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## Vegetable lecithins: A review of their compositional diversity, impact on lipid metabolism and potential in cardiometabolic disease prevention

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2 **Vegetable lecithins: a review of their compositional**  
3 **diversity, impact on lipid metabolism and**  
4 **potential in cardiometabolic disease prevention**

5  
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17  
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28 read and approved the final manuscript.

29 **Highlights**

- 30 • Vegetable lecithins possess an immense compositional diversity arising from **genetic,**  
31 **agronomical and processing factors**, which grants them with a wide range of  
32 biochemical and physiological properties
- 33 • There is an evident lack of data concerning the impact of vegetable lecithins other than  
34 soybean on lipid metabolism and metabolic health
- 35 • Despite controversial data on lipid absorption specifically, there is substantial evidence  
36 that vegetable lecithins are capable of modulating lipoprotein metabolism, decreasing  
37 hepatic lipogenesis and blood cholesterol levels, as well as delivering specific fatty acids  
38 to target tissues
- 39 • Their pleiotropic physiological effects imply that vegetable lecithins may act as  
40 potential preventive or therapeutic agents for cardiometabolic diseases  
41

42 **ABSTRACT**

43 Vegetable lecithins, widely used in the food industry as emulsifiers, are a mixture of naturally  
44 occurring lipids containing more than 50% of phospholipids (PL). PL exert numerous important  
45 physiological effects. Their amphiphilic nature notably enables them to stabilize endogenous  
46 lipid droplets, conferring them an important role in lipoprotein transport, functionality and  
47 metabolism. **In addition, beneficial** effects of dietary lecithin on metabolic disorders have been  
48 reported since the 1990s. This review attempts to summarize the effects of various vegetable  
49 lecithins on lipid and lipoprotein metabolism, **as** well as their potential application in the  
50 treatment of dyslipidemia associated with metabolic disorders.

51 Despite controversial data concerning the impact of vegetable lecithins on lipid digestion  
52 and intestinal absorption, the beneficial effect of lecithin supplementation on plasma and  
53 hepatic lipoprotein and cholesterol levels is unequivocal. This is especially true in  
54 hyperlipidemic patients. Furthermore, the immense compositional diversity of vegetable  
55 lecithins endows them with a vast range of biochemical and biological properties, which remain  
56 to be explored in detail. Data on the effects of vegetable lecithins alternative to soybean, **both**  
57 **as supplements and as ingredients**, is undoubtedly lacking. Given the exponential demand for  
58 vegetable products alternative to those of animal origin, it is of primordial importance that  
59 future research **is** undertaken in order to elucidate the mechanisms by which individual fatty  
60 acids and PL from various vegetable lecithins modulate lipid metabolism. The extent to which  
61 they may influence parameters associated with metabolic disorders, such as intestinal integrity,  
62 low-grade inflammation and gut microbiota must also be assessed.

63

64 **Keywords:** *Lecithin, vegetal phospholipid, food additive, lipoprotein, metabolic diseases*

## 65 **1. Introduction**

66

67 Food additives represent an increasingly growing market within the food industry, estimated  
68 to reach USD 25 billion by 2024 in Europe only [1]. In response to this and due to a rise in  
69 consumer awareness regarding health consciousness, food additives are under intense scrutiny  
70 and are constantly being assessed and revised for health concerns. Concomitantly, the demand  
71 for natural products has increased dramatically. Lecithin, commonly used in the food industry  
72 under the number E322 for their emulsifying and stabilizing properties, are a mixture of  
73 naturally occurring lipids containing more than 50% of phospholipids (cf. section 2 for official  
74 definition). Phospholipids, as major constituents of cell membranes in ubiquitous tissues,  
75 components of bile, and active messengers involved in cell signal transduction, exert numerous  
76 important physiological effects. They enable the micellar solubilisation of lipids in the lumen  
77 and hence facilitate lipid hydrolysis and absorption within the enterocyte. Their amphiphilic  
78 nature makes them important components of the coat of lipid droplets and lipoproteins,  
79 attributing them an important role in lipid transport and metabolism. In this way, they have been  
80 shown to modulate lipoprotein metabolism, decrease cholesterol levels and exert beneficial  
81 effects on hepatic function. These pleiotropic beneficial health effects have generated much  
82 interest and many studies have investigated the potential role of lecithins in the prevention  
83 and/or treatment of metabolic diseases. A growing interest in marine PL has appeared in the  
84 last few years, which has yielded promising results regarding the effects of lecithin of marine  
85 origin on metabolic health (as reviewed by Lordan et al. [2]). But data is still lacking when it  
86 comes to vegetable lecithin. We have found no systematic review that effectively resumes and  
87 concludes on the effects of vegetable lecithin on lipid metabolism and their potential role in  
88 metabolic disorder prevention. With an expanding need to restrain from animal and marine  
89 sourced ingredients, vegetable products are expected to explode on the food market and it is  
90 crucial that their nutritional, bioactive properties are known. This mini-review will hence  
91 attempt to gather the existing literature and succinctly conclude on the role of lecithin of  
92 vegetable origin on fatty acid bioavailability and metabolism.

## 93 2. Dietary vegetable lecithins: major sources and composition

94 The term lecithin must first be clearly defined. Many studies, especially within the field of  
95 medicine, have used the terms “lecithin” and “phosphatidylcholine” (PC) interchangeably [3].  
96 In this review, the term lecithin refers to the mixture of lipids composed predominantly of  
97 phospholipids (>50%) derived from animal or vegetable origin. This is in agreement with the  
98 definition reported in the *Codex Alimentarius* presented by FAO/WHO and by EFSA [4].  
99 Conversely, PC refers to a glycerophospholipid composed of a phosphatidic acid linked to a  
100 choline polar head group by a phosphoester bond.

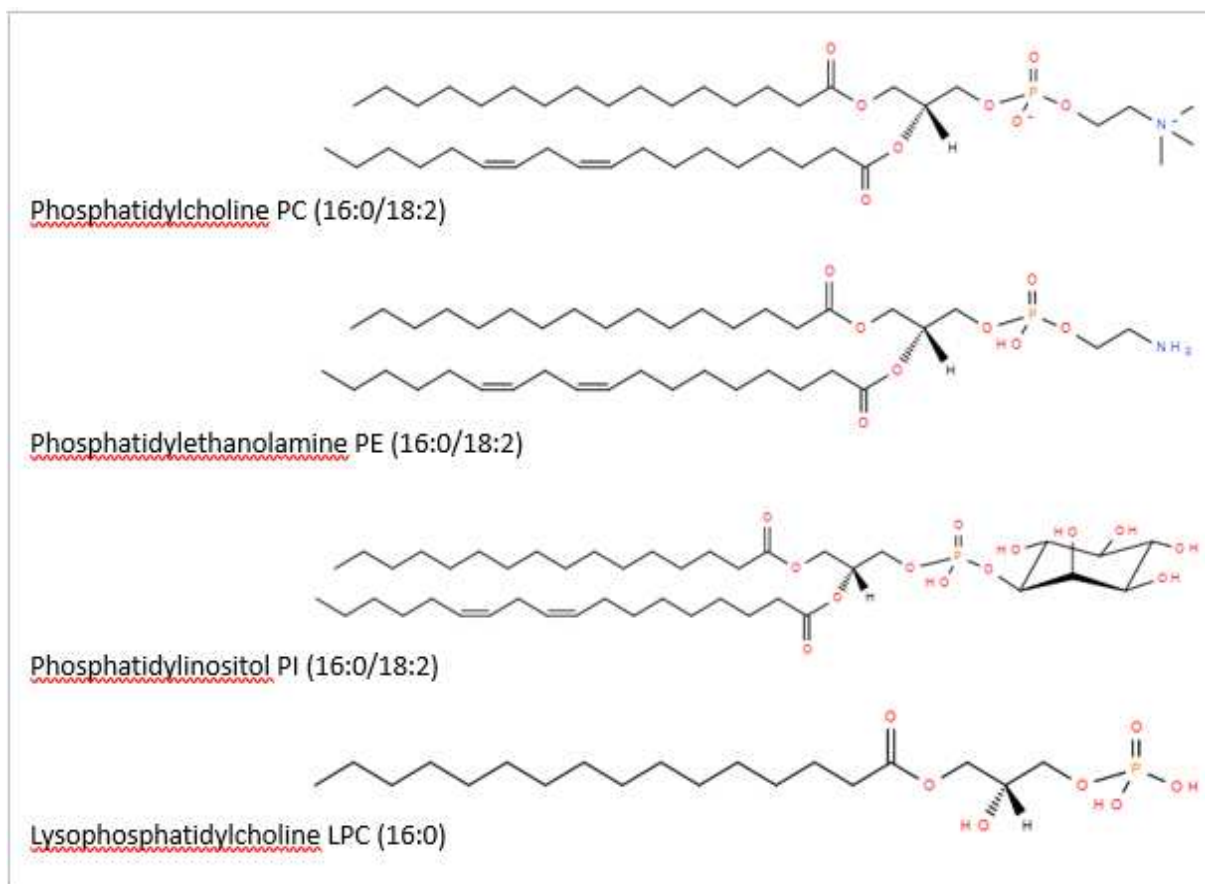
### 101 2.1. Dietary lecithin composition and structure

