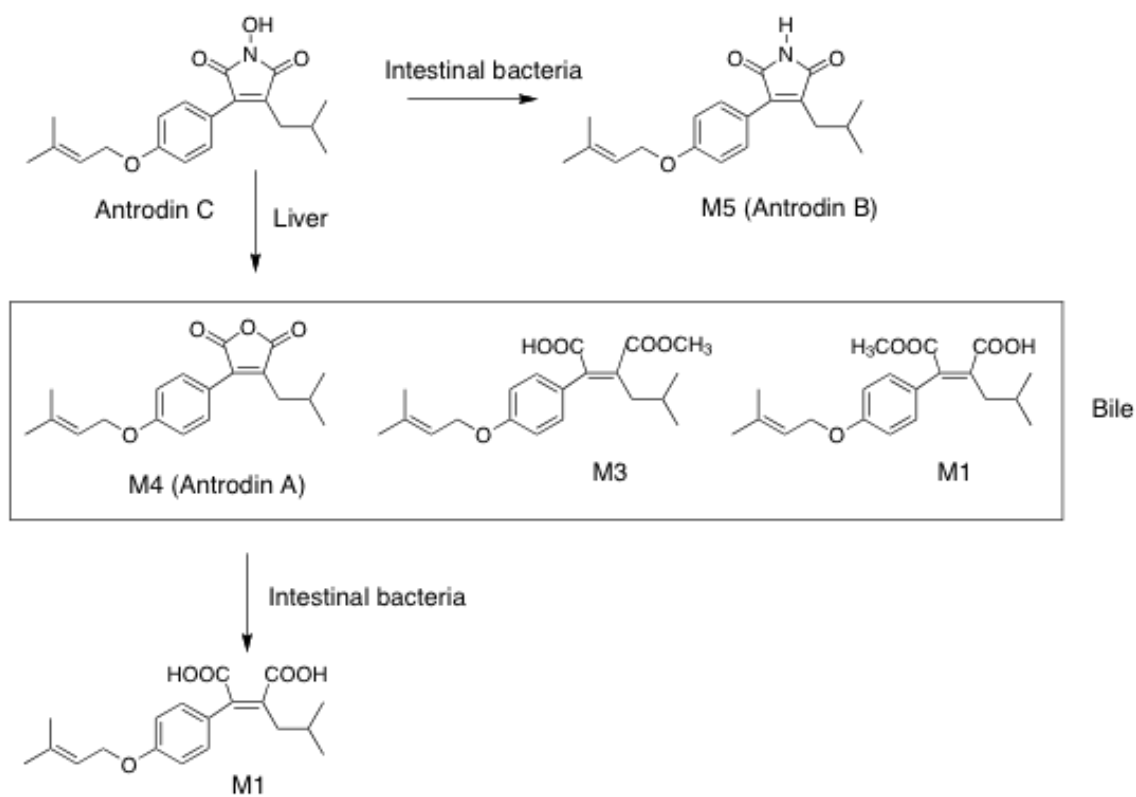


Antrodin C



Metabolism of antrodin C in rats

代謝実験

動物代謝 ラット

腸内細菌代謝 ラット腸内細菌フローラ

単一化合物 antrodin C

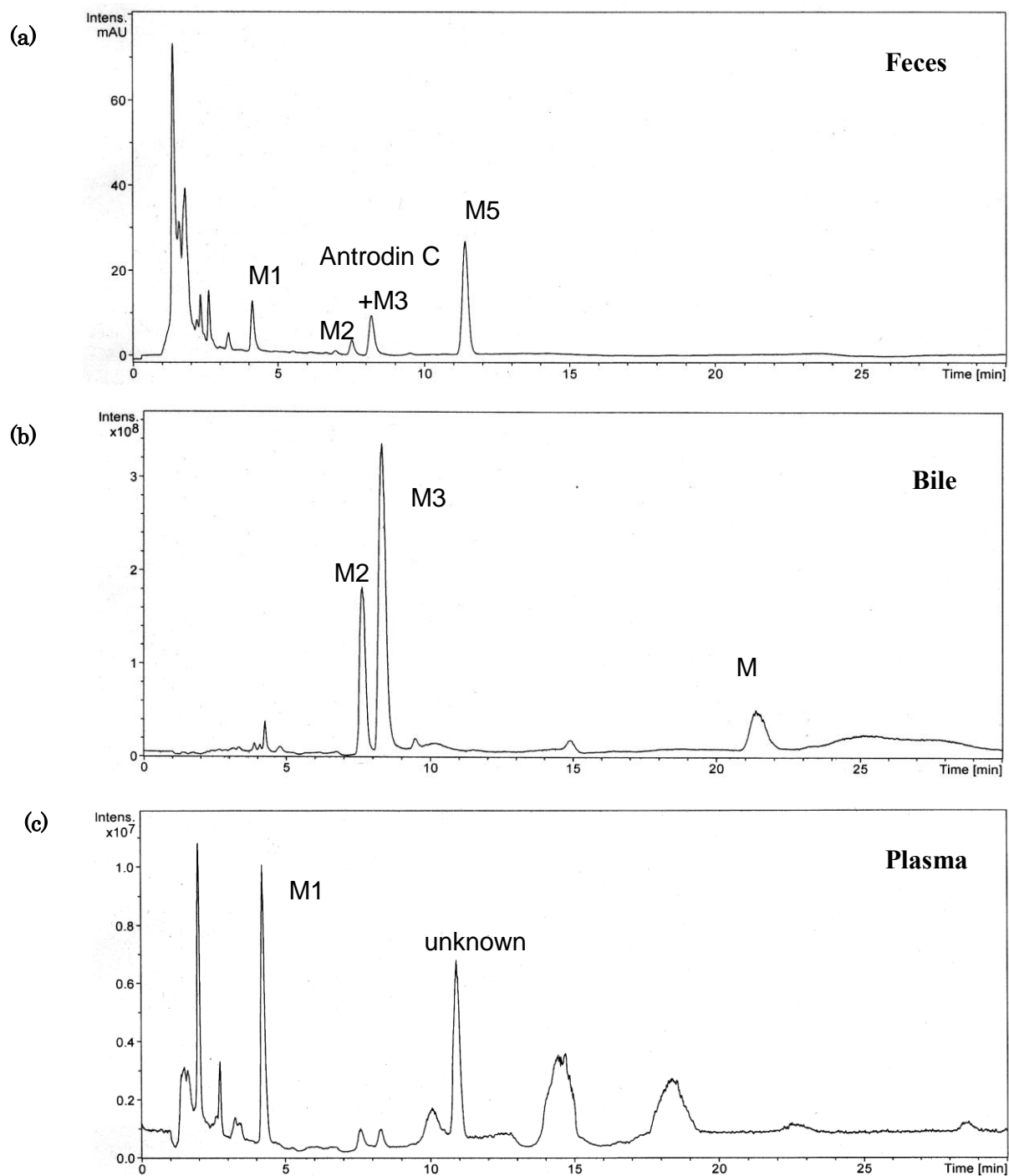


Fig. 1. Total ion chromatogram (TIC) of feces (a), bile (b) and plasma (c) sample after oral administration of antrodin C at a dose of 50 mg/kg.

