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Absorption and distribution of dietary fatty acids from different sources

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Abstract

Lipids have physical, chemical, and physiological properties that make them important factors in human nutrition. They form a group of compounds of varied chemical nature that have the common property of being soluble in organic solvents but insoluble in water. This basic property affects their digestion, absorption, and transport in the blood and metabolism at cellular level. Firstly, fatty-acid chain length and number of double bonds influence fat absorption. Thus, medium-chain fatty acids (MCFA) are better absorbed than long-chain fatty acids. Secondly, the positional distribution of fatty acids (FA) in dietary triglycerides (TG) determine whether FA are absorbed as 2-monoglycerides (2-MG) or free fatty acids (FFA), and hence, influences the composition of chylomicroms (CM) because triglycerides (TG) are resyntethysed in the intestinal mucosa using 2-MG from dietary lipids. Generally, the absorption of FA in the *sn*-2 position of TG is favored, whereas no specificity has been found for the fatty acids in the *sn*-1 and *sn*-3 positions. Finally, some FA of nutritional interest, namely, long-chain polyunsaturated fatty acids (LCP), are present in dietary lipid sources as both TG or phospholipids (PL). Fatty acids esterified as PL or TG may show different availability. In fact, some authors have suggested a better absorption of LCP-PL. Moreover, dietary LCP in form of TG or PL differently affects the composition of HDL and LDL PL.

Keywords: Long-chain polyunsaturated fatty acids; Palmitic acid; Structuted triglycerides; Phospholipids; Fat absorption; Lipoproteins

Abbreviations: CM, Chylomicroms; FA, Fatty acids; FFA, Free fatty acids; LCP, Long-chain polyunsaturated fatty acids; MCFA, Medium-chain fatty acids; 2-MG, 2-Monoglycerides; PL, Phospholipids; TG, Triglycerides.

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1. Introduction

Fatty-acid chain length and unsaturation number influence fat absorption. It is well known that medium-chain fatty acids (MCFA) are better absorbed than longer fatty acids because they can be solubilized in the aqueous phase of the intestinal contents, absorbed bound to albumin and transported to the liver by the portal vein [1]. Moreover, dietary triglyceride structure influences the bioavailability of its component fatty acids (FA). Fat from human milk is better absorbed than that from infant formulas partly due to the presence of palmitic acid in the *sn*-2 position of glycerol backbone [2].

Finally, dietary fat is mainly composed of triglycerides (TG), on a small proportion is contributed by phospholipids (PL) (3–6%) [3]. However, some important FA can be provided by the diet esterified to PL. In recent years, there has been an increasing awareness that long-chain polyunsaturated fatty acids (LCP) may be conditionally essential for preterm infants. Some studies have shown an association between dietary LCP and visual development [4]. A number of polyunsaturated dietary lipid sources are currently available for supplementing infant formulas with LCP, namely: egg yolk lipids, fish oils, and oils from unicellular organisms (fungi and algae). These lipid sources differ in their structure (TG or PL, position of FA in their backbone), FA composition and presence of other components. These differences may affect the absorption, distribution and tissue uptake of these important FA.

2. Mechanism of fat digestion and absorption

The first step of fat digestion occurs in the stomach and is catalyzed by lingual or gastric lipase [3]. These enzymes are similar in structure and characteristics, but differ in origin among species, which is either oral (pregastric esterase in ruminants and lingual lipase mainly in rodents), or gastric lipase (rabbit, dog, guinea pig, human) [5,6]. The major digestion products of this gastric phase are diacylglycerol and free fatty acids (FFA) [3], which facilitate the intestinal phase of digestion acting as emulsifying agents [8]. Pancreatic lipase cleaves the *sn*-1 and *sn*-3 position of TG yielding to 2-monoglycerides (2-MG) and FFA [9]. Pancreatic cholesterol esters hydrolase completely hydrolyzes cholesterol esters into FFA and free cholesterol [9]. Dietary phospholipids are hydrolyzed by activated pancreatic phospholipase A_2 yielding to 1-lysophospholipids and FFA [9]. Pancreatic lipase is relatively inefficient in digesting marine oils and arachidonic acid-containing TG [10]. Cholesterol ester hydrolase may also play a role in the digestion of triglycerides that contain LCP [9]. Bile-salt stimulated lipase from human milk plays an important role in the TG digestion in breast-fed infants [14]. It is an unespecific enzyme, and, unlike gastric and pancreatic lipase, leads to the complete hydrolysis of TG [11]. In addition, it is of importance for the efficient use of human milk LCP [12].

