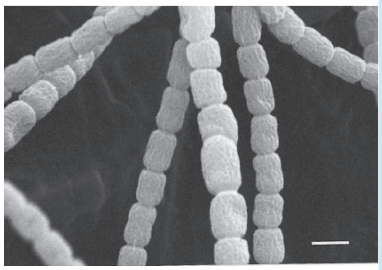
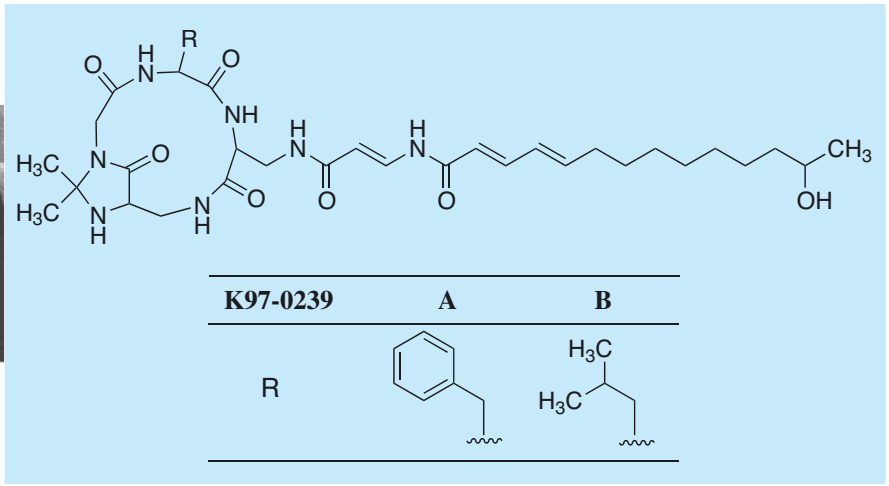
K97-0239

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

K97-0239A and B were isolated from the culture broth of the actinomycete strain K97-0239[1,2)] and identified as inhibitors of macrophage foam cell formation in a cell-based assay. Their structures were cyclic lipopeptides related to those of enamidonin[2)].



Streptomyces sp. K97-0239



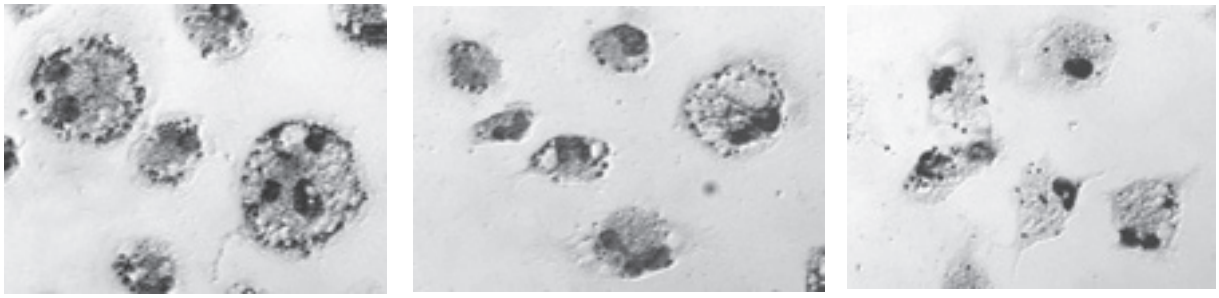
2. Physical data (K97-0239 A)[1)]

White powder. $C_{37}H_{53}N_7O_7$; mol wt 707.40. Sol. in MeOH, EtOH, acetone, CH_3CN, EtOAc, $CHCl_3$. Insol. in H_2O, hexane.

3. Biological activity[1)]

1) Inhibition of lipid droplet formation in mouse peritoneal macrophages.

Inhibitory activity against lipid droplet formation in macrophages (See also "Beauveriolide" (p. 105) was tested in a cell assay using mouse peritoneal macrophage. K97-0239A and B caused a reduction in the number and size of cytosolic lipid droplets in macrophages at 15 μM without any cytotoxic effects on the macrophages.



Control 1.5 μM 15 μM

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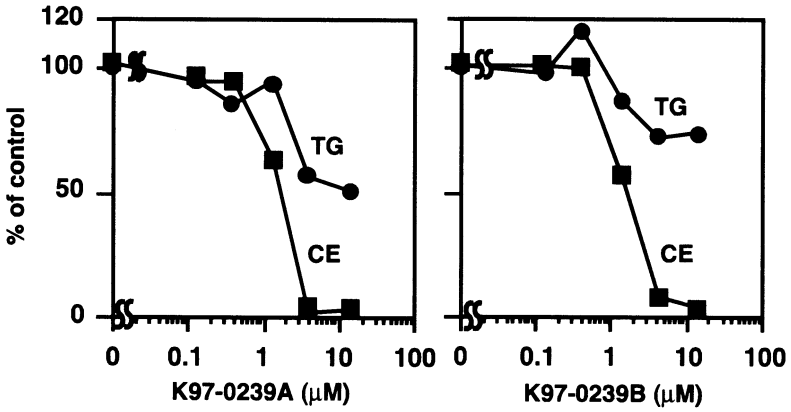
2) Inhibition of neutral lipid synthesis in macrophages.
Inhibitory activity against the syntheses of neutral lipids (cholesteryl ester (CE) and triacylglycerol (TG)) in the cytosolic lipid droplet was tested. [^{14}C]CE synthesis from [^{14}C]oleic acid of macrophages was inhibited by K97-0239A and B with IC_{50} values of 1.5 μM and 1.7 μM, respectively. [^{14}C] TG synthesis was only moderately inhibited (30~50%) by the drugs at the highest dose, 15 μM.



3) Antimicrobial activity[1)]
K97-0239 showed antimicrobial activity against several Gram-positive bacteria such as *Bacillus subtilis*, *Micrococcus luteus* and *Staphylococcus aureus* at a concentration of 10 μg/disk.

4. References

1. [802] I. Namatame *et al*., *Proc*. *Jap*. *Acad*. **78**, 45-50 (2002)
2. S. Koshino *et al*., *J*. *Antibiot*. **48**, 185-187 (1995)