102 Lipids represent an extremely vast range of molecules with diverse structures and functions.  
103 While the majority of dietary lipids are present as triacylglycerols (TAG), PL account for 3-6%  
104 of total lipid intake [5]. **Indeed**, PL are ubiquitous components of biological membranes, and as  
105 such, are present in foods of animal, marine and vegetable origin. Commercial lecithin may  
106 thus be obtained from a wide range of sources, the most common being eggs, milk, fish or oil-  
107 bearing seeds (notably soybean).

108 PL are made up of a hydrophobic tail consisting of two fatty acid chains esterified at the *sn*-  
109 1 and *sn*-2 positions of a glycerol moiety, to which a phosphate group with a hydrophilic residue  
110 is attached at the *sn*-3 position. The *sn*-2 position of PL usually carries an unsaturated fatty acid,  
111 such as oleic acid, linoleic acid or alpha-linolenic acid, whereas a saturated fatty acid typically  
112 occupies the *sn*-1 position [2]. This is only true however when concentrations of unsaturated  
113 fatty acids are high. When these concentrations are low, unsaturated fatty acids are equally  
114 distributed between the *sn*-1 and *sn*-2 positions [6]. **This non-random regiodistribution of fatty**  
115 **acids in PL is seemingly similar amongst vegetal and animal species, and may result from the**  
116 **intrinsic properties of the enzymes involved in the synthesis pathway for PL in eukaryotes, the**  
117 **so-called “Kennedy pathway”. Indeed, the acyltransferase involved in the esterification of the**  
118 **glycerol backbone at the *sn*-1 position tends to favour saturated fatty acids, whereas that**  
119 **involved in the succeeding esterification at the *sn*-2 position preferentially binds unsaturated**  
120 **fatty acids [7]. The fatty acid moiety at the *sn*-2 position of vegetal PL may further be modified**  
121 **by the Land’s cycle [8]. Enzymes involved in this cycle (notably lysophospholipid**  
122 **acetyltransferases and phospholipases A<sub>2</sub>) also tend to favour PUFA as substrates [7]. This then**  
123 **results in the typical PL structure containing a saturated fatty acid at the *sn*-1 position and an**  
124 **unsaturated fatty acid at the *sn*-2 position.**

125 The most common bioactive PL in biological vegetable cells are phosphatidylcholine,  
 126 phosphatidylethanolamine (PE), phosphatidylinositol (PI) and phosphatidylserine (PS). While  
 127 animal cells also contain sphingomyelin (SM), a PL containing a choline head and a sphingosine  
 128 moiety instead of the glycerol backbone, it is absent in vegetable cells. Vegetable lecithin are  
 129 therefore devoid of SM. Vegetable lecithin may also contain lyso-phospholipids, which consist  
 130 of PL whose fatty acid chain has been **hydrolysed** at the *sn*-1 or the *sn*-2 position. Other lipids,  
 131 such as triacylglycerols, glycolipids and sterols, as well as liposoluble vitamins may be found  
 132 in negligible quantities in vegetable lecithin.

133



134 **Figure 1.** Structures of the major phospholipids found in soybean lecithin. Lipid structures were  
 135 drawn using LIPID MAPS tools.

136

## 137 2.2. Phospholipids: biological function

138 PL are essential components of all cellular and sub-cellular membranes, in association with  
 139 cholesterol, glycolipids and peripheral and integral proteins. The biological importance of PL  
 140 derives from their amphiphilic properties. They are **indeed** capable of forming selectively  
 141 permeable lipid bi-layers, which act as barriers between cells or organelles and their

142 surroundings. In doing so, they provide a unique, biologically rich environment, suitable for  
143 proteins and other bioactive compounds. Along with cholesterol, they are responsible for the  
144 formation of lipid rafts, which are involved in cell signalling and apoptosis. The inherent  
145 amphiphilic nature of PL additionally allows them to act as important constituents of the coat  
146 of lipid droplets and lipoproteins, attributing them an important role in lipid transport and  
147 metabolism. This intrinsic property endows PL with potent emulsifying capacities: **they are**  
148 **capable** of stabilising lipid droplets endogenously, but also within a food matrix, where they  
149 contribute to the texture and palatability of foods. Lecithin are consequently extremely  
150 widespread food emulsifiers: their market is projected to reach USD 350 million by 2024 [1].

151 In addition, PL, along with bile salts and cholesterol, enable the micellar solubilisation of  
152 lipids in the lumen and hence facilitate lipid hydrolysis and absorption of lipolysis products  
153 within the enterocyte. Certain PL also act as lipid mediators of inflammation or as secondary  
154 messengers in cell signaling. In this way, PL possess pleiotropic properties, which are, not least  
155 of all, dictated by their fatty acid composition. **Indeed**, the fatty acid composition of PL defines  
156 and determines its structural and functional properties [9]. The higher the degree of  
157 unsaturation, the less rigid its molecular structure will be and hence the more fluid the  
158 membrane. In this way, the ratio of saturated to unsaturated fatty acid in phospholipids has a  
159 direct impact on the functionality of the cellular membrane, lipid droplet or lipoprotein coat  
160 which they form. Consequently, cellular functions, as well as the activity of membrane bound  
161 enzymes, carriers and receptors may be modulated by dietary PL. In addition to their structural  
162 roles, as integral components of cell membranes, PL are also involved in cell signalling, as  
163 precursors of lipid mediators and are therefore essential for communication and interaction  
164 between the body cells.

165 In this way, PL participate in a variety of metabolic, neurological, and intracellular signalling  
166 processes [10] such as cell development, necrosis and apoptosis, transport, DNA replication,  
167 neuronal signalling, or secretion [11].

