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Structured Lipids : Enzymatic Synthesis, Health Benefits and Nutraceutical Characteristics - A Review

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***Abstract* – Structured lipids (SLs) are generally defied as triacylglycerols (TAGs) that have been modified to change the fatty acid composition and/or their positional distribution in glycerol molecules by chemical and/or enzymatic reactions and/or by genetic engineering processes. They are designed for obtaining TAGs with improved functional properties (i.e. fats with specific physical properties for food applications) and/or for medical and nutritional applications, especially to meet for the growing need for healthier foods and to prevent obesity, cancer and cardiovascular disease cardiovascular disease. The production of SLs by enzymatic procedures has a great potential in the future market because of the specificity of lipases and phospholipases used as the biocatalysts. Enzymatic synthesis of SLs and commercial products examples are discussed in this review. Moreover, nutritional and medical uses of SLs and their effect on human health are also reviewed in this paper.**

***Keywords* – Structured Lipids, Enzymatic Synthesis, Lipase, Modified Fats, Nutraceutical Characteristics, Interesterification.**

I. INTRODUCTION

Lipids have long been recognized for the richness they impart to foods as well as their satiety value in the diet. Lipid is an important component of the diet, because it provides both energy and essential fatty acids (EFAs). It is the most concentrated energy source in the diet, with an average energy value of 9 kcal/g compared to 4 kcal/g for carbohydrates and proteins. They serve several important biological functions including: 1) acting as structural components of all membranes; 2) serving as storage form and transport medium of metabolic fuel; 3) serving as a protective cover on the surface of several organisms; and 4) being involved as cell-surface components concerned with cell recognition, species specificity and tissue immunity [1],[2]. The role of dietary lipids in health and disease -notably coronary heart disease, obesity, hyperlipidemia, diabetes and cancer- is one of the most active areas of research in modern food science, nutrition, and biochemistry [3], [4].SLs can be prepared chemically or enzymatically. The use of enzymes as biocatalysts has several advantages over chemical methods, thereby providing alternative and possible routes for the chemical catalysts in the synthesis of SLs for a variety of different applications. The most remarkable feature of enzymes is selectivity or specificity, which cannot be achieved by chemical catalysts, resulting in a few or no formation of byproducts. Second, enzymatic reactions are performed under mild conditions, leading to a reduction in the loss of original attributes of temperature-sensitive substrates and products (namely, SLs). Finally, the use of enzymes reduces the use of energy and deleterious reagents and makes it easy to recover products, resulting in a more environment-friendly and safer alternative for these applications [5].

Although lipases and phospholipases have several advantages over chemical catalysts for the SLs synthesis, their industrial application has been slow because of their high cost. The use of immobilized enzymes helps to overcome much of this economic problem because it allows easy recovery and several reuses of the enzymes. Researchers and manufacturers of SLs prefer to use commercial immobilized lipases of which the catalytic behaviors and properties are well-known in several reaction systems. The representative examples of the commercial products include Lipozyme RM IM (*Rhizomucormiehei* lipase immobilized on a macro porous anion exchange resin, sn-1,3-specific), Lipozyme TL IM (*Thermomyceslanuginosus* lipase immobilized on silica gel, sn-1,3-specific), and Novozym 435 (*Candida antarctica* lipase B immobilized on a macro porous acrylic resin, sn-1,3-specific or nonspecific depending on the substrates) from Novozymes (Denmark, Bagsvaerd, Denmark). On the contrary, there are few commercial immobilized phospholipases. Accordingly, several researchers have attempted to immobilize commercial free phospholipases (for example, Lecitase Ultra, PLA1 from Novozymes) as well as commercial free lipases and lipases developed independently in their laboratories and use the resulting immobilized enzymes as the biocatalyst for the synthesis of SLs [6].

The guidelines for a healthy diet issued in various countries recommend lowering the diet fat content to 20-35% of total energy content. A reduction of energy intake through a reduction of dietary fat intake is easier said than done because fat contributes strongly to the sensory characteristics of our food such as taste, appearance and texture. New developments in food technology now allow the partial replacement of dietary fat with substitutes called structured lipids (SLs), which combine unique characteristics of component fatty acids such as melting behavior, digestion, absorption, and metabolism to

enhance their use as functional lipids and as nutraceuticals of much lower energetic value and many health benefits [7].

