Original Article

Omega-3 fatty acids in wild plants, nuts and seeds

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Human beings evolved consuming a diet that contained approximately equal amounts of omega-6 and omega-3 essential fatty acids. Over the past 100–150 years there has been an enormous increase in the consumption of omega-6 fatty acids due to the increased intake of vegetable oils from seeds of corn, sunflower, safflower, cotton and soybeans. Today, in Western diets, the ratio of omega-6 to omega-3 fatty acids ranges from 10 to 20:1 instead of the traditional range of 1–2:1. Studies indicate that a high intake of omega-6 fatty acids shifts the physiologic state to one that is prothrombotic and proaggregatory, characterized by increases in blood viscosity, vasospasm, and vasoconstriction and decreases in bleeding time, whereas omega-3 fatty acids have anti-inflammatory, antithrombotic, anti-arrhythmic, hypolipidemic, and vasodilatory properties. These beneficial effects of omega-3 fatty acids have been shown in the secondary prevention of coronary heart disease and hypertension, as for example, in the Lyon Heart Study, the GISSI Prevenzione Trial, and in the The Dietary Approaches to Stop Hypertension Study. Most of the studies have been carried out with fish oils (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)). However, α-linolenic acid (ALA), found in green leafy vegetables, flaxseed, rapeseed, and walnuts, desaturates and elongates in the body to EPA and DHA and by itself may have beneficial effects in health and in the control of chronic diseases. The present paper identifies multiple sources of ALA from plants, legumes, nuts and seeds and emphasizes the importance of the ratio of omega-6 to omega-3 fatty acids for proper desaturation and elongation of ALA into EPA and DHA. α-linolenic acid is not equivalent in its biological effects to the long-chain omega-3 fatty acids found in marine oils. Eicosapentaenoic acid and DHA are more rapidly incorporated into plasma and membrane lipids and produce more rapid effects than does ALA. Relatively large reserves of linoleic acid in body fat, as are found in vegans or in the diet of omnivores in Western societies, would tend to slow down the formation of long-chain omega-3 fatty acids from ALA. Therefore, the role of ALA in human nutrition becomes important in terms of long-term dietary intake. One advantage of the consumption of ALA over omega-3 fatty acids from fish is that the problem of insufficient vitamin E intake does not exist with high intake of ALA from plant sources.

Key words: docosahexaenoic acid, eicosapentaenoic acid, metabolism of omega-6 and omega-3 fatty acids, ratio of omega-6:omega-3 fatty acids, secondary prevention of coronary heart disease sources of α-linolenic acid.

Introduction

Over the past 20 years many studies and clinical investigations have been carried out on the metabolism of polyunsaturated fatty acids (PUFA) in general and on omega-3 fatty acids in particular. Today we know that omega-3 fatty acids are essential for normal growth and development and may play an important role in the prevention and treatment of coronary artery disease, hypertension, diabetes, arthritis, other inflammatory and autoimmune disorders, and cancer.[1–10] Research has been done in animal models, tissue cultures, and human beings. The original observational studies have given way to controlled clinical trials. Great progress has taken place in our knowledge of the physiologic and molecular mechanisms of the various fatty acids in health and disease. Specifically, their beneficial effects have been shown in the prevention and management of coronary heart disease,[11–14] hypertension,[15–17] type 2 diabetes,[18,19] renal disease,[20,21] rheumatoid arthritis,[22] ulcerative colitis,[23] Crohn's disease[24] and chronic obstructive pulmonary disease.[25] However, this review focuses on the evolutionary aspects of diet, the biological effects of omega-6 and omega-3 fatty acids, terrestrial sources of α-linolenic acid (ALA), and the effects of dietary ALA on coronary heart disease and hypertension.

Evolutionary aspects of diet

On the basis of estimates from studies in Paleolithic nutrition and modern-day hunter–gatherer populations, it appears that human beings evolved consuming a diet that was much lower in saturated fatty acids than is today's diet.[26] Furthermore, the diet contained small and approximately equal amounts of omega-6 and omega-3 PUFA (ratio of 1–2:1) and much lower amounts of *trans* fatty acids than does today's diet (Fig. 1).[27,28]

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The current Western diet is very high in omega-6 fatty acids (the ratio of omega-6 to omega-3 fatty acids is 10–20:1) because of the indiscriminate recommendation to substitute omega-6 fatty acids for saturated fats to lower serum cholesterol concentrations.[29] Table 1 compares the omega-6:omega-3 intake of various populations.[30–34] The population of Crete obtained a higher intake of ALA from purslane and other wild plants, walnuts and figs, whereas the Japanese obtained it from canola oil and soybean oil.[30]

