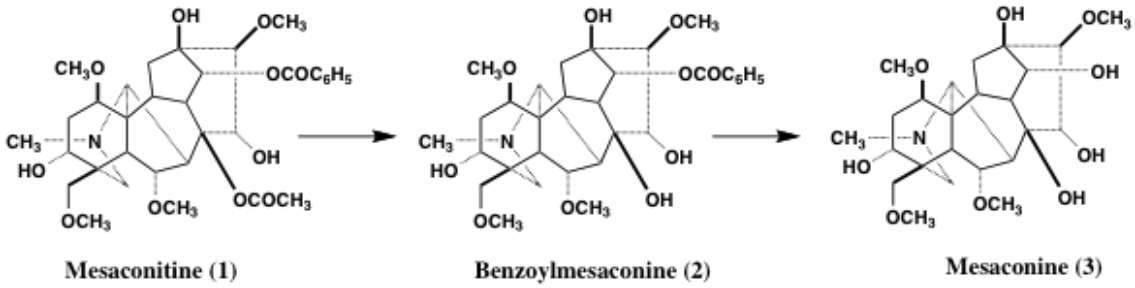
Mesaconitine



Metabolic processes of mesaconitine

代謝実験

代謝動物　Wistar ラット

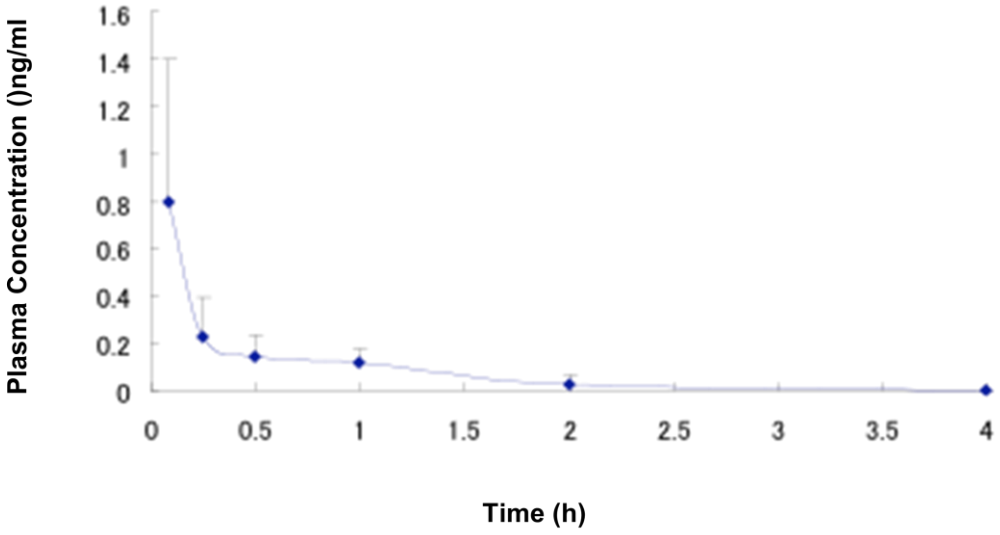


Fig. 1. Plasma concentration of mesaconitine after intravenous administration to Wistar rats at the dose of 0.005 mg/kg. [Zhao *et al*., *J. Trad. Med*., **20**, 201-207 (2003)]

Standard curve of mesaconitine (1)

2.5×10^{4}-fold diluted As-DEAG in 50 µl of buffer A, 50 µl of serially diluted mesaconitine (5×10^{-4}—50 ng/tube) or 50 µl of buffer A as a blank, and 25 µl of 10^{3}-fold diluted DEAG-β-Gal were incubated at room temperature for 2 h. Afterward, 20 µl of 10^{2}-fold diluted normal rabbit serum and 50 µl of 10-fold diluted goat antiserum to

rabbit Ig G were added to the reaction system, which was allowed to stand at 4 °C overnight. After measurement of fluorescence, B/B_0 values were calculated as the percentage of the enzyme activity of the labeled antigen bound to the antiserum in the presence of various concentrations of mesaconitine (B) to that in the absence of mesaconitine (B_0). [Zhao *et al*., *J. Trad. Med*., **20**, 201-207 (2003)]

Measurement of plasma concentration of mesaconitine (1) after intravenous and oral administration

Seven-week old male Wistar rats about 220 g each, were fasted one day before the pharmacokinetic study. After intravenous administration at a dose of 0.005 mg/kg or oral administration at a dose of 1 mg/kg to rats, blood was collected by haperinated capillaries at 5 min, 15 min, 0.5 h, 1 h, 2 h, 4 h and 8 h after injection or continued at 12 h and 24 h after oral administration. [Zhao *et al*., *J. Trad. Med*., **20**, 201-207 (2003)]