II. Component Fatty Acids

A variety of fatty acids are used in the synthesis of SLs, taking advantage of the functions and properties of each to maximize the benefits of a given SL. The component fatty acids and their position in the TAG molecule determine the functional and physical properties, the metabolic fate, and the health benefits of an SL. Therefore, careful analysis of the function and metabolism of component fatty acids is merited.

A. Short Chain Fatty Acids

Short chain fatty acids (SCFAs) range from 2 to 6 carbons long, and are also known as volatile fatty acids. Traditional sources of SCFAs include bovine milk and butter fat. Due to their water soluble nature, molecular size, and short chain length, they are more rapidly absorbed in the stomach than other fatty acids. Additionally, SCFAs attached to the sn-3 position of TAGs will be completely hydrolyzed in the lumen of the stomach and small intestine, due to the positional and chain length specificity of human pancreatic gastric lipase. SCFAs have lower heat of combustion than other fatty acids, making them lower in calories. Caloric values of common SCFAs are as follows: C2:0, 3.5 kcal/g; C3:0, 5.0kcal/g; C4:0, 6.0 kcal/g; and C6:0, 7.5 kcal/g [8].

B. Medium Chain Fatty Acids

The primary sources of MCFAs, which range in length fromC6:0 to C12:0, are coconut and palm kernel oils. MCFAs are preferentially transported via the portal vein to the liver, because of their smaller size and greater solubility compared to LCFAs [9]. For entry into the mitochondria of all tissues, MCFAs are not carnitine-dependent [10]. Additionally, MCFAs are metabolized as rapidly as glucose in the body with little tendency to deposit as stored fat, because they are not readily re-esterified intotriacylglycerols. Although MCFAs may be useful in the control of obesity, they can potentially raise serum cholesterol levels. Therefore, it appears that MCFAs are most useful in a structured lipid that combines their inherent mobility, solubility, and ease of metabolism with more healthful polyunsaturated fatty acids [8].

C. Long Chain Fatty Acids

Long chain fatty acids (LCFAs), ranging from C14 to C24, are common to animal fats and vegetable and marine oils. LCFAs are absorbed and metabolized more slowly than either medium or short chain fatty acids; much of the LCFAs may be lost as calcium-fatty acid soap in the feces. LCFAs cannot be absorbed or transported in the blood, due to their increased hydrophobic character compared to SCFA and MCFA. Instead they must be first packaged into micelles, and then enter the intestinal cells where chylomicrons are formed. Chylomicrons are secreted into the lymphatic system and ultimately enter the systemic circulation. Carnitine is then required to transport LCFAs into the mitochondria of cells [11].

Several types of LCFAs exist, and the important ones in SL production will be discussed here. Omega-6 fatty acids cannot be synthesized by humans and are therefore considered essential fatty acids (EFAs). Linoleic acid (18:2n-6), found in most vegetable oils and plant seeds, is an EFA that can be desaturated further, and elongated to arachidonic acid (20:4n-6). Arachidonic acid is aprecursor for eicosanoid formation. Another type of EFA is theomega-3 fatty acid, such as linolenic acid (18:3n-3), which is found in soybean and linseed oils. Eicosapentaenoic acid, 20:5n-3 (EPA), and docosahexaenoic acid, 22:6n-3 (DHA), found in fish oil, are other n-3 polyunsaturated fatty acids (PUFAs) of interest in SL production. The n-3 fatty acids are essential in growth and development throughout the human life cycle and should be included in the diet. The n-3 PUFAs inhibit tissue eicosanoid biosynthesis and reduce inflammation. Diets rich in n-3 PUFAs also increase high density lipoprotein (HDL) cholesterol, while decreasing low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol levels. Omega-9 fatty acids, found as oleic acid (18:1n-9) in many vegetable oils, are not EFAs, but play a moderate role in reducing plasma cholesterol in the body. Conjugated linoleic acid (CLA), which has been shown to exhibit potent anticancer properties in animal models of carcinogenesis, can also be used for designing SLs. The major dietary source of this important class of PUFA is from the meats and fats of ruminant animals. Commercial sources of food grade quantities of this unusual non-methylene-interrupted fatty acid will be required before the therapeutic benefits are realized in humans [12].