#### 168 **2.4. The compositional diversity of vegetable lecithins**

169 The lipid composition of PL membranes varies amongst tissues and organisms, and as such,  
170 the lipid composition of lecithin reflects that of its origin. Generally, the fatty acid composition  
171 of vegetable lecithin typically reflects that of the corresponding oil-bearing seed [12]. As a  
172 result, rapeseed lecithin, like rapeseed oil, generally possess high concentrations of mono-  
173 unsaturated fatty acids (MUFA), notably oleic acid, whereas soy lecithin contain a high  
174 proportion of n-6 polyunsaturated fatty acids (PUFA), most of which is represented by linoleic



175 acid. **Table 1** presents the typical phospholipid and fatty acid composition of soy, sunflower  
 176 and rapeseed lecithin. An early study has demonstrated that these fatty acids are equally  
 177 distributed amongst the different classes of PL (such as PC, PE, PI) within lecithin [6].

178

179 **Table 1.** Summarised data on phospholipid composition [4] and fatty acid composition [13] of  
 180 three liquid vegetable lecithins (soy, sunflower and rapeseed).

	Soy lecithin	Sunflower lecithin	Rapeseed lecithin
<b>Phospholipid composition (%) [4]</b>			
PC	12.69 – 16.7	14.34 – 17.23	16.74 – 18.18
PI	6.47 – 11.84	12.30 – 14.92	10.45 – 12.30
PE	6.45 – 13.57	4.85 – 6.82	6.46 – 8.03
PA	2.28 – 5.96	1.32 – 3.21	2.44 – 3.59
<b>Fatty acid composition (%) [13]</b>			
16:0	16	11	7
18:0	4	4	1
18:1	17	18	56
18:2	55	63	25
18:3	7	0	6
Others	1	4	5

181

182 The phospholipid and fatty acid profiles of lecithin also hugely depend on the agronomical,  
 183 genetic and environmental parameters of the seed crops they originate from [12]. Agronomical  
 184 conditions, such as storage and extraction conditions, have been shown to modulate the lipid  
 185 composition of vegetable lecithin [13]. Vegetable lecithin are by-products of the refining of oil.  
 186 They may be obtained via diverse extraction methods, such as **physical** or enzymatic  
 187 degumming. Canola lecithin obtained from enzymatic degumming demonstrated higher  
 188 emulsion stability than that derived from water degumming and this was attributed to the  
 189 phospholipid composition of the lecithin [14]. The **crop- or process-induced** variability within  
 190 one vegetable lecithin source may hence be higher than that between **lecithin** sources [13].  
 191 However, Nguyen et al. demonstrated via the use of biplots and principal component analysis  
 192 that, despite their heterogeneity, vegetable lecithins could be distinguished according to their  
 193 origin [12]. They found rapeseed lecithin to be the most different amongst soybean, sunflower  
 194 and rapeseed lecithin. In comparison to soy and sunflower lecithin, rapeseed lecithin tended to

195 possess the highest relative concentration of PC. Sunflower lecithin displayed the highest and  
196 lowest concentration of PI and PE respectively [6,12,15].

197 This composition data plays an important role, as the phospholipid composition of lecithin  
198 determines its emulsifying capacity. PC, which forms a lamellar layer at the lipid/water  
199 interface, and lysoPC, which engenders a hexagonal phase, promote oil-in-water emulsion  
200 stability, whereas PE (reverse hexagonal phase) facilitates water-in-oil emulsions [16]. **The  
201 amount of neutral lipids, such as TAG, present in lecithins also modulates emulsifying  
202 properties. Lecithins that have undergone a deoiling fractionation process and hence contain  
203 reduced neutral lipid concentrations, possess enhanced oil-in-water dispersion functionality  
204 [17].**

205 Furthermore, different lecithin from various sources (soy, rapeseed) or with **differing PL  
206 compositions have been reported to exert varying antioxidant properties [18]. PL may indeed  
207 act as antioxidative agents: they are able of chelating pro-oxidative metals, forming anti-  
208 oxidative Maillard reaction products, changing the location of primary antioxidants or  
209 regenerating primary antioxidants. These mechanisms are clearly summarised by Cui et Decker  
210 [19] and may be, in part, attributed to the negatively charged phosphate head group, which can  
211 bind pro-oxidative metals, thereby inhibiting lipid oxidation. The basic amino functions and  
212 intramolecular hydroxyl groups of the side-chain moieties of PL have also been reported to be  
213 implicated in such mechanisms [20]. However, the antioxidative activities of PL depend  
214 massively on the conditions and food matrices in which they are contained. In addition,  
215 processing conditions may further alter the antioxidant capacity of lecithin. It has been shown  
216 *in vitro* that rapeseed lecithin obtained via both chemical or water-degumming displayed higher  
217 antioxidant capacities than soy lecithin when associated with fish oil [21]. The presence of  
218 phenols, such as sinapic acid and canolol, in rapeseed lecithin appears to increase its antioxidant  
219 and ion-chelating capacities, most probably due to the synergism between phenols and  
220 phospholipids [22]. This synergistic effect has also been observed between quercetin and  
221 lecithin [23]. The role of individual fatty acids inherent to each vegetable lecithin must not be  
222 undermined with regards to the antioxidant activity of lecithin. N-3 PUFA such as  
223 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) possess higher antioxidant  
224 properties, for example, than saturated fatty acids. Extraction processing may also affect the  
225 oxidative stability of lecithins. The deoiling process of lecithin reduces significantly the content  
226 of phenolic compounds in rapeseed lecithin and consequently its antioxidant effect [18].**

227

## 228 **2.4. Socio-economic and environmental preoccupations concerning soy lecithin**

229 Soybean lecithin dominates over the vegetable lecithin market, representing more than 90%  
230 of available lecithin products [24]. With arising concerns about genetically modified organisms  
231 (GMOs) and awareness concerning environmental issues, there is an expanding demand/need  
232 for the development of alternative sources of vegetable lecithin. In Europe, the market for  
233 sunflower and rapeseed lecithin, which are locally produced, is increasing [13]. However, the  
234 majority of studies using vegetable lecithin have used soy lecithin and data concerning rapeseed  
235 or sunflower lecithin are lacking. The presence of concomitant compounds such as pollutants  
236 and phytoestrogens in soy lecithin must also be evaluated and subsequent impact on metabolic  
237 and intestinal health must be studied [25,26].

238

## 239 **3. Vegetable lecithins influence lipid digestion and intestinal absorption**

240 Vegetable lecithin provide food-derived PL with specific fatty acid profiles that, once  
241 incorporated in host membranes, have the potential to modulate membrane-dependant cellular  
242 functions. Whereas there is an expanding knowledge regarding the mechanisms by which PL  
243 are digested and absorbed, their incorporation into membranes *in vivo* and their ability to exert  
244 subsequent beneficial health effects remain to be elucidated.

