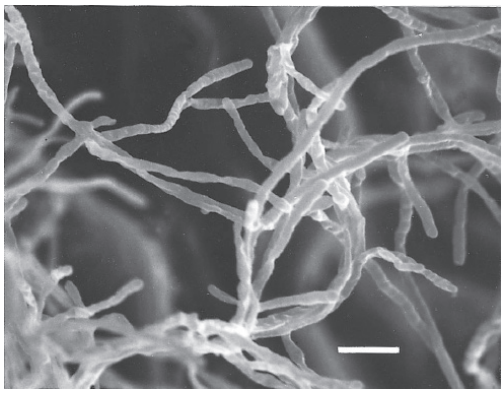
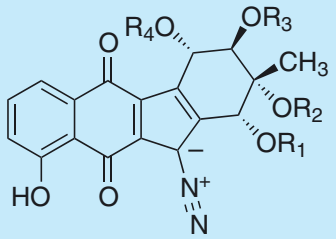
Kinamycin

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

Kinamycins were found from the culture broth of the actinomycete strain KA-295 and recognized as antimicrobial substances active against Gram-positive bacteria. The proposed structure was revised by Gould *et al*.[7)] The first total synthesis of kinamycin C was achieved by John Jr. *et al*.[9)] and biosynthesis of kinamycin was achieved by Gould e*t al*.[12-17)]



Streptomyces murayamaensis KA-295
Bar: 5 μm



	R_1	R_2	R_3	R_4
Kinamycin A	H	$COCH_3$	$COCH_3$	$COCH_3$
B	H	$COCH_3$	H	H
C	$COCH_3$	H	$COCH_3$	$COCH_3$
D	$COCH_3$	H	$COCH_3$	H

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

Yellow needles. $C_{25}H_{23}N_2O_{10}$; mol wt 497.13. Sol. in MeOH, $CHCl_3$, EtOAc. Insol. in hexane, H_2O.

3. Biological activity[1,18)]

1) Antimicrobial activity of kinamycins A, B, C, and D

Test organism	MIC (μg/ml)			
	A	B	C	D
Bacillus subtilis PCI219	0.024	0.012	0.19	0.012
Bacillus anthracis	0.19	0.012	0.19	0.024
Staphylococcus aureus FDA209P	0.78	0.012	0.78	0.024
Staphylococcus albus	0.024	0.012	0.39	0.024
Mycobacterium smegmatis ATCC 607	25	6.25	6.25	6.25
Escherichia coli NIHJ	>100	3.12	100	12.5
Vibrio comma	>100	0.19	25	12.5
Vibrio comma Inaba 904	50	0.09		
Klebsiella pneumoniae	>100	12.5	100	25
Salmonella typhosa 901 W	>100	6.25	>100	12.5
Shigella dysenteriae	>100	25	>100	25
Proteus vulgaris OX-19	>100	12.5	>100	6.25
Neisseria gonorrhoeae	>50	>12.5	>100	>50

2) Cell growth inhibition[8,10,11)]

Both kinamycin A and kinamycin C strongly inhibited cell growth of CHO cells.

Kinamycin A was the more potent of the two compounds and with a 72-h drug treatment the IC_{50} was in the low nanomolar range. The growth inhibitory effects of both these compounds were strong even with drug exposure times of 1 h or less. Assuming that the compounds were washed out of the cells, these results suggest that both kinamycin A and kinamycin C acted quickly on their cellular targets to inhibit cell growth.

3) Cell cycle[8,10)]

Experiments were carried out on CHO cells synchronized through serum atarvation (normal doubling time of 12 h) to determine whether kinamycin A exerted a cell cycle block. The untreated cells were still highly synchronized 5 h after serum reletion as evidenced by the low levels of S and G2/M phase cells

4) Inhibit topoisomerase II catalytic activity[8,10)]

Kinamycin A and kinamycin C inhibited the activity of topoisomerase II α. Kinamycin F inhibited the decatenation activity of human topoisomerase II α with an IC50 of 0.85±0.26 μ M

4. References

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