# Characterization of the lipotropic potential of plant-based foods

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**Abstract**

Lipotropes are food components that limit excessive hepatic triglyceride contents or steatosis. Hepatic steatosis is often associated with obesity and type 2 diabetes, and may lead to more serious pathologies such as steatohepatitis, hepatic fibrosis and cirrhosis, or cancer. Yet, whereas hepatic steatosis concerns several millions people worldwide, the lipotropic potential of foods has never been studied; and lipotrope-rich foods remain quite unknown. The objective of this work has been to characterize and quantify the lipotropic potential of plant-based foods from lipotrope contents found in literature and nutritional tables. Thus, 132 plant-based foods and 8 lipotropes (betaine, choline, *myo*-inositol, methionine, niacin, pantothenic acid, folates and magnesium) could have been selected. Main results showed that vegetables are the best source of lipotropes on a 100 kcal-basis and that plant-based foods are a more diversified source - but complementary - of lipotropes compared to animal-based products. We then expressed the lipotropic potential into a new index, the Lipotropic Capacity (LC) that integrates the sum of the 8 lipotropic densities relative to a reference food. Technological processes reduce plant-based foods lipotropic potential by around 20%: while refining is the most drastic treatment, fermentations have little effect, and may even tend to increase lipotrope densities. Then, by comparing lipotrope consumption *via* both French standard diet (INCA 2 survey) and Food guide pyramid, we evaluated that our consumption in betaine, choline and *myo*-inositol may be increased: this can be easily reached by choosing lipotrope-dense foods like beetroot, spinash or coffee.  On a one euro-basis, grains products (*i.e.* cereals, and leguminous and oleaginous seeds) are the best compromise between a high LC and a cheap supply in lipotropes. However, it remains indispensable to carry out studies in humans to relate LC and prevalence of hepatic steatosis.

**Keywords**: Lipotropes ; Hepatic steatosis ; Plant-based foods ; Lipotropic capacity ; Technological processes ; Consumption

**Introduction**

Increased consumption of fruits, vegetables and whole-grain cereals tends to be associated with a reduced risk of developing type 2 diabetes, obesity, cancers, and cardiovascular diseases[1]. The reason lies in their high density of protective bioactive compounds, mainly fibre compounds, vitamins, minerals, oligo-elements and associated phytochemicals such as carotenoids and polyphenols. Their antioxidant, hypolipidaemic, hypoglycaemic, anti-carcinogenic and/or anti-inflammatory properties are among their most studied physiological effects in animals and/or in vitro, and secondarily in humans.

Another physiological property that is common to several phytochemicals is the ability to counteract the development of fatty liver or hepatic steatosis, called the "lipotropic effect". *Sensu stricto*, a lipotrope prevents the liver from excess triglyceride deposits by hastening their removal, limiting their uptake, increasing fatty oxidation and/or reducing fatty acid and triglyceride synthesis. The detailed physiological mechanisms by which lipotropes act *in vivo* have been described in a previous review[1]. Briefly, they involve methyl donation for methionine synthesis to favour hepatic phospholipid synthesis, these latter being constitutive of VLDL/LDL that export excess triglycerides outside the liver (Figure 1A). The reduction of lipogenic enzyme activities and activation of fatty acid oxidation enzymes are also implicated (Figure 1B). In addition, the gene expression of PPARα (peroxisome proliferator-activated receptor) and SREBP (sterol regulatory element binding proteins), which both play a role in lipid metabolism regulation, may be, respectively, up- and down-regulated[1].

Hepatic steatosis may be associated with excess alcohol consumption[2], obesity/overweight and diabetes[3], insulin resistance[4], increased oxidative stress[5], hyperlipidaemia[6], risk factors of the metabolic syndrome[7] and hepatocarcinogenesis[8]. Hepatic steatosis may also result from choline deficiency[9,10]. Hepatic steatosis is otherwise the first step that may lead to more severe pathologies, *i.e.*, steatohepatitis, fibrosis and cirrhosis. In 2000, it has been estimated that more than 30 million American people may have suffered from steatosis[11]. Therefore, the capacity of foods to prevent hepatic steatosis development or to reduce it is undoubtedly of the utmost interest within the context of preventive nutrition and public research.

Yet, there are very few observational studies that report an association between increased PBF or phytochemical consumption and the prevalence of hepatic steatosis. These studies were concerned with beverages only: for example, baseline high-coffee consumption (≥ 3 cups/day) in patients with advanced hepatitis C-related liver disease was associated with less severe steatosis[12]. Conversely, 80% of 60 patients with NAFLD consumed excessive soft drinks, mainly sodas that are generally carbohydrate-rich, compared to 17% in healthy controls[13]. In addition, NAFLD patients significantly consume more fructose than controls[14], and liver fat scores in sedentary abdominally obese men were significantly and positively associated with alcohol consumption and average total caloric, fat, saturated fat and simple carbohydrate intake over 10 days[15]. It is therefore not surprising that caloric restriction was shown to be efficient in reducing hepatic steatosis in both type 2 diabetic subjects and NAFLD patients[16,17]. To the best of our knowledge, the association between a reduction of the hepatic steatosis prevalence or risk and the consumption of solid plant-based food has never been investigated.

The same was true for human interventional studies: they are quite rare. The most striking interventional studies are studies led during ~2 to 12 months in patients suffering from NAFLD for whom the chronic daily consumption of n-3 poly-unsaturated fatty acids supplements (from ~0.8 to 4 g), betaine anhydrous solution (20 g), L-carnitine (2 g) or tea pigment capsules (375 mg) has significantly reduced or improved the degree of hepatic steatosis and/or hepatic functions - as reflected by the improvement of the levels of circulating liver enzyme[18-24]. Other human studies are quite old and are concerned with reported clinical cases of hepatic dysfunction or troubles (*e.g.*, as a result of alcoholism) that were improved in some cases via administration of choline chloride[25], commercial lipotrope complex (Ornitaine®, which notably contains betaine and magnesium)[26,27] or lipotrope tablets[28]. Other studies were mainly carried out in animal models, primarily using rats and mice but also hamsters and guinea pigs[1].

