The effect of artichoke on lipid profile: A review of possible mechanisms of action

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Abstract

Cardiovascular disease is a highly prevalent issue worldwide, and one of its main manifestations, dyslipidaemia, needs more attention. Cooked artichoke (Cynara scolymus) hearts or artichoke leaf extract (ALE) are believed to be helpful in the treatment of dyslipidaemia. In this narrative review, we provide a brief overview of the potential impact of artichoke consumption on lipid profile. We appraised the Cochrane, MEDLINE and Web of Science databases, and included articles published between 2000 and June 2018 on intervention in humans only. The main potential of ALE administration observed on lipid profile relates to decreased serum LDL, total cholesterol and triglyceride concentrations, although no strong evidence for increasing HDL appears to exist. Evidence suggests that decreases of 8–49 mg/dL for LDL concentration, 12–55 mg/dL for total cholesterol, and 11–51 mg/dL for triglycerides, can be attributed to 2 to 3 g/d of ALE, in which its components luteolin and chlorogenic acid may play a key role. On the other hand, the effects of cooked artichoke hearts can be attributed mainly to its soluble fibres, particularly inulin. Despite the convincing evidence on its health benefits, additional long-term clinical trials are pivotal to fully elucidate the potential effects of ALE administration on positive cardiovascular outcomes.

Keywords

Artichoke, Cynara scolymus, Dyslipidaemia Lipids Phytotherapy

1. Introduction

Cardiovascular disease is the major cause of death globally, and dyslipidaemia is a significant risk factor [1,2]. Dyslipidaemia is associated with other risk factors, including genetic risk, sedentary lifestyle, smoking, and the intake of unhealthy and ultraprocessed foods [3,4]. It is extensively accepted that compliance to a heathier diet favours positive health outcomes, but recent evidence shows that nutraceutical compounds have been more widely employed for the adjuvant treatment of dyslipidaemia due to their attributed phytotherapic properties, deemed as safe and useful [5,6].

Cynara scolymus (Asteraceae), commonly known as artichoke, is farmed in several countries [7], but other known cultivars of artichoke, such as the Jerusalem artichoke (Helianthus tuberosus) and the Chinese artichoke (Stachys affinis) [[8], [9], [10]] are also widely prevalent. Globe artichoke is the portion of the plant which contains the flower buds before their blossoming, with the stem cut. Globe artichoke is normally cooked but the consumed part, after discarding the leaves, is known as heart artichoke. Nonetheless, the artichoke leaves are commonly consumed as herbal supplement, in the form of artichoke leaf extract (ALE) [7,11,12]. ALE, particularly the one produced from the Cynara scolymus cultivar, has been identified as a potent phytotherapic agent for several comorbidities, including cardiovascular, hepatic and gastric diseases [7]. Phenolic compounds such as cynarin, luteolin and chlorogenic acid, in conjunction with the soluble fibres inulin and pectin, are the main substances believed to be involved with the mechanisms of action attributed to artichoke [13,14].

Several studies employing experimental models have described various beneficial effects of artichoke [[15], [16], [17]], but such findings cannot be straightforwardly transferred over to larger epidemiological settings. Therefore, the potential effects of artichoke consumption on lipid profile should be further investigated before it can be identified as a useful nutraceutical compound for that purpose. Such investigations should include the analysis of metabolic biomarkers and pathways in cell lipid biochemistry.

The aim of this review is to appraise and incorporate the main results of clinical trials that have investigated the effects of artichoke administration on lipid profile, focusing on ranges of classical biomarkers including high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC), and serum triglycerides (TG) concentrations. The present study will also briefly address mechanisms of action of the main phytochemicals found in artichoke involved with lipid-lowering properties.

2. Method

This review was performed employing the Cochrane, MEDLINE and Web of Science databases. The search for articles was based on the following keywords: “artichoke leaf extract”, “artichoke cholesterol”, “artichoke LDL”, “artichoke triglycerides”, “artichoke dyslipidemia”, “artichoke metabolic syndrome”, “Cynara scolymus”, “globe artichoke” and “artichoke heart”. This search included articles published between 2000 and June 2018, and we appraised publications that covered lipid profile analyses in human interventions.

3. Lipid profile

Evidence currently available shows that artichoke administration can improve lipid profile in patients with hypercholesterolemia, metabolic syndrome, overweight, type 2 diabetes mellitus, non-alcoholic fatty liver disease and non-alcoholic steatohepatitis [[18], [19], [20], [21], [22], [23], [24], [25], [26],

[27], [28], [29]]. The main effects of artichoke administration on lipid profile are related to the observed reductions in LDL, TC and TG serum levels. Reductions in LDL concentrations were observed within a range of 8–49 mg/dL, TC within 12–55 mg/dL, and TG within 11–51 mg/dL. However, in the opposite trend, the study of Lupattelli et al. [23] showed an increase of 9 mg/dL in serum TG concentrations (Table 1). Regarding HDL, no strong evidence for its increased serum levels could be found. At the same time as the studies of Nazni et al. and Rondanelli et al. [24,29] identified increased HDL levels within the range of 8–9 mg/dL, the study of Panahi et al [25] observed decreased levels, in the range of 4.7 mg/dL (Table 1).

