Biological and Medical Aspects of Fats[1]

C. G. KING, Institute of Human Nutrition, School of Public Health and Administrative Medicine, Columbia University, New York, New York

Abstract

A key problem in structural studies of fatty acid glycerides is imposed by the sensitivity of shifts between the beta and alpha positions. The analogous aromatic esters, halides and ring structures tend to be more stable. Hence structures reported before 1923, when systematic studies were developed, were nearly all wrong or uncertain. The second major hurdle was to identify and control the position and configuration of the ethylene groups. Then two great leaps forward developed, in parallel, particularly in biological and medical research, when isotopes and micro chromatography became available. Now it is clear that each fatty acid has significant roles to play in normal biological functions and in relation to major problems in health and agriculture. These relationships are particularly fascinating and significant in relation to linoleic acid and the prostaglandins.

My first interest in research at the post doctorate level was in relation to fats. In preparation for a seminar I read two of Emil Fischer's last journal papers. He had started reporting on a systematic study of the molecular structure of the fatty acid glycerides, pointing out that almost nothing had been done in this field on a critical basis, and that there appeared to be much confusion. His classical work on amino acids, sugars and tannins were well known, and apparently he was just starting to develop lipid chemistry in a similar manner when he died.

When appointed to the permanent staff at the University of Pittsburgh in 1923, the study of molecular structure and physical properties of the glycerides was undertaken with graduate students and continued through a number of years—until I came to New York in 1942. B. F. Daubert (General Foods) and H. E. Robinson (Swift & Co.), well known to many of you, were in the early group. Dr. Daubert continued on the staff for several years and gave good leadership in the study of mono-, di- and triglycerides in which one could be certain of the position of each fatty acid. The correlations between structure, stability and physical properties were remarkably consistent (melting point, solubility, index of refraction, x-ray data on crystal structure, specific heat, pH sensivity, etc.) including sensitivity to enzymes.

A central problem in dealing with the position of acids in glycerides is to recognize that the fatty acids are very sensitive to shifting from the beta position to the alpha position, but aromatic acids and the halides are relatively resistant to the rearrangements. Many of the aldehyde, ketone and ether condensation products of glycerol show similar wide ranges in their sensitivity to hydrolysis or rearrangement. Failure to recognize these characteristics in previous work meant that until 1923 practically everything in the literature which involved the fatty acid position in glycerides was wrong or uncertain.

We became increasingly interested in the biochemistry of the lipids, and when research funds became available we invited H. E. Longenecker (Tulane University), also known to many of you, to join the group. Dr. Longenecker was very successful in building up the biochemical studies to supplement the work in organic and physical chemistry.

One of the items was to establish the normal fatty acid content of human and cow's milk as a fundamental piece of information needed in the field of human nutrition. There was practically nothing of a quantitative nature in the literature beyond the content of crude fat and approximate measures of a few acids. My appointment as scientific director of the Nutrition Foundation in 1942 made it possible to support and integrate related studies on a national scale.

To get enough human milk under medical nutritional supervision for analysis we had to set up a program in cooperation with Icie Macy Hoobler at the Children's Fund of Michigan to collect milk from mothers in good health and on known good diets, and send a huge amount of the fat to Dr. Longenecker and A. R. Baldwin (Cargill) to run a fractional distillation of the esters, and follow down through the old classical procedure for measuring changes in index of refraction for corrections and all that sort of thing. A parallel supply of cow's milk fat was obtained from a well controlled dairy herd at Cornell University. Now one could go to the Rockefeller University, where E. H. Ahrens, Jr., is working and find them doing far more accurate and complete analyses with one-drop samples. A major problem is keeping the samples small enough so that they don't clog the apparatus used in chromatographic analysis. And the time required is in terms of hours instead of weeks or months.

An experience at the American Chemical Society meeting in New York, about 1935, indicates the general situation at that time. When speaking before the Agricultural and Food Chemistry Division, I urged those working in the area of lipid chemistry to undertake really basic studies of the functions of the individual fatty acids in foodstuffs, pointing out that we knew practically nothing about the physiological function or health relationships of the individual fatty acids. But the reaction of the audience was very casual, with an implication that I was more visionary than practical.

Professor G. O. Burr had shown, of course, that linoleic acid was an essential fatty acid, but no one knew how linoleic acid was formed or functioned. No one knew where cholesterol came from except as it occurred in foods. No one knew the metabolic correlation of one type of lipid with others, in any detail. Very little was known of the relationships with vitamins or hormones or trace minerals.

The present comments include some points of special interest in relation to the biochemistry and health relationships of the fatty acids. First, a brief note on the molecular structure of fatty acids; second, the prostaglandins represent a relatively new group of hormones that are derived primarily from linoleic acid; third, the chain length of fatty acids is steadily becoming more significant; and fourth, a brief comment on food patterns that appear to be quite closely related to health.

The fatty acids of primary relationship to linoleic acid leading to the biosynthesis of arachidonic are indicated in the following sequence:

$$\mathrm{CH_3—(CH_2)_4—(CH=CH—CH_2)_2—(CH_2)_6—COOH}$$

linoleic

$$\downarrow\ -2\mathrm{H}$$

$$\mathrm{CH_3—(CH_2)_4—(CH=CH—CH_2)_3—(CH_2)_3—COOH}$$

y-linolenic

$$\downarrow\ +2\mathrm{C}$$

$$\mathrm{CH_3—(CH_2)_4—(CH=CH—CH_2)_3—(CH_2)_5—COOH}$$

homo-y-linolenic

$$\downarrow\ -2\mathrm{H}$$

$$\mathrm{CH_3—(CH_2)_4—(CH=CH—CH_2)_4—(CH_2)_2—COOH}$$

arachidonic

The structural relationship of arachidonic acid to the prostaglandins is indicated by the following example:

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