Long chain saturated fatty acids are generally believed to increase serum cholesterol levels. However, stearic acid (18:0) is neutral with respect to cholesterol levels in the blood, partly because it has a melting point that is higher than body temperature and it is readily desaturated to oleic acid in vivo. Additionally, TAGs with high amounts of long chain saturated fatty acids are poorly absorbed in humans. Controlling the positional distribution of component fatty acids in the final TAG is also important. During digestion, TAGs are degraded to sn-2 monoacylglycerols (MAGs) and free fatty acids in the small intestine by pancreatic lipase. The sn-2 MAG and free fatty acids are then absorbed by the enterocytes. In the intestinal mucosa cells, sn-2 MAGs are re-esterified with fatty acids of exogenous or endogenous origin to form new TAGs. These are then packed into chylomicrons and excreted into the lymph. The rate of hydrolysis of TAGs by pancreatic lipase is affected by chain length and unsaturation of the fatty acids at the sn-1 and -3 positions, with medium chain triacylglycerols (MCTs) being degraded faster than long chain triacylglycerols (LCTs) [9].

III. Production of Structured Lipids

A. Enzymatic Synthesis

Lipases occur widely in nature and are active at the oil-water interface in heterogeneous reaction systems. Lipase

catalyzed interesterification reactions offer the advantage of greater control over the positional distribution of fatty acids in the final product, due to lipases' fatty acid selectivity and regiospecificity. Lipases hydrolyze TAGs to monoacylglycerols, diacylglycerols (DAGs), free fatty acids (FFA), and glycerol. In addition to the ester-interchange reaction discussed in the previous section, lipases can also catalyze direct esterification, acidolysis, and alcoholysis reactions [13].

Direct esterification:

R_1 -CO-OH + R-OH R_1 -CO-OR + H_20

Acidolysis:

R_1 -CO-OR + R_2-CO-OH R_2-CO-OR + R_1 -CO-OH

Alcoholysis:

R-CO-OR_1 + R_2-OH R-CO-OR_2 + R_1 -OH

Lipase-catalyzed reactions are a combination of esterification and hydrolysis (reverse reaction) reactions. Water must be continuously removed from the reaction medium in order to increase esterification reactions, while minimizing hydrolysis in order to obtain high conversion rates to products. When excess water is present, hydrolysis predominates, resulting in the accumulation of glycerol, FFAs, MAGs, and DAGs. However, some water is essential for enzymatic catalysis because it maintains enzyme dynamics during non-covalent interactions. To "optimize" 1-step lipasecatalyzed reactions, it is necessary to strike a balance between hydrolysis and esterification. Willis and Marangoni [14] recently proposed splitting the reactions into 2 component hydrolytic and esterification phases and then optimizing the reaction conditions for each individual phase, in order to improve productivity and potentially make lipase-catalyzed reactions economically viable. The results of their study indicated that using chemical esterification of oil for the 1st phase of the reaction and enzyme hydrolysis in the 2nd phase offered the best control over the fatty acid positional distribution in the final product and required the least amount of reaction time. There were drawbacks associated with the chemical reaction, and further studies are needed in order to reduce product charring, degree of hydrolysis, and decomposition.

Structured lipids can be produced with lipases in organic solvent, where substrates are soluble and hydrolysis can be minimized. The type of organic solvent employed can dramatically affect the reaction kinetics and catalytic efficiency of an enzyme. The extent to which the solvent affects the activity or stability of the enzyme and the effect of the solvent on the equilibrium position of the desired reaction must both be considered when choosing a solvent for bio catalysis. Hydrophilic or polar solvents can penetrate into the hydrophilic core of proteins and alter their functional structure. They also strip off the essential water of the enzyme. Hydrophobic solvents are less likely to cause enzyme inactivation in esterification reactions [8].

Most lipases are optimally active between 30 and 40 C [15]. As the temperature increases, enzyme molecules unfold by destruction of bonds, such as sulfide bridges, and may lead to hydrolysis of peptide bonds and deamination of asparagine and glutamine residues. However, these processes can be avoided in a water-free environment. Immobilization of enzymes also results in greater thermostability. Additionally, genetically engineered lipases are now available for the synthesis of SLs. It is hoped that the use of biotechnology will reduce the cost of lipases, making the enzymatic route to SLs economically viable. Other factors affecting enzymatic activity and product yield include pH, substrate molar ratio, enzyme activity and load, incubation time, specificity of enzyme to substrate type and chain length, and regiospecificity [8]. Two of the most attractive reasons for choosing enzymatic over chemically catalyzed reactions for SL production are the energy saved and minimization of thermal degradation.

