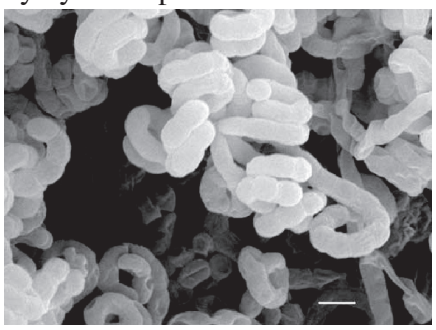
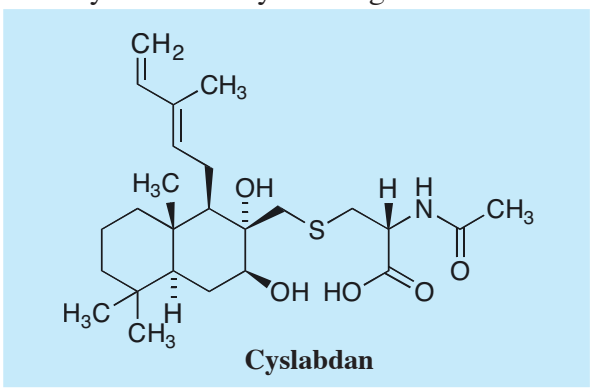
# Cyslabdan

## 1. Discovery, producing organism and structures[1-3)]

Cyslabdan was isolated from the culture broth of the *Streptomyces cyslabdanicus* strain K04-0144$^T$ as a potentiater of imipenem activity against MRSA. Cyslabdan has a labdane-type diterpene skeleton connecting with an *N*-acetylcysteine *via* thioether. The relative configuration of the diterpene part was determined by NOE experiments and the absolute configuration of the *N*-acetylcysteine part was elucidated as L-form by HPLC analysis using a chiral column[2)].



*Streptomyces cyslabdanicus* K04-0144$^T$




**Cyslabdan**

## 2. Physical data

White powder. $C_{25}H_{41}NO_5S$; mol wt 467.66. Sol. in $H_2O$, $CH_3CN$, MeOH. Insol. in EtOAc, $CHCl_3$.

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

The MIC value of imipenem against MRSA was reduced from 16 to 0.015 μg/ml in combination with cyslabdan. Study on anti-MRSA activity of other typical antibiotics in combination with cyslabdan showed that the potentiating activity was limited to β-lactam antibiotics.

| | β-Lactam | MIC (μg/ml) | | Ratio |
|---|---|---|---|---|
| | | Cyslabdan (-) | Cyslabdan (+) | (-/+) |
| Penam | Ampicilin | >1024 | 64 | 16 |
| | Penicillin G | 512 | 64 | 8 |
| | Cloxacilin | 512 | 16 | 32 |
| Cephem | Cefazolin | 512 | 64 | 8 |
| | Cefalexin | 1024 | 256 | 4 |
| | Cefotaxime | 1024 | 64 | 16 |
| | Cefmetazole | 128 | 4 | 32 |
| Carbapenem | Imipenem | 16 | 0.015 | 1024 |
| | Biapenem | 16 | 0.032 | 512 |
| | Panipenem | 32 | 0.032 | 1024 |
| | Meropenem | 16 | 0.125 | 128 |

The concentration of cyslabdan was set up at 10 μg/ml.

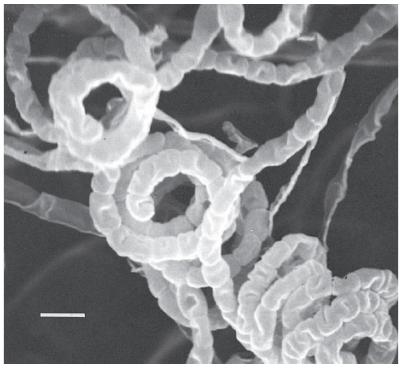
## 4. References


1. [977] A. Fukumoto *et al*., *J. Antibiot*. **61**, 1-6 (2008)
2. [978] A. Fukumoto *et al*., *J. Antibiot*. **61**, 7-10 (2008)
3. [1178] A. Take *et al*., *J. Antibiot*. **68**, 322-327 (2015)
4. N. Koyama *et al*., *PLoS One* **7**, e48981 (2012)

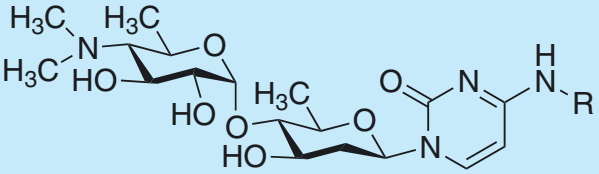
# Cytosaminomycin

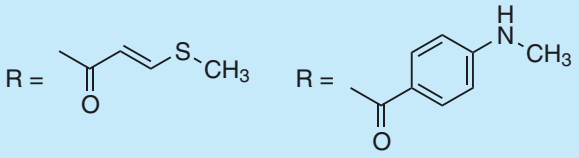
## 1. Discovery, producing organism and structures[1-3)]

Cytosaminomycins were isolated from the culture broth of *Streptomyces amakusaensis* strain KO-8119 and identified as anticoccidial substances. The structurally-related compound, oxyplicacetin, a known antibiotic[3)], was also isolated.

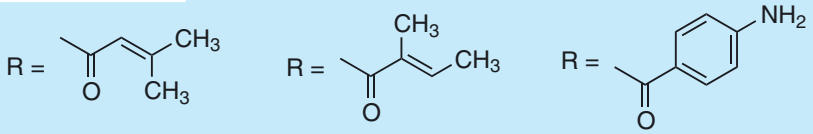


*Streptomyces amakusaensis* KO-8119





**Cytosaminomycin A** **Cytosaminomycin B**



**Cytosaminomycin C** **Cytosaminomycin D** **Oxyplicacetin**

## 2. Physical data (Cytosaminomycin A)

Pale yellow powder. $C_{22}H_{34}N_4O_8S$; mol wt 514.21. Sol. in DMSO, MeOH, $CHCl_3$. Insol. in $H_2O$, hexane.

## 3. Anticoccidial activity[1)]

Anticoccidial activity was evaluated by an *in vitro* assay using chicken embryonic and BHK-21 cells as hosts and monensin-resistant *Eimeria tenella* as a parasitic protozoan.

| Compound | | Minimum effective concentration (μM) | | | |
|---|---|---|---|---|---|
| | | Chicken embryonic cells | | BHK-21 cells | |
| | | Anticoccidial* activity (A) | Cytotoxicity** (C) | Anticoccidial* activity (A) | Cytotoxicity** (C) |
| Cytosaminomycin | A | 0.6 | 19 | 0.3 | 0.6 |
| | B | 1.1 | 9.1 | 2.3 | 4.6 |
| | C | 1.3 | 10 | 2.5 | 10 |
| | D | 5.0 | 20 | 20 | >20 |
| Oxyplicacetin | | 9.4 | >19 | 2.3 | 9.4 |

* No mature shizonts were observed in the cells at the indicated drug concentration or higher.
**No host cells were observed at the indicated drug concentration or higher.

## 4. References


1. [549] K. Haneda *et al.*, *J. Antibiot.* **47**, 774–781 (1994)
2. [550] K. Shiomi *et al.*, *J. Antibiot.* **47**, 782–786 (1994)
3. C. Yong-Le *et al.*, *Kangshengsu* **10**, 285–295 (1985)