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Beyond energy storage: food lipids as modulators of metabolism, inflammation, and organ function

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ABSTRACT

Dietary lipids are increasingly recognized as complex bioactive components whose physiological effects extend far beyond their contribution to energy intake. Recent advances in analytical technologies revealed an extraordinary diversity of lipid species in foods and highlighted how their biological activity depends not only on fatty acid composition but also on molecular structure, food matrix organization, processing conditions, and interactions with host metabolism. These findings challenged traditional nutritional paradigms based solely on total fat intake and have promoted a more integrated view of dietary lipids.

This review discusses current knowledge on the complexity of food lipids and the mechanisms through which their structure, organization, and metabolic transformations influence digestion, bioavailability, and physiological responses. Particular emphasis is placed on recent insights provided by food lipidomics and on the emerging concept that individual lipid species, rather than total lipid content alone, may differentially affect metabolic health. The growing integration of lipidomics with nutrition science is opening new perspectives for understanding diet–health relationships and may contribute to the development of functional foods and precision nutrition strategies aimed at improving metabolic health and reducing disease risk.

1. Introduction

Dietary lipids have traditionally been regarded as energy sources and structural components of biological membranes, and nutritional research has long focused on total fat intake and the conventional classification of fatty acids according to their effects on cardiovascular health. Recently, advances in molecular nutrition have shifted attention toward the structural diversity and bioactivity of specific lipid species, highlighting that the physiological effects of dietary lipids depend not only on fat quantity but also on lipid composition, food matrix, and metabolic fate. (Smilowitz et al., 2013). Recent improvements in analytical chemistry and high-resolution mass spectrometry have reshaped this perspective, revealing the extraordinary structural complexity and functional diversity of food lipids. Beyond their caloric contribution, lipids are now recognized as dynamic bioactive compounds involved in a wide range of physiological processes, including membrane organization (Lingwood & Simons, 2010), intracellular signaling (Wymann & Schneiter, 2008), immune regulation (Gilroy & David Bishop-Bailey, 2019), intestinal homeostasis (Li et al., 2026), and neurodevelopment (Okai-Mensah et al., 2025).

Food lipidomes are highly complex systems composed of several molecular species differing in polarity, chain length, degree of unsaturation, stereochemistry, and head-group composition (Fig. 1). In addition to the major neutral lipids, such as triacylglycerols (TAGs), foods contain minor yet biologically relevant lipid classes, including phospholipids (PL), sphingolipids (SL), glycolipids (GL), sterols, oxidized lipids, and signaling lipid mediators. Minor lipid fractions are increasingly attracting scientific interest due to their potential bioactive properties. In particular, membrane-associated polar lipids such as phosphatidylcholines (PC), phosphatidylethanolamines (PE), phosphatidylserines (PS), and sphingomyelins (SM) emerged as important regulators of membrane organization, cell signaling, immune responses, and intestinal physiology (Fappani et al., 2026). Their biological effects are often disproportionate to their concentration and are strongly influenced by their molecular structure, supramolecular organization, and interactions with the surrounding food matrix (Martínez-Ramírez et al., 2013; Z. Ye et al., 2021).

Importantly, the biological activity of food lipids can be profoundly influenced by technological processing, digestion, and microbial metabolism. Processes such as fermentation, thermal treatment, enzymatic

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hydrolysis, and storage can induce extensive lipid remodeling, generating new lipid molecular species and modifying the bioavailability and functionality of existing compounds. Fermented foods, for example, represent highly dynamic biochemical systems in which microbial metabolism can reshape both neutral and polar lipid fractions through lipolysis, phospholipid remodeling, and sphingolipid metabolism (Manis, Casula, Chessa, et al., 2025).

In parallel, high-resolution mass spectrometry (HRMS), combined with advanced chromatographic separation techniques, now allows the simultaneous detection and annotation of hundreds to thousands of lipid species differing in chain length, unsaturation, head-group composition, and structural organization (Quehenberger & Dennis, 2011). In particular, tandem mass spectrometry (MS/MS) fragmentation approaches have become essential for distinguishing lipid subclasses, identifying fatty acyl composition, and improving structural annotation confidence, especially in complex food matrices and processing-induced lipid remodeling studies (Damiani et al., 2023).

Despite considerable advances in food lipidomics, current reviews have predominantly focused on individual lipid classes, fatty acid composition, or specific aspects of lipid metabolism. Comparatively less attention has been devoted to the dynamic interplay linking lipid chemical diversity with processing-induced remodeling, food matrix organization, digestion, tissue-specific biological functions, and the emerging concept of precision nutrition. Therefore, rather than considering food lipids as static sources of energy or isolated nutrients, the present review adopts an integrative framework in which lipid chemistry, technological processing, matrix-dependent bioaccessibility, organ-specific functions, and individual metabolic responses are viewed as interconnected determinants of lipid functionality. By integrating evidence from food chemistry, lipidomics, nutrition, and metabolism, this review aims to provide a comprehensive perspective on dietary lipids as dynamic molecular systems whose biological effects extend far beyond their caloric contribution and are ultimately shaped by structural organization and metabolic interactions. Accordingly, the review is structured to progressively link lipid chemical diversity with processing-induced remodeling, matrix-dependent bioaccessibility, organ-specific biological functions, and the emerging paradigm of precision nutrition.

2. Chemical diversity of food lipids

2.1. Neutral lipids

Neutral lipids represent the predominant lipid fraction in most foods and the principal form of energy storage in both plant and animal tissues. The storage of fatty acids, fatty alcohols, and sterols as neutral lipids represents an efficient metabolic strategy that allows organisms to preserve hydrophobic molecules for subsequent utilization in essential physiological processes, including membrane biosynthesis, maintenance of epidermal barrier integrity, bile acid production, lipoprotein assembly and transport, and steroid hormone synthesis (Turkish & Sturley, 2009).

The neutral lipids group mainly include triacylglycerols (TAGs), diacylglycerols (DAGs), monoacylglycerols (MAGs), and free fatty acids (FFAs), compounds characterized by low polarity and marked hydrophobicity. Among these, TAGs account for most dietary lipids and play a central role in determining the nutritional, physicochemical, and sensory properties of foods (Mu & Høy, 2004). Structurally, TAGs are composed of three fatty acids esterified to a glycerol backbone. Their physicochemical properties are influenced by fatty acid chain length, degree of unsaturation, and stereospecific distribution within the glycerol molecule. These structural characteristics affect melting behavior, crystallization, oxidative stability, and digestibility, ultimately influencing both food functionality and postprandial metabolic responses (Mu & Høy, 2004). In particular, TAGs rich in saturated fatty acids generally exhibit higher melting temperatures and oxidative stability, whereas unsaturated TAG species are more fluid but also more susceptible to lipid oxidation. The positional distribution of fatty acids within TAG molecules is biologically relevant because gastric and pancreatic lipase preferentially hydrolyzes ester bonds located at the *sn*-1 and *sn*-3 positions, generating free fatty acids and 2-monoacylglycerols (Casula,

