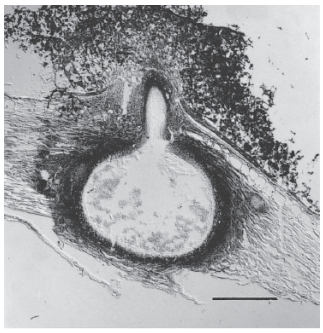
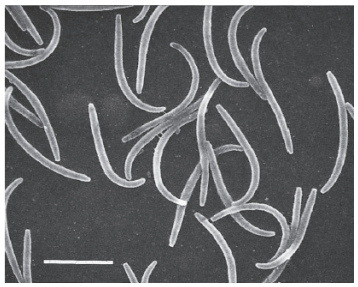
# Phenochalasin

## 1. Discovery, producing organism and structures[1,2)]

Phenochalasins A and B were isolated from the culture broth of *Phomopsis* fungal strain FT-0211[1, 2)] and recognized based on a cell-based assay, to be inhibitors of macrophage foam cell formation. Although phenochalasins belong to the cytochalasan family, phenochalsin A has the only cytochalasan skeleton containing a phenyl moiety.

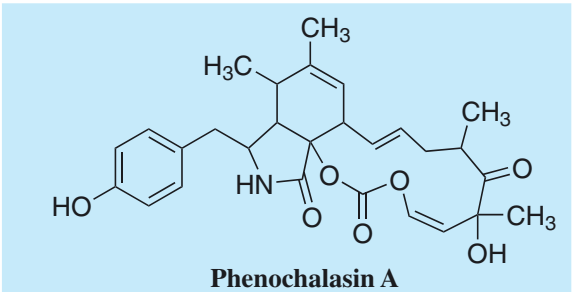


Conidioma, Bar: 200 μm

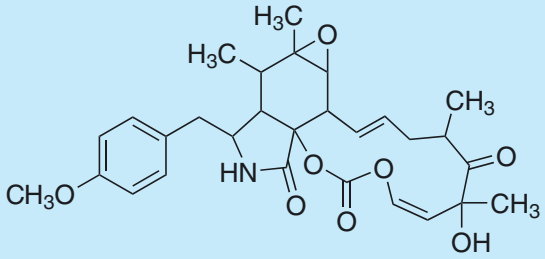


Conidia, Bar: 10 μm

*Phomopsis* sp. FT-0211




**Phenochalasin A**




**Phenochalasin B**

## 2. Physical data (Phenochalasin A)[1)]

White powder. $C_{28}H_{33}NO_7$; mol wt 495.23; Sol. in MeOH, EtOH, acetone, $CH_3CN$, EtOAc, $CHCl_3$. Insol. in $H_2O$, hexane.

## 3. Biological activity[1,3,4)]

1) Inhibition of lipid droplet formation in mouse peritoneal macrophages[1,3)].

Inhibitory activity against lipid droplet formation in macrophages (See also “Beauveriolide” (p. 64)) by cytochalasans was tested in a cell assay using mouse peritoneal macrophages. Phenochalasin A inhibited lipid droplet formation in a dose-dependent manner up to 20 $\mu$M without morphological changes in the macrophages. The other cytochalasans inhibited lipid droplet formation over a narrow concentration range and morphological changes in macrophages were observed.

2) Inhibition of neutral lipid synthesis in macrophages[1,3].
Inhibitory activity against neutral lipid synthesis (cholesteryl ester (CE) and triacylglycerol (TG)) in the cytosolic lipid droplet was tested. Phenochalasin A and cytochalasins D and E inhibited CE synthesis, while the other cytochalasans inhibited both CE and TG synthesis.

Effects of cytochalasans on cholesteryl ester and triacylglycerol synthesis, morphology and toxicity in mouse macrophages.

| Compound | $IC_{50}$[a] | | Morphology[b] | Cytotoxicity[c] | Cytotoxicity / $IC_{50}$ of CE |
|---|---|---|---|---|---|
| | CE | TG | | | |
| Phenochalasin A | 0.61 | >19 | >19 | >20 | >32.8 |
| Phenochalasin B | 0.2 | 0.38 | 0.18 | 0.5 | 2.2 |
| Cytochalasin B | 2.9 | 11.4 | 1.8 | 10 | 3.4 |
| Cytochalasin D | 2.4 | >19 | 1.8 | >20 | >8.3 |
| Cytochalasin E | 0.20 | >19 | 0.19 | 2.0 | 10 |
| Aspochalasin F | 3.0 | 5.0 | 2.3 | 2.0 | 0.67 |
| Aspochalasin G | 1.0 | 2.0 | 2.4 | 1.0 | 1.0 |

a: Concentration of a compound which inhibits [$^{14}$C]CE or [$^{14}$C]TG synthesis from [$^{14}$C]oleic acid by 50% in macrophages.
b: Minimal concentration of a compound which shows morphological changes in macrophages.
c: Concentration of a compound which causes 50% viability of macrophages in a MTT assay.

Phenochalasin A showed no activity against ACAT1 and ACAT2 as compared with the $IC_{50}$ values of CE synthesis (0.6 μM) in the macrophage assay, indicating that their molecular targets in macrophage are not ACAT.[4]

**4. References**

1. [728] H. Tomoda *et al., J. Antibiot.* **52**, 851-856 (1999)
2. [729] H. Tomoda *et al., J. Antibiot.* **52**, 857-861 (1999)
3. [740] I. Namatame *et al., J. Antibiot.* **53**, 19-25 (2000)
4. [955] T. Ohshiro *et al., J. Antibiot.* **60**, 43-51 (2007)