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LIPOLYSIS AND FAT ABSORPTION

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According to the current hypothesis of fat absorption [Verzár & McDougall, 1936], lipolysis is an essential preliminary to absorption. The absorption of unhydrolysed triglyceride is regarded as an impossibility. If this were true, one would expect that neutral fat would give an identical picture to fatty acid during and after absorption. It can be shown that this is not the case [Frazer, 1938]. It is possible that fat is absorbed partly as a hydrolysed fraction and partly as unhydrolysed triglyceride and that lipolysis determines the route and destination of the absorbed fatty material. The object of this paper is to put forward further evidence in support of this conception of lipolysis in relation to fat absorption.

Methods

Animals. Black and white adult rats from our own breeding stocks were used.

Materials. The fat used was olive oil B.P., the lipase preparation was 'Holadin' (Fairchild Bros.) and the sodium cetyl sulphate was obtained as 'Lissapol A' (I.C.I.).

Assessment of absorption. This was determined by analyses of the residual intestinal contents 6 hr. after administration of a known weight of fat. Absorption was confirmed by frozen sections showing the presence or absence of fat in the intestinal cells. The pathway taken by the fatty material after absorption was demonstrated by systemic and portal chylomicrographs. The eventual destination of the fat in the body was traced by the use of Sudan-stained fats which could be seen in the fat depots or the liver respectively. Human chylomicrographs were carried out under the standard conditions previously described [Frazer & Stewart, 1939].

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Results

The effect of added lipase in the rat

Fifty rats were used in these experiments. Groups of animals were fed with neutral fat to which was added an excess of active lipase. To control groups identical quantities of fat were fed with pancreatic extract in which the ferments had been destroyed by heat. The control groups showed the characteristic appearances found after neutral fat feeding. The animals which had extra lipase showed the changes usually associated with fatty acid feeding, namely, a fine granular deposit in the intestinal cells, no milkiness of the lacteals, a portal instead of a systemic lipaemia and deposition in the liver rather than the fat depots. The main findings are given in Table 1.

The effect of inhibition of lipolysis in the rat

Schulman [1941] showed that long-chain sulphates such as sodium cetyl sulphate inhibit the hydrolysis of ethyl butyrate by lipase. On testing the effect of this substance on the hydrolysis of triglyceride by lipase *in vitro*, it was found that 1/1000 sodium cetyl sulphate completely prevented lipolysis. This concentration must be slightly increased to ensure inhibition in the presence of bile.

Using fifty adult rats, groups of animals were fed upon olive oil mixed with a solution of 1/200 sodium cetyl sulphate while the control animals received a mixture of olive oil and water. The amount of fat absorbed was identical in the two groups, being slightly greater in those having cetyl sulphate. The histological picture, the chylomicrograph and the deposition of stained fat were all as found after triglyceride feeding. The results are tabulated below (Table 1).

Table 1. Results of ingestion by rats of neutral fat, fatty acid, neutral fat and lipase, and neutral fat and cetyl sulphate. Comparable amounts were absorbed in all groups. Average rate: 1 g. per 24 hr.

	Material ingested			
	Neutral fat	Fatty acid	Neutral fat + lipase	Neutral fat + cetyl sulphate
Intestinal cells	Large globules	Fine granules	Fine granules	Large globules
Lacteals	Milky	Nil	Almost clear	Milky
Systemic chylomicrograph	Normal max. 200	Low max. 20	Low max. 50	High max. 250
Fat depots	Heavy staining	Nil	Very little staining	Very heavy staining
Portal chylomicrograph	Low max. 20	Normal max. 200 +	Normal max. 200 +	Low max. 10
Liver	Small amount of staining	Heavy staining	Heavy staining	Very small amount of staining

In order to make certain that there was inhibition of lipolysis in the lumen of the rat's intestine under these conditions, samples of the intestinal contents were taken from some groups. This material was incubated and aliquots were

titrated at half-hourly intervals. There was no appreciable increase of fatty acid over a period of 6 hr. To further samples extra lipase was added but again lipolysis was found to be inhibited.

Effect of added lipase in man

Most of the observations made on rats cannot be checked in man. One striking change can, however, be demonstrated. The chylomicrograph may show differences between one individual and another, but any one subject

