Medium-Chain Triglycerides—Their Composition, Preparation, and Application

V. K. BABAYAN, Stokely-Van Camp Inc., Indianapolis, Indiana

Abstract

Medium-chain triglycerides, prepared from fractionated fatty acids of vegetable oils ranging from caproic to lauric, have been prepared and used in the treatment of patients suffering from malabsorption syndromes. Commercial practices for processing of the kernel oils to obtain such fractionation of fatty acids are described, and the practical sources for such medium-chain fatty acids are given. Medium-chain esters of synthetic fatty acids and modifications of such esters for special medicinal and nutritional uses are suggested for future consideration and application.

Introduction

ALTHOUGH A WIDE VARIETY of fats and oils are available from animal, vegetable, and marine kingdoms, there is not any readily available ester solely consisting of such medium-chain fatty acids. By utilizing the kernel oils as a source for such fatty acids, with commercial processing techniques, esters have been synthesized which have specific compositions that are suitable for metabolism via the portal system. It is in order now to set up some standards for the raw material, specification of finished products, and the projection of some future modifications for broader investigation of the application of such medium-chain esters. This paper attempts to clarify the terminology used thus far in order to avoid misnomers concerning the term "medium-chain triglycerides."

Preparation and Specifications

From various sources (1–4) it is possible to ascertain that the kernel oils, such as coconut, palm kernel, babassu, etc., are the most common and available sources for the medium-chain fatty acids. Furthermore industry, having established large-scale usage for the various fractions of the fatty acids of these kernel oils, can supply medium-chain fatty acids at reasonable prices to serve as raw material for the preparation of such medium-chain triglycerides.

Since coconut oil is processed in large volume for industrial and edible uses, we shall follow the processing operation of that oil to illustrate how the C_6–C_{12} fatty acids become available for our use. The crude coconut oil, as it is received from the Philippines and other Asian or African ports, is hydrolyzed (split under high pressure with steam) to recover glycerin and fatty acids. The fatty acids, in turn, are fractionally distilled into specific fractions for various specialty uses. In the fractionation of coconut oil fatty acids, usually three fractions are taken. Figure 1 is a schematic presentation of the fatty acids of coconut oil with the respective cuts or fractions taken in the fractionation of such acids. The approximate percentage of the composition of the original oil is given to illustrate the supply available for the fractionation. The fractionation points have been taken as practical considerations in commercial operations to dictate the most advantageous fractions for supplying the market needs and demands. Since fractionation is not an absolute, clear-cut separation in commercial

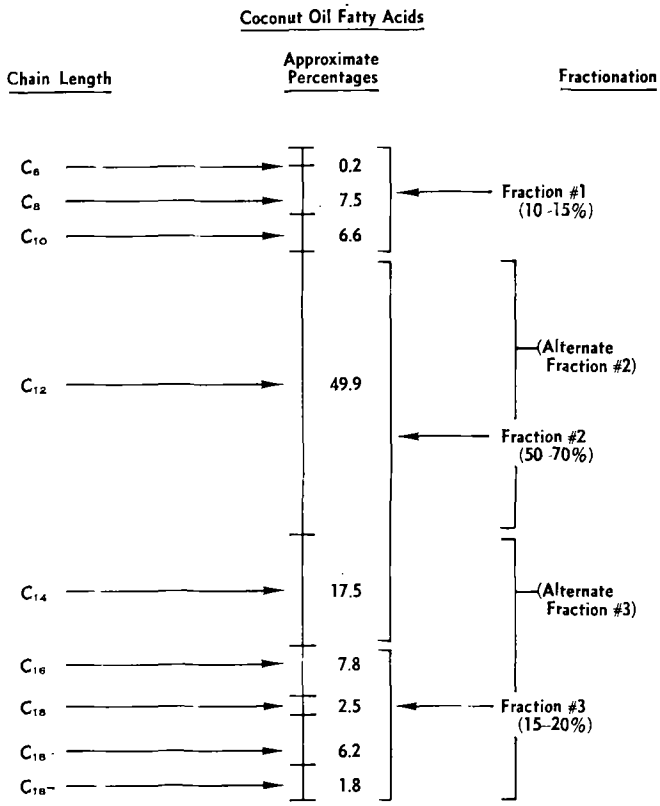

FIG. 1. Medium chain triglycerides—their composition, preparation and application.

practice, some contamination and overlap of fractions may occur. Double distillation is used to further purify the fractions and make specific fractions as needed.

