

Remarks on the Specificity of Action of Pancreatic Lipase

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I WOULD like to say just a few words about some experiments we made during the past few years in the field of the digestion of lipids. In 1954 when we started this series of experiments,¹ we could show that pancreatic juice, obtained from permanent fistulas in the rat, acting *in vitro* on various natural triglyceride substrates, various seed oils and some animal fats, removed the most saturated fatty acids first. The iodine value of the liberated fatty acids in our experiments was always below the iodine value of the fatty acids of the substrates and increased very regularly during the course of the hydrolysis.

As it had not yet been demonstrated that pancreatic lipase manifested a steric specificity, we thought that the pancreatic lipase might have an affinity for the most saturated fatty acids. Very shortly, the interesting experiments of Borgstrom,² Mattson and Beck³ and Desnuelle and Savary⁴ demonstrated that lipase removes first the fatty acids located in the α - α' position (carbons 1 and 3 of the molecule of the glycerol).

We reported for the first time at the meeting in Ghent in 1955,⁵ that it was possible to explain the removal of the most saturated fatty acids if, in natural fats and oils, the fatty acids in positions 1 and 3 were generally more saturated than the fatty acids in position 2.

In the meantime Mattson showed that pancreatic extracts acting on lard as glyceride substrate removed the most unsaturated fatty acids first. We recently repeated these experi-

ments with pancreatic juice and lard and found results in good agreements with the results of Mattson. However, we must say that we tried a very large number of other natural fats and oils and that the lard was the only exception to the general rule. We do not know at the moment what explanation can be given for these observations.

We would like to add that we are very impressed by recent experiments of Mattson⁶ with synthetic substrates of known structure, and by the difference he observed when pancreatin acts on natural lard or lard after the fatty acids have been rearranged in the triglyceride molecule by hydrolysis and random reesterification. These last experiments, particularly, like those of Savary and co-workers⁷ seem very conclusive and speak against the conception of a "chain specificity" of the lipase.

However, it must be recognized that until recently we did not know very much about the structure of the natural triglycerides and we cannot discard completely the hypothesis that the lipase manifests, in addition to its steric specificity, a special affinity for certain kinds of triglyceride substrates present in natural fats and oils.

On the other hand, it is very interesting to note that the pancreatic cholesterol esterase esterified preferentially the most unsaturated fatty acids as we have seen,⁸ in good agreement with the experiments of Swell and co-workers.⁹

It may be that in the intestinal tract a certain interrelation exists in the action of the enzymes of the pancreatic juice for esterification and hydrolysis which permit an adequate repartition of the fatty acids between the different lipid constituents. This hypothesis is well supported by results obtained on the composition of the lipid present in the intestinal lumen¹⁰ and in the lymph.¹¹

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