245

### 246 **3.1 Digestion and intestinal absorption of dietary phospholipids**

247 Phospholipids, unlike TAG, are not hydrolysed by gastric lipases. Their digestion begins in  
248 the intestinal lumen, where they are readily hydrolysed by phospholipases A<sub>1</sub> (PLA<sub>1s</sub>) or  
249 phospholipases A<sub>2</sub> (PLA<sub>2s</sub>), which catalyze the hydrolysis of the ester bond of the acyl group  
250 at the *sn*-1 or the *sn*-2 position of the PL respectively, to produce one lyso-phospholipid  
251 (LysoPL) and a free fatty acid [27]. It has been demonstrated that other pancreatic enzymes,  
252 such as pancreatic lipase related protein 2 (PRLP2) and cholesterol ester hydrolase (CEL) also  
253 possess phospholipase activity of the PLA<sub>1</sub> type [28]. Inhibition of PLA<sub>2</sub> reduces fatty acid  
254 absorption in rats, suggesting the importance of this hydrolysis step in maintaining normal lipid  
255 absorption [29]. Nearly the entirety of dietary PL are absorbed (>90%) into enterocytes, where  
256 they are resynthesized, incorporated into the surface layer of chylomicrons (CM), and to a lesser  
257 extent, of **intestine-derived** very low density lipoproteins (VLDL) and liberated into the lymph  
258 to finally reach the systemic circulation [30]. In the bloodstream, CM are catabolised by  
259 lipoprotein lipase (LPL) which hydrolyses TAG contained within the core of CM and liberates  
260 free fatty acids, which are then available for uptake by receiving tissues. Once the TAG-rich  
261 lipoproteins such as CM are degraded by LPL, a part of the PL located on the CM interface is

262 hydrolysed by the endothelial lipase (EL), whose activity is similar to that of PLA1. The non-  
263 hydrolysed PL may be incorporated into high-density lipoprotein (HDL) fractions [31].  
264 Interestingly, certain studies carried out in human intestinal Caco2-cells [32] and rats [33] have  
265 demonstrated that a non-negligible amount of PL in the lumen is absorbed passively and  
266 preferentially integrated into HDL fractions already present in the intestine [30,34]. In this way,  
267 the fatty acid composition of dietary lecithin affects the composition of lipoproteins in the  
268 bloodstream, in turn influencing the lipid composition and functionality of the various receiving  
269 tissues. The efficiency of PL in delivering specific fatty acids has recently generated much  
270 interest, notably for their potential in increasing the bioavailability of fatty acids of nutritional  
271 importance. In the current context of the epidemic explosion of obesity and metabolic disorders,  
272 limiting the intake of total lipids while increasing that of essential fatty acids such as n-3 PUFAs  
273 has become one of the major challenges of nutrition scientists.

274

### 275 3. 2. PL vs TAG as vectors of fatty acids of nutritional importance

276 Growing evidence indicates beneficial biological activities of PL compared to that of dietary  
277 TAG [2,35]. Notably, there is a current explosion in the number of studies concerning marine  
278 PL as preferential vectors of the long chain n-3 PUFA (LC n-3PUFA), EPA and DHA. Burri et  
279 al concluded in his review on marine PL that research so far tended to indicate a higher  
280 bioavailability of n-3 PUFAs when they were incorporated into PL comparatively to TAG [34].  
281 A systematic review by Ulven also compared EPA and DHA bioavailability in PL-rich krill oil  
282 vs. TAG-rich fish oil in 14 studies [36]. They concluded that krill oil, rich in PL, presented a  
283 potential beneficial role compared to fish oil, but that more studies were required to certify this  
284 claim and to affirm positive effects on lipid metabolism. A study by [37] focused on  
285 lysophospholipids and demonstrated no differences in EPA and DHA bioavailability between  
286 TAG-bound or LysoPL-bound EPA and DHA in male Wistar rats. Although the effect of marine  
287 PL on lipid absorption are so far inconclusive, the efficiency with which these PL deliver  
288 specific fatty acids in receiving tissues is now recognised. For instance, studies have shown PL  
289 to be preferential carriers of DHA in the brain [38–40] and other tissues, such as liver, white  
290 adipose tissue and muscle [34] (cf. section 4.1 for further information and mechanisms).

291 Marine PL are not the subject of this review and readers curious to learn more may refer to  
292 the various reviews and studies listed above. Nonetheless, it could be extrapolated based on the  
293 plethora of evidence concerning marine PL that the bioavailability of FA present in vegetable  
294 lecithin would be increased comparatively to vegetable oil (TAG). But data concerning the  
295 optimal vectorization of typical vegetable fatty acids as either PL or TAG is lacking and more

296 research must be undertaken to study these differences. This is all the more necessary as  
297 vegetable lecithin, although devoid of LC n-3 PUFA, contain other fatty acids of nutritional  
298 importance. Rapeseed and, to a lesser extent, soybean lecithin, contain alpha-linolenic acid  
299 (ALA), an essential fatty acid and precursor of the LC n-3 PUFA, EPA and DHA. The intake of  
300 ALA is particularly important, as it may not be synthesised endogenously in humans. Its  
301 presence in human cells relies on its uptake from the diet. Oleic acid, another major fatty acid  
302 in vegetable lecithin, is one of the staple components of the Mediterranean diet, which is proven  
303 to be one of the most beneficial diets in terms of cardio-metabolic health. It is important to  
304 determine whether PL have the potential to increase the bioavailability of these fatty acids,  
305 comparatively to TAG.

306 Nonetheless, dietary lecithins have been shown to impact lipid metabolism in other ways than  
307 merely by delivering specific fatty acids. They have been reported to exert beneficial anti-  
308 dyslipidaemia effects by modulating postprandial lipid absorption and metabolism.

309

### 310 **3. 3. Impact on gastro-intestinal (GI) lipid digestion**

311 Lipid metabolism is a complex process that involves a number of succeeding steps.  
312 Phospholipids play an important role in lipid metabolism since its early stages: the micellar  
313 solubilisation of lipids in the lumen. Lipids are hydrophobic by definition and their transport  
314 across the intestinal lumen towards enterocytes relies on the addition of biliary lipids. Bile salts  
315 secreted into the small intestine form lipid micelles with dietary lipids capable of withstanding  
316 the hydrophilic conditions of the intestinal lumen. Bile salts are hence essential for lipid  
317 micellisation and digestion, and their absence has been shown to result in severe intestinal fat  
318 malabsorption [41]. Bile is naturally rich in PL and more specifically in PC, which represents  
319 more than 95% of biliary PL. In fact, the contribution of endogenous PC to bile is much higher  
320 (10-15 g/day) than that of dietary, exogenous PC (1-2 g/day) [42]. The intrinsic amphiphilic  
321 structure of biliary phospholipids enables them to stabilise lipid micelles in the lumen and their  
322 presence hence facilitates micellar lipid solubilisation, increasing the surface of lipid droplets  
323 required for hydrolysis by digestive enzymes and ultimately leading to a higher bioavailability  
324 of fatty acids for uptake by the enterocyte. This increase in lipid droplet dispersion has been  
325 suggested as a limiting step in lipolysis [43]. In this way, it is now widely acknowledged that  
326 the pre-emulsification process of an oil enhances the digestion of the fatty acids it contains [44–  
327 47]. According to *in vitro* and human studies, fine emulsions made up of small lipid droplets  
328 (~0,5µm) are more efficiently hydrolysed than those comprised of larger particles (>1.5µm)  
329 [48,49]. Lipid hydrolysis kinetics are not only affected by the size of lipid droplets, but also