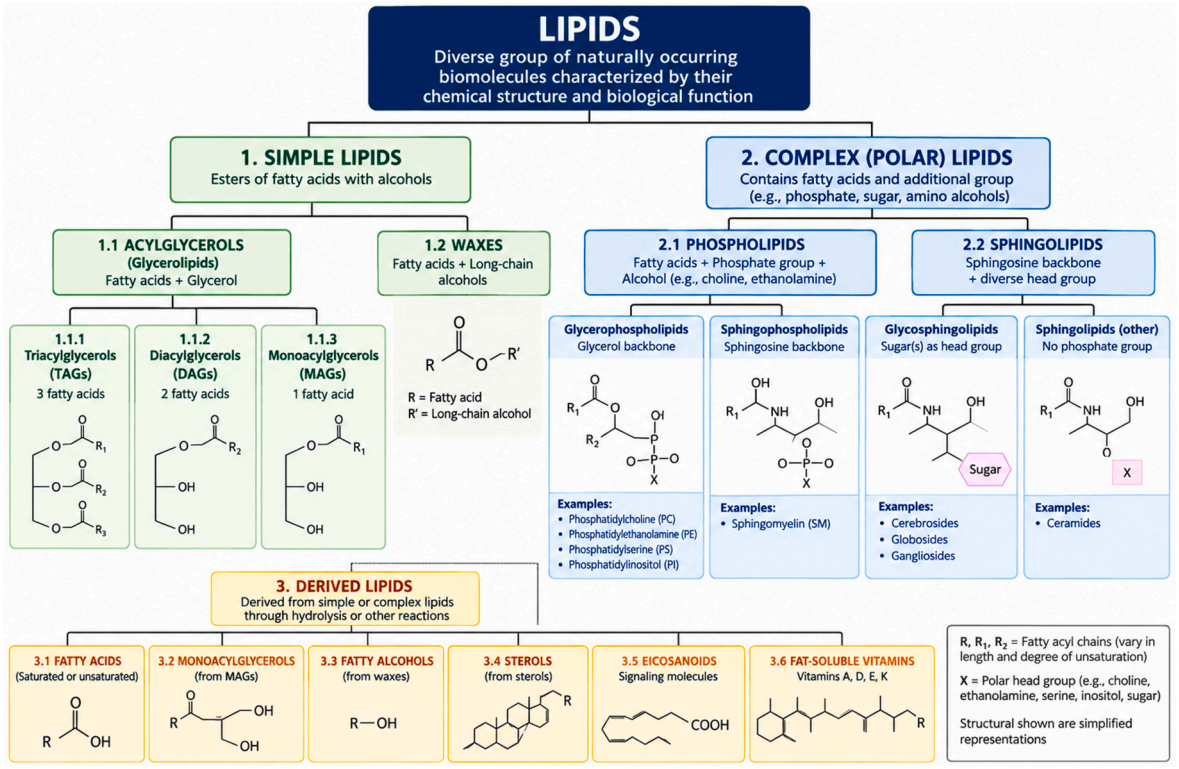

Fig. 1. Classification of dietary lipids according to their chemical structure.

Manis, et al., 2024). Consequently, the regiospecific arrangement of fatty acids influences lipid digestion, bioavailability, and metabolic fate (S. E. E. Berry, 2009). In addition to TAGs, their hydrolysis-derived products, diacylglycerols (DAGs) and monoacylglycerols (MAGs), are increasingly recognized as biologically active molecules. Generated through enzymatic hydrolysis of triacylglycerols during digestion and cellular lipid turnover, DAGs participate in intracellular signaling pathways through activation of protein kinase C (PKC), thereby contributing to the regulation of cell proliferation, membrane trafficking, and insulin signaling (Carrasco & Mérida, 2007). Dietary DAG-rich oils have also attracted attention for their potential effects on lipid metabolism and body weight regulation, with some studies reporting reduced postprandial triglyceridemia and enhanced fatty acid oxidation compared with conventional TAG-rich oils (Nagao et al., 2000).

Neutral lipids are therefore dynamic food components whose nutritional properties are determined by their structural and compositional remodeling.

2.2. Polar lipids

Polar lipids constitute a structurally diverse class of amphiphilic molecules characterized by the coexistence of hydrophobic fatty acyl chains and hydrophilic polar head groups. Depending on the nature of the polar moiety, which may include choline, ethanolamine, serine, or inositol residues, polar lipids comprise several phospholipid subclasses, including phosphatidylcholines (PC), phosphatidylethanolamines (PE), phosphatidylserines (PS), phosphatidylinositols (PI), N-acyl-phosphatidylethanolamines (NAPE), as well as lysophospholipid derivatives such as lysophosphatidylcholine (LPC) and lysophosphatidylethanolamine (LPE) (Tan et al., 2020). Owing to this dual chemical nature, polar lipids are essential components of biological membranes and play critical roles in membrane organization, cellular signaling, lipid transport, and intercellular communication. Among phospholipids, PC is generally the most abundant species in mammalian membranes and lipoproteins, while PSs, for example, are particularly enriched in neuronal membranes and are involved in synaptic activity, cognitive processes, apoptosis signaling, and membrane-dependent enzyme activation (Kim et al., 2014). PI and their phosphorylated derivatives also represent important signaling lipids involved in intracellular communication pathways regulating cell growth, metabolism, vesicle trafficking, and inflammatory responses. Although present in relatively low concentrations, phosphoinositides play central roles in membrane-associated signaling cascades and metabolic regulation (Balla, 2013).

In foods, polar lipids are particularly abundant in dairy products (Contarini & Povolo, 2013), eggs (Blesso, 2015), marine foods (Ahmmed et al., 2020; Manis et al., 2026), and cellular membranes of plant (Mamode Cassim et al., 2019) and animal tissues (Lordan et al., 2017). Different foods exhibit characteristic polar lipid fingerprints reflecting species origin, tissue organization, metabolic activity, and technological processing. In plant-derived foods, polar lipids mainly occur as structural membrane components, particularly PC, PE, and glycolipids associated with chloroplast and cellular membranes, whereas neutral storage lipids such as TAGs generally predominate in seeds and oleaginous tissues. Conversely, animal-derived foods typically display more complex polar lipid profiles enriched in phospholipids and sphingolipids. Phospholipids are particularly enriched in polyunsaturated fatty acids (PUFAs), making them more susceptible to oxidative degradation during processing and storage.

The nutritional relevance of polar lipids extends beyond membrane structure and signaling, influencing intestinal lipid absorption, cholesterol metabolism, gut barrier integrity, and microbiota composition. As observed for neutral lipids, the biological functions of polar lipids are strongly influenced by molecular composition and structural organization. Minor modifications in fatty acyl composition or head-group structure may alter membrane properties, lipid-protein interactions, and signaling pathways. Consequently, polar lipids are increasingly recognized as highly dynamic bioactive molecules involved in multiple physiological and pathological processes.

