Egypt. J. Chem. **Vol. 67,** No. 6 pp. 33 - 41 (2024)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Plants Effective in the Control of Hyperlipidemia and Hypercholesterolemia: A Review

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Abstract

Hyperlipidemia is characterized by the elevation of cholesterol, triglyceride, and LDL (low-density lipoprotein) blood concentrations. Hyperlipidemia is a risk factor for cardiovascular diseases, in addition to nonalcoholic fatty liver disease and hepatic cancer. Current treatment strategies for hyperlipidemia include lifestyle changes and lipid-lowering medications, which have serious side effects. Therefore, the aim of this review is describing what is known to date as lipid-lowering alternatives of natural source and therefore have fewer side effects. Many phenolic-rich plants were found to be effective in regulating lipid metabolism, as cassia bark, clove buds, coffee seeds, eucalyptus kino and leaves, ginger rhizomes, hops strobiles, juniper berry leaves, licorice roots, milk thistle seeds, peppermint leaves, pomegranate rind, and turmeric rhizomes.

Keywords: Curcuma, herbal medicines, hops, hypercholesterolemia, hyperlipidemia, NAFLD.

1. Introduction:

Dyslipidemia is a collective term used to describe abnormal levels of triglycerides, cholesterol, and/or high-density lipoproteins. Dyslipidemia is a common feature in individuals with type 2 diabetes and metabolic syndrome [1], it is characterized by a complex interplay of various lipid components, including elevated triglycerides (TG) and TG-rich lipoproteins, along with increased postprandial TG levels [2]. The reduced levels of high-density lipoprotein cholesterol (HDL-C) and apolipoprotein A-I (apo A-I) further exacerbate the imbalance [3]. The dyslipidemia is marked by an increase in apolipoprotein B (apo B), reflecting higher levels of atherogenic lipoproteins [4]. Notably, there is an elevation in LDL particle number, particularly the small, dense LDL particles, which are associated with increased cardiovascular risk [5]. Moreover, dyslipidemia in these individuals is characterized by an increase in oxidized and glycated lipids, highlighting the role of oxidative stress and glycation in lipid metabolism abnormalities associated with type 2 diabetes and metabolic syndrome [6]. The intricate chemistry of dyslipidemia underscores the multifaceted nature of lipid dysregulation in these metabolic disorders, providing insights into potential therapeutic targets for managing cardiovascular risk in affected individuals.

Dyslipidemia can be mediated by genetic factors, diet, such as unhealthy and ultraprocessed foods, and lifestyle, such as sedentary lifestyle and smoking, and certain types of drugs [7]. Dyslipidemia can be a primary disease condition, or it can be secondary to certain disease conditions such as diabetes mellitus. Dyslipidemia contributes as a risk factor in fatal cardiovascular complications leading to the increase in risk of mortality [7–10].

Excessive accumulation of liver lipids contributes to inflammation and lipid metabolism disorders, causing nonalcoholic fatty liver disease (NAFLD). NAFLD contributes as a major cause of hepatic cancer [11]. Therefore, controlling lipid levels would be a promising strategy for combating NAFLD and liver cancer.

Currently, achieving control of dyslipidemia is usually with multi-drug treatment, preferably accompanied with lifestyle and dietary adjustments and restrictions to be effective [12]. However, patients may have low compliance in following lifestyle changes [12]. In addition, long-term use of lipid-lowering medications can cause serious side effects. Therefore, finding alternatives of natural source and therefore fewer side effects can be of great merit [8, 10].

Many phenolic compounds were found to be effective in regulating lipid metabolism. Flavonoids can target lipid metabolism by inhibiting sterol regulatory binding protein-1 (SREBP-1), leading to the inhibition of fatty acid synthase and associated enzymes [11]. Rutin was found to downregulate transcription of SREBP-1c in hepatic cell line, decreasing the levels of triglycerides and cholesterol. Taxifolin also downregulated transcription of SREBP-1c in mice fed with high fat-diet [11].

