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Lack of effect on Myleran derivatives on the synthesis of uridine nucleotides and glycogen

(*Received* 20 *September* 1962; *accepted* 26 *September* 1962)

THE pyrimidine moieties of nucleic acids are derived, directly or indirectly, from uridine 5′-diphosphate or -triphosphate (UDP, UTP), which arise from uridine 5′-monophosphate (UMP). In liver UMP is normally formed, under the action of orotidylate pyrophosphorylase (Code No. EC 2.4.2.10) and orotidylate decarboxylase (EC 4.1.1.23), from orotic acid, which arises from carbamylaspartic acid by two enzymic steps (dihydroorotase, EC 3.5.2.3, and dihydroorotate dehydrogenase, EC 1.3.3.1). An alternative pathway,[1] perhaps particularly important in liver tumours,[2] is from uridine under the action of uridine kinase (EC 2.7.1.21). Derivatives of UMP are important not only for nucleic acid synthesis but also for other processes such as synthesis of glycogen, the latter arising from UDPglucose by the action of UDPglucose-α-glucan glucosyltransferase (EC 2.4.1.11). The possibility that certain of these reactions in liver may be influenced by dimethylmyleran (2:5-dimethanesulphonoxyhexane, DM) or mannitolymyleran (1:6-dimethanesulphonylmannitol, MM) has now been examined, with negative results.

TABLE 1. TESTS OF MYLERAN DERIVATIVES FOR EFFECTS ON CERTAIN ENZYME PROCESSES

The values represent the mean percentage difference from controls, and are followed, where more than three experiments were done, by the standard error of the mean (number of experiments in parentheses). Values shown thus in square brackets represent mean activity in controls, as μmole/g/min.

	Derivative	Effect when injected	Effect *in vitro*
Orotate formation from carbamylaspartate, "free' activity [0·002]	DM		−17% (1)
Uridine nucleotide formation: from orotate* [0·008]	DM	+24 (3) ⎫ −1	+18 (6) ⎫ +6
	MM	−26 (3) ⎭ ±22%	−19 (3) ⎭ ±12%
Uridine nucleotide formation: from uridine [0·03]	DM		−15 (2) ⎫ 0
	MM	−18% (3)	+8 (4) ⎭ ±10%
Glycogen formation from UDPglucose [0·7]	MM	−18% (2)	−7% (2)

* Data for the individual products (UMP, UDP, UTP and UDPglucose) have been combined; there were no selective effects on the yield of any one product, or on the amount of uridine formed.

Young adult male rats of the Institute albino strain were given two intraperitoneal injections, each 6 mg/kg body wt., of DM in arachis oil or of MM in saline solution; the first injection was given 4 days and the second 1 day before killing. Alternatively, DM as a fine suspension in 0·25 M sucrose solution or MM dissolved in sucrose solution was added to liver samples from untreated rats prior to homogenizing; the amount was usually such as to give 0·5 mg/ml in the medium. Enzyme activities were assayed as in work described elsewhere.[2] The formation of uridine nucleotides from orotate was assayed essentially according to Stone and Potter,[3] with liver homogenates freed from nuclei and mitochondria. For uridine kinase, the procedure was similar to that used in Reichard's laboratory.[4] Glycogen synthesis was assayed essentially as in Leloir's laboratory,[5] with unfractionated homogenates to which UDPglucose labelled in the glucose moiety was added.

In some experiments on UMP synthesis, DM or MM was tested *in vitro* at several concentrations, ranging from 0·05 mg/ml to 2·5 mg/ml; since, however, there was no trend in the results with variation of the concentration, the results were averaged to give a single value. These and the other values obtained are given in Table 1. It is clear that none of the processes studied was markedly affected by the treatments investigated.

Acknowledgements—The investigation was supported by grants to the Institute from the Medical Research Council, the British Empire Cancer Campaign, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

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BOOK REVIEW

Nervous Inhibition: Proceedings of the Second Friday Harbor Symposium. Edited by E. FLOREY. Pergamon Press, Oxford, 1961. pp. 475, £5.

THIS Conference of fifty people took place at Friday Harbor, where the University of Washington has a marine biological station. Its object was to review the state of knowledge about inhibitory processes and to promote an exchange of ideas between workers normally concerned with vertebrates and those with experience on invertebrates. Nearly two thirds of the papers dealt with the electrophysiological side of the problem, both on vertebrate and invertebrate tissues. There were few anatomical papers, among which that by Szentágothai was most striking by the demonstration that classical anatomical methods may yet prove of great help to the unravelling of modern physiological problems. Chemical progress in the identification of inhibitory transmitters has been slow, and on those lines much of the work remains to be done. The last paper, by van der Kloot, exposed a totally different and fascinating aspect of long-lasting inhibitions found in a variety of insects and crustaceans. The processes all have in common that nervous activity elicits inhibitory phenomena, sometimes apparent only in the next generation, and brought about either by the release or by the prevention of the release of a hormone at a critical stage in development.

The book is well produced and its publication was assisted by the National Science Foundation which also subsidized the Symposium itself. It will make interesting reading to a great number of physiologists and biologists.

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