contradiction can be easily explained if we admit (SCHRAMM[8]) that the virus particle is constituted of a great number of smaller units, genetically identical, and which multiply independently in the host cell. We may suppose that the thiouracil incorporated in our experiments is not in sufficient amount to inhibit the multiplication of all the elementary units of each particle. Each virus particle will thus remain infective, but the proportion of its elementary units capable of duplication in the host is reduced.

We are well aware of the tentative character of this interpretation and have presented it in order to show that there is no necessary contradiction between COMMONER's results[7] and our own.

TABLE I

Exp. No.	*Duration of virus growth (days)*	*Concentration of infective solut. %*	*Protein N ppt. by antiserum (γ Protein N p. mg Prot. N of leaves)*		*% Drop in the amount of newly formed virus*	*% Drop of concentration of normal virus sol. producing same effect*
			Normal virus	*Thiouracil-containing virus*		
12–10	3	0.1	51	46	9.8	28
		0.3	76	40	47.5	92
5–10	3	0.3	89	68	23	80
29–8	3	0.46	71	53	25	65
23–6	4	1	6	3.7	38.4	68
	7	1	42	32	24	—
	8	1	40	33	17	—

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EFFECT OF TAURO-CHOLIC ACID ON THE pH/ACTIVITY CURVE OF RAT PANCREATIC LIPASE

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The bile acids have generally been assumed to activate the pancreatic lipase[1,2,3,4]. These accelerating effects of bile acids on pancreatic lipolysis have mostly been studied in the pH range 8.5–8.9, but at an acid pH an activating effect has also been found[5]. Any detailed study of the effect of pH on the pancreatic lipolysis in the presence of bile acids does not, however, seem to have been undertaken.

The effect of different concentrations of synthetic tauro-cholic acid, at different pH values, on the rate of hydrolysis of olive oil by rat pancreatic lipase has been studied. The results of this investigation are summarized in Fig. 1.

In the absence of tauro-cholic acid the pH/activity curve for the rat pancreatic lipase shows an optimum at pH about 8. With increasing concentrations of tauro-cholic acid the pH optimum is changed to about 7.2 at 0.05 %, pH 6.7 at 0.1 % and about pH 6 at 0.2 % tauro-cholic acid. With increasing concentrations of tauro-cholic acid a second pH optimum also appears at a pH of about 9.

This second pH optimum is already indicated at a concentration of tauro-cholic acid of 0.1 %. Between the two pH optima a pH minimum develops which is most apparent at a concentration of about 0.2 % and is found at about the same pH as the pH maximum in the absence of bile acids.

To get an idea of the importance of the bile acids for the rate of pancreatic hydrolysis of long-chain glycerides under *in vivo* conditions a knowledge of the pH and the bile acid concentration of the contents of the small intestine during digestion is necessary.

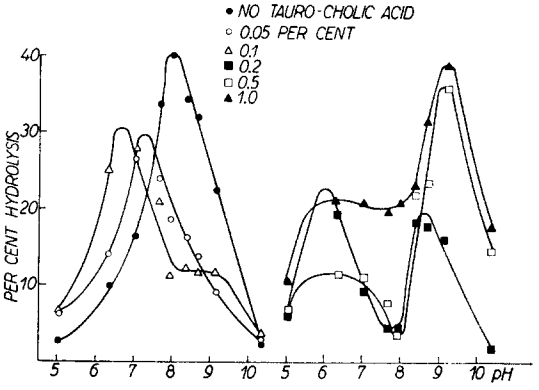

Fig. 1. Effect of different concentrations of tauro-cholic acid on the pH/activity curves of rat pancreatic lipase. Substrate 20 mg olive oil. Buffer: pH 5.0–7.6, 0.1 *M* phosphate; pH 7.9–10.3, 0.1 *M* NH_4Cl/NH_4OH. Enzyme: lyophilized rat pancreatic juice[7]. The substrate and 4 ml of the respective buffers were added to 10 ml test tubes. To each tube was then added the synthetic tauro-cholic acid[8] dissolved in 1 ml water and 1 ml solution of the dry pancreatic powder corresponding to 0.005 ml of the fresh juice. The tubes were closed and rotated for 30 minutes in a water bath at 38°. The fatty acids liberated on hydrolysis were extracted and titrated according to the method described by DAVIS[9].

The pH of the intestinal contents in the upper part of the small intestine has been found to be about 6.5. At this pH pancreatic lipase in the absence of bile acids has a low activity. Reliable information about the bile acid concentration in the contents of the small intestine during digestion is not to be found in the literature. The concentration of bile acids in rat bile is, however, about 300 mg %[6]. The bile is then diluted with pancreatic juice and also by gastric contents, the volume of which of course is dependent on the water intake, in all giving about a 2-fold dilution. Roughly the bile acid concentration in the contents of the small intestine would then be something between 0.1 and 0.2 %. At this bile acid concentration the pH optimum of the pancreatic lipase is shifted to between 6 and 7 as is evident from Fig. 1.

The optimum for pancreatic lipase at higher bile acid concentrations at pH about 9 probably has no physiological importance.

In a recent publication MINARD[4] has given figures for the effect of bile acids on the rate of hydrolysis of a corn oil emulsion at pH 8.5, and found an activating effect of bile acids in concentrations from 0.05 to 0.3 %. With these concentrations and at this pH our results show only inhibitory effects on the rate of hydrolysis of olive oil.

The explanation of these differences probably is to be found in the fact that MINARD has used enzyme and bile acid preparations less pure than those used in this investigation, *viz.* synthetic tauro-cholic acid[8] and rat pancreatic juice[7].

The results of this investigation thus show that *in vitro* tauro-cholic acid, in the concentrations most probably found in the small intestinal contents during digestion, shifts the pH optimum of pancreatic lipase from pH about 8 to pH values between 6 and 7, *i.e.* the pH range found in the contents in the upper part of the small intestine. This shifting of the pH optimum for pancreatic lipase appears to be an important physiological function of the bile acids in fat digestion.

The explanation of the ways in which tauro-cholic acid affects the rate of hydrolysis of triglycerides of long-chain fatty acids at different pH values remains to be elucidated.

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