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Lipid Lowering with Soluble Dietary Fiber

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Abstract Consumption of dietary soluble fibers has been associated with health benefits such as reduced lipid levels, lower blood pressure, improved blood glucose control, weight loss, improved immune function, and reduced inflammation. Many of these health benefits relate to a reduced risk of developing cardiovascular disease. In this paper, we have reviewed recent studies on the hypocholesterolemic effects of dietary soluble fibers as well as fiber-rich foods. Findings include the following: (a) consumption of water-soluble, viscous-forming fibers can reduce total and low-density lipoprotein cholesterol levels by about 5–10 %; (b) minimal changes of high-density lipoprotein cholesterol or triglyceride levels were observed; (c) cholesterol-lowering properties of soluble fibers depend on their physical and chemical properties; and (d) medium to high molecular weight fibers are more effective in reducing lipid levels. Hypocholesterolemic benefits were also observed with some fiber-rich foods, such as whole oats, whole barley, legumes, peas, beans, flax seeds, apples, and citrus foods.

Keywords Diet · Fiber-rich food · LDL cholesterol · Cardiovascular risk · Microbiome

This article is part of the Topical Collection on *Nutrition*

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Introduction

Consumption of soluble dietary fibers (SDF) is reported to provide several health benefits such as reduced lipid levels, lower blood pressure, improved blood glucose control, weight loss, improved immune function and reduced inflammation, and reduced cardiovascular disease (CVD) risk [1–5]. The US Food and Drug Administration (FDA) has approved a claim stating that diets low in saturated fat (<10 % of total daily calories) and cholesterol, and high in fruits, vegetables, and whole grains, have a decreased risk of leading to coronary heart disease (CHD) [6].

The cholesterol-lowering effect of SDF has been known for over 40 years [7–10]. Vegetarians can have lower levels of total (TC) and low-density lipoprotein cholesterol (LDL-C) than omnivores [11]. SDF lowers serum TC and LDL-C levels in both adults and children [2, 12, 13] more effectively than insoluble dietary fibers (IDF). The cholesterol-lowering efficacy of SDF depends on a number of factors, including fiber type, amount consumed, and length of adaptation and nature of the overall diet. Pereira et al. reported that a 10-g/day increase in intake of SDF can lower the risk of coronary events by 14 % and the risk of coronary death by 27 % with minimal side effects compared to the use of statins [14].

Regarding underlying mechanisms, studies to date indicate that dietary fiber increases the rate of bile acid excretion, leading to reductions in TC and LDL-C levels [8, 14, 15]. Further, SDF produces short-chain fatty acids (SCFAs) in the colon potentially affecting cholesterol synthesis [8, 9, 16–22].

Dietary Fibers

Dietary fibers are found mostly in grains, peas/legumes and beans, some fruits and vegetables, and seeds and nuts.

Definition

There is no agreed upon definition of dietary fiber. The three most widely used definitions are given by: (a) the Institute of Medicine (IOM) of the National Academy of Sciences, (b) the American Association of Cereal Chemists (AACC), and (c) the World Health Organization (WHO). The IOM defines dietary fiber as edible materials consisting of non-digestible carbohydrates and lignin, intrinsic and intact in plants. The definition differentiates between fiber endogenous to a food (dietary fiber) and fiber extracted and/or synthesized (functional fiber), i.e., isolated, non-digestible carbohydrates. The AACC defines dietary fibers as edible parts of plants or carbohydrate polymers resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine [23]. The WHO suggested a small variation to the AACC definition for dietary fibers, stating that dietary fiber is a polysaccharide with 10 or more monomeric units not hydrolyzed by endogenous enzymes in the small intestine [24].

Classification

Dietary fiber can be classified based on (a) type of source (plant polysaccharides, animal polysaccharides, and polysaccharides derived from native or synthetic sources), (b) type of polysaccharide structure (linear or nonlinear molecular structure), and (c) solubility. The most widely used classification is based on water solubility: SDF and IDF. Most foods contain both types of fibers, approximately one-third soluble and two-third insoluble dietary fiber [25].

Soluble Dietary Fibers (SDF) Some of the important properties of SDF are (a) water solubility, (b) ability to form viscous solutions, and (c) fermentability. Examples of SDF include β-glucan, psyllium, pectins, guar gum, arabinoxylans, and inulins. SDF are present in whole grains (e.g., oats, barley, and wheat), peas and beans (e.g., lentils, split peas, guar beans, pinto beans, black beans, kidney beans, garbanzo beans, and lima beans), some fruits and vegetables (apples, oranges, and carrots), and seeds and nuts (e.g., flax seed and psyllium seed). The composition, source, and properties of some SDFs are given in Table 1. SDF bypasses the digestion in the small intestine and are fermented by the microflora of the large intestine.

Insoluble Dietary Fibers (IDF) IDF can have properties such as water insolubility, decreased fermentability, and stool bulk forming. Examples of IDF include lignin, cellulose, and some hemicelluloses. IDF can be present in foods such as whole-wheat flour, wheat bran, brown rice, nuts, beans, and some vegetables (e.g., cabbage, celery, cauliflower, brussel sprouts), and skins of fruits and vegetables. IDF have a laxative effect but a lower hypolipidemic response compared with SDF.

