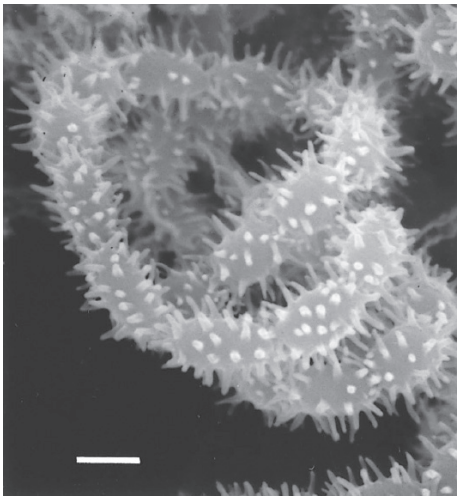
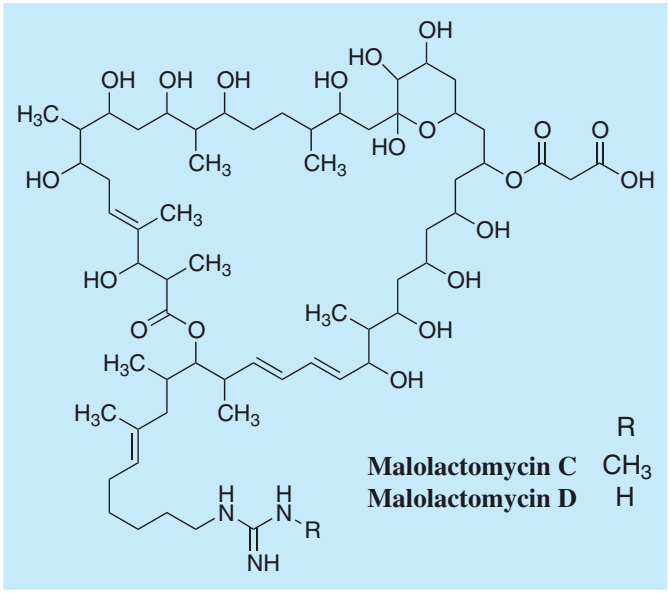
# Malolactomycin

## 1. Discovery, producing organism and structure[1)]

Malolactomycins C and D were isolated from the culture broth of the actinomycete strain KP-3144 and found to be antifungal compounds. They are 40-membered polyol macrolides similar to malolactomycin A[2)].



*Streptomyces* sp. KP-3144




## 2. Physical data (Malolactomycin C)

White powder. $C_{62}H_{109}N_3O_{20}$; mol wt 1216.55. Sol. in DMSO, MeOH, acetone, EtOAc. Insol. in $H_2O$, $CHCl_3$.

## 3. Biological activity

1) Antifungal activity of malolactomycin C[1)]

| Plant pathogenic fungi | MIC ($\mu$g/ml) | Plant pathogenic fungi | MIC ($\mu$g/ml) |
|---|---|---|---|
| *Fusarium oxysporum f.* sp. *lycopersici* | >100 | *Cladosporium fluvum* | 25 |
| *Phytophthora infestans* | 100 | *Botrytis cinerea* | 25 |
| *Trichoderma viridae* | >100 | *Pyricularia oryzae* | 25 |
| *Rhizoctonia solani* | >100 | *Glomerella cingulata* | >100 |
| *Verticillium dahliae* | >100 | *Cercospora beticola* | 100 |
| *Alternaria kikuchiana* | >100 | | |

2) Protective effect (%) of malolactomycins against gray mold of kidney bean[1)]

| Test compound | 1,000 | 500 | 200 | 100 | 40 | 20 (ppm) |
|---|---|---|---|---|---|---|
| Malolactomycin C | 100 | 100 | 100 | 60 | 0 | 0 |
| Malolactomycin D | 100 | 100 | 60 | 60 | 60 | 0 |

3) Inhibitory effect (%) of malolactomycin C on spore germination of *Botrytis cinerea*[1)]

| Concentration (ppm) | One day after treatment | One day after removal of malolactomycin C |
|---|---|---|
| 100 | 100 | 59.4 |
| 25 | 100 | 44.0 |
| 6.25 | 100 | 14.3 |
| 1.56 | 7.3 | ND |
| 0 | 1.7 | ND |

4) Inhibition of Ras signal by malolactomycin D[3)]

Malolactomycin D selectively inhibited transcription from Ras-responsive element (RRE) with an $IC_{50}$ value of 0.9 $\mu$g/ml. The expression of matrix metalloproteinases MMP-1 and MMP-9, which have RRE in their promoters, was reduced by treatment with malolactomycin D at translational and transcriptional levels. Analysis of activity of MAP kinases, which play important roles in Ras signal transduction, showed that malolactomycin D inhibited the activation of p38 MAP kinase and JNK but had no effect on ERK1 or 2.

**4. References**

1. [656] Y. Tanaka *et al*., *J. Antibiot*. **50**, 194-200 (1997)
2. K. Kobinata *et al*., *J. Antibiot*. **46**, 1912-1915 (1993)
3. M. Futamura *et al*., *Oncogene* **20**, 6724-6730 (2001)