The Liver and Theory of Fatty Acid Desaturation

by

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In the body the liver is the one organ in which the fat content is subject to wide variations. This fatty change is readily brought about by excessive alimentation or methods which cause a mobilization of the depot fat. This unique intermediary position of the liver in fat metabolism was established at the beginning of the century by Lebedeff[1] and Rosenfeld[2], whose work not only demonstrated that the mobilized liver fat was characteristic of the depot fat but that the increase in liver fat depended upon the nutritive state of the animal—in other words, the richness of the depots.

It was then shown that the fatty acids of the liver and other organs were more highly unsaturated than those of the depots (adipose, intramuscular). The fatty acids of the liver ordinarily have an iodine number ranging between 130 and 140. Leathes and Meyer-Wedell[3] fed animals cod liver oil which yields fatty acids with an iodine number of 150. The livers of these animals contained fatty acids with iodine numbers ranging from 160 to 185 and even greater in some cases. This result did not obtain in the other tissues. It was evident that the liver in some way was concerned with fatty acid metabolism.

Hartley[4] attacked the problem in a different fashion by examining the character of the individual fatty acids in pig's liver. He found that the oleic acid in pig's liver had the double bond in the Δ^{12-13} position (from the carboxyl end) while the oleic acid of the adipose tissue (ordinary oleic acid) has the double bond in the Δ^{9-10} position. He also isolated a C_{20} acid with four double bonds which has since been shown to be arachidonic ($C_{20}H_{32}O_2$).

Certain facts regarding the liver in relation to fat metabolism are therefore evident. When fat is mobilized it appears in the liver, the amount depending upon the content of the adipose tissues and the intensity of the mobilization. The greater the increase in the liver fat the nearer it approaches the character of the storage fat, measured in terms of the iodine number of the fatty acids. The iodine values of the liver fatty acids are higher than other organ and adipose tissue fatty acids. However, the fatty acids of the liver are subject to wide fluctuations and are readily influenced by diet. The unsaturation of the liver fatty acids may exceed that of the dietary fatty acids. Furthermore in one species, the pig, there is found an oleic acid, as well as a highly unsaturated acid of twenty carbon atoms foreign to the ingested food.

This array of data led Leathes[5] in 1908 to propose the well known theory of fatty acid desaturation by the liver. It is probably best described in his own words:

> "It looks as if the work of the liver consisted in an operation which may be compared to the drying of gunpowder. The fats we take in our food are remarkably unreactive substances and it has always been one of the most astonishing chemical achievements of animal cells that they should be able to burn up completely and cleanly as they do so stable a structure as saturated fatty acids like palmitic or stearic acids. They are wet gunpowder. And the body stores its gunpowder wet, and safely removed from the inflammatory operations of busily working cells. When the orders for mobilization are issued this wet powder is conveyed to the drying chambers in the liver, and from there distributed to the fighting line in a proper condition for use. There are times when the stress of this work is manifestly too great. Too active a mobilization of stored fat, or too little activity in dealing with it on the part of the liver, will result in an accumulation of the unfinished product in that organ. A fatty liver is then the result, and the fatty acids which it contains are found to have a low iodine value. There is an accumulation of wet powder."

Joannovics and Pick[6] in 1910 presented evidence which tended to support Leathes' hypothesis. They confirmed Leathes' observation that the fatty acids of the liver, after cod liver oil feeding, had a higher iodine number than those of the cod liver oil ingested. The phospholipids were not changed in percentage but contained fatty acids more highly unsaturated than the liver phospholipids in the fasting state. In the short period of twenty-four hours after the feeding of the oil the iodine number of the liver fatty acids had again reached the lower values of the fasting state. When the portal circulation (blood from the intestines) was diverted so as not to enter the liver, the above-mentioned changes in the liver fatty acids did not occur after feeding cod liver oil. Furthermore, when iodized fat was fed it was scarcely detectable in the liver. Thus, two ideas regarding the function of the liver in fatty acid metabolism became a point of contention. One was that the liver was able to desaturate or saturate fatty acids; the other, the liver exerted a selective action on the fatty acids arising in the portal circulation—absorption of the unsaturated acids in preference to the saturated ones.

In 1914, Imrie[7] presented evidence favoring the view that accumulation of connective tissue fat in the liver was of a physiological nature whereas accumulation in other organs such as the heart and kidney was more in the order of a pathological process. That the liver is concerned in some manner with fatty acid metabolism seems obvious. Are fatty acids actually desaturated in the liver or is the presence of highly unsaturated acids in this organ merely evidence of its selective action?

Recently Burr and Burr[8] reported that rats raised on a diet, rendered as free of fat as experimentally possible, exhibited a dermatitis and failed to grow. Linoleic acid and linolenic acid were each capable of curing this deficiency. The saturated acids as well as oleic were of

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no value as curative agents. Arachidonic acid was ineffective also. This work seemed fairly conclusive proof that warm-blooded animals needed fatty acids more unsaturated than oleic and that they were dependent upon the diet for these acids. The synthetic power of the body and supposedly of the liver was therefore limited to one double bond. In addition, Turner[9] showed that the oleic acid of sheep liver was the ordinary Δ^{9-10} acid. Channon and co-workers[10] reinvestigated pig's liver and found that 85 per cent of the oleic acid present was the ordinary Δ^{9-10} acid in contradiction to Hartley's original observation. The main structure supporting the theory of fatty acid desaturation by the liver seemed to be destroyed.

