

Lipids in healthcare and medicine

Abstract

Lipids are biologically active in a variety of ways in plants, animals, and people. In addition to providing energy and necessary fatty acids, they are also significant parts of our daily diet. They also act as transporters of fat-soluble vitamins and aid in their absorption. The texture, mouth feel, and flavor of food are all influenced by lipids, which are essential as a heating medium for food processing. Structured lipids (SL) are triacylglycerols (TAG) that have undergone chemical or enzymatic modification to change the fatty acid makeup and/or where they are located within the glycerol backbone. Target fatty acids may be delivered most effectively via SL for nutritional or therapeutic objectives, as well as to treat particular diseases and metabolic problems. The chemistry, content, classification, use, presence in food, and biological functions of lipids are covered in this document. It also clarifies several facets of structured lipids, such as their applications, methods of synthesis (chemical vs. enzymatic), use in aquaculture, and potential future developments.

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Introduction

A collection of chemically diverse substances known as lipids are soluble in non-polar solvents but either hardly or completely insoluble in water. They perform a number of crucial biological tasks, such as acting as structural elements of all membranes, storing and transporting metabolic fuel, protecting various organisms' surfaces, and participating in cell recognition, species specificity, and tissue immunity. They also act as structural elements of all membranes. The daily diet also includes a significant amount of lipids, which are a source of energy and vital fatty acids. The fat-soluble vitamins A, D, E, and K are also transported by lipids, which aids in absorption. Finally, lipids function as a heating medium throughout the food processing process and have an impact on the flavor, mouthfeel, and texture of food.¹

Chemistry and composition of lipids

Fatty acids

The basic chemical framework of fats is made up of fatty acids. Triacylglycerols (TAG) make up between 80% and 95% of all lipids. Three fatty acids and one glycerol molecule make up one TAG molecule. TAG's physical characteristics vary according on the source from which they are obtained. Lard, butter, and other products made from animal fats are solid at room temperature, but cod liver oil, olive oil, and other products made from plant and marine oils are liquid. The two primary types of fatty acids are saturated and unsaturated, with the latter further broken down into monounsaturated (MUFA) and polyunsaturated (PUFA). According to where the initial double bond from the methyl end group of the fatty acid is located, there are two primary classes of PUFA: n-3 (also known as omega-3), and n-6 (also known as omega-6). Saturated and monounsaturated fatty acids are also synthesized by the human body, but polyunsaturated fatty acids (PUFA) cannot; they must instead be received from diet. PUFA are therefore regarded as essential fatty acids (EFA).

Saturated fatty acids

In the aliphatic chain, saturated fatty acids only have single carbon-carbon bonds, while all other possible bonds are occupied by hydrogen atoms. In animal and plant tissues, straight-chain molecules with 10, 12, 14, 16 and 18 carbon atoms make up the majority of saturated fatty acids. Saturated fats are typically solid at normal

temperature. Margarine, shortening, coconut, and palm oils, as well as meals of animal origin, are the main sources of these fats. The melting point rises with the length of the chain does for a chain of saturated fatty acids. The melting point of a saturated fatty acid will typically decrease when double bonds are added.

Short-chain fatty acids (SCFA)

The C2:0 to C4:0 range of short-chain fatty acids (SCFA) includes acetic (C2:0), propionic (C3:0), and butyric acids. They are the byproducts of fermentation of carbohydrates in the human gastrointestinal system.² Due to their higher water solubility, smaller molecular size, and shorter chain length, SCFA are rapidly absorbed in the stomach³ and have fewer calories than medium-chain fatty acids (MCFA) or long-chain fatty acids (LCFA) (acetic acid, 3.5 kCal; propionic acid, 5.0 kCal; butyric acid, 6.0 kCal).