Intake of omega-3 fatty acids is much lower today because of the decrease in fish consumption and the industrial production of animal feeds rich in grains containing omega-6 fatty acids, leading to production of meat rich in omega-6 and poor in omega-3 fatty acids.[35] The same is true for cultured fish[36] and eggs.[37] Even cultivated vegetables contain fewer omega-3 fatty acids than do plants in the wild.[38,39] In summary, modern agriculture, with its emphasis on production, has decreased the omega-3 fatty acid content in many foods: green leafy vegetables, animal meats, eggs, and even fish. Although recommended dietary allowances (RDA) do not officially exist, the adequate intake (AI) of essential fatty acids has been established,[40] as well as the ratio of 18:2ω6 to 18:3ω3.[41]

Biological effects of omega-6 and omega-3 fatty acids

Linoleic acid (LA; 18:2ω6) and ALA (18:3ω3) and their long-chain derivatives are important components of animal and plant cell membranes. When humans ingest fish or fish oil, the ingested eicosapentaenoic acid (EPA; 20:5ω3) and docosahexaenoic acid (DHA; 22:6ω3) partially replace the omega-6 fatty acids (especially arachidonic acid (AA; 20:4ω6)) in cell membranes, especially those of platelets, erythrocytes, neutrophils, monocytes and liver cells (reviewed in 1). As a result, ingestion of EPA and DHA from fish or fish oil leads to (i) decreased production of prostaglandin E_2 metabolites; (ii) decreased concentrations of thromboxane A_2, a potent platelet aggregator and vasoconstrictor; (iii) decreased formation of leukotriene B_4, an inducer of inflammation and a powerful inducer of leucocyte chemotaxis and adherence; (iv) increased concentrations of thromboxane A_3, a weak platelet aggregator and vasoconstrictor; (v) increased concentrations of prostacyclin prostaglandin $(PG)I_3$, leading to an overall increase in total prostacyclin by increasing PGI_3 without decreasing PGI_2 (both PGI_2 and PGI_3 are active vasodilators and inhibitors of platelet aggregation); and (vi) increased concentration of leukotriene B_5, a weak inducer of inflammation and chemotactic agent.[42,43]

Because of the increased amounts of omega-6 fatty acids in the Western diets, the eicosanoid metabolic products from AA, specifically prostaglandins, thromboxanes, leukotrienes, hydroxy fatty acids, and lipoxins, are formed in larger quantities than those formed from omega-3 fatty acids, specifically EPA. The eicosanoids from AA are biologically active in small quantities and if they are formed in larger amounts, they contribute to the formation of thrombi and atheromas; the development of allergic and inflammatory disorders, particularly in susceptible people; and cell proliferation. Thus, a diet rich in omega-6 fatty acids shifts the physiologic state to one that is prothrombotic and proaggregatory, with increases in blood viscosity, vasospasm, and vasoconstriction and decreases in bleeding time. Bleeding time is shorter in groups of patients with hypercholesterolemia,[44] hyperlipoproteinemia,[45] myocardial infarction, other forms of atherosclerotic disease, type 2 diabetes, obesity, and hypertriglyceridemia. Atherosclerosis is a major complication in type 2 diabetes patients. Bleeding time is longer in women than in men and in younger than in older persons. There are ethnic differences in bleeding time that appear to be related to diet. As shown in Table 2, the higher the ratio of omega-6 to omega-3 fatty acids in platelet phospholipids, the higher is the death rate from cardiovascular disease.[46] As

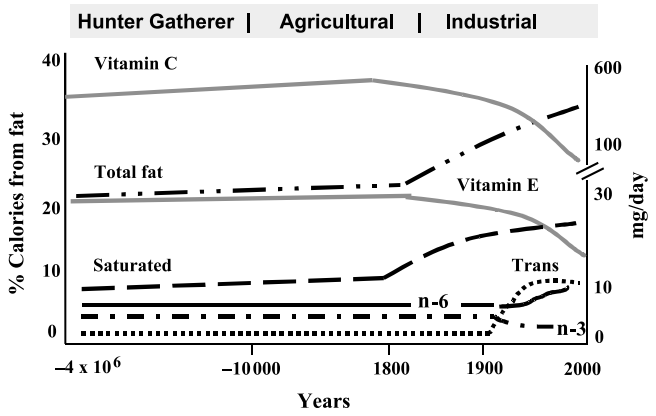

Figure 1. Hypothetical scheme of fat, fatty acid (ω-3, ω-6, *trans* and total) intake (as % of calories from fat) and intake of vitamins E and C (mg/day). Data were extrapolated from cross-sectional analyses of contemporary hunter–gatherer populations and from longitudinal observations and their putative changes during the preceding 100 years.

