Ann. For. Res. 65(1): 11213-11228, 2022
ISSN: 18448135, 20652445

ANNALS OF FOREST RESEARCH
https://www.e-afr.org/

HEALTH IMPLICATIONS OF TREE NUTS IN RELATION TO MAJOR LIFESTYLE DISORDERS

Aanisah Shafi[1], Dr Naila Irshad[2], Rakia Koul[3]

1. MPH student, University of Glasgow, Scotland, G12 8QQ, UK.
2. Senior Assistant Professor, Institute of Home Science, University of Kashmir, Hazratbal, Jammu and Kashmir, 190006, India.
3. Research Scholar, Institute of Home Science, University of Kashmir, Hazratbal, Jammu and Kashmir, 190006, India.

Abstract

Emerging research from epidemiologic studies and clinical studies is demonstrating that nut consumption could be a healthy dietary strategy to prevent and treat Type 2 Diabetes Mellitus (T2DM) and related cardiovascular diseases (CVDs). The objective of this review is to understand the health implications of tree nut intake, the functional mechanism behind nut intake in promoting good health and busting myths associated with the consumption of tree nuts. The distinctive nutritional makeup and bioactive substances in nuts may be the cause of the beneficial benefits of nuts. Research studies have shown that nut intake has a cholesterol-lowering effect, and there is also emerging evidence of beneficial effects on inflammation, oxidative stress and vascular reactivity. Nuts contain compounds that favorably influence glucose homeostasis, and prevent onset of CVDs. It has been seen that regular nut consumption is unlikely to contribute to obesity and may even help in weight loss. Safety related to the infrequent occurrence of nut allergy in children is limited. Further investigations are required to be conducted on those experiencing CVDs, diabetes, hyperlipidemia, and obesity. This will have new insights into the health benefits of nuts and also to validate the time and the form of consumption influencing the effect of nuts on lipoprotein or blood serum levels.

Key words: Nuts, Diabetes, CVD, Inflammation, Oxidative stress, Vascular reactivity, Appetite, Allergic reaction.

Introduction

Tree nuts are dry fruits that have one seed and whose ovary wall becomes hard at maturity. The common edible tree nuts include almonds (Prunusamigdalis), walnuts(Juglansregia), hazelnuts (Corylusavellana), pine nuts (Pinuspinea), pistachios (Pistachiavera), pecans(Caryaillinoiensis), macadamias (Macadamia integrifolia), cashews (Anacardiumoccidentale), and Brazil nuts (Bertholletiaexcelsa). Peanuts (Arachis hypogea) are also included in the category of tree nuts which are actually groundnuts or legumes [1].

Among the first disorders that man has known, is diabetes mellitus (DM). It was first reported about 3000 years ago in Egyptian manuscript. A clear distinction between type 1 and type 2 was made in year 1936 and in year 1988 T2DM was described as the component of metabolic syndrome which is formerly known as non-insulin dependent diabetes mellitus. It is characterized by hyperglycemia, insulin resistance and relative insulin deficiency. Those suffering from type 2

diabetes mellitus are vulnerable to both short and long term complications, which often lead to premature death [2].

Cardiovascular disease is the single cause of death all over the world. CVD is not a single disease, but a cluster of disease that affect the structure and or functioning of the cardiovascular system including arrhythmias, heart valve disease, heart muscle disease, (cardiomyopathy), heart defect and blood vessel disease [3].

Nuts are beneficial plant based food items that has proven to play an important role in reducing various health risk (diabetes, cardiovascular diseases, cancer, etc.). This is due to the fact that nuts contain an array of macro and micro nutrients that prevents from the potential health risks such as;

- Magnesium which regulates blood sugar levels.
- Fiber which reduces gastric emptying and in turn decreases CHO breakdown and glucose absorption.
- L-arginine an amino acid essential for vascular function.
- Phytochemicals which exert an anti-inflammatory and anti-oxidant action.
- MUFA and PUFA (unsaturated fatty acids) having anti-inflammatory and lipid-lowering effects. [4] .

The prevalence of diabetes is increasing at a very fast rate around the world. According to 2017 status, 425 million people are suffering from diabetes in the world. It has been estimated that by year 2045 there will be 151 million rise in diabetes cases [5] . Diabetes is treatable, even when glucose levels are under control, but it increases the risk of various cardiovascular events (stroke)[6] . There is 17% increase for CVD if there is 1mmol/L increase in fasting glucose levels. The major reasons behind T2DM are; abdominal obesity, lack of physical exercise, sedentary life style, genetics, smoking, bad eating habits and family history [7] .

Epidemiological studies and prior reviews have suggested that regular inclusion of nuts in 'heart healthy diets' of an individual improves various health problems such as obesity, blood glucose, lipid profile, hypertension, diabetes mellitus, cardio-vascular diseases. It also has proven a beneficial impact on chronic diseases such as oxidative stress, inflammation, visceral adiposity, hyperglycemia, insulin resistance, endothelial dysfunction and metabolic syndromes. Moreover, the nutrients present in nuts modify various health processes related to;

- Cancer development,
- Reduces tumor initiation, promotion and progression
- Protects and regulates DNA of immunological and inflammatory responses [8] .