Numerous herbs are acknowledged for their potential impact on lipid profiles, yet comprehensive investigations into their mechanisms, particularly concerning their influence on gene expression and regulatory proteins, remain

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Receive Date: 04 August 2023, Revise Date: 10 November 2023, Accept Date: 16 November 2023
DOI: 10.21608/EJCHEM.2023.227181.8364

incomplete. Therefore, we have meticulously chosen a variety of herbal samples (refer to Figure S1) renowned for their reputed lipid-lowering properties in both traditional medicine and scientific literature. Our objective is to probe into the intricate biological activities and elucidate the mechanisms of action of these selected herbs. The botanical specimens under scrutiny encompass Cassia bark, Clove buds, Coffee seeds, Eucalyptus kino and leaves, Ginger rhizomes, Hops strobiles, Juniper berry leaves, Licorice roots, Milk thistle seeds, Peppermint leaves, Pomegranate rind, and Turmeric rhizomes.

2. Experimental:

In order to find only trusted scientific studies on herbs that are effective in the control of hyperlipidemia and hypercholesterolemia, many scientific websites and articles were extensively combed through. Example of these are the Web of Science, Google Scholar, EBSCO Information Services, ProQuest, the Egyptian Knowledge Bank databases, Science Direct, and PubMed. Only Recent reports, review articles, book references, and clinical studies were studied, reviewed, and mentioned herein. Information that was found to lack the desired specific goal and unreviewed literature were discarded.

3. Results and Discussion

Herein, several examples of plants with promising anti-hyperlipidemic activity are reviewed.

3.1 Cassia (*Cinnamomum cassia* family Lauraceae):

Cinnamomum cassia, also known by its common names Chinese cassia or cinnamon, is an aromatic tree that originated in the south of China and is cultivated in China, India, and surrounding regions. The part used consists of the inner bark of the tree [13]. It is extensively used for its aroma, flavour, and therapeutic properties. It was found to have anti-microbial, anti-inflammatory, anti-oxidant, antidiabetic, antitumor, and anti-hyperlipidemic properties [13–15].

Cassia was found to contain various aromatic compounds, as cinnamaldehyde, cinnamic acid, cinnamate, eugenol, camphor, trans-cinnamyl acetate, in addition to caryophyllene, bergamotene, alphacopane, and caryophyllene oxide [13, 15]. The commercial value of cassia depends on its content of its volatile oil's eugenol and its derivatives [16]. The preliminary phytochemical screening of the cassia bark ethanolic extract gave positive results regarding alkaloids, carbohydrates, tannins, terpenoids, quinones, total protein, flavonoids, coumarin, phenols, and anthraquinones, while the methanolic extract gave positive results with alkaloids, carbohydrates, tannins, total protein, flavonoids, and phenols [15].

Many studies proved the anti-hyperlipidemic activity of cassia bark. For instance, the administration of cassia bark ethanol extract in mice given streptozotocin to induce diabetes significantly decreased the disturbed levels of blood lipids caused by streptozotocin administration with no adverse effects reported [15]. Furthermore, in normal adult albino rats given a daily dose 2 gram/kg body weight of cassia extract for 30 days, total cholesterol in serum was lowered (decreased by 2.10%), triglycerides (decreased by 3.65%), and LDL-C by 10.37% [13]. Finally, an umbrella meta-analysis of 11 meta-analyses found that cassia significantly lowered the serum levels of total cholesterol (WMD = -1.01mg/dl; 95% CI: -2.02, -0.00, p = 0.049), serum levels of LDL (WMD = -0.82mg/dl; 95% CI: -1.57, -0.07, p = 0.032) and significantly increased the blood levels of HDL (WMD = 0.47 mg/dl; 95% CI: 0.17, 0.77, p = 0.002), giving supporting evidence to the lipid-lowering potential of cassia bark [17].

3.2 Clove (*Syzygium aromaticum* L. or *Eugenia caryophyllata* family Myrtaceae):

Clove is a traditional spice and is used for its therapeutic properties in folk medicine. The part used in traditional medicine is the dried flower bud collected before the blossoming of the flowers. Clove is thought to be indigenous to Indonesia's Maluku islands, and is currently cultivated in several Asian and African countries, as Madagascar, Sri Lanka, Indonesia, and China [18–20].