IV. Studies on The Enzymatic Synthesis of Medium And Long Chain Triacylglycerols (MLCTs)

Long-chain TAGs (LCTs) are the predominant form of common edible oils and serve as a source of long-chain FAs (LCFAs)including essential FAs (EFAs). However, LCTs are metabolized slowly and mostly tend to be deposited in human adipose tissue. In contrast, medium-chain TAGs (MCTs) provide quick delivery of energy via oxidation of the more hydrophilic medium-chain Fas(MCFAs) and have lower tendencies to be deposited in the adipose tissue because of their direct transportation via the portal vein to the liver rather than through the lymphatic system. However, MCTs have the problem of EFA deficiencies. This has created the need for the development of specific SLs retaining the benefits of both LCTs and MCTs, called medium- and long-chain TAGs(MLCTs) [6].There are 4 different types of FA arrangement on the glycerol backbone of MLCTs, namely MLM, MML, LML, and LLM. Among them, MLM-type MLCTs of which MCFAs are esterified at the sn-1,3 positions and LCFAs at the sn-2 position are considered to be the desired structure of MLCTs because they can act as an efficient carrier of LCFAs compared with other types of MLCTs. That is, the 2-MAGs retaining LCFAs are produced by pancreatic lipase digestion during metabolism of MLM-type MLCTs and are well absorbed through the intestinal wall [16].

Table 1 shows many studies have dealt with the enzymatic preparation of MLCTs, indicating that MLCTs is one of the major topics in the field of SLs synthesis. sn-1,3-Specific lipase-catalyzedacidolysis of LCTs with MCFAs has been and now is the best approach to prepare MLM-type MLCTs. Many of recent studies have produced MLM-type MLCTs from diverse kinds of plant oils (mainly soybean, corn, olive, canola, rice bran, avocado, mustard, borage, echium, and pine nut oils and palm olein) and MCFAs, such as caprylic (8:0) and capric acids (10:0). These published studies employed free or immobilized sn-1,3-specificlipases developed in laboratories of Kim and others [17], Nunes and others [18], If eduba and Akoh [19], and Qin and others[20], as well as commercial immobilized sn-1,3-specific lipases, such as Lipozyme RM IM and Lipozyme TL IM [21] –[30].

In particular, the use of PBRs is preferred in the enzymatic preparation of MLM-type MLCTs because rupture of the supporting materials for immobilized lipases, which facilitates acyl migration that causes the formation of other types of MLCT species can be avoided in these reactors [31]. Although many research activities have been toward the industrial production of MLM-type MLCTs, to the best of our knowledge they are not yet commercially available. Rather, typical commercial MLCTs (for example, Healthy Resseta from Nisshin Oillio, Yokohama, Kanagawa, Japan) are a mixture of MLM, MML, LML, and LLM. The reason is because they are generally produced through lipase-catalyzed interesterification of plant oils (usually soybean, rapeseed, and cottonseed oils) with MCTs (such as coconut and palm kernel oil). In similar manners to the industrial production of MLCTs, several recent studies have attempted to produce non MLM-type MLCTs via interesterification of LCTs with MCTs using sn-1,3-specific or nonspecific lipases as the biocatalyst [32] – [37].Non-MLM-type MLCTs were also obtained through acidolysis of LCTs with MCFAs [38] or direct esterification of glycerol with a mixture of LCFAs and MCFAs in the presence of a nonspecific lipase [39]or acidolysis of LCTs with a mixture of LCFAs and MCFAs using an sn-1,3-specific lipase as the biocatalyst [40].

Table 1. Recent studies on the enzymatic synthesis of medium- and long-chain triacylglycerols (MLCTs).