330 largely depend on the nature of the surfactant molecule used to stabilise the lipid emulsion.  
331 Couëdelo et al. reported that soy lecithin-stabilised emulsions displayed higher lipolysis rates  
332 in an *in vitro* digestion model than those stabilised by either sodium caseinate or Tween 80 [50].  
333 This is in accordance with a previous study by Vors et al. comparing sodium caseinate-stabilised  
334 and soy lecithin-stabilised emulsions [51]. A study by Lecomte et al. however demonstrated an  
335 increase in lipid hydrolysis with milk PL comparatively to soy PL [50]. This could be attributed  
336 to the presence of SM, a characteristic dairy phospholipid absent in vegetable lecithin. The  
337 impact of emulsifier type on subsequent lipolysis kinetics are mainly due to physicochemical  
338 parameters. Different emulsifiers interact differently with bile salts, generating varying  
339 molecular assemblies at the interface of lipid micelles, which affect the ability of bile salts to  
340 remove fatty acids from lipid droplets [52]. Moreover, the nature of the emulsifier determines  
341 its ability to modulate the activity of lipolytic enzymes [53]. Early *in vitro* studies have  
342 demonstrated that bile PL exert a regulatory effect on the binding of lipases onto the surface of  
343 lipid droplets [54]. LysoPC exerts an inhibitory effect on pancreatic lipase-mediated hydrolysis,  
344 by reducing both substrate affinity and lipase activity, effect which is counterbalanced however  
345 by the presence of bile salts [55]. Gargouri et al. reported that vegetable lecithin, naturally rich  
346 in PC, is capable of increasing the activity of gastric lipase and, as such, may enhance lipolysis  
347 efficiency [56]. PL contained in vegetable lecithin differently modulate gastric lipase activity:  
348 lipid droplets coated with PC, PI or PS induce a higher activity of gastric lipase, compared to  
349 PE or SM [57]. Nonetheless, the mere presence of soy phospholipids without any emulsification  
350 process has also been shown to increase lipolysis rates. Lin et al. demonstrated via an *in vitro*  
351 digestion model that emulsification of algal oil with soy lecithin increased the initial lipolysis  
352 rate and DHA accessibility compared to that of bulk oil and to a non-emulsified mixture of  
353 similar composition containing soy lecithin [58]. However, the extent of lipolysis was similar  
354 between the bulk oil, the emulsified and the non-emulsified mixtures.

355 In this way, research so far demonstrated the efficiency by which soy lecithin impacts one  
356 of the initial steps of lipid metabolism: their solubilisation and hydrolysis in the lumen. Future  
357 research must be undertaken to study other sources of vegetable lecithin on such parameters.

358

### 359 **3. 4. Impact on intestinal lipid absorption**

360 Lipids released from lipid micelles at the unstirred layers of the brush-border membrane (pH  
361 gradient) are then absorbed by the intestinal microvilli of enterocytes via passive or active  
362 pathways. The hydrolysis products are then resynthesized into TAG and PL within enterocytes,  
363 and liberated into the lymph via CM and, to a lesser extent, VLDL particles.

364 Early research investigating the biological activities of lecithin on intestinal lipid absorption  
365 was carried out in the 1970s up to the end of the 1990s and focused mainly on the role of  
366 endogenous phosphatidylcholine. Studies undertaken in bile-diverted rats showed that  
367 endogenous PC is required for and enhances the intestinal absorption of lipids and their  
368 lymphatic transport [59,60]. **Indeed**, by providing the surface coats of CM, promoting  
369 apolipoprotein B48 (ApoB48) synthesis and maintaining adequate enterocyte membrane  
370 composition, biliary PL facilitate the transport of dietary lipids from the lumen into lymph [61].  
371 Importantly, small lipid droplets present a greater surface/core ratio than large lipid droplets  
372 and consequently require larger amounts of surface compounds such as PL. Consistently, it has  
373 been demonstrated that impaired biliary PL secretion in genetically modified rodents leads to  
374 delayed intestinal lipid absorption and engenders the secretion of significantly larger  
375 lipoproteins in lymph [61–63]. On the contrary, rodents with excess biliary PL secretion  
376 synthesize small CM particles [61]. This effect on lipoprotein size has major biological impacts.  
377 In effect, lipoprotein size and composition play an important role in the postprandial lipoprotein  
378 metabolism and TAG appearance in plasma [64]. **At similar lipid load**, smaller CM possess a  
379 lower affinity for LPL and their plasma clearance is considerably slower than that of larger  
380 lipoproteins [65].

381 Whereas endogenous PC enhances lipid intestinal absorption, the impact of dietary PC is  
382 much more controversial. Nakano et al. reported that oral administration of soybean lecithin  
383 and its hydrolysates promoted lymphatic TAG output in rats [66]. On the contrary, Davidson et  
384 al. reported that endogenous PC increased ApoB48 expression, but excess dietary PC did not  
385 enhance its expression any further [67]. A study by Sadouki and Bouchoucha demonstrated no  
386 difference in intestinal lipid absorption nor in fecal fatty acid excretion when 30% of lipids  
387 (4.5% of total diet) were replaced by lecithin compared to the control group in rats [68].  
388 Likewise, Sugasini et al. observed no statistical difference in lymphatic TAG or PL  
389 concentrations in rats fed linseed oil in its non-emulsified form or when it was emulsified by  
390 phospholipids or whey protein [69]. In this way, the addition of dietary PL at low PL/TAG ratios  
391 (1/16 – 1/7) in several studies did not generate an increase in lipid lymphatic output [70,71].  
392 However, Nishimikuai et al. demonstrated in two follow-up studies that supplementation with  
393 a high dose of soybean PC (PC/TAG with a 1/3 ratio) was capable of enhancing TAG absorption  
394 and output in lymph, as well as plasma TAG concentrations in rats [71]. The authors **concluded**  
395 that, based on their previous findings, this increase of TAG absorption by soybean PC must be  
396 due to an increase in CM secretion. Consistently, Couédelo et al. observed an increase in the  
397 mRNA expression of proteins involved in chylomicron secretion and exocytosis (Mttp, ApoB

398 and Sar1b) in the duodenum of rats fed linseed oil emulsified with soy lecithin compared to  
399 control rats (not gavaged), while rats fed linseed oil devoid of lecithin showed no difference in  
400 gene expression vs control rats [50]. Of note, although the expression of these genes were the  
401 highest in the soy lecithin group, there was no statistically significant difference between the  
402 oil and the oil+lecithin group. However, ApoB48 concentrations in the lymph were doubled in  
403 presence of soybean lecithin. Since each CM can only contain one Apob48 molecule, Apob48  
404 concentrations are recognised as accurate measures of CM quantity [50]. Hence, it may be  
405 concluded that soy lecithin increases the number of CM particles, leading to an increase in  
406 interfacial lipoprotein surface.

407 Altogether, studies concerning the effect of vegetable lecithin have yielded contradicting  
408 results and remain rather inconclusive. In addition, there is a debate on whether the effect of  
409 lecithin arises from PC or from its hydrolysed products. Nakano et al. demonstrated that LysoPC  
410 and not PC enhanced TAG lymphatic output [66]. This highlights the need for further research  
411 on the impact of vegetable lecithin and the role of their individual PL on lipid absorption. In  
412 addition, CM coats composed of PUFA-rich PL have been shown to be more effectively cleared  
413 from plasma than those composed of saturated fatty acids [63]. Vegetable lecithin, with their  
414 high content of PUFA, may therefore exert beneficial effects on lipid intestinal absorption,  
415 which may be of use in the prevention of metabolic disorders.

416 To specifically study lipid intestinal absorption and uptake into enterocytes, *in vitro* models  
417 using intestinal cells such as Caco-2 cells or lymph-cannulated animal models are required. The  
418 data thus obtained in lymph or in the culture media is a reflection of the absorption of dietary  
419 lipids, since these have not yet been subjected to hepatic metabolism and been diluted within  
420 the endogenous plasma pool.

421 However, unlike lymphatic lipids, the lipid profile of plasma is not merely defined by the  
422 lipids absorbed at the intestinal level, but is a reflection of whole body homeostasis resulting  
423 from the lipid metabolism of individual tissues. Determining the impact of vegetable lecithin  
424 on plasma lipemia is therefore crucial in order to grasp a complete understanding of the effect  
425 of vegetable lecithin on lipid metabolism and homeostasis.