Table 1. Omega-6:omega-3 ratios in various populations

Population	omega-6:omega-3	Reference
Paleolithic	0.79	31
Greece prior to 1960	1.00–2.0	32
Current US	16.74	31
Current UK and Northern Europe	15.00	33
Current Japan	4.00	34

Table 2. Ethnic differences in fatty acid concentrations in thrombocyte phospholipids and percentage of all deaths from cardiovascular disease†

	Europe and USA	Japan	Greenland eskimos
AA (20:4ω6) %	26	21	8.3
EPA (20:5ω3) %	0.5	1.6	8.0
Omega-6:omega-3	50	12	1
Mortality from CVD %	45	12	7

†Data modified from 46.

AA, arachidonic acid; EPA, eicosapentaenoic acid; CVD, cardiovascular disease.

Table 3. Effects of omega-3 fatty acids on factors involved in the pathophysiology of atherosclerosis and inflammation[47]

Factor	Function	Effect of omega-3 fatty acid on factor concentrations
Arachidonic acid	Eicosanoid precursor, aggregates platelets, and stimulates white blood cells	↓
Thromboxane A_2	Platelet aggregation, vasoconstriction, increases intracellular Ca^{2+}	↓
Prostacyclin	Prevents platelet aggregation, vasodilator, increases cyclic AMP	↑
Leukotriene B_4	Neutrophil chemoattractant increases intracellular Ca^{2+}	↓
Tissue plasminogen activator	Increases endogenous fibrinolysis	↑
Fibrinogen	Blood clotting factor	↓
Red blood cell deformability	Decreases tendency to thrombosis and improves oxygen delivery to tissues	↑
Platelet-activating factor	Activates platelets and white blood cells	↓
Platelet-derived growth factor	Chemoattractant and mitogen for smooth muscles and macrophages	↓
Oxygen free radicals	Causes cellular damage, enhances LDL uptake via the scavenger pathway, stimulates arachidonic acid metabolism	↓
Lipid hydroperoxides	Stimulates eicosanoid formation	↓
Interleukin-1 and tumor necrosis factor	Stimulates neutrophil oxygen free radical formation, lymphocyte proliferation, and platelet activating factor; expresses intercellular adhesion molecule 1 on endothelial cells; and inhibits plasminogen activator and thus is procoagulant	↓
Endothelial-derived relaxation factor	Reduces arterial vasoconstrictor response	↑
Very-low-density lipoprotein	Related to LDL and HDL concentrations	↓
High-density lipoprotein	Decreases the risk of coronary heart disease	↑
Lipoprotein(a)	Atherogenic and thrombogenic	↓
Triacylglycerols and chylomicrons	Contribute to postprandial lipemia	↓

↑, increases; ↓, decreases; AMP, adenosine monophosphate; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

the ratio of omega-6 PUFA to omega-3 PUFA increases, the prevalence of type 2 diabetes also increases.[18]

The hypolipidemic, antithrombotic, and anti-inflammatory effects of omega-3 fatty acids have been studied extensively in animal models, tissue cultures, and cells (Table 3).[47] As expected, earlier studies focused on the mechanisms that involve eicosanoid metabolites. More recently, however, the effects of fatty acids on gene expression have been investigated and this focus of interest has led to studies at the molecular level (Tables 4,5). Previous studies have shown that fatty acids, whether released from membrane phospholipids by cellular phospholipases or made available to the cell from the diet or other aspects of the extracellular environment, are important cell-signaling molecules. They can act as second messengers or substitute for the classic second messengers of the inositide phospholipid and cyclic adenosine monophosphate (AMP) signal transduction pathways.[61] They can also act as modulator molecules mediating responses of the cell to extracellular signals.[61] It has been shown that fatty acids rapidly and directly alter the transcription of specific genes.[62]

Effects of dietary α-linolenic acid compared with long-chain omega-3 fatty acid derivatives on physiologic indexes

Several clinical and epidemiologic studies have been conducted to determine the effects of long-chain omega-3 PUFA on various physiologic indexes.[7] Whereas the earlier studies

Table 4. Effects of polyunsaturated fatty acids on several genes encoding enzyme proteins involved in lipogenesis, glycolysis, and glucose transport