Medium-chain fatty acids (MCFA)

Tropical plant oils like those of the coconut and palm kernel undergo hydrolysis to produce medium-chain fatty acids (MCFA), which have 6–12 carbon atoms.^{4,5} Pure medium-chain triacylglycerols (MCT) do not contain essential fatty acids and have a caloric value per gram of 8.3.^{6,7} Compared to long-chain fatty acids (LCFA), MCFA are more hydrophilic. Low viscosity, low melting point, and good oxidative stability are only a few of the unique characteristics of MCFA.⁸ MCT are different from other fats and oils because they can be absorbed through the portal system without hydrolysis and re-esterification since they are moderately soluble in water.

They also have unique structural and physiological features. MCT have a faster rate of -oxidation to produce acetyl CoA end products, which are further oxidized to produce CO₂ in the Kreb's cycle and do not need to form chylomicrons to transport from blood to cells.⁹ MCTs have a similar rate of absorption and metabolism to glucose and contain almost twice as many calories as proteins and carbs. They don't seem to build up body fat very easily. To enter mitochondria, medium-chain triacylglycerols do not require carnitine, an enzyme required for fatty acid transport across the inner mitochondrial membrane. Compared to long-chain fatty acids, MCFA are considerably easier to absorb, transport, and metabolize due to their higher solubility and smaller molecular size. Compared to long-chain triacylglycerols (LCT), MCT are digested by pancreatic lipase more swiftly and thoroughly. With minimal pancreatic or biliary function, the intestinal mucosa may directly absorb them.¹⁰

Lauric acid (C12:0), which is present in very high concentrations in tropical plant oils like those from coconut and palm kernels (around 50%), is also known as linoleic acid. Additionally, they contain sizable amounts of myristic (C14:0), capric (C10:0), and caprylic (C8:0) acids. A combination of MCT and LCT is used in several medicinal diets to supply both quickly and slowly absorbed fuel as well as important fatty acids. Fat malabsorption symptoms might result from any abnormality in any of the numerous enzymes or processes that are necessary for LCT digestion. As a result, when MCTs are included in the diet of individuals with specific disorders, such as Crohn's disease, cystic fibrosis, colitis, and enteritis, they exhibit improved symptoms.¹¹ Clinical uses for MCT include the treatment of obesity, malnutrition, lipid malabsorption, and carnitine deficiency. According to certain studies, MCT may lower cholesterol levels in humans and animals' tissues and serum even more than conventional polyunsaturated oils.¹² However, Cater et al.,¹³ found that slightly hypercholesterolemic males who consumed MCT, palm oil, or high oleic sunflower oil diets had higher plasma cholesterol and TAG levels.

Long-chain fatty acids

The majority of lipids, also known as long-chain triacylglycerols (LCT), are made up of long-chain fatty acids (>C12). Almost all vegetable oils, fish oils, and the body fat of terrestrial animals all include palmitic acid (16:0), a commonly occurring saturated fatty acid. Palm oil, cottonseed oil, lard, and tallow are just a few of the foods that contain large amounts of palmitic acid. Another significant saturated fatty acid is stearic acid (C18:0), which is also a key ingredient in cocoa butter. In part because of their higher melting point than body temperature and poor emulsion characteristics, triacylglycerols with large concentrations of long-chain saturated fatty acids, particularly stearic acid (C18:0), are poorly absorbed in humans.¹⁴ Long chain saturated fatty acids are excellent candidates for the production of low-calorie structural lipids (SL) due to their limited absorption. SLs are fats or oils that have had their fatty acid compositions or where they are located within the glycerol backbone altered. For instance, Nabisco Food Group made use of the C18:0 property to create Salatrium, a line of low-calorie SL that mostly contains stearic acid and long-chain saturated fatty acids.¹⁵

Unsaturated fatty acids

In its aliphatic chain, unsaturated fatty acids have carbon-carbon double bonds. These lipids are often pliable at room temperature. One double bond between carbon atoms can be found in monounsaturated fatty acids. Polyunsaturated fatty acids (PUFA), on the other hand, have two or more carbon-carbon double bonds. Because the double bonds are stiff and prevent the fatty acids from clustering tightly together, the PUFA are liquid at normal temperature. They often have low melting points and are oxidation-prone. The majority of PUFA are typically referred to as oils because they are liquid at normal temperature. PUFA is frequently found in grains, nuts, vegetables, and seafood.