Fiber Content of Various Foods

A summary of the fiber content of various foods is given in Table 2 and in Tables 8, 9, and 10 of reference [26].

Lipid-Lowering Benefits of Soluble Dietary Fibers

Examples of studies on lipid-lowering effects of different fibers are listed in Table 3.

β-Glucan

β-Glucan is a linear polysaccharide of glucose monomers with β(1→4) and β(1→3) linkages containing up to about 250,000 glucose units found in the endosperm of cereal grains, primarily oats and barley, and also present in yeast, bacteria, and fungi. Its concentration in oats and barley varies from 3.9 to 6.8 % [52, 53]. While wheat and rice do not contain β-glucan, the latter is water soluble and forms highly viscous solutions even at low concentrations [54].

The US FDA, Health Canada, and European Food Safety Authority have approved health claims regarding the cholesterol-lowering effects of SDF from oat products/oat β-glucan, and several studies have indicated that β-glucan can lower both TC and LDL-C levels by about 5–10 % [2, 27, 55, 56]; see Table 3. Whitehead et al. [30•] analyzed the results of 28 RCTs conducted between 1966 and 2013 and found that (a) diets containing ~3 g/day of oat β-glucan reduced TC and LDL-C levels by 0.30 and 0.25 mmol/L, respectively; (b) no significant effect on HDL-C or triglyceride levels was observed even with a broad range of oat β-glucan doses (3.0–12.4 g/day); and (c) a higher LDL-C lowering effect was observed in subjects with type 2 diabetes and subjects with higher baseline LDL-C levels. Trials with barley β-glucan appear to result in similar lipid-lowering outcomes. In a meta-analysis to assess the effects of β-glucan consumption (from oats and barley) on TC, LDL-C, and triglyceride levels, Tiwari et al. reported that β-glucan consumption (a) reduced TC levels by 0.60 mmol/L, and LDL-C levels by 0.66 mmol/L; (b) led to a modest increase in HDL-C levels (0.03 mmol/L); and (c) resulted in no significant reductions in triglyceride levels [31•]. Wang et al. conducted a RCT to investigate the effect of cholesterol-lowering efficacy of barley β-glucan with different molecular weights (MW) as well as to determine any gene-diet interaction [32, 57]. The findings of the study indicate that high-MW β-glucan was more effective than low-MW β-glucan in reducing TC levels in mildly hypercholesterolemic adults. It is also noted that individuals carrying the *CYP7A1* SNP rs3808607-G allele were more responsive than

Table 1 Source, composition, and health benefits of soluble dietary fibers

Fiber	Source	Composition	Health benefits
β-Glucan	Oats and barley	β-1,4 D-Glucose and β-1,3 D-glucose	Reduced cholesterol levels
Mucilages	Psyllium seeds	Psyllium (polymer of arabinoxylans with 1,4 and 1,3 linkages)	Reduced cholesterol levels
Pectin	Fruits and vegetables (apple, citrus, sugar beets, etc.)	α-1,4-L-Galacturonic acid backbone/neutral sugar side chains, some ester groups	Decreases gastric emptying and small intestine transit time, reduces serum cholesterol levels
Gums (guar gum)	Guar beans	(Galactomannan residue)	Lipid-lowering effect, glucose-lowering effect, fermented by colon microbiota
Gum (gum arabic)	African bush, *Acacia Senegal*	β-D-Galactose backbone, L-arabinose, L-rhamnose, and D-glucuronic acid	Prebiotic effect, lipid-lowering effect
Arabinoxylans	Barley, wheat, rye, rice, sorghum, oats, and corn millet	Non-cellulose polysaccharide, a polymer of xylose in which arabinofuranosyl is substituted	Fecal-bulking effect, prebiotics effect, lipid-lowering effect
Inulin and fructo-oligo--saccharides	Chicory, onions, Jerusalem artichoke, banana, garlic, and wheat	Linear fructose polymer usually with terminal glucose, DP 3-60	Rapid fermentability, fermented by colon microbiota, low viscosity
Chitosan	Crustacean chitins	2-amino-2-deoxy-β-D-glucose	Lipid-lowering effect

TT-allele carriers. In a review of 11 trials from 1989 to 2008, AbuMweis et al. noted that barley β-glucan lowered TC and LDL-C concentrations by 0.30 and 0.27 mmol/L, respectively [33•].

Mucilages—Psyllium

Psyllium is a bulk-forming laxative, not absorbed by the small intestine, and absorbs water in the gut, facilitating bowel movements. It is found in laxatives, ready-to-eat cereals, and dietary supplements. The FDA has approved health claims like: "Diets low in saturated fat and cholesterol that include 7 g/d of SDF from psyllium may reduce the risk of heart disease" [6]. Among mild-moderate hypercholesterolemic patients, subjects receiving 14 g/day of psyllium-containing husk along with a low-saturated-fat diet for 8 weeks had a relative reduction of TC by 6 %, LDL-C by 6 %, triglycerides by 21.6 %, apoB-100 by 6.7 %, and oxidized LDL-C by 6.82 U/L [37•]. The degree of viscosity appears to influence the effects of psyllium. In a RCT that compared the lipid-lowering efficacy of low-viscosity wheat bran (WB, 10.8 g/day), medium-viscosity psyllium (PSY 9 g/day), and a high-viscosity viscous fiber blend (VFB 5.1 g/day), LDL-C levels decreased significantly with VFB compared to PSY (−12.6 %) and WB (−14.6 %). The LDL-C reduction was positively associated with apparent viscosity, and a smaller quantity of VFB lowered LDL-C levels to a greater extent than lower-viscosity fibers [39].

