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Almonds and Cardiovascular Health: A Review

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Abstract

Background: Several preventive strategies to reduce dyslipidaemia, have been suggested of which dietary modification features as an important one. Addition of almonds in our daily diets has been proposed to beneficially impact the lipid profile. This review critically examines the available evidence assessing the effect of almonds on dyslipidaemia in the South Asian (particularly Indian) context.

Methods: An extensive review comprising of epidemiological studies, clinical trials, meta-analyses and systematic reviews was conducted from published literature from across the world. Studies examining the effect of almonds on different aspects of dyslipidaemia viz. high LDL-C, low HDL-C, triglyceridaemia, high total cholesterol levels have been included.

Results: Dyslipidaemia is a major risk factor for coronary heart disease and strategies to manage dyslipidaemia have been shown to reduce the incidence of CVD. Although there are proven pharmacological therapies to help manage this condition, there are not many nutritional interventions which can impact dyslipidaemia. Almonds have been shown to reduce LDL-C which is a known risk factor for CHD, in several studies and the effect of almonds has been well documented in systematic reviews and meta-analysis of clinical trials.

Conclusions: Addition of almonds in the diet has been shown to not only to reduce LDL-C levels, but also to maintain HDL-C levels. This review informs about the use of this simple nutritional strategy which may help manage known major risk factors for heart disease such as high LDL-C and low HDL-C levels especially in the context of South Asians.

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Keywords

almonds; lipids; heart disease; cardiovascular disease; nuts; dyslipidaemia; cholesterol; low density lipoprotein; high density lipoprotein

Abbreviations

CVD: Cardiovascular Disease

CAD: Coronary Artery Disease

LDL-C: Low Density Lipoprotein-Cholesterol

HDL-C: High Density Lipoprotein-Cholesterol

MUFA: Monounsaturated fatty acid

PUFA: Polyunsaturated fatty acid

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Introduction:

India, like many other developing nations in the world, has been facing the dual burden of malnutrition with under nutrition on one hand and diet related chronic diseases on the other. Of all the chronic diseases, cardiovascular diseases (CVD) appear to be a major public health concern and warrants the attention of public health scientists, clinicians and policy makers. Although pharmacological approaches have been in practice, life style modifications, particularly diet, physical activity and smoking cessation are amongst the best preventive strategies.

Indians have a higher risk for heart diseases owing to their genetic make-up and this has been documented in several epidemiological studies [1]. The theory of Indians having a lower threshold for risk factors for heart disease due to their genetic makeup can be applicable to the large Indian diaspora across the globe, which has been estimated to be around 31 million and to be the largest in the world [2]. Cardiovascular diseases account for 28% of total mortality in India surpassing all other causes [3]. The age-standardized death rate from CVD is 272 per 100,000 populations in India in comparison to the global average of 235[4]. The impact of CVDs as measured by the years of lives lost to the disease, was 37 million in the year 2010, rising from 23.2 million (nearly 60% more) in just 20 years [4]. Risk factors for CVDs, especially Coronary Heart Disease (CHD), like high LDL cholesterol(LDL-C), low HDL cholesterol (HDL-C) and abnormal apolipoprotein A-1: B ratio, are increasing at a steady pace. It is essential to prevent further rise in its incidence and prevalence[5].Indians are at a higher risk of CHD due to changing lifestyles resulting in an increasing number of people with conditions like abdominal obesity (visceral adiposity), insulin resistance, dyslipidaemia and inflammation [6].Increases in apolipoprotein B100/apolipoprotein A-I ratio is more prevalent in

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South Asians (43.8 %) than people from other geographies (31.8%)[7].This is a major risk factor out of the 8 risks factors that explains more than 90% of deaths due to myocardial infarction (MI) amongst Indians[8].