Besides their nutritional relevance, phospholipid profiles emerged as valuable compositional markers for food authentication and quality assessment. Owing to their species-specific distribution and susceptibility to processing-induced modifications, phospholipids have been successfully applied to discriminate dairy products, seafood species, edible oils, and fermented foods, as well as to monitor technological treatments and storage conditions (Fong et al., 2007; Rezzi et al., 2007; Manis et al., 2023; Hatzakis et al., 2008).

Overall, the remarkable structural diversity and biological versatility of phospholipids make them valuable components not only for membrane organization and cellular regulation, but also for food quality assessment, authenticity evaluation, and nutritional characterization. Among polar lipids, sphingolipids have emerged as a key class of bioactive molecules regulating membrane organization, cell signaling, and multiple physiological processes.

2.2.1. Sphingolipids

Sphingolipids constitute an important class of complex bioactive lipids characterized by the presence of a sphingoid backbone rather than the glycerol backbone typical of phospholipids. This family includes sphingomyelins (SM), ceramides (Cer), glycosphingolipids (GSL), and other complex sphingolipid species. Sphingolipids are increasingly recognized as highly bioactive molecules involved in membrane organization, lipid raft formation, signal transduction, apoptosis, inflammatory regulation, and cell differentiation. In particular, Cer play a central role in sphingolipid metabolism and act as key mediators of cellular stress responses, oxidative damage, and programmed cell death.

The extensive structural heterogeneity of sphingolipids, including variations in sphingoid backbone structure, fatty acyl-chain length, hydroxylation pattern, and degree of saturation, may substantially affect their digestion, absorption, metabolic fate, and biological activity. Such molecular complexity has therefore stimulated growing interest in food sphingolipidomics and in the investigation of the nutritional and functional significance of dietary sphingolipids. The abundance and composition of food sphingolipids strongly depend on the biological origin of the matrix. Dairy products represent one of the richest dietary sources of sphingolipids, particularly sphingomyelin species enriched in long-chain saturated and very-long-chain fatty acids. These lipids are mainly localized within the milk fat globule membrane (MFGM), together with glycosphingolipids and ceramide derivatives, contributing to membrane architecture and interfacial organization (Contarini & Povolo, 2013; Lopez et al., 2008, 2010). Eggs and animal-derived tissues are also important sources of SM and Cer associated with plasma and organelle membranes, whereas marine foods contain distinctive sphingolipid species enriched in long-chain polyunsaturated fatty acids and unusual sphingoid bases adapted to marine environments (Pruett et al., 2008). Conversely, plant-derived foods generally contain lower levels of SM but are relatively rich in glycosylceramides and phytosphingolipids, particularly in cereals, legumes, soybeans, and rice bran (Imai et al., 1997; Yumoto et al., 2021). These plant sphingolipids differ markedly from animal sphingolipids in their sphingoid base composition, influencing their physicochemical properties, digestion, and membrane interactions.

3. Food processing as a driver of lipid remodeling

Food processing profoundly influences lipid composition and may generate substantial modifications in both neutral and polar lipid fractions. Thermal treatments, oxidation, enzymatic hydrolysis, fermentation, and storage conditions can induce lipid degradation, isomerization, hydrolysis, and membrane remodeling, ultimately affecting food quality and biological activity. The major processing technologies, lipid classes affected, resulting molecular modifications, and their implications for

matrix organization, bioaccessibility, and physiological responses are summarized in Table 1.

Among processing technologies, microbial fermentation represents one of the most important drivers of lipid remodeling. During fermentation, microbial lipases and phospholipases hydrolyze complex lipids, releasing free fatty acids and generating new phospholipid and sphingolipid species. Fermented dairy products such as yogurt, kefir, and aged cheeses exhibit lipid profiles distinct from the original milk matrix, characterized by changes in PEs, lysophospholipids, and SMs (Furse et al., 2019). In artisanal and industrial fermentation, microbial activity reshapes the lipidome through the action of specific enzymes from lactic acid bacteria (LAB) and yeasts. Studies on fermented dairy products from small ruminants like Gioddu demonstrate that LAB-derived phospholipases (A1, A2) and sphingomyelinases degrade complex membrane lipids, leading to a significant accumulation of lysophospholipids (e.g., LPE) and a reduction in sphingomyelins (Manis, Casula, Chessa, et al., 2025). Furthermore, fermentation acts as a driver for the enrichment of odd-chain fatty acids (C15:0, C17:0) and induces a remodeling of the PE profile to reflect the composition of the bacterial cell envelope (Furse et al., 2019). The extent of lipid remodeling strongly depends on microbial composition and fermentation dynamics. Kefir, characterized by a complex symbiotic consortium of lactic acid bacteria, acetic acid bacteria, and yeasts, often displays more extensive metabolic transformations compared to yogurt, which is produced by a more restricted bacterial consortium.

Thermal processing may induce oxidation of unsaturated fatty acids, oxylipin formation, and membrane lipid remodeling. At the industrial level, partial hydrogenation of vegetable oils promotes geometric and positional isomerization, profoundly altering lipid structure (Kummerow, 2009). This process shifts natural *cis*-configurations to "unnatural" trans-isomers (*e.g.*, elaidic acid) and causes double bonds to migrate along the carbon chain, creating a complex mixture of isomers that interfere with essential fatty acid metabolism and prostacyclin synthesis. Thermal treatments, particularly deep-frying, induce remodeling through two primary mechanisms: thermo-oxidation and structural complexation. Culinary oils rich in PUFA are highly susceptible to thermo-oxidation at 180 °C, leading to the generation of toxic lipid oxidation products, such as α,β-unsaturated aldehydes (*e.g.*, *(E)*-2-alkenals and (*E,E*)-2,4-alkadienals) (Ampem et al., 2023). Simultaneously, high-temperature frying, introduce a structural dimension to lipid remodeling by promoting the formation of starch-lipid complexes (V-type amylose) (Hu et al., 2022). High temperatures facilitate the migration of hydrophobic fatty acid ligands into the spiral structure of starch, creating highly ordered crystalline domains that significantly reduce enzymatic digestibility and increase the content of resistant starch. Meat lipids are particularly susceptible to thermal degradation because muscle tissues contain abundant membrane phospholipids enriched in PUFA. Cooking promotes the disruption of cellular membranes, increasing the exposure of phospholipids to oxygen and transition metals, particularly iron, thereby accelerating lipid oxidation (Cheng, 2016). Elevated temperatures also promote decomposition of primary hydroperoxides into secondary volatile compounds, including aldehydes and ketones, which contribute to off-flavors and rancid smells. (Broncano et al., 2009). Beyond organoleptic decline, thermal degradation leads to the loss of essential fatty acids and vitamins, while inducing the generation of toxic cholesterol oxidation products (Alfaia et al., 2010).