Through the years the demand for lauric acid and/or lauric-myristic acid combinations has dominated the industry planning and operations. The synthetic detergents, such as amine condensates and amides with lauric acid or lauric-myristic acid compositions, have necessitated that fractional distillation cuts be Fraction 2 or Alternate Fraction 2 as the prime consideration of operation. Mono, di-, and polyhydric alcohol esters, as well as ethylene oxide adducts, have helped to create the market for more specific fatty acid compositions. Today one can purchase, for a price, relatively pure grades of individual fatty acids or blends of specific percentage ratios of two or more acids. It is sufficient to say that the initial fractional distillation of coconut oil fatty acids should give the medium-chain acids from C_6–C_{10} as the first cut or fraction. Industry can divert Fractions 2 and 3 or its alternate fractions into other areas of operation and use. The commercial feasibility of fractionating coconut oil fatty acids and having uses for the fatty acids from C_{12}–C_{18} however make it possible to have a ready source of C_6–C_{10} acids for the preparation of the MCT oils.

Initially the MCT oils, which were prepared and submitted to Hans Kaunitz (5–10) and his colleagues

at Columbia University for the animal feeding tests, essentially constituted the compositions and ratios of fatty acids made available from coconut oil fatty acid fractionation. The products in use today by the various investigators are quite similar to the original preparations investigated by Dr. Kaunitz. It is fortunate that the final selections have turned out this way, but it is not a coincidence. The selection was made after intensive investigation of the products resulting from the systematic isolation, preparation, and clinical testing of the pure esters of fatty acids from butyric acid to stearic acid. Ahrens (11,12) and his colleagues studied the metabolism of the pure triglycerides of C_4–C_{18} saturated fatty acids to establish the range of portal vein transport. Hashim and Van Itallie (13–18) confirmed the findings of Ahrens in studies that involved both animals and human beings. They also extended the MCT clinical investigations to cover a wide range of MCT compositions where the fatty acids, their ratios, and their positions in the triglyceride were altered for the metabolic studies. Beveridge (19), Kritchevsky (20,21), Isselbacher (22,23), Furman (24), and many others (25–35) who were working with minor variations of the MCT preparations, investigated various aspects of the applications and uses of MCT. The culminations of the clinical studies carried out by all these investigators established the fact that MCT oils could have great flexibility in composition, providing that certain safeguards were maintained. There appeared to be little difference in the clinical acceptability of MCT whether the composition was at random distribution or a physical mixture of two or more glycerides. There could be variations in physical form and/or chemical constants and in the characteristics of the MCT preparations because of the fatty acid compositions and ratios. Such differences however resulted in very little, if any, difference in the metabolism of the preparations in both animals and human beings as long as the length of fatty acid chain was kept below lauric acid. With these accumulated data as a guide the final MCT specifications and compositions were established to conform with sensible, practical, and commercial operations while rigid quality control was maintained for uniformity and consistency.

The MCT available to clinical investigators at present is the product which, in the last analysis, has been found to be the best all-around composition for the unique applications and uses contemplated. The MCT preparation uses a double-distilled fraction of coconut oil fatty acids as its starting material, followed by esterification with glycerin and the use of a metallic or slightly acidic catalyst. The crude ester which is formed is subjected to refining, bleaching, and deodorizing operations. It should be kept in mind that the solubility and volatility characteristics of such a product are somewhat different from the conventional vegetable oils and animal fats.

The esterification step in the preparation of MCT requires the utmost care since it is essential that complete esterification take place and thus insure that

TABLE I
Raw Material Specifications Fatty Acids for MCT Oil

Free fatty acid (as oleic)	185% min.
Iodine value (Wijs)	1.0 max.
Color (Lovinbond)	10 Y./1.0 R.
Unsaponifiables	0.5% max.
Fatty acid composition	
C_6	1–2%
C_8	65–75%
C_{10}	25–35%
C_{12}	2% max.

TABLE II
MCT Oil Specifications

Free fatty acids (as oleic)	0.05% max.
Saponification value	345–355
Iodine value (Wijs)	1.0 max.
Acetyl value	5.0 max.
Setting point	−5°C max.
Color (Lovibond)	10 Y./1.0 R
Unsaponifiables	0.5 max.

the final product is a neutral oil with bland flavor and odor characteristics. A typical fatty acid feed stock for MCT is given in Table I. A typical MCT oil specification is given in Table II; the fatty acid composition falls in the range of that shown in Table I.

Under the conditions of esterification the resulting triglyceride will be pretty much at random distribution, and the ratios of the esters present will be predicated on the ratio of the fatty acids used in the feed. With the feed stock based upon a specification that is essentially composed of C_8 and C_{10} fatty acids, the predominant structures present in the MCT are shown in Figure 2. Figure 2 is essentially that of Eckey (36), where C_8 and C_{10} triglycerides have been substituted for the saturated and unsaturated fatty acids in his graph.