However, there is evidence for another view of this theory. What about the arachidonic acid found by Hartley? Here is a C_{20} acid with four double bonds. No highly unsaturated acid of more than 18 carbon atoms has been discovered in the plant world except in the case of algae, marine flora, which Tsujimoto[11] has shown to contain the polyethylenic acids of the C_{20} and C_{22} series. In 1925 Wesson[12] reported an extensive study of arachidonic acid. Using rats he found a larger content of arachidonic acid in the tissues during active fat metabolism. This increase was greatest in the liver. No changes were noted when the rats were deprived of dietary fat or when they were fed a vitamin A deficient diet. Wesson offered the suggestion that arachidonic acid is an intermediate product (built up in the liver) in the metabolism of at least part of the fatty acids which contain fewer than 20 carbon atoms. Incidentally, he demonstrated the presence of arachidonic acid in all the tissues of the dog. Müller[13] reported that the arachidonic acid content of the liver of human beings was independent of the total fat and total iodine number of the liver. He believes that the level of arachidonic acid in the liver is an index of its fat-splitting activity. Bloor[14] studied bovine tissues and found arachidonic acid to be "greatest in the brain, next in the liver and kidney, then lung, then pancreas." Bloor and Snider[15] reported that 31 per cent of the unsaturated fatty acids of beef liver is arachidonic acid. Brown[16] confirmed the work of Hartley in demonstrating the presence of arachidonic acid in pig's liver and states that it is the only highly unsaturated fatty acid present in appreciable quantities. Brown and Ault[17] asserted that beef, sheep, and hog brains are alike in their arachidonic acid content. Turner[9] found it present in sheep liver. Klenk and Schönebeck[18] also demonstrated the presence of archidonic acid in beef liver in which they contend that the unsaturated C_{20} acids are more abundant than the C_{22} unsaturated acids; in the brain, however, C_{22} acids are the more plentiful.

Arachidonic acid apparently is a common constituent of the fatty acids of the various organs (notably the liver) of omnivores, carnivores, and herbivores alike. But arachidonic acid is not the only highly unsaturated fatty acid present in animal tissues. Numerous investigators (15, 17, 18 and 19) have reported the presence of highly unsaturated C_{22} acids (clupanodonic acid with 4 double bonds) and C_{24} acids. Arachidonic acid is not a common constituent of the diet, especially of the herbivorous animal. Acids of C_{22} and C_{24} atoms of a high degree of unsaturation are still less common. Where then do these acids arise from if not through the synthetic powers of the animal body? It appears that, in general, in the animal kingdom wherever there are notable amounts of unsaturated fatty acids, they are likely to contain mostly 18, 20, and 22 carbon atoms. Acids of 18 carbon atoms are less important in animals, while in plants the highly unsaturated acids are mostly of this series.

It is interesting to note in the work of Burr and Burr[8] regarding the essential nature of linoleic and linolenic acids that Snider and Bloor[15] have shown that linoleic acid is the most important unsaturated fatty acid in beef liver lecithin. It constituted 45 per cent of the unsaturated acids whereas arachidonic and linoleic acid amounted to 31 per cent and 21 per cent respectively. No evidence of linolenic, the C_{18} three double bond acid was found. Turner[9] found linoleic acid in sheep liver, but no linolenic acid. Klenk and Schönebeck[18] reported similar results on beef liver.

It would seem that linoleic is quite important as an unsaturated fatty acid in the liver. Oleic acid is the normally occurring unsaturated acids of the depots. The depot fat of beef was found by Klenk and Schönebeck[18] to contain no unsaturated fatty acids of higher carbon content than C_{18} while the neutral fat of the liver contained highly unsaturated fatty acids of C_{20} and C_{24} atoms. Normally the quality of the liver fat is quite different from that of the depots, but tends to become more like them under the stress of mobilization.

Burr and Burr's[8] work seems to have demonstrated that linoleic acid cannot be synthesized in the animal body at least in sufficient quantities to permit growth. It has been shown that linoleic acid is probably the most important unsaturated fatty acid in the liver. Linolenic acid will replace linoleic acid but is not required if linoleic is supplied. Linolenic acid is not found in the liver. We can therefore look upon linoleic acid as being a necessary constituent of the food together with certain amino acids, vitamins, salts, etc. However, this does not disprove the fatty acid desaturation theory. Certainly arachidonic acid and clupanodonic acid must be synthesized since they do not occur in the food—this is especially true of the herbivorous dietary. Sinclair[20] has studied the fat of growing rats ingesting a practically fat-free diet and finds that the synthetic fat has a greater iodine number than oleic acid and points out that the amount synthesized precludes the possibility of it arising from the small amount that might have been present in the food. Undoubtedly the liver does exert a selective action on the unsaturated fatty acids in preference to the saturated acids as they come to it. Nevertheless the ubiquitous distribution throughout the tissues of significant quantities of such highly unsaturated fatty acids as arachidonic, the C_{22} and C_{24} acids, all of which are foreign to most dietaries, appears to be conclusive evidence in favor of the desaturation theory—if not desaturation at least of the synthetic power of the body to produce highly unsaturated fatty acids. Whether or not this process occurs in the liver is an unsettled question.