Finally, biological and post-harvest factors drive hydrolytic remodeling during storage and traditional curing. In matrices like oil palm fruits, post-harvest duration triggers the activation of endogenous lipases and phospholipases (*e.g.*, PTL, NPC4), which degrade membrane glycerophospholipids (PC, PE, PG) into FFAs like lauric and eicosenoic acid (Liu et al., 2025). In high-fat matrices like Bottarga and salt-dried yellow, exposure to oxygen and light during processing creates a distinct degradation gradient (Cai et al., 2017; Manis et al., 2026). The outer layers exhibit accelerated accumulation of FFAs and lysophospholipids, whereas the inner core better preserves high-value lipids like cardiolipins and triacylglycerols. Furthermore, lipidomic investigations shown that marine lipids are highly sensitive to oxidation and processing conditions, resulting in the formation of lysophospholipids, oxidized fatty acids, and hydrolysis products during salting, drying, or thermal treatment (Rosa et al., 2009).

However, controlled oxidation processes may also generate biologically active lipid mediators with signaling properties. In animal tissues, the relationship between lipolysis and oxidation is often paradoxical; while FFAs are precursors for oxidation, their accumulation can sometimes exert antioxidant effects by neutralizing heme proteins (Tatiyaborworntham et al., 2022). Understanding processing-induced lipid remodeling is essential to link technological modifications with lipid digestibility, bioaccessibility, and nutritional function.

4. Food matrix, digestion, and lipid bioaccessibility

The physiological effects of dietary lipids depend not only on their molecular composition but also on food matrix structure. Through its three-dimensional organization and interactions among food components, the food matrix regulates lipid digestibility, bioaccessibility, and ultimately their biological effects. Lipid droplet size, emulsion structure, membrane composition, and interactions with proteins, carbohydrates, and minerals may substantially affect lipid digestion kinetics, micelle formation, and intestinal absorption. Accordingly, the food matrix emerges as a major determinant of lipid digestion and biological activity across different food systems.

Dairy Matrices. The milk fat globule membrane represents a paradigmatic example of how food structure modulates lipid functionality. This trilayer membrane, naturally surrounding milk fat globules,

Table 1
Effects of food processing technologies on dietary lipids. Summary of the main food processing technologies, the lipid classes affected, the principal molecular modifications induced, and their consequences for food matrix structure, lipid bioaccessibility, and potential physiological effects.

Processing technology	Lipid classes affected	Main molecular modifications	Consequences for matrix and bioaccessibility	Potential physiological implications	Representative examples
Fermentation	TAG, PL, SL	Lipolysis, phospholipid remodeling, ceramide formation	Modified matrix structure and digestibility	Changes in bioactivity and gut interactions	Fermented milk, yogurt, kefir, Gioddu
Thermal treatments	PUFA, PL, sterols	Oxidation, aldehyde and oxysterol formation	Reduced stability and altered bioaccessibility	Oxidative stress and lower nutritional quality	Pasteurization, cooking
Deep frying	TAG, PUFA	Hydrolysis, oxidation, polymerization	Formation of degradation products	Altered lipid quality	Vegetable oils and fried foods
Storage and aging	PL, PUFA	Hydrolysis and lipid oxidation	Loss of structural integrity	Reduced nutritional value	Bottarga, meat products
Cheese ripening	TAG, PL, SL	Lipolysis and microbial remodeling	Changes in matrix structure and flavor	Modified digestibility and bioavailability	Cheese maturation
Plant-based processing	GL, PL	Enzymatic hydrolysis and oxidation	Changes in membrane organization	Altered lipid release and digestion	Soy products, cereals
Emulsification and encapsulation	TAG, PL	Structural reorganization	Improved dispersion and lipid delivery	Altered bioaccessibility and digestion kinetics	Infant formulas and functional foods

contains phospholipids, sphingomyelins, cholesterol, and membrane proteins that influence lipase accessibility, intestinal absorption, and microbial interactions. Homogenization disrupts this native structure by fragmenting milk fat globules into submicron droplets and replacing the original membrane with a protein-rich interface mainly composed of caseins and whey proteins (Bourlieu et al., 2015). The resulting increase in droplet surface area enhances lipase access and accelerates lipolysis, making surface area the primary determinant of gastric lipid digestion kinetics (Barbé et al., 2013). Consequently, homogenized dairy products and infant formulas are digested more rapidly than minimally processed milk. Comparative *in vitro* digestion studies demonstrated that different cheese matrices exhibit distinct disintegration behaviors and lipolysis kinetics during gastrointestinal digestion. Mozzarella cheese, for example, showed higher matrix disintegration, free oil release, and fatty acid liberation compared with Cheddar cheeses (Lamothe et al., 2012), likely due to the *pasta filata* stretching process, which promotes rupture and coalescence of fat globules into pools of non-emulsified fat entrapped within the protein matrix (Rowney et al., 2004). Additional studies comparing cheese, yogurt, and milk further demonstrated that compact solid matrices are generally more resistant to lipid digestion, whereas homogenized milk displays higher lipolytic activity due to the smaller size and increased surface area of homogenized fat globules (Berton et al., 2012; Lamothe et al., 2017).

Animal-based Matrices. The lipid fraction of muscle foods, which typically accounts for 1–40% of fresh weight depending on animal species, anatomical location, and fatness, is mainly composed of triacylglycerols stored in intramuscular adipocytes and phospholipids associated with cellular and organelle membranes (Marzocchi et al., 2018). This heterogeneous distribution is a key structural feature of the muscle matrix, as the accessibility of these lipid pools during digestion depends on the progressive disruption of muscle fibers and connective tissue rather than on lipid composition alone. During mastication and gastrointestinal digestion, the muscle matrix undergoes progressive structural disintegration. Mechanical fragmentation, gastric acidification, and proteolytic enzymes gradually disrupt myofibrillar proteins and connective tissue, exposing intracellular lipid droplets and membrane phospholipids to digestive lipases (Bax et al., 2013). The post-mortem conversion of muscle into meat further influences lipid digestion by modifying the organization of myofibrillar proteins. In particular, changes in the actomyosin complex regulate the accessibility of digestive proteases, thereby indirectly affecting the release of intracellular lipids and the kinetics of lipid digestion (Huff-Lonergan & Lonergan, 2005). Mechanical processing, such as grinding, also disrupts muscle membranes and promotes the release of membrane-associated phospholipids, increasing their availability for enzymatic hydrolysis (Marzocchi et al., 2018). These observations demonstrate that the structural integrity of the muscle matrix is a major determinant of lipid bioaccessibility, highlighting food matrix structure as a key factor governing the nutritional properties of lipids in meat-based foods.