Function and gene	Reference	LA	ALA	AA	EPA	DHA
Hepatic cells						
Lipogenesis						
FAS	48–51	↓	↓	↓	↓	↓
S14	48–51	↓	↓	↓	↓	↓
SCD1	52	↓	↓	↓	↓	↓
SCD2	53	↓	↓	↓	↓	↓
ACC	51	↓	↓	↓	↓	↓
ME	51	↓	↓	↓	↓	↓
Glycolysis						
G6PD	54	↓				
GK	54	↓	↓	↓	↓	↓
PK	55	–	↓	↓	↓	↓
Mature adiposites						
Glucose transport						
GLUT4	56	–	–	↓	↓	–
GLUT1	56	–	–	↑	↑	–

AA, arachidonic acid; ALA, α-linolenic acid; LA, linoleic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Table 5. Effects of polyunsaturated fatty acids on several genes encoding enzyme proteins involved in cell growth, early gene expression, adhesion molecules, inflammation, β-oxidation, and growth factors

Function and gene	Reference	LA	ALA	AA	EPA	DHA
Cell growth and early gene expression						
c-fos	57	–	–	↑	↓	↓
Egr-1	57	–	–	↑	↓	↓
Adhesion molecules						
VCAM-1 mRNA†	58	–	–	↓	‡	↓
Inflammation						
IL-1β	59	–	–	↑	↓	↓
β-oxidation						
Acyl-CoA oxidase§	51	↑	↑	↑	↑↑	↑
Growth factors						
PDGF	60	–	–	↑	↓	↓

†Monounsaturated fatty acids (MONO) also suppress VCAM1 mRNA, but to a lesser degree than does DHA. AA also suppresses to a lesser extent than DHA.

‡EPA has no effect by itself but enhances the effect of DHA.

§MONO also induce acyl-CoA oxidase mRNA.

AA, arachidonic acid; ALA, α-linolenic acid; CoA, concanavalin A; LA, linoleic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; IL, interleukin; PDGF, platelet-derived growth factor; VCAM, vascular cell adhesion molecule; ↓, suppresses or decreases; ↑, induces or increases.

were conducted with large doses of fish or fish-oil concentrates, more recent studies have used lower doses.[14] α-linolenic acid, the precursor of omega-3 fatty acids, can be converted to long-chain omega-3 PUFA and can therefore be substituted for fish oils. The minimum intake of long-chain omega-3 PUFA needed for beneficial effects depends on the intake of other fatty acids. Dietary amounts of LA as well as the ratio of LA to ALA appear to be important for the metabolism of ALA to long-chain omega-3 PUFA. Indu and Ghafoorunissa showed that while keeping the amount of dietary LA constant, 3.7 g ALA appears to have biological effects similar to those of 0.3 g long-chain omega-3 PUFA with conversion of 11 g ALA to 1 g long-chain omega-3 PUFA.[63] Thus, a ratio of 4 (15 g LA:3.7 g ALA) is appropriate for conversion. This ratio is also consistent with the Lyon Heart Study.[12] In human studies, Emken *et al.* showed that the conversion of deuterated ALA to longer-chain metabolites was reduced by approximately 50% when dietary intake of LA was increased from 4.7% to 9.3% of energy, as a result of the known competition between omega-6 and omega-3 fatty acids for desaturation.[64]

Indu and Ghafoorunissa further indicated that increasing dietary ALA increases EPA concentrations in plasma phospholipids after both 3 and 6 weeks of intervention.[63] Dihomo-γ-linolenic acid (20:3ω6) concentrations were reduced but AA concentrations were not altered. The reduction in the ratio of long-chain omega-6 PUFA to long-chain omega-3 PUFA was greater after 6 weeks than after 3 weeks. Indu and Ghafoorunissa were able to show antithrombotic effects by reducing the ratio of omega-6 to omega-3 fatty acids with ALA-rich vegetable oil. After ALA supplementation there was an increase in long-chain omega-3 PUFA in plasma and platelet phospholipids and a decrease in platelet aggregation. The ALA supplementation did not alter triacylglycerol concentrations. As shown by others, only long-chain PUFA have triacylglycerol-lowering effects.[65]

In Australian studies, ventricular fibrillation in rats was reduced with canola oil as much or even more efficiently than with fish oil, an effect attributable to ALA.[66] Further studies should be able to show whether this result is a direct effect of ALA per se or occurs as a result of its desaturation and elongation to EPA and DHA.