Berend[21] reports the extraction from the pancreas of an enzyme (dehydrogenase) capable of desaturating the fatty acids. He finds this enzyme, also, to be present in liver tissue.

That the body is able to synthesize fatty acids of a greater degree of unsaturation than oleic seems evident. While the liver may not be the only site of such synthesis, it appears to be the most important organ concerned in the elaboration of these fatty acids. Linoleic acid appears to be an essential fatty acid. Whether the body is incapable of the high rate of synthesis demanded by the growing organism for this particular fatty acid or whether it is unable to actually synthesize linoleic acid due to the particular position of the unsaturated linkages in the chain, is not evident. The latter would seem to be the more tenable conclusion.

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A GENERAL COMPARISON OF THE PROPERTIES OF

PALE WOOD AND GUM ROSINS*

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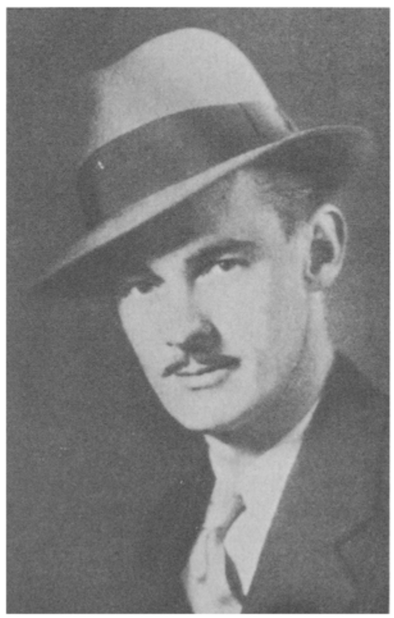
This is a rather non-technical paper, discussing briefly how wood rosin is made and comparing the chemical properties of Pale Wood Rosins to those of the Pale Gum Rosins, a raw material with which all soap manufacturers are familiar.

Gum rosin has been produced in this country for centuries, and since its inception, the soap industry has been one of the principal consumers of this raw material. In view of the age of the industry and the importance of the raw material to the soap chemist, it is not surprising that you well understand the physical and chemical properties of gum rosin and the part it plays in the production of good soap.

In the year 1910, the first large unit of a new industry was completed, based on research that had been carried on for many years previous to that date. In that year wood rosin, made by the steam and solvent process, was produced commercially by Homer T. Yaryan. From the beginning the process and industry was destined to be successful, and thus in twenty-four years has grown to be a major factor in the Naval Stores world. In 1933, the production of all grades of wood rosin reached 226,500,000 pounds, or approximately 23 per cent of the total production of rosin in the United States. All manufacturers are vitally interested in all sources of supply of the raw materials they use and so it is not surprising that the soap industry has become interested in wood rosin. We hope that what we have to say about wood rosin in the following paragraphs will help you to better understand this soap-making raw material.



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Wood rosin is produced by the steam and solvent process from the oleoresin in Southern long-leaf and slash pine stump wood. This is the same type of oleoresin from which gum rosin is produced. The gum rosin producer bleeds the oleoresin from the living tree. When the tree is cut down, the stump, rich in oleoresin, is available to the wood rosin producer as a raw material from which to make his rosin. So we point out that both gum and wood rosins come from the same natural source.

The first step in the production of wood rosin is the pulling of the stumps, grading, and shipping them into the plant. Only highly productive wood is used. At the plant the wood is put through chippers, where it is comminuted into small chips and is so prepared for the process.

This wood is charged into large vertical digesters and first exposed to steam. The steam passes through the wood chips, volatilizing the greater portion of the volatile oils, such as turpentine and pine oil, and carries them off to condensers where they are recovered. After the volatile oils are removed, the steam is turned off and a hot solvent turned into the digesters. This hot solvent dissolves out all of the rosin and the remainder of the oils and carries them into evaporators where the solvent and oils are evaporated off and the rosin obtained. The rosin as it comes from the evaporators is generally dark ruby red in color and known as an FF grade of rosin. FF Wood Rosin can be further processed to pale grades of rosin by selective solvent or other types of refining to remove color bodies.

The soap industry consumes principally the medium pale grades of rosins, such as I and M Rosins. There is comparatively little rosin as dark as F Rosin used and comparatively small quantities of grades as light as WG or WW going into the soap kettle. In view of this, we will confine the comparison of wood and gum rosin to the most widely used pale grades, such as I and M grades of rosin.

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