The INTERHEART study, which was conducted in 52 countries, including India, mentions dyslipidaemia as a potentially modifiable risk factor for MI [8]. The secular trend seen in the rise of CVDs in India is also due to the consumption of saturated fats, trans-fats, refined carbohydrates and processed foods among Indians[9].The prevalence of low HDL-C and hypertriglyceridemia are associated with Coronary Artery Disease (CAD) in Indian patients[10]. In a large study conducted by the Indian Council of Medical Research (ICMR) in 4 regions of India,79% of the participants were found to have some form of dyslipidaemia. The ICMR study also identified that 72.3% of the total participants had low HDL-C levels, 29.5% had hypertriglyceridemia and almost 12% had high LDL-C levels[11].

Strategies to manage dyslipidaemia have been shown to reduce CVD in several studies. Systematic reviews and meta-analyses of several clinical trials show the reduction in LDL-C levels are directly proportional to the reduction in the CVD risk[12]. All the studies in these systematic reviews or meta-analyses looked at pharmacological therapies that help to lower LDL-C levels, of which statins were prominent. Notwithstanding the benefits of statins in reducing LDL-C levels in dyslipidaemia, the use of this class of drugs also leads to adverse effects like myalgia[13].A study called the Prediction of Muscular Risk in Observational Conditions (PRIMO) project, in which a cohort of 7924 hyperlipidaemic patients received high-dose statin therapy, 10.5% of patients reported myalgia like symptoms [13]. A meta-analysis of 90 observational, cross-sectional and cohort studies found a

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strong positive association (OR: 2.63; 95% CI; 1.50-4.61) of statins and myopathy [14].

Systematic reviews document a special role for lifestyle modification on the prevention of CVD and its risk factors and therefore these need to be emphasized as part of strategies to prevent or manage CVD[15]. Nutritional interventions to help manage dyslipidaemia by mainly reducing LDL-C levels and increasing HDL-C levels have to be a part of lifestyle modifications along with enhanced physical activity levels.

Prospective studies on nut consumption on a regular basis have shown reduction in the risk of heart disease as well as mortality in cohort studies [16,17].In a large systematic analysis for the Global Burden of Disease study, low consumption of nuts and seeds as risk factors for cardiovascular and circulatory diseases was observed [18]. There was an inverse association seen between nut consumption and sudden cardiac deaths in a prospective data of 21,454 male participants in the US Physicians' Health Study [17].Incorporation of nuts especially almonds in the diet of Americans have been shown to improve nutrient quality in both children and adults and could be adopted as a strategy to replace unhealthy snacks[19,20].

Almonds and dyslipidaemia:

Almonds are a part of the prunus family, which are rich sources of mono- and polyunsaturated fatty acids (MUFAs and PUFAs) and are widely accepted in India as a nutritive food for several benefits [21].A 100gof almonds contain around 50gof healthy fats, most of which (40g) are MUFAs and PUFAs, along with 4gof saturated fats[22]. Almonds are a rich source of several minerals as well as vitamins like calcium, copper, iron, magnesium, phosphorus, potassium, zinc, manganese,

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thiamine, riboflavin, niacin, and vitamin E. The health benefits of almonds can be attributed to their healthy fatty acid composition, high Vitamin E and fibre content, as well as other nutrients **(Table 1)**. Almond skin flavonoids have been shown to possess anti-oxidant activity in in-vitro models, to be bioavailable and to synergistically act along with vitamin E to prevent oxidation of LDL in hamster models [23]. Almonds are rich in lipids but the bio-accessibility of lipids from almonds has been shown to be poor in different studies which could be attributed to the cell wall of almonds,rich in non-starch polysaccharides thus preventing or reducing lipid release[24].The way almonds are consumed determines the measured metabolisable energy (ME). The measured ME of whole natural almonds, whole roasted almonds and chopped almonds were shown to be significantly less than the measured ME of almond butter whereas the ME of whole natural almonds were lesser than that of whole roasted almonds[25].

The nutraceutical effect of almonds in reducing lipid levels, especially LDL-C levels, helps us take a dietary approach to manage dyslipidaemia, one of the major drivers of CVD in Indians.