Clove contains bioactive phytoconstituents as sesquiterpenes, monoterpenes, hydrocarbons, and phenolic compounds, and it has potent antibacterial, antiviral, antifungal and antioxidant activities [18–20]. The hydroethanolic extract of clove was found to be rich in flavonoids, (64.63+/-0.35 mg gallic acid equivalent/gram). Other detected classes of compounds included alkaloid (17.33+/-2.31 mg/g), tannins (1.93+/-0.031 mg/g), and cardiac glycosides (0.13+/-0.03 mg/g) [21]. Isolated bioactive molecules from clove included eugenol, beta-caryophyllene, alpha-humulene, 4-hydroxy-3-methoxybenzaldehyde or vanillic aldehyde, maslinic acid, kaempferol, rhamnetin, eugenin chromone and its methyl derivative eugenitin, , ellagic acid, gallic acid, biflorin, an chromone C-glucosides, myricetin, campesterol, stigmasterol, oleanic acid, bicornin, quercetin, and carvacrol [18, 19]. Regarding clove's volatile oil, eugenol is the main constituent of the oil (More than 50%), contributing to the oil's pain-relieving, antioxidant, anti-tumor, anti-depressant, antispasmodic, anti-inflammatory, and anti-microbial properties. Clove oil also contains other phenolic constituents as eugenol acetate, beta-caryophyllene, and alpha-humulene (10-40%) [18, 19].

The effect of clove on lipid profiles was tested on Wistar rats with artesunate toxicity. Administration of the hydroethanolic extract of clove for 21 days in a dose of 400 and 800 mg/kg reversed the increased levels of lipids caused by artesunate toxicity, decreasing the elevated levels of cholesterol, triglycerides, and LDL, while raising the decreased levels of high density lipoproteins (HDL) [21].

3.3 Green coffee (*Coffea arabica* L., family Rubiaceae):

Coffee is mainly cultivated in Brazil, Colombia, Indonesia, and Vietnam [22]. Green coffee seeds are superior to roasted coffee seeds regarding their content of phenolic compounds and antioxidant activity [23], as active compounds are partially destroyed during the roasting process [22]. Green coffee seed was found to achieve protection against obesity, Alzheimer's, hypertension, and bacterial infections [23]

Green coffee seeds were reported to contain carbohydrates as cellulose, hemicellulose, sucrose, glucose, fructose and galactose; lipids as triacylglycerols, sterols, tocopherols, and diterpenes; aminoacids and proteins; alkaloids as caffeine and trigonelline; and phenolic chlorogenic acid derivatives [22].

In a study done on Sprague–Dawley albino rats, administering green coffee methanolic extract reversed the histological damage done to liver cells and significantly improved the altered parameters induced by carbon tetrachloride toxicity due to green coffee's antioxidant activity, increasing HDL levels and decreasing the levels of cholesterol, TG and LDL [23]. This activity could be attributed to green coffee's phenolic content, specially its

rich content of chlorogenic acid, which was reported to improve lipid metabolism due to the activation of AMPK [24]. In addition, a randomized, cross-over, controlled study found that consuming 6 grams per day of a mixture of green and roasted coffee (35:65) lowers serum lipids [25]. Another randomized, double-blind clinical trial placebo-controlled found that a daily dose of 400 mg of green coffee extract for a period of 8 weeks significantly decreased serum total cholesterol, LDL, and plasma-free fatty acids in the intervention group [26].

3.4 *Eucalyptus globulus* L. leaves obtained from a tree of the myrtle family (Myrtaceae).