Plant-Based Matrices. In plant-based foods, particularly nuts such as almonds, walnuts, and peanuts, the food matrix may act as a complex cellular structure capable of physically entrapping lipids within intact cell walls, thereby limiting lipase accessibility and reducing lipid bioaccessibility during digestion (Paz-Yépez et al., 2019). Unlike dairy lipids, which become relatively accessible once the surrounding membrane structure is disrupted, lipids in nuts are physically encapsulated within intact plant cell walls composed of complex polysaccharide networks such as cellulose and pectin (Grundy et al., 2016). Since these structural components are largely resistant to human digestive enzymes, a substantial proportion of intracellular lipid bodies may remain inaccessible unless the cellular structure is mechanically disrupted during mastication or food processing, thereby limiting lipid release and bioaccessibility during gastrointestinal digestion (Paz-Yépez et al., 2019). Mechanical disruption through mastication, grinding, or industrial milling represents the primary mechanism enabling lipid release from nut matrices during digestion. However, mastication is frequently incomplete and generates only partial fragmentation of the plant tissue, so that lipid release mainly occurs from cells located at fractured particle surfaces, whereas lipids entrapped within intact internal cells remain largely inaccessible to digestive enzymes (Creedon et al., 2023; Grundy et al., 2015). Even when small fissures in the cell wall permit limited lipase penetration, diffusion of hydrolysis products such as long-chain fatty acids remains restricted, substantially slowing lipid digestion kinetics. Consequently, whole nuts behave as a slow-release lipid matrix, in marked contrast to processed products such as nut butters or refined oils, where mechanical disruption of the cellular structure markedly increases lipid bioaccessibility and digestibility (Grundy et al., 2015).

Ultra-Processed Food Matrices. In different ultra-processed and formulated foods, lipids are no longer retained within their native biological structures but are extracted and subsequently reorganized into emulsified or encapsulated lipid systems. This processing creates new lipid–water interfaces whose composition and organization may differ substantially from those of naturally occurring lipid droplets, such as milk fat globules or plant oil bodies. In model infant formulas, for example, homogenization produces submicron lipid droplets whose native membrane is replaced by newly formed interfaces containing adsorbed proteins and other emulsifying components. Comparison with minimally processed milk emulsions demonstrated that this structural reorganization substantially modifies gastric lipolysis kinetics, with the interfacial properties of the droplets representing a major determinant of lipid digestion (Bourlieu et al., 2015). Experimental manipulation of food-emulsion interfaces demonstrated that the emulsifiers used to stabilize lipid droplets can modify bile-salt and lipase adsorption and consequently alter intestinal lipolysis kinetics (Michels et al., 2025). Thus, industrial lipid structuring can modify gastrointestinal lipid processing not simply through disruption of the native food matrix, but also through the creation of new interfacial environments that regulate lipid accessibility to digestive components. However, whether these structural effects translate into consistent differences in postprandial lipid metabolism after consumption of complex ultra-processed foods remains insufficiently established in humans.

Physicochemical Modulation. Food matrix may also modulate lipid digestion and absorption through physicochemical interactions occurring during gastrointestinal transit. Several surface-active components, such as proteins, phospholipids, and small molecule surfactants are capable of inhibiting the activity of lipases at oil–water interfaces by reducing the contact between the oil and the lipase (A. Ye et al., 2013).

In dairy matrices rich in calcium, such as cheese, long-chain fatty acids released during lipolysis can interact with calcium ions to form insoluble calcium soaps, reducing lipid absorption and increasing fecal fat excretion (Soerensen et al., 2014). This mechanism has been proposed as one of the factors contributing to the different metabolic effects observed between cheese and butter despite their comparable saturated fat content. During intestinal lipolysis, calcium can interact with long-chain free fatty acids at the oil–water interface, promoting their precipitation and removal from mixed micelles, thereby limiting their intestinal absorption. Interfacial studies demonstrated that calcium influences the organization of lipolysis products at the surface of lipid droplets, leading to the formation of viscoelastic calcium–soap networks that alter lipid digestion kinetics and fatty acid bioaccessibility (Torcello-Gómez et al., 2018). As a consequence, a proportion of dietary lipids remains unavailable for uptake and is subsequently excreted. Interestingly, although calcium ultimately reduces lipid bioavailability, it may simultaneously accelerate lipolysis during the initial stages of small intestine digestion by removing free fatty acids from the oil–water interface, thereby limiting product inhibition of lipases and facilitating continued enzymatic hydrolysis (Zangenberg et al., 2001). These effects have important physiological consequences, including increased fecal fat excretion and attenuation of postprandial and circulating lipid levels, particularly LDL cholesterol (Soares & Chan She Ping-Delfos, 2010). The magnitude of these effects appears to be strongly influenced by the food

matrix. In dairy products, calcium soap formation appears to be more pronounced in solid matrices such as cheese than in raw milk or other liquid dairy products, likely due to the higher local availability of calcium and the structural characteristics of the cheese matrix, which can influence lipid digestion and fatty acid sequestration (Ayala-Bribiesca et al., 2017). Furthermore, beyond its direct involvement in soap formation, calcium can interact with bile salts and lipid digestion products. Calcium therefore emerges as a key regulator of lipid digestion and bioaccessibility, with its effects largely determined by food matrix structure.

5. From dietary lipids to endogenous lipid pools: absorption, transport, and metabolic remodeling

The biological effects of dietary lipids cannot be directly inferred from their molecular composition in foods, as most lipid species undergo extensive digestion, absorption, transport, and metabolic remodeling before reaching peripheral tissues. As discussed above, food matrix structure strongly influences the accessibility of lipids to digestive enzymes and therefore determines the nature and amount of lipid-derived products available for intestinal uptake. Once released, triacylglycerols are hydrolyzed predominantly by pancreatic lipase at the *sn*-1/*sn*-3 positions into free fatty acids and 2-monoacylglycerol, with the resulting product profile shaped by the intramolecular structure of the parent triacylglycerol and not only by its overall fatty acid composition (Mu & Høy, 2004). Dietary phospholipids are hydrolyzed mainly by pancreatic phospholipase A2 (PLA2G1B) at the *sn*-2 position into a free fatty acid and a lysophospholipid, whereas sphingomyelins undergoes sequential hydrolysis to ceramides and subsequently to sphingosine and a free fatty acids. Among these metabolites, sphingosine, rather than intact sphingomyelin or ceramide, is absorbed by enterocytes (Yang & Chen, 2022). Consequently, the lipid molecular species originally present in foods do not necessarily correspond to those entering the systemic circulation or ultimately accumulating in tissues.