This review captures an in-depth analysis of effect of almonds on managing lipid levels, thus providing clinical evidence for mitigating risk factor of dyslipidaemia. **Table 2** has a list of studies that looked at the effect of almonds on different lipid parameters.

Almonds and LDL-C levels:

A meta-analysis observed a significant reduction in LDL-C levels with almond consumption [26].Almonds have been shown to have a dose-dependent effect on the reducing LDL-C in several well conducted studies[27-29].A recent systematic review

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found that eating almonds results in significant reductions in total cholesterol, LDL-C and triglycerides levels, while having no significant impact on HDL-C levels [30].A sub-group analysis showed that blood lipid levels substantially improved in the studies in which the dose of almonds was at least 45 g/day in individuals with altered lipid profiles. The analysis which included 18 published randomized controlled trials (selected from a pool of 1697 publications) and a total of 837 participants showed the reduction in total cholesterol by 0.153 mmol/L (5.92 mg/dL). Yet another sub-group analysis of studies where the amount of almonds consumed was at least 45 g/day (~1.5 oz/day), the reduction in total cholesterol was 0.212 mmol/L (8.20 mg/dL) which suggested that the effects of almonds on total cholesterol are dose-dependent. A similar pattern was observed for LDL-C with the calculated reduction of 0.124 mmol/L (4.80 mg/dL) in the pooled data and reductions of 0.132mmol/L (5.10 mg/dL) after a sub-group analyses of those studies in which at least 45 g (~1.5 oz) of almonds were consumed per day[30].

The effect of almond consumption on lipids was seen in several studies, one of earliest of which was published in 1992 in which the diet of the participants was modified by adding 100grams of almonds to it [31].There was a reduction in the total plasma cholesterol levels by 21 mg/dL($P<0.05$) in a period of 9 weeks. Several studies followed the study done by Spiller et al, 1992 which showed similar results of almonds on the reduction of cholesterol and LDL-C levels [27,29,32-37]. In a recently concluded large randomised controlled crossover study, conducted over a period of 6 weeks,the consumption of almost 45gof almonds (1.5 ounces) reduced LDL-C levels andnon-HDL-C levels significantly while maintaining HDL-C levels[38]. The study also demonstrated that almond intake reduced abdominal fat which is known to be a major factor in metabolic syndrome and Ischaemic Heart Disease (IHD). A

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198 study from India in subjects with metabolic syndrome demonstrated a significant
199 decrease in LDL-C and total cholesterol levels after consumption of 30 grams of
200 almonds for a period of 6 weeks [39]. The randomised controlled study also showed
201 statistically significant reduction in waist circumference, BMI and systolic blood
202 pressure in the group that consumed almonds as part of the intervention. In another
203 recent study from India, almonds were shown to reduce LDL-C, serum triglycerides
204 and cholesterol levels along with markers of metabolic syndrome such as
205 glycosylated haemoglobin and abdominal obesity in patients with type 2
206 diabetes[40]. The intervention duration in this study was 24 weeks during which 20%
207 of the participant energy intake was replaced with almonds.
208 A theoretical modelling study compared the effects of relative almond intake (defined
209 as almonds consumed per body weight) and that of reduction of dietary saturated
210 fats alone. The study observed that increased almond intake was more beneficial
211 than by the reduction of dietary saturated alone and that replacing saturated fats with
212 almonds on a regular basis could help reduce LDL-C levels further [41].
213
214 **Almonds and HDL-C levels:**
215 Low HDL-C is a key CVD risk factor as seen in several epidemiological studies
216 [42,43]. Low HDL-C levels have been found to be prevalent in people with insulin
217 resistance even without the presence of type 2 diabetes mellitus [44]. A large
218 multicentre study done in India estimated that nearly 72% of Indians have low HDL-C
219 levels [11]. According to The Indian Heart Association, every 10-point increase in
220 HDL-C may reduce the risk of heart disease by half [45]. Physicians worldwide are
221 intrigued and find it difficult to enhance HDL-C levels even after prescribing strict
222 exercise regimes and the addition of pharmacological therapies like high doses of