The n-9 fatty acids

The ninth and tenth carbon atoms from the methyl end group are where a double bond exists in the n-9 fatty acids, also known as monounsaturated fatty acids. They can be found as oleic acid (18:1n-9) in vegetable oils as high-oleic sunflower, olive, almond, hazelnut, canola, and peanut. Of all the fatty acids, oleic acid is the most prevalent and the most abundantly generated. Rich sources of this fatty acid are olive oil (60% to 80%), hazelnut oil (60% to 70%), and almond oil (60% to 70%).¹⁶ Oleic acid is not regarded as an essential fatty acid

because it is a molecule that the human body can make on its own. Although increasing the absorption of oleic acid in young, healthy adults is known to raise plasma high density lipoprotein (HDL) and decrease TAG, it also plays a modest influence in decreasing plasma cholesterol in the body.¹⁷

Essential fatty acids (EFA)

As previously stated, PUFA with two or more double bonds in their backbone structures are termed EFA since they cannot be produced by the body. The n-3 and n-6 fatty acids are the two types of EFA. They are identified by the double bond in the molecule closest to the chain's methyl terminus. The initial double bond is located between the third and fourth carbon atoms in the n-3 group of fatty acids and between the sixth and seventh carbon atoms in the n-6 group of fatty acids. Linoleic acid (LA, 18:2 n-6) and -linolenic acid (ALA, 18:3 n-3) are the parent molecules of the n-6 and n-3 families of fatty acids, respectively. Through a sequence of alternating desaturation (in which an extra double bond is inserted by removing two hydrogen atoms) and elongation (in which two carbon atoms are added) stages, these parent compounds are metabolized in the body.¹⁸

The n-3 fatty acids

Numerous health benefits of n-3 fatty acids, including -linolenic acid (ALA), eicosapentaenoic acid (EPA; 20:5n-3), and docosahexaenoic acid (DHA; 22:6n-3), have been linked to immunological response, diabetes, hypertension, and renal diseases.¹⁹ Epidemiological studies have connected the high dietary intake of n-3 PUFA in Greenland Eskimos with their low incidence of coronary heart disease.^{20,21} DHA is necessary for the proper operation of the central nervous system and newborns' visual acuity, according to research.¹⁹ The n-3 fatty acids should be a part of a healthy diet because they are crucial for optimal growth and development throughout the human life cycle. The impact of n-3 fatty acids on cardiovascular disease (CVD) has been thoroughly investigated. Research findings have demonstrated that these FA in marine oils may protect CVD by lowering serum TAG and functioning as anti-therapeutic and antithrombotic agents.¹ However, the precise mechanism by which these benefits are given is yet unknown.

Marine oils, particularly EPA and DHA, are abundant sources of n-3 fatty acids. About 30% of the EPA and DHA in cod liver, menhaden, and sardine oils are omega-3 fatty acids.¹⁹ The parent of n-3 fatty acids, alpha-linolenic acid (ALA; 18:3n-3), can be biologically transformed to DHA by desaturation and elongation processes. However, the efficiency of ALA to DHA conversion in human adults is quite low (around 4%), and it is even lower in babies (1%).²² Long-chain polyunsaturated fatty acids (LC PUFA) like DHA and EPA are required for good health but are only conditionally necessary in specific illness states when the rate of conversion of ALA to DHA and/or EPA is substantially lower.²² ALA makes up between 50% and 60% of flaxseed oil. Through dietary absorption, ALA transforms into long-chain PUFA with an n-3 terminal structure in animals. Additionally, significant n-3 fatty acids include EPA and DHA. The gray matter of the brain and the retina of the eye both contain a significant amount of DHA. Infants fed on mother's milk had better IQs and levels of intellect than infants fed on formulas devoid of DHA since human milk also includes a significant amount of DHA.²³ Additionally, due to its antithrombotic activity, EPA is a precursor to a number of eicosanoids and plays a significant role in preventing heart attacks.²⁴ EPA was also shown to raise bleeding time and to decrease serum cholesterol levels [24]. In conclusion, LC PUFA have multiple roles in the human body, including the promotion of health and the prevention of disease. They are known to increase the