Table 1. The impact of artichoke administration on lipid profile.

Authors	N	Study Design (Length of the Intervention)	Type of artichoke	Daily dose of artichoke	Outcomes (mg/dL)			
					HDL-c	LDL-c	TC	TG
Barrat et al. [18]	94, subjects with hypercholesterolemia	Randomized placebo-controlled trial (16 w)	Artichoke leaf extract, policosanols and red yeast rice	200 mg	↔	↓22	↓26	↔
Bundy et al. [19]	68, subjects with mild to moderate hypercholesterolemia	Randomized, double-blind placebo-controlled trial (12 w)	Artichoke leaf extract	1280 mg	↔	↔	↓11.60	↔
Cicero et al. [20]	40, moderately hypercholesterolemic patients with metabolic syndrome	Double-blind, cross-over, randomized clinical trial (6 w)	Artichoke extract, red yeast rice, banaba extract, coenzyme Q10, vitamin B3, B6, B9 and B12	500 mg	↔	↓30.3	↓34.1	↓19.8
Englisch et al. [21]	143, hyperlipoproteinemia patients	Double-blind, randomized, placebo controlled, multi-centre clinical trial (6 w)	Artichoke dry extract	1800 mg	↔	↓48.73	↓55.3	↔
Huber et al. [48]	17, patients with chronic hepatitis C	Open, prospective pilot study (12 w)	Artichoke leaf extract	3200 mg	NA	NA	↔	NA
Huseini et al. [22]	72, hypercholesterolemia type 2 diabetic patients	Randomized double-blind placebo-controlled clinical trial (8 w)	fibre-free artichoke leaf extract	400 mg	↔	↓8	↓15	↔

Authors	N	Study Design (Length of the Intervention)	Type of artichoke	Daily dose of artichoke	Outcomes (mg/dL)			
					HDL-c	LDL-c	TC	TG
Lupattelli et al. [23]	28, moderately hyperlipidaemic patients	Non-randomized interventional study (6 w)	Frozen artichoke juice	20 mL	↔	↓14	↓17	↑9
Nazni et al. [24]	30, type 2 diabetic individuals	Non-randomized interventional study (12 w)	Processed globe artichoke powder	6000 mg	↑9.01	↓9.18	↓10.75	↓19.94
Ogier et al. [94]	39, moderate hypercholesterolemia	Double-blind, randomized, parallel controlled study (16 w)	Artichoke leaf dry extract, red yeast rice, garlic dry extract, pine bark extract and micronutrients supplementation	200 mg	↔	↓32.47	↓35.25	↓10.98
Panahi et al. [25]	89, non-alcoholic fatty liver disease	Pilot double-blind randomized controlled trial (8 w)	Artichoke leaf dry extract	600 mg	↓4.7	↓36.5	↓46.0	↓51.2
Rangboo et al. [26]	60, non-alcoholic steatohepatitis (NASH)	Randomized double-blind clinical trial (8 w)	Artichoke leaf extract	2700 mg	↔	↓14.14	↓23.6	↓38.87
Rezazadeh et al. [27]	68 metabolic syndrome patients	Double-blind placebo-controlled randomized clinical trial (12 w)	Hydro-alcoholic artichoke leaf extract	1800 mg	↔	NA	NA	↓17.7
Roghani-Dehkordi and Kamkhah [30]	98 patients with mild hypertension	Randomized, placebo-controlled trial	Concentrated artichoke leaf juice	50 and 100 mg	↔	↔	↔	↔
Rondanelli et al. [95]	49, overweight subjects	Randomized, double-blind, placebo-controlled clinical trial (8 w)	*Cynara scolymus*flowering buds extract	600 mg	↔	↔	↔	↔
Rondanelli et al. [29]	92, overweight subjects with primary mild hypercholesterolemia	Double-blind, randomized, placebo-controlled trial (8 w)	Artichoke leaf extract	500 mg	↑8.00	↓21.69	↓15.35	↔

Authors	N	Study Design (Length of the Intervention)	Type of artichoke	Daily dose of artichoke	Outcomes (mg/dL)			
					HDL-c	LDL-c	TC	TG
Rondanelli et al. [28]	55, overweight subjects with naïve impaired fasting glycaemia	Double-blind, placebo-controlled, randomized clinical trial (8 w)	Artichoke extract	600 mg	↔	↓19.33	↓17.01	↔
Skarpanska-Stejnborn et al. [96]	22, competitive rowers	Double-blind, placebo-controlled, randomized clinical trial (5 w)	Artichoke leaf extract	1200 mg	↔	↔	↔	↔