The diets of Western countries have contained increasingly larger amounts of LA, which has been promoted for its cholesterol-lowering effect. It is now recognized that dietary LA favors oxidative modification of low-density lipoprotein (LDL) cholesterol,[67,68] increases platelet response to aggregation,[69] and suppresses the immune system.[70] In constrast, ALA intake is associated with inhibitory effects on the clotting activity of platelets, on their response to thrombin[71,72] and on the regulation of AA metabolism.[73] In clinical studies, ALA contributed to lowering of blood pressure.[74] In a prospective study, Ascherio *et al.* showed that ALA is inversely related to the risk of coronary heart disease in men.[75]

α-linolenic acid is not equivalent in its biological effects to the long-chain omega-3 fatty acids found in marine oils. Eicosapentaenoic acid and DHA are more rapidly incorporated into plasma and membrane lipids and produce more rapid effects than does ALA. Relatively large reserves of LA in body fat, as are found in vegans or in the diet of omnivores in Western societies, would tend to slow down the formation of long-chain omega-3 fatty acids from ALA. Therefore, the role of ALA in human nutrition becomes important in terms of long-term dietary intake. One advantage of the consumption of ALA over omega-3 fatty acids from fish is that the problem of insufficient vitamin E intake does not exist with high intake of ALA from plant sources.

Terrestrial sources of omega-3 fatty acids

In view of the fact that a number of studies indicate that 18:3ω3 (ALA) is converted to EPA and DHA in human beings, it is important to consider terrestrial sources of omega-3 fatty acids in the food supply. α-linolenic acid, the precursor to EPA and DHA, was first isolated from hempseed oil in 1887.[76] In plants, leaf lipids usually contain large proportions of 18:3ω3, which is an important component of chloroplast membrane polar lipids. Mammals who feed on these plants convert 18:3ω3 to EPA and DHA, the long-chain omega-3 fatty acids found in fish.

Wild animals and birds who feed on wild plants are very lean, having a carcass fat content of only 3.9%,[77] and contain approximately fivefold more polyunsaturated fat per g than is found in domestic livestock.[35,78] Most importantly, 4% of the fat of wild animals contains EPA, whereas domestic beef

Table 6. Fatty acid content of plants (mg/g of wet weight)[38]

Fatty acid	Purslane	Spinach	Buttercrunch lettuce	Red Leaf lettuce	Mustard
14:0	0.16	0.03	0.01	0.03	0.02
16:0	0.81	0.16	0.07	0.10	0.13
18:0	0.20	0.01	0.02	0.01	0.02
18:1ω9	0.43	0.04	0.03	0.01	0.01
18:2ω6	0.89	0.14	0.10	0.12	0.12
18:3ω3	4.05	0.89	0.26	0.31	0.48
20:5ω3	0.01	0.00	0.00	0.00	0.00
22:6ω3	0.00	0.00	0.001	0.002	0.001
Other	1.95	0.43	0.11	0.12	0.32
Total fatty acid content	8.50	1.70	0.601	0.702	1.101

contains very small or undetectable amounts because cattle are fed grains that are rich in omega-6 fatty acids and poor in omega-3 fatty acids.[79] A deer that forages on ferns and mosses also contains omega-3 fatty acids in its meat.

Lipids of liverworts, ferns, mosses and algae include 16:4ω3, 18:3ω3, 20:5ω3 and 22:6ω3. These are of particular interest because, unlike the higher plants in which 18:3ω3 and 16:3ω3 are the more abundant, they contain long-chain omega-3 fatty acids such as 20:5ω3 (liverwort, 9–11%) depending on their state of development. Mosses growing in or near water contain higher percentages of C20 and C22 PUFA and are morphologically simpler than those that live in dry habitats. Thus both the plants, and the animals that feed on them, are good sources of omega-3 fatty acids for human consumption.

Table 6 includes the amount of omega-3 fatty acids in mg per g wet weight of purslane and other commonly eaten leafy vegetables (spinach, buttercrunch lettuce, red leaf lettuce, and mustard greens). As indicated in Table 6, purslane contains 8.5 mg of fatty acids per g of wet weight. In contrast, other plants are relatively low in lipid content: spinach contains 1.7 mg/g, mustard greens 1.1 mg/g, red leaf lettuce 0.7 mg/g, and buttercrunch lettuce 0.6 mg/g.

Purslane, with 4 mg/g wet weight, is a good non-aquatic source of 18:3ω3. Based on the information available from the provisional US Department of Agriculture (USDA) table[80] and our studies,[38,39] purslane, a wild growing plant, is the richest source of omega-3 fatty acids of any leafy vegetable yet examined.

Purslane is one of the plants that was part of the diet of hunter–gatherers in the Pacific Northwest section of the USA. The large native population encountered at contact (*ca* 1790–1850) was non-agricultural and obtained their food by foraging, harvesting and sometimes managing, natural, localized species of plants and animals. In a recent study, Norton *et al.* studied the vegetable food products of the foraging economies of the Pacific Northwest and found them to be valuable sources of calcium, magnesium, iron, zinc and ascorbic acid.[81] Norton *et al.* state the following.

