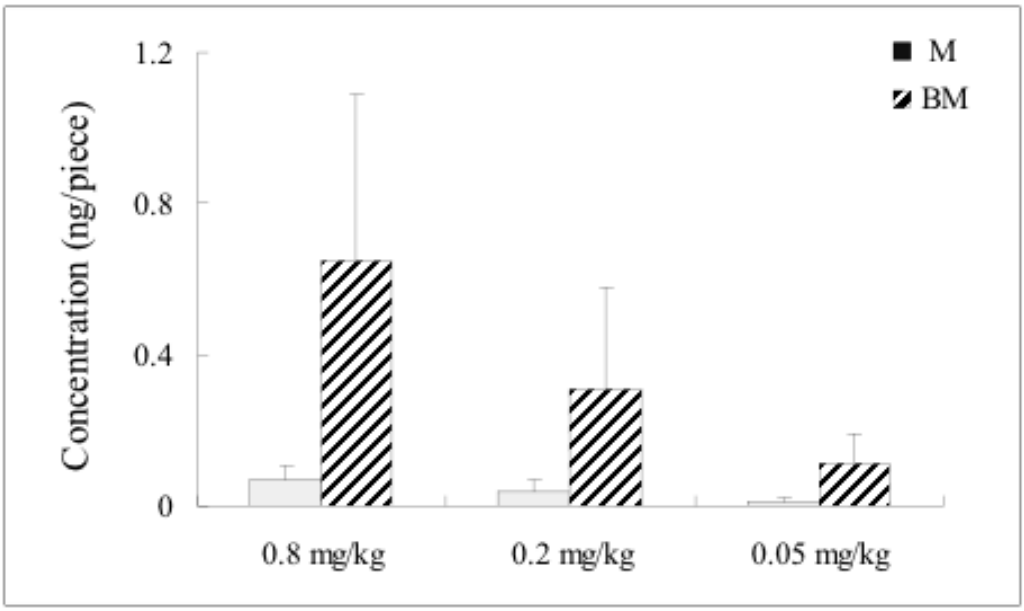

Fig. 3. The concentrations of mesaconitine (**1**) and benzoylmesaconine (**2**) 1 h after oral administration of **1** in sera (I) and in spinal cord (II) samples

M, mesaconitine (**1**); BM, benzoylmesaconine (**2**) [Zuo *et al*., *J. Nat. Med*., **60**, 313-321 (2006)]

Disposition of mesaconitine (1) after oral administration in rats

One hour after oral administration of **1** at doses of 0.8, 0.2, 0.05 mg/kg in rats, under general anesthesia, the blood and spinal cord (L1-L4) were collected, and their mesaconitine (**1**) and benzoylmesaconine (**2**) contents were determined by the respective enzyme immunoassay systems. [Zuo *et al*., *J. Nat. Med*., **60**, 313-321 (2006)]

参考論文

1) Zuo F., Zhao J., Nakamura N., Gao J. J., Akao T., Hattori M., Oomiga Y., and Kikuchi Y.: Pharmakokinetic stydy of benzoylmesaconine in rats using an enzyme immunoassay system. *J. Nat. Med.*, **60**, 313-321 (2006).

2) Zhao Z., Sun X. F., Nakamura N., Zuo F., Yang X. W., and Hattori M.: Development of an enzyme immunoassay system for mesaconitine and its application to the disposition study on mesaconitine. *J. Trad. Med*., **20**, 201-207 (2003).