In a previous review, from rat studies, we distinguished among lipotropes: 1) the main lipotropes, which are betaine, choline, methionine, *myo*-inositol and carnitine; 2) magnesium, niacin, pantothenic acid and folates that support the overall lipotropic effect of other compounds; 3) fibre-type compounds, including soluble and insoluble fibre, phytic acid (or *myo*-inositol hexakisphosphates, IP), oligofructose and resistant starch (RS); 4) polyphenol-type compounds, including some polyphenols from the 4 main classes (*i.e.* phenolic acids, flavonoids, lignans and stilbenes), curcumin, saponins and γ-oryzanol; 5) other specific isolated compounds that are some organosulphur compounds, some unsaturated fatty acids, acetic acid, coumarin, phosphatidylinositol, caffeine, deoxynojirimycin and melatonin; and 6) various plant extract, notably proteins from lupin and soybean, and oxidized oils [1]. Although they significantly reduce hepatic total lipid and/or triglyceride contents, the phytochemicals of groups 3, 4 and 5 have never been cited as being lipotropic in the literature. The reasons for this remain unclear. It remains that the lipotropic effect of the majority of these compounds has to be demonstrated in humans.

Foods rich in lipotropes are not known. Yet, plant-based foods are potential sources of lipotropes for human nutrition. However, up today, no studies have defined the lipotrope content of PBFs, either raw or processed. Their lipotropic capacity (LC) therefore needs to be characterized. The main objective of this work was therefore to find a way to simply characterize the lipotropic potential of food to prevent hepatic steatosis development or to guide nutritional choices for people with moderate hepatic steatosis. This work was carried out in three steps: 1) characterization of the lipotropic potential of plant products; 2) the study of the influence of technological treatment on lipotropic potential, and 3) the evaluation of the contribution in lipotropic a standard French regime in comparison with the recommendations of the food pyramid.

## Methods

The systematic study of the literature has allowed identifying compounds that may exert a lipotropic effect[1]. We then sought to express the lipotropic potential of plant-based foods (PBF) in a simple and integrative way to classify and compare them[29], to study the effect of technological treatments on it[30], and to evaluate the daily consumption in lipotropes[31].

A significant number of PBF for which the contents of the main lipotropes were known were first selected[29]. Thus, 132 PBF were selected from food composition tables[32-36]. Among these 132 PBF, *myo*-inositol contents could not have been calculated for 61 products. These 132 foods were then classified into 6 groups: grain products, legumes, vegetables, fruits, nuts and seeds, and beverages. The products have also been classified as raw and processed products to study the influence of technological processes on the lipotropic densities, and as edible and non-edible products to calculate daily consumption in lipotropes.

Data from literature allowed selecting eight compounds: betaine, choline, *myo*-inositol, methionine, magnesium, niacin, pantothenic acid and folates. Although recognized as having a significant lipotropic activity, carnitine could not have been selected because there are too few data in the literature on carnitine content in plant products. However, few data suggest that the levels of carnitine are probably quite low, and about 100 to 1000 times lower than in animal tissues[37,38].

As a first step, the lipotropic contents were expressed in mg/100 kcal (lipotropic density, LD) because the caloric basis is recommended for the nutrients we want to encourage consumption[39]. From the LDs, the PBF lipotropic profiles were compared using the principal component analysis (PCA) in order to identify foods with closed lipotropic profiles.

To easily and rapidly compare PBF, the Lipotropic Capacity (LC) - which allows giving the same theoretical weight for the 8 DL and integrating them into a single value - has been defined as follows:

$$CL_{food}\ (\%) = (\Sigma[(DL_{food}/DL_{raw\ asparagus})\ x\ 100])\ /\ 8\ (\text{nombre de lipotropes sélectionnés})$$

Where $[(DL_{food}/DL_{raw\ asparagus})\ x\ 100]$ was calculated for each lipotrope and represents the ratio of the density of a given lipotrope to that of the same lipotrope in the reference food[29]. The raw asparagus was chosen as the reference food as it ranks first among the 38 raw PBFs based on the average rank obtained for the 8 LDs (see Table 1).

Due to the non-Gaussian distribution of LDs for each of the 8 selected lipotropes, the tailed non-parametric Mann-Whitney test was used to measure the effects of technological treatments as a whole - raw vs. processed PBFs - on the LDs and LCs. The effect of specific technological treatments (thermal, refining and fermentation) on the LDs has been measured by the non-parametric Wilcoxon test for paired samples (*e.g.*, raw beans vs. boiled beans).

The daily intake in lipotropes was calculated on the basis of the French survey INCA 2 (2006-2007) that gives the average daily consumption by food group[35]. Then, daily intakes were compared to those that would be obtained by following the recommendations of the food pyramid[40].

Finally, the amount of lipotropes provided by one euro from PBFs and animal products was calculated. The prices were estimated using two different sources: data collected from TNS Worldpanel 2007 and updated for the majority of products, and the data collected from the Web sites of several supermarkets and suppliers (17 March 2011) for some cereal products and animal products. In the end, the price of 108 PBFs and 14 animal products were obtained.

## Results and Discussion

### *The lipotropic potential of raw plant-based foods*

By considering the 38 raw PBFs, vegetables are the best source of lipotropes (means = 419 mg/100 kcal), followed by cereals (226 mg/100 kcal), legumes (235 mg/100 kcal) and fruits (224 mg/100 kcal). Due to their high energy density, nuts and seeds (*e.g.*, walnuts, hazelnuts, almonds, etc.) come last (133 mg/100 kcal). Yet, nuts and seeds are the richest source of lipotropes on a fresh weight-basis (804 mg/100 g): also, when consumed in moderation, which is often the case, they can be a significant source of lipotropes.

Based on the average rank for the 8 LDs, 13 vegetables are among the first 14 PBFs. Blackberry, the only exception among fruits, ranks eighth. Other fruits, nuts and seeds rank rather low.

