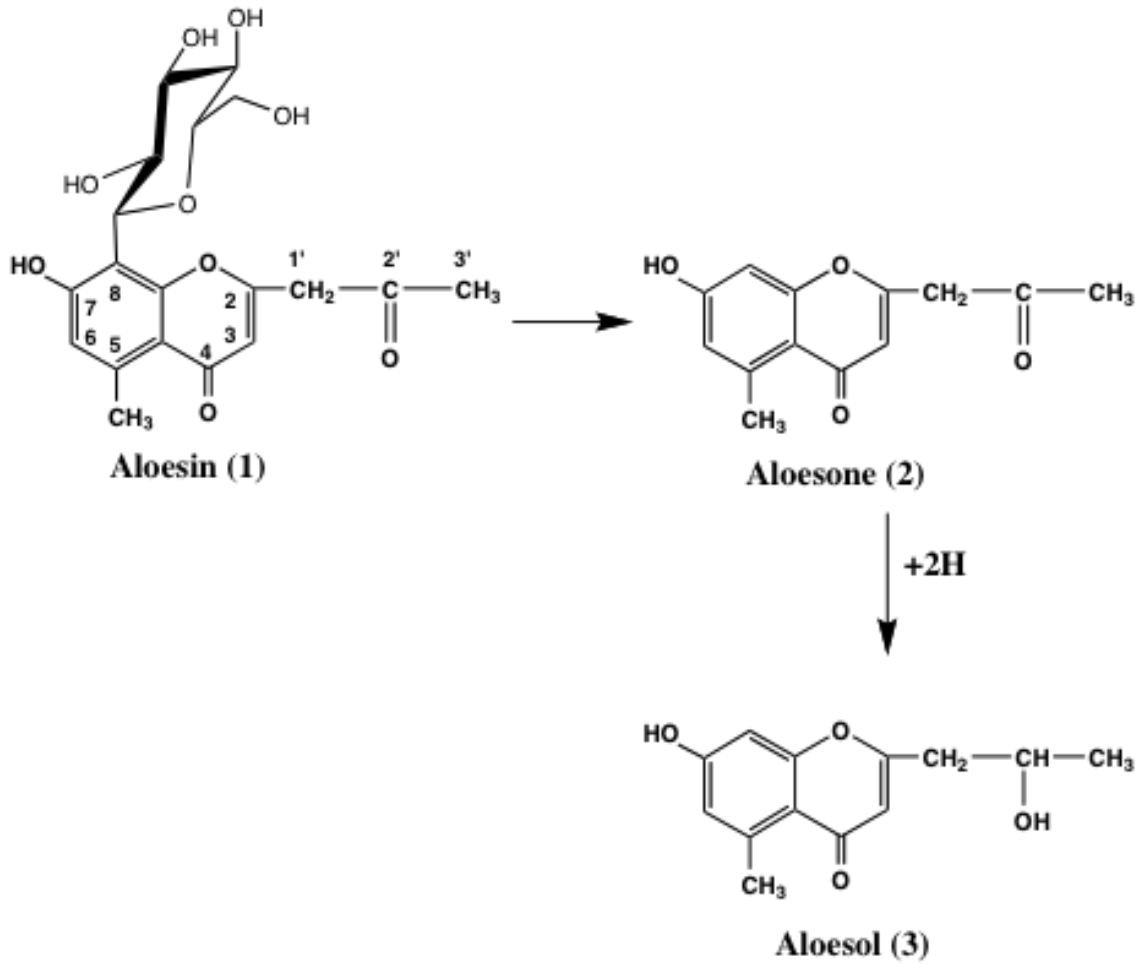


## Aloesin



Metabolic processes of aloesin by human intestinal microflora

代謝実験

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### **Metabolism by a bacterial mixture from human feces**

Fresh feces from a healthy man were thoroughly suspended in 50 volume of 0.2 M phosphate buffer (pH 7.2), filtered through layers of gauze to eliminate the sediment. The filtrate was used as an intestinal bacterial mixture.

A tube containing aloesin (**1**) (10.7 mg) and an intestinal bacterial mixture (10 ml) was incubated at 37 °C in an anaerobic box. A portion (0.5 ml) of the mixture was taken out at intervals, and vigorously mixed with BuOH (0.5 ml). An aliquot of the BuOH layer was applied to a TLC plate and the plate was developed with CHCl<sub>3</sub>-MeOH-H<sub>2</sub>O (50 : 10 : 1). *R<sub>f</sub>* values of aloesin (**1**), aloesone (**2**) and *dl*-aloesol (**3**) were 0.06, 0.59 and 0.44, respectively. The metabolites separated on the plate were quantitatively analyzed with a TLC scanner at 290 nm in the single scan mode. The calibration line was prepared with an authentic sample.

### **Incubation of aloesin (1) with an intestinal bacterial mixture**

Aloesin (1.0 g, **1**) was added to an intestinal bacterial mixture (500 ml) and incubated for 3 d at 37°C in an anaerobic box. The mixture was extracted three times with BuOH (500 ml each). The combined BuOH solutions were evaporated *in vacuo* to give a residue (*ca.* 1.8 g). The residue was applied to a column of silica gel (20 cm x 3 cm i.d.; 45 g), which was eluted successively with CHCl<sub>3</sub>, CHCl<sub>3</sub>-MeOH (95 : 5) to give 2-acetyl-7-hydroxy-5-methylchromone (**2**) and 7-hydroxy-2-(2'-hydroxypropyl)-5-methylchromone (**3**) (240 and 20 mg, respectively). The metabolites were further purified by crystallization from EtOH.

