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NUTRITIONAL IMPORTANCE OF WALNUTS IN PREVENTION OF CARDIOVASCULAR DISEASE

SUMMARY

The aim of the paper was to point out the significance of the walnut use in nutrition with the purpose of cardiovascular disease incidence reduction.

The paper demonstrated and analyzed the published data about the role of walnut in nutrition in control of some of the risk factors for development of cardiovascular disease, above all, about the role of lipid status. We provided an analysis of energetic value and nutritional walnut composition, as well as health significance of its cardio-protective ingredients.

The results obtained by epidemiological research indicated that the frequent use of nuts reduces mortality and risk of cardiovascular disease development.

In clinical studies, after introduction of walnuts in nutrition, statistically significant reduction of total cholesterol (TC) has been achieved, as well as that of LDL-cholesterol. The values of other investigated parameters (HDL-cholesterol, triglyceride) after introduction of walnuts into nutrition were significantly affected. The walnut diet increased endothelium-dependent vasodilatation and reduced levels of vascular cell adhesion molecule and inflammatory cytokines.

The results undoubtedly indicated that walnuts should be an important part of nutrition for cardiovascular patients and subjects at high risks of cardiovascular disease development, especially subjects with hypercholesteremia.

Key words: **walnut, nutrition, cardiovascular disease, prevention**

INTRODUCTION

For the prevention of cardiovascular diseases (CVD), diet is of essential importance. In this respect, the Mediterranean diet is considered especially beneficial because mortality rates from CVD and cancer are low in the traditional Mediterranean populations (1).

Nuts, including walnuts (*Juglans regia* L.), are a traditional part of Mediterranean diets. They are ingredients of sauces, stuffings, entrees, appetizers, and desserts. Nuts are also being studied for their potential health benefits.

The risks of having a stroke (2), of developing type 2 diabetes (3), of developing prostate cancer (4), advanced macular degeneration (5), and of gallstones (6) have all been found to be lowered by eating nuts. That fact that nuts, including walnuts may reduce the risk of coronary heart disease (CHD) is the fact acknowledged by the U.S. FDA (Food and Drug Administration) (7).

The aim of this systematic review was to evaluate the scientific evidence related to the effects of walnut consumption on risk factors for CVD, including a consideration of the nutritional components in walnuts.

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Composition of walnuts

Since walnuts, like other nuts, are high in fats (65 g/100g edible portion); also, they are high in calories (654 kcal/ 100g) – *Table 1* (8).

Table 1. Composition of nuts (per 100 g edible portion) (8)

Nutrient	per 100 g edible portion
Energetic value	654 ckal/ 2738kj
Total Fat	65 g
Saturated Fat	6 g
Monosaturated Fat	9 g
Polyunsaturated Fat	47 g
Linoleic acid (18:2)	38 g
Linolenic acid (18:3)	9,08 g
Cholesterol	0 mg
Protein	15 g
Carbohydrate (by difference)	14 g
Dietary Fiber	7 g

However, walnuts are low in saturated fatty acids (6%), monounsaturated fatty acids (9%) and high in polyunsaturated fatty acids (47%). Compared to most other nuts, which contain monounsaturated fatty acids (MUFA), walnuts are unique because they are rich in n-6 (linoleate) and n-3 (linolenate) polyunsaturated fatty acids (PUFA). The sources of n-3 (linolenate) - α -linolenic acid (ALA), especially in our national nutrition are rare (9). ALA is a type of omega 3 acid, similar to those found in cold-water fish, but also in flex seed and 9% of edible portion of walnuts.

Epidemiologic studies and clinical trials demonstrate substantial cardioprotective effects of ALA (10-14). Recommended daily intake is 2,22 grams of ALA for men and women, respectively (15). With 2.7 grams of ALA, 30 grams of walnuts contain ALA more than daily requirement.

Walnut is relatively high in protein (15g / 100g edible portion). The amino acid composition of walnuts is highest in glutamic acid (2.8 g) and arginine (2.3g). L-arginine can be converted to nitric oxide (natural dilator of small arteries) (16) and may lower blood pressure (17,18). Walnuts also contain aspartic acid, leucine, serine, glycine, valine, phenylalanine, alanine, proline, isoleucine, and threonine. The concentrations of methionine and cystine are low.

Walnuts contain dietary fiber (7 g/100g), of which 25% is soluble fiber. Analysis of 67 controlled clinical trials indicated that diets high in soluble fiber decrease total cholesterol (TC) and LDL cholesterol (LDL-C) (19).

Walnuts are good sources of several other important micronutrients *(Table 2)*, including potassium and magnesium (8).

Table 2. Composition of nuts (per 100 g edible portion)- micronutrients (8)

Micronutrients	per 100 g edible portion
Minerals	
Calcium	98 mg
Iron	3 mg
Magnesium	158 mg
Phosphorus	346 mg
Potassium	441 mg
Sodium	2 mg
Zinc	3,09 mg
Manganese	3,4 mg
Selenium	4,60 mcg
Vitamins	
Riboflavin	0,15 mg
Niacin	1,99 mg
Vitamin B6	0,54 mg
Folate	98 mcg
Vitamin E	2,92 ATE

Adequate dietary intake of potassium lowers the blood pressure and is protective against stroke and cardiac arrhythmias (20). Low magnesium status can contribute to hypertension (21,22).