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niacin, fibric acids or bile acid sequestrants. International guidelines in the Adult Treatment Panel III (ATP III) increased the healthy HDL-C threshold from less than 35 mg/dL to less than 40 mg/dL in males and to 50 mg/dL in females [46]. But the same guidelines suggest that the goals for HDL-C should be at least 50 mg/ dl for Indians [45].One of paradoxes of lifestyle interventions is that dietary strategies for reducing LDL-C and cholesterol levels like reduction of dietary saturated fats has also been shown to reduce HDL-C levels [47].Therefore, it is important for maintaining or even increasing HDL-C levels while lowering LDL-C levels. A recent randomised controlled study conducted in Pakistan investigated the effect of almonds on HDL-C levels in patients suffering from coronary artery disease (CAD). This is a seminal study that tried to look at the effects of almonds exclusively in a South Asian population. The study assessed 1489 patients suffering from CAD for recruitment eligibility, from which 150 subjects were recruited into the study. Of these 113 were men and 37 were women. The study showed that almonds significantly increase HDL-C levels up to an average of 14% in patients with CAD in just 6 weeks. The participants were given a daily dose of 10 grams of soaked and peeled almonds as an intervention, which is also a traditional way of consuming almonds in India [48].

Another recent study examined the effect of nuts (almonds and hazelnuts) in different forms (ground, sliced and whole) on the HDL-C levels after 6 weeks of intervention and found a statistically significant reduction in LDL-C levels along with an increase in HDL-C levels [49].

Recent literature mentions that absolute HDL-C levels alone may not be cardioprotective but this effect may be dependent on the HDL-C functions as well as the sub-species of HDL-C e.g. plasma apoA-I–containing HDL-C subspecies [50].In

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248 a recent study consumption of 43 grams of almonds over 6 weeks, showed an
249 improvement of a-1 HDL-C levels in comparison to the control group[51].
250 The above-mentioned studies have been able to demonstrate significant
251 improvement in HDL-C levels thus suggesting a viable dietary approach for
252 management of an important CVD risk factor.
253
254 **Almonds and other lipid parameters:**
255 Hypertriglyceridaemia is an important risk factor for CVD especially in the context of
256 rising trends of obesity and insulin resistance worldwide [52].An analysis of 101
257 studies has found a causal relationship between hypertriglyceridaemia and CAD
258 [52]. South Asians have been shown to have a pattern of dyslipidaemia which is
259 different from people of other ethnicity which could be one of the reasons for the
260 early propensity for coronary heart disease in this population. This pattern of
261 dyslipidaemia in South Asians consists of, low HLD-C levels, increased lipoprotein-A
262 levels as well and increased number of atherogenic particles in comparison to
263 people of other origins with similar LDL-C levels [53]. South Asians have been
264 shown to have lower HDL-C and higher triglyceride levels in comparison to their
265 Caucasian counterparts[54].
266 A study conducted in a population suffering from CAD has shown the effect of
267 almonds in reducing the levels of triglycerides in people with CAD at 6 and 12 weeks
268 of intervention with 10 grams of almonds ($p<0.05$), but more studies need to be
269 conducted to further investigate this effect [48]. New biomarkers like LDL particle
270 number and LDL particle size have been found to be associated with CVD with some
271 studies suggesting these markers to be more sensitive than LDL-C or HDL-C
272 [55].There is a need for research on the effects of almonds not only on the

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conventional biomarkers for CVD but also for newer ones like LDL particle size and number.

Almonds have been a part of the traditional Indian diet since time immemorial and have been a part of several Indian cuisines. Traditionally almonds in India are soaked and peeled to be eaten early in the morning and has had several positive connotations with respect to health. Almonds are rich in nutrients like vitamin E, proteins, MUFAs, PUFAs, magnesium, potassium and dietary fibres, which are all useful for good cardiovascular health. There is strong clinical evidence that proves the beneficial effect of almonds in dyslipidaemia management. Several well conducted studies from across the world have shown that almonds have a potential to reduce cardiovascular risk factors like dyslipidaemia, namely high LDL-C and low HDL-C levels. Addition of almonds to a lifestyle modification model along with increased physical activity can be a natural way to prevent and manage cardiovascular disease risk factors, particularly dyslipidaemia, which is a major concern for the Indian population.

