

with added leucine) to minimize the possible nutritional effects of amino-acids and other materials. Crude extract caused an increase of about 35 per cent, whereas the pyridine eluate from 'Amberlite IR-100' produced 12 per cent inhibition and the whole acid fraction about 79 per cent inhibition. Since the inhibitory fractions were considerably more potent than the crude extract against infections *in vivo*, it is doubtful whether the growth stimulation originally observed is related to the effectiveness against the infection. The antistaphylococcal activity probably may be attributed to as yet unidentified acid substances.

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<sup>3</sup> Block, B. J., Durrum, E. L., and Zweig, G., "A Manual of Paper Chromatography and Paper Electrophoresis", 160 (Academic Press, New York, 1955).

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### A Probable Peptidase in Carcinoid Tumours

CARCINOID tumours (argentaffin carcinomas) are considered to arise from the argentaffin (enterochromaffin, Kultschitsky) cells of the intestine. These tumours contain and secrete 5-hydroxytryptamine<sup>1</sup>, and histochemical investigations<sup>2</sup> make it likely that enterochromaffin cells do likewise. In three cases of argentaffin carcinoma recently investigated, we have observed a strong esterase (Fig. 1) capable of hydrolysing a variety of substrates. Using

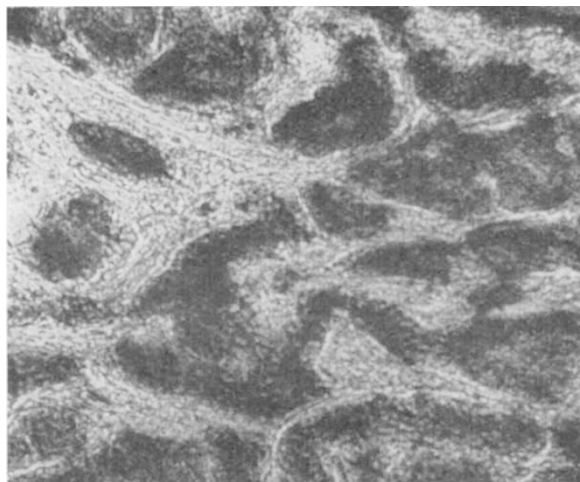


Fig. 1. Frozen section (15 $\mu$ ) of human ileum. Carcinoid tumour infiltrating serous coat. Indoxyl esterase (1 $\frac{1}{2}$  hr., no counter-stain). ( $\times$  175)

Table 1. EFFECT OF INHIBITORS ON CARCINOID ESTERASE (Figures represent visual estimate)

Inhibitor and concentration	Activation (per cent)	Inhibition (per cent)
Diethyl- <i>p</i> -nitrophenyl phosphate, $\times 10^{-4}$ M	—	100
Silver nitrate, $2 \times 10^{-5}$ M	—	100
Sodium fluoride, $\times 10^{-3}$ M	—	—
Sodium taurocholate, $\times 10^{-3}$ M	20	—
Cysteine, $\times 10^{-3}$ M	30	—
Hydroxylamine, $\times 10^{-3}$ M	30	—
Hydrocinnaic acid, $\times 10^{-3}$ M	—	—
Sodium dodecyl sulphate, $\times 10^{-3}$ M	—	30

O-acetyl-5-bromoindoxyl as substrate and an incubation time of 4 hr., inhibition studies gave the results shown in Table 1.

Inhibition by diethyl-*p*-nitrophenyl phosphate (E600) confirms the general identity of the enzyme as a carboxylic acid esterase. Enzymes of this class are known to function as peptidases, and several of the latter can split indoxyl acetates. Although the results with taurocholate and dodecyl sulphate do not exclude the possibility of a lipase, we believe, on the basis of other work<sup>3</sup>, that the pattern of activation and inhibition given above indicates the presence of an intracellular peptidase.

Enterochromaffin cells in man, rat and guinea pig could not be shown by histochemical methods to contain any type of esterase or peptidase. We thus have to consider a tumour containing an enzyme which is absent from the presumed parent cell. This is the reverse of what is usually found by biochemical and histochemical methods.

An esterase with similar properties to the carcinoid esterase is found in the mucous-secreting cells of the intestinal glands, and these were believed by Popoff<sup>4</sup> to give rise to enterochromaffin cells. His theory has had little support, the majority of workers subscribing to the neural crest theory of origin. Although our results preclude neither theory, they make necessary a reconsideration of the ancestry of the cells which give rise to carcinoids, and invite speculation as to the connexion of the enzyme with the behaviour of these tumours.

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### Acylacrylic Acids and Biological Activity

It has recently been reported<sup>1</sup> that  $\beta$ -acetylacrylic acid and its (ethyl) ester are rather poisonous to mice, about 1 mgm. given subcutaneously to a 25-gm. mouse being lethal. There was also an increase in leucocytes, which in the case of the ester appear after about three weeks and in the case of the acid after a few hours. In the latter case the effect disappeared after about a day and this increase was assumed to be due to acidosis. This has now been found to be almost certain, because injection of