Artichoke juice was one of the means of administration employed in a few of the studies appraised; however, the juice volume must be considered in view of the observed improvement in lipid profile. Lupatteli et al. [23] employed a dose of 20 mL frozen artichoke juice for the observed decreases in LDL and TC levels. However, Roghani-Dehkordi and Kamkhah [30] employed artichoke juice concentrate in capsules of 50 and 100 mg twice a day and found no improvement in lipid profile. The latter adopted an amount much lower than the concentration found in artichoke leaf extract.

4. Artichoke, its polyphenols and phytosterols: mechanisms of action

Artichoke is a rich source of polyphenolic compounds deemed as beneficial for their nutritional properties [31]. The concentration of macronutrients and micronutrients found in 100 g of cooked artichoke is not nutritionally remarkable (Table 2). For that reason, the polyphenolic compounds and phytosterols found in artichoke are believed to be the main promoters of lipid profile improvement.

Table 2. Nutrition facts per 100 g of wet weight of artichoke compared to other vegetables of its family and the cruciferous family.

Nutrition facts	Artichoke, globe, cooked, drained. Asteraceae family.	Jerusalem-artichokes, raw. Asteraceae family.	Lettuce, green leaf, raw. Asteraceae family.	Yacon, pulp. Asteraceae family. Brassicaceae family.	Broccoli, Chinese, cooked. Brassicaceae family.	Cabbage, raw. Brassicaceae family.	Cauliflower, cooked. Brassicaceae family.
Energy (kcal)	53	73	15	44	22	25	23
Protein (g)	2.89	2.00	1.36	0.43	1.14	1.28	1.84
Total lipid (g)	0.34	0.01	0.15	0.06	0.72	0.10	0.45
Carbohydrates, by difference (g)	11.95	17.44	2.87	10.32	3.81	5.80	4.11
fibre, total dietary (g)	5.7	1.6	1.3	1.31	2.5	2.5	2.3

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fibre, soluble (g)	3.39	0.39	0.16	NA	0.45	0.65	0.65
fibre, soluble insoluble (g)	2.31	1.21	1.14	NA	2.05	1.85	1.65
Calcium (mg)	21	14	36	6.3	100	40	16
Magnesium (mg)	42	17	13	3.7	18	12	9
Potassium (mg)	286	429	194	171.7	261	170	142
Vitamin C (mg)	7.4	4	9.2	NA	28.2	36.6	44.3

In addition to reductions of TC and TG concentrations, ALE may feature a potentially preventive effect due to its ability to attenuate oxidative stress and inhibit inflammatory pathways [32,33]. ALE hinders lipid peroxidation by reducing malondialdehyde (MDA) levels and increasing the concentrations of superoxide dismutase (SOD) and glutathione (GSH) in rodent models of liver disease [33,34]. Tang and colleagues [33] found less intense degeneration of hepatic tissue in the treated group as compared to the control ones, as well as downregulated toll-like receptor 4 (TLR4) and nuclear factor kappa B (NF-κB) expression in liver tissue. These results suggest that the levels of aspartate transaminase levels (AST) and alanine transaminase (ALT) are potentially improved.

One of the cholesterol-lowering properties attributed to ALE may be related to its capacity to hinder cholesterol biosynthesis from 14C-acetate in primary cultured rat hepatocytes [35], possibly via inhibition of hydroxymethylglutaryl-CoA-reductase (HMG-CoA reductase). The inhibition of non-saponifiable neutral lipid biosynthesis from 14C-acetate appears to be attributed to the effects of chlorogenic acid, luteolin and cynaroside [35]. Briefly, chlorogenic acid and luteolin are found in considerable amounts in artichoke, and are likely to be important players amongst other polyphenolic compounds in lipid lowering mechanisms (Fig. 1).

The dosage of ALE deemed to be effective ranges from 2 to 3 g/d [21,26,27], and the amount of chlorogenic acid found at those levels is higher when compared to its amount in green coffee extract [36,37]. Green (or raw) coffee is an important source of chlorogenic acids, reaching levels of up to 14% in dry matter [36,37]. The dosage of green coffee extract found to exhibit health benefits is in average 400 mg/d, containing 170 mg of chlorogenic acid [36,38,39]. Interestingly, however, as the chlorogenic acid content found in commercially available ALE is in average 15%, the amount of ALE needed to reach 170 mg of chlorogenic acid is equivalent to approximately 1.13 g [40].