Conclusion:

Almonds have been shown to reduce LDL-C, which is a known risk factor for coronary heart disease in several well conducted clinical trials. Studies have also looked at the effect of almonds on HDL-C and it has been found that consumption of almonds have helped maintain or even increase HDL-C levels. Daily consumption of around 45 grams of almonds can help reduce one the most important risk factors for CVD in Indians, viz. dyslipidaemia. Addition of whole almonds in the diet is a safe and practical nutritional strategy that can be recommended to manage dyslipidaemia. Further studies need to be conducted to investigate the mechanism of

action responsible for the effect of almonds on dyslipidaemia as well its effect on lipid particle size and vascular health.

Declarations

Ethics approval and consent to participate

NA

Consent for publication

NA

Availability of data and material

NA

Competing interests

This review was sponsored by the Almond Board of California. The authors have no other conflicts of interest to declare.

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Authors' contributions

All authors contributed substantially to the review as a part of the review panel for the same.

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523 **Table1: Almond Composition**

524

NUTRIENTS	UNITS	Value per 100g whole almonds
PROXIMATES		
Calories	kcal	579
Water	g	4.41
Protein	g	21.15
Lipids (total)	g	49.93
Dietary fiber (Total)	g	12.5
Sugars (Total)	g	4.35
Ash	g	2.97
MINERALS		
Calcium	mg	269
Iron	mg	3.71
Magnesium	mg	270
Phosphorus	mg	481
Potassium	mg	733
Sodium	mg	1
Zinc	mg	3.12
Copper	mg	1.03
Manganese	mg	2.18
VITAMINS		
Vitamin E (alpha-tocopherol)	mg	25.63
Thiamin	mg	0.21
Riboflavin	mg	1.14
Niacin	mg	3.62
Pantothenic acid	mg	0.47
Vitamin B6	mg	0.14
Folate, food	mcg	44
FATTY ACIDS		
SATURATED (TOTAL)	g	3.80
16:0 Palmitic	g	3.08
18:0 Stearic	g	0.70
Monounsaturated (total)	g	31.55
16:1 Palmitoleic	g	0.23
18:1 Oleic	g	31.29
Polyunsaturated (total)	g	12.33
18:2 Linoleic	g	12.32

525 USDA 2016 SR28 Nutrient Database No.12061 Nuts, almonds.

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Table 2: Studies on the effect of almonds on lipids

Study	Participants	Intervention (Almonds and study duration)	Outcome Measurements Related to Blood Lipids	Design	Results
Spiller et al. (1998)[27]	Dyslipidaemic adults (n=30) not on drugs Mean age=53±10 y	3.5 oz (100 g) 4 weeks	Total CH LDL-C HDL-C Total CH:HDL-C TG	Randomized 3-arm parallel study, 1-week run-in (diet NR)	↓Total CH ↓LDL-C
Easwaran et al. (2002)[56]	Men with dyslipidaemia (n=24) not on drugs Mean age=NR (age range of 35 to 60 y)	0.16 oz (4.5 g) 4 weeks	Total CH LDL-C HDL-C VLDL-C TG	Randomized 7-arm parallel study	No observed effect
Jenkins et al. (2002)[33]	Dyslipidaemic adults (n=27; 15M, 12 postmenopausal F) Mean age=64±9 y	1.3 oz (≈37 g) 2.6 oz (≈73 g) 4 weeks	Total CH LDL-C HDL-C Total CH:HDL-C LDL-CH:HDL-C TG ApoA-1 ApoB ApoB:ApoA-1 Lp(a)	Randomized 3-arm CO study, ≥2-week WO period	↓Total CH ↓Total CH:HDL-C Full-dose WA vs. C: ↓Total CH ↓LDL-C ↑HDL-C ↓Total CH:HDL-C ↓LDL-C:HDL-C ↓ApoB ↓ApoB:ApoA-1 ↓Lp(a)
Sabaté et al. (2003)[29]	Healthy adults (n=25; 14M, 11F) Mean age=41±13 y	1.2 oz (34 g) 2.4 oz (68 g) 4 weeks	Total CH LDL-C HDL-C LDL-C:HDL-C TG ApoA ApoB ApoB:ApoA Lp(a)	Randomized 3-arm CO study, 2-week run-in	↓Total CH for high WA ↓LDL-C for high WA ↓LDL-C:HDL-C for high WA ↓ApoB for high WA ↓ApoB:ApoA for high WA
Jia*et al.*(2006)[57]	Healthy adult smokers(n=30M) Mean age=22.1 y (age range of 18 to 25 y)	3 oz (84 g) 6 oz (168 g) 4 weeks	Total C TG	Randomized 3-arm parallel study	No observed effect