Pectin

Pectin is a methylated ester of polygalacturonic acid, composed of 300 to 1000 galacturonic acid moieties, plus neutral sugars such as L-rhamnose, D-galactose, and L-arabinose units in 1α→4 linkages. The degree of esterification affects the gelling properties of pectin. Pectin fibers, a type of SDF, are found in high amounts in some fruits (e.g., citrus fruits, apples, etc.) and in lower amounts in other vegetables, legumes, and nuts. Citrus fruit contains anywhere from 0.5 to 3.5 % of pectin with a larger concentration located in the white portion of the peel. Pectin bypasses enzymatic digestion of the small intestine and is degraded by the microflora of the colon yielding predominantly acetate. Several studies have indicated that pectin fibers are effective in lowering the TC and LDL-C levels [58, 59]. The European Panel on Dietetic Products, Nutrition and Allergies concluded that consumption of 6 g of pectin per day can contribute to the maintenance of cholesterol levels [60].

As with glucans and psyllium, the viscosity and MW of pectins may influence lipid-lowering effects. Brouns et al. assessed cholesterol-lowering properties of different types of pectins (citrus pectin, apple pectin) in mildly hypercholesterolemic men and women. The study reported a 7–10 % reduction in LDL-C levels with 15 g/day of citrus pectin and apple pectin fibers [35]. A recent systemic review and meta-analysis by van der Gronde et al. concluded that pectin fibers reduced LDL-C and TC, and possibly very-low-density lipoprotein cholesterol (VLDL-C) levels [36].

Gums (e.g., Gum Arabic, Guar Gum)

Gum arabic (GA) is a natural gum made of the hardened sap of various species of the acacia/seyal trees. Several studies have reported on the lipid-lowering effects of

Table 2 Fiber content of some foods particularly rich in soluble fiber

Food Item	Amount	Weight g	Total Dietary Fiber g	Insoluble Fiber g	Soluble Fiber g
Legumes and Grains					
Beans, lima	1 c	188	13.6	6.2	7.4
Beans, navy	1 c	182	15.4	6.6	5.2
Chick peas	1 c	164	9.5	5.7	3.8
Peas, split	1 c	196	6.3	4.1	2.2
Oatmeal, cooked	1 c	234	3.6	1.7	1.9
Fruits					
Apple with skin	1 med	138	2.8	1.8	1.0
Banana	1 med	114	2.2	1.6	0.6
Cantaloupe	½ med	461	3.7	1.5	2.2
Grapefruit	½ med	145	1.8	0.7	1.1
Mango	1 med	207	4.1	2.2	1.9
Nectarine	1 med	136	2.2	1.1	1.1
Orange	1 med	131	3.1	1.2	1.9
Papaya	1 c	140	3.5	1.3	2.2
Peach	1 med	87	1.4	0.5	0.9
Plums	1 med	66	1.0	0.3	0.7
Vegetables					
Artichokes	1 c	168	5.6	2.5	3.1
Broccoli	1 c	184	5.2	2.8	2.3
Cabbage	1 c	150	3.0	1.9	1.1
Corn, whole kernel	1 c	164	6.1	3.4	2.6
Kohlrabi	1 c	165	4.4	1.4	3.0
Okra	1 c	185	5.9	2.4	3.5
Squash, winter	1 c	245	6.9	2.9	3.9
Sweet potatoes	1 c	255	7.7	4.6	3.1
Zucchini	1 c	130	2.0	0.7	1.3

GA [61, 62]. Guar gum is a viscous soluble fermentable fiber that has been associated with reductions in TC and LDL-C levels [16, 63–65]. Even though guar gum did not appear to alter fecal SCFA levels, it appeared to alter the amount of beneficial bacteria (e.g., bifidobacteria) and pathological microbiota (e.g., *Clostridium* genera) [66, 67•].

Isolated Arabinoxylans and Inulin-Type Fructans

Arabinoxylans, a non-starch polysaccharide, is present in many grains and cereals (e.g., wheat, psyllium, rye, corn). Animal studies suggest that arabinoxylans may affect the intestinal barrier function which could influence the absorption of free fatty acids and levels of SCFAs. While there is support for an effect of arabinoxylans on SCFAs, no recent RCTs have reported on the effects of isolated arabinoxylans on serum cholesterol levels [68, 69].