Ionized FFA and 2-MG enter into bile micelles, to form with phospholipids, mixed micelles which help apolar lipids to go thought the unstirred water layer and reach the microvillous membrane where they are absorbed. Absorbed lipids are re-esterified to newly form TG and PL in the smooth endoplasmic reticulum. Triglycerides can be

synthesized via 2-MG or via 3-glycerol-phosphate, although in the fed state the 2-MG pathway predominates [11]. Triglycerides, PL, cholesterol and apoproteins are used to synthesize chylomicroms (CM), which are secreted to the lymph, and then to the general blood stream through the thoracic duct. In the peripheric tissues, they are cleaved by lipoprotein lipase losing TG and giving CM remnant. Chylomicrom remnants interchange components with other plasma lipoproteins and finally, are taken up by the liver.

2.1. Effects of fatty acid chain length and saturation

Unsaturated fatty acids and MCFA are more efficiently absorbed than long-chain saturated fatty acids. Because of the way that MCFA are digested, they can be absorbed in the stomach, after hydrolysis of MCT by gastric lipase [15], and can also be solubilized in the aqueous phase of the intestinal contents, where they are absorbed bound to albumin and transported to the liver via the portal vein [1]. For these reasons, medium-chain TG has been used as an energy source in syndromes having pancreatic-enzyme deficiency such as cystic fibrosis [7].

With increasing chain lengths of saturated fatty acids, an increasing proportion is absorbed into the lymphatic pathway and a decreasing proportion is absorbed by way of the portal venous blood [3]. There is some limited evidence that a substantial amount (over 50%) of infused linoleic and linolenic acids bypass the lymphatic pathway [3]. An important proportion of LCP might pass through the enterocyte cytosol and go directly to the portal venous flow [3]. However, some studies have reported lymphatic transport of 20:5$n-3$ and 22:6$n-3$ [15,16], although this pathway may depend on the position to which those FA are esterified in the TG molecule.

3. Effect of dietary lipid structure

The positional distribution of FA in dietary TG determined whether FA are absorbed as 2-MG or FFA, and hence, influences the composition of the newly formed CM because triglycerides are resyntethysed in the intestinal mucosa using 2-MG from dietary lipids. However, little specificity is shown towards the unesterified FA that are re-esterified to the *sn*-1 and *sn*-3 positions [13].

Long-chain saturated fatty acids such as 16:0 are not well absorbed from the lumen as FFA, because of its melting point substantially above body temperatures and because of a strong tendency to form insoluble calcium soap with divalent cations at the alkaline pH of the small intestine [2]. Palm oil and its derivatives are used mixed with other vegetable oils to increase the content of 16:0 in infant formulas up to the percentage found in human milk. However, infants fed formulas containing 50% of total fat as palm olein showed a lower fat and calcium absorption than infants fed a soy-based formula [17].

The use of dietary TG with 16:0 mainly in the *sn*-2 position (obtained by enzymatic interesterification) has highlighted the importance of FA positional distribution and *sn*-2 position of TG on fat absorption both in experimental animals and in newborn infants

[18–22]. Moreover, The presence of 16:0 in the *sn*-2 position may influence the composition and size of CM after the digestion process and also the metabolism of cholesterol esters and LCP [21,23].

Likewise, the position of LCP in the lipid structure influences their absorption and metabolism. Most of the LCP-enriched fats have a characteristic fatty acid composition and distribution. By means of enzymatic analyses we have found that 21% of 20:4$n-6$ and more than 50% of total 22:6$n-3$ were located at the *sn*-2 position of glycerol in fungal and tuna TG, respectively. Moreover, 22:6$n-3$ was mainly esterified to the *sn*-2 position of PE fraction in egg phospholipids [24].

Christensen et al. [15] have reported that the absorption of 20:5$n-3$ and 22:6$n-3$ was higher when those FA where predominantly in the *sn*-2 position than when they were distributed at random between the three positions of TG molecule. Furthermore, the incorporation of both FA into lipids of plasma lipoprotein fractions was related to their distribution between the inner and outer positions of TG [25].

