This brief review provides a plausible explanation for the absence of hypertriglyceridemia following butterfat feeding in apparent contradiction to the effect of the C12-C16 saturated fatty acids fed individually as triacylglycerols. The mechanism is based on differences in the structure of butterfat and the synthetic triacylglycerols, which results in lipolysis products that are absorbed at different rates via the phosphatidic acid and the 2-monoacylglycerol pathways, respectively. The hypothesis is supported by previous work with alkyl esters of fatty acids and 1,3-diacylglycerol oils.

A large number of metabolic studies and epidemiological surveys have claimed that consumption of milk fat increases serum total and low-density lipoprotein (LDL) cholesterol, which increases the risk for developing heart disease. This consensus has been reached largely on the basis of feeding high concentrations of the major butter fatty acids, lauric, myristic and palmitic, as triacylglycerols with myristic acid being the most potent while stearic acid and the short-chain saturated fatty acids being considered by some workers to be neutral.

Effect on cholesterol

In the case of milk fat, however, a persistent problem has been the difficulty in measuring the true consumption of dairy fat and the confounding effect of cholesterol. Recently, much of this ambiguity has been eliminated by using tissue levels of C15 and C17 fatty acids as valid markers of dairy fat intake, as introduced by Annika Smedman and her colleagues at Uppsala University in Sweden.

These biomarkers have revealed negative associations between intake of milk products and body mass index, waist circumference, high-density lipoprotein (HDL) triacylglycerols, LDL/HDL ratio, and fasting plasma glucose, whereas relations to HDL cholesterol and apoprotein A-I tended to be positive. The change in the LDL/HDL ratio was of particular interest because dietary interventions which focus on reducing saturated fatty acids and cholesterol usually lower both LDL-cholesterol and HDL-cholesterol, thereby not improving the lipoprotein profile. Likewise, significant negative correlations between markers and serum triacylglycerols, cholesterol, insulin, leptin, plasminogen activator inhibitor and a first acute myocardial infarction were found between high proportions of 15:0 and 17:0 in serum phospholipids.

A recent study by Anne Sofie Biong and colleagues published in the February 2006 issue of the European Journal of Clinical Nutrition (60:236-244, 2006) showed that intake of dairy fat or some other component of dairy products, as reflected by C15:0 as marker in adipose tissue, may protect persons at increased risk from having a first myocardial infarct, and that the causal effects may relate to other factors than serum cholesterol. The explanation for the inverse associations between the intake of milk products and certain cardiovascular risk factors is not known. It is therefore of interest to consider a possible metabolic basis for the paradoxical effects of feeding butterfat and its major fatty acids as synthetic triacylglycerols.

Early work by the late Jim Beveridge and colleagues at Queen’s University, Kingston, Ontario, Canada, demonstrated that the hypercholesterolemic effect of butter is due to the presence of cholesterol. Ingestion of butteroil distillation residues stripped of cholesterol caused only a minimal increase in serum cholesterol, while reconstitution of the cholesterol content to the level in the original oil resulted in hypercholesterolemia (Figure 1). This demonstrated that butteroil triacylglycerols per se were not hypercholesterolemic. [In other experiments, Beveridge et al had showed that butterfat fed along with sitosterol, which interfered with cholesterol absorption, also did not result in a hypercholesterolemia attributable to the high content of lauric, myristic and palmitic acids. Clearly, the feeding of lauric, myristic and palmitic acid esters in the form of sterol-stripped butter or butteroil distillates differed from feeding these acids as simple triacylglycerols or their interesterified mixtures.]

Figure 1. Time course of recovery of lymph total triacylglycerols after feeding menhaden oil or corresponding fatty acid ethyl esters.
Hydrolyzation

A possible explanation for this apparent paradox emerged later when the structure of milk fat triacylglycerols was established. We determined it is now known that butterfat, which contains up to 30% of its acids as C4-C8 homologues, is characterized by a specific association of the short chain acids with the sn-3-position of the triacylglycerol molecule. Therefore, butterfat is composed largely of triacylglycerols containing one C4-C8 fatty acid in combination with two long or medium chain length fatty acids. Ingestion of butterfat would then lead to a rapid formation of sn-1,2-long and medium chain length diacylglycerols due to the action of lingual and gastric lipases, which attack the short chain fatty acids preferentially. Furthermore, at the low pH of the medium of the stomach, the sn-1,2-diacylglycerols would rapidly isomerize to the 40:60 equilibrium mixture with sn-1,3-diacylglycerols, respectively, which would be hydrolyzed by pancreatic lipase to free fatty acids and glycerol, and a minimum of 2-monoacylglycerols. While the released short chain fatty acids would be transferred for absorption to the portal circulation, the liberated long chain fatty acids would depend on the less efficient phosphatidic acid pathway for their incorporation into triacylglycerols and absorption into the lymph in absence of 2-monoacylglycerols (Figure 2).