Nutrient Composition

Nuts contain matrix of bioactive compounds that are known to be important for healthy living such as, vitamins (niacin, vit. E, folic acids and choline), minerals (potassium, calcium, magnesium and phosphorus), phenolic compounds, phytosterols and carotenoids [9] . The sodium

Content of roasted or raw, but otherwise unprocessed nuts is very low, ranging from undetectable in hazelnuts (0 mg) and 18mg in 100 g of raw peanuts. A combination of high intake of calcium, magnesium and potassium, together with a low sodium intake, is related with protection against

overall cardiovascular risk, insulin resistance, bone demineralization and arterial hypertension. But it is quite obvious that the advantage of the low sodium content of nuts is lost if they are consumed as a salted product [1]. Among the 50 quintessential foods, some nuts have highest antioxidant capacity. The only tree nut that contains significant amount of lutein and zeaxanthin that are xanthophyll carotenoids are pistachios which appear to protect from age related macular degeneration. Pistachios are also rich in ß-carotenes that have a protective role against T2DM. On dry roasting the concentration of some compounds present in tree nuts is decreased [9] . Nuts are good source of fiber (especially nuts covered with skin) and polyphenols. In US diets, in 2008 and in Europe nuts provided 162 mg per day polyphenols [10] . Polyphenols and tocopherols present in nuts have proven to be rapidly available to the gut due to which they have maximum possibility of getting absorbed in the upper small intestine, thus contributing the beneficial relationship between nut consumption and health related outcomes [9] . Nuts are one of the best plant source foods that contain essential fatty acids (MUFA and PUFA) and a low amount of bad fat (saturated fatty acids-4-5% only). The MUFA present in nuts is oleic acid and the PUFA present is linoleic acid with the exception being macadamia nuts. Walnuts contain highest amount of linolenic acid (9%), PUFA (47%) and linoleic acid (38%). Along with these essential nutrient components, nuts are a great energy source [10] .

Nutrient	Almond	Walnut	Peanut	Pistachio	Hazelnut	Brazil-nut	Pecan	Pine-nut	Cashew	Macadamia
Water (g)	4.41	4.07	6.5	4.37	5.31	3.42	3.52	2.28	5.2	1.36
Energy (kcal)	579	654	567	560	628	659	691	673	553	718
Protein (g)	21.15	15.23	25.8	20.16	14.95	14.32	9.17	13.69	18.22	7.91
Total fat (g)	49.93	65.21	49.24	45.32	60.75	67.1	71.97	68.37	43.85	75.77
SFA	3.802	6.126	6.279	5.9	4.464	16.134	6.18	4.899	7.783	12.061
MUFA	31.551	8.933	24.426	23.3	45.652	23.879	40.801	18.764	23.797	58.877
PUFA	12.329	47.174	15.558	14.4	7.92	24.399	21.614	34.071	7.845	1.502
Carbohydrates (g)	21.55	13.71	16.13	27.2	16.7	11.74	13.86	13.08	30.19	13.82
Fiber (g)	12.5	6.7	8.5	10.6	9.7	7.5	9.6	3.7	3.3	8.6
Ca (mg)	269	98	92	105	114	160	70	16	37	85

Mg (mg)	270	158	168	121	163	376	121	251	292	130
Fe (mg)	3.71	2.91	4.58	3.92	4.7	2.43	2.53	5.53	6.68	3.69
Na (mg)	1	2	18	1	0	3	0	2	12	5
K (mg)	733	441	705	1025	680	659	410	597	34.1	368
P (mg)	481	346	376	490	290	725	277	575	593	188
Zinc (mg)	3.12	3.09	3.27	2.2	2.45	4.06	4.53	6.45	5.78	1.3
V A ,RAE (µg)	0	1	0	126	1	0	3	1	0	0
V D (D2+D3) (µg)	0	0	0	0	0	0	0	0	0	0
V E (mg) (α tocopherol)	25.63	0.7	8.33	2.86	15.03	5.65	1.4	9.33	0.9	0.54
V K (phylloquinone) (µg)	0	2.7	0	-	14.2	0	3.5	597	34.1	Na
V C (mg)	0	1.3	0	5.6	6.3	0.7	1.1	0.8	0.5	1.2
V B_1 (mg)	0.025	0.341	0.64	0.87	0.643	0.617	0.66	0.364	0.423	1.195
V B_2 (mg)	1.138	0.15	0.135	0.16	0.113	0.035	0.13	0.227	0.058	0.162
V B_3 (mg)	3.618	1.125	12.066	1.3	1.8	0.295	1.167	4.387	1.062	2.473
V B_6 (mg)	0.137	0.537	0.348	1.7	0.563	0.101	0.21	0.094	0.417	0.275
Folate(µg)	44	98	240	51	113	22	22	34	25	11
V B_{12} (µg)	0	0	0	0	0	0	0	0	0	0
Lutein-zeaxanthin (µg)	1	9	0	2903	92	0	17	9	22	Na
β-carotene (µg)	1	12	0	305	11	0	29	17	0	Na
α-carotene (µg)	0	0	0	10	3	0	0	0	0	Na
Phytosterols (mg)	197	110.2	NA	214	122	123.5	158.8	236.1	151	116

Source - United States Department of Agriculture (USDA) Nutrient Database Standard Reference. [11]

Epidemiological studies on nuts in relation with Diabetes and CVDs

Numerous studies have been carried out to show the relationship between nut consumption and management of CVD and diabetes.