Product type	Reaction scheme	Reaction type	Enzyme	Reactor type	Study
MLM-type	Avocado oil + 8:0	Acidolysis	RM IM or TL IM	Cylindrical glass vessel	[29]
MLM-type	High-stearidonic soybean oil + 8:0	Acidolysis	*Rhizomucormiehei* lipase (immobilized on Celite powder, prepared in thelaboratory)	Batch (undefined)	[19]
MLM-type	Soybean oil + 8:0	Acidolysis	*Geobacillus* sp. T1 lipase (free)	Batch (undefined)	[20]
MLM-type	Mustard oil + 10:0	Acidolysis	TL IM	Batch (undefined)	[30]
MLM-type	Echium oil + 12:0	Acidolysis	RM IM	30-mL reactor flask	[28]
MLM-type	Tricaprin + marine n-3 FA ethyl ester concentrate	Interesterification	RM IM	100-mL round bottom flask	[41]
MLM-type	Palm olein + 8:0 and 10:0	Acidolysis	RM IM	Batch (undefined; vacuum)	[24]
MLM-type	Step 1: Redistribution of FAs in pine nutoil Step 2: FAs-redistributed pine nut oil + 10:0	Intraesterification (for step 1) Acidolysis (for step 2)	N 435 (for step 1) RM IM (for step 2)	50-mL Erlenmeyer flask(for step 1) PBR (column dimension: 7.62 cm × 4.8 mm i.d.; forstep 2)	[25]
MLM-type	Case 1: Olive oil + 8:0Case 2: Olive oil + 10:0	Acidolysis(for both cases)	*Rhizopusoryzae* heterologous lipase (immobilized on Eupergit C or Lewatit VP OC 1600, prepared in the laboratory)	Cylindrical glass vessel	[18]
MLM-type	Canola oil + 8:0	Acidolysis	TL IM	Flask	[26]
MLM-type	Canola oil + 8:0	Acidolysis	RM IM	25-mL round bottom flask	[27]
MLM-type	Mustard oil + 10:0	Acidolysis	TL IM	PBR (column dimension: 50 cm × 10 mm i.d.)	[23]
MLM-type	Case 1: Rice bran oil + 10:0Case 2: Ground nut oil + 10:0Case 3: Mustard oil + 10:0	Acidolysis (for all cases)	N 435	Stirred-tank reactor	[42]
MLM-type	Tripalmitin + 10:0	Acidolysis	RM IM	10-mL vial	[43]
MLM-type	Fish oil + 10:0	Acidolysis	RM IM	PBR (column dimension: 16.2 × 2.5 cm2 i.d.)	[44]
MLM-type	Rice bran oil + 8:0	Acidolysis	RM IM	PBR (column dimension: 50 × 4.7 cm2 i.d.)	[21]
MLM-type	Borage oil + 8:0	Acidolysis	RM IM or lipase from *Pichia lynferdii* NRRL Y-7723 (free)	25-mL Erlenmeyer flask	[17]
MLM-type	Corn oil + 8:0	Acidolysis	TL IM	30-mL Reaction flask	[22]

Non-MLM-type	Soybean oil + MCTs	Interesterification	TL IM	50-mL round bottom flask PBR (column dimension: 20 cm × 11.5 mm i.d.)	[35]
Non-MLM-type	Glycerol + 8:0, 10:0, and 18:1n-9	Direct esterification	N 435	250-mL three necked round bottom flask (vacuum)	[39]
Non-MLM-type	Flaxseed oil + tricaprylin	Interesterification	TL IM	30-mL reactor flask	[36]
Non-MLM-type	Flaxseed oil + tricaprylin	Interesterification	N 435	30-mL reactor flask	[37]
Non-MLM-type	Tricaprylin + trilinolenin	Interesterification	RM IM or N 435	50-mL Erlenmeyer flask	[32]
Non-MLM-type	Case 1 : Olive oil +8:0Case 2: Olive oil + 10:0	Acidolysis (for both cases)	*Yarrowia lipolytica* lipase 2 (immobilized on Accurel MP1000, prepared in the laboratory)	Cylindrical glass tube	[38]
Non-MLM-type	Flaxseed oil + tricaprylin	Interesterification	RM IM, TL IM, N 435 or Amano DF (free *Rhizopus oryzae* lipase, Amano, 30-mL reactor flask Japan)	30-mL reactor flask	[33]
Non-MLM-type	Tricaprylin + trimyristin	Interesterification	*Thermomyces lanuginosus* lipase (immobilized on Immobead 150, Sigma–Aldrich, U.S.A.) or *Candida antarctica* lipase B (immobilized on Macroporous resin, Sigma–Aldrich, U.S.A.)	Batch (undefined)	[34]
Non-MLM-type	Terebinth fruit oil + 8:0 and 18:0	Acidolysis	RM IM	Batch (undefined)	[40]

V. Nutraceutical Applications of SLs

The interesterifiation and genetic engineering processes have been used in the production of structured lipids with specific physical properties such as having a desired melting point, slow rancidification, and also for the production of functional structured lipids possessing specific compositions and nutritional properties. **Table 2** summarizes the potential uses of functional structured lipids.