Eucalytus trees are believed to have originated in Australia [27], but are commonly cultivated elsewhere including Egypt [28, 29]. Eucalytus trees reach a height of 60-80 metres [27]. The color of the bark ranges from brown to yellowish-brown [27]. The color of the leaf is initially blue-green and turns greenish-white as the age of the tree increases [27]. Although Eucalyptus trees are normally cultivated for their wood [30], *Eucalyptus globulus* trees are known for their essential oil which is of medicinal, nutritional, and ornamental value [27]. The medicinal properties of the essential oil include antimicrobial, antioxidant, chemotherapeutic, wound healing, and chemoprotective properties, and respiratory and gastrointestinal disorder treatment [30, 31]. The volatile oil of eucalyptus is mainly extracted from the leaves [27], although research was also conducted on the extracts of the eucalypt tree bark and exudate [28, 29]. The GC-MS analysis of the essential oil proved 1,8-cineol (eucalyptol) to be the major constituent (51.25%), in addition to other compounds that are mainly bicyclic monoterpenes, aromatic terpenoids, cyclic ether, or terpenes such as camphor (9.58%), borneol (7.63%), and camphene (3.77%) [27].

Analysis of the leaf methanol extract using HPLC-DAD-ESI-MS/MS detected the presence of compounds (including tannins, phenolic acids, and flavonoids) of which the major ones were gallic acid derivatives, isorhamnetin 3-O-β-d-glucuronoside , quercetin derivatives, cypellocarpin C, eicosanoic acid, and valoneic acid dilactone [31].A study on the acetone extract of eucalyptus tree leaves detected the presence of gallotannin, ellagitannin and flavonol derivatives [32].

Upon treatment with 0.05, 0.1, 0.2 and 0.4 gram/kg body weight of eucalyptus leaves ethanolic extract for 21 days in rats treated with streptozotocin to induce diabetes, the levels of serum triglyceride and cholesterol were significantly decreased when compared with control diabetic rats [33].

On the other hand, Eucalytus is also known for its phenolic rich exudate named *Eucalyptus globulus* L. kino, a trunk exudate produced by the eucalypt trees. Eucalyptus kino is known for its astringent properties due to its content of tannins, characterised by its deep reddish color and rich in phenolic compounds including phenolic acids and flavonoids [28]. Eucalyptus kino was found to have significant anti-oxidant and anti-tumor activity through the inhibition of matrix metalloproteinase-9 (MMP-9) and Transforming growth factor beta (TGF-β) gene expression [28, 34].

3.5 Ginger (*Zingiber officinale* R., family Zingiberaceae):

Ginger is an ancient food ingredient, spice, and nutraceutical native to Asia, but cultivated elsewhere such as Africa and tropical regions [35]. Ginger is a perennial plant and has nodal rhizomes with a yellow or brown and a yellowish-brown outer membrane. The rhizome consists of cells containing oleoresin [35]. The amount of oil in ginger ranges between 1-3%. Ginger rhizomes are known to have anti-hyperlipidemic properties while causing minimal side effects [36]. In addition to being an anti-hyperlipidemic, ginger also possesses immune-modulating, anti-tumorigenesis, anti-inflammatory, anti-apoptosis, antioxidant, anticoagulation, antidiabetic, antioxidative, anti-inflammatory, anti-oncogenic, and anti-nausea properties [35–37].

At least 400 compounds have been reported in ginger extract, while over 50 compounds have been reported in the oil, among which the major is 6-gingerol [35, 37]. Gingerols are phenolic compounds that are responsible for the pungency of ginger, which upon dehydration the powdered gingerol are converted to shogoals [35]. Other reported compounds included zingerones, zingerols, paradols, gingerdiols, diaryl heptanoids, and ferollic acid derivates [35].

Several clinical trials found that ginger is effective in controlling blood lipids in humans [35]. A randomized, double-blind, placebo-controlled clinical study done on 41 diabetes mellitus (II) patients found that the supplementation of 2 grams of ginger powder per day for 12 weeks significantly decreased the levels of apolipoprotein B, the ratio of apolipoprotein B to apolipoprotein A-I, and the levels of malondialdehyde in the ginger group in comparison to the baseline, as well as in comparison to the control group, while increasing the level of apolipoprotein A-I [38]. Another randomized double-blind placebo-controlled clinical study done on 63 diabetes mellitus (II) patients found that the supplementation of 1600 mg per day of ginger for 12 weeks significantly lowered the levels of serum triglyceride and total cholesterol comparison to the placebo group [39] One study done on hamsters due to the similarity of lipid metabolism between humans and hamsters found that the consumption of ginger in hyperlipidemic hamsters had many positive outcomes on the lipid metabolism, including the reduction of lipids accumulated in the liver through different mechanisms such as the lowering of oxidative stress and endoplasmic reticulum stress and the increase of cholesterol efflux [37].