PCA highlights the disparity of lipotropic profiles for vegetables (Figure 2: in green) while the profiles of cereals/pseudo-cereals, legumes, and nuts and seeds are more homogeneous (Figure 2: in orange, blue and and brown, respectively). Vegetables are characterized by high levels of betaine, choline and folate while legumes tend to have a higher methionine - and to a lesser extent magnesium - density; and fruit a higher *myo*-inositol density compared to other groups.

These findings may have practical applications for choosing foods with a high lipotropic potential, especially for choosing PBFs with a balanced profile in each of the 8 lipotropes if it is considered preferable to promote the synergistic action of several lipotropic compounds with different mechanisms of action (Fig. 1A-B) rather than only one in high amount.

However, these analyses are not easy to interpret, notably when aiming at rapidly choosing PBFs. Lipotropic potential of PBFs has been therefore defined more simply as an integrative index, the LC. Compared with raw asparagus, spinach, beetroot, quinoa and blackberry have high LC (Table 1). Except citrus and blackberry, other fruits have a rather low LC (<35%) as nuts and seeds due to their high energy density.

However, if the LC allows relative comparisons, in absolute, one cannot tell if a value of 30, 70 or 150% has a physiological sense or not: in other words, is a value of 30, 70 or 150% is well reflected *in vivo* with a significant effect on the reduction of fatty liver? To validate in vivo the LC, a first step could be to relate the LC quintile daily consumed with the prevalence of hepatic steatosis in a cohort and to identify from which quintile the prevalence of hepatic steatosis was significantly lower than that observed for the lowest quintile. One might also consider using the *in vitro* model of hepatic steatosis (which consists of HepG2 cells accumulating triglycerides following stimulation by oleic acid[41]) to investigate the ability of digestive food extracts - obtained after in vitro digestion - to reduce the accumulation of triglycerides in these cells.

***Effect of technological treatments on the lipotropic potential***

*Effects of technological treatments on the whole*

On the basis of each of the 8 LDs, processed products tend to be ranked lower, the effect being more pronounced for lipotropic micronutrients (magnesium and B vitamins) for the main lipotropes (choline, betaine, *myo*-inositol and methionine )[30]. Thus, considering the 121 raw and processed in our initial database, significant differences among average ranks were obtained for the magnesium (-16 ranks, p <0.05), pantothenic acid (-19, p <0.05), folate (-19, p <0.05) and *myo*-inositol (-9, p <0.05) densities of processed products compared to raw products[30]. No significant difference was obtained for the other LDs.

*Effects of specific technological treatments*

Thermal treatments include cooking in boiling water, canning, baking, drying and toasting. Considering 18 pairs of raw vs. processed PBFs, these treatments lead to a decrease in LD of ~25% (*P* <0.05) for B vitamins - pantothenic acid density being the most affected (-32%, *P* <0.05) -, 9% (not significant, NS) for magnesium, 24% (*P* <0.05) for betaine, 54% for *myo*-inositol (NS due to the small number of products for which the content of *myo*-inositol could be obtained) and 8% for methionine (NS). Only the choline density increases (+6%, NS).

Refining includes all treatments resulting in significant losses of food ingredients (notably the fibre fraction) from the original product as the transformation of fruit into juices or sodas, cereals into refined flours, tomatoes into concentrate, or potatoes into potato chips. Considering 14 pairs of raw vs. processed PBFs, refining appears much more drastic than thermal treatments with significant decreases in methionine density (-33%), magnesium (-46%) and vitamin B (-33%). Choline density decreases by 33% but the effect is at the limit of significance (*P* = 0.07). The betaine density does not change and that of *myo*-inositol decreases by 43% but the effect is not significant due to the small number of PBFs.

Fermentation processes include fermentation of cabbage into sauerkraut, the grapes into wine, barley into beer, cucumbers into pickles and wheat flour into bread. Thus considering 6 pairs of raw vs. processed PBFs, fermentation appears to be the least drastic technological process with a single significant decrease of -21% for niacin. Levels of betaine, choline, magnesium, folates and *myo*-inositol increased but the effects are not significant.

*Effects of technological treatments on the lipotropic capacity*

Within the limit of 38 raw and 21 processed products for which the *myo*-inositol levels have been calculated, we can see that the processed products have generally lower LCs (median 18 against 38 for the raw product; Table 1). Note the two main exceptions that are canned beetroot with a LC of 536% against 390% for raw beetroot, and tea (LC = 196%). The high LC of tea is mainly due to its low energy density, such as for coffee (LC = 537% based on 7 LDs, the density of *myo*-inositol excluded since not available). All refined and/or energy-rich products have a low LC, less than 30%.

*Conclusions*

Technological processes reduce the overall lipotropic potential of PBFs by ~20%, refining being the most drastic treatment, either to the LDs or LCs. Second, technological treatments tend to degrade or reduce micronutrient densities (magnesium and B vitamins) more significantly than for the 4 main lipotropes (betaine, choline, *myo*-inositol and methionine). Among the B vitamins, folates densities are more often adversely affected than for pantothenic acid or niacin.

This study also highlighted the positive effects of fermentation processes in their ability to increase - or at least not changing - LDs and LCs. This favourable effect of fermentation on the content of bioactive plant products has been already emphasized in the literature, particularly for cereals [42-44]. Indeed, fermentation processes tend to release bioactive compounds originally linked to other components - mainly fibre - due to the activation of enzymes. For example, B vitamins are generally in both bound and free form within complex food matrices. As fermentation, canning increases the LD and LF of beetroots and beans, probably by releasing bioactive compounds, all lipotropic considered in this study being water soluble.

Finally, we know that technological treatments can increase the levels of resistant starch in foods[45]. Or resistant starch exerts lipotropic effects well documented in rats[1]. Given the daily consumption of resistant starch in the framework of a standard Western diet - between 8 and 40 g[46]-, it could be interesting, then, to include this compound in the calculation of the LC. Technological treatments can also increase the content of free *myo*-inositol in cereal partially by degrading phytic acid[47].