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Kurlandsky *et al*. (2006) [58]	Healthy women (n=47) Mean age=43.7 y	2.1 oz (60 g) 6 weeks	Total C LDL-C HDL-C TG	Randomized 4-arm parallel study, 4-week run-in	No observed effect
Jambazian et al (2005)[36]	Healthy adults (n=16; 8 M, 8 F) Mean age=41 + 13 years	0%, 10% (approx. 1 oz / 28 g) or 20% (approx. 2 oz / 56 g) of total energy intake	Plasma alpha-tocopherol Total CH LDL-C HDL-C TG	Randomized controlled clinical trial, 2 week run-in	↑ alpha-tocopherol ↓Total CH ↓LDL-C
Tamizifar et al. (2005) [59]	Dyslipidaemic adults not on drugs (n=30; 17M, 13F)	0.88 oz (25 g) 4 weeks	Total CH LDL-C HDL-C Total CH:HDL-C TG	Randomized 2-arm CO study, 5- to 7-d WO period between treatment periods	↓Total CH ↓LDL-C
Lamarche et al (2004)[35]	12 adults with dyslipidaemia	15 g almonds 4 weeks	Medium LDL Small LDL	4-week randomized clinical study	↓Medium LDL ↓Small LDL
Jalali-Khanabadi, et al (2010) [66]	Healthy men with dyslipidaemia (n=30) Mean age = 45.5±7.1 y	2.1 oz (60 g) 4 weeks	Total CH LDL-C HDL-C TG Lp(a) Apo-A1 Apo B100	Single arm study	↓Total CH ↓LDL-C ↓Apo B100
Ruisinger JF et al (2015) [67]	Adults(n=48) with dyslipidaemia controlled by statins; baseline LDL-C = 102 mg/dL Mean age = 60 years	3.5 oz (100 g) 4 weeks	Total CH LDL-C HDL-C Non-HDL-C VLDL-C TG Lp(a) Body weight	Parallel design, 4-week intervention in adults already receiving statin drugs to treat dyslipidemia	↓Non-HDL-CH ↓VLDL-C Also, no change in body weight despite additional calories consumed from almonds.