Other compounds found in artichoke that could contribute to its lipid-lowering properties include the family of phytosterols, once previous studies have described a beneficial effect of phytosterol supplementation on specific lipid-related biomarkers [41]. Beta-sitosterol and stigmasterol are the main phytosterols found in artichoke, which are believed to reduce cholesterol absorption from the intestine into the bloodstream. Beta-sitosterol and stigmasterol correspond to 45.6% and 16.2%, respectively, of the artichoke seed oil phytosterol composition [42].

However, at least 1–2 g/d of isolated phytosterols are necessary to decrease LDL and cholesterol concentrations [43,44], and phytosterol concertation in ALE is relatively very low, particularly when looking at a general recommendation of ALE at 2–3 g/d. This amount of phytosterol would not be found in a typical 100 g portion of cooked artichoke heart either. As shown in Table 2, this portion size contains only approximately 0.34 g of total fat, but only a relatively high amount would be able to provide 1–2 grams of phytosterol. For instance, the amount of phytosterols found in 100 mL of vegetable oils is 909 mg in corn oil, 411 mg in sunflower oil, 320 mg in soybean oil, 300 mg in olive oil and 183 mg in almond oil [45].

5. Liver parameters

Circulating lipids are not only associated with cardiovascular pathophysiology, they are a direct outcome of liver metabolism, where lipoproteins are synthesized [46,47]. In double-blind randomized clinical trials, Rangboo et al. and Englisch et al. found improvements in lipid profile and liver biomarkers induced by the administration of 1800 to 2700 mg/d of ALE [21,26]. Rangboo et al. found reductions in ALT levels, from ∼82 mg/dL to ∼38 mg/dL, and in AST from ∼46 mg/dL to ∼25 mg/dL, in patients with non-alcoholic steatohepatitis who took 2700 mg of ALE daily for two months [26]. However, unparallel results were found in a pilot study showing that the administration of 3200 mg/d of ALE for 3 months did not reduce ALT, AST or gamma-glutamyltransferase (GGT) levels in patients with hepatitis C, some of whom also had cirrhosis and liver fibrosis [48].

The probable mechanism of ALE in amelioration of liver metabolism is illustrated in Fig. 2. Chlorogenic acid and cynarin, which are caffeic acid derivatives, in conjunction with luteolin, are antioxidant compounds found in ALE that most probably modulate hepatic pathways [49,50]. Cynarin and caffeic acid per se show significant hepatoprotective activity in cultured rat hepatocytes [51]. Interestingly, the hepatoprotective activity of cynarin can be more remarkable than silybin from the herbal medicine Silybum marianum [52], a plant known to improve liver parameters in humans [53,54]. Caffeic acid, in turn, contributes to the modulation of the redox balance in the liver by reducing the concentration of reactive oxygen species, as well as increasing antioxidant enzyme activity [55].

6. Artichoke fibres – possible pathways for lipid improvement and prebiotic effects

Artichoke is widely regarded as a rich source of soluble fibre [[56], [57], [58]]. Although there is no Dietary Reference Intake (DRI) currently established for soluble or insoluble fibre, the Adequate Intake (AI) towards dietary total fibre is 25 g for adult women, and 38 g for adult men, which is equivalent to approximately 14 g / 1000 kcal / day, of which 2.5–10 g should include soluble fibre [59,60]. As the daily consumption of 3 g of soluble fibre is known to provide health benefits on

decreasing LDL levels, a 100 g serving of artichoke heart would be sufficient to provide that amount, exhibiting comparable potential as the usual serving of oat and psyllium [61].

Artichoke total fibre content is proportionally higher than other plants of the same family, and of the cruciferous family; however, it is lower than the fibre content found in nuts, psyllium, beans, cocoa powder, avocado, oats and various types of whole grains [62,63]. In order to achieve an intake of 10 g of soluble fibre from general foods, 120–130 g of total fibre would be required [58,64]. However, this volume of fibre may induce transient side effects including diarrhoea, bloating, nausea, flatulence, eructation and increased bowel movements. More importantly, such volume may impair the absorption of nutrients, especially micronutrients [65]. In this way, the consumption of artichoke heart, which features a valuable ratio of soluble to insoluble fibre, may be appropriate, alongside the consumption of oats and psyllium in a food plan.

Soluble fibre, which is found in relevant amounts in artichoke heart, may decrease cholesterol biosynthesis through biliary sequestration (Fig. 3). When ingested in substantial amounts (3–20 g/d), inulin induces partial diversion of the enterohepatic cycle, favouring the increased conversion of free cholesterol into cholic acid and bile acids through expression of CYP7A1 [66,67]. The CYP7A1 is a liver enzyme of the cytochrome p450 complex responsible for converting cholesterol to 7-alpha-hydroxycholesterol, which is a precursor of bile acids. Therefore, in conditions of high inulin content in the intestinal lumen, the availability of cholesterol for VLDL synthesis is reduced, and less LDL is formed. Decreased circulating cholesterol is also an outcome observed through this pathway, attributed to the increased excretion of bile acids into the intestine [68].