It therefore seems possible *via* technology to maximize the lipotropic potential of PBFs.

### ***Consumption and prices of lipotropes***

The daily consumption of lipotropes was estimated from the 106 edible PBFs extracted from the 132 PBFs initially selected[29].

*Lipotropic densities profiles of edible products*

The application of PCA easily allows identifying products with close lipotropic profiles as avocado vs. potato chips, sesame seeds vs. canned beans, peanut vs. wholemeal bread, tomatoes vs. bell peppers, and lettuce vs. algae (results not shown). Although there is no significant group effect if one considers the only sum of the 8 LDs ($P$ = 0.069), we can however separate groups according to three trends: vegetables and legumes that provide more than 300 mg lipotropes per 100 kcal; fruits that provide an average of ~200 mg per 100 kcal, and cereals, nuts and seeds, and beverages that provide an average of ~100 mg per 100 kcal. Always on the basis of 100 kcal, grain products, vegetables, fruits and legumes are rich in betaine, choline+magnesium, *myo*-inositol and methionine, respectively. Concerning beverages, because of the heterogeneity of their composition and origin, it is more relevant to study them individually or to group them by type. Thus, tea and coffee have the highest LD, and sodas/lemonade the lowest. Apart from tea and coffee, the best sources for lipotropes for 100 kcal are fruit juices, followed by soybean and coconut milks, tomato soup and alcohols.

However, the analysis by food groups is somewhat limited because it does not emphasize the heterogeneity of products within a group, which is particularly the case for the vegetables products extracted from the roots, stem, leaves, flowers or fruit of the plant.

*Lipotrope consumption based on a standard French diet*
Based on edible PBFs, apparent deficiency in B vitamins is at minimum (the smallest number of servings recommended by the Food Guide Pyramid for AOV) 11 614 mg and of at least 638 mg for other lipotropes (magnesium, betaine, choline, *myo*-inositol and methionine). Even adding the contributions of beverages, minimal differences are greater than zero.

Despite these differences between the real (INCA 2) and ideal (food pyramid), the standard French diet - considering both plant and animal products - meets the daily recommended intakes for methionine, magnesium (420 and 320 mg/day for men and women, respectively), niacin (16 and 14 mg for men and women, respectively) and pantothenic acid (5 mg for both men and women). There is a folates deficiency (174 vs. 400 µg/day recommended for both men and women) and choline (262 vs. 550 and 425 mg for men and women, respectively). Considering *myo*-inositol and betaine, there are no official recommendations. Calculations show that the French standard diet provides about 112 mg of betaine/day and 269 mg *myo*-inositol/day. The betaine consumption is below values reported in a Greek study, namely 306 mg for men (range 52-1120 mg/day) and 314 mg for women (range 79-681 mg/day)[48]. There is not, to our knowledge, data in the literature for the consumption of free *myo*-inositol (*i.e.*, not from phytate). The only value obtained is 900 mg *myo*-inositol/day, fractions of *myo*-inositol from phytate being included, the authors estimating that more than 56% corresponds to fractions of *myo*-inositol bound to membrane lipids[49 15082]. Taking into account the consumption of phytate and applying this factor of 56%, the INCA 2 French standard diet provides ~1040 mg of potential *myo*-inositol fractions, which is not too far from the value of 900 mg[49].

More generally, the calculations show that there is substantial margin for increasing consumption of choline and betaine, and probably that of free *myo*-inositol without deleterious effects associated with overdose; preferably via PBFs (for which increased consumption is generally recommends). The increased consumption of foods rich in choline is also recommended by other authors estimating that daily quantities consumed are below recommendations[50].

To increase the consumption of lipotropes, especially in betaine, choline and *myo*-inositol, one can increase its consumption of PBFs rich in these three lipotropes or with a high LC. Thus, on a daily basis, the consumption of canned beetroots, spinach, canned beans, orange juice, asparagus, coffee, toasted wheat germ, wholemealbread and blackberries can largely offset the aforementioned differences in consumption between lipotropes consumed via a standard French diet vs. food pyramid.

*The cost of dietary lipotropes*
Per euro, the PBFs provide ~3.2 mg of vitamin B and 298 mg of the 8 lipotropic selected, whereas animal products provide ~4.5 and 847 mg/euro, respectively. Based on the food groups, it is interesting to note that the grain-type products, including cereals, legumes, and nuts and seeds are the cheapest sources of B vitamins and total lipotropes: 1481, 1422 and 1044 mg/euro respectively, well above fruits and vegetables (<300 mg/euro). This confirms the high cost of these products to reach high densities in protective bioactive compounds. Always on the basis of 1 euro, products of animal origin appear as an intermediate source of lipotropes between grains/seeds and fruits/vegetables.

**Conclusions**

Although the approach developed in this work is still rather theoretical, it has the merit of focusing on a nutritional property neglected by nutritionists, namely the lipotropic potential (there is not only the antioxidant potential!). Lipotropic potential should be therefore considered to guide food choices, especially for subjects at the beginning of steatosis or simply as part of the nutritional prevention in the same way that the glycemic index is used to guide food choices for diabetics. Indeed, hepatic steatosis affects several million people around the world. For example, it was estimated in 2000 that about 30 million Americans were affected by hepatic steatosis[11]. And 20 to 30% of the so-called developed Western countries have been reported as having excess hepatic fat deposits[51].

Nevertheless, the only knowledge of the lipotrope contents of food is not sufficient. Ideally, the LC should be corrected by the real bioavailable lipotropic fraction in the body. But bioavailability data are unfortunately very difficult and expensive to obtain *in vivo*. Therefore, one could use in a more systematic and standardized way *in vitro* digestors to assess this parameter in a standard Western diet. The LC defined in this article is also an evolutionary index based on new scientific data that could be obtained, namely contents in lipotropic compound and validation of their lipotropic effect in humans. We can then consider incorporating carnitine levels, polyphenols, phytic acid and resistant starch: the formula for calculating the LC will fit then based on these new data. The reference food may also change when more data for more foods will be available.