Following intestinal uptake, lipid digestion products undergo extensive metabolic reassembly within enterocytes. For example, absorbed sphingosine can be reutilized for endogenous sphingolipid synthesis. Stable-isotope tracing in Caco-2/TC7 enterocyte cultures demonstrated that exogenous deuterated sphingosine was taken up and partly converted into sphingosine-1-phosphate, ceramide, and sphingomyelin species, with a small fraction also secreted basolaterally as ceramide (Calzada et al., 2024). Furthermore, long-chain fatty acids and monoacylglycerols are largely re-esterified into triacylglycerols via the MGAT/DGAT pathway (Yen et al., 2015), incorporated into chylomicrons together with cholesterol, phospholipids, and other lipid components and secreted into the lymphatic circulation before entering the bloodstream. Once in circulation, chylomicron triacylglycerols are progressively hydrolyzed by lipoprotein lipase (LPL), releasing fatty acids that can be taken up by peripheral tissues, particularly adipose tissue and skeletal muscle, while the resulting chylomicron remnants are subsequently cleared by the liver (Cooper, 1997). Human tracer studies further demonstrate that dietary fatty acids undergo tissue-specific trafficking and can contribute to different endogenous fatty acid pools rather than remaining associated with the molecular structures in which they were originally consumed (Fielding, 2011). Importantly, the mechanistic evidence supporting these metabolic pathways derives from different experimental settings, ranging from *in vitro* and animal models to human tracer studies. Consequently, their translational relevance to human physiology should be interpreted in light of the experimental model and level of evidence available. The metabolic fate of the major dietary lipid classes, together with the experimental evidence supporting these pathways, is summarized in Table 2.

Structural information obtained from food lipidomics should therefore not automatically be interpreted as evidence of direct delivery of the same lipid species to target organs. Accordingly, the relationship between food lipid composition and physiological function should be considered a dynamic metabolic continuum rather than a direct correspondence between dietary and tissue lipid species. Biological responses to dietary lipids may thus result from intact absorbed molecules, products generated during digestion, or subsequent intestinal, hepatic, and peripheral metabolic transformations, including changes in endogenous lipid pools and signaling mediators. The relative contribution of these processes depends on lipid class and molecular structure, food matrix, metabolic status, and tissue-specific lipid metabolism. Distinguishing dietary lipid exposure from endogenous lipid function is therefore essential when interpreting associations between food lipid composition and health outcomes. Within this framework, the organ-specific effects discussed in the following section should be considered as the integrated outcome of dietary exposure, bioaccessibility, systemic transport, and endogenous lipid remodeling, rather than as evidence of direct transfer of food lipid profiles to individual tissues.

6. Organ-specific biological functions of food lipids

Beyond their role as energy substrates, dietary lipids exert a wide range of biological functions that are highly dependent on their molecular structure, bioavailability, and metabolic fate. Following digestion and absorption, and metabolic remodeling, dietary lipid exposure can influence tissue-specific biological processes through complex metabolic and signaling pathways. Consequently, the biological effects of food lipids extend far beyond caloric intake and influence the function of multiple organs and systems.

Brain and Nervous System. The human brain contains approximately 50–60% lipids by dry weight and relies on tightly regulated lipid homeostasis together with an adequate supply of essential dietary fatty acids. Beyond their structural role in neuronal membranes and synaptic architecture, lipids participate in signaling networks regulating neurodevelopment, synaptic transmission, and neuronal survival. Among

Table 2
Metabolic fate of major dietary lipid classes from gastrointestinal digestion to endogenous lipid pools. The table summarizes the principal digestion products, intestinal absorption and transport routes, demonstrated tissue fate, and current level of experimental evidence for major dietary lipid classes. Evidence levels reflect the experimental models supporting each metabolic pathway and highlight the distinction between dietary lipid exposure and subsequent incorporation or remodeling within endogenous lipid pools.

Lipid class	Digestion products	Absorption/transport route	Tissue fate demonstrated	Evidence level
Triacylglycerols	Free fatty acids, 2-monoacylglycerol	Re-esterification in enterocyte → chylomicron	Peripheral uptake via LPL; hepatic remnant clearance	Human + animal (Mu & Høy, 2004)
Phospholipids	Free fatty acid, lysophospholipid	PLA2G1B-dependent; brush-border PLB compensates (no lysoPL)	Lysophospholipid suppresses hepatic FA oxidation, ↑VLDL	Mouse knockout only (Richmond et al., 2001; Labonté et al., 2010)
Sphingomyelin	Ceramide → sphingosine + FA	Sphingosine absorbed intact; re-synthesized to Cer/SM in enterocyte	Confirmed re-incorporation into endogenous sphingolipid pools	Cell model, isotope-confirmed (Calzada et al., 2024)
Dietary FA (general)	—	Chylomicron-TAG transport; LPL-mediated FA release and postprandial NEFA spillover	Pool-specific, tissue-specific uptake and partitioning of dietary fatty acids, particularly toward adipose tissue, liver, and skeletal muscle	Human stable-isotope tracer studies (Fielding, 2011)

these, sphingolipids emerged as key regulators of neurogenesis, membrane organization, and cell–cell communication within the central nervous system. Consequently, altered sphingolipid metabolism has been linked to impaired neuronal plasticity and neurodevelopmental and neurodegenerative disorders (Hussain et al., 2019). These observations highlight the importance of lipid homeostasis for brain function and provide a biological framework for investigating how dietary lipid exposure and metabolic remodeling may influence neurological health.

The structural and functional integrity of the human brain relies heavily on long-chain n-3 PUFAs, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). These fatty acids are key components of neuronal membranes and play essential roles in brain development, synaptic plasticity, cognitive function, and the regulation of neuroinflammatory processes (Mallick et al., 2021). Despite their recognized importance, the effectiveness of dietary n-3 PUFA supplementation may depend on the molecular form in which these lipids are delivered. Indeed, the brain preferentially takes up omega-3 fatty acids as lysophosphatidylcholine (LPC) through the Mfsd2a transporter at the blood–brain barrier, whereas most conventional supplements provide them as triacylglycerols (Nguyen et al., 2014). Moreover, the benefits of n-3 PUFAs appear to be influenced by the developmental stage, with higher maternal DHA status during pregnancy being associated with neurodevelopmental benefits in infants (Braarud et al., 2018). This aspect is particularly relevant given the limited endogenous conversion of α-linolenic acid (ALA) into DHA in humans, which is generally estimated to be below 9% (Greupner et al., 2018). When present at adequate levels, DHA and EPA contribute to neuronal function by modulating membrane organization and inflammatory signaling pathways, thereby supporting cognitive performance and brain health throughout life (Ramakrishnan et al., 2016).

Importantly, growing evidence indicates that many biological effects attributed to dietary lipids depend on interactions between lipid metabolism, gut microbiota, and immune signaling, highlighting the complexity of nutrilipidomic networks. For example, excessive dietary cholesterol may increase levels of oxysterol 27-OH-Chol, which crosses the blood-brain barrier to impair estrogen-related neuroprotection and promote Alzheimer's-like pathology (Brooks et al., 2017). Simultaneously, diet-induced intestinal dysbiosis may promote the translocation of lipopolysaccharides (LPS) into the circulation, compromising blood-brain barrier integrity and triggering microglial activation (Melo et al., 2019).

Gastrointestinal and Immune Functions. The gastrointestinal (GI) tract represents a key interface where dietary lipids influence both barrier integrity and immune homeostasis. Western dietary patterns, which are typically rich in saturated fatty acids (SFAs) and n-6 PUFAs, have been associated with increased intestinal permeability and metabolic endotoxemia (Konjar et al., 2025). These alterations may facilitate the translocation of lipopolysaccharides (LPS) from the gut lumen into the systemic circulation, promoting the activation of inflammatory pathways through TLR4-mediated signaling. As a consequence, the expression of tight junction proteins, including zonula occludens-1 (ZO-1) and occludin, may be reduced, contributing to impaired epithelial barrier function and the development of chronic low-grade inflammation (Guo et al., 2013).