426

## 427 **4. Vegetable lecithins impact lipid homeostasis**

### 428 **4. 1. Lecithins in the regulation of blood lipid profile**

429 The impact of vegetable lecithin on blood lipid profile has been demonstrated in several  
430 manners.



431 Firstly, the pre-emulsification of an oil with vegetable lecithin has been shown to increase  
432 the systemic bioavailability of certain fatty acids, without increasing total plasma lipid  
433 concentrations. In this way, Sugasini et al. observed no statistical difference in lymphatic TAG  
434 or PL concentrations in rats fed non-emulsified or PL-emulsified linseed oil, but reported higher  
435 plasma alpha-linolenic acid (ALA) concentrations in the PL-emulsified group [69]. Similar  
436 observations using flaxseed oil emulsions stabilised by soy lecithin were related by Couëdelo  
437 et al. [50]. Studies exploring the effect of vegetable lecithin supplementation on fatty acid  
438 bioavailability without pre-emulsification have generally led to the same conclusions. Geurden  
439 et al. demonstrated in carps that the combination of dietary PC and TAG enhanced postprandial  
440 plasma TAG concentrations, compared to TAG alone [72]. In rats, combined long-term  
441 supplementation of DHA-rich oils and deoiled soy lecithin promoted higher DHA and n-3  
442 PUFA concentrations in erythrocytes and plasma than either DHA or lecithin supplementation  
443 alone [73]. The authors suggest that the observations result from a synergistic effect of n-3  
444 PUFA and crude lecithin. The mechanisms behind this specific improvement of fatty acid  
445 bioavailability are not well understood and require further research, but synergistic effects  
446 between PUFA and PL seem plausible [2]. This may be explained by the impact that lecithins  
447 may on specific genes, such as FADS2 and PPAR $\gamma$  and fatty acid binding proteins, notably  
448 CD36 and FATP4 [42]. In addition, this may stem from the fact that fatty acids bound to PL are  
449 less prone to beta-oxidation, than when they are present as TAG, hence the n-3 and n-6 PUFA  
450 largely present in soybean, sunflower and rapeseed lecithin are more shielded from beta-  
451 oxidation than those contained in the respective vegetable oils.

452 Aside from their impact on systemic fatty acid bioavailability, vegetable lecithins have been  
453 shown to influence the plasmatic concentrations of other major lipid classes. Notably, PL exert  
454 hypocholesterolemic effects and supplementation with soybean PL in patients with primary  
455 hyperlipidemia has been reported to significantly reduce blood cholesterol levels [30]. In a  
456 study conducted in hypercholesterolemic rabbits, both purified soybean PC and non-purified  
457 soybean lecithin (containing 23% PC) significantly decreased plasma total and esterified  
458 cholesterol concentrations [74]. Wilson et al. also reported that soybean PC supplementation in  
459 hypercholesterolemic monkeys and hamsters enhances the cholesterol-lowering effects of a  
460 lipid-lowering diet, while maintaining plasmatic HDL levels [75]. In this way, dietary PC not  
461 only reduces blood cholesterol levels, but it also increases HDL cholesterol, subsequently  
462 reducing serum LDL/HDL ratio, a marker of metabolic syndrome [76]. In diabetic patients, it  
463 was observed that a 2-month supplementation of polyenylphosphatidylcholine (PPC) purified  
464 from soybean lecithin generated elevated HDL cholesterol and Apolipoprotein A-I levels in

465 plasma [77]. The increase in HDL following vegetable PL supplementation may be explained  
466 by the fact that PL are preferentially incorporated into HDL particles. Moreover, PL are  
467 substrates for lecithin-cholesterol acyl-transferase (LCAT), an enzyme which catalyzes the  
468 esterification of cholesterol, enabling the maturation of plasma HDL and consequently  
469 promoting cholesterol uptake from peripheral tissues by HDL particles [78]. Increase in Apo A-  
470 I also stimulates reverse cholesterol transport [79]. It has also been speculated that PL exert  
471 their hypocholesterolemic effect by reducing microsomal HMG-CoA reductase activity and  
472 increasing biliary cholesterol excretion [80]. In addition to their impact on enzyme activity and  
473 lipoprotein metabolism, vegetable PL promote fatty acid oxidation and impair the uptake of  
474 cholesterol by enterocytes [70]. PL are indeed capable of interacting with the membranes of  
475 enterocytes, thereby reducing their cholesterol binding capacity [81]. Some authors have  
476 reported that the degree of saturation and the length of fatty acids bound to PL control the  
477 quantity of cholesterol absorbed in the intestine. The higher the degree of saturation and the  
478 longer the chain length of the FA, the less cholesterol is absorbed [70,82,83]. One possible  
479 explanation for this finding is the fact that PL carrying saturated fatty acids are poor substrates  
480 for pPLA<sub>2</sub>, therefore hindering the enzyme from accessing the micellar lipids (formed mainly  
481 of cholesterol, mono- and diglycerides, and coated with saturated PL) and in consequence  
482 impairing the cholesterol uptake [70].

483 It must be noted however that these effects are mainly described under dyslipidemic conditions  
484 [30]. Whereas the cholesterol-lowering effects of lecithin are widely validated under  
485 dyslipidemic conditions and in hypercholesterolemic patients, they remain more controversial  
486 in normal lipidemic conditions [30,84]. In a scientific opinion report, the EFSA concluded that  
487 there was insufficient evidence to establish a cause and effect relationship between the  
488 consumption of soy PC and the maintenance of normal cholesterol levels in humans [85].  
489 Nonetheless, this concerns PC specifically and data have revealed a promising role of PE and  
490 PI as a lipid-lowering agents [86–88].

491 The same conclusion may be made concerning the effect of lecithin on triglyceride  
492 metabolism. Whereas certain studies affirm a hypotriglyceridemic effect of lecithin in plasma,  
493 this causal relationship is far from unequivocal. The lack of convergence of existing data may  
494 be explained by the diversity and specificity of the lipid metabolism of each tissue. Of these,  
495 the liver and adipose tissue are central organs in the regulation and maintenance of whole body  
496 lipid homeostasis; hence alterations of their lipid profile by dietary factors may have major  
497 impacts on lipid metabolism as a whole.

498

#### 499 4. 2. Impact on lipid metabolism in liver and adipose tissue

500 The liver plays a central role in lipid metabolism, hence investigating the impact of lecithin  
501 on this organ is crucial. The partial replacement of dietary TAG by vegetable, and more  
502 specifically soybean, lecithin has been associated with an amelioration of the lipid profiles in  
503 the liver and most importantly, a reduction of hepatic TAG levels [89–91]. Buang et al. reported  
504 that the replacement of 20% of TAG by PC with similar fatty acid composition in a rat model  
505 diminished hepatic TAG accumulation by two thirds through a simultaneous downregulation of  
506 *de novo* fatty acid synthesis (PAP and FAS mRNA expression) and upregulation of  
507 mitochondrial beta-oxidation in the liver [92]. Similarly, Rouyer et al. demonstrated in fasted  
508 re-fed rats that diets containing 4% of soybean or safflower phospholipids markedly decreased  
509 hepatic fatty acid synthase and malic enzyme activity and mRNA expression in comparison to  
510 diets containing soybean oil [93]. Hence, the beneficial physiological effects of vegetable  
511 lecithin seem to result, in part, from an inhibitory effect on the activity and gene expression of  
512 enzymes involved in fatty acid synthesis. In addition, soy lecithin is associated with reduced  
513 hepatic and VLDL cholesterol levels, similar to those previously described in plasma [81,89].  
514 Furthermore, PL metabolism in the liver plays an important role in hepatocyte lipid metabolism,  
515 as illustrated by the important role of LCAT and phospholipid transfer protein (PLTP) in hepatic  
516 lipid metabolism [94]. These enzymes are indeed modulated in NAFLD, leading to  
517 dyslipidaemia [95]. It may be extrapolated that PL imported via the intake of dietary lecithin  
518 modulate the activity of these enzymes, subsequently modulating hepatic lipid metabolism.  
519 This hypothesis deserve to be tested.