Otherwise, this study provides new arguments to promote the consumption of fruit, vegetables and minimally processed grains. These products are good sources of lipotropes, including vegetables based on 100 kcal, and products such as grains and seeds on the basis of one euro. Consumption of highly processed products should be therefore limited. The fruits are particularly interesting for their content in *myo*-inositol but literature data are still limited. Nuts and seeds may be recommended if they are consumed in moderation because of their high energy density. Concerning beverages, they are very heterogeneous, both with respect to applied technological processes and their botanical origin. Beer and wine are seen as valuable sources of betaine, but being rich in alcohol, have to be consumed with moderation; sodas, when consumed in large quantities should be avoided because they are steatogenous[13]; coffee appears as a relevant food with a high lipotropic potential for regular drinkers in agreement with the study by Freedman et al. who shows a lower prevalence of hepatic steatosis in coffee drinkers (> 3 cups/day, $P$ for trend = 0.047)[12]; and it is interesting to note that with the tea - also with a strong lipotropic potential - both are widely consumed beverages in the world.

Finally, this study provides new arguments to promote the consumption of PBFs such as cereal grains and legumes for their good ratio lipotropic density/price. They are also - especially legumes - foods with a good satiating effect and a high nutritional density in bioactive compounds and fibre. Specifically concerning legumes (beans, lentils ...), the INCA 2 study estimated that their average daily consumption was about 9.7 g[52], which is low and leaves a large margin to increase their consumption, especially as their price is quite low and that these products are easy to store and cook. Consumption of legumes should be more widely promoted and encouraged.

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## Figure legends

**Figure 1A-B.** The different mechanisms by which the main lipotropes can prevent excessive deposits of fat in the liver (from Fardet & Chardigny [1]): A - The action of choline, betaine, *myo*-inositol, methionine and folates (vitamin B9) in the transmethylation pathway for the synthesis of phosphatidylcholine and phosphatidylinositol; B - The action of pantothenic acid (vitamin B5), magnesium and carnitine in β-oxidation of lipids.
*Abbréviations* : AMP, Adenosine MonoPhosphate; ATP, Adenosine TriPhosphate; BHMT, Betaine Homocysteine MethylTransferase; CoA, Coenzyme A; LDL, Low Density Lipoprotein; MS, Methionine Synthetase; PEMT, PhosphatidylEthanolamine-*N*-MethylTransferase; THF, TetraHydroFolate; VLDL, Very Low Density Lipoprotein

**Figure 2.** Principal component analysis for the 38 selected raw vegetable products based on 8 lipotropics densities for betaine, choline, *myo*-inositol, methionine, magnesium, niacin, pantothenic acid and folates (based Fardet et al.[29]).

**Table 1**. Lipotropic Capacity of raw and processed plant-based foods*

| Raw (n = 38) | LC (%) | Processed (n = 21) | LC (%) |
|---|---|---|---|
| Spinash | 672 | Canned beetroot | 536 |
| Beetroot | 390 | Tea | 196 |
| Quinoa | 155 | Boiled green beans | 79 |
| Blackberry | 107 | Orange juice | 49 |
| Raw asparagus | 100 | Canned beans | 40 |
| Lettuce | 92 | Wholemeal bread | 39 |
| Broccoli | 90 | Boiled cabbage | 38 |
| Algae | 84 | Lime juice | 34 |
| Celery | 76 | French/Vienna bread | 27 |
| Peeled cucumber | 74 | Tomato soup | 20 |
| Tomato | 70 | White wheat bread | 18 |
| Bell pepper | 66 | Wine | 14 |
| Cabbage | 65 | Catsup | 13 |
| Radish | 63 | Potato chips | 13 |
| Orange | 51 | Apple juice | 13 |
| Grapefruit | 46 | Cooked white rice | 10 |
| Kiwifruit | 44 | Grape juice | 8 |
| Amaranth | 42 | Dried flaked coconut meat | 5 |
| Mandarin orange | 41 | Raisin | 4 |
| Raw bean | 36 | Carbonated orange juice | 1 |
| Peach | 33 | Carbonated cola | 1 |
| Carrot | 33 | | |
| Soyabean | 33 | | |
| Strawberry | 28 | | |
| Watermelon | 28 | | |
| Whole-grain oat flour | 28 | | |
| Sesame seed | 26 | | |
| Onion | 24 | | |
| Plum | 23 | | |
| Peanut | 20 | | |
| Avocado | 20 | | |
| Pineapple | 20 | | |
| Almond | 14 | | |
| Apple | 14 | | |
| Blueberry | 12 | | |
| Banana | 12 | | |
| Pear | 11 | | |
| Grapes | 7 | | |
| | | | |
| Median | 38 | Median | 18 |
| Average rank[a] | 25.6 ±15.2 | Average rank | 37.0 ±17.9[a] |

*From Fardet et al. [30]

[a]The effect of technological processes is significant (*p* = 0.015, two-tailed non-parametric Mann-Whitney's test)