A. Breast Milk fat Substitute

Lipids are the major source of energy in human milk or infant formulas. Hence, modification of fats and oils for infant formulas in order to obtain not only the correct fatty acid (FA)composition but also the same positional distribution as in human milk fat (HMF) via interesterification had been widely investigated. Christensen and Holmer [45] prepared a HMF analogue using a *Rhizomucormiehei* lipase-catalyzed modification of butter oil. Unilever produced a milk fat substitute named Betapol for infant formulas. Also, Yang et al. [46] modified lard by lipase to produce HMF substitutes.

B. Margarine fats

Chemical and enzymatic interesterifiation has been specially employed in the formulation of margarines and shortenings with no trans FAs while still maintaining physical properties, taste and stability. The vegetable oils including corn, palm, peanut, cottonseed, canola, and sunflower oils can be randomly interesterified with fully hydrogenated soybean oil or fully hydrogenated cottonseed hard fats to produce desirable fat compositions for margarines and shortenings [47].

C. Cocoa Butter Equivalents

Due to high cost and fluctuations in the supply and demand of cocoa butter, cocoa butter equivalent (CBE) with a TAGs composition similar to cocoa butter is used as an alternative source. Recently, vegetable oils such as Mahua, Kokum and mango fats, palm oil, tea seed oil, and olive oil have been used to prepare CBE through enzymatic catalyzed interesterification until a similar composition of cocoa butter is obtained. The triacylglycerol composition of oils was redesigned so that properties such as the melting point, solid fat content and fat crystal network microstructures of the structured oil and cocoa butter were very much similar [48].

D. Frying Oils

Genetic engineering process had been used for the production of modified oils that have a lot of benefits which include high oxidative stability, zero trans-fat and low saturated FAs, non-hydrogenated, high oleic content, liquid at room temperature, and excellent taste and flavor [49]. Recently, genetically modified soybean oil has been introduced that eliminates the need for hydrogenation to be used in bakery goods and for frying. The oil also has a healthier FA composition. High-oleic sunflower oil having better oxidative stability in deep frying applications and extended shelf life compared to traditional sunflower oil has been developed using selective breeding and

mutagenesis [50].Other example includes canola oil seed mutants with low linolenic/high oleic acid content [51].

Table 2. Potential uses of functional structured lipids

Potential uses	SL related to food application	References
Margarine, butter, spreads, shortening, dressings, dips, and sauces	Benefat, Neobee and Olestra	[52] -[54]
Cocoa butter equivalents	Caprenin and Benefat	[55], [56]
Confectioneries and soft candies	Caprenin and Laurical	[57], [55]
Baking chips, baked goods	Benefat and Olestra	[52], [53]
Snack foods	Caprenin, Captex	[55]
Low caloric food	Caprenin, Benefat, Neobee	[58] - [60]
Frying oil	Genetically modified soybean oil, high-oleic sunflower oil and canola oilseed mutants with low linolenic/higholeic acid content.	[50], [51]
Infant food formulas	SLs containing EFAs and MCFAs such as Betapol	[61], [62]
Dairy products	Benefat	[56]

VI. Health Benefits of SLs

One of the earliest uses of SL was in enter a land parenteral nutrition followed by its application in a range of clinical settings including prevention of thrombosis, improved nitrogen balance, and enhanced immune function. Low-calorie structured lipids (SLs) are mainly designed for special nutritional applications, especially to meet the growing need for healthier foods and to prevent obesity [63], [64].Data from several short-term investigations suggest that SLs are well tolerated and rapidly oxidized and cleared from the plasma [65] - [67].

A. Enteral and Parenteral Nutrition

The advantages of enterally fed SLs may well relate to differences in absorption and processing. Structure TAGs that contain MCFA may provide a vehicle for rapid hydrolysis and absorption, due to their smaller molecular size and greater water solubility in comparison to long-chain TAGs [68].The TAGs in total parenteral nutrition (TPN) are normally administered as an emulsion. These emulsions are suspected of suppressing the immune function because pneumonia and wound infection often occur in patients treated with TPN. Kruimel et al. [69] attempted to explain this phenomenon, the results indicated that physical mixtures caused higher peak levels and faster production of oxygen radicals; compared to SLs. Chambrier et al. [70] conducted a similar study comparing the effect of physical mixtures and SL on postoperative patients. They did not see the hepatic function disturbances in patients given the SL, which are often observed with TPN.