Inulin-type fructans (fructose polymers) can be found in various vegetables and plants such as wheat, cereal grains, onions, bananas, and chicory. Inulin is a soluble fiber that can improve transit time/stool consistency and may act as a prebiotic (for certain populations, e.g., bifidobacteria population) in the large intestine [70]. A recent study reported that an intake of 10 g of inulin resulted in a mild reduction in triglyceride levels and there are variable reports on the effects of inulin on production of SCFA [41, 70].

Whole Foods (Grains, Peas, Beans, and Seeds)

Most fibers are consumed as part of whole foods and examples of studies are listed in Table 3.

Whole Grains Many whole grains (whole wheat, whole oats, brown rice, wild rice, whole-grain corn, whole-grain barley, whole-wheat bulgur, and whole rye) are

Table 3 Soluble dietary fiber studies—individual fiber components

Source	Study type/subjects	Major findings	Ref
β-Glucan			
Oat β-glucan of at least 3 g/day	Meta-analysis of RCTs (from 1998 to 2011)	Reductions in TC and LDL-C levels by 5–10 % (on average: associated with 5 and 7 % reductions) in normocholesterolemic or hypercholesterolemic subjects	[27]
Oat β-glucan of 1.5 to 3 g/day	A 6-week RCT in 87 mildly hypercholesterolemic men and women	Reductions in TC of ~8 % and LDL-C of ~8 %; intake of 1.5 g/day was nearly as effective as 3 g/day oat β-glucan	[28]
Oat and barley β-glucan	Meta-analysis of 17 RCTs (from 1991 to 2012)	Reductions in TC −0.26 mmol/L (95 % CI −0.33 to −0.18) and LDL-C −0.21 mmol/L (95 % CI −0.27 to −0.14)	[29•]
Oat β-glucan of >3 g/day	Meta-analysis of 28 RCTs (from 1966 to 2013)	Reductions in TC and LDL-C levels by about 0.30 and 0.25 mmol/L, respectively	[30•]
Oat and barley β-glucan of 3 g/day	Meta-analysis of 30 RCTs (from 1991 to 2009)	Reductions in TC and LDL-C levels by about 0.60 and 0.66 mmol/L, respectively	[31•]
Barley β-glucan: 3–5 g of high molecular weight (HMW) β-glucan/day vs. low molecular weight (LMW) β-glucan	A 14-week randomized, controlled crossover trial (5 weeks on barley-4 weeks of washout-5 weeks on control) in 30 mildly hypercholesterolemic males and females aged 27–78 years	Reductions in TC by −0.12 mmol/L (95 % CI −0.24, −0.006 mmol/L) in HMW β-glucan rather than LMW β-glucan. Individuals carrying the CYP7A1 SNP rs3808607-G allele are more responsive to the cholesterol-lowering effect of β-glucan with HMW than the TT carriers	[32]
Barley β-glucan	Meta-analysis of 11 RCTs (from 1998 to 2008)	Reductions in TC and LDL-C levels by about 0.30 and 0.27 mmol/L, respectively	[33•]
Oat β-glucan with different molecular weights (MW) of 3–5.4 g/day	A 4-week RCT in 347 Caucasians and non-Caucasians	Reductions in TC and LDL-C were noted to be more effective in 3 and 4 g/day medium and 4 g/day high-MW β-glucans than low-MW β-glucans	[34]
Pectin			
Citrus and apple pectin of 6 to 15 g/day	RCT (7 to 8 weeks: 4 and 3 weeks): cross-over studies in mildly hypercholesterolemic subjects	6 g/day pectin, reduced LDL-C level by 6–7 %. High molecular weight and degree of esterification may be important for cholesterol lowering	[35]
Pectin	Systematic review of studies, including clinical trials on pectin	Reductions in LDL-C and total cholesterol	[36]
Mucilages—psyllium			
Psyllium/*Plantago ovata* 14 g/day	An 8-week RCT in 258 individuals with mild-to-moderate hypercholesterolemia (age 43–67 years)	Reductions approximately of TC by −6 %, LDL-C by −6 %, oxidized LDL by a mean of −6.82 U/L, triglyceride by −21.6 %, and apolipoprotein B-100 by −6.7 %	[37•]
7.0 g psyllium was given to the intervention group	An 8-week RCT in 51 individuals with mild-to-moderate hypercholesterolemia (age 6–19 years)	Reductions in total cholesterol of 7.7 % (−0.39 mmol/L) and LDL-C of 10.7 % (−0.36 mmol/L)	[38]
Low-viscosity wheat bran (WB) 10.8 g/day, medium-viscosity psyllium (PSY) 9 g/day, and a high-viscosity viscous fiber blend (VFB) 5.4 g/day	A 3-week RCT in 23 participants	LDL-C levels decreased significantly with high-viscosity viscous fiber blend compared to the medium-viscosity psyllium and low-viscosity wheat bran	[39]
6 g/day of psyllium or placebo	A 6-week RCT in 47 healthy adolescent males aged 15–16 years; 44 % of subjects were overweight or obese	Reduction in LDL-C of 0.12 mmol/L (6 %)	[40]
Inulin			
5 g inulin	A 12-week RCT in 144 women (age 18–50 years) with BMI ≥ 25 kg/m^2	Decreased triglyceride by ~4 %	[41]

Table 3 (continued)