The results of the various clinical investigations will identify MCT oil as the investigators have received it. Sometimes the similarity of the analyses of two or more investigators will be noted, and at other times there will be definite differences. These are not variations in their analytical techniques but rather are the variations of the particular batch of MCT supplied. For the purpose of the clinical investigators, triglycerides were prepared from specific fatty acids and combinations thereof. In some cases 99% purity acids were used. Triglycerides of such purity were used to study the mechanism of the transport and to establish the specific pathways of assimilation. Triglycerides were also prepared where mixed acids were at random distribution in one case and physical mixtures of such pure triglycerides in other cases. For example, C_8 and C_{10} triglycerides which were prepared from 99% pure C_8 and C_{10} acids were in physical admixture of C_8 triglyceride and C_{10} triglyceride in one case and

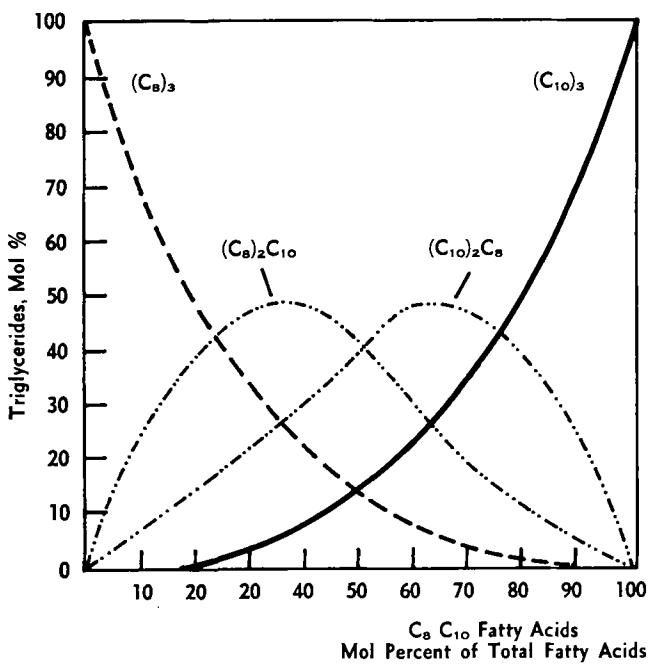

FIG. 2. Medium chain triglycerides—their composition, preparation and application.

were rearranged in the same ratios at random distribution. The metabolic studies did not show any differences in their acceptability or utilization.

Since such products from pure triglycerides did not show any differences in metabolism experiments when compared with triglycerides which were prepared from the mixed fatty acids, the preparation procedure adopted became that which uses the mixed fatty acids available from the fractionation of coconut oil. C_6 and C_{12} are essentially present in minor amounts and can be considered contaminants. Usually the C_8 and C_{10} acids constitute better than 95% of the fatty acid feed stock; the C_{12} acids are kept below 2%, and the C_6 acids are taken at the level found in the feed. The C_{12} acid limitation is placed to safeguard the fractionation of the fatty acids and to insure that the MCT oil prepared is completely metabolized from the gut via the portal system rather than the lymphatics. There is also some slight preference shown by the patients for MCT which is kept low in the C_{12} acid composition. Such MCT oil, low in C_{12} acid ratio, is completely alcohol-soluble and may lend itself more easily for formulations and applications.

In some experiments MCT with small and large amounts of the ethyl ester of linoleic acid, the glycerin ester of linoleic, linolenic, and arachidonic acids were prepared and used, along with safflower oil, soybean oil, and corn oil. Clinical investigators examined both the physical mixtures and the rearranged products. It was found quite feasible to prepare such variations of MCT oil with varying amounts of polyunsaturated fatty acid esters, either by the physical admixture of MCT or a pure C_8 triglyceride and a triglyceride high in polyunsaturates, such as safflower oil or the same composition after rearrangement. Swern (37) shows another way of illustrating the same type of system and the fatty acid compositions present in such esters. With mixed fatty acid esters, naturally the possibilities are increased and the picture is more complex. VanderWal (38,39) has reported on some of the more complex systems and the probabilities of the compositions available in such systems for saturated and unsaturated fatty acid triglycerides of the longer chain-length, but his projections would be equally valid for the medium-chain triglycerides.

Aside from the MCT oils derived from such vegetable oils as coconut oil and other kernel oils, a few words should be supplied about the possibilities in preparing further modifications of such medium-chain triglycerides which can be considered from synthesis and/or sources other than edible oils.

Since there are new processes for the synthesis of fatty acids via fermentation and even more immediate sources such as those from oxidation of paraffins, ozonolysis of oleic, linoleic, and tall oil acids, a host of synthetic fatty acids, both odd-carbon and even-carbon chain lengths, are at hand (40). Synthetic fatty acids of C_5–C_{13} have been utilized to make similar esters for clinical investigation. By using the odd-carbon chain acids with glycerin, propylene glycol, etc., esters have been prepared and are being investigated clinically. Hashim and Van Itallie (41) have already reported on some of their initial results in using such odd-carbon chain acids and esters. More will be forthcoming in the next few years since there are many new avenues to explore in the further extension of the medium-chain fatty esters. It is indeed a fertile field for the medical researcher.

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