### **2-Acetyl-7-hydroxy-5-methylchromone (2)**

Colorless needles, mp 218—221 °C, EI-MS *m/z* (rel. int. ): 232 (M<sup>+</sup>, 62%), 190 (86%), 161 (24%), 151 (42%), 43 (CH<sub>3</sub>CO, 100%). IR  $\nu$  cm<sup>-1</sup>: 3450 (OH), 1650, 1545, 1360, 1280. <sup>1</sup>H-NMR (270MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.22 (3H, s, 3'-H<sub>3</sub>), 2.66 (3H, s, 5-Me), 3.86 (2H, s, 1'-H<sub>2</sub>), 6.04 (1H, s, 3-H), 6.59 (1H, *J*=2.4Hz, 8-H), 6.61 (1H, br d, *J*=2.4Hz, 6-H), 10.58 (1H, s, 7-OH).

### **7-Hydroxy-2-(2'-hydroxypropyl)-5-methylchromone (3)**

Colorless needles, mp 175-178 °C. [ $\alpha$ ]<sub>D</sub> 0° (*c* = 0.044, MeOH). IR  $\nu$  cm<sup>-1</sup>: 3400, 1630, 1540, 1360, 1285. EI-MS *m/z* (rel. int.): 234 (M<sup>+</sup>, 65%), 190 (85%), 161 (20%), 151

(36%), 124 (15%), 91 (13%), 45 (42%), 18 (100%). <sup>1</sup>H-NMR (270MHz, CD<sub>3</sub>OD) δ: 1.27 (3H, d, *J*=6.3Hz, 3'-H<sub>3</sub>), 2.65 (1H, dd, *J*= 14.2, 7.6 Hz, 1'-Ha), 2.68 (1H, dd, *J*= 14.2, 5.6 Hz, 1'-Hb), 2.72 (3H, s, 5-Me), 4.19 (1H, m, 2'-H), 6.06 (1H, s, 3-H), 6.63 (1H, br d, *J*=2.0Hz, 6-H), 6.66 (1H, d, *J*= 2.0Hz, 8-H).

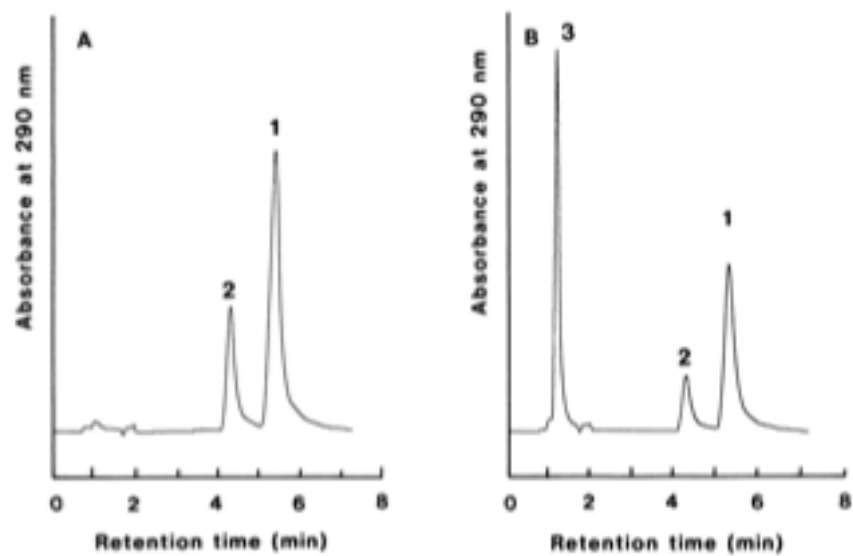


Fig. 1. Elution profiles of the metabolites of aloesin (A) and aloeresin A (B) obtained by anaerobic incubation with a bacterial mixture from human feces

The metabolites were extracted with BuOH and analyzed by HPLC. HPLC was performed with an ODS-5 column (Nomura Chem. Co.) under conditions: mobile phase, CH<sub>3</sub>CN-H<sub>2</sub>O (1:3); flow rate, 1.0 ml/min; detection at 290 nm. Peak 1, aloesone (2); peak 2, *dl*-aloesol (3); peak 3, *E*- and *Z*-*p*-coumaric acids.

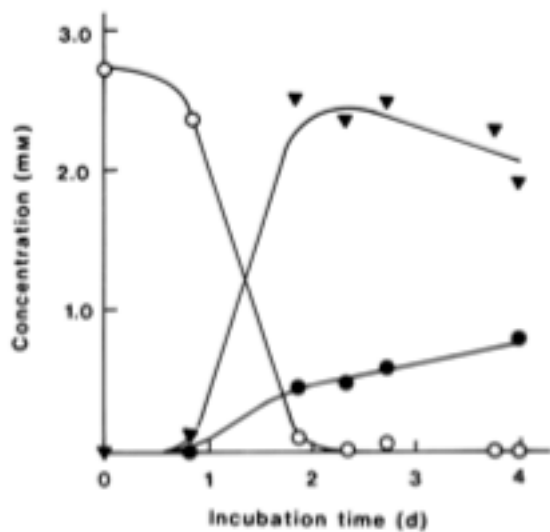


Fig. 2. Time course of the metabolism of aloesin (1)

Aloesin (1) was anaerobically incubated with an intestinal bacterial mixture at 37 °C. The metabolites were analyzed by TLC-densitometry. (○), aloesin (1); (▼), aloesone (2); (●), *dl*-aloesol (3).

#### 参考文献

1) Che Q. M., Akao T., Hattori M., Kobashi K. and Namba T.: Metabolism of aloesin and related compounds by human intestinal bacteria: A bacterial cleavage of the C-glucosyl bond and the subsequent reduction of the acetyl side chain. *Chem. Pharm. Bull.*, **39**, 704-708 (1991).