Structured lipids synthesized from fish oil and MCFA were administered to patients undergoing surgery for upper gastrointestinal malignancies. This diet was compared to a control diet that differed only in its fat source. The SL diet was tolerated significantly better, led to improved hepatic and renal function, and reduced the number of infections per patient [71].In a recent study, a novel SL was designed and synthesized based on lipase-catalyzed interesterifiation of camellia oil fatty acid methyl esters and triacetin. The SL product contains relatively high amounts of unsaturated fatty acids and has a lower risk of safety problems[72]. Triacetin was found to be metabolically beneficial in hypermetabolic states, it improves protein utilization and structural components of the small and large bowel and reduces the development of intestinal mucosal atrophy associated with conventional parenteral nutrition in burn injury [73].The use of fish oil emulsions in patients undergoing stent implantation resulted in lower incidences of atrial fibrillation and the length of intensive therapy unit ITU and hospital stay is reduced, compared to the therapy with soybean oil-based emulsions [74]. SLs containing MCFAs and n-3 PUFAs could be a therapeutic or medical lipid source, and may be useful in enteral and parenteral nutrition. These SLs provided an efficient way to supplement n-3 PUFAs and to provide energy from the MCFAs, which were the preferred substrate for oxidative metabolism [75]. No signs of central nervous system toxicity were noted in patients given the SL, and there was no tendency to ketosis [76]. Additionally, SLs were safe and efficient when provided to patients on home parental nutrition on a long-term basis because they may be associated with possible reduction in liver dysfunction [77].

B. Immune Function

The essential constituents of structured lipids in terms of their effects on the immune system are fatty acids, which are composed of the hydrocarbon chain of various lengths. Fatty acids used in structured lipids can affect the immune system via several mechanisms. The first mechanism involves incorporation of lipids into the structure of the cell membranes and thus affecting their fluidity, permeability of ion channels and functions of membranous receptors. The second mechanism is associated with penetration of fatty acids to the cell where they can affect the production of eicosanoids, resolvins, cytokines, pathways responsible for signal transduction into the cell, and expression of genes. Moreover, fatty acids can alter cell apoptosis and production of reactive oxygen species [78].

Studies reporting on novel emulsions based on olive and fish oils, structured lipids or mixed-type emulsions in which various lipid species replace conventional long-chain triglycerides indicate that these lipids are generally well tolerated. While long-chain triglycerides may promote inflammation due to conversion of n-6 polyunsaturated fatty acids into arachidonic acid-derived eicosanoids, structured lipids and olive oil emulsions

appear more immune-neutral [79], [80]. The structured lipid diet named Impact, containing low levels of linoleic acid, resulted in decreased length of hospital stay compared to other enteral formulae. Bower et al [81] also demonstrated a decrease length of hospital stay and infection rate when using diets with low level of linoleic acid added fish oil.

Fish oil-based emulsions contain mainly long-chain n-3 polyunsaturated fatty acids. They have inhibitory effects on signal transduction and expression of genes involved in the inflammation, they also modify significantly the cytokine profile and increase the EPA levels in serum [82]. Moreover, its use was demonstrated to enhance the production of DHA and EPA metabolites without affecting the production of AA, whose products show pro-inflammatory effects [83]. Importantly, recent investigations indicate beneficial effects of parenteral fish oil on relevant clinical outcome measures. Leukocyte-activating effects of medium-chain triglycerides in experimental studies await further characterization in vivo, although the recent data indicate that MCTs are not indifferent to the functioning of the immune system [84].

C. Thrombosis

Thombosis is the formation of blood clots. Blood clotting involves the clumping together of platelets into large aggregates and is triggered when endothelial cells lining the artery walls are damaged. If the platelet membranes are rich in long-chain n-3 PUFAs, formation of certain eicosanoids such as prostacyclin I3 and thromboxane A3 is promoted. These do not trigger platelet aggregation as much as the corresponding eicosanoids, prostacyclin I2 and thromboxane A2, that are formed from n-6 PUFA. Therefore, long-chain n-3 PUFAs may help to reduce the tendency for blood to clot [85].