Source	Study type/subjects	Major findings	Ref
10 g/day inulin	An 8-week RCT in 49 type 2 diabetic females	Reductions in total cholesterol (12.9 %), LDL-C (35.3 %), and triglyceride (23.6 %)	[42]
3 g/day inulin in an enriched cookie	A 4-week RCT in 34 subjects	Reductions in total cholesterol (6 %) and LDL-C levels (7 %)	[43]
Whole grain			
Oat vs. rice: 70 g/day of oats (3 g β-glucan) for the first 4 weeks and they were switched to 70 g/day rice porridge (control product) for the next 4 weeks	A randomized, crossover 8-week RCT in 24 adults with hypercholesterolemia	Reduced TC by 5 % and LDL-C by 10 % in oat consumption; TC and LDL-C levels were also lower than the levels observed with rice consumption	[44]
Oat: 25–135 g/day for oat bran/45–90 g/day for whole-grain oat cereal, 60–150 g/day for oatmeal	Meta-analysis of 69 studies; 59 % of studies had less than 30 subjects in the oat intervention group	Reduction in TC between 2 and 19 % in 58 % of studies; reduction in LDL-C between 4 and 23 % in 49 % of studies	[45•]
Whole-grain compared with non-whole-grain foods	Meta-analysis of 24 studies	Reduction in TC and LDL-C levels by about 0.12 and 0.09 mmol/L respectively. Whole-grain oat had the greatest effect on TC ~−0.17 mmol/L. In the majority of the studies, LDL-C reduction was due to effect of oats. No effect on HDL-C levels. Triglyceride lowered by 0.04 mmol/L	[46•]
Peas and beans			
Pulses: 130 g/day of pulses (e.g., chick peas, lentils, peas, and beans)	Meta-analysis of 26 studies; men and women 30–60 years, studies at least 3 weeks in duration	Reduction in LDL-C levels of ~0.17 mmol/L. No effect on apolipoprotein B and non-HDL-C levels	[47•]
Non-soy legume: 80 to 130 g/day of peas, lentils, or beans for 3–8 weeks	Meta-analysis of 10 studies with a minimum of 3 weeks duration: 268 men and women aged 20–60 years	Reductions in TC 11.8 mg/dL and LDL-C by 8.0 mg/dL	[48]
Flax			
Diet with flax seed fiber drink (3/day) (flax drink) and a diet with flax seed fiber bread (3/day) (flax bread)	RCT in 17 subjects	Reductions in TC and LDL-C levels by about 12 and 15 %, respectively, with flax drinks; smaller reductions in TC and LDL-C levels, 7 and 9 %, respectively with flax bread	[49]
30 g/day of roasted flax seed powder	A 12-week RCT in 50 subjects with dyslipidemia	Reduction in TC of ~24 mg/dL (16.9 %) and LDL-C of ~26 mg/dL (19.3 %)	[50]
30 g/day of milled flax seed or 30 g of whole wheat	A 52-week RCT in 111 patients with peripheral artery disease	In the flax seed group: reduction in TC at 1 month (11 %) and 6 months (11 %), but no difference noted at 12 months; reduction in LDL-C at 12 months of 8.5 %	[51•]

good or excellent sources of dietary fiber. In a systematic review of 64 studies, Thies et al. assessed the consumption of whole-grain oat-based products (oat bran, whole-grain oat cereals, oatmeal) on CVD risk factors [45•]. Findings included (a) regular consumption of oats or oat bran had a beneficial effect on TC and LDL-C levels, with a reduction of 2–19 and 4–23 %, respectively, in hypercholesterolemic subjects, and (b) few studies described any significant effects on HDL-C or triglyceride levels.

Hollaender et al. conducted a meta-analysis to assess the effects of whole-grain foods on changes in lipid levels [46•]. The major findings based on 24 studies were as follows: (a) whole-grain intake lowered TC and LDL-C levels; (b) whole-grain oat had the largest effect on TC levels; (c) no effect on HDL-C was seen; and (d) whole-grain foods tended to lower triglycerides.

Peas and Beans Many whole peas/legumes and beans are good or excellent sources of dietary fiber. Legume consumption has been associated with lower risks of CHD in observational epidemiologic studies [71, 72] and has been shown to decrease TC and LDL-C levels in clinical trials [73, 74]. Several components of legumes are likely to contribute to their cholesterol-lowering effects. Ha et al. conducted a systematic review and meta-analysis of 26 RCTs ($n = 1037$) assessing effects of dietary peas and beans (beans, chick peas, beans whole flour) intake on lipid levels and CVD risk reduction [47•]. Intake of beans (median 130 g/day) resulted in a modest reduction of LDL-C levels (0.17 mmol/L, corresponding to a 5 % reduction from baseline). No significant changes in apoB-100 and non-HDL-C levels were observed.

Bazzano et al. conducted a meta-analysis of 10 RCTs ($n = 268$) to evaluate overall effects of non-soy legume consumption on blood lipids [48]. The results indicated that a diet rich in legumes other than soy decreases TC and LDL-C levels.