Olmedilla-Alonso et al., 2008 conducted a research study on impact of consumption of restructured meat products with added walnuts having a cholesterol-lowering effect in subjects at high CV risk. A crossover unblinded dietary intervention study (5 weeks) in subjects at risk (n = 25) was done. Dietary intervention included meat products with or without walnuts for 5 weeks with one-week washout in between. The blood samples were taken overnight on days 0, 12, 21, 28 and 35, coinciding with body weight and blood pressure recording. The participants were asked to records their daily dietary intake during these 5 weeks. It was observed that walnut enriched meat products provoke decrease in total cholesterol, LDL-cholesterol, body weight and increased gamma-tocopherol[12] . Predimed randomized study conducted by Salas-Salvadó et al., 2008 to evaluate the effect of Mediterranean diet supplemented with nut on metabolic syndrome. The study revealed that a traditional MedDiet enriched with nut can be a useful tool in management of the metabolic syndrome [13].

Nut consumption lowers cardiovascular disease risk. To study the likely effect of pistachio on CVD, a randomized cross over controlled feeding study was conducted on 28 individuals by Gebauer et al., 2008. The study participants were given the pistachio diet which was calculated as 10% and 20% total energy. It was observed that the pistachio diet decreases total cholesterol, LDL-cholesterol, non HDL-cholesterol, apoB/apoA and plasma SCD activity [14] . In 2009, it was observed that regular nut consumption and peanut butter is associated with a lower risk of CVD in women with T2DM [15].

Daily ingestion of pistachio either 42g or 70g for 12 weeks does not lead to any weight gain or increase in waist-to-hip ratio in Chinese subjects with metabolic syndrome. In fact, pistachio intake can improve the risk associated with the metabolic syndrome [16].

Prospective studies in non-Mediterranean populations have shown that increased frequency of nut consumption >3 servings/week provide protective effect against CVD and cancer mortality in individuals at high cardiovascular risk (Guasch-Ferré et al., 2013) [17]. A controlled randomized parallel study was conducted to see the effect of hazelnut consumption on T2D. Fifty qualified participants were split into the control and intervention groups. 10% of total daily calorie intake was replaced with hazelnuts in the intervention group. After 8 weeks, there were significant differences seen in high-density lipoprotein-cholesterol (HDL-C) concentrations between the two groups. Although Hazelnut group achieved a greater reduction in triglyceride (TG) concentrations than the control group, these changes were not statistically significant. Neither between-group changes nor within-group changes were significant for FBS, total cholesterol (TC), TG, and low-density lipoprotein-cholesterol (LDL-C) levels. The findings of the study revealed that incorporation of hazelnuts into the diet can prevent reduction of HDL-C concentrations in patients

with type 2 diabetes, but had no effect on FBS or other lipid profile indices (Damavandi et al., 2013) [18] .

People suffering from DM have an increased risk for cardiovascular diseases. A regular nut consumption can help to reduce this risk. Inclusion of pistachio in moderate fat diet favorably reduces the risk of CVD. A randomized crossover controlled feeding study done on 28 subjects having LDL level ≥ 2.86 mmol/l there was significant decrease seen in LDL level, reduction in TAG levels and increased serum HDL particles (Holligan et al., 2014) [19] . A similar randomized trial was conducted in the year 2015 in which 30 adults were enrolled with well-controlled type 2 diabetes, to evaluate the effect of pistachio on the glucose level. 20 % of total energy was provided from pistachio to the subjects for 2 weeks and separated from a 2-week washout (a diet without pistachio). It was observed that there was a significant reduction in serum lipid level and a significant reduction in fructosamine. The research study concluded that including 20% of energy from pistachio lessens the effect of CVD and T2D risk in well-controlled adults (Sauder et al., 2015) [20] . Daily almond consumption, a substitute for high caloric diet can prevent the onset of cardio metabolic disease in healthy individuals (Berryman et al., 2015) [21] .