3.6 Hops (*Humulus lupulus* L., family Cannabaceae).

The strobiles (also known as cones or female inflorescence) of *Humulus lupulus* are commonly named hops. The genus *Humulus* originated in China, but many cultivars have spread worldwide in temperate zones [40, 41].

The main secondary metabolites in hops are polyphenols, essential oils, and resins [41]. Other compounds reported in hops are terpenes, phloroglucinol bitter acids (5–20% of weight, mainly humulone, cohumulone, adhumulone, lupulone, colupulone, and adlupulone), prenylflavonoids (mainly the chalcone xanthohumol), flavonol glycosides (as kaempferol, quercetin, rutin), and catechins (as catechin and epicatechin gallate) [42].

Hops has a bitter taste due to its content of bitter acids; and is therefore used in the brewing industry to give flavor, as well as to increase the shelf life. This is due to its polyphenolic compounds and acyl phloroglucides content [40, 42]. In addition, hops is a traditional remedy used in the treatment of inflammation, pneumonia, indigestion, insomnia, and dysentery [42]. Some of its traditional uses have been scientifically supported such as its stomachic, antibacterial and antifungal activities [42]. Hops was found to have many medicinal properties mainly due to its content

of bitter acids, prenylated chalcones as xanthohumol, and phytoestrogens as 8-prenylnaringenin, such as anti-inflammatory, immune-modulatory, anti-obesity, and cancer as well as metabolic disorders prevention properties [40, 43].

Supplementation of hops extract in mice fed a high-fat diet was found to prevent obesity (Sumiyoshi and Kimura's 2013). Isohumulones were found to control dyslipidemia and reduce insulin resistance in humans [41]. Isohumulones were also found to control obesity, boost lipid metabolism, and decrease systemic inflammation in high fat-fed animal models [41].

3.7 Juniper (*Juniperus communis* L., Family Cupressaceae).

Juniper communis is an evergreen aromatic shrub that reaches a height of 10 meters and has green needle-like leaves and bitter astringent fruits that are berry-like cones which turn from green to purple-black as they ripen [44]. Juniper is distributed throughout Asia, Europe and North America [44].

Juniper is rich with secondary metabolites, such as volatile oil, resin, gums, lignins, and polyphenolics (as catechin, leucoanthocyanidin, flavonoids, and tannins). In traditional medicine, juniper is known for being used as diuretic, anti-arthritic, anti-diabetic, and antiseptic [44]. Juniper berries were proven to have many medicinal properties such as having antioxidant, antibacterial, antiviral and antifungal, anti-inflammatory, cytotoxic, hypoglycemic and hypolipidemic properties [44].

In a study carried out on Wistar albino rats, the administration of 50, 100 and 200 mg/kg body weight of juniper extract prevented the increase in lipid cholesterol and oxidized LDL levels caused by the consumption of cholesterol [45]. Another study in Streptozotocin-nicotinamide induced diabetic rats showed that the administration of 100 and 200mg/kg juniper methanol extract produced a significant dose-dependent reduction in total cholesterol, triglycerides, LDL, Very low-density lipoproteins (VLDL) with the elevation of HDL levels [46].

3.8 Licorice (*Glycyrrhiza glabra* L., family Fabaceae.):

Licorice, also spelled as “liquorice”, has been a well-known traditional remedy in Chinese medicine since ancient times, known for its pharmacological properties on the digestive, immune, and cardiovascular systems. In addition to its adrenocortical hormone-like effects due to the triterpenoidal saponin content [47]. Licorice also has anti-inflammatory, antibacterial, antiviral, antioxidative and anti-allergenic properties and antitumor effects [47].