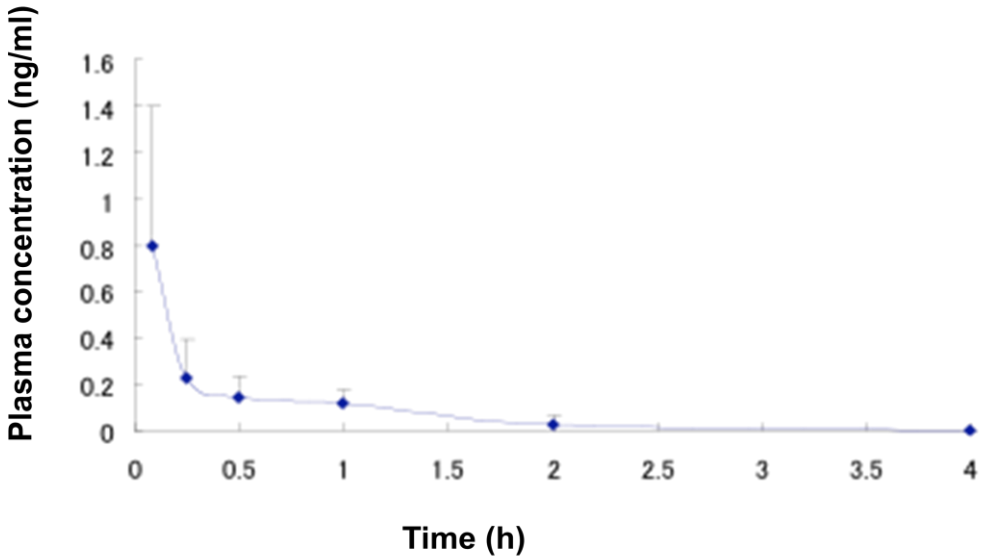


Fig. 2. Plasma concentration of mesaconitine after oral administration at 1 mg/kg to Wistar rats. [Zhao *et al*., *J. Trad. Med*., **20**, 201-207 (2003)]

Table 1. Pharmacokinetic parameters of mesaconitine (**1**) after intravenous and oral administrations to Wistar rats.

1) Parameters after intravenous administration at 0.005 mg/kg to Wistar rats.

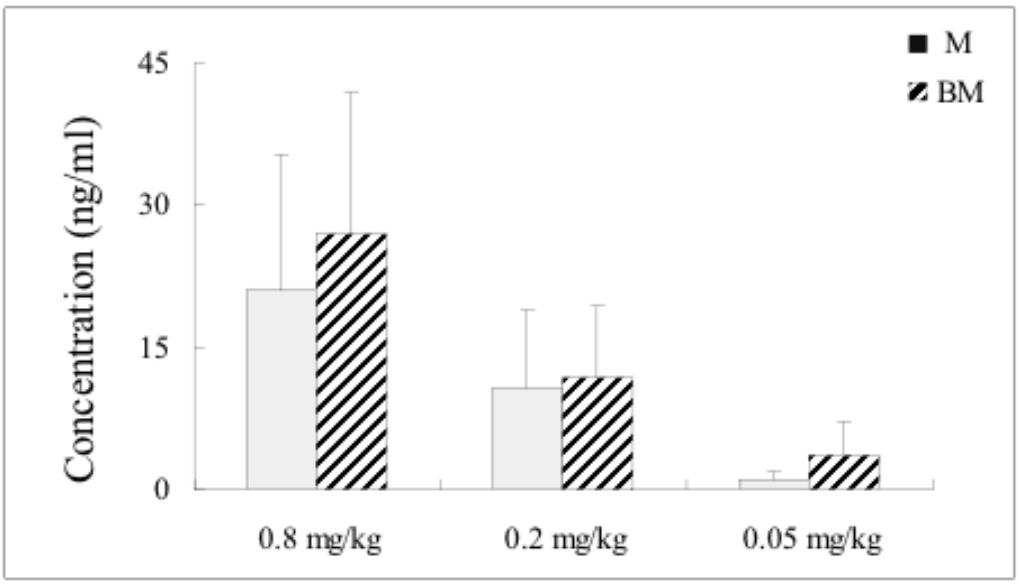
Parameter	Dose (mg/kg)
	0.005
A (ng/ml)	2.63±0.37
α (h^{-1})	11.05±3.04
B (ng/ml)	0.12±0.13
β (h^{-1})	0.42±0.18
T1/2α (h)	0.0652±0.0179
T1/2β (h)	1.823±0.767
Vc (l/kg)	0.397±0.069
Vdss (l/kg)	4.620±2.536
Cl (l/h kg)	1.704±0.247
AUC (ng/ml h)	0.652±0.094

2) Parameters for mesaconitine after oral administration to Wistar rats.