Flax Seeds Flax seeds contain ~30 % dietary fibers with water-soluble polymers including arabinoxylans and various amounts of galactose and fructose residues [75]. They also contain some pectins and omega-3 fatty acids [76, 77]. Flax seed fibers form highly viscous solutions upon hydration [78, 79]. Kristensen et al. investigated the effect of flax seed dietary fibers in different food matrices and reported that flax drinks lowered fasting TC and LDL-C levels by about 12 and 15 %, respectively [49]. No effects were seen on fasting triglyceride, HDL-C, glucose, or insulin levels. Saxena et al. evaluated the therapeutic potential of flax seeds in patients with dyslipidemia [50]. Administration of roasted flax seed powder for three months resulted in a significant reduction in TC, LDL-C, triglyceride, and VLDL-C levels as well as an elevation in HDL-C levels.

Fiber Supplements

Fiber supplements, often from a single type of fiber, are available in many forms from capsules to powders to chewable tablets and are largely aimed at preventing constipation. Examples of commonly used fiber supplements are Fiber Choice (inulin), Citrucel (methylcellulose), Metamucil (psyllium), and Benefiber (wheat dextrin). Cyclodextrin (α-CD) is a cyclic oligosaccharide derived from corn (trade name: Mirafit fbcx). Comerford et al. conducted a RCT to investigate the effects of α-CD on glucose and lipid levels in overweight humans [80]. They reported that (a) α-CD decreased TC (−5.3 %), LDL-C (−6.7 %), and apoB-100 (−5.6 %) levels in the absence of any other dietary modifications; (b) participants who had the highest baseline TC and LDL-C levels tended to show the largest reductions; and (c) participants with hypertriglyceridemia had more than twice the reduction in TC levels as compared to normotriglyceridemic participants. Jarosz et al. conducted a RCT to examine the effect of 2 g/day of α-CD on postprandial responses in healthy adults and showed that consumption of α-CD with a fat-containing meal reduced postprandial triglyceride levels [81].

Dietary Guidelines

Products made with refined flour (e.g., breads, buns, pizza crust, pasta) contribute substantially to dietary fiber consumption in typical American diets. In a National Health and Nutrition Examination Survey (NHANES)-based study (2009–2010 data), the mean fiber intake was 17 g/day from a variety of sources (grains > fruits > vegetables > legumes) [82]. Based on NHANES data from 2001 to 2010, it was noted that adults from ages 19 to 51 years had fiber intakes of ~17 g and ages >51 years had fiber intakes of ~26 g [83]. Based on the percent of recommended daily fiber intake, food can be labeled as a "good source of fiber" (10 % or ~2.5 g/serving) or as "excellent source of fiber" (20 % or ~5 g/serving). The Dietary Guidelines for Americans note that foods high in fiber may not only promote a sense of fullness and laxation but also help to reduce the risk of CVD [84, 85]. While there is no clear upper limit for total fiber intake, the definition for adequate fiber intake has been based on age, gender, and proposed effects of fiber on lowering cardiovascular risk [84]. To meet the fiber intake recommendation, the Academy of Nutrition and Dietetics recommends that Americans should increase consumption of beans and peas, vegetables, fruits, whole grains, and foods with naturally occurring fiber [86].

Safety Concerns

An excess of fiber intake may cause abdominal discomfort, gas, and/or difficulty with bowel movements. In individuals with irritable bowel syndrome, it can worsen constipation symptoms. Diabetics with severe gastroparesis can also experience variable blood glucose levels with increased fiber intake. In some individuals, some fiber supplements may potentially cause additional side effects including allergic reactions, asthma, gastrointestinal distress, and drug and nutrient interactions. Intake of fiber supplements may impact on metabolic properties of some drugs when taken concomitantly. Psyllium may reduce absorption of drugs such as lithium, carbamazepine, digoxin, and warfarin [87]. Guar gum may influence absorption and plasma levels of digoxin, acetaminophen, metformin, and penicillin [88]. There are few studies that explore the impact of concomitant fiber and statin use. Pectin has been reported to influence the absorption of lovastatin [89]. Other studies have noted that different forms of fiber may act in a synergistic or antagonistic fashion to bioavailability of statins. In general, medications should be taken at least one hour before or two hours after fiber supplements.

Mechanism of Action

Fiber has been associated with beneficial physiological effects, e.g., decreasing intestinal transit time, increasing stool bulk, lowering TC, LDL-C, postprandial glucose and insulin levels, production of SCFAs, and influencing immune function. The lipid-lowering physiological effects of dietary fiber are influenced by water solubility, water-holding capacity, viscosity, particle size, degradability/degree of fermentation, colon pH alteration, cation exchange properties, and organic acid absorption. The soluble, viscous fiber types can affect absorption from the small intestine due to gel formation that attenuates postprandial blood glucose and lipid levels. Although the exact mechanism responsible for the hypocholesterolemic effects of SDF is unclear, several suggestions have been proposed (Fig. 1).