A Latin square parallel study revealed that 56 gm of daily walnut intake improves endothelial function, total and low density lipoprotein (LDL) and cholesterol, thus reducing risk for diabetes and CVD (Njike et al., 2015) [22]. A randomized controlled clinical trial was conducted in Aga Khan University hospital to observe whether the almond consumption reduced LDL level and improved HDL serum level in coronary artery disease patients. 150 patients were selected to conduct the research study having LDL levels of ≤100 mg/dl and HDL cholesterol ≤40 mg/dl. The subjects were divided into 3 groups (50 in each) and the groups were named as No-Intervention group (NI), the Pakistan Almond group (PA) and the American almond group (AA). The PA and AA group were asked to consume almonds (10mg/dl) by traditional method (soaking almond overnight and removing the peel before consuming on empty stomach). The study revealed that the serum LDL level was reduced and HDL level was increased after 6 and 12 weeks of assessment (Jamshed et al., 2015) [23]. People who consume nuts ≥4 servings/week have reduced risk of developing T2D as compared to those who consume < 1 serving /week of nuts (Asghari et al., 2016) [24]. A prospective randomized controlled trial was conducted, to assess the effect of isocaloric replacement of macronutrients with walnut on plasma lipid levels, consisting of 194 healthy subjects (134 females) and divided into 2 separate groups of 96 individuals in 1 group and 98 in other. The subjects in the 1stgroup were given walnut (43g/day) diet in the first phase of 8 weeks and then walnut free diet in the 2nd phase of the same time period and the reversal of walnut and walnut free diet in the 2nd group. During the walnut diet, either carbohydrate or fat or both were restricted in both groups which significantly showed a reduction in fasting cholesterol, non HDL cholesterol, TAG, LDL cholesterol, and apoB. There was seen an increase in HbA1c level. Thus including walnut in healthy subjects' diet may be an effective mean for lowering the risk of CVD (Bamberger et al., 2017) [25]. Almond supplementation has been seen to improve HbA1c level, reducing T2D risk and CVD (Gulati et al., 2017) [26] .

Summary of epidemiological studies

S.no.	Author	Study name	Number of Subjects	Exposure	Observation
1.	Olmedilla-Alonso et al., 2008.	Randomized, crossover, placebo-controlled study	25	Restructured meat products with added walnuts	Decreased total cholesterol, LDL-cholesterol, body weight and increased gamma-tocopherol in high risk CV subjects
2.	Salas-Salvadó et al., 2008.	**PREDIMED randomized trial**	1224	**Mediterranean diet supplemented with nuts**	Managed metabolic syndrome
3.	Gebauer et al., 2008.	**A dose-response study**	28	**10% and 20% total energy from pistachio**	Decreased total cholesterol, LDL-cholesterol, non-HDL cholesterol, apoB/apoA and plasma SCD activity
4.	Li et al., 2009.	**Prospective cohort study**	54,656	**Impact of nuts and peanut butter**	Reduces CV risk in women with T2DM
5.	Wang et al., 2012.	**Randomized study**	90	**Effect of pistachio**	Pistachio intake does not lead to weight gain and improves risk associated with metabolic syndrome.
6.	Guasch-Ferré et al., 2013.	Prospective study	7216	>3 servings /week vs. (almost) never	Lowered mortality in CVD high risk population

7.	Damavandi et al., 2013.	Controlled randomized parallel study	50	10% of daily energy from hazelnuts	Preserved HDL level in T2DM patients
8.	Holligan et al., 2014.	Randomized cross-over controlled feeding	28	Controlled diet (without pistachios), Diet with one serving of pistachios (30%of TF), Diet with two pistachio serving (34% of TF).	Pistachios with a moderate fat diet have a beneficial effect on individuals with increased risk of CVD
9.	Sauder et al., 2015.	Randomized cross-over controlled feeding	30	20% of daily energy from pistachios	Improved lipid profiles in controlled diabetic patients
10.	Berryman et al., 2015.	Randomized cross-over controlled feeding study	48	1.5 oz. almonds /day	Improved lipid profile and reduction in incidence of CVDs
11.	Njike et al., 2015.	Randomized controlled modified Latin square parallel design	112	56gm walnut /day	Improved lipid profile, endothelial function and diet quality
12.	Jamshed et al., 2015.	Randomized controlled trial	150 (50/group)	7 almonds (10gm/day)	Improved HDL levels in CAD patients

13.	Asghari et al., 2016)	TLGS (prospective study)	1984 (920 men 1064 women)	>4 servings /week or <1 serving /week	Decreased risk of developing T2DM
14.	Bamberger et al., 2017.	Prospective randomized controlled trial	194 (134 females) Group I – 98 Group II - 96	43gm walnut /day	Improved total lipid profiles which reduces the risk of CVDs
15.	Gulati et al., 2017.	A 24 week intervention	50	20% of energy from almonds	Reduced HbA1c levels and improved risk factors of T2DM and CVDs

Potential mechanism

The mechanism -

Fiber

Nuts contain a high amount of fiber due to which there is a decreased postprandial serum glucose level, which in turn increases insulin sensitivity and thus reducing the several risk factors of T2DM and CVD.