Dose	T_{max} (h)	C_{max} (ng/ml)	AUC_{0-8} (ng h/ml)
1.0 mg/kg	2.10±0.08	6.01±2.04	17.6606±3.3888

Each point represents the mean±SD (n=3). [Zhao *et al*., *J. Trad. Med*., **20**, 201-207 (2003)]

I



II

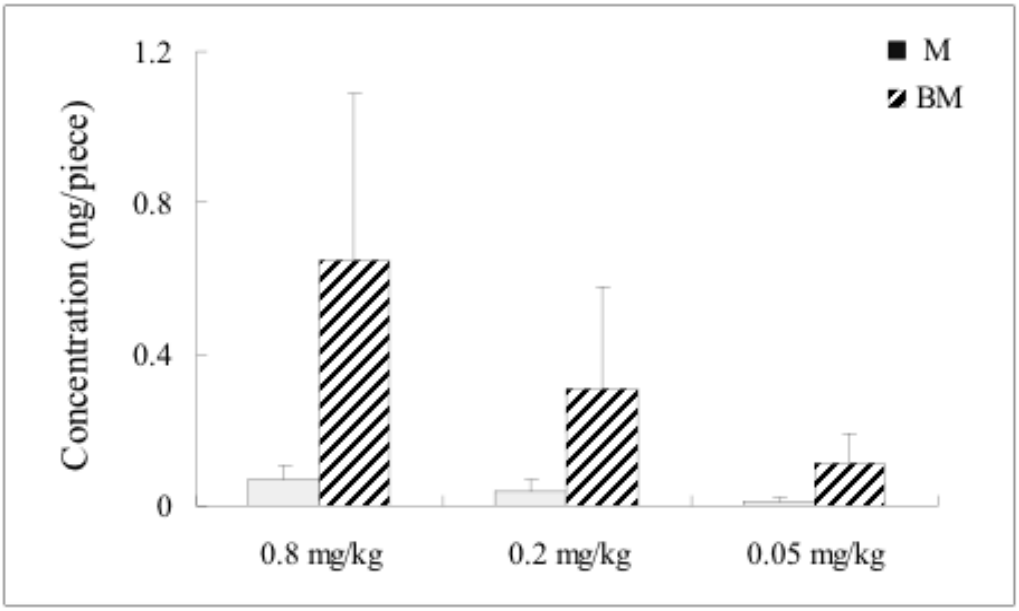


Fig. 3 The concentrations of mesaconitine (**1**) and benzoylmesaconine (**2**) 1 h after oral administration of mesaconitine (**1**) in sera (I) and in spinal cord (II) samples

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

Disposition of mesaconitine (1) after oral administration in rats

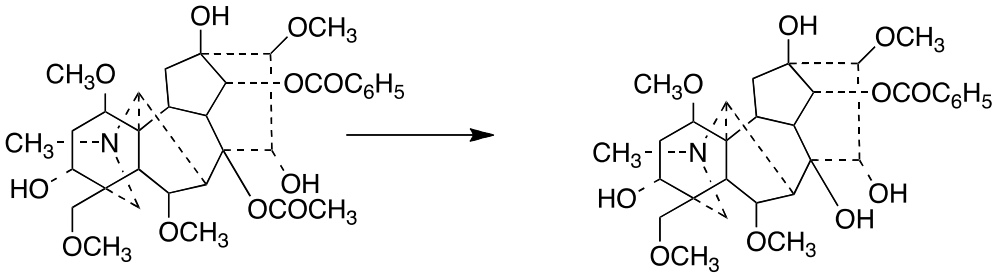
One hour after oral administration of mesaconitine (**1**) at doses of 0.8, 0.2, 0.05 mg/kg in rats, under general anesthesia, the blood and spinal cord (L1-L4) were collected, and the samples treated as described above. [Zuo *et al*., *J. Nat. Med.*, **60**, 313-321 (2006)]

参考論文

1) 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).

2) 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).

Mesaconitine（追加）



Mesaconitine (1)　　Benzoylmesaconine (2)

【化合物】Mesaconitine

"SHEN-FU" injectable powder by SAN-JIU PharmaceuticalCompany of Ya-An in China was applied to humans, and their sera were used for analysis of aconite alkaloids. The "SHEN-FU" injectable powder was approved by State Food and Drug Administration of China (No. 2004L02334). At present, it was under clinical trial in phase I in National Clinical Trial Center of Traditional Chinese Medicine of China. The main active components of "SHEN-FU" were ginsenosides and *Aconitum* alkaloids. [Zhang et al., *J. Chromato. B,* **873**, 173–179 (2008).]

【化合物の起源 生薬お呼び薬用植物】

【対象】動物（ヒト）

【測定機器】LC-MS/MS

【代謝実験】

"SHEN-FU" injectable powder was applied to 18 healthy volunteers by intravenous drop infusion. Six volunteers were involved in each experiment. The blood samples were collected at intervals after intravenous drop infusion. The pharmacokinetics demonstrated that the concentrations of aconitine, mesaconitine, and hypaconitine were at very low levels with < 0.2, < 0.2, and < 0.7 ng/mL or under detection limit for all) and the content of benzoylmesaconine was highest. [Zhang et al., *J. Chromato. B,* **873**, 173–179 (2008).]

【参考文献】

Fan Zhang, Ming-hai Tang, Li-juan Chen, Rui Li, Xian-huoWang, Jun-guo Duan, Xia Zhao, Yu-quanWei, Simultaneous quantitation of aconitine, mesaconitine, hypaconitine, benzoylaconine, benzoylmesaconine and benzoylhypaconine in human plasma by liquid chromatography–tandem mass spectrometry and pharmacokinetics evaluation of “SHEN-FU” injectable powder. *J. Chromato. B,* 873, 173–179 (2008).