The first potential mechanism underlying hypocholesterolemic effects of SDF is based on a lower overall energy intake [2, 90, 91]. Lower energy intake occurs due to two mechanisms: (1) fiber-rich foods contain fewer calories and take longer time to digest [12, 92] and (2) SDFs promote increases of bulk forming and satiety. Water-soluble fibers with increased viscous properties can decrease gastric emptying time and influence the amount of nutrient absorption. While IDFs can decrease transit time in the digestive system and subsequently decrease absorption of nutrients, they do not appear to significantly lower lipid levels. However, the increased satiety leads to reduced calorie intake and this can indirectly lower lipid levels.

The second mechanism suggests that consumption of fiber increases the rate of bile acid excretion and reduces bile acid re-absorption from the small intestine, resulting in reduced TC and LDL-C levels. SDF increase the fecal excretion of cholesterol and bile acids [12, 15, 90, 92, 93] by entrapping bile acids by means of viscosity [20], adsorption [9, 20, 94], and inhibition of micelle formation [15, 20, 35, 58]. The increased bile acid excretion leads to lower reabsorption of bile acids with fecal loss. Since the daily fecal loss in bile acids nearly equals hepatic de novo bile acid synthesis, the liver increases the intake of cholesterol by LDL receptor upregulation, leading to lower serum TC and LDL-C concentrations.

The third proposed mechanism invokes the formation of SCFAs, such as propionate, acetate, and butyrate, in the colon. Fermentation of SDF by anaerobic intestinal bacteria produces SCFAs associated with reduced cholesterol synthesis [8, 9, 16, 17, 20–22, 90]. The type of SCFAs formed depends on the nature and amount of SDF, microbiome diversity and activity, and gut transit time. Fiber intake can alter proportions of the human gut flora, including *Bacteroides*, Firmicutes, and *Prevotella*. Agrarian diets high in fruit/legume fiber are associated with greater microbial diversity and predominance of *Prevotella* over *Bacteroides* compared to Western diets which have lower levels of beneficial bacteria and lower total amounts of SCFAs produced [95••]. In addition, a high fat, high refined sugar, high animal protein with low fermentable fiber diet (e.g., Western diet) appears to promote bacteria from Proteobacteria phylum (e.g., gut pathogens, *E. coli*) [95••]. In addition, formation of large amounts of SCFAs can affect the pH in the colon and this can alter the composition of the colonic microbiota and modify SCFA production [96••]. Fiber sources that contain high amounts of β-glucan, resistant starch, and α-galactosides appear to yield higher amounts of SCFAs. The presence of different fibers in different whole-grain products (e.g., barley) may also influence the proportion or composition of the microbiota species [97, 98].

SCFAs can influence metabolism and lipid levels through multiple pathways. While the majority of butyrate appears to be utilized by the colonic bacteria as a source of energy, some SCFAs (e.g., acetate, proprionate) can influence multiple metabolic pathways, including fatty acid synthesis, fatty acid oxidation, fatty acid lipolysis, and cholesterol synthesis [96••, 99]. As propionate and acetate can be absorbed and subsequently enter into the portal vein, it has been suggested that increased levels of propionate may contribute to the inhibition of acetate conversion into lipids and cholesterol synthesis in the liver [96••, 100••]. This may also affect intrahepatocellular lipid levels, liver triglyceride and cholesterol content, and hepatic cholesterol synthesis [96••, 100••]. In support of this, propionate has been shown to inhibit activity of 3-hydroxy-3-methylglutaryl-CoA reductase [96••]. Some of the interactions between SCFAs and FFA receptors are thought to influence AMP-activated protein kinase levels and this has been surmised to affect lipid/cholesterol metabolism substrates [96••].