body's load on natural antioxidants such as -tocopherol when consumed and are particularly vulnerable to oxidation when stored. As a result, it is crucial to stabilize oils high in LC PUFA during storage by adding the proper antioxidants and packaging techniques.

The n-6 fatty acids

Operate throughout the human body. The primary tasks of these fatty acids are connected to their contributions to membrane structure and to the creation of eicosanoids, which are short-lived derivatives that regulate various aspects of cellular activity. The integrity of the skin's water-impermeable barrier is preserved by the n-6 fatty acids. Additionally, they control how cholesterol is transported throughout the body. The most prevalent fatty acid of this category is linoleic acid (LA; 18:2n-6). All vegetable oils include LA, which is necessary for healthy growth, reproduction, and development. LA is a precursor to the family of n-6 fatty acids, which are created through chain elongation and desaturation with the retention of the terminal (n-6) structure. Arachidonic acid (AA; 20:4n-6) is particularly significant among them since it is a crucial component of membrane phospholipids and a precursor to eicosanoids. However, -linolenic acid (GLA; 18:3n-6), a crucial intermediary in the biosynthesis of AA from LA, is a part of some seed oils, including evening primrose and borage, and has been the focus of extensive research.^{25,26} The intake of 1% to 2% LA in the diet is thought to be sufficient to guard against chemical and clinical problems in babies. Lack of LA in the diet has been linked to the occurrence of a number of diseases, including scaly dermatitis, decreased growth and reproduction, excessive water loss through the skin, and impaired wound healing.²⁷

Biological effect of dietary lipids

It is well known that dietary lipids have an impact on the makeup and composition of adipose tissue.²⁸ This proves the adage "we are what we eat" true for many of the studied species. Iverson and her coworkers²⁹ shown through a series of research on seals and fish that it was simple to identify food lipids in their circulatory lipids and adipose tissues. The fatty acid and TAG deposition in adipose tissue is specifically influenced by the dietary fat composition. In turn, lipid mobilization and the release of fatty acids into the circulatory system are influenced by the makeup of the fat in adipose tissue.²⁸ Chain length, degree of unsaturation, and positional isomerization of fatty acids are some of the factors that influence lipid mobilization from adipose tissue, which is not a random process. Fatty acids of 16–20 carbon atoms and four–five double bonds are the most quickly mobilized, but very long unsaturated and monounsaturated fatty acids are less so.²⁸ Additionally, trans isomers' direct impact on the metabolism of fat cells may be linked to the lower fat deposition in animals fed trans fatty acids.³⁰ Numerous studies have shown that changes in the amount and type of dietary fat can alter the size (hypertrophy) and/or number (hyperplasia) of adipose cells.²⁸ It is widely acknowledged that a diet heavy in fat can cause hypertrophy and/or hyperplasia. According to Launay et al.,³¹ the amount of unsaturation in dietary lipids may increase the rate at which adipose tissue multiplies. On the other hand, Shillabeer & Lau³² showed that saturated dietary fat led to a greater degree of fat cell hyperplasia than unsaturated dietary fat. In contrast to the results mentioned above, dietary n-3 PUFA that preferentially restrict fat cell size and/or quantity in a depot-dependent manner have been found to have more consistent effects on adipose cellularity.³³

Classes of lipid

Oils are liquid at normal temperature, whereas fats are solid. Lipids are also categorized based on their polarity (polar and neutral

lipids), their human necessity (essential and non-essential FA), and their structure (simple, compound, and fat-derived). Simple fats are composed of a glycerol plus one, two, or three fatty acids (monoacylglycerol, diacylglycerol, or triacylglycerol). The second category, known as compound, is made up of simple fats that have been combined with other moieties; phospholipids are an illustration of this type of lipid. Sterols are a good example of a chemical that falls into the category of "lipid-derived compounds," which are simple to assemble and do not include any fatty acids.