Similar to other types of soluble fibre, inulin is resistant to digestion in the upper parts of the intestinal tract and is later fermented in the colon. Moreover, inulin has an important bulking effect, due to the increased microbial biomass that results from its fermentation [69]. A serving of 100 g artichoke heart contains an amount of soluble fibre – inulin and pectin being prevalent ones – that is deemed sufficient for increased faecal mass [69].

The daily intake of 5 to 10 g of inulin from artichoke heart shows bifidogenic effects and contributes to the suppression of potential pathogenic bacteria in human faeces, and at the same time, this dosage is not shown to increase the content of faecal short-chain fatty acids (SCFAs) [13,70,71]. However, SCFA faecal excretion provides little information about the actual status of intestinal SCFA metabolism; its excretion does not truly reflect their concentration and production in the intestine as most SCFAs are taken up by enterocytes [72].

7. Artichoke heart versus ALE

Cooked artichoke heart provides a relevant amount of fibre, which is necessary for the achievement of its lipid lowering properties. However, a diet that aims to focus on moderate to high amounts of artichoke in a daily basis may not be realistically achievable for every individual, and the sourcing of dietary fibre from a variety of food items is a recommendation. In addition to that, artichoke leaves are removed when cooking the actual artichoke heart, and as such, its preparation may be more difficult and less cost competitive as compared to other fibre-rich foods [73].

ALE may be a useful option when looking at the health benefits of artichoke and leaf bioactive compounds; its administration in capsules may be more easily managed. Moreover, ALE can be found on the market without too much difficulty given that several pharmaceutical companies have made their products more easily accessible [74,75].

8. ALE versus lipid-lowering agents

The number of ALE capsules that must be administered in order to achieve positive health outcomes is relatively high [26,48]. A few studies have administered ALE 2–3 times a day, resulting in a total of 6–10 daily capsules, which may be inconvenient for the individual [26,48]. This particular issue is further exacerbated when in conjunction with other pharmacotherapies. For instance, the intake of multiple medicines, i.e. the polypharmacy, is relatively common in older populations, which in a daily basis could vary between five to ten different types of medicines [76,77]. Adherence to polypharmacy is already very difficult per se; adding ALE capsules may further disturb the prescribed dyslipidaemia therapy due to the large amount of capsules involved [78]. Lipid-lowering drugs such as statins or proprotein convertase subtilisin/kexin type 9 (PCK9) inhibitors are extremely useful due to their very well established efficacy for dyslipidaemia with a relatively lower number of capsules [[79], [80], [81], [82], [83]]. In light of that, the purpose of ALE administration would be to play an optional coadjutant therapy, and not intended as substitute for prescribed lipid-lowering agents.

9. Tolerability, safety and risks

Artichoke belongs to the culture and food habits of many populations throughout the centuries, evidencing its safety. In regards to ALE specifically, it is well tolerated and has few side effects within recommended dosages [7]. ALE toxicity has been identified as very low; its median lethal dose (LD50) is >2000 mg/kg for Wistar rats [48].

Intraperitoneal LD10 of hydroalcoholic total ALE solution containing 19% caffeoylquinic acids was identified as >1000 mg/kg for male rats. However, the purified extract containing 46% caffeoylquinic acids presents an oral LD40 and intraperitoneal LD50 of 2000 mg/kg and 265 mg/kg respectively (84). The LD50 of cynarin for mice has been identified as 1900 mg/kg body weight. Upon intraperitoneal administration to rats at 800 mg/kg, or intravenous to rabbits at 1000 mg/kg/hour, cynarin produced no apparent side effects or signs of toxicity [84]. Interestingly, a study employing a rat model of paracetamol-induced hepatotoxicity showed that ALE oral administration at 1.5 g/kg/d protected liver tissue and its biomarkers, improved the antioxidant status and reduced apoptosis, in relation to the non-ALE group [85].

ALE has been used as hepatoprotective herbal supplement for humans [21,26], and to the best of our knowledge, no intoxication to orally administered ALE has so far been observed in humans. The conclusion of the European Medicines Agency on the pharmaceutical forms of Cynara scolymus L. regarding clinical safety is overall acceptable. Nevertheless, as rare allergic and eczematous reactions have been reported after occupational exposure and skin contact with the fresh plant or its dried parts, allergy should be considered a contraindication for ALE internal use [7].