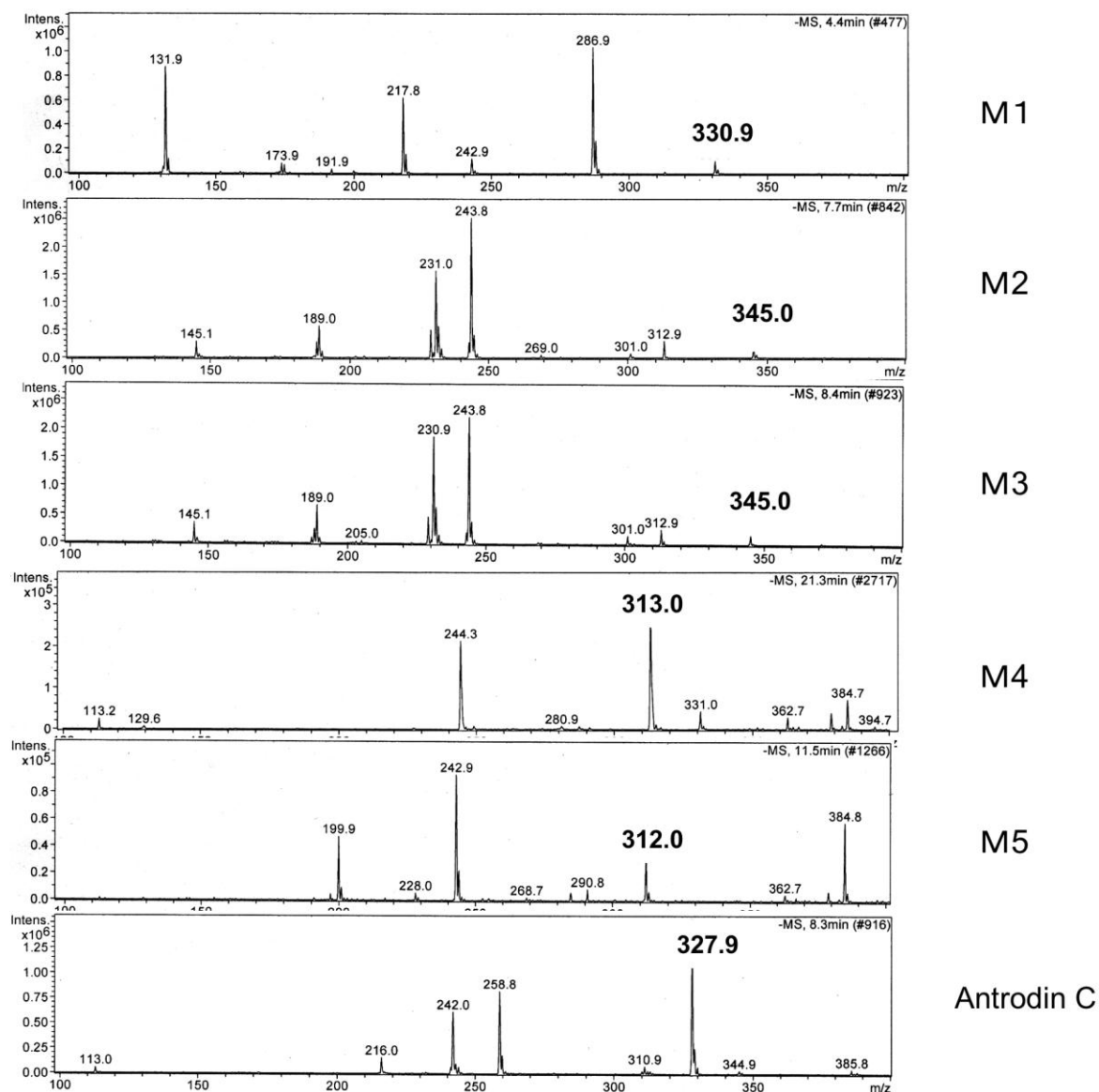