Licorice roots contains many bioactive compounds, such as saponins, triterpenoids, flavonoids, polysaccharides, coumarins, and alkaloids[47]. The main active constituents are flavonoids, of which the major is glabridin, in addition to liquirtins and coumarins [47, 48]. Licorice roots also contains triterpenoidal saponins, such as the sweetening agent glycyrrhizin [47, 48].

The antihyperlipidemic effect of the alcoholic powdered root extract was tested in Wister rats given streptozotocin to induce diabetes. The reduction in cholesterol and triglyceride concentrations resulting from the treatment with licorice root extract were similar to the results obtained by the treatment with glibenclamide [48]. Another study was done to compare the anti-hyperglycemic and anti-hyperlipidemic effect of licorice with the drugs metformin and glimepiride on Wistar albino rats given streptozotocin to induce diabetes. Licorice extract concentrations of both 200 and 400 mg/kg body weight for 28 days showed significant decrease in total cholesterol (TC), and the triglycerides (TG) levels [49].

3.9 Milk thistle (*Silybum marianum* L., family Asteraceae).

Milk thistle is known as a plant with hepatoprotective properties and used for the treatment of hepatic diseases. Its Fruits, leaves, and seeds are used in the traditional Egyptian medicine for depression, migraine, and as a general analgesic, stimulant, laxative, and for treating liver disorders and mushroom poisoning [50]. Milk thistle is also known in Chinese folk medicine as a clearing and detoxifying agent [51]. Milk thistle is believed to be native to many regions including Northern Africa, Southern Europe, Southern Russia and Anatolia [52].

Both the seeds and fruits of milk thistle contain the active constituent silymarin, a flavonolignan complex that consists of compounds such as silybin (40−65%), isosilybin (10−20%), silychristin and silydianin (20−45%), and dihydrosilybin, [51]. Milk thistle also contains flavonoids (as taxifolin, dihydrokaempferol, and quercetin) and fatty acid oil (phospholipids and unsaturated fatty acids) [51]. Other than being a well-known hepatoprotective agent, milk thistle was also found to have antimicrobial, anticancer, antioxidant, and antidiabetic properties [51]. Among the various hepatic disorders milk thistle was found to be effective against, nonalcoholic fatty liver disease and alcoholic liver disease are notable as their pathogenesis includes disrupted lipid metabolism and fat accumulation within the liver [51].

In a study carried out on HepG2 cells treated by the free fatty acids, oleic acid and palmitic acid in a ratio of 2:1, in order mimic a Hepatic steatosis model, pretreatment with silibinin (10 uM) resulted in 22% reduction in lipid accumulation in comparison with the control group that was treated with the free fatty acid mixture only [53]. Silibinin was also found to significantly downregulate the sterol regulatory element binding proein-1 (SREBP-1) protein expression [53].

3.10 Peppermint (*Mentha piperita* L., family Lamiaceae).

Peppermint is a strongly scented perennial plant mainly grown in temperate regions as in Europe, Asia, United States, India and Mediterranean countries including Egypt [54]. It is a short plant that can reach up to 90 cm with an erect rectangular stem and oblong-ovate green leaves [54]. The traditional medicinal uses of peppermint include treatment of fever, cold, digestive disorders, and oral mucosa and throat inflammation [54] and the dried leaves of peppermint were found in the Egyptian pyramids [55]. Scientific studies showed that peppermint has numerous bioactive properties, such as anti-oxidant, anti-microbial, anti-inflammatory, anticancer, radioprotective and anti-diabetic properties [54].

The active constituents of peppermint mainly consist of essential oils (mainly menthol, menthone, pulegone, menthofuran, menthyl acetate and isomenthone), phenolics, flavonoids, lignans and stilbenes [54, 56].

In a study of the effect of Mentha piperita leaf juice on the blood sugar levels and lipid profiles of the offspring of pregnant diabetic Wistar rats given streptozotocin to induce diabetes, the leaf juice (100 gram/L) significantly reduced glucose, LDL-c, cholesterol and triglycerides levels and significant rise in HDL-c in the offspring of the diabetic female rats in comparison to the control group [57]. Further,

in a study carried out to investigate the effect of peppermint on serum lipid levels of albino rats fed with fructose, the aqueous extract (100 mg/Kg, 250 mg/Kg given orally daily for 3 weeks) indicated that the water extract of peppermint significantly decreased the elevated levels of cholesterol, triglycerides, VLDL, LDL and also increased the HDL levels [56].