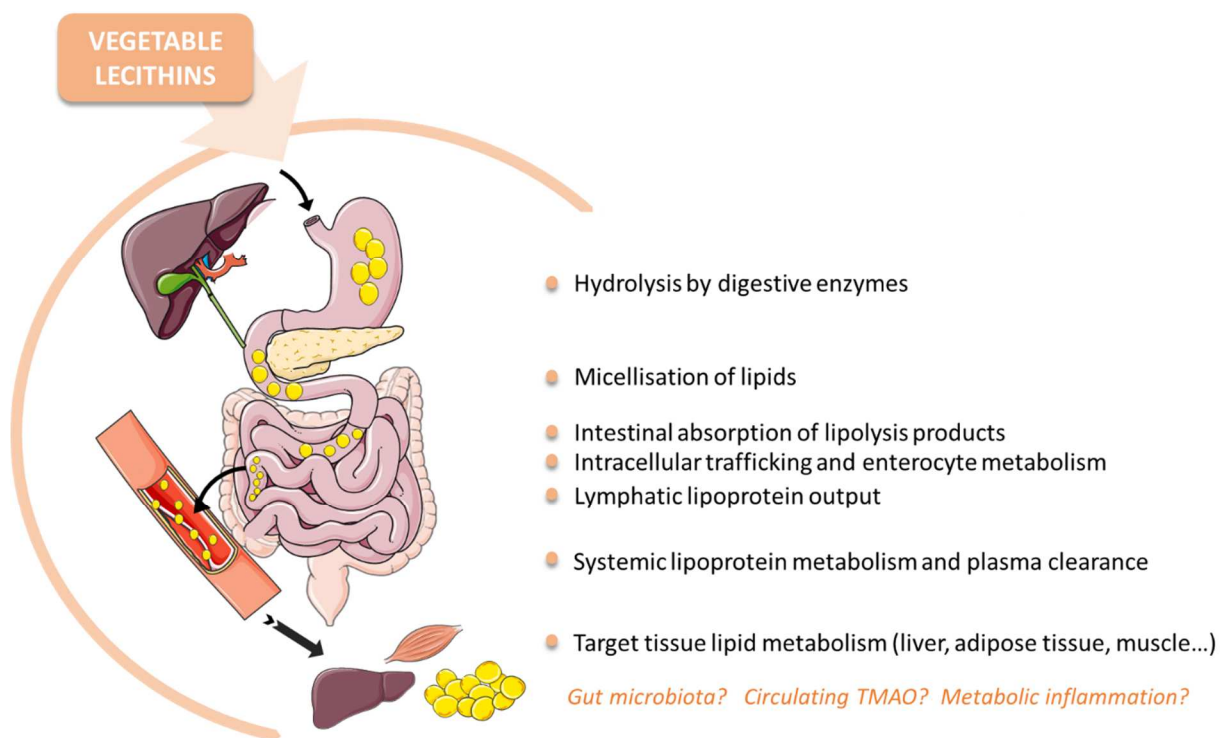
520 Moreover, the phospholipid composition of hepatocytes and, more specifically, their PC/PE  
521 ratio has been reported to be crucial in insulin signalling [96]. A stable PC/PE ratio in the liver  
522 is required for proper glucose and energy metabolism [97] and its alteration is associated with  
523 liver disease [98]. PE is essential for health and mice lacking either of the two major PE-  
524 producing pathways are **not viable** [99]. A considerable proportion of PE is converted to PC in  
525 the liver, via a reaction catalysed by PE methyltransferase (PEMT) [100]. The subsequent  
526 PC/PE ratio may hence be a result of both the activity of this enzyme and the amount of these  
527 phospholipids delivered from endogenous and exogenous pools. Vegetable lecithin,  
528 predominantly composed of PC and PE, may hence contribute to balance this PL ratio, which  
529 may partially explain its beneficial effect on hepatic lipid metabolism.

530 Several studies have also described the impact of marine or vegetable lecithin on adipocytes.  
531 Awada et al. reported that DHA-rich marine PL in a high fat diet induce lower adipose tissue  
532 mass with smaller adipocytes that, DHA-rich TAG in mice [101]. Soy PC supplementation was

533 also associated with smaller adipocytes in high fat fed mice [102]. Nonetheless, data concerning  
 534 the impact of vegetable lecithin, and notably of lecithin sources other than soy, on adipose tissue  
 535 and its lipid profile remains scarce. Considering the crucial role of adipocyte lipid profile and  
 536 metabolism in metabolic disorders, it is of primordial importance that further research be carried  
 537 out on the impact of such commonly used emulsifiers on adipose tissue.

538 Despite this lack of evidence, the data obtained so far concerning vegetable lecithin tends  
 539 towards a beneficial impact on lipid profile (cf **figure 2**), which represents a non-negligible  
 540 potential within the current upsurge of dyslipidaemia and associated metabolic disorders.

541



542

543

544 **Figure 2.** Plausible impacts of vegetable lecithins on lipid and lipoprotein metabolism.

545

## 546 **5. Vegetable lecithins: towards a preventive role in dyslipidaemia associated** 547 **with metabolic disorders**

### 548 **5.1. Potential of vegetable lecithin on obesity and associated metabolic disorders**

549 The prevalence of obesity is rising at unprecedented rates in developed countries, so that it  
 550 now represents one of the main public health issues in the world [103]. Obesity is associated  
 551 with a number of cardio-metabolic chronic diseases, such as type II diabetes mellitus, non-  
 552 alcoholic fatty acid liver disease (NAFLD) and cardiovascular diseases (CVD). All of these

553 disorders are characterised by hyperlipidaemia, that is to say abnormally elevated plasma  
554 triglyceride and cholesterol levels [104]. Based on the plethora of evidence concerning the  
555 crucial role of endogenous biliary PL on lipid metabolism, as well as the aforementioned lipid-  
556 lowering capacities of lecithin, it is not surprising that several studies have recently attempted  
557 to investigate the potential of lecithin on the prevention and amelioration of obesity-related  
558 metabolic disorders [89,92,102].