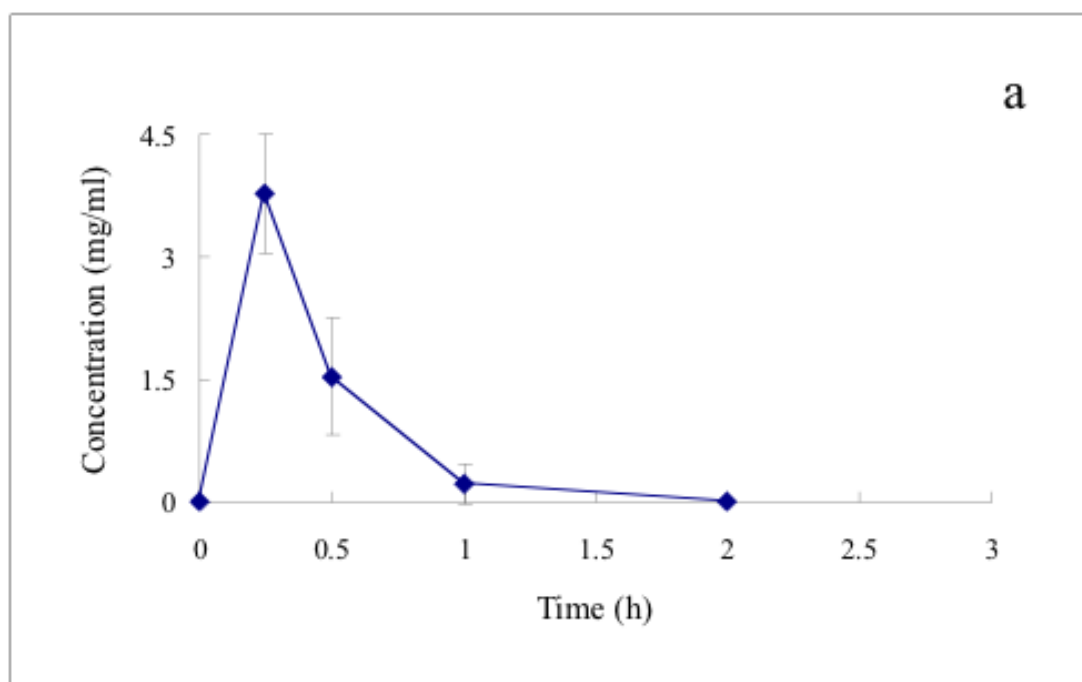