3.11 Pomegranate (*Punica granatum* L., family Punicaceae).

Pomegranate is an ancient shrub or small tree and is believed to be native to the Himalayas in northern India. The roots, flowers, fruits, peel, seeds of the pomegranate plant are used as medicinal materials and contain many phytochemicals, mainly tannins, organic acids, flavonoids, alkaloids, and volatile oils. The bioactive properties of pomegranate include antioxidant, antimicrobial, anti-inflammatory, antibacterial, antiviral, lipid-regulatory, immunomodulatory and anti-oncogenic [58, 59].

The pomegranate peel or rind is the main part used in Traditional Chinese Medicine. This is due to its tannin contents including ellagic acid, chlorogenic acid, casuariin, punicalagin, punicalin, strictinin, casuarinin, gallic acid, granatin A, granatin B, punigluconin, and tellimagrandin. Besides its flavonoid constituents (quercitin, apigenin, acacetin-7-O-rutinoside, hespereti n, hesperidine, isoquercetrin, kampferol, astragalin, kaempferol-3-O-β-d-glucopyranoside, luteolin, naringenin, naringin, pelargonidin, apigenin-4′-O-β-D-glucoside, cyanidin, rutin, and (+)-epicatechin) may also be responsible as well as alkaloids (such as hygrine, caffeine, pelletierine (punicine), norhygrine, norpseudopelletierine, pseudopelletierine, sedridine, and 2,3,4,5-tetrahydro-6-propenyl-pyridine) [59].

A study was done to test the effect of purified pomegranate peels polyphenols (gallic acid, punicalagin, catechin, chlorogenic acid, caffeic acid, epicatechin, rutin, ellagic acid) on the lipid metabolism regulation in a steatosis hepatic cell model. The results indicated that pomegranate peels polyphenols possessed significant lipid-lowering effects reducing the accumulation of triglycerides and cholesterol within the hepatic cells [60].

3.12 Turmeric (*Curcuma longa* L., family Zingiberaceae).

Turmeric is a globally utilized spice, especially in Asia, and is extensively cultured in the tropical areas of Asia [61]. The turmeric plant can reach a height of of 3–5 feet and its leaves are oblong with yellowish funnel-shaped flowers, and the most extensively used part in medicine is the root [61]. Its rhizome is known for its yellow pigment attributed to its main active constituents, curcuminoids.

Curcumin is a member of the phenolic curcuminoids, along with demethoxy-curcumin and bis-demethoxy-curcumin [62]. Turmeric rhizomes were found to have numerous pharmacological activities including anti-inflammatory, antioxidant, antitumor, antimutagenic, antimicrobial, anti-obesity, antihyperlipidemic, cardioprotective, and neuroprotective effects [61].

Studies have found that turmeric and its main active constituent curcumin can produce antihyperlipidemic effects by increasing the uptake of fatty acids , and anti-obesity effects by reducing the process of lipogenesis [62]. Curcumin was also found to significantly decrease triglyceride and LDL serum levels [63]. In a randomized controlled trial carried out in diabetes mellitus type II patients, curcuminoids (1000 mg per day plus piperine 10 mg per day for 12 weeks) were found to reduce serum levels of atherogenic lipid indices including non HDL-cholesterol and lipoprotein(a) [64].

4. Conclusion:

In conclusion, the comprehensive examination of various phenolic-rich plants in this review, drawing on clinical trials, animal studies, and in-vitro investigations, substantiates their potential as valuable sources of bioactive compounds for the treatment of hyperlipidemia and hypercholesterolemia. The evidence gathered underscores the promising lipid-regulating properties of these plants, with examples such as Cassia bark, Clove buds, Coffee seeds, Eucalyptus kino and leaves, Ginger rhizomes, Hops strobiles, Juniper berry leaves, Licorice roots, Milk thistle seeds, Peppermint leaves, Pomegranate rind, and Turmeric rhizomes.