Walnuts also provide other compounds with biological activity such as folic acid, vitamin B6, vitamin E, flavonoids, sterols and melatonin.

The amount of homocysteine in the blood is regulated by three vitamins: folate, vitamin B12 and vitamin B6. The results of more than 80 studies indicate that even moderately elevated levels of homocysteine in the blood increase the risk of CVD (23). Polyphenol- rich extracts from walnuts are effective inhibitors in vitro plasma LDL oxidation (24).

Epidemiologic studies (25) have shown that flavonoid intake is significantly and inversely associated with coronary heart disease (CHD) mortality.

Walnuts contain 72 milligrams of phytosterols which are chemically similar to cholesterol, and block the absorption of cholesterol into the bloodstream (26).

Walnuts are important sources of the antioxidant vitamin E, but the results of studies do not support the concept that this agent is cardioprotective (20).

Reiter et al. quantified the amount of melatonin present in walnuts, in bioavailable form. They have demonstrated that eating walnuts increases antioxidant activity in the bloodstream in

animals, in which case they could be protective against CVD (27).

Intervention studies with walnuts

Because walnuts have a favorable fatty acid profile and contain several bioactive compounds, there is an interest in evaluating the role of walnuts in cholesterol-lowering diets *(Table 3)* (28) .

In 4/7 studies of walnut consumption (40–84 g/d), there was a significant decrease in TC (4–12%) and LDL-C (6–16%) compared with consumption of Step I (29), Mediterranean (30,31), and Japanese (32) diets. Three studies (33,34,35) did not show any significant change in the lipid profile of subjects. In 2 (33,35) walnut intervention trials (64–78 g/d), the lipid profiles of subjects were not affected, possibly because of the large difference in the percentage of fats between the nut diet (38 and

Table 3. Effects of walnuts on the blood lipid profile in human intervention trials [1,2] Adopted by Mukuddem-Petersen et al. (28)

Reference et subjects	Control diet	Walnut (g/day) / Duration	% Total fat		Nut diet end vs. control diet end [2]			
			Walnut diet	Control diet	TC	LDL C	HDL C	TG
29 n=18 M (helthy)	Step I diet	84 / 4wk	31.3	29.3	-12.4 p<0.001	-16.3 p<0.001	-4.9 p=0.009	-8.3 ns
33 n = 21M (hyperlipidemic)	Low-fat diet	78 / 4 wk	38	30	-2 ns	-3.9 ns	2.5 ns	7.5 ns
30 n = 49; 26M, 23W (hypercholesterolemic)	Mediterranean diet	41–56 / 6 wk	33.2	31.2	-4.1 p<0.001	-5.9 p<0.001	3.2 ns	-6.1 ns
34 n = 10M (hypercholesterolemic)	Mediterranean diet	41–56 / 6 wk	31.8	30.9	-4.2 ns	-6 ns	0 ns	-5.1 ns
35 n = 42: 17M, 25W (hypercholesterolemic)	Step I diet	64 / 6 wk	45	33	-3.3 ns	-3 ns	6.7 ns	-6.3 ns
32 n = 40; 20M, 20W (healthy)	Japanese diet	44–58 / 4 wk	26	24	-4.5 p=0.01	-9.8 p=0.01	-1.3 ns	0 ns
31 n = 20: 8M, 12W (hypercholesterolemic)	Mediterranean diet	40–65 / 4 wk	33	33.2	-4.3 p=0.01	-6.7 p=0.01	-1.3 ns	8.3 ns

1 Abbreviations used: M, men; W, women; NS, insignificant; American Heart Association/National Cholesterol Education Program Step I diet with 30% of energy from fat
2 In cases in which the percentage difference was not indicated, we used the formula:
(End value nut diet – End value control diet)/End value control diet x 100. When baseline values were compared to nut intervention end values the formula was: (End value nut diet – Baseline value)/Baseline value x 100.

All studies were of short duration (3-6 weeks on a diet). Participants were mainly Caucasian, young or middle-aged, with either normal lipid profiles or mild-to-moderate hyperlipidemia and few cases of established coronary heart disease.

45%, respectively) and the control diets (30 and 33%, respectively). In the study by Munoz et al. (34), consumption of the walnut diet compared with the Mediterranean diet did not affect the lipid profile.

In most of the walnut studies, HDL-C was not significantly affected, compared with control

diets. Only in walnut study by Sabate and al., the HDL-C concentrations decreased significantly compared with consumption of a Step I diet (29). New researches show that walnuts also improve cholesterol profile in subjects with type 2 diabetes (36,37).