Nuts are rich in complex carbohydrates and fiber which is associated with reduced insulin sensitivity, reduced plasma insulin level and promoting better glycemic control in diabetic patients. Ingesting fiber-rich food speeds the carbohydrate absorption and lowers the concentration of postprandial glucose because soluble fiber elevates gastric distention, viscosity in the GI tract and gradual absorption of macronutrients. The digestion of fiber in the large intestine produces the SCF. The SCFa reduces the production of hepatic glucose and stimulates secretion of GLP1 [incretins]. GLP1 and gastric inhibitory polypeptide promotes the release of insulin by βcells thus favoring the maintenance of normal blood glucose level[9].

Carbohydrate

Nuts have a low glycemic index as they have relatively low carbohydrate content. There is less insulin secretion after nut intake which in-turn doesn't increase the blood glucose level. So the inclusion of nuts as a source of carbohydrate decreases the chance of elevated blood glucose level in patients with T2D[9].

Fats

The essential fatty acids MUFA and PUFA are required by the body because they are not produced within. Nuts are the best source of the fatty acids, they contain a high amount of MUFA and PUFA. These fatty acids change glucose levels in the blood by affecting insulin sensitivity. It is believed that the cell membrane which itself is made up of different unsaturated fatty acids, influences the insulin action by altering the action of insulin on its receptors and facilitating the glucose receptor on the cell surface[9] .

MUFA decreases the risk factor of CHD and its onset. CHD risk factors which include plasma lipid and lipoprotein and LDL oxidation susceptibility and favorably reduced by intake of MUFA [27] .

On the other hand, PUFA (omega-3) prevents CAD and other heart diseases by acting as anti-arthogenic agent, lowering serum triacylglycerol's, lowering BP, improving endothelial function, inhibiting platelet aggregation, thrombosis and decreases the incidence of arrhythmias. Nuts have a cholesterol-lowering effect, as they are free of cholesterol their fatty fraction contains phytosterols in sizable amounts [27] .

Protein

The L-arginine is the main amino acid present in the nuts. L-arginine is an essential amino acid required for maintaining vascular tone and blood pressure as it is the main substrate for synthesizing endothelium-derived nitric acid [28] .

Minerals

Nuts improve hypertension[29]. They have an optimum density of some beneficial minerals such as Ca, Mg, K and contains a low amount of Na. Ingesting high amount of Ca, Mg, K with low intake of Na improves hypertension [28]. On acute hyperglycemia, the body is not able to absorb Mg which leads to low mineral blood level, so including nuts in a healthy well-balanced diet improves the Mg level and this, in turn, improves insulin action and response. Mg is also essential for the metabolic reaction for producing ATP. Deficiency of Mg results in the reduction of metabolic function which can lead to T2DM. This explains the relationship of consuming nuts and increased risk of developing T2DM [9].

Bioactive components

The current studies and researches indicate the beneficial effect of bioactive components (phytochemicals and antioxidants) in the prevention, reduction, and management of CVD [27] . The bioactive components are present in various plant foods such as fruits, vegetables and also nuts. Mostly the antioxidants present in nuts are present in the pellicle (outer most soft shell). Roasting and peeling the nuts decline the efficacy of tree nuts. So, it is advised to include nuts in "heart healthy diets" in raw or unpeeled form [28]. It has been studied that certain polyphenols have antidiabetic properties such as 'quercetin'. Quercetin inhibits the alpha-glycosidase and alpha-amylase activity and prevents the lipid peroxidation of pancreatic tissue. Another polyphenol such as 'ellagic acid' may reduce the symptoms of the chronic metabolic disease by lessening the chronic inflammation [9] . Phytosterols and cholesterol have a similar structure due to which there is lesser

cholesterol absorption from the gut. This less cholesterol in the plasma, in turn, reduces CV risk (atherosclerosis) [27] .

Benefits, beyond CVD and Diabetes

Inflammation has been associated to many cellular mechanisms which in turn are associated to tumor development. Inflammation is also said to be associated to genomic instability through several mechanisms that are also associated with different mechanism involved in metastasis development, for instance nuts contain several components like MUFA, magnesium, fiber, linolenic acid, L-arginine, quercetin and resveratrol that have anti-inflammatory properties which have proven to reduce the action of inflammatory mediators including cytokines, chemokines, free radicals, prostaglandins, growth and transcription factors, microRNAs, and enzymes as, cyclooxygenase and matrix metalloproteinase. These inflammatory mediators increase the survival chances of cancer cells and promote their eruption by stimulating the up regulation of adhesion molecules and are thus involved in protecting against tumor development and cancers.

Antioxidants such as phytosterols, carotenoids, phenols (proanthocyanidins, flavonoids, resveratrol), vitamin E (α-tocopherol, β-tocopherol, and γ-tocopherol), selenium and magnesium present in nuts inhibits lipid peroxidation. It has been studied that the accumulation of reactive oxygen species leads to onset of cell proliferation, cell survival, migration and metastasis through various mechanisms. ROS also leads to oxidation of PUFA and initiates lipid peroxidation which in turn generates free radical chain and products that regulate gene expression and cell proliferation. It has been shown that ROS also oxidize proteins leading to modification of DNA bases. Thus including antioxidants in diet from nuts source provide protection against oxidation.