Fig. 2. MS spectra (negative ion mode) of M1-M5 and antrodin C in rat feces, bile and plasma samples

LC/MS-MS Condition.

The LC/MS-MS equipment comprised a column containing TSK gel ODS-80 Ts

(particle size, 5 μm ; 4.6×150 mm i.d., Tosoh Co., Tokyo, Japan). Samples were eluted through a column with 0.1% AcOH and acetonitrile (35:65) at a flow rate of 1 ml/min at 30°C. The standard negative ion mode was selected under the following conditions: full scan range, 50-800 m/z ; scan resolution, 13000 m/z /sec; nebulizer, 50.0 psi; dry gas, 10.0 l/min; dry temperature, 360°C.



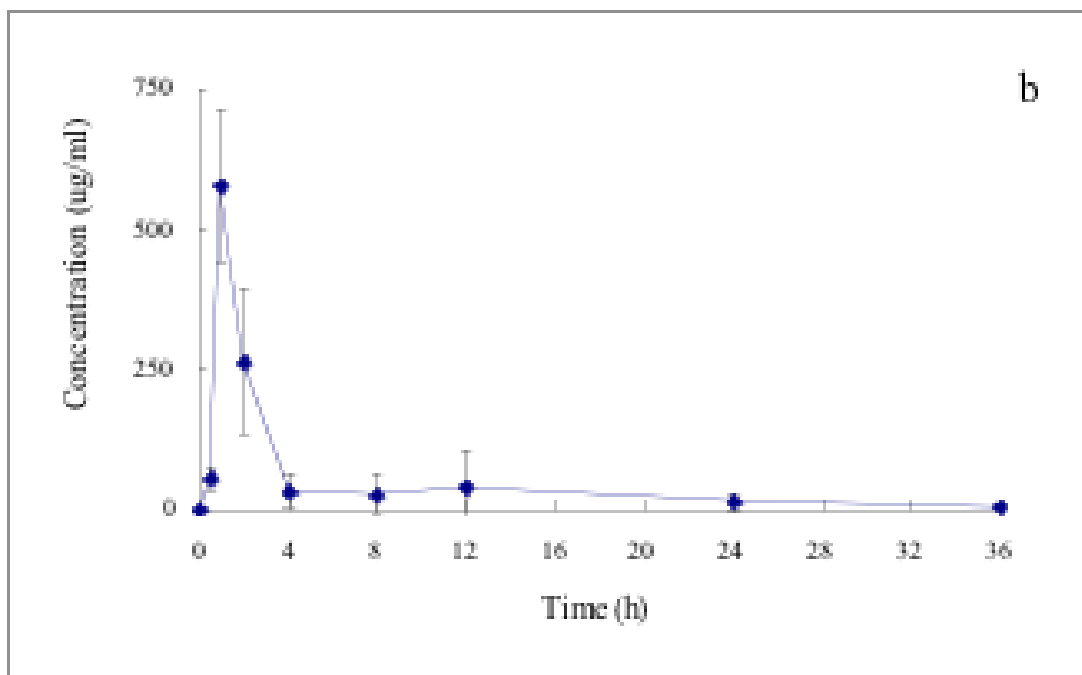


Fig. 3. Concentration-time curve of M1 in bile samples after administration of antrodin C at doses of (a) 10 mg/kg i. v. and (b) 50 mg/kg p.o.

Animal Experiments.

Male Wistar rats (9 weeks old) purchased from SLC Co. (Hamamastu, Japan), were fed with standard laboratory chow for one week, fasted overnight and given free access to water before drug administration. Urine and feces samples were collected while the rats remained isolated in metabolic cages. The animals were light anesthetized with diethyl ether during surgical procedures. Bile samples (n=5) was collected by cannulating a polyethylene tube (PE-10) into a rat bile duct at intervals of 0, 0.25, 0.5, 1, 2, 4, 8, 12, 24, 36 and 48 h after oral (50 mg/kg) and intravenous (10 mg/kg) administration of antrodin C. The blood sample was collected from the inferior vena cava using a heparinized injector when the abdomen was exposed by a midline abdominal incision after administration. The blood samples were centrifuged at $8000 \times g$ for 15 min to separate the plasma, and then all samples were stored at -20°C for later analysis.

Table 1. Pharmacokinetic parameters of M1 in rat bile samples after p.o. and i.v. administration of antrodin C.

P.O. (50 mg/kg)		I.V. (10 mg/kg)			
$t_{1/2(k\alpha)}$	$t_{1/2(k\beta)}$	AUC _{0-lim}	AUC _{0-lim}	Cl _{m,b.}	F _{m,b.}
(h)	(h)	(h mg/ml)	(h mg/ml)	(ml/h kg)	(%)
0.95±0.07	12.64±2.24	1.61±0.58	1.68±0.31	5.96	19.43

Pharmacokinetic Analysis.

The concentration-time data in rat bile (n=5) were computer fitted using a program of Pharmacokinetics 3p97 edited by the Mathematics Pharmacological Committee, Chinese Pharmacological Society. The following pharmacokinetic parameters were obtained: half-time of absorption phase ($t_{1/2(k\alpha)}$) and half-time of elimination phase ($t_{1/2(k\beta)}$) in the bile samples after oral administration of antrodin C at a dose of 50 mg/kg.

The area under the concentration–time curve (AUC_(i.v.) and AUC_(p.o.)) was calculated by the statistical moment method of non-compartmental pharmacokinetic analysis.

Clearance (Cl_{m,b}) and absolute bioavailability (F_{m,b}) were calculated by an equations as follows: Cl_{m,b} (ml/h·kg) = Dose_(i.v.)/AUC_(i.v.) and F_{m,b} (%) = AUC_(p.o.) · Dose_(i.v.)/ [AUC_(i.v.) · Dose_(p.o.)]. Data were expressed as the mean and standard deviation (S.D.) for each group.

参考文献

1) Zuo F., Wada A., Ma C. M., Nakamura N., and Hattori M., Metabolism and disposition of antrodins C, a cytotoxic major principle from the mycelium of *Antrodia cinnamomea*, in rats. Unpublished results.