

Summary. Experiments in which cysteine and X-ray dosage were varied over a wide range revealed that the protective action afforded by cysteine is proportional to the dosages of cysteine and radiation employed

and that cysteine increases the time to 50% mortality and the average survival time of animals dying within 30 days post irradiation.

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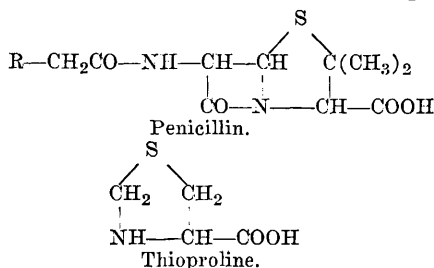
Bacterial Inhibition by a Penicillin Moiety.* (17625)

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Little is known concerning the exact mode of action of most natural antibiotics, other than that they produce several general changes in bacterial morphology and respiration. Since biological activity can often be referred to specific groups in the molecule, metabolic studies involving smaller moieties of antibiotic molecules might possibly provide an approach to this problem. A preliminary attempt along these lines involving the nucleus of the penicillin molecule is described in this paper.

Experimental. 4-Thiazolidinecarboxylic acid, thioproline, was synthesized by the method of Armstrong and du Vigneaud(1). The organ-



ism, medium, and technics employed were those previously described and extensively

used in analogue-metabolite inhibition studies(2). The results are summarized in Table I. Thioproline effectively inhibits the growth of *Escherichia coli* in mineral salts-glucose medium, and the inhibition is reversed to a limited extent by proline, despite the fact that the inhibitor is not isosteric with proline. To a somewhat lesser extent, a large number of other amino acids can also reverse the inhibition. Vitamins, purines, pyrimidines, and increased levels of glucose, however, are inactive in this regard. Combinations of amino acids manifest an even greater reversing ability than any single substance.

Discussion. A consideration of the data suggests that thioproline may inhibit bacterial growth by preventing the conversion of a large number of amino acids to some product or products essential for growth. It is apparently most effective in preventing proline utilization, perhaps because of its structural similarity to this amino acid. The known facts regarding penicillin action are not out of line with the possibility that penicillin prevents bacterial protein synthesis.

* Part of this work was conducted under Dr. William Shive at the University of Texas in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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TABLE I.
The Effect of Various Amino Acids in Reversing the Toxicity of Thioproline for *Escherichia coli*. Organism incubated 16 hr at 37°C.

No.	Reversing agent	Mg per 10 ml medium	Galvanometer readings* Thioproline (μg per 10 ml)			
			0	300	1000	3000
1.	Blank	—	52	53	3	3
2.	DL-isoleucine	1	51	50	8	3
3.	L-histidine	1	50	50	49	4
4.	DL-leucine	1	52	51	53	5
5.	DL-valine	1	51	53	52	3
6.	DL-cystine	1	50	49	42	3
7.	DL-hydroxyproline	1	52	50	50	4
8.	DL-methionine	0.1	51	49	25	3
9.	L-aspartic acid	1	53	50	52	2
10.	L-glutamic acid	1	52	51	53	3
11.	L-lysine	1	49	50	51	3
12.	L-proline	1	50	52	53	12
13.	Glycine	1	54	50	17	3
14.	DL-alanine	1	51	49	49	3
15.	L-arginine	1	52	49	49	3
16.	DL-serine	1	54	49	3	3
17.	DL-threonine	1	51	52	3	3
18.	L-tyrosine	1	50	51	7	3
19.	L-tryptophan	1	49	53	4	3
20.	DL-phenylalanine	1	51	50	46	3
21.	1-5 above	.05 of each	53	52	52	25
22.	6-12 "	.05 " "	52	49	50	42
23.	13-17 "	.05 " "	50	52	51	34
24.	18-20 "	.05 " "	53	51	52	3
25.	1-12 "	.05 " "	53	54	51	42
26.	1-5, 13-17 above	.05 " "	51	52	52	43
27.	6-17 above	.05 " "	50	50	51	40
28.	Proline and cystine	.05 " "	50	51	51	42

* A water blank gives a zero reading; an opaque object reads 100.

Prolongation of Penicillin Blood Level by Implantation of Procaine Penicillin Tablets.* (17626)

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Many attempts have been made to prolong the penicillin blood level. Numerous procedures have been used to prolong the levels of penicillin in the blood. The three methods most commonly employed have been: *a*) a mixture of calcium penicillin with peanut oil and beeswax(1), *b*) the blockade of the renal elimination by carinamide(2,3), and *c*) the parenteral administration of relatively insoluble

penicillin, such as procaine penicillin(4,5, 6). It has recently been demonstrated that implantation of tablets of procaine penicillin

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