> These members of the Lily, *Purslane*, Barberry, Currant, Rose, Parsley, Heath, Honeysuckle, Sunflower and Water-Plantain families are among those regularly collected by these foraging groups whose economic strategies were keyed to the use of multiple resources and the storage of large quantities of processed foods. Stored vegetable food along with dried fish provide ample and nutritious diets during the seasonal periods of resource non-productivity . . . Analyses show that these native foods are superior to cultigens in necessary fiber, minerals and vitamins making substantial contributions to precontact diets.

The results of this study revealed that a wide variety of foods were used to meet nutritional needs and that native preparation and preservation techniques were important factors in retaining nutrients and in maintaining a balanced diet during seasons of low productivity. The study indicates that vegetable foods were systematically gathered and processed in quantity. The wide variety of vegetables eaten along the Mediterranean and by foragers contrasts with the relatively narrow variety of crops produced by horticulturists and traditional agriculturists today.

Table 7 indicates the amount of 18:3ω3 in fruits, which contain only small amounts of linolenic acid (0.1 g per 100 g edible portion). Table 8 shows the amount of omega-3 in grains. Oats is the highest source, at 1.4 g per 100 g edible portion, followed by wheat germ at 0.7 g/100 g, whereas rice, corn and wheat contain only between 0.1 and 0.3 g/100 g edible portion. Table 9 indicates the amount of 18:3ω3 in legumes. Soybeans contain the highest amount of ALA at 1.6 g per 100 g edible portion. Table 10 indicates the amount of 18:3ω3 in vegetables. Soybeans contain the highest amount of ALA, at 3.2 g per 100 g edible portion. Table 11 indicates the amount of 18:3ω3 in nuts and seeds. Butternuts contain the highest amount of ALA, at 8.7 g per 100 g edible portion, followed by English walnuts at 6.8 g/100 g.

Table 7. Terrestrial sources of omega-3 fatty acids: fruits (100 g edible portion, raw)

Fruits	18:3 (g)
Avocados, raw, California	0.1
Raspberries, raw	0.1
Strawberries	0.1

Adapted from US Department of Agriculture table.[80]

Table 8. Terrestrial sources of omega-3 fatty acids: grains (100 g edible portion, raw)

Grains	18:3 (g)
Barley, bran	0.3
Corn, germ	0.3
Oats, germ	1.4
Rice, bran	0.2
Wheat, bran	0.2
Wheat, germ	0.7
Wheat, hard red winter	0.1

Adapted from US Department of Agriculture table.[80]

Table 9. Terrestrial sources of omega-3 fatty acids: legumes (100 g edible portion, raw)

Legumes	18:3 (g)
Beans, common, dry	0.6
Chickpeas, dry	0.1
Cowpeas, dry	0.3
Lentils, dry	0.1
Lima beans, dry	0.2
Peas, garden, dry	0.2
Soybeans, dry	1.6

Adapted from US Department of Agriculture table.[80]

Table 12 indicates the amount of 18:3ω3 in g per 100 g of edible seed oils. Linseed (flaxseed), at 53.3 g, is the richest common source of ALA. As with the case of phytoplankton, the linolenate content depends on the condition of cultivation, light period, temperature, and the species or variety of flax. Other good sources of 18:3ω3 are rapeseed oil (11.1 g/100 g), walnut oil (10.4 g/100 g), wheat germ oil (6.9 g/100 g) and soybean oil (6.8 g/100 g of edible seed oils).

Table 10. Terrestrial sources of omega-3 fatty acids: vegetables (100 g edible portion, raw)

Vegetables	18:3 (g)
Beans, navy, sprouted, cooked	0.3
Beans, pinto, sprouted, cooked	0.3
Broccoli, raw	0.1
Cauliflower, raw	0.1
Kale, raw	0.2
Leeks, freeze-dried	0.2
Lettuce, butterhead	0.1
Radish seeds, sprouted, raw	0.7
Seaweed, Spirulina, dried	0.8
Soybeans, green, raw	3.2
Soybeans, mature seeds, sprouted, cooked	2.1
Spinach, raw	0.1

Adapted from US Department of Agriculture table.[80]

Table 11. Terrestrial sources of omega-3 fatty acids: nuts and seeds (100 g edible portion, raw)

Nuts and Seeds	18:3 (g)
Butternuts, dried	8.7
Walnuts, English/Persian	6.8
Chia seeds, dried	3.9
Walnuts, black	3.3
Beechnuts, dried	1.7
Soybean kernels, roasted and toasted	1.5
Hickory nuts, dried	1.0

