MECHANISM OF ACTION OF LIVIDOMYCIN A, A NEW AMINOGLYCOSIDIC ANTIBIOTIC

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Lividomycin A, a new aminoglycoside[1,2], was observed to inhibit protein synthesis more than nucleic acid syntheses in growing cells of *Escherichia coli*.

In a cell-free system, f2 phage RNA-directed protein synthesis was markedly inhibited by the antibiotic. A similar inhibition was observed with streptomycin (Fig. 1).

Polyphenylalanine synthesis directed by poly U in *E. coli* extract was also significantly affected by lividomycin A (Fig. 2). Inhibition of poly U-directed polypeptide synthesis was lower when 1 M NH_4Cl-washed ribosomes and S-100 were employed. The methods and materials followed those described previously.[3]

The incorporation of leucine, isoleucine and serine (miscoding) into polypeptide in the presence of poly U was increased by the addition of lividomycin A. The *in vitro* miscoding activity seemed to correspond to that of kanamycin (Table 1).

The acetylphenylalanyl-puromycin reaction, and T factor- and G factor associated GTPase reactions were not significantly affected by lividomycin A.

The results indicate that the primary site of action of lividomycin A is in the bacterial system of protein synthesis. The mechanism of action of lividomycin A seems to be similar to that of other aminoglycosides such as streptomycin, kanamycin, paromomycin, *etc.*

Table 1. *In vitro* miscoding produced by lividomycin A in poly U system.

Antibiotics	Relative incorporation of			
	Phenyl-alanine	Leucine	Iso-leucine	Serine
—	100	5	1	0
Lividomycin A 0.15 μg/ml	62	7	3	1
Kanamycin 5 μg/ml	26	7	4	1

The reaction mixture contained in 0.2 ml: *E. coli* S-30 1.4 mg, poly U 3 μg, tRNA 100 μg, ^{14}C-amino acid 0.02 μCi, ATP 1 mM, PEP 5 mM, pyruvate kinase 4 μg, GTP 0.03 mM, Tris-HCl, pH 7.6, 50 mM, NH_4Cl 100 mM, $MgCl_2$ 20 mM, and 2-mercaptoethanol 6 mM. It was incubated at 37℃ for 40 minutes. 100=30.2 pmoles.

Fig. 1. Effects of antibiotics on f2 RNA-directed protein synthesis.

The reaction mixture contained in 1.0 ml: *E. coli* Q13 ribosomes (washed with 1 M NH_4Cl) 58.2 A_{260}, S-150 2 mg, initiation factors 345 μg, f2 RNA 400 μg, 19 amino acids except valine 0.025 mM, tRNA 200 μg, fMet-tRNA 150 μg, ^{14}C-valine (169 mCi/mmole) 0.2 μCi, pH 7.8, Tris-HCl 50 mM, NH_4Cl 100 mM, $Mg(AcO)_2$ 8 mM, DTT 1 mM, ATP 1 mM, PEP 5 mM, pyruvate kinase 4 μg, and GTP 0.03 mM.

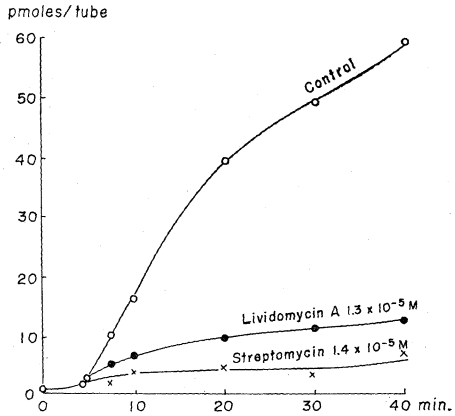
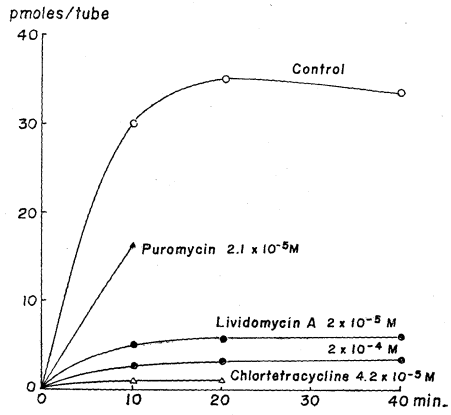


Fig. 2. Effects of antibiotics on polyphenylalanine synthesis.

The reaction mixture contained in 0.2 ml: *E. coli* S-30 870 μg protein, poly U 10 μg, tRNA 10 μg, ^{14}C-phenylalanine (405 mCi/mmole) 0.04 μCi, ATP 1 mM, PEP 5 mM, pyruvate kinase 4 μg, GTP 0.03 mM, pH 7.8, Tris-HCl 50 mM, NH_4Cl 100 mM, $MgCl_2$ 10 mM, and 2-mercaptoethanol 6 mM.



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