Desertomycin, a New Crystalline Antibiotic with Antibacterial and Cytostatic Action

A REPORT was recently published[1] of a new antifungal antibiotic, flavofungin, from a previously unreported *Streptomyces* strain, *Streptomyces flavofungini*. This species produces, besides flavofungin, another antibiotic. Its presence was demonstrated by the paper-chromatographic examination of the fermentation fluid and of the crude flavofungin. The *Streptomyces* strain originally isolated produces much more of this antibiotic than of flavofungin, in contrast to its natural variant, which synthesizes flavofungin more abundantly. The second antibiotic can be extracted from the fermentation broth as well as from the mycelium with organic solvents. We succeeded in obtaining hexagonal crystals from various solvent systems (Fig. 1). This new antibiotic was named 'desertomycin', after the source (African desert sand) of the *Streptomyces* strain which produces it.

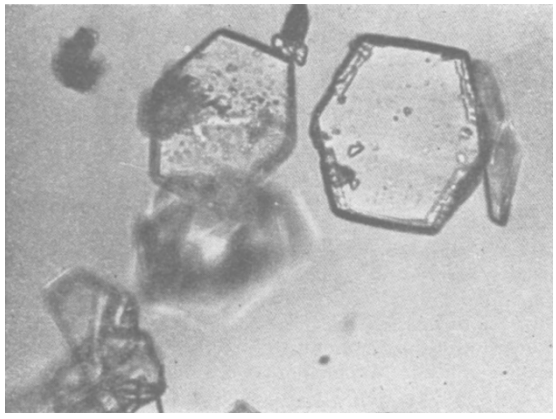

Fig. 1 Desertomycin crystals

Desertomycin is a uniform snow-white, glittering, crystalline product. Its tentative empirical formula is: $C_{33}H_{60-62}O_{14}N$. It melts at 189–190° C. The solubility in water or in absolute alcohols, ether and acetone is low, but it is higher in alcohols which contain some water. Its neutral aqueous solution is very stable. Desertomycin contains no sulphur, halogen, N-methyl or acetyl groups, but it has a C methyl group. The substance gives acetylated and hydrogenated derivatives; it decolorizes a solution of permanganate or bromine and gives positive ninhydrin and Kuhn–Roth C-methyl tests.

Crystalline desertomycin was tested against a number of bacteria by a serial dilution method. The minimum inhibitory concentration varies between 5 and 25 μgm./ml. for various micro-organisms. The antimicrobial activity of desertomycin is shown in Table 1.

Desertomycin proved to be markedly toxic for mice. The intravenous, intraperitoneal, subcutaneous and oral *LD*50 of desertomycin in mice was found to be 1·35 mgm./kgm., 2·6 mgm./kgm., 5·3 mgm./kgm. and 12–15 mgm./kgm. body-weight, respectively.

Desertomycin exhibits a very significant cytotoxic effect. Our *in vitro* experiments show that it inhibits the life-activity of leukæmic cells and of Ehrlich ascites cells in a quantity of 0·7 μgm. and 10 μgm., respectively[2]. It exhibits a cytostatic (10 μgm.) and in higher concentrations (50–100 μgm.) a cytolytic

Table 1

Micro-organism	Inhibitory concentration (μgm./ml.)
B. subtilis, NTCC 6633	1–5
B. subtilis (streptomycin resistant)	1–5
B. subtilis (penicillinase producing)	1–5
B. megatherium	1–5
Staphylococcus aureus Duncan	10
Staphylococcus aureus (penicillin resistant) (three strains)	10
B. cereus 569	10
E. coli 111	10–25
E. coli S. (mouse-pathogen)	10–25
Staphylococcus aureus (mouse-pathogen) (two strains)	25
Staphylococcus aureus (four strains)	25
Staphylococcus aureus (poly-resistant)	25
Staphylococcus aureus (penicillin resistant) (five strains)	25
Micrococcus ureae	25
Enterococcus	>25
E. typhosa H	>25
E. coli commune	>25
Pneumobacillus Friedländer	>25
Pseudomonas pyocyanea	not inhibited

action on fibroblast, HeLa and Crocker cells, studied by the tissue culture method (Kelner, B., *et al.*, personal communication). Once more the inhibition of the growth of bacteria is seen to be connected with the inhibition of tumour cells.

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[1] Úri, J., and Békési, I., *Nature*, **181**, 908 (1958).
[2] Vályi-Nagy, T., Hernádi, F., and Bászler, G. (in the press).

Adrenalectomy and Tissue Amines

WE have recently suggested[1] that the secretion of the adrenal cortex exerts a functional control over the levels in tissue of both histamine and 5-hydroxytryptamine. This evidence was obtained by injecting synthetic corticosteroid substances into normal rats as well as into rats in which tissue histamine had been previously depleted. Further experiments have now been carried out on animals the adrenal glands of which have been removed before drug treatment.

Groups of rats (100–125 gm. in weight) were bilaterally adrenalectomized and maintained for four days on a cube diet and either drinking water or normal saline solution. Other groups were mock-adrenalectomized and similarly maintained. The animals were then killed and several tissues extracted and tested for histamine and 5-hydroxytryptamine activity. Striking differences between the amine-levels in the groups were noted. Whereas the histamine-levels in the skin, ears, feet, liver and lung of adrenalectomized rats maintained on normal saline solution did not differ significantly from those of mock-adrenalectomized animals, the histamine-levels in these tissues of adrenalectomized rats maintained on water were increased two to six times. When cortisone (but not deoxycorticosterone acetate) was given to such animals, the histamine-levels in the tissues fell dramatically to normal levels or below. This is therefore a further demonstration of the control exerted by glucocorticoid substances on tissue histamine-levels, and as suggested by Schayer and his