PROCEEDINGS OF THE BIOCHEMICAL SOCIETY

The 521st Meeting of the Society was held at the Imperial College of Science and Technology, London S.W.7, on Monday and Tuesday, 20 and 21 December 1971, when the following papers were presented:

COLLOQUIUM ON 'FUNGAL BIOCHEMISTRY'

The Chemistry and some Biological Effects of the Cytochalasins

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The cytochalasins are a group of fungal metabolites produced by a variety of mould species. Cytochalasins A and B, the first to be isolated and studied (Carter, 1967; Aldridge *et al.*, 1967), were obtained from *Helminthosporium dematioides*.

Although differing considerably in potency and to some extent in their qualitative effects, the cytochalasins tend to share a common pattern of biological activity, which may be exemplified by the action of cytochalasin B on cultured mammalian cells. At a concentration of 1 $\mu\text{g/ml}$ this compound increases cell adhesion to glass, and inhibits cell locomotion and cytoplasmic cleavage. At higher concentrations (10 $\mu\text{g/ml}$) it causes extrusion of the cell nucleus.

The effect on cell adhesion is complex. When cells in suspension are exposed to the compound they adhere more readily to glass but spread more slowly than untreated cells. Subsequently, however, the degree of spreading may exceed the normal, so that the cells become greatly flattened and occupy a greater area of substrate.

When attached cells are treated with the compound, cell locomotion ceases immediately, and ruffling movements at the cell periphery and most internal cell movements also become quiescent. This effect is readily reversible on washing the cells with fresh medium. Although nuclear division proceeds normally, cytoplasmic cleavage may begin in the usual way but fails to go to completion. A succession of nuclear divisions in the absence of cleavage results in very large multinucleate cells.

Nuclear extrusion at higher concentrations of the compound may lead to total enucleation. Cells that have been enucleated in this way and restored to normal medium are viable for at least 24 h.

Among many other biological effects, cytochalasin B has also been shown to interfere with morphogenetic movements (Wessels *et al.*, 1971) and phagocytosis (Davis *et al.*, 1971).

The regular association of all these effects suggests that a common factor may underly the many cell

activities with which these compounds interfere. The elucidation of the mode of action of the cytochalasins could therefore throw valuable light on a number of ill-understood aspects of cell behaviour and function.

The cytochalasins are characterized as a group, not only by their effects on mammalian cells, but also by a common biosynthetic derivation, which leads to certain shared structural features. The compounds are formed by condensation of a long chain, derived from acetate and the C_1 pool, with phenylalanine. The common structural features are indicated in structure (I). The large ring A may be a carbocycle

or a lactone, and varies from 11 to 14 atoms in size; considerable variation occurs in the part of the ring represented by the broken line. Ring B contains a double bond, which can be at any of the positions represented by the dotted line. The heterocyclic ring C is common to all the cytochalasins.

- Aldridge, D. C., Armstrong, J. J., Speake, R. N. & Turner, W. B. (1967) *J. Chem. Soc. C* 1667
Carter, S. B. (1967) *Nature (London)* 213, 261
Davis, A. T., Estensen, R. & Quie, P. G. (1971) *Proc. Soc. Exp. Biol. Med.* 137, 161
Wessels, N. K., Spooner, B. S., Ash, J. F., Bradley, M. O., Luduena, M. A., Taylor, E. L., Wrenn, J. T. & Yamada, K. M. (1971) *Science* 171, 135