Acylglycerols

The TAG is made up of three fatty acids esterified to a glycerol backbone. Edible oils may also include trace amounts of partial acylglycerols such mono- and diacylglycerols. Nature uses enzyme systems to create these substances. The majority of lipids, between 80% and 95%, are made up of TAG. Depending on the kind and position of the three fatty acid components involved, the TAG is displayed in a variety of ways. Simple TAGs are those that only contain one kind of fatty acid in each of the three places, and they get their name from that fatty acid. The trivial names, however, are more frequently employed in specific circumstances. Triolein, also known as trioleylglycerol, is an illustration of this. A more complicated approach is used to name TAGs that include two or more distinct fatty acids.¹⁶ Diacylglycerols (DAG) and monoacylglycerols (MAG) are two important partial acylglycerols that play important roles in the biosynthesis and catabolism of TAG and other classes of lipids. One of the crucial stages in the production of TAG and other lipids is 1,2-DAG. On the other hand, during the enzymatic hydrolysis of TAG, 2-MAG is created as intermediates or end products.

Structured lipids

Structured lipids applications

Through chemical or enzymatic techniques, structured lipids (SL) are TAG changed to alter the fatty acid composition and/or their placement in the glycerol backbone.³⁴ Structured lipids have received a lot of attention recently because of their potential biological functions and nutritional benefits, such as lowering serum levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and TAG,³⁵ enhancing immune function, preventing thrombosis,¹¹ reducing protein breakdown,^{36,37} improving absorption of other fats,³⁸ and preserving reticuloendothelial system function.³⁹ Genetically modified oilseed crops, the creation of oils rich in polyunsaturated fatty acids, and chemically or lipase-assisted interesterification reactions are only a few techniques for modifying lipids. Chemical or enzymatic processes, such as direct esterification (reaction of fatty acids and glycerol), acidolysis (transfer of an acyl group from an acid to an ester), and alcoholysis (exchange of an alkoxy group from an alcohol to an ester), can be used to create SL depending on the kind of substrate that is available.⁹ The typical processes for producing SL, however, are based on interactions between two triacylglycerol molecules (interesterification) or between a triacylglycerol and an acid (acidolysis) (Figure 1).

Synthesis of structured lipids

Chemically-catalyzed interesterification: It is affordable and simple to scale up chemically-catalyzed interesterification using an alkali like sodium methoxide. The positional distribution of fatty acids in the finished product can be controlled to a limited or no extent by such processes, which lack specificity.⁹ Additionally, reactions that take place in hostile environments with high temperatures (80°–90°C) produce byproducts that are challenging to remove.⁴⁰

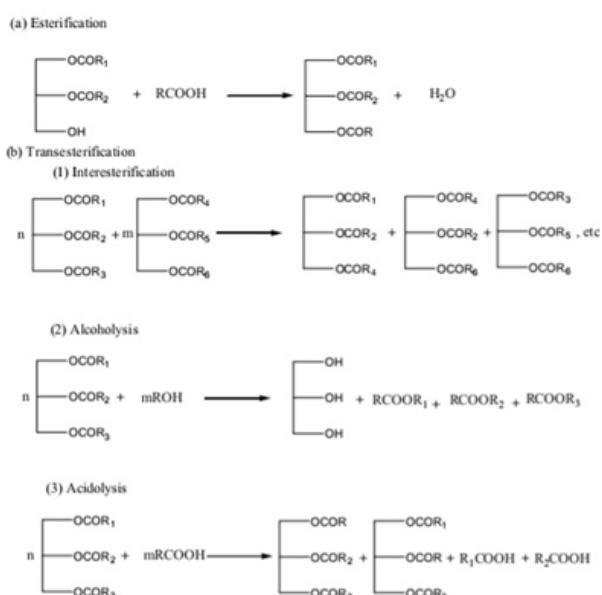


Figure 1 Schematic representation of lipid modification techniques aided by lipases for the creation of structured lipids.