**Figure 1A.**

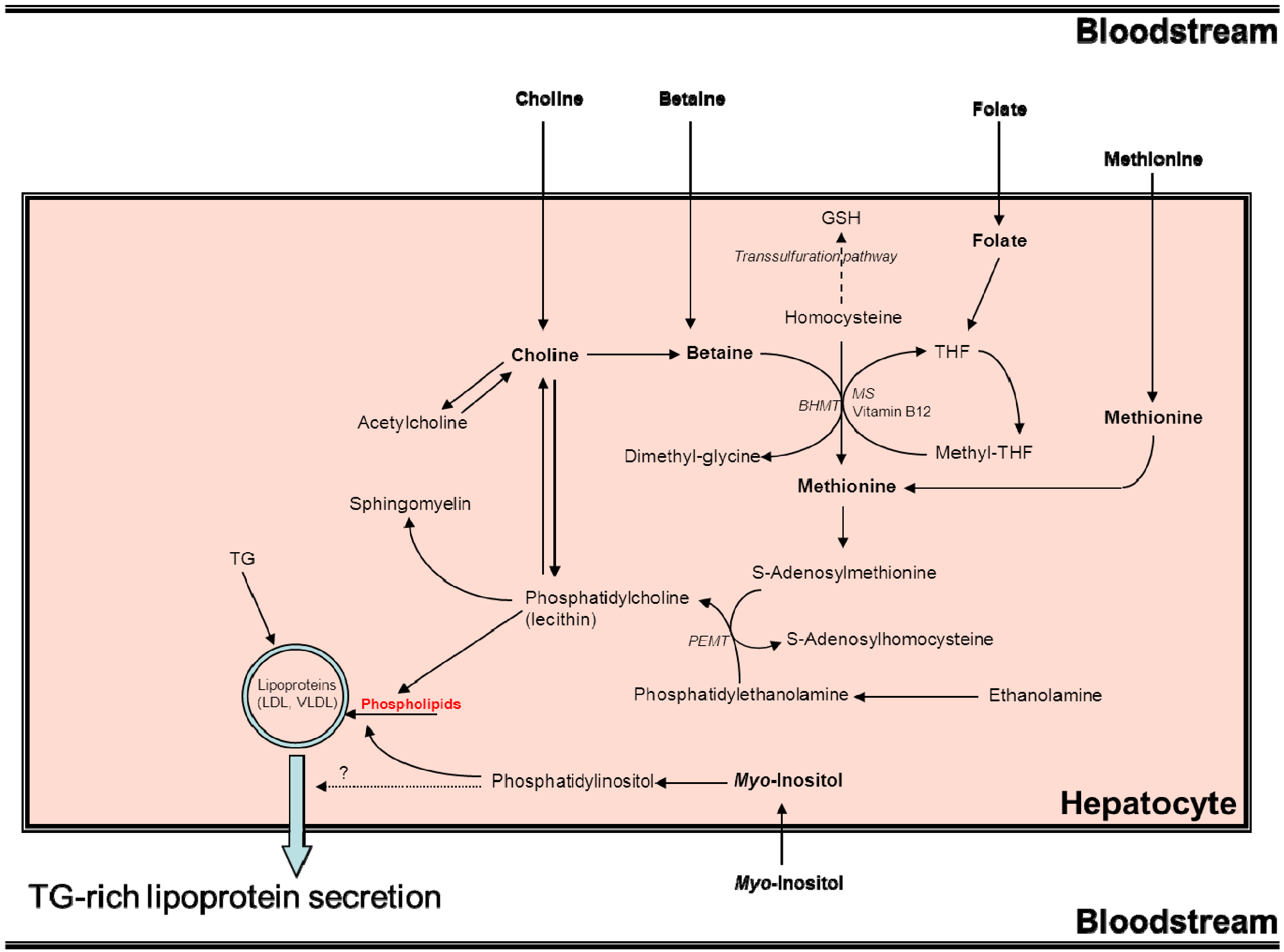