10. Novelty and clinical aspects

The present study offers a point of view for dietitians, physicians and pharmacists on the clinical aspects of ALE supplementation, reiterating its potential for conditions such as dyslipidaemia and liver diseases. Bringing together the main findings of experimental studies and randomized clinical trials, this review attempted to address the mechanisms of actions of ALE components and how they modulate lipid biomarkers often investigated by clinicians.

Artichoke is unarguably an important source of fibre [[56], [57], [58]], but one that may be difficult to achieve by its sole means; a 100 g serving of artichoke heart can be difficult to manage by some patients. Another downside relates to cooking difficulties and costs, once a substantial part of the plant must be removed to obtain its heart. Taken together, these factors contribute to the justification of the usefulness of ALE, alongside its rich antioxidant compound composition.

An inherent limitation of this review, however, refers to the lack of studies that have investigated the effects of artichoke heart consumption, specifically. Consequently, we can only reiterate the importance of clinical trials that investigate artichoke heart consumption as a medicinal food.

11. What is still missing in scientific investigations?

Randomized clinical trials with dietary control are still required to further investigate the effects of ALE and its chlorogenic acid content on lipid profile, in comparison to other natural sources of chlorogenic acid such as green tea and green coffee. Furthermore, interventional studies with reliable dietary control would provide stronger scientific evidence for the effects of artichoke as a food item, be it artichoke hearts or its juice. Of note, meticulous attention to dietary fibre is needed, once the soluble fibre content in artichoke is a key player on its mechanism of action.

Randomized clinical trials may also feature the advantage of providing more reliable evidence of ALE effects well beyond lipid profile, for example its potential effects upon hypertension, hyperglycaemia and inflammation. Serum luteonin is a biomarker that can be investigated in response to ALE administration or artichoke heart intake, due to the usefulness of reflecting its own ingestion [86]. Finally, long-term clinical studies are necessary to elucidate whether ALE is, or is not, an aid to reduce negative cardiovascular outcomes. Follow-up studies of 5–10 years duration would provide valuable information on mortality and health outcomes such as cardiovascular disease [87].

12. Conclusion

The evidence so far available suggests that artichoke, employed either as food item or herbal supplement, can offer additional support for the treatment of dyslipidaemia. As food item, for intended improvement in lipid parameters, the consumption of considerable servings of cooked artichoke heart, as much as 100 g daily, may be necessary. The artichoke leaf extract, in turn, may be an accessible option as it can be more easily ingested as capsules, offering an arguably superior

adherence for the coadjutant treatment of dyslipidaemia. Several investigations have favoured the study of artichoke leaf extract as capsules, as opposed to other forms of artichoke administration, for example its juice or cooked artichoke heart.

The daily administration of approximately 2–3 g of artichoke leaf extract is seen as effective for improvements in lipid profile. Such improvement is evidenced as decreased LDL, triglycerides and total cholesterol blood levels have been reported, but apparently no changes to HDL levels. Long-term clinical trials are decisive to confirm the beneficial effects of artichoke leaf extract administration upon cardiovascular outcomes.

Conflict of interests

The authors have no competing interests to declare.