Conversely, several lipid classes contribute to the maintenance of intestinal homeostasis. Among these, bioactive sphingolipids, including sphingomyelin and gangliosides, are important structural components of the apical membrane and can limit pathogen adhesion by acting as competitive binding sites at the epithelial surface (Rohrhofer et al., 2021). Altered ceramide and glycosphingolipid metabolism has been reported in IBD, underscoring the importance of endogenous sphingolipid homeostasis in intestinal inflammation. Dietary sphingolipids may additionally influence the intestinal environment through their luminal digestion products and interactions with the microbiota, although these mechanisms should be distinguished from the function of endogenous epithelial sphingolipid pools (Hussain et al., 2019).

The protective effects of dietary lipids also involve interactions with the gut microbiota. In particular, n-3 PUFAs such as EPA and DHA have been associated with an increased abundance of beneficial bacterial species, including *Akkermansia muciniphila*, and enhanced production of short-chain fatty acids (SCFAs) (Bellenger et al., 2019). Among SCFAs, butyrate plays a central role in maintaining epithelial barrier function by promoting tight junction assembly and reducing intestinal permeability (Canani et al., 2011). In addition, dietary lipids directly contribute to immune regulation. Long-chain n-3 PUFAs and MUFAs, such as oleic acid, are recognized for their anti-inflammatory properties. By modulating membrane composition and inflammatory signaling pathways, these lipids contribute to the attenuation of immune activation and the maintenance of immune homeostasis (Tosti et al., 2018). Their incorporation into membrane phospholipids also limits arachidonic acid-derived eicosanoid production, reducing the generation of pro-inflammatory mediators. Collectively, these findings highlight the multifaceted role of dietary lipids in shaping the gut barrier, host–microbiota interactions, and immune responses, reinforcing their importance in gastrointestinal and systemic health.

Cardiovascular and Metabolic Health. The relationship between dietary lipids and cardiometabolic health is increasingly interpreted through the "food matrix" concept. The stereospecific distribution of fatty acids within triacylglycerols contributes to their metabolic effects. During digestion, pancreatic lipase preferentially hydrolyzes ester bonds at the *sn*-1 and *sn*-3 positions, preserving the fatty acid esterified at the *sn*-2 position. TAGs sharing similar fatty acid compositions may exert different physiological effects depending on the positional arrangement of fatty acids. This aspect is particularly important in dairy lipids and human milk, where palmitic acid is predominantly esterified at the *sn*-2 position, favoring intestinal absorption and calcium utilization in infants. Conversely, when palmitic acid is located at the *sn*-1 and *sn*-3 positions, as commonly observed in vegetable oils, its digestion releases free palmitic acid, which may form insoluble calcium soaps and reduce lipid and mineral absorption (Lien, 1994).

TAGs enriched in long-chain n-3 PUFA, particularly EPA and DHA, have been associated with reduced inflammatory responses and improved cardiovascular health through modulation of eicosanoid synthesis, cytokine production, and membrane composition. EPA and DHA can also serve as precursors of specialized pro-resolving mediators, including resolvins and protectins, which contribute to the resolution of inflammation (Calder, 2017). In contrast, excessive intake of TAGs enriched in certain long-chain saturated fatty acids, particularly palmitic acid, has been associated with altered lipid metabolism, increased LDL cholesterol levels, and enhanced cardiometabolic risk, although these effects appear to be strongly influenced by food matrix and overall dietary context (Astrup et al., 2020).

In general, diet rich in saturated fatty acids (SFA), trans-fatty acids (TFA), and cholesterol, can contribute to cardiometabolic diseases by promoting white adipose tissue (WAT) dysfunction and chronic low-grade inflammation (Custers et al., 2022). Chronic expansion of WAT through hypertrophy and hyperplasia leads to the release of pro-inflammatory cytokines and FFA that activate the TLR4-CD14 system, contributing to metabolic endotoxemia and the progression of atherosclerosis.

In contrast, MUFAs and n-3 PUFAs exert well-established cardioprotective effects by suppressing pro-inflammatory genes and reducing visceral adiposity (Custers et al., 2022). Specifically, milk polar lipids and SM have demonstrated a clinical capacity to lower cholesterol absorption and reduce atherogenic lipoprotein markers (LDL-C and VLDL-C) by promoting a gut sphingomyelin-cholesterol interplay (Vors et al., 2020). Furthermore, the microbial metabolism of dietary precursors (e.g., choline and L-carnitine) can produce atherogenic trimethylamine N-oxide (TMAO), whereas the fermentation of fibers into short-chain fatty acids (SCFAs) like butyrate mitigates inflammation and reduces diastolic blood pressure (Simó & García-Cañas, 2020). Finally, at the endogenous level, targeted lipidomics studies have

identified specific circulating lipid species, including ceramides and certain sphingomyelins, as important mediators and biomarkers of cardiovascular disease (Gaggini & Vassalle, 2023).

Liver and Energy Metabolism. The liver plays a central role in the regulation of whole-body energy metabolism by coordinating lipid uptake, storage, oxidation, and export according to nutritional status. As the primary site for the processing of dietary lipids, it integrates signals from adipose tissue, skeletal muscle, and the gastrointestinal tract to maintain metabolic homeostasis, orchestrating the critical balance between de novo lipogenesis (DNL), fatty acid oxidation, and the secretion of very-low-density lipoproteins (VLDL) (Zou & Wang, 2023). Dietary patterns enriched in specific lipid classes can influence hepatic metabolic homeostasis, whereas excessive consumption of saturated fats and energy-dense diets promotes hepatic lipid accumulation, insulin resistance, and metabolic dysfunction (Custers et al., 2022). Mechanistically, SFAs promote lipotoxicity through TLR4 activation and the accumulation of bioactive ceramides, which impair Akt phosphorylation and activate hepatic stellate cells, thereby accelerating the progression from simple steatosis to fibrosis (Scorletti & Byrne, 2013). In contrast, EPA and DHA may improve hepatic lipid handling by downregulating key transcription factors such as SREBP-1c and ChREBP to inhibit DNL, while simultaneously upregulating PPARα to promote mitochondrial β-oxidation and autophagic degradation (Scorletti & Byrne, 2013). However, the clinical impact on serum liver enzymes (ALT/AST) remains inconsistent, highlighting a persistent translation gap and a need for standardized dosing in human trials (Parker et al., 2011). Furthermore, specialized dietary patterns modulate energy metabolism through distinct molecular sensors: the Mediterranean diet utilizes MUFAs and antioxidants to reduce reactive oxygen species (ROS) and stimulate autophagy, whereas the ketogenic diet leverages carbohydrate restriction to activate the AMPK and SIRT1 pathways, facilitating rapid lipolysis and ketogenesis to provide an alternative energy source for the brain (Zou & Wang, 2023). These findings demonstrate that liver function and energy metabolism are regulated by specific dietary lipid classes rather than by total fat intake alone. In this context, future metabolic health strategies must move toward a targeted lipidomics approaches that may help to identify endogenous lipid signatures associated with hepatic dysfunction and determine how these pools respond to specific dietary interventions (Gaggini & Vassalle, 2023).