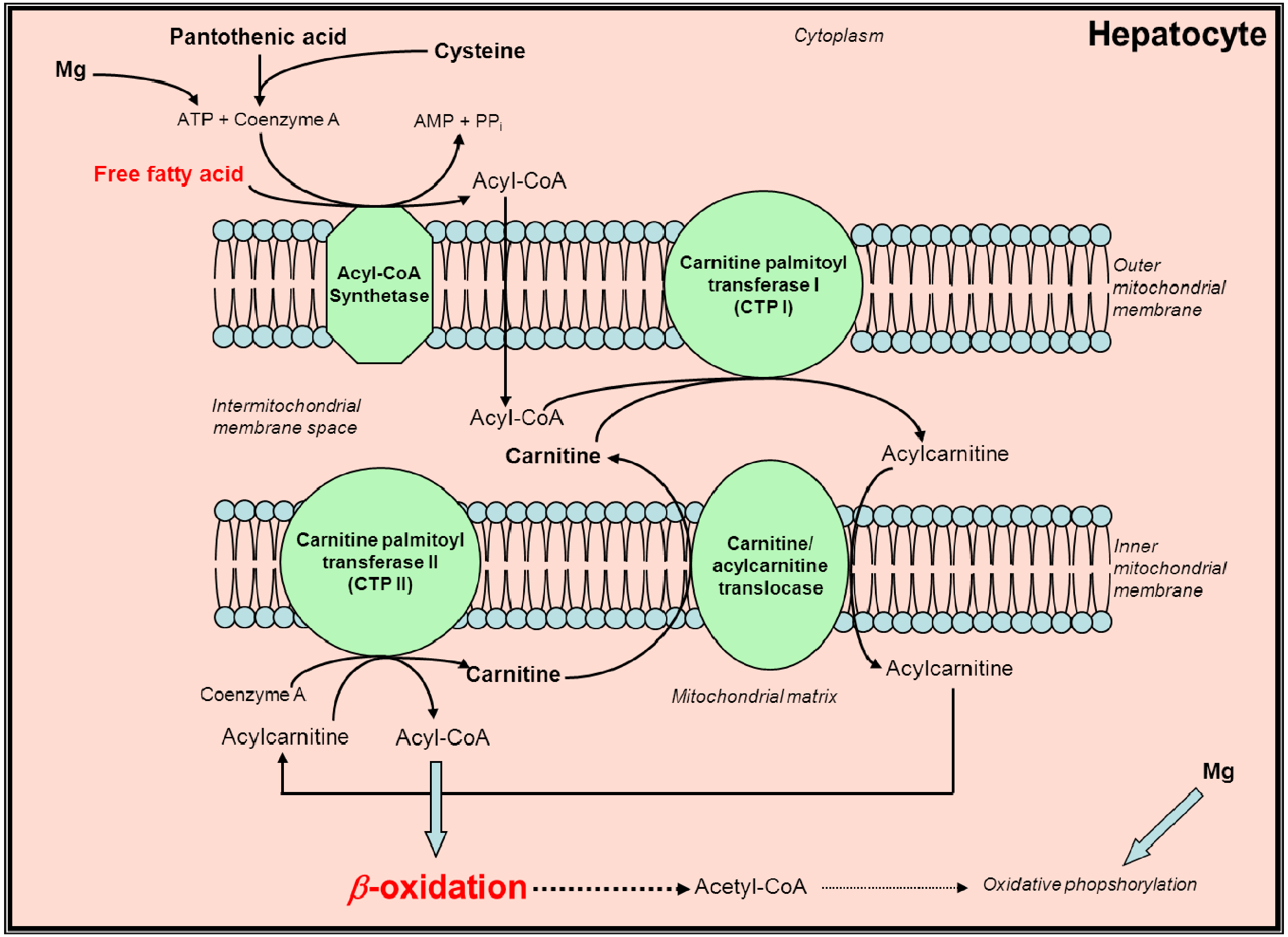
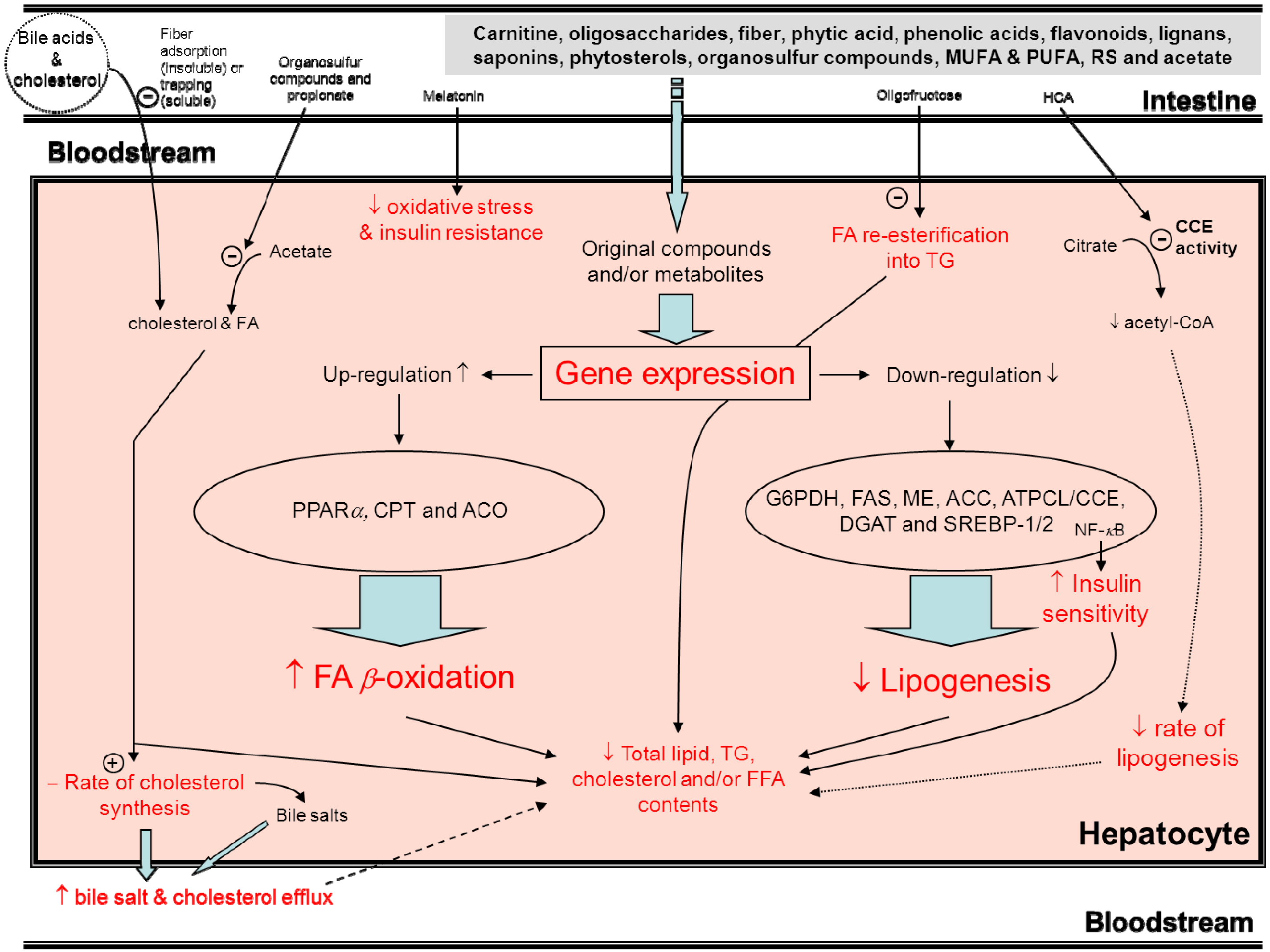