Food intake is an important factor that affects vascular reactivity. The walnut diet increased endothelium-dependent vasodilatation and reduced the levels of vascular cell adhesion molecule (31). Supplemental walnuts also reverse the postprandial endothelial dysfunction associated with consumption of a fatty meal. The plasma concentrations of soluble inflammatory cytokines and adhesion molecules decreased after the walnut meal (38).

Serum components, such as lipoproteins, coagulation factors (factor VII, tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1), fibrinogen), and homocysteine have been associated with CVD. In study of Morgan et al. (35), at the end of walnut diet, no statistical effects on homocysteine or the coagulation factors were observed.

A cross-sectional study of a population of farmers in the region of France (39) investigated a possible association between walnut consumption (walnut oil and kernels) and blood lipids. Healthy subjects (n=793) had completed a FFQ (Food Frequency Questionnaire) covering the previous year. Blood TC, lipoprotein-cholesterol, and apoprotein levels were measured. Increased HDL-C and apo A-1 were associated with walnut consumption, but not TC, LDL-C, or apo B.

Observational studies on consumption of nuts and coronary heart disease

Four large epidemiologic studies showed an inverse relation between nuts (including walnuts) consumption and the reduction and prevention of coronary heart disease. Summaries of these observational studies (Adventist Health Study (40), Iowa Women's Health Study (41), Nurses' Health Study (42), and Physician's Health Study (43)) are presented in *Table 4*.

All these studies demonstrated a dose response-related inverse association between coronary heart disease and the frequent daily consumption of small amounts of nuts, including walnuts.

Table 4. Results of prospective studies

Reference end subjects	Duration of study	Conclusion
Adventist Health Study (40) n=31208 white Adventist	6y	Subjects who consumed nuts ³ 5 times/week decreased their risk of fatal CHD by 48%, and those who ate nuts only 1-4 times/week decreased their risk of fatal CHD by 24%, compared to those who ate nuts less than once a week
Iowa Women's Health Study (41) n=3484 females	5y	154 females free of CHD at baseline died of CHD, and coronary mortality was inversely associated with the nut intake.
Nurses Health Study (42) n=86016 females	14y	Women consuming ³ 5ounces of nuts/week had reduced the risk of total CHD by 35%, and by 32% compared to those who consumed less than one ounce/week.
Physician's Health Study (43) n=21454 men	17y	Compared with men who rarely or never consumed nuts, those who consumed nuts ³ 2 times/week had lowered the risk of sudden cardiac death by 47 % and lower risk of total CHD death by 30%.

CONCLUSION

It is evident that the favorable fatty acid profile of walnuts (high in unsaturated fatty acids and low in saturated fatty acids) with contribution of other bioactive constituents in walnuts (potassium, manganese, folic acid, flavonoids and sterol) may confer additional cardioprotective effects.

In clinical studies, healthy diets supplemented with walnuts decreased the serum concentrations of LDL-C and TC and improved endothelial function. The future researches should use feeding studies with larger sample sizes and longer duration. Four large epidemiologic studies have consistently demonstrated beneficial effects of nut consumption (including walnut) on CHD morbidity and mortality in different population groups.

Based on the results of these studies, it is appropriate to recommend that normo- and hyperlipidemic individuals consume walnuts 30 g at least 5 times/week.

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NUTRITIVNI ZNAČAJ ORAHA U PREVENCIJI KARDIOVASKULARNIH BOLESTI

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SAŽETAK

Cilj rada bio je da ukaže na značaj korišćenja oraha u ishrani radi smanjenja rizika za nastanak kardiovaskularnih bolesti.

U radu su revijski predstavljeni i analizirani objavljeni podaci o ulozi oraha unetih hranom u kontroli nekih faktora rizika za nastanak kardiovaskularnih bolesti i to, pre svega, lipidnog statusa. Energetska vrednost i nutritivni sastav oraha prikazani su sa posebnim osvrtom na zdravstveni značaj njegovih kardioprotektivnih sastojaka.

Rezultati četiri obimne prospektivne epidemiološke studije ukazuju da česta upotreba jezgrastog voća (uključujući i orah) u ishrani smanjuje smrtnost i rizik od nastanka kardiovaskularnih bolesti. Rezultati većine kliničkih studija ukazuju da uvođenje oraha u ishranu dovodi do značajnog smanjenja vrednosti ukupnog (TC) i holesterola male gustine (LDL-C), ali ne i triglicerida (TG) i holesterola velike gustine (HDL-C). Dodavanjem oraha u ishranu značajno je povećana i endotelijum zavisana vazodilatacija i smanjena ćelijska adhezija krvnih sudova ispitanika i vrednosti inflamatornih citokina.

Dobijeni rezultati nedvosmisleno ukazuju da bi orah trebalo da bude važan deo ishrane kardiovaskularnih bolesnika i osoba sa rizikom za nastanak kardiovaskularnih bolesti a naročito osoba sa hiperholesterinemijom. Zbog visoke energetske vrednosti i prevencije gojaznosti, dovoljno je koristiti jednu porciju oraha dnevno, nekoliko puta nedeljno.

Ključne reči: **orah, ishrana, kardiovaskularne bolesti, prevencija**