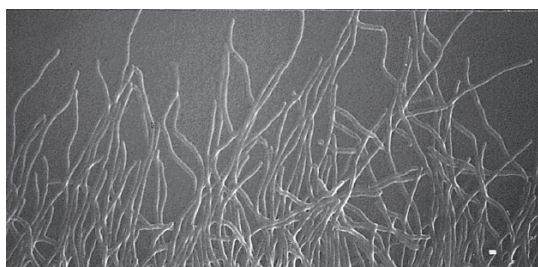


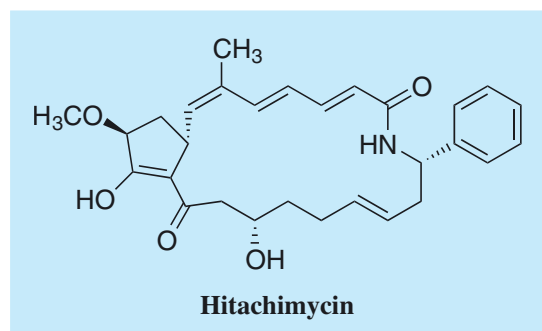
Hitachimycin

1. Discovery, producing organism and structure¹⁻⁴⁾

Hitachimycin is an antiprotozoal antibiotic isolated from the culture broth of *Streptomyces scabrisporus* strain KM-4927¹. Later, the antibiotic was found to be identical to an antitumor antibiotic, stubomycin¹⁾. The relative and absolute stereochemistry was defined via NMR and X-ray crystallographic analyses^{2,3)}. The total synthesis was reported by Smith *et al.*^{5,6)} (See Appendix-I).



Streptomyces scabrisporus KM-4927¹



2. Physical data

Colorless plates. C₂₉H₃₅NO₅; mol wt 477. Sol. in DMSO, pyridine, DMF, MeOH. Insol. in H₂O, CHCl₃, Et₂O.

3. Biological activity⁷⁻⁹⁾

1) Antimicrobial activity⁷⁾

Test organism	MIC (μg/ml)
<i>Bacillus subtilis</i> PCI 219	0.025
<i>Staphylococcus aureus</i> FDA 209 P	0.78
<i>Micrococcus Luteus</i> PCI 1001	0.4
<i>Mycobacterium smegmatis</i> ATCC 607	6.25
<i>Escherichia coli</i> NIHJ	100
<i>Klebsiella pneumoniae</i> PCI 602	100
<i>Pseudomonas aeruginosa</i>	100
<i>Xanthomonas oryzae</i>	100
<i>Candida albicans</i>	3.12
<i>Saccharomyces cerevisiae</i>	50
<i>Aspergillus niger</i>	25
<i>Microsporium gypseum</i>	0.78
<i>Trichophyton interdigitale</i>	0.2
<i>Sclerotinia cinerea</i>	0.2
<i>Alternaria kikuchiana</i>	0.78
<i>Pyricularia oryzae</i>	0.4
<i>Mucor racemosus</i> IFO 4851	50
<i>Mycoplasma gallisepticum</i> KP-13	0.4
<i>Acholeplasma laidlawii</i> PG-8	0.4
<i>Trichomonas foetus</i>	2.0
<i>Trichomonas vaginalis</i>	5.0

2) Antitumor activity of hitachimycin and its derivatives⁷⁻⁹⁾

Derivative	Cytotoxicity ^{a)}	Hemolysis ^{b)}	Total dose (mg / kg)	ILS ^{c)} (%)	Survivors ^{d)}
Hitachimycin	0.39	6.3	75	188.6	1/5
11-Et, 15-Et	1.56	25	150	323.1	2/5
15-Me	1.56	> 25	150	280.8	1/5
11-Prl, 15-Bul	1.56	3.9	75	539.5	3/5
15-L-Gly	3.13	> 25	150	298.3	3/5

^aIC₅₀ (μg/ml) against HeLa S3 cell

^bIC₁₀₀ (μg/ml)

^cInoculum size; 2.5 X 10⁶ cells of sarcoma 180/mouse (ICR, 6-week old, female)

^dNumber of surviving mice at day-60 (survival/total)

Prl: propionyl, Bul: Butyryl

4. References

- [252] S. Ōmura *et al.*, *Tetrahedron Lett.* **23**, 4713-4716 (1982)
I. Umezawa *et al.*, *J. Antibiot.* **34**, 259-265 (1981)
- [435] A. B. Smith, III *et al.*, *J. Org. Chem.* **55**, 1133-1135 (1990)
- [489] A. B. Smith, III *et al.*, *J. Am. Chem. Soc.* **114**, 8003-8007 (1992)
- [860] P. Xu *et al.*, *Int. J. Syst. Evol. Microbiol.* **54**, 577-581 (2004)
- A. B. Smith, III *et al.*, *J. Org. Chem.* **55**, 1136-1138 (1990)
- A. B. Smith, III *et al.*, *J. Am. Chem. Soc.* **114**, 8008-8022 (1992)
- [391] K. Shibata *et al.*, *J. Antibiot.* **41**, 614-623 (1988)
- [411] K. Shibata *et al.*, *J. Antibiot.* **42**, 718-726 (1989)
- [420] K. Shibata *et al.*, *J. Antibiot.* **42**, 1114-1123 (1989)