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Figure 1

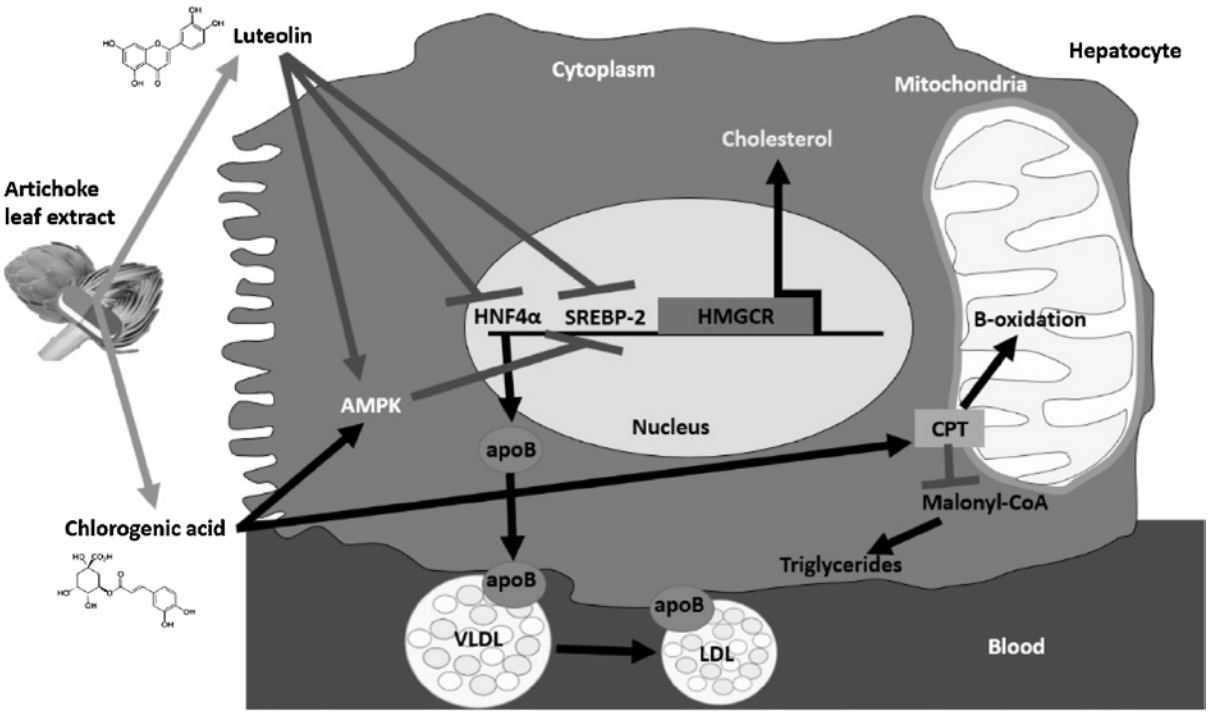

Fig. 1. The impact of artichoke leaf extract (ALE) on lipid profile. Modulation of lipid profile induced by ALE occurs mainly through the actions of luteolin and chlorogenic acid. In the hepatocyte nucleus, luteolin decreases HNF4α expression, consequently decreasing cholesterol synthesis due to inhibition of SREBP-2 and HMGCR [[88], [89], [90]]. Reduced HNF4α expression also decreases the synthesis of apoB, consequently decreasing VLDL and LDL levels [88]. Chlorogenic acid decreases cholesterol synthesis due to stimulation of AMPK and consequent inhibition of SREBP-2 [[91], [92], [93]]. Chlorogenic acid may also lower triglyceride levels by CPT stimulation, which increases β-oxidation and inhibits Malonyl-CoA [92,93]. apoB: apolipoprotein B; AMPK: AMP-activated protein kinase; CPT: Carnitine Palmitoyl Transferase; HMGCR: 3-Hydroxy-3-Methylglutaryl-CoA Reductase; HNF4α: Hepatocyte nuclear factor 4α; SREBP-2: Sterol-regulatory element-binding protein; VLDL: very low-density lipoprotein.