In contrast, the lauric, myristic and palmitic acid containing triacylglycerols would be hydrolyzed to 2-monoacylglycerols, which along with the released acids would be rapidly taken up and resynthesized into triacylglycerols via the 2-monoacylglycerol shunt pathway. The delayed absorption of dietary fat via the phosphatidic acid pathway is best demonstrated by feeding of fatty acid methyl or ethyl esters in comparison to the corresponding triacylglycerols. We have found that the lymphatic recovery of the triacylglycerols resulting from the alkyl ester feeding is greatly delayed when compared to that observed following feeding the corresponding triacylglycerols. The slower absorption of the fatty acids from the alkyl ester feeding could not be attributed to a slower hydrolysis of the alkyl esters by pancreatic lipase. Since the hydrolysis products of the alkyl esters were absorbed in absence of 2-monoacylglycerol, it was concluded that the released free fatty acids were resynthesized into triacylglycerols via the phosphatidic acid pathway and that the phosphatidic pathway was responsible for the delayed fat absorption. In comparison to the 2-monoacylglycerol shunt, the synthesis of triacylglycerols via the phosphatidic acid pathway involves several additional enzymatic steps, including the formation of sn-glycerol-3-phosphate.

Diacylglycerols

The above discussed intestinal absorption of the alkyl esters of fatty acids, as well as that of the sn-1,3-diacylglycerols released by the lingual and gastric lipases during the initial stages of butterfat digestion, resembles the absorption of synthetic diacylglycerol oils enriched in X-1,3-diacylglycerols. These diacylglycerol oils also would yield an excess of free fatty acids (in comparison to 2-monoacylglycerols) during hydrolysis by pancreatic lipase. In the absence of 2-monoacylglycerols, the released fatty acids would have to be absorbed via the phosphatidic acid pathway, which would delay their absorption and appearance in lymph. The delay in the absorption of the fatty acids from the diacylglycerol oil feeding was estimated to be 50% lower than that resulting from triacylglycerol feeding, which is comparable to the delay observed during fatty acid alkyl ester feeding. Interestingly, Ikeda and Yanagita and Gotoh and Shimasaki attribute the apparent antiobesity activity of the dietary 1,3-DAG oil results to the delayed lymphatic transport of the chylomicron triacylglycerols derived from the 1,3-diacylglycerol fatty acids via the glycerol 3-phosphate (phosphatidic acid) pathway.

Since the X-1,3-diacylglycerols would exist in a 60:40 ratio with X-1,2-diacylglycerols, it would be anticipated that significant amounts of 2-monoacylglycerol would also be formed during pancreatic lipolysis of the synthetic diacylglycerol mixture. Therefore the delay in the overall fat absorption must have resulted from only a partial supplementation of the dietary fat by X-1,3-diacylglycerols.

Although a detailed understanding of the intestinal metabolism of diacylglycerols is limited, various researchers have provided evidence that dietary diacylglycerols rich in 1,3-diacylglycerols decrease serum triacylglycerol levels, prevent postprandial hyperlipidemia, and suppress visceral fat accumulation in animals and man in comparison to triacylglycerols with similar fatty acid composition. These effects constitute a remarkable coincidence with the above discussed seemingly paradoxical positive metabolic effects like reduced body mass index, waist circumference, LDL/HDL ratio, serum triacylglycerols and blood pressure, associated with consumption of dairy products using C15 and C17 fatty acids as markers for butterfat absorption. The less efficient operation of the phosphatidic acid pathway would appear to provide a plausible explanation for the reduction in lymph and plasma serum triacylglycerol and accompanying cholesterol content following ingestion of both butterfat and the 1,3-diacylglycerol-rich oils. Since the transformation of butterfat triacylglycerols to the 1,3-diacylglycerol rich diacylglycerol mixture depends on the activity of the lingual and gastric lipases and acidic isomerization, some variation may be encountered in the gastrointestinal metabolism of butterfat that might affect the relative yield of 2-monoacylglycerols and hence the contribution of the 2-monoacylglycerol pathway to the fat absorption.

It remains to be established whether or not the delayed absorption of butterfat also accounts for the suggestion made by several research groups that consumption of milk products may be associated with a small reduction in the risk of heart disease and stroke. These results are hard to reconcile with the opinion that high intakes of milk products, including the “hypercholesterolemic” C12-C16 fatty acids and cholesterol, are connected with increased risk of
ischemic heart disease. While diet intervention remains the initial choice for the prevention and treatment of cardiovascular disease, the nature of the dietary modification remains controversial. A review by Robert Nicolosi and colleagues at the University of Massachusetts, Lowell, Massachusetts, USA, have reviewed dietary interventions that lower LDL-cholesterol without affecting HDL-cholesterol levels, including plant sterols, and have suggested looking beyond saturated fatty acids and cholesterol. In the absence of a true dietary effect of butterfat, Margaret Moss and David Freed at the Nutrition and Allergy Clinic at Stockport, Cheshire in the United Kingdom have proposed that, in the absence of a true dietary effect of butterfat, theories of causation of coronary heart disease should now concentrate on the non-fat moieties of milk, especially those which are destroyed by fermentation.

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Further reading


International Committee Management

AOCS, through the American National Standards Institute, hosts a number of Technical Advisory Groups representing US interests within the framework of ISO/TC 34 Food Products. This activity provides a forum for all interested parties to participate in ISO activities. A major focus is the harmonization among international partners of methods of analysis relevant to the fats and oils industry. As a standards development organization (SDO), AOCS is also an international non-governmental organization (NGO) recognized by the FAO and an active participant in the Codex Committees on Fats and Oils, as well as Measuring, Analysis, and Sampling.

AOCS organizes and participates in international collaborative studies, which lead to the global harmonization of analytical methodology. Multi-laboratory, multi-national groups cooperate with leading international organizations such as FOSFA, ISO, and IUPAC to enhance and streamline the methods development process.