Adapted from US Department of Agriculture table.[80]

Table 12. Terrestrial sources of omega-3 fatty acids: oils (100 g edible portion, raw)

Oils	18:3 (g)
Linseed oil	53.3
Rapeseed oil (Canola)	11.1
Rice bran oil	1.6
Soybean oil	6.8
Tomato seed oil	2.3
Walnut oil	10.4
Wheat germ oil	6.9

Adapted from US Department of Agriculture table.[80]

Clinical intervention studies with dietary patterns rich in omega-3 fatty acids from plants, nuts and seeds

In recent cardiovascular studies, investigations of dietary patterns, rather than single nutrients, have been very useful in measuring their effects on new cardiovascular events or total mortality. For example, in the Lyon Heart Study, de Lorgeril *et al.* used a diet based on a modified diet from the island of Crete and compared it with the American Medical Association (AHA) Step I diet.[12]

De Lorgeril *et al.* used the modified diet of Crete because there was evidence from the Seven Countries Study that Cretans had a lower rate of coronary heart disease than other participants, including those from other Mediterranean countries.[82] Therefore, using a Mediterranean diet rather than the diet of Crete would not have been scientifically accurate. The population of Crete had three times as much ALA in their cholesteryl esters as the population of Zutphen, indicating higher intake of ALA.[83]

The characteristics of the Cretan diet are: moderate in total fat but high in monounsaturated fat (because olive oil is the predominant cooking oil), low in saturated fat, lower in omega-6 fatty acids than typical Western diets, low in *trans* fatty acids, high in omega-3 fatty acids, and rich in fruits and vegetables, particularly wild plants, which are especially rich in ALA and in vitamins E, C, beta-carotene, and glutathione.[84] Comparing the control diet, which was the Step I AHA diet, with the experimental diet based on that of Crete, Table 13 shows that whereas the amount of cheese intake was the same in both diets, the experimental diet was lower in other dairy products and meat but higher in fish and ALA from canola margarine.

After 2 years of follow up, the patients on the experimental diet had no sudden deaths and a decrease in total mortality of 70%. The same subjects at 4 years of follow up had a significant decrease in cancer mortality. After adjustment for age, sex, smoking, leukocyte count, cholesterol level, and aspirin use, the reduction of risk in experimental subjects compared with controls was 56% for total deaths, 61% for cancers, and 56% for the combination of deaths and cancers.[85]

The Dietary Approaches to Stop Hypertension (DASH) Clinical Trial is the only study that investigated the effects of three different diets on lowering blood pressure.[86] The study enrolled 459 adults age 22 years and older with body mass index (BMI) less than 35, systolic blood pressure less than 160 mmHg, and diastolic pressures of 80–95 mmHg. Approximately half were women and nearly 60% were African American, who tend to develop hypertension earlier and more often than Caucasians.

For 8 weeks participants were fed one of three diets: a control diet; a fruit and vegetable diet; or a combination diet. The DASH study was designed to test whether blood pressure in randomly assigned subjects in four clinical centers would differ between the control diet and the fruit and vegetable diet and the combination diet. The greatest lowering of blood pressure occurred between the control and combination diets. The nutrient composition of the control

Table 13. Lyon Heart Study: dietary intake (g/day; mean (SEM)) in the two groups†

Foods	Control $n = 192$		Experimental $n = 219$		P
Vegetables	288	(12)	316	(10)	0.07
Fruits	203	(12)	251	(12)	0.007
Delicatessen	13.4	(2.4)	6.4	(1.5)	0.01
Meat	60.4	(5.5)	40.8	(5.0)	0.009
Poultry	52.8	(6.0)	57.8	(5.0)	0.42
Cheese	35.0	(2.6)	32.2	(2.0)	0.25
Fish	39.5	(5.7)	46.5	(5.6)	0.16
Butter and cream	16.6	(1.6)	2.8	(0.6)	<0.001
Oil	16.5	(0.9)	15.7	(0.8)	0.65
Bread	145	(7)	167	(6)	0.01
Cereals	99.4	(11)	94.0	(10)	0.22
Legumes	9.9	(3.0)	19.9	(4.3)	0.07
Margarine	5.1	(0.6)	19.0	(1.0)	<0.001

Table modified from 12.

†Intake of the main foodstuffs after 1–4-year follow up in the two groups.

Control, American Heart Association's Step I diet; Experimental, based on the diet of Crete.