559 The findings obtained so far, mostly in preclinical models, conveys rather encouraging  
560 information concerning the ameliorative effects of lecithin on obesity-related dyslipidaemia.  
561 Amongst many reasons, this is in part due to the aforementioned physiological effects of PL on  
562 lipid gastro-intestinal metabolism. Long-term soybean-derived PC supplementation in mice fed  
563 a high-fat (HF) diet has been shown to alleviate obesity-related complications and normalize  
564 plasma lipid profiles, notably by reducing plasma triglycerides, cholesterol and leptin levels  
565 and diminishing the LDL/HDL ratio [102]. PC supplementation also attenuates HF-induced  
566 ApoE expression in the aorta in these mice [102]. In another study conducted in rats, diets  
567 supplemented with soybean lecithin presented decreased gastric emptying and food intake,  
568 most probably due to the increase in the secretion of gut hormone cholecystinin (CCK) [105].  
569 These effects observed in preclinical studies show the potential of soybean lecithin in the  
570 prevention of obesity and metabolic disorders, as food intake and satiety are important  
571 contributing factors of obesity. **The possible impact of lecithin in different foods or supplements**  
572 **on satiety and food intake must be confirmed in humans.** An additional study performed on  
573 obese Otsuka Long-Evans Tokushima Fatty (OLETF) rats, an animal model for obesity- and  
574 metabolic syndrome- related complications, reported that omega 3-PC (i.e. EPA and DHA) and  
575 not egg PC alleviated obesity-related dyslipidaemia, via reduction of hepatic fatty acid synthesis  
576 and increase in beta-oxidation and serum adiponectin levels [106]. Unlike egg PC, omega-3 PC  
577 acted by suppressing the gene expression of SREPB1 and PPAR $\delta$ , two nuclear receptors  
578 involved in the regulation of lipid and energy homeostasis [107]. This clearly demonstrates that  
579 the origin of PL and its fatty acid composition determine and modulate their subsequent  
580 physiological effects. Such preclinical observations highlight the need for further research  
581 investigating the difference between PL from different vegetable sources. To our knowledge,  
582 only one review has attempted to gather and compare the effects of individual PL compounds  
583 on long-term cardiometabolic health parameters [88]. The review explores the effects of PC,  
584 PE and PI on dyslipidaemia, in both animal models and humans, and concludes on the high  
585 potential of the use of these PL, especially PI, as alternative or adjunctive therapy for  
586 dyslipidaemia in the context of metabolic disorders.

587 More widely reported are the effects of lecithin supplementation on obesity-related liver  
588 diseases, such as NAFLD and steatosis [92]. Indeed, historically, PL have been widely  
589 prescribed in the treatment of alcohol-induced liver damage and viral hepatitis. The beneficial  
590 impact of plant PL on such hepatic disorders are described in depth in two recent reviews  
591 [30,108]. The hepatic lipid-lowering properties of vegetable lecithin endows them with  
592 beneficial effects on liver metabolism with potential application in the treatment of hepatic  
593 diseases such as NAFLD [88].

594 Lecithins have also been reported to possess potent anti-inflammatory properties [30,109].  
595 This is of particular interest, since metabolic disorders are highly associated with chronic low-  
596 grade inflammation in plasma and adipose tissue [110]. As reviewed in [30,109], beneficial  
597 anti-inflammatory properties of vegetable lecithin as a supplement have been reported in a  
598 number of inflammatory diseases, including arthritis and ulcerative colitis. However in a dietary  
599 context, regarding HF-induced metabolic low-grade inflammation in mice, soy PL (1.2 wt% in  
600 a HF diet) have recently been associated with higher markers of adipose tissue inflammation  
601 than milk PL [111]. Additionally, the addition of soy PL to a HF diet rich in flaxseed oil also  
602 induced higher markers of adipose tissue inflammation in mice than the HF diet enriched with  
603 flaxseed oil devoid of lecithin [112]. As outlined in a recent EFSA report, this supports the need  
604 for further research investigating the mechanisms and the effects of vegetable lecithin on  
605 metabolic inflammation [4] and warrants research in humans.

606 In addition, a study by Karantonis et al. reported that the polar lipid compartment (which  
607 constitutes vegetable lecithin) and not the neutral lipids of seed oils generated biologically  
608 active, antithrombotic and anti-atherogenic properties [113]. Vegetable lecithin may then play  
609 a promising role in the prevention of atherosclerosis. Interestingly, the study demonstrated the  
610 superiority of lecithin derived from olive oil compared to that of other seed oils (sunflower,  
611 corn or soybean) as a platelet aggregation factor (PAF) antagonist. This highlights once again  
612 the need for more research concerning individual phospholipids and different lecithin sources.  
613 More research must also to be undertaken, which takes into consideration the other minor  
614 components of dietary vegetable lecithin. Notably, phyto-oestrogens may be present in non-  
615 negligible amounts. Phytosterols, such as those found in rapeseed lecithin, may equally play a  
616 synergistic role [18]. The presence of lipid soluble vitamins, such as vitamin E, may further  
617 explain certain observed effects of lecithin on lipid metabolism and homeostasis [22].

618

619

620

## 621 **5. 2. Impact on gut microbiota**

622 A plethora of recent research has demonstrated the importance of gut microbiota on lipid  
623 metabolism and homeostasis [114,115]. As such, microbiota affects lipid absorption and, vice  
624 versa, ingested lipids influence the number, diversity and health status of the gut microbiota. It  
625 has recently been demonstrated that intestinal microbiota converts dietary phosphatidylcholine  
626 to trimethylamine (TMA), which is then further metabolised by flavin monooxygenase 3  
627 (FMO3) and other FMO proteins in the liver into pro-atherogenic trimethylamine N-oxide  
628 (TMAO) [116]. High TMAO concentrations in plasma are associated with increased cardio-  
629 metabolic disease and atherosclerosis risk [116,117]; hence, it is thought that excess dietary PC  
630 increases the levels of TMAO resulting in a pro-inflammatory and pro-thrombotic state leading  
631 to insulin resistance, type II diabetes, and cardiovascular disease [116,118]. However, recent  
632 research indicates that the conversion of choline to the TMAO precursor, TMA, results from  
633 the presence of specific gut bacteria, rather than from excess dietary choline [2]. The authors of  
634 these studies specify that the need for further research is required in order to clearly understand  
635 the relationship between dietary PL and the microbiota-dependent production of TMAO.  
636 The present knowledge regarding the importance of gut microbiota on lipid metabolism and  
637 metabolic health renders obligatory that further research on the effect of vegetable lecithin on  
638 TMAO production and gut microbiota in general be explored. This is all the more important as  
639 the market of vegetable lecithins is expanding at unprecedented rates.

640

## 641 **6. Conclusion and future prospects**

642 Vegetable lecithins provide food-derived PL that, similarly to endogenous PL, have the  
643 potential to modulate numerous membrane-dependent cellular functions, as well as exert lipid-  
644 regulating, anti-inflammatory and antioxidant effects [2]. Despite the lack of converging  
645 evidence concerning their effects on lipid digestion and intestinal absorption, it is clear that  
646 dietary vegetable lecithin exert an overall beneficial effect on lipid and lipoprotein metabolism.  
647 In this way, they have been proposed as novel therapeutic agents for the treatment of  
648 hyperlipidaemia associated with metabolic and cardiovascular diseases [89]. Supporting this  
649 idea is the fact that PL are capable of forming unique lipid droplets, referred to as liposomes,  
650 which have been investigated as drug carriers for decades and which have been associated with  
651 ameliorated blood and hepatic lipid profiles [119].

652 Importantly, this review highlights the evident lack of existing data concerning vegetable  
653 lecithin from sources other than soybean, and their effects on lipid metabolism and metabolic



654 health. The immense compositional diversity of vegetable lecithins, arising from both  
655 agronomical and genetic factors, grants them with a vast range of biochemical and biological  
656 properties, which remain to be explored. Faced with the current epidemical outburst of obesity  
657 and the staggering growth rates of the lecithin market, future research must be undertaken in  
658 order to determine the health effects of vegetable lecithins, **both as supplements and as**  
659 **ingredients in different foods**. More specifically, it is of primordial importance that researchers  
660 attempt to elucidate the various mechanism by which individual fatty acids and PL from various  
661 vegetable lecithin modulate lipid metabolism and the extent to which they may influence  
662 parameters associated with metabolic disorders, such as intestinal integrity, low-grade  
663 inflammation and gut microbiota.

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