Figure 2

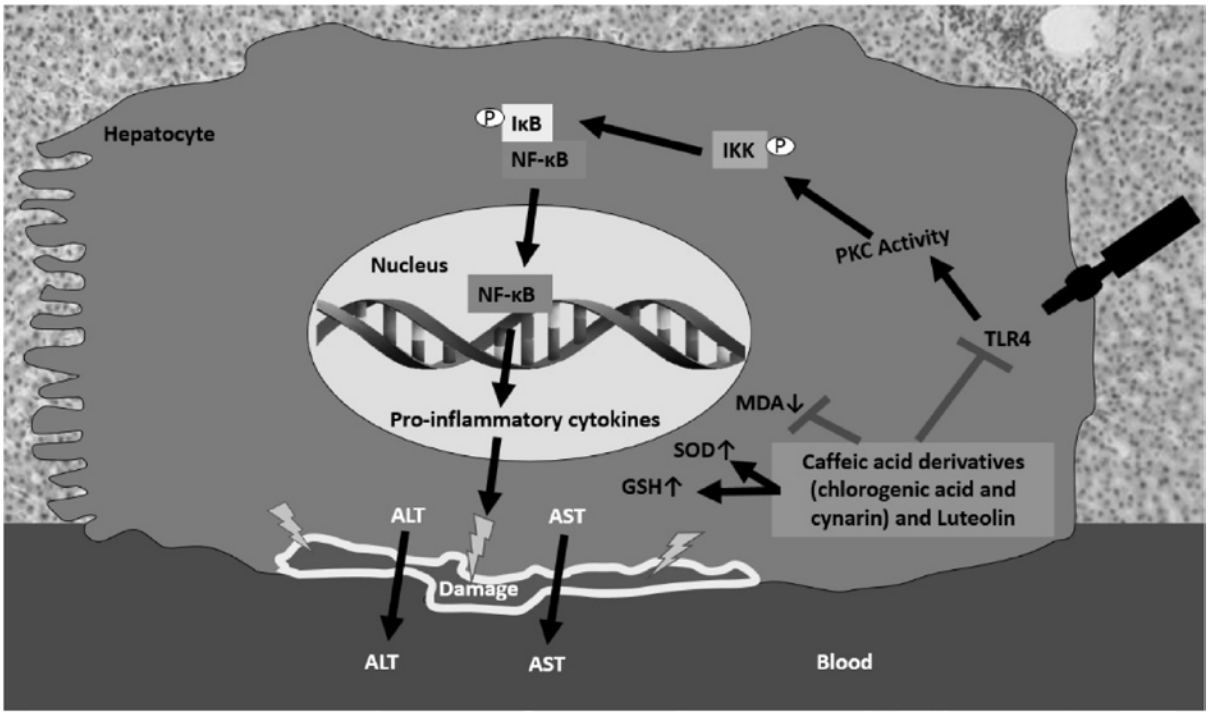

Fig. 2. The hepatocyte antioxidant system can be modulated by artichoke components, the main ones possibly being caffeic acid and its derivatives, and luteolin. These substances have the potential to supress the TLR4 signalling cascade, which activates the NF-κB pathway. In the nucleus, activated NF-κB stimulates various pro-inflammatory cytokines that damage the cell and its membrane. Through cell membrane injury, ALT and AST enzymes leak into the blood. The hepatoprotective effects attributed to artichoke components corroborate the observed decreases in ALT and AST concentrations. Additionally, artichoke components increase the activity of the SOD and GSH antioxidant enzymes, and decrease MDA levels, biomarkers of oxidative stress [33].

ALT: alanine aminotransferase; AST: aspartate transaminase; GSH: glutathione; IKK: IκB kinase; MDA: malondialdehyde; NF-κB: nuclear factor-kappa B; P: phosphate; PKC: protein kinase C; SOD: superoxide dismutase; TLR4: toll-like receptor 4.

Figure 3

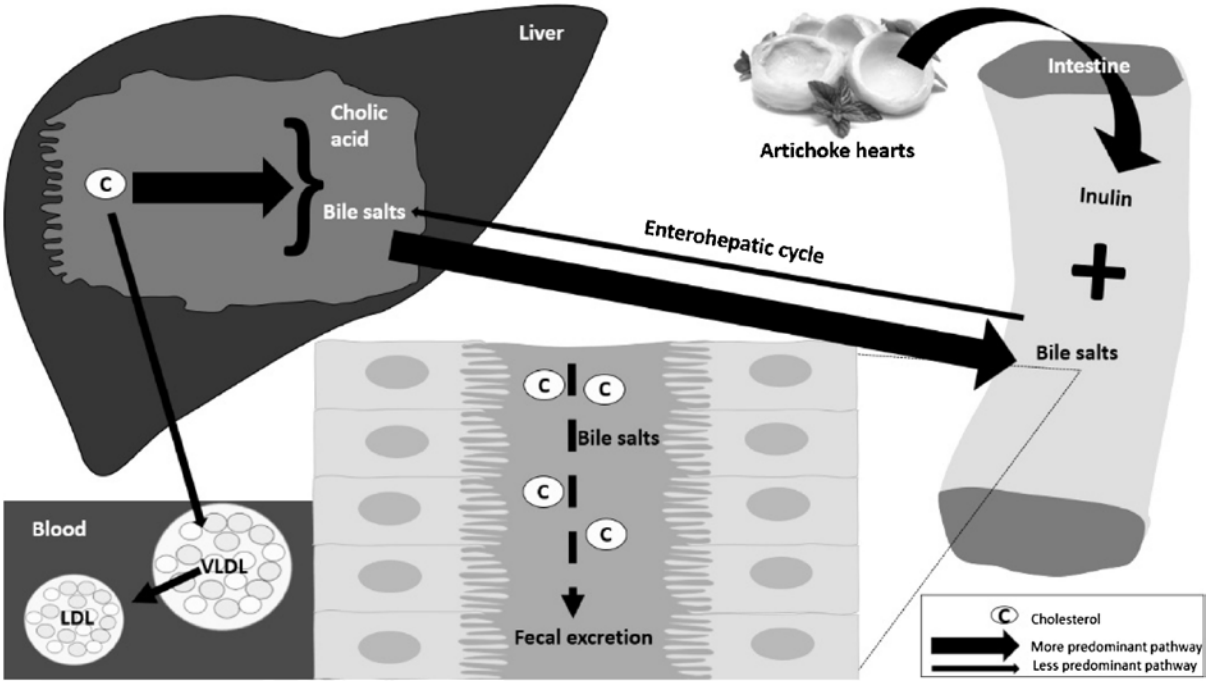

Fig. 3. Inulin and modulation of lipid profile. Inulin, which can be found abundantly in artichoke heart, can modulate lipid profile through the enterohepatic cycle [66,67]. If ingested in sufficient amounts, inulin in the intestine increases the demand for bile salts in situ, and decreases their return to the liver. In the liver, cholesterol bioconversion to bile salts for excretion is increased, subsequently decreasing VLDL and LDL serum levels [68]. C: cholesterol; LDL: low-density lipoprotein; VLDL: very low-density lipoprotein.