Bloodstream
Choline
Betaine
Folate
Methionine
GSH
Transsulfuration pathway
Folate
Homocysteine
Choline
Betaine
THF
BHMT
MS
Vitamin B12
Acetylcholine
Methionine
Dimethyl-glycine
Methyl-THF
Methionine
Sphingomyelin
TG
S-Adenosylmethionine
Phosphatidylcholine
(lecithin)
PEMT
S-Adenosylhomocysteine
Lipoproteins
(LDL, VLDL)
Phospholipids
Phosphatidylethanolamine
Ethanolamine
?
Phosphatidylinositol
*Myo*-Inositol
Hepatocyte
TG-rich lipoprotein secretion
*Myo*-Inositol
Bloodstream

**Figure 1B.**



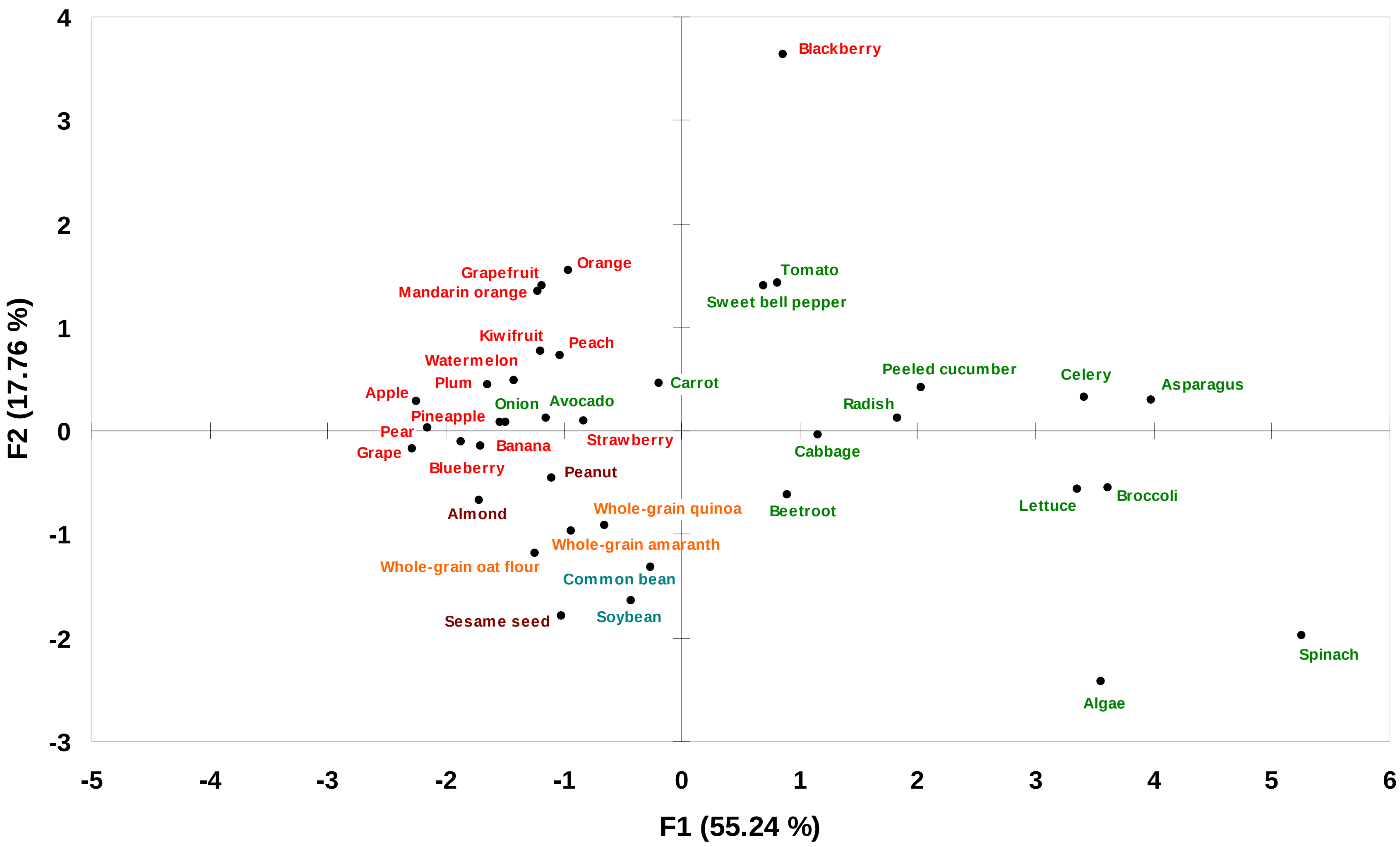
Hepatocyte
Cytoplasm
Mg
Pantothenic acid
Cysteine
ATP + Coenzyme A
AMP + PP$_i$
Free fatty acid
Acyl-CoA
Acyl-CoA Synthetase
Carnitine palmitoyl transferase I (CTP I)
Outer mitochondrial membrane
Intermitochondrial membrane space
Acyl-CoA
Carnitine
Acylcarnitine
Carnitine palmitoyl transferase II (CTP II)
Carnitine/ acylcarnitine translocase
Inner mitochondrial membrane
Carnitine
Acylcarnitine
Coenzyme A
Mitochondrial matrix
Acylcarnitine
Acyl-CoA
Mg
β-oxidation
Acetyl-CoA
Oxidative phopshorylation

**Figure 1C.**



Bile acids & cholesterol
Fiber adsorption (insoluble) or trapping (soluble)
Organosulfur compounds and propionate
Melatonin
Carnitine, oligosaccharides, fiber, phytic acid, phenolic acids, flavonoids, lignans, saponins, phytosterols, organosulfur compounds, MUFA & PUFA, RS and acetate
Oligofructose
HCA
Intestine
Bloodstream
↓ oxidative stress & insulin resistance
Acetate
Original compounds and/or metabolites
FA re-esterification into TG
Citrate
CCE activity
cholesterol & FA
↓ acetyl-CoA
Up-regulation ↑
Gene expression
Down-regulation ↓
PPARα, CPT and ACO
G6PDH, FAS, ME, ACC, ATPCL/CCE, DGAT and SREBP-1/2
NF-κB
↑ Insulin sensitivity
↑ FA β-oxidation
↓ Lipogenesis
↓ rate of lipogenesis
↓ Total lipid, TG, cholesterol and/or FFA contents
– Rate of cholesterol synthesis
Bile salts
Hepatocyte
↑ bile salt & cholesterol efflux
Bloodstream

**Figure 2.**



Blackberry
Orange
Grapefruit
Mandarin orange
Tomato
Sweet bell pepper
Kiwifruit
Peach
Watermelon
Plum
Carrot
Apple
Onion
Avocado
Pineapple
Pear
Grape
Banana
Strawberry
Blueberry
Peanut
Almond
Peeled cucumber
Celery
Asparagus
Radish
Cabbage
Beetroot
Lettuce
Broccoli
Whole-grain quinoa
Whole-grain amaranth
Whole-grain oat flour
Common bean
Soybean
Sesame seed
Spinach
Algae
F2 (17.76 %)
F1 (55.24 %)