Structured TG provide new possibilities for designing special lipids with particular purposes in human nutrition. Triglycerides containing MCFA in the *sn*-1 and *sn*-3 positions and essential fatty acids or LCP in the *sn*-2 of the same TG molecule can be used in malabsorption and cystic fibrosis syndromes providing energy as well as essential fatty acids in a more absorbable manner [7].

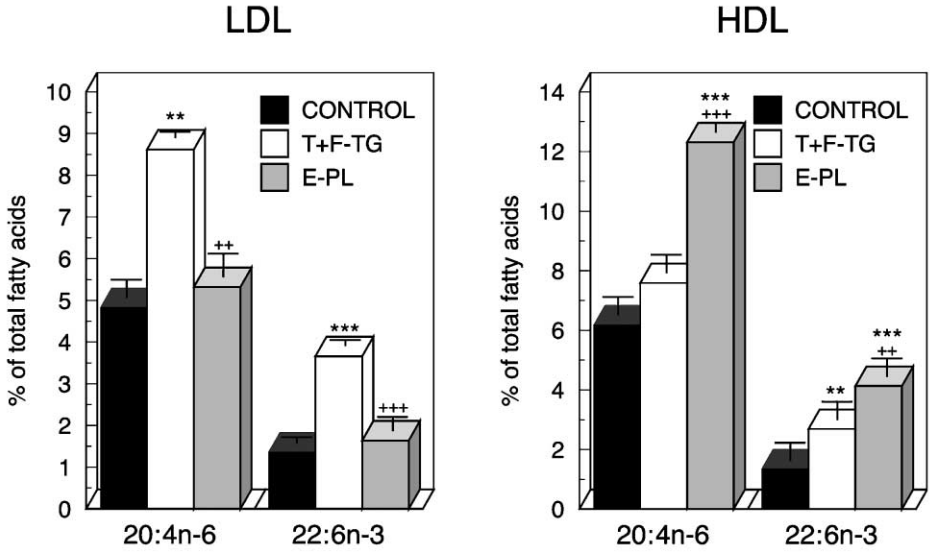

Fig. 1. Percentage of arachidonic and docosahexaenoic acids in LDL and HDL phospholipids in lactating piglets fed for 4 weeks a control diet without LCP, a diet with LCP from tuna and fungal triglycerides (T + F-TG) or a diet with LCP from egg yolk phospholipids (E-PL). $^{**}p<0.01$, $^{***}p<0.001$ vs. the control group. $^{++}p<0.01$, $^{+++}p<0.001$ vs. the T + F-TG.

4. Effect of the chemical form of lipids

The mechanism of TG digestion and absorption has been well studied. However, little attention has been paid to the processes affecting dietary PL because they are minor component of the diet. As explained above, TG and PL yield to different products at the intestinal level. Moreover, PL contains a phosphate group and a nitrogen base that may interact in several metabolic pathways [26].

On the other hand, some studies in newborn infants have indicated that dietary PL may be better absorbed than TG and thus, may enhance total fat absorption. Morgan et al. [27] found that fat absorption was higher in term infant fed a formula containing LCP from egg yolk PL than in those fed a standard formula without LCP. Carnielli et al. [28] studied a group of preterm infants fed preterm breast milk, a group fed a formula without LCP, a group fed a formula with LCP from egg yolk PL and a group of infants fed a formula with LCP from TG from unicellular microorganisms. The absorption of 22:6$n-3$ was higher in the infants receiving the PL-LCP formula than in infants receiving breast milk or the TG-LCP formula.

Finally, dietary PL may affect the composition and metabolism of lipoproteins. It has been reported that lipoproteins secreted by the rat small intestine after the infusion of triolein were CM, whereas those secreted after egg PL infusion were VLDL-size particles [29]. We have recently found that piglets fed a LCP-TG formula had higher LCP content in LDL phospholipids than those fed the same formula with LCP-PL. The opposite results were found in HDL phospholipids, indicating that dietary LCP in form of TG or PL differently affect the composition of HDL and LDL phospholipids [30] (Fig. 1).

5. Conclusion

Lipid sources of similar fatty acid composition might not be biologically equivalent because of the structural characteristics of the lipids they contain. This property may be useful for designing new fat blends for particular purposes in infant nutrition. Further studies to elucidate the biological responses to different lipid sources of similar fatty acid composition are needed to shed more light on this intriguing question.

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