Short Communications

On the Biological Methylation of Histamine. 5. Inhibition by Histamine Analogues

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Histamine is attacked mainly by two enzymes, one being diamineoxidase, which is fairly well known. This enzyme can be inhibited effectively by aminoguanidine. When diamine oxidase is thus inhibited *in vivo* by injection of aminoguanidine, the other histamine-metabolizing enzyme, S-

adenosylmethionine — histamine methyltransferase continues histamine inactivation to completion¹.

It is evident that a potent inhibitor of the histamine methyltransferase could help in clarifying the physiology of histamine. So far only nonspecific inhibitors have been reported²⁻⁴. Therefore some histamine analogues were examined for possible inhibition of histamine methyltransferase.

The method for the assay of the enzyme has been described recently⁴. A new method for purification of the enzyme using TEAE-cellulose chromatography and Sephadex-filtration has since been used and will be described in detail elsewhere. The histamine analogues were obtained through the courtesy of Drs Kahlson and White at the Physiological Institute, University of Lund, Sweden.

Table 1. The effect of some histamine analogues on histamine methyltransferase. The roman figures refer to Lee and Jones⁵.

Compound	Inhibition in % at different inhibitor concentrations			
	2.5×10^{-3} M	1×10^{-3} M	1×10^{-4} M	1×10^{-5} M
V	30	17	5	0
VIII	42	8	0	0
IX	80	18	24	13
XIII	65	37	4	3
XXIV	75	51	19	12

The compounds tested are listed in Table 1, which shows their inhibitory effect on histamine methyltransferase. The roman figures refer to the investigation by Lee and Jones⁵, in which they examined the effect of the same compounds on isolated guinea pig ileum and on the blood pressure of the anesthetized cat. Compounds Nos. V, VIII, and IX had some activity, but XIII and XXIV were devoid of histamine-like activity. Evidently there is no correlation between the biological activity and the enzyme inhibition.

Table 2. Inhibitory effect of 3- β -aminoethylpyrazole (XXIV) on histamine methyltransferase at different histamine concentrations. The inhibitor concentration was 2.5×10^{-3} M.

Histamine concentration, mM	Inhibition, %
0.034	79
0.067	72
0.168	41
0.337	1

In Table 2 it is shown that the inhibition by compound XXIV is of competitive nature. This finding makes it doubtful if the compound can be used with any success as an inhibitor *in vivo*, although its lack of biological activity would permit rather high doses.

A full report of these experiments will be published.

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The Structures of Three Mesomorphic Phases in the Sodium Caprylate-Decanol-Water System

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Of the liquid-crystalline phases that under certain conditions separate from concentrated aqueous association colloid systems, the so-called middle soap phase has a two-dimensional hexagonal structure. This was proposed already by McBain and Marsden¹ in the cases of dodecylsulphonic acid and triethanolamine laurate. These authors concluded that the phase in question consists of long fibres, rods or ribbons that are arranged in a hexagonal network with water occluded between the fibres. Luzzati and co-workers² have recently established that association colloids of different types including the salts of higher fatty acids ($C_{12}-C_{18}$) form middle soaps with a two-dimensional hexagonal structure and were able to present detailed information about the inner structure and unit dimensions of the phases.

We have studied the middle soap formation by a fatty acid soap with a shorter chain, sodium caprylate (C_8)³⁻⁴. A liquid-crystalline phase separates at 20°C from aqueous solutions of this soap when the concentration exceeds 40.5 %. Between 46.0 and 51.5 % sodium caprylate this mesomorphic phase is homogeneous. The phase is both macroscopically (it is a transparent, rigid "gel") and microscopically (it has a fanlike and angular texture: 222.5 and 226.1 in Rosevear's system⁵) similar to the middle soaps of some higher fatty acid soaps and its X-ray diffraction pattern reveals a hexagonal structure. We therefore felt justified in drawing the conclusion that the middle soap of sodium caprylate has a inner structure resembling the structure of the middle soaps of the higher soaps. Subsequent X-ray studies have confirmed this conclusion. We have recorded for the middle soap of sodium caprylate, besides a weak diffuse reflection at the position $s = 1/4.5 \text{ \AA}^{-1}$ ($s = 2 \sin \theta/\lambda$), as many as three sharp reflections with Bragg spacings of 25.9, 15.0, and 13.0 Å in the central part of the X-ray diffraction pattern. The positions of these lines do not vary over