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The action of xanthomycin

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XANTHOMYCIN A, and xanthomycin B, are toxic antibiotics with a strong effect on Gram-positive microorganisms and a weak effect on Gram-negative ones.[1] Xanthomycin A and xanthomycin B are interconvertible compounds.[2,3] A similar substance, the antibiotic gancidin[4, 5], proved to be anti-carcinogenic. Xanthomycin was found by Csányi[6] to also show the same effect, when given in subtoxic doses. In this paper, a short report is given on the mode of action of xanthomycin. The xanthomycin used in these experiments was purified by the counter current distribution method.[1] The preparation obtained after evaporation contained 80% of xanthomycin A (the pure A-fraction is partly converted into B during preparation).

The accumulation of uridine nucleotides. Staphylococcus aureus P 209 has been found to accumulate uridine nucleotides as a result of the action of xanthomycin when tested under the circumstances used by Strominger *et al.*[7] for studying the mode of action of penicillin (Fig. 1). A similar effect is observed in the case of several antibiotics, such as penicillin[10–12], D-cycloserine[13, 14], bacitracin[15], novobiocin[16], vancomycin[17, 18], ristocetin[19].

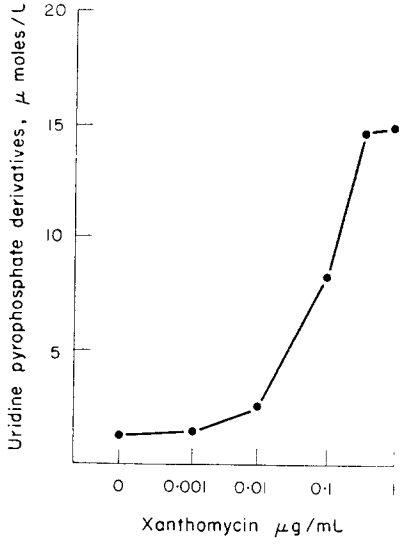

FIG. 1. *Staphylococcus aureus* at about half maximum of growth, is centrifuged, washed and suspended in an equal volume of fresh medium[10] containing xanthomycin. After 90 min the culture is centrifuged, washed and following de-proteination by trichloro-acetic acid, the uridine-5-pyrophosphate-N-acetyl-amino sugar compounds are hydrolysed[8] and measured with the Elson–Morgan[9] reagent.

Inhibition of the synthesis of desoxiribonucleic acid. It is known that anticarcinogenic antibiotics inhibit the synthesis of nucleic acids, e.g. mytomycin-C[30] inhibits DNA synthesis, actinomycins[21] inhibit RNA synthesis.

The effect of xanthomycin upon the nucleic acid metabolism of *Escherichia coli* K_{12} has been investigated and it was observed, with bacteria in the exponential phase of growth, that a concentration of the antibiotic of about 0·1 μg/ml inhibited more distinctly the synthesis of DNA than that of RNA and proteins. The effect mentioned can be observed by varying the concentrations within narrow limits. Because of the variability of the results, the method of Harold and Ziporin[22] for mustards was

adopted, i.e. the coli cells in exponential growth were exposed to the effect of xanthomycin (0·6 μg/ml) for 10 min. In order to remove the antibiotic, the cells were centrifuged and suspended in fresh medium. The rates of the protein-, RNA- and DNA-syntheses were then measured. Under the circumstances described, it was shown that no change occurs in the rate of synthesis of proteins and only a slight inhibition of RNA synthesis could be detected. Whereas the synthesis of DNA was temporarily decreased, the latter effect being similar to that of the mustards (Fig. 2).

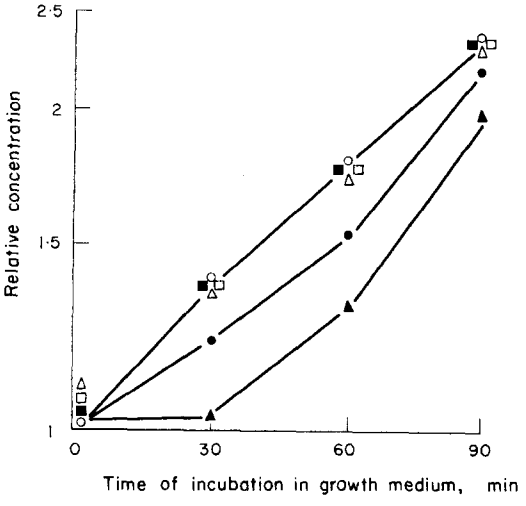

FIG. 2. In a medium containing glucose and salt,[23] when the culture has reached half maximum growth, 0·6 μg/ml of xanthomycin are added. After further incubation for 10 min, the *E. coli* cells are centrifuged, washed twice and suspended in an equal volume of fresh medium. Protein is determined according to Lowry *et al.*[24] Following treatment with cold perchloric acid, nucleic acids are extracted repeatedly with 0·5 N hot perchloric acid[22]. DNA is determined according to Burton,[25] RNA according to Ceriotti.[26]

$$\text{Ordinate} = \frac{\text{Concentration of proteins and nucleic acids at time} = t}{\text{Concentration of proteins and nucleic acids at time} = 0} \text{ plotted on a logarithmic scale.}$$

Symbols
□——□ protein..
△——△ DNA ..No xanthomycin
○——○ RNA ..
■——■ protein..
▲——▲ DNA ..0·6 μg/ml xanthomycin
●——● RNA ..

In conclusion, it can be stated that xanthomycin acts in two different ways: on the one hand, it inhibits the synthesis of cell walls, as shown by the accumulation of uridine phosphate compounds, and on the other hand, it selectively decreases the rate of DNA-synthesis, inhibiting to a lower extent the synthesis of RNA.

This double effect of xanthomycin resembles that of fluorouracil which has been shown to inhibit both cell wall[27, 28] and nucleic acid syntheses[29, 30]. This similarity is perhaps due to the inhibitory effect exerted by xanthomycin at a certain step of the pyridine metabolism.

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Effect of thalidomide on *Tribolium confusum* Duval

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THE association of human fetal abnormalities with thalidomide has led to an increasing amount of experimental work on various laboratory animals during the past two years. In the present communication we have investigated the effect of thalidomide on *Tribolium confusum*. This insect was selected for the study because of its short life span and distinct life stages.* In addition, such an investigation might be of interest for comparative purposes.

* Life cycle of *T. confusum* may be divided into five well-defined stages: (i) embryonic (6 days); (ii) larval (14 days), a growth phase, duration of which is considered a criterion for growth; (iii) pre-pupal (3 days); (iv) pupal (6 days); (v) adult (up to 2 years).