Mori et al. [86] suggested that n-3 fatty acid intake from fish consumption in conjunction with a low-fat diet was most beneficial in terms of reducing cardiovascular disease. Studies indicate that the n-3 fatty acids, especially EPA and DHA, may be effective in reducing the clinical risk of cardiovascular disease by favorably altering lipid and hemostatic factors such as bleeding time and platelet aggregation [87]. EPA incorporating into the atheromatous plaque decreases the number of foam cells and T lymphocytes, reduces the inflammatory process and increases the stability of platelets [88].

D. Cholesterol and Triacylglycerols Concentrations

Long-term feeding studies with an SL containing MCFAs and fish oil fatty acids showed that SL modified plasma fatty acid composition, reflecting dietary intake and induced systemic metabolic changes that persisted after the diet was discontinued [89]. When SL (emulsion of MCT + fish oil composed of 50% MCT, 40% fish oil, and 10% canola oil) and soybean oil were provided to rats enterally, TAG and cholesterol levels in liver were lowered in the SL group [90]. Rats were fed a diet containing coconut oil, coconut oil-sunflower oil blend (1:0.7 w/ w) or structured lipid enriched with omega 6 PUFA at 10% levels for a period of 60 days. The SL lowered serum cholesterol levels by 10.3 and 10.5% respectively in comparison with those fed coconut oil and blended oil. Similarly the liver cholesterol levels were also decreased by 35.9 and 26.6% respectively in animals fed structured lipids when compared to those fed on coconut oil or the blended oil. Most of the decrease observed in serum cholesterol levels of animals fed structured lipids was found in LDL fraction. The triglyceride levels in serum showed a decrease by 17.5 and 17.4% while in the liver it was reduced by 45.8 and 23.5% in the structured lipids fed animals as compared to those fed coconut oil or blended oil respectively [91]. SL containing caprylic and n-3 polyunsaturated fatty acids was synthesized and this enzymatically produced SL vs soybean oil (20% of diet weight) were fed to female mice for 21 days. The result showed that the concentration of total cholesterol, LDL cholesterol, and triacylglycerol were significantly decreased in SL-fed group [92].

E. Reduced Calorie Fats

With increasing consumer awareness of the risks associated with high fat intake, a market for reduced calorie fats and fat replacers has opened up. Carbohydrate and protein-based fat replacers are currently available, but cannot be exposed to high temperatures. Therefore, lipid-based fat substitutes are the only option for use in cooking and deep-frying applications and for mimicking all the attributes of a natural fat. Reduced calorie SLs are designed by taking advantage of either limited absorption of long-chain saturates or the low caloric value of SCFAs.The majority of reduced calorie fats and fat substitutes available today contain fatty acids that are not naturally present in edible oils and fats, but may match the chemistry and functions of natural fats. Typically, such products lack nutritionally important EFAs. For example, Akoh and Yee [93] interesterified tristearin with tricaprin (C10:0) or tricaprylin (C8:0) with sn-1,3-specific immobilized lipase to produce a low calorie SL.

One group of researchers synthesized an SL from natural vegetable oils so it would contain EFAs and natural antioxidants. They incorporated behenic acid into thesn-1 and sn-3 positions of sunflower oil through a transesterification reaction catalyzed by lipases. The synthesized product delivered 5.36 kcal/g and had an improved plastic nature, which increases the potential food applications for such a product, especially since it is a trans-free solid fat. After producing the SL, it was fed to rats and compared to a control group fed sunflower oil. No differences were observed in the amount of food consumed, which indicates that the palatability and taste of the SL was very similar to the native sunflower oil. Additionally, no differences were observed between the groups regarding the levels of major fatty acids of the plasma total lipids [94].

VII. CONCLUSIONS

Although much remains unstudied in the field of SLs, one cannot read this review and feel that the consumers will not benefit from at least one aspect of SLs. Whether it be through improvement in functionality or physical properties of a food, reduction in caloric value of foods that normally contain high amounts of fat, or the medicinal

properties of rapidly absorbing TAGs composed of MCFAs and PUFAs, structured lipids definitely provide attributes that consumers will find valuable. Therefore, it is important that further research be conducted that will allow for better understanding and more control over the various esterification processes and reduction in costs associated with large-scale production of SLs.

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