Nuts are the greatest source of protein L-arginine that reduces various events of CV diseases. The L-arginine is an essential component required for endothelial function. If there is decreased bioavailability of endogenous vasodilators NO synthesized from L- arginine, it can lead to regulation of many CV events like atherogenesis [30].

Safety of nut intake

Nuts and body weight

Nuts have a potential benefit of suppressing hunger and reducing the chances of getting overweight. Nuts intake decreases hunger and provides fullness after their consumption. The mechanism lying behind this is due to properties of tree nuts (physical, sensory and nutrient) which alter the gut secretion and appetite response. Nuts helps in reducing satiety (decrease in the frequency of meals) and satiation (decrease in the amount of food eaten in single meal). Satiety is induced by 2 gut hormone:

1. Cholecystokinin (CCK) that is released from duodenal-entero endocrine cells into bloodstream in response to either fatty acids or protein.
2. Glucagon like peptide-1 that is produces in the ileum, induced by intake of fatty acids and carbohydrates.

Both plays major role in food intake control as satiety hormone.

The other mechanism involved behind weight gain is due to the fat quality of nuts determining the thermogenic response. Apart from this, nuts are also great source of fiber and protein which are known to increase satiety and giving feeling of fullness following consumption [31].

Nuts and allergy

One of the major causes of food allergy is nut. Allergic reaction due to nut is because of the allergic seed storage protein that induce specific IGE antibodies. Children during their young age are usually affected and it can be severe and also life threatening. Children who are likely to develop life threatening allergic reaction to nuts are those who are suffering from coexisting atopic disease like asthma, rhintis and eczeme. Some children with nuts and peanut allergy are able to develop tolerance with time [1].

Discussion

The findings of numerous studies suggest that nuts have a potential benefit of improving the general health status of individuals, in addition to improving the various cardiometabolic syndromes like CVD and diabetes. The reason behind cardiometabolic disorders is increased serum lipid levels, obesity, unhealthy lifestyle, excessive carbohydrate, and fat intake and sedentary lifestyle.

The tree nuts provide cardiometabolic benefits that are predicted to be caused by changes in TAG: HDL ratio, as changes in TAG: HDL ratio can lead to insulin resistance, the incidence of hypertension and diabetes. The available literature also shows a similar result i.e., tree nuts almond, hazelnut, walnut, pistachio, peanut consumption improves HDL cholesterol concentration and reduces LDL, VLDL, TG levels, thus improving serum lipid level and reducing the risk of CVD and diabetes.

The subjects in all nut feeding trials were recommended to replace the carbohydrate or fat (energy) with nuts. Different amounts were suggested to be taken in different studies e.g. 10 or 20% of energy from pistachio, 10mg of almonds, 43 gm of walnuts and were suggested to be taken as a meal or snack.

Majority of the studies conducted to evaluate the effect of walnut, recommended the individuals to include it as a meal or snack. Most of the studies conducted describing the effect of almonds, revealed that the beneficial effect was most noticeable on metabolic syndrome when nuts were consumed as a snack. This owes to the fact that nuts as snack provided satiety and led to a reduction in the total energy intake. On the other hand, almond consumption as meal reduced postprandial glucose due to slow digestion which in-turn respond by reducing the serum cholesterol level. However, the inclusion of nuts in "heart healthy diets" of the individual as a snack or meal is still not clear from the above literature.

Moreover, various studies have been put forth suggesting different views regarding the intake of nuts and its impact on HbA1c levels. A feeding trial done for 8 weeks on healthy subjects suggested an intake of 43gm of walnuts daily, which resulted in an increase in the HbA1c levels. Contrarily, another study conducted on type 2 diabetes mellitus patients, suggesting an intake of 20% of energy in the form of almonds, showed a decrease in the HbA1c levels.

In the preceding study, the increase in HbA1c level was found to be due to various reasons e.g., an increased calorie intake or the implementation of statin therapy (which decreased LDL levels). Besides genetic variant LDL (which negatively affect the glucose level) or the shortage of time in conducting the study were also found to be responsible for the said inflation.

So it is clear from the above discussion that nuts have a beneficial role to play on improving the HbA1c levels thereby improving the health status of individuals at risk of developing T2DM, only when nuts are taken as a part of a moderate fat diet or else replacing the fat or carbohydrate intake with tree nuts.

The significant increase in HbA1c levels has been demonstrated to be associated with the greater waist circumference and serum triglyceride levels. The nut feeding trial on almond consumption conducted for 24 weeks showing a decrease in HbA1c level provides strong evidence that almond consumption reduces the waist circumference besides decreasing the HbA1c level improving serum lipid levels.

The result from the studies showed similar response regarding the anthropometric parameters. Besides, there were no changes either in BMI and weight or fasting glucose and serum insulin levels.

