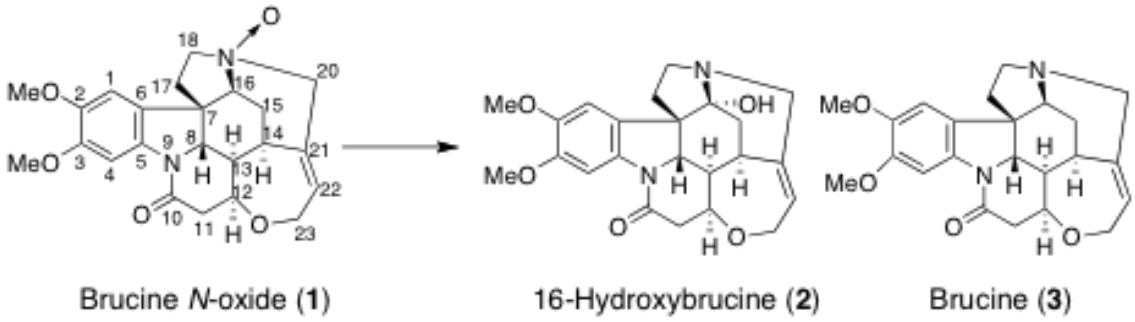
Burcine *N*-oxide



Transformation of brucine *N*-oxide by human intestinal bacteria

代謝実験

腸内細菌代謝 ヒト腸内細菌株 *Lactobacillus acidophilus*

Screening of bacterial strains for their ability to metabolize brucine *N*-oxide (1)

Brucine *N*-oxide (10 mg; **1**) in DMSO (0.1ml) was incubated with each bacterial suspension (10 ml) under anaerobic conditions for 4 d and the metabolites were quantitatively analyzed by HPLC using CH_3CN–0.03 M Na_2HPO_4 (45 : 55) as a mobile phase. [El-Mekkawy *et al., Planta Med*., **59**, 347-350 (1993)]

Incubation of brucine *N*-oxide (1) with *Lactobacillus acidophilus*

Brucine *N*-oxide (**1**, 500 mg) was anaerobically incubated for 4d. The residue after the evaporation of solvent was applied to preparative TLC (solvent system B) to isolate metabolites (**2** and **3**). [El-Mekkawy *et al., Planta Med*., **59**, 347-350 (1993)]

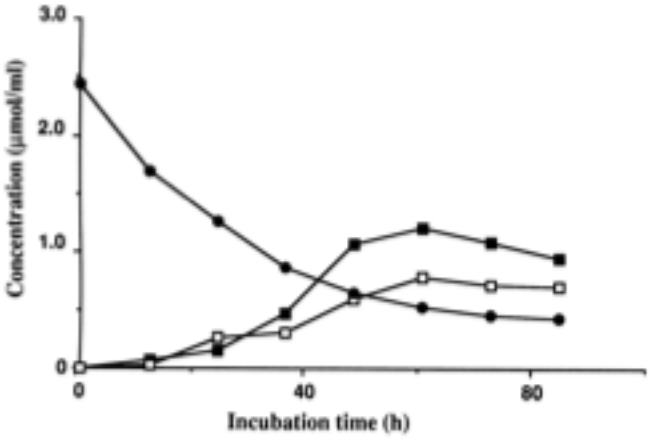
Compound 2 (16-Hydroxyburcine)

Colourless needles from acetone (6 mg, 1.2%), mp 209-211 °C. $[\alpha]_D$: −19.7° (*c* 0.05; $CHC1_3$–MeOH). MS *m/z* (rel. int.): 410 (M^+, 63%), 394 (100%). IR ν_{max} (KBr) cm^{-1}: 3400 (OH), 1640 (lactam). UV λ_{max} nm (EtOH) (log ε): 265 (4.3), 298 (4.1). ^{1}H-NMR (400 MHz, $CDC1_3$): δ 1.37 (1H, ddd, *J*= 10, 4, 3 Hz, 13-H), 1.78 (1H, dd, *J*= 13, 7 Hz, 17-Hb), 1.82 (1H, dd, *J*= 14, 3 Hz, 15-Hb), 2.22 (1H, dd, *J*= 14, 4.5 Hz, 15-Ha), 2.31 (1H, dd, *J*= 13, 7 Hz, 17-Ha), 2.60 (1H, dd, *J*= 17, 3.5 Hz, 11-Hb), 2.61 (1H, s,

exchangeable with D_2O, 16-OH), 2.81 (1H, dd, *J*= 10, 7 Hz, 18-Hb), 2.83 (1H, d, J= 15 Hz, 20-Ha), 3.09 (1H, dd, *J*= 17, 8 Hz, 11-Ha), 3.19 (1H, dd, *J*= 10, 7 Hz, 18-Ha), 3.28 (1H, br. s, 14-H), 3.80 (1H, d, *J*= 10 Hz, 8-H), 3.85 (3H, s, 2-OCH_3), 2.87 (1H, dd, *J*= 15, 2 Hz, 20-Ha), 3.90 (3H, s, 3-OCH_3), 4.06 (1H, dd, *J*= 14, 6.5 Hz, 23-Ha), 4.15 (1H, dd, *J*= 14, 6.5 Hz, 23-Hb), 4.20 (1H, ddd, *J*= 8, 3.5, 3 Hz, 12-H), 5.93 (1H, t, *J*= 6.5 Hz, 22-H), 7.40 (1H, s, l-H),7.84(lH, s, 4-H). [El-Mekkawy *et al., Planta Med*., **59**, 347-350 (1993)]

Compound 2 (Brucine)

Colourless needles from acetone (40mg, 8 %), mp 172-173 °C. $[\alpha]_D$: – 78.7° (c 0.05; $CHCl_3$–MeOH). MS *m/z* 394 (rel. int.): (M^+, 100%). IR ν_{max} (KBr) cm^{-1}: 1650 (lactam). UV λ_{max} nm (EtOH) (log ε): 263 (4.1), 301 (3.9). The ^1H and ^{13}C-NMR spectra were in agreement with the reported data of brucine. [El-Mekkawy *et al., Planta Med*., **59**, 347-350 (1993)]



Time course for the metabolism of 1

A precultured bacterial strain of *L. acidophilus* was inoculated into GAM broth (500 ml) and cultivated for 24 h at 37 °C. The culture was centrifuged at 7800 x g for 10 min. The pellets were suspended in 0.1 M phosphate buffer (50 ml, pH 7.3). Brucine *N*-oxide (**1**, 50 mg each) was added to each bacterial suspension and the mixture was incubated at 37 °C under anaerobic conditions. A 5 ml aliquot was taken at intervals, made basic, and extracted twice with EtOAc (5 ml). The EtOAc solution was evaporated to dryness,

and the residue was dissolved in $CHCl_3$–MeOH (1:1 v/v, 200 μl) and analyzed by HPLC. [El-Mekkawy *et al., Planta Med*., **59**, 347-350 (1993)]

参考文献

1) El-Mekkawy S., Meselhy M. R., Kawata Y., Kadota S., Hattori M., and Namba T.: Metabolism of strychnine *N*-oxide and brucine *N*-Oxide by human intestinal bacteria. *Planta Med*., **59**, 347-350 (1993).