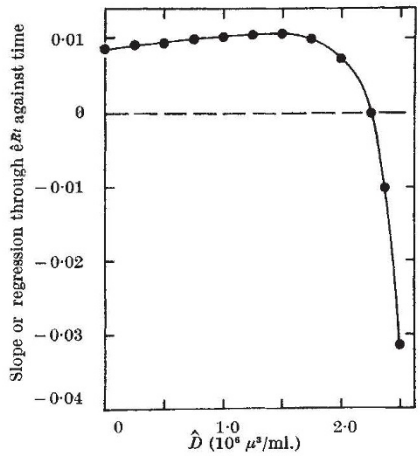

Fig. 2. The slopes of the regressions of e^{Rt} against time.

The slopes of $\hat{e}^{Rt}$ against time for various values of D are plotted in Fig. 2. Where the line joining these points intercepts zero ($\hat{D} = 2{\cdot}25$), $\hat{D} = D$. From the regression log $(V - D)$ or P on time (probability $P < 0{\cdot}02$), $P_c = 0{\cdot}680$ μ^3/ml., $D = 2{\cdot}250$ μ^3/ml., and $\hat{e}^{Rt} = 1{\cdot}62$/day. The resultant fitted curve and the observed values of V are plotted in Fig. 3. The assumption that D is constant is likely to be valid because the experiment was carried out in a bottle.

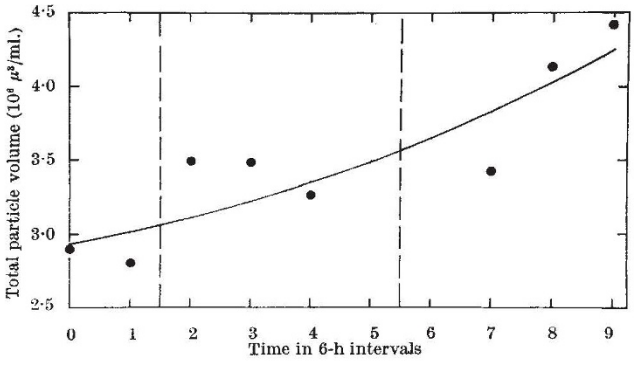

Fig. 3. Observed and fitted values of V. The vertical dotted lines represent midnight on two successive days.

The disadvantages of this system are: (1) the assumption that R is constant; Fig. 3 shows that there is a diurnal variation in the rate of production just as there is in photosynthetic processes, the fitted line averaging the changes in production rate for more than 2 days; (2) samples have been concentrated from a fine net; it is hoped that it will become possible to concentrate sea water satisfactorily by using a continuous centrifuge.

The advantages are: (1) the algal production rate is measured at sea; (2) both production and standing crop are determined from the same set of measurements; (3) living material is separated from the dead; (4) high accuracy is possible with heavy replication of samples.

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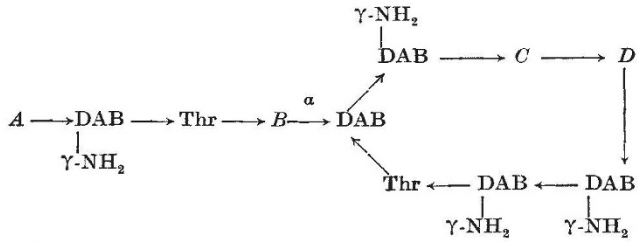
PHARMACOLOGY

Structures of the Polymyxins *A* and the Question of Identity with the Polymyxins *M*

THE elucidation of the structures of the polymyxins and the related antibiotic circulin *A* has so far revealed a remarkable consistency. Polymyxins *B*1 and *B*2 (refs. 1 and 2), polymyxins *E*1 and *E*2 (identical with colistins *A* and *B*, respectively)[3,4], and circulin *A* (ref. 5) are now known to be cyclic decapeptides, each possessing a ring of seven amino-acids and a chain of three amino-acids attached to the ring at the α-amino-group of an αγ-diaminobutyric (DAB) acid component. As shown in the accompanying formula, differences occur in the nature of the accompanying aliphatic acid and of certain amino-acid constituents.



In common with polymyxins *B* and *E*, polymyxin *A* has now been shown to be composite, separable by counter-current distribution into two components, polymyxin *A*1 and polymyxin *A*2. From the sequential analysis of the fragments obtained by partial acid hydrolysis and enzyme degradation, the structures of these two antibiotics have been determined and, as the formula shows, conform to the basic pattern. In contrast to the polymyxins *B* and *E* the polymyxins *A* have two D-amino-acids, which may account for the high degree of nephrotoxicity. It will be recalled that two D-amino-acids, D-serine and D-leucine, also occur in polymyxin *D*, the other nephrotoxic antibiotic of this group.

Table 1

	A	*B*	*C*	*D*
Polymyxin *B*1	MOA	DAB	D-Phe	Leu
Polymyxin *B*2	IOA	DAB	D-Phe	Leu
Polymyxin *E*1 (= colistin *A*)	MOA	DAB	D-Leu	Leu
Polymyxin *E*2 (= colistin *B*)	IOA	DAB	D-Leu	Leu
Circulin *A*	MOA	DAB	D-Leu	Ileu
Polymyxin *A*1	MOA	D-DAB	D-Leu	Thr
Polymyxin *A*2	IOA	D-DAB	D-Leu	Thr

MOA is (+)-6-methyloctanoic acid, and IOA is isooctanoic acid.

Polymyxin *M*, isolated by Khokhlov[6] in 1956, has now similarly been shown to be a mixture of antibiotics, giving, on hydrolysis, the same aliphatic acids, (+)-6-methyloctanoic acid and isooctanoic acid, found in the other polymyxins. The amino-acid composition, electrophoretic and chromatographic behaviours, optical rotation and nephrotoxicity of polymyxin *M* so parallel those of polymyxin *A* that there can be little doubt that these two antibiotics are identical.

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