Limitations

Majority of the studies taken into consideration have been conducted on healthy individuals, or individuals at risk of developing diseases, rather than on those who were already suffering from any cardiometabolic syndrome, hyperlipidemia or obesity.

Another limitation is an unclear view of nut consumption as a meal or a snack, either of the two forms, having a more pronounced beneficial effect on individuals suffering from either CVD, diabetes, hyperlipidemia or at risk of developing any of them.

Future work

The future studies are suggested to be conducted on those experiencing CVD, diabetes, hyperlipidemia, and obesity. This will have new insights into the health benefits of nuts. Further trials are also suggested to validate the time and the form of consumption influencing the effect of nuts on lipoprotein or blood serum levels.

Conclusion

Nuts are energy-dense foods rich in various bioactive component, macronutrients, micronutrients, and phytochemicals. They have a unique nutrient composition due to which they have proven of providing health benefits. The evidences from epidemiologic and clinical studies have shown beneficial effects of nut intake on risk of CHD, including sudden cardiac death, as well as on diabetes in women, and on major and emerging cardiovascular risk factors. Beyond these health benefits, inclusion of nuts in 'heart healthy diets' of individuals have proven health benefits against various cancers.

Appendices and Full Forms

ApoB	Apolipoprotein B
BMI	Body Mass Index

CAD	Coronary Artery Disease
CHD	Coronary Heart Disease
CHO	Carbohydrate
CVD	Cardiovascular Diseases
FBS	Fasting Blood Sugar
GI tract	Gastrointestinal Tract
GLP1 [incretins]	Glucagon-Like Peptide 1
HbA1c	Glycated Hemoglobin
HDL	High-Density Lipoprotein
HDL-C	High-Density Lipoprotein-Cholesterol
LDL	Low-Density Lipoprotein
LDL-C	Low-Density Lipoprotein-Cholesterol
MeTs	Metabolic syndrome
MUFA	Monounsaturated Fatty Acids
PUFA	Polyunsaturated Fatty Acids
ROS	Reactive Oxygen Species
SCD	Stearoyl-CoA desaturase
SCFa	Short-Chain Fatty Acids
SFA	Saturated Fatty Acids
T2D	Type 2 Diabetes
T2DM	Type 2 Diabetes Mellitus
TAG	Tri-Acyl Glyceride
TG	Triglyceride
VLDL	Very Low-Density Lipoprotein

References

1. Ros, E. (2010). Health benefits of nut consumption. *Nutrients, 2*(7), 652-682.
2. Charan Kumar, C., & Murthy, S. D. S. (2016). A review on management of blood glucose in type 2 diabetes mellitus. *Int J Plant Sciences*, *6*, 114-120.
3. Nason, E. (2008). An overview of cardiovascular disease and research.
4. Kamil, A., & Chen, C. Y. O. (2012). Health benefits of almonds beyond cholesterol reduction. *Journal of agricultural and food chemistry*, *60*(27), 6694-6702.
5. IDF SEA members, Indian Diabetic Federation, (2017). Retrieved on October 15, 2018, from https://www.idf.org/our-network/regions-members/south-east-asia/members/94-india.html.
6. American Heart Association,(2015).Retrieved on October 15, 2018, from https://www.heart.org/en/health-topics/diabetes/why-diabetes-matters/cardiovascular-disease--diabetes

7. Kim, Y., Keogh, J., & Clifton, P. (2017). Benefits of nut consumption on insulin resistance and cardiovascular risk factors: Multiple potential mechanisms of actions. *Nutrients*, *9*(11), 1271.
8. Grosso, G., Yang, J., Marventano, S., Micek, A., Galvano, F., & Kales, S. N. (2015). Nut consumption on all-cause, cardiovascular, and cancer mortality risk: a systematic review and meta-analysis of epidemiologic studies. *The American journal of clinical nutrition*, *101*(4), 783-793.
9. Hernández-Alonso, P., Camacho-Barcia, L., Bulló, M., & Salas-Salvadó, J. (2017). Nuts and dried fruits: An update of their beneficial effects on type 2 diabetes. *Nutrients*, *9*(7), 673.
10. Kim, Y., Keogh, J., & Clifton, P. (2017). Benefits of nut consumption on insulin resistance and cardiovascular risk factors: Multiple potential mechanisms of actions. *Nutrients*, *9*(11), 1271.
11. United States Department of Agriculture Agricultural Research Service USDA Food Composition Databases. Version Current: May 2018. Available online:http://www.ars.usda.gov/ba/bhnrc/ndl (accessed on 3 February 2019).
12. Olmedilla-Alonso, B., Granado-Lorencio, F., Herrero-Barbudo, C., Blanco-Navarro, I., Blázquez-García, S., & Pérez-Sacristán, B. (2008). Consumption of restructured meat products with added walnuts has a cholesterol-lowering effect in subjects at high cardiovascular risk: a randomised, crossover, placebo-controlled study. *Journal of the American College of Nutrition*, *27*(2), 342-348.
13. Salas-Salvadó, J., Fernández-Ballart, J., Ros, E., Martínez-González, M. A., Fitó, M., Estruch, R., ...& Flores, G. (2008). Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. *Archives of internal medicine*, *168*(22), 2449-2458.
14. Gebauer, S. K., West, S. G., Kay, C. D., Alaupovic, P., Bagshaw, D., & Kris-Etherton, P. M. (2008). Effects of pistachios on cardiovascular disease risk factors and potential mechanisms of action: a dose-response study. *The American journal of clinical nutrition*, *88*(3), 651-659.
15. Li, T. Y., Brennan, A. M., Wedick, N. M., Mantzoros, C., Rifai, N., & Hu, F. B. (2009). Regular consumption of nuts is associated with a lower risk of cardiovascular disease in women with type 2 diabetes. *The Journal of nutrition*, *139*(7), 1333-1338.
16. Wang, X., Li, Z., Liu, Y., Lv, X., & Yang, W. (2012). Effects of pistachios on body weight in Chinese subjects with metabolic syndrome. *Nutrition journal*, *11*(1), 20.
17. Guasch-Ferré, M., Bulló, M., Martínez-González, M. Á., Ros, E., Corella, D., Estruch, R., ...&Lapetra, J. (2013). Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. *BMC medicine*, *11*(1), 164.
18. Damavandi, R. D., Eghtesadi, S., Shidfar, F., Heydari, I., &Foroushani, A. R. (2013). Effects of hazelnuts consumption on fasting blood sugar and lipoproteins in patients with type 2 diabetes. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, *18*(4), 314.