Enzymatically-catalyzed interesterification: The enzymatic production of SL utilizing various lipases is an alternative to the chemical manufacture of the substance. Compared to chemical interesterification, lipase-assisted interesterification has various benefits. Because it integrates a certain fatty acid at a precise position of the glycerol moiety, it creates fats or oils with a clearly defined structure. It calls for benign experimental settings with less chance of adverse effects, decreased energy use, lessened heat damage to reactants, and simple product purification.^{5,41} However, using lipase to bio-convert lipids is more expensive than using chemical processes. As a result, it is preferable to immobilize lipids on suitable supports because doing so enables the reuse of enzymes. For industrial use, it would be ideal to screen fresh lipases from organisms or create a thermostable or sn-2-specific lipase by bioengineering. Another strategy is to use bioengineering to create structured lipids. The California company Calgenes Inc. of Davis was successful in producing 40% lauric acid (C12:0) high-laurate canola oil. It is now offered and sold under the name Laurical and utilized in filling fats, coffee whiteners, whipped toppings, and coatings for confections. However, the necessary fatty acids in this genetically engineered oil are lacking. Recently, Hamam and Shahidi⁴²⁻⁴⁵ were successful in adding EPA, DPA, and DHA to a variety of high-laurate canola oil varieties.

Structured lipids and aquaculture: Aquaculture must continue to expand at a 10% annual rate in order to meet the average annual fish intake requirement of 13 kg/person. Aquaculture is predicted by scientists to consume almost 75% of the world's fish oil by 2010. Fish oil is used in aqua diets primarily because it is an excellent source of n-3 fatty acids (EPA and DHA). Vegetable oils are becoming more competitive on the market because of the rising demand for high-quality fish oil, which is keeping the price high and causing it to stay that way. This will lead to the creation of modified oils that have the necessary levels of n-3 fatty acids and are of adequate grade.⁴⁶

Future considerations: PUFA-containing fish and marine oils as well as borage oil, which is high in linolenic acid, have successfully absorbed MCFA (caprylic or capric acids) over the past 20 years.^{26,47-52} Despite having health benefits, SL containing PUFA are unstable due

to their susceptibility to fast oxidative degradation. Therefore, more research is required to develop effective antioxidants and packaging techniques that will stabilize these changed oils throughout storage. It is necessary to support the inclusion of SL containing n-3 PUFA in foods with data obtained from animal research and clinical trials. The metabolism, therapeutic value, and viability of producing SL with a variety of n-3 fatty acids on a wide scale should be the main areas of future study. Designing SL with specific fatty acids at specific locations of the TAG for use in medicine needs more studies. For example, it may be desirable to develop a SL for patients with cystic fibrosis that contains PUFA (e.g. EPA or DHA) at the sn-2 position, and MCFA at the sn-1, 3 positions.⁵³

Conclusion

In conclusion, the nutritional, functional, and sensory qualities of fats and oils have been recognized. They offer a more concentrated source of energy compared to proteins and carbs. Concern over the connection between specific illness problems, such as cardiovascular disease, obesity, and cancer, and a high intake of some fatty acids or an optimal balance of various fatty acids in the diet is growing. Therefore, it is evident that there is a demand for speciality lipids that offer certain health advantages while maintaining the physical, functional, and sensory properties of regular lipids.

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Conflicts of interest

Authors declare that there is no conflict of interest.

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