Emerging Functions of Minor Dietary Lipids. Recent advances in food lipidomics revealed that several minor dietary lipid species, although present at low concentrations, can exert significant biological effects that exceed what would be expected based on their abundance alone. The discovery of Fatty Acid Esters of Hydroxy Fatty Acids (FAHFAs) as a novel class of bioactive lipids expanded the understanding of dietary lipids biological functions, shifting attention from the effects of bulk lipid classes toward specific molecular species capable of regulating metabolic and inflammatory pathways. FAHFAs, particularly palmitic acid esters of hydroxy stearic acids (PAHSAs), were first identified in mammalian adipose tissue and showed effective anti-inflammatory and insulin-sensitizing properties (Yore et al., 2014). Experimental studies demonstrated that PAHSAs can improve glucose homeostasis by stimulating insulin-dependent glucose uptake and promoting glucagon-like peptide-1 (GLP-1) secretion through the activation of G-protein-coupled receptors, including GPR120 and GPR40 (Syed et al., 2018). Although FAHFAs are endogenously synthesized, recent evidence demonstrated that their biosynthesis can be catalyzed by adipose triglyceride lipase (ATGL) through a transacylation reaction (Patel et al., 2022), their levels are critically responsive to dietary intake. Although FAHFAs have been identified in a variety of commonly consumed foods, including meat, milk, eggs, mushrooms, and cereals, they are generally present at relatively low concentrations, typically ranging from 45 to 320 ng/g of fresh weight (Zhu et al., 2020). Recent lipidomic investigations expanded the occurrence of FAHFAs to plant-derived foods. Notably, cold-pressed hemp seed oil contains several linoleic acid-derived FAHFAs (Manis et al., 2025), and these bioactive lipids have also been reported in microalgae (Casula, Manis, et al., 2024). Given the increasing interest in plant-based diets and algae-derived superfoods as sustainable sources of bioactive compounds, these findings suggest that non-animal foods may represent additional potential dietary sources of FAHFAs. Nevertheless, their absorption, bioavailability, and metabolic fate in humans remain largely unexplored.

7. Precision nutrition

The integration of food lipidomics with human lipidomics and metabolomics offers a potential framework for moving from population-based dietary recommendations toward more individualized strategies. Substantial interindividual variability has been observed in postprandial responses to identical meals, particularly in circulating triglycerides, indicating that the metabolic consequences of dietary lipid exposure cannot be predicted solely from food composition (S. E. Berry et al., 2020). As discussed above, dietary lipid species undergo extensive digestion, absorption, and metabolic remodeling, and their physiological effects therefore depend not only on their abundance and molecular structure in foods but also on the metabolic phenotype of the individual. Consequently, integrating the molecular characterization of food lipids with individual lipidomic and metabolomic profiles could help identify metabolic phenotypes associated with differential responses to dietary fat quality and support the development of more individualized dietary strategies. Recent lipidomic studies provide initial support for this concept. Lipidomic profiling of controlled dietary interventions has shown that replacing saturated with unsaturated dietary fats induces coordinated changes across multiple circulating lipid species. In particular, Eichelmann et al. (2024) developed a multilipid score reflecting the lipidomic response to improved dietary fat quality and showed that this lipid signature was associated with lower cardiometabolic risk across independent cohorts (Eichelmann et al., 2024). These findings illustrate how lipidomics can provide an intermediate molecular phenotype linking dietary fat quality with metabolic response and may ultimately contribute to identifying individuals who could benefit from specific modifications in dietary lipid intake.

Nevertheless, translating lipidomic information into individualized dietary recommendations remains challenging. Circulating lipid profiles reflect the combined influence of dietary exposure and endogenous metabolism and are additionally affected by genetic background, gut microbiota, metabolic status, lifestyle, and environmental factors. Moreover, differences in analytical platforms, lipid annotation, data processing, and study design currently limit comparability across lipidomic studies. Most importantly, prospective intervention studies demonstrating that dietary recommendations guided by individual lipidomic profiles provide greater long-term clinical benefit than conventional dietary approaches remain scarce. Thus, lipidomics currently represents a promising tool for metabolic phenotyping and individual stratification rather than an established basis for routine personalized dietary prescription.

8. Conclusions and future perspectives

Dietary lipids comprise a remarkably diverse group of molecules that extend far beyond their traditional role as energy sources. Advances in analytical technologies, particularly lipidomics, revealed the extensive food lipids structural complexity and highlighted how differences in lipid class, molecular composition, and supramolecular organization can significantly influence their biological properties. As discussed throughout this review, dietary lipids are unevenly distributed among food matrices and are continuously modified by processing, fermentation, and storage, generating dynamic lipid profiles that ultimately affect their nutritional value and physiological effects.

Importantly, the physiological effects of dietary lipids are determined by the interplay between lipid composition and food matrix

structure. The lipids physicochemical organization within foods influences digestion, bioaccessibility, and absorption, thereby modulating the bioactive lipid species availability and their interactions with metabolic pathways. Growing evidence demonstrates that individual lipid classes, including phospholipids, sphingolipids, fatty acid esters of hydroxy fatty acids (FAHFAs), and other minor lipid species, exert distinct organ-specific functions contributing to the regulation of neural, cardiovascular, gastrointestinal, immune, and metabolic health.

The increasing application of lipidomics is shifting nutritional research from a quantitative focus on total fat intake toward a molecular understanding that recognizes the biological relevance of specific lipid species. In this context, food lipidomics emerge as a powerful tool for characterizing food composition, identifying novel bioactive lipids, and elucidating the mechanisms linking dietary lipids to health outcomes.

Future advances integrating food lipidomics with human metabolomics, nutrigenomics, and microbiome research are expected to provide a more comprehensive understanding of individual responses to dietary lipids, providing bases for personalized dietary interventions tailored to individual metabolic profiles and health needs. Such advances may ultimately support the development of more targeted nutritional strategies and contribute to the transition toward precision nutrition and preventive healthcare. Ultimately, a deeper knowledge of lipid molecular diversity and food matrix effects will contribute to the development of next-generation dietary recommendations based not only on lipid quantity, but also on lipid quality, functionality, and biological activity.

Author contributions

Cristina Manis: Conceptualization, Methodology, Validation, Visualization, Writing – original draft, Writing – review and editing.

Mattia Casula: Writing – original draft, Writing – review and editing.

Pierluigi Caboni: Supervision, Visualization, Writing – original draft, Writing – review and editing.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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