19. Holligan, S. D., West, S. G., Gebauer, S. K., Kay, C. D., & Kris-Etherton, P. M. (2014). A moderate-fat diet containing pistachios improves emerging markers of cardiometabolic syndrome in healthy adults with elevated LDL levels. *British Journal of Nutrition*, *112*(5), 744-752.
20. Sauder, K. A., McCrea, C. E., Ulbrecht, J. S., Kris-Etherton, P. M., & West, S. G. (2015). Effects of pistachios on the lipid/lipoprotein profile, glycemic control, inflammation, and endothelial function in type 2 diabetes: A randomized trial. *Metabolism*, *64*(11), 1521-1529.
21. Berryman, C. E., West, S. G., Fleming, J. A., Bordi, P. L., & Kris-Etherton, P. M. (2015). Effects of daily almond consumption on cardiometabolic risk and abdominal adiposity in healthy adults with elevated LDL-cholesterol: a randomized controlled trial. *Journal of the American Heart Association*, *4*(1), e000993.
22. Njike, V. Y., Ayettey, R., Petraro, P., Treu, J. A., & Katz, D. L. (2015). Walnut ingestion in adults at risk for diabetes: effects on body composition, diet quality, and cardiac risk measures. *BMJ Open Diabetes Research and Care*, *3*(1), e000115.
23. Jamshed, H., Sultan, F. A. T., Iqbal, R., &Gilani, A. H. (2015). Dietary almonds increase serum HDL cholesterol in coronary artery disease patients in a randomized controlled trial. *The Journal of nutrition*, *145*(10), 2287-2292.
24. Asghari, G., Ghorbani, Z., Mirmiran, P., &Azizi, F. (2017). Nut consumption is associated with lower incidence of type 2 diabetes: The Tehran Lipid and Glucose Study. *Diabetes & metabolism*, *43*(1), 18-24.
25. Bamberger, C., Rossmeier, A., Lechner, K., Wu, L., Waldmann, E., Stark, R., ...&Parhofer, K. (2017). A walnut-enriched diet reduces lipids in healthy Caucasian subjects, independent of recommended macronutrient replacement and time point of consumption: A prospective, randomized, controlled trial. *Nutrients*, *9*(10), 1097.
26. Gulati, S., Misra, A., & Pandey, R. M. (2017). Effect of Almond Supplementation on Glycemia and Cardiovascular Risk Factors in Asian Indians in North India with Type 2 Diabetes Mellitus: A 24–Week Study. *Metabolic syndrome and related disorders*, *15*(2), 98-105.
27. Amarowicz, R. (2016). Consumption of Tree Nuts in the Prevention of Coronary Heart and Cardiovascular Disease. *International Journal of Cardiology and Lipidology Research, 3,* 47-53.
28. Ros, E. (2015). Nuts and CVD. *British Journal of Nutrition*, *113*(S2), S111-S120.
29. Barbour, J. A., Howe, P. R., Buckley, J. D., Bryan, J., & Coates, A. M. (2014). Nut consumption for vascular health and cognitive function. *Nutrition research reviews*, *27*(1), 131-158.
30. Falasca, M., Casari, I., &Maffucci, T. (2014). Cancer chemoprevention with nuts. *Journal of the National Cancer Institute*, *106*(9), dju238.
31. Lutz, M., & Luna, L. (2016). Nuts and body weight: an overview. *J Nutr Health Sci*, *3*(1), 105.