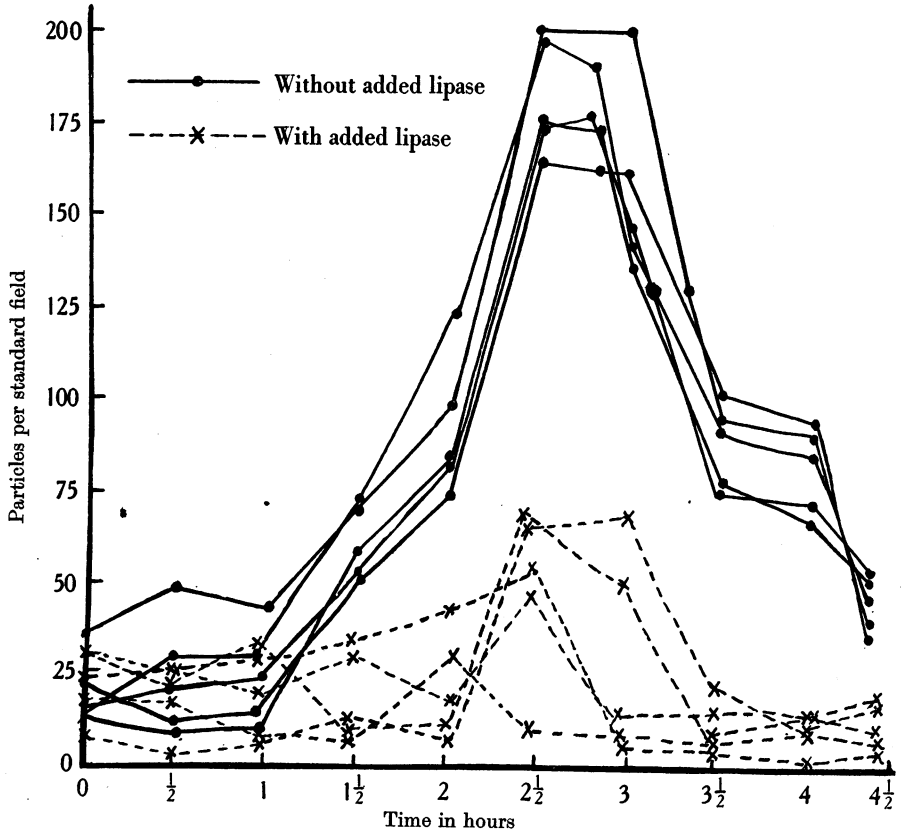

Fig. 1. Five normal human chylomicrographs following ingestion of 30 g. neutral fat with and without added lipase.

ingesting a standard amount of fat gives a reasonably constant lipaemic curve. If 30 g. neutral fat are ingested, the peak lipaemia will usually be in the region of 150–200 particles per field, but if to the 30 g. neutral fat is added some potent lipase (two 3 gr. capsules of 'Holadin'), the maximal systemic lipaemia is reduced by more than 75%. If the pancreatic extract is inactivated by heating before addition to the neutral fat it causes no such change

in the lipaemic curve. The depression of the post-absorptive lipaemia in a group of five human subjects by the simple addition of lipase is shown in Fig. 1. The average peak lipaemia in fifteen human experiments was 185 particles per field (range 100–300) after ingestion of 30 g. neutral fat, but when lipase was added to the 30 g. neutral fat the average peak lipaemia was only 45 particles per field (range 20–75).

Discussion

If the breakdown of the triglyceride molecule is essential before it can be absorbed, the simple addition of lipase would not be expected to cause any profound change in the form, route or destination of absorbed fatty material. The first group of experiments, however, show that in the rat all these occur. The results fully confirm previous observations [Frazer, 1938] which were made after feeding with neutral fat or equivalent amounts of fatty acid respectively. While ingestion of neutral fat normally leads to a characteristic appearance of the intestinal cells, to milkiness of the lacteals, to a marked systemic lipaemia and to deposition of fat in the fat depots, the simple addition of potent lipase to the ingested neutral fat changes all these sequelae. Instead of large globules in the intestinal cells there are very fine granules, the lacteals remain almost clear, the systemic blood shows but a slight lipaemia, and deposition in the depots is much decreased. The portal blood and liver, which show only slight changes after neutral fat ingestion, exhibit marked lipaemia and deposition respectively if lipase is added to the neutral fat. The results following the ingestion of neutral fat and lipase are thus similar to those seen after the administration of fatty acid.

In the human subject it is only possible to check one of the essential observations. The normal chylomicrograph for any human subject under standard conditions is reasonably constant. It is possible to suppress almost completely the post-absorptive systemic lipaemia by the simple addition of lipase to the standard fat-containing meal. This observation correlates with the findings in the rat and it seems probable that the reason for the suppression of the systemic lipaemia is the diversion of the fat from the lymphatic pathway into the portal blood. It cannot be attributed to interference with, or delay in, the absorption of the fatty material.

The second group of experiments confirm the observations of Schulman that long-chain sulphates inhibit lipolysis. The inhibitory action of sodium cetyl sulphate in the rat's intestine has been carefully checked. There seems to be no reasonable doubt that fat is being absorbed in these experiments in the absence of any appreciable degree of lipolysis. It may be significant, however, that sodium cetyl sulphate is a strongly surface active substance and an excellent emulsifying agent. These experiments do seem to indicate that triglycerides may be absorbed without previous hydrolysis, although it

is probable that the presence of a surface active compound is important. From these experiments it appears that it is not essential to hydrolyse triglycerides for them to be absorbed.

These observations provide further support for the view that hydrolysis determines the mechanism of absorption, the route and destination of the absorbed fatty material. It is suggested that the current conception that hydrolysis of triglycerides is a necessary step in their absorption is incorrect, and that lipolysis should be regarded as a determining factor in the fate of absorbed fat and possibly as a means of providing essential raw materials for the synthesis of lecithin and the formation of soaps. This latter possibility will be discussed in a subsequent paper.

Summary

1. Rats fed with neutral fat with added lipase show sequelae normally associated with the ingestion of fatty acid, such as fine granular deposition in the intestinal cells, portal rather than systemic lipaemia, and deposition in the liver instead of in the fat depots.

2. In human subjects under standard conditions, the systemic post-absorptive lipaemia can be almost entirely prevented by the simple addition of lipase to the fat-containing food.

3. The complete inhibition of lipolysis by sodium cetyl sulphate in rats does not prevent triglyceride absorption in amounts comparable with, or rather greater than, those absorbed by the control groups in the same time.

4. The significance of these findings is discussed and it is suggested that lipolysis is not an essential step in triglyceride absorption, but that firstly it determines the fate of absorbed fatty material and secondly it provides fatty acid for soap and phospholipid formation.

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