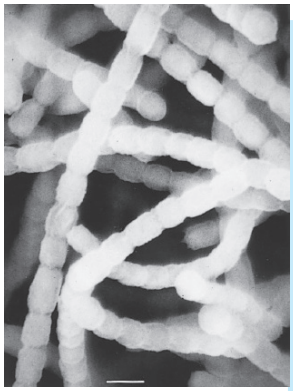
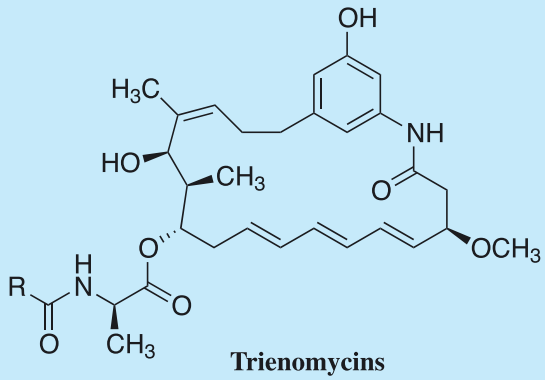
Trienomycin

1. Discovery, producing organism and structures[1-7)]

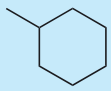
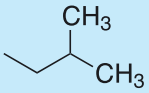
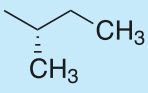
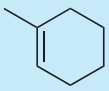
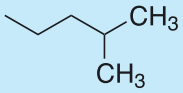
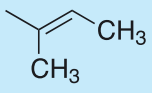
Trienomycins were isolated and identified as antitumor antibiotics from the culture broth of the actinomycete strain 83-16. The stereostructures of trienomycins were elucidated by a chemical synthetic method[4,6,7)]. The first paper on the total synthesis of trienomycins A and B, C and F has been reported by Smith *et al*.[8,9)] (See Appendix-I).



Streptomyces sp. 83-16



Trienomycins

	A	B	C	D	E	F
R						

2. Physical data (Trienomycin A)[1)]

Colorless powder. $C_{36}H_{50}N_2O_7$; mol wt 622.36. Sol. in MeOH, EtOH, acetone, EtOAc, BuOAc, $CHCl_3$, CH_2Cl_2, THF. Insol. in H_2O, hexane.

3. Biological activity[10,11)]

1) Cytocidal activity[10)]

Trienomycin	IC_{50} (μg/ml)	
	HeLa S_3	P388
A	0.005	0.02
B	0.2	1.6
C	0.1	0.1
D	0.022*	NT
E	0.104*	NT

*: MIC, NT: not tested.

2) Antitumor activity of trienomycin A[11)]

Dose (mg/kg)	Sarcoma 180		P388 leukemia		IMC carcinoma	
	MSD	ILS (%)	MSD	ILS (%)	MSD	ILS (%)
Saline	10.1 ± 0.8	0	10.4 ± 0.5	0	16.6 ± 2.6	0
32 X 10	22.8 ± 3.9*	128	18.2 ± 2.3*	75	27.4 ± 4.3*	65
16 X 10	24.8 ± 3.4*	148	17.0 ± 2.2*	64	21.6 ± 2.7*	30
8 X 10	22.4 ± 5.9*	124	15.2 ± 1.1*	46	20.2 ± 1.6*	22
4 X 10	13.0 ± 1.8*	0	13.6 ± 0.5*	31	18.4 ± 2.6	11

Dose (mg/kg)	B16 melanoma		Lewis lung carcinoma		Ehrlich carcinoma	
	MSD	ILS (%)	MSD	ILS (%)	MSD	ILS (%)
Saline	19.4 ± 1.9	0	16.6 ± 0.5	0	18.5 ± 1.3	0
32 X 10	NT		NT		37.0 ± 2.6*	100
16 X 10	22.2 ± 0.4*	14	20.6 ± 0.9*	24	25.6 ± 7.2	38
8 X 10	21.0 ± 2.3	8	19.2 ± 2.2	15	18.3 ± 1.5	0
4 X 10	22.0 ± 1.4	13	16.4 ± 3.	10	18.8 ± 1.5	1

* $P < 0.05$
NT: not tested

3) Antimicrobial activity[11)]

Test organism	MIC (μg/ml)
Pyricularia oryzae KF 180	100
Mucor racemosus KF 223 (IFO 4581)	>100
Saccharomyces cerevisiae KF 26	>100
Candida albicans KF 1	>100
Penicillium herquei KF 227(IFO 4674)	100
Aspergillus niger KF 103 (ATCC 6275)	>100

4) Inhibitory activity of ICAM-1 expression[12)]
Trienomycin A inhibited ICAM-1 expression. The inhibitory activity is closely related to the ability to prevent translation. IC_{50} values against ICAM-1 expression incubated with TNF-α and with IL-1α were 0.61 μM and 3.0 μM, respectively.

5) Cell growth inhibition[13)]
Trienomycin A inhibited cell growth of HeLa cells with IC_{50} values of 30 ng/ml. Trienomycin A exhibited inhibitory activities against thapsigargin-induced XBP 1-luciferase activation with IC_{50} values of 32 ng/ml. Trienomycin A is inhibitor of ER stress-induced XBP1 activation.

6) Inhibitory activity of NO production[14)]
Trienomycin A inhibited dose-dependently NO production in LPS-stimulated BV-2 cells with EC_{50} value of 25.4 nM.

4. References

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