Effect of Antibiotics on Indole Synthesis by *Escherichia coli* 7-4

It has been shown (Gibson, Jones and Teltscher[1]) that indole is formed from glucose and ammonium chloride by washed-cell suspensions of a mutant, *Escherichia coli* 7-4, blocked in the conversion of indole to tryptophan. The effect of some antibiotics on the formation of indole has now been studied.

It was found that chloramphenicol, terramycin, aureomycin and streptomycin inhibited indole formation, but penicillin had little effect (Table 1). The minimum concentrations of chloramphenicol, terramycin and aureomycin needed to inhibit indole synthesis corresponded closely to the bacteriostatic concentrations for *E. coli* 7-4 in the liquid synthetic medium described by Davis and Mingioli[2]. As an example of such inhibition, the effect of terramycin on total growth and indole synthesis is shown in Fig. 1.

Table 1. Effect of Antibiotics on Indole Synthesis by *E. coli* 7-4

Addition to indole synthesis system*	Indole formed (mμ*M*./mgm. dry wt. cells)
None	260
Terramycin (1 μgm./ml.)	41
Aureomycin (1 μgm./ml.)	71
Chloramphenicol (5 μgm./ml.)	44
Streptomycin (10 μgm./ml.)	231
(150 μgm./ml.)	35
Penicillin (100 units/ml.)	274
(1,000 units/ml.)	196

* Indole synthesis system. Washed cells from heart infusion agar (0·8 mgm./ml. dry wt.); glucose (0·1 *M*); DL-serine (0·01 *M*); ammonium chloride (0·005 *M*); phosphate buffer (0·1 *M*, *p*H 7·7). Test incubated 5 hr. at 37°.

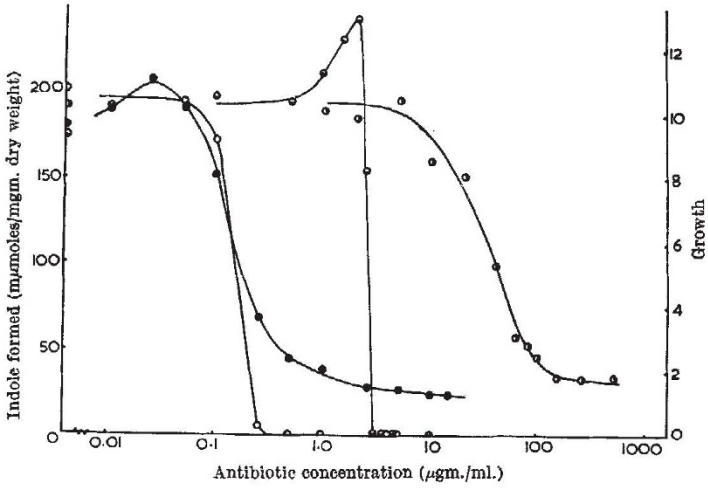

Fig. 1. Effect of terramycin and streptomycin on growth and indole synthesis by *E. coli* 7-4.
—○—○—, Terramycin, growth (expressed as turbidity with *E.E.L.* portable colorimeter); —●—●— terramycin, indole synthesis; —◒—◒—, streptomycin, growth (expressed as turbidity with *E.E.L.* portable colorimeter); —◑—◑—, streptomycin, indole synthesis.
Indole synthesis. Substrates and cells as in Table 1. Antibiotics added with substrates and test incubated 4 hr. at 37°.
Bacteriostatic tests. Davis minimal medium plus DL-tryptophan (10^{-4} *M*) incubated 24 hr. at 37°

Chloramphenicol, terramycin and aureomycin have been shown to suppress the formation of adaptive enzymes in *E. coli*[3]; but their interference with indole synthesis is different since the addition of any of these drugs to adapted cells still inhibited synthesis (Fig. 2). Thus the action of these antibiotics on the formation of adaptive enzymes may be secondary to the inhibition of the synthesis of essential aromatic compounds.

Streptomycin differed from the other antibiotics tested in that it did not inhibit indole synthesis at the concentration needed to prevent growth (3 μgm./ml.), but was effective at higher concentrations (Table 1, Fig. 1). Furthermore, the addition of streptomycin (150 μgm./ml.), once indole formation was proceeding at maximum rate, did not interfere with its synthesis (Fig. 2). It appears that streptomycin inhibits some adaptive process concerned in the formation of indole.

Various workers have suggested that antibiotics may interfere with protein synthesis or with the biosynthesis of the aromatic amino-acids (see ref. 4). That chloramphenicol, terramycin and aureomycin may interfere with the same metabolic pathway is suggested by the finding that strains of *E. coli* made resistant to any one of the three drugs showed a cross-resistance to the other two[5].

The present results provide evidence that some antibiotics, at bacteriostatic concentrations, inhibit reactions associated with aromatic synthesis in *E. coli*.

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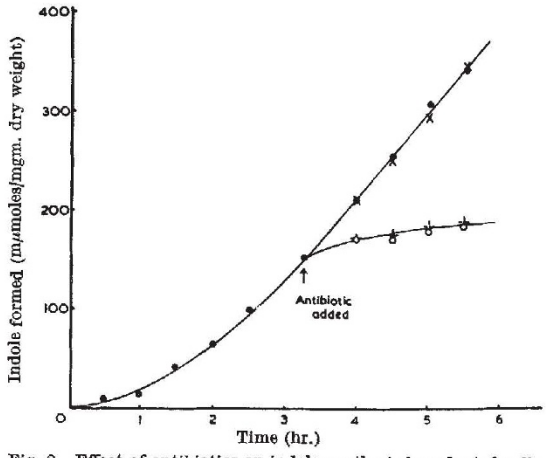

Fig. 2. Effect of antibiotics on indole synthesis by adapted cells. Indole synthesis system. Substrates as for Table 1; cells (0·7 mgm./ml.). Test incubated at 37° and antibiotics added as follow: —●—●—, No addition; —○—○—, terramycin (1 μgm./ml.); —+—+—, chloramphenicol (5 μgm./ml.); —×—×—, streptomycin (150 μgm./ml.)

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