Delicatessen: ham, sausage, and offal; margarine: special canola margarine providing 2 g of α-linolenic acid (LNA, an omega-3 fatty acid) and less than 2–5% *trans* fatty acids.

diet was typical of the diets of a substantial number of Americans. The macronutrient profile and fiber content corresponded to average consumption, whereas the potassium, magnesium, and calcium levels were close to the 25th percentile of USA consumption.[87]

The combination diet was rich in fruits and vegetables and had reduced amounts of saturated fat, monounsaturated fat, total fat, and cholesterol because of the consumption of low-fat dairy products; fewer snacks; less intake of fats, oils and salad dressings; one-third less intake of beef, pork and ham in servings per day (1.5 for the control diet *vs* 0.6 for the combination diet); less poultry (0.8 control *vs* 0.6 combination); but greater consumption of fish (0.2 control *vs* 0.5 combination).

The combination diet included 10 g less of saturated fat than the control diet, but was similar in the content of polyunsaturated fatty acids, and higher in protein, carbohydrates, and fiber. Whereas the control diet did not include any servings of nuts, seeds, or legumes, the combination diet included 0.7 servings per day (Table 14). Nuts, seeds, and legumes are rich in essential fatty acids, particularly the omega-3 fatty acid ALA. The diet provided potassium, magnesium, and calcium at levels close to the 75th percentile of USA consumption.

The dietary patterns and nutrient composition of the diet of Crete,[84] the Lyon Heart Study[12] and the DASH study[86] are all very similar. They are low in saturated fat and polyunsaturated fatty acids and are balanced in omega-6 and omega-3 essential fatty acids. The diets are low in meat; high in fish, protein and fiber; and rich in fruits, vegetables, and legumes. Calcium was provided by cheese in the Lyon study and by low-fat dairy products in the DASH study.

Such a dietary pattern is similar to the Paleolithic diet (the diet to which our genetic profile was programmed to respond) although the Paleolithic diet was much higher in protein.[31,32] Those dietary patterns provided low amounts of sodium but high amounts of potassium, calcium (from fish bones and plants during the Paleolithic period), and magnesium, high amounts of anti-oxidants, and balanced omega-6 and omega-3 fatty acids.

The results from the Lyon Heart Study, the GISSI study and the DASH study confirm the importance of a dietary pattern consistent with human evolution in the secondary prevention of coronary heart disease and in lowering blood pressure. Because the traditional diet of Greece as exemplified by the diet of Crete is associated with a decreased rate in coronary

Table 14. DASH Study: average daily servings of foods

Foods	Control diet	Combination diet
Vegetables	2.0	4.4
Fruits and juices	1.6	5.2
Beef pork, and ham	1.5	0.5
Poultry	0.8	0.6
Fish	0.2	0.5†
Fats, oils, and salad dressing	5.8	2.5
Low-fat dairy	0.1	2.0
Regular-fat dairy	0.4	0.7
Grains	8.2	7.5
Snacks and sweets	4.1	0.7
Nuts, seeds and legumes‡	0.0	0.7

Modified from 86.

†Increase in fish intake indicates an increase in omega-3 fatty acids, specifically EPA and DHA.

‡Nuts, seeds, and legumes are rich in α-linolenic acid.

DASH, Dietary Approaches to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid.

heart disease and cancer and an increased life expectancy, it could serve as a prototype in the primary prevention of coronary heart disease.[88] Of interest is the fact that other traditional diets (i.e. the Japanese diet) are similar in composition to the diet of Crete, particularly relative to the essential fatty acids.

Conclusions

It is now evident that human beings evolved on a diet that was balanced in the essential fatty acids. Changes in agricultural practices have decreased the content of omega-3 fatty acids (18:3ω3, 20:5ω3, 22:6ω3) in the food supply while there has been an increase in the intake of 18:2ω6 from vegetable oils and 20:4ω6 from meat and dairy products. Leafy wild plants contain more 18:3ω3 and less 18:2ω6 whereas cultivated plants and seeds are higher in 18:2ω6 with the exception of flax. The time has come to return the omega-3 fatty acids into the food supply. Progress in this regard is being made.[89,90] In the past, industry focused on improvements in food production and processing, whereas now and in the future, the focus will be on the role of nutrition in product development.[90] This will necessitate the development of research for the nutritional evaluation of the various food products and educational programs for professionals and the public.[90] The definition of food safety will have to expand in order to include the adverse effects of nutrient structural changes (i.e. *trans* fatty acids) and food composition (i.e. ratio of omega-6:omega-3 fatty acids).[91] The dawn of the 21st century will enhance the scientific base for product development and expand collaboration among agricultural, nutritional and medical scientists. This should bring about a greater involvement of nutritionists and dietitians in industrial research and development to respond to an ever-increasing consumer interest in the health attributes of food.

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