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Nishi et al (2014) [60] : The Kendall Study	Adults with elevated LDL-C who were otherwise healthy (n=27) Mean LDL-C = 167 mg/dL Mean age=64 y	25-100 g (~1-4 oz) depending on participant energy requirements 4 weeks	Estimated 10-year risk of CHD Oleic acid in TAG and NEFA fractions MUFA in TAG and NEFA fractions Body weight	Randomized CO design, 4-week interventions with2 weeks Wash Out	↓ 10-year risk (3.5% for every 30 g/d almonds) ↑MUFA in NEFA fraction ↑Oleic acid in NEFA Fraction
Berryman et al (2015)[32]	Adults with dyslipidaemia (n=52) Mean LDL-C 148 mg/dL at baseline Mean TC 227 mg/dL Mean age=49.9 years	1.5 oz whole almonds 6 weeks	Total CH LDL-C Non-HDL C HDL-C LDL-C:HDL-C Total CH:HDL-C TG Apo B C-reactive protein Abdominal fat mass Waist circumference Leg fat mass	Randomized CO design, 6-week interventions with 2 week Wash Out	↓Total CH (-5.1 mg/dL) ↓LDL-C (-5.3 mg/dL) ↓non HDL-C (-6.9 mg/dL) ↓LDL-C:HDL-C (-0.23) ↓ApoB ↓abdominal fat ↓waist circumference ↓leg fat
Lovejoy et al. (2002)[28]	Adults with Type 2 Diabetes (n=30; 13M, 17F)xvi Mean age=53.8±1.9 y	2 to 4 oz (57 to 113 g) 4 weeks	Total CH LDL-C HDL-C LDL-C:HDL-C Total C:HDL-C TG	Randomized 4-arm CO study, 2-week Wash Out period between treatment periods	None
Li et al. (2011) [61]	Adults with Type 2 Diabetes (n=20; 9M, 11F) Mean age=58±2 y	2 oz (56 g) 4 weeks	Total CH LDL-C HDL-C LDL-C:HDL-C TG ApoA-1 ApoB ApoB:ApoA-1 NEFA	Randomized 2-arm CO study, 2- wk Wash Out period betweentreatment periods	↓Total CH ↓LDL-C ↓LDL-C:HDL-C ↓ApoB ↓ApoB:ApoA-1 ↓NEFA
Cohen and Johnston (2011) [62]	Adults with Type 2 Diabetes (n=13; 7M, 6F) Mean age=66±3.3 y	1 oz (28 g) 5 days/week 12 weeks	Total CH LDL-CH TG	Randomized 2-arm parallel study	None

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Wien et al. (2010)[63]	Pre-diabetic adults (n=65; 17M, 48F) Mean age=53±9 and 54±11 y for WA and Control groups, respectively	2.1 oz (60 g) 16 weeks	Total CH LDL-C HDL-C Total C:HDL-C TG	Randomized 2-arm parallel study	↓LDL-C
Wien et al. (2003) [64]	Overweight and obese adults (n=65; 28M, 37F) Mean age 53±2 and 57±2 y for WA and C groups, respectively	3 oz (84 g) 24 weeks	Total CH LDL-C HDL-C LDL-C:HDL-C TG	Randomized 2-arm parallel study	↓ HDL-C
Foster et al. (2012) [65]	Overweight and obese adults not on medication (n=123; 11M, 112F) Mean age 46.8±12.4 y	2 oz (56 g) 18 months	Total CH LDL-C HDL-C VLDL-C Total CH:HDL-C TG	Randomized 2-arm parallel study	None
Jamshed, 2015[48]	Adults with CAD (n=150; 117 M, 33 F) Age: 32-86 y	.353 oz(10g) 12 weeks	Total CH LDL-C HDL-C VLDL-C TG	Randomized 3-arm parallel study	↓ CH ↓ LDL-C ↑HDL-C ↓VLDL-C ↓TG
Tey, 2015[49]	Healthy Adults (n=74, 34 M, 40 F)	1.05 (30g) 5 days	Total-C HDL-C LDL-C Total CH :HDL	Randomised crossover study with six treatments in it	↓ LDL-C ↑HDL-C ↓Total CH:HDL-C

528

529 ApoA=apolipoprotein A; ApoA-1 = apolipoprotein A-1; ApoB=apolipoprotein B; ATP = Adult

530 Treatment Panel; BMI=body mass index; WA=whole almond; CO = Crossover study design;

531 TAG = Triacylglycerol; NEFA = Non-esterified fatty acids

532 ↑= Increase; ↓ = decrease

533 All increases (↑) or decreases (↓) are statistically significant where p<= 0.05.