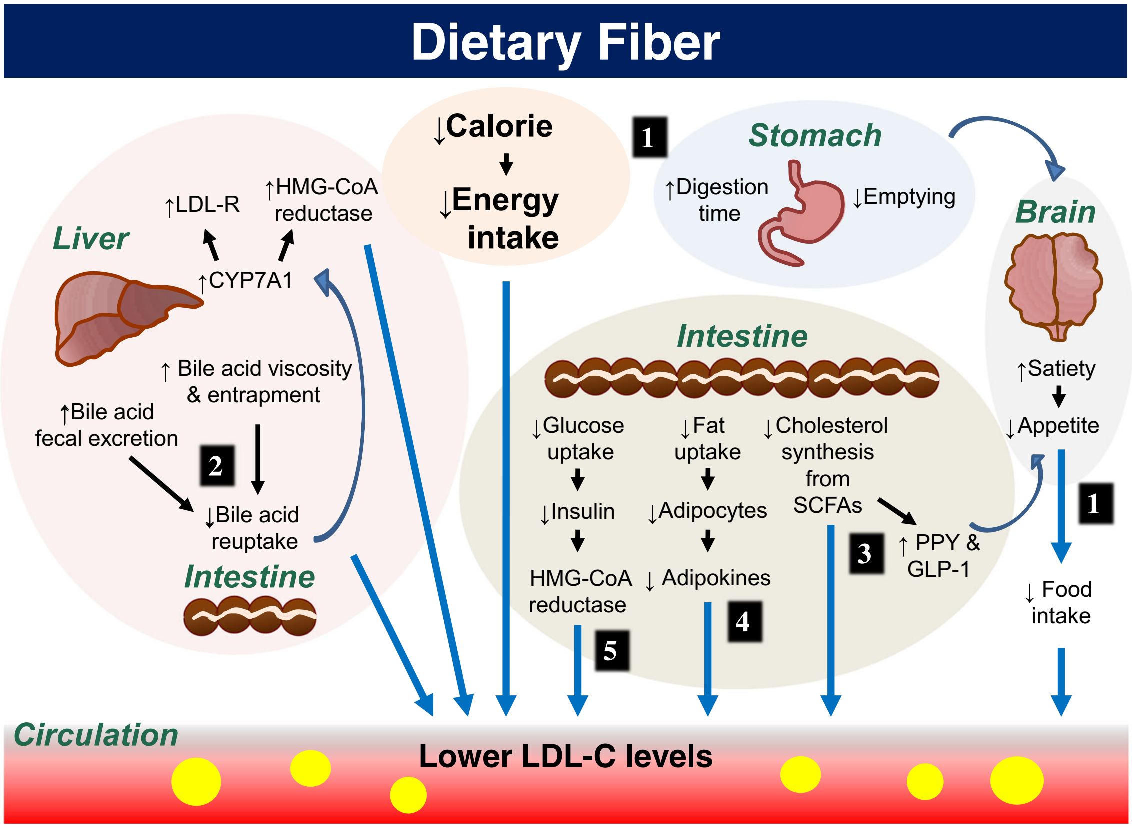

Fig. 1 Potential mechanisms underlying lipid lowering by soluble dietary fiber. First, lower calorie intake associated with consumption of dietary fiber, a longer digestion time with delayed gastric emptying, an increase in bulk-forming and satiety, as well as viscosity-induced reduced absorption of cholesterol, contribute to lower LDL-C concentration (*1*). Second, dietary fiber increases the fecal excretion of bile acid, reduces its re-absorption in the small intestine, and prevents bile acid permeation. A decreased enterohepatic pool of bile acid upregulates the rate-limiting enzyme involved in bile acid production (CYP7A1) which, in turn, promotes liver uptake of LDL-C from blood via upregulation of LDL-R and CYP51, and impacting HMG-CoA reductase (*2*). Third, decreased cholesterol synthesis from short-chain fatty acids (SCFAs) produced by fiber fermentation in the intestine contributes to lower LDL-C concentration. Some SCFAs (propionate) stimulate the release of peptide YY (PYY) and glucagon-like peptide 1 (GLP-1), both of which may help to decrease LDL-C concentration (*3*). Fourth, reduced fat uptake due to fiber alters production of adipokines (leptin, resistin, and TNF-α) that play important roles in lipid metabolism by fat cells and leads to improved cholesterol concentration (*4*). Furthermore, fiber viscosity (gel-forming) delays intestinal absorption of glucose which, in turn, decreases insulin secretion. Insulin activates HMG-CoA reductase; thus, lower insulin could contribute to lower LDL-C concentration (*5*)

In addition, some SCFAs, particularly propionate, have been shown to stimulate the release of peptide YY (PYY) and glucagon-like peptide 1 (GLP-1) potentially affecting hepatic FFA accumulation and possibly reducing hepatic steatosis [100••]. It is suspected that the increased GLP-1 activity may lead to increased uptake of FFA into skeletal muscle [100••]. The increase in GLP-1 can also result in lower glucose intake which may attenuate hepatic synthesis of fatty acid and cholesterol [9].

The fourth potential mechanism is based on adipokines, produced by fat cells. Increased fiber intake may indirectly result in decreased adipokine production. High fat diets result in increases of leptin, resistin, and tumor necrosis factor α (TNF-α) levels and a decrease of adiponectin [93, 101, 102]. Adipokines are important for glucose regulation and lipid metabolism, including cholesterol [8, 17, 93, 101, 103]. Additionally, delayed glucose absorption due to fiber viscosity in the intestine can lead to lower insulin secretion.

Conclusions

The major findings of clinical studies carried out over the last few years on hypocholesterolemic effects of SDFs are as follows: (a) consumption of water-soluble, viscous-forming fibers can reduce TC and LDL-C levels by 5–10 %; (b) a minimal increase of HDL-C level was observed with some fibers; (c) no statistically significant reduction in triglyceride level was seen in most studies; (d) the extent of cholesterol lowering depends on the type of dietary fiber, amount of fiber consumed, length of adaptation period, and nature of the diet; (e) medium- to high-viscosity gel-forming fibers were found to be more effective in reducing cholesterol levels; (f) medium and high MW β-glucans were more effective; (g) TC and LDL-C reductions were found to increase with fiber intake; and (h) dose-response models showed that a 3-g/day dose of oat or barley β-glucan was sufficient to decrease the TC level. The mechanism of action of SDFs in lowering cholesterol levels is not yet fully delineated. Studies carried out so far support the role of increased bile acid excretion, reducing TC and LDL-C levels. Finally, SDF produces SCFAs which may impact cholesterol synthesis. Future mechanistic and clinical studies using various types of dietary fiber can help to fully elucidate mechanisms underlying hypocholesterolemic effects of dietary fibers as well as their effects on clinical outcomes to improve overall cardiovascular health.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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