Despite the compelling findings, further explorations through advanced phytochemical and pharmacological studies are imperative to unravel the precise mechanisms of action responsible for the hypolipidemic and hypercholesterolemic effects of these plants. This necessity is accentuated by the complex interplay of factors in dyslipidemia, such as genetic influences, dietary habits, lifestyle choices, and the potential side effects associated with conventional lipid-lowering medications.

As the quest for alternative, naturally sourced remedies gain significance, continued research endeavours will deepen our understanding of the intricate biology behind lipid metabolism and offer insights into novel therapeutic avenues. In essence, this review lays the foundation for future investigations aimed at isolating and characterizing specific bioactive compounds responsible for the observed lipid-modulating effects, ultimately paving the way for the development of targeted and efficacious interventions for individuals grappling with lipid-related disorders.

Table 1. The major properties of the different herbal samples discussed in the article.

Herbal Sample	Major Properties
Cassia bark	Significantly reduced the elevations in blood lipids caused by streptozotocin in diabetic mice. Significantly reduced the serum concentrations of cholesterol, triglycerides, and LDL in albino rats. Significantly reduced the serum concentrations of total cholesterol and LDL, and significantly increased the serum concentrations of HDL in randomized control trial in humans.
Clove buds	Reversed the increased serum concentrations of cholesterol, triglycerides, and LDL caused by artesunate toxicity in Wistar rats, while raising the decreased levels of HDL.
Coffee seeds	Reversed the histological damage done to the hepatic cells and significantly reduced the elevated levels of cholesterol, TG and LDL caused by carbon tetrachloride toxicity in Sprague–Dawley albino rats and increased the HDL blood levels. Significantly reduced serum lipids (cholesterol, LDL, and free fatty acids) in humans in clinical trials.
Eucalyptus leaves	Significantly decreased blood triglycerides and cholesterol in rats treated with streptozotocin to induce diabetes.
Ginger rhizomes	Significantly lowered serum triglycerides and total cholesterol and significantly decreased apolipoprotein B levels, apolipoprotein B/apolipoprotein A-I ratio and malondialdehyde in diabetes mellitus (II) patients. Reduction of hepatic lipids accumulated in hamsters.
Hops strobiles	Prevented obesity in high-fat diet fed-mice. Hops isohumulones reduced dyslipidemia in humans, in addition, isohumulones decreased obesity and boosted lipid metabolism in animal models fed a high fat-diet.
Juniper berry leaves	Prevented the increase in lipid cholesterol and oxidized LDL levels caused by the consumption of cholesterol in Wistar albino rats. Significantly reduced cholesterol, triglycerides, LDL, very low-density lipoproteins (VLDL) plasma levels in rats treated with streptozotocin to induce diabetes, with the elevation of HDL levels.
Licorice roots	Decreased cholesterol and triglyceride concentrations in Wister rats treated with streptozotocin to induce diabetes with results similar to glibenclamide.
Milk thistle seeds	Pretreatment of HepG2 cells with milk thistle silibinin resulted in the reduction of lipid accumulation and significantly downregulated the SREBP-1 protein expression.
Peppermint leaves	Produced a significant lowering in the elevated plasma concentrations of cholesterol, triglycerides, VLDL, and LDL and increased HDL-C levels in fructose-fed albino rats. Peppermint leaf juice significantly lowered cholesterol, LDL, and triglycerides levels and significant increased HDL in the offspring of the diabetic streptozotocin (STZ) diabetic induced female Wistar rats.
Pomegranate rind	Pomegranate peels polyphenols significant lowered the accumulation of triglycerides and cholesterol in a steatosis hepatic cell model.
Turmeric rhizomes	Turmeric and curcumin increase the uptake of fatty acids and decrease lipogenesis. Curcumin significantly lowered triglyceride and LDL serum levels. Curcuminoids reduced serum concentrations of atherogenic lipid indices in diabetes mellitus type II patients.

5. Conflicts of interest

There are no conflicts to declare.

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