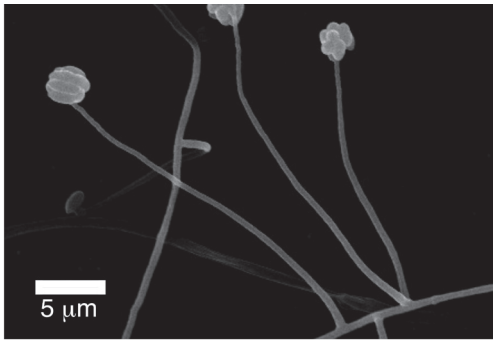
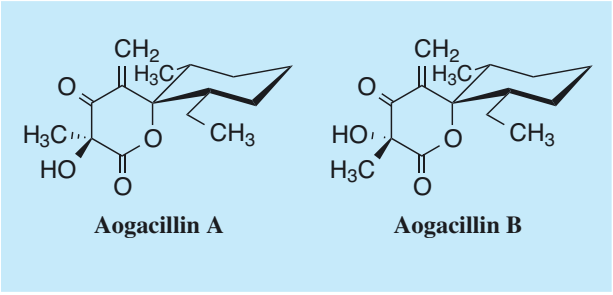
Aogacillin

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

Aogacillins A and B were discovered in a culture broth of a fungal strain, *Simplicillium cylindrosprum* FKI-5985, and found to be circumventors of arbekacin resistance in MRSA. They have novel skeletons, consisting of a β-keto-γ-methyliden-δ-lactone ring connected to a 2-ethyl-6-methylcyclohexane ring by spiro conjugation.



Simplicillium cylindrosporum FKI-5985



2. Physical data (Aogacillin A)

Yellow syrup. $C_{15}H_{22}O_4$; mol wt 266.33. Sol. in MeOH, $CHCl_3$, Insol. in EtOAc, CH_3CN.

3. Biological activity[1)]

1) Circumvention activity of arbekacin resistance in MRSA

Aogacllins A and B only showed an effect on arbekacin-resistant MRSA in the agar diffusion method when the media contained arbekacin. Of the two, aogacillin A displayed potent circumvention activity even at 0.03 μg/disc.

Compound	Amount μg/disc	Inhibition zone (mm)	
		Arbekacin (-)	Arbekacin (+)
Aogacillin A	0.03	–	10.2
Aogacillin B	0.1	–	11.6

2) Aogacillins A and B markedly reduced the MIC value of arbekacin against the MRSA, from 256 μg/ml to 8 μg/ml (32-fold).

4. References

1. [1158] K. Takata *et al*., *Org*. *Lett*. **15**, 4678-4681 (2013)
2. [ ] K. Nonaka *et al*., *Mycoscience* **54**, 42-53 (2013)