MARVALOUS

Join The Tribe

An update on Salvia Sclarea oil

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Salvia Sclarea oil introduction

Salvia Sclarea is produced from one of the breeds of sage; the family of sage has more then 2400 different breeds, grown for different use in different places around the globe.

Salvia Sclarea is originate in the east Mediterranean and southern Europe, region that contain wild habitancy of this species. The species is widely cultivated throughout the temperate regions of the world. Systematically it is belonging to the Salvia (Sage) genus in the Lamiaceae family. There are almost one thousand different species within the Salvia genus with global distribution from among many are known for their therapeutic and culinary excellencies.

Salvia Sclarea is known as one of the oldest medicinal plants, Nowadays its floral extracts are utilized in the food industries as flavor additive for soft and alcoholic beverages, extensively used in frozen dairy desserts, candy, baked goods, gelatins and puddings, condiments and relishes. While the essential oil esteemed for its aroma therapeutic properties, both, essential oil and its components, are being used in the cosmetic and hygienic industries as fragrances in soaps, detergents, creams, lotions and perfumes.

Dweck described the folklore and cosmetic use of various Salvia species;
Salvia Sclarea is antispasmodic and balsamic in nature and has been used both fresh and dry for digestive difficulties as a stomachic. It has also been employed in kidney disease with good results. The mucilage of the seeds has been used in ophthalmic disorders and a decoction of the herb was considered by herbalists to be efficacious in any complaint of the eyes. Mucilage of the seeds is used in tumours. Cold extract of Salvia Sclarea will help draw out thorns and splinters and reduce inflammation. The dried roots, crushed and powdered, can be used like snuff to clear the head and ease a headache. An ointment made with Salvia Sclarea leaves will help draw out inflammation and bring boils and spots to a head.

It was used by the native Jamaicans, who considered it cooling and cleansing for ulcers, and who also used it for inflammation of the eyes. A decoction of the leaves boiled in coconut oil was considered beneficial for the stings of scorpions. Available data indicate the essential oil to be generally non-toxic.
After the essential oil is removed the crude material is a source of sclareol which is converted to the sclareolide; both are used to flavour tobacco. sclareolide is also used in the production of an ambergris substitute.

In the extensive essay of Grieve, Salvia Sclarea is mentioned with relation to wine merchant of Germany, who employed it as adulterant, infusing it with Elder flowers, and then adding the liquid to the Rhenish wine, which converted it into the likeness of Muscatel. In this piece it had be mentioned that the herb and leaves, used both fresh and dry, dried in the same manner as the garden sage. Formerly the root was used dry, in domestic medicine, and also the seeds. In the Encyclopedia of Herbs and Their Uses it said that the leaves of Salvia Sclarea have been used to make fritters and the flowers added to salads and to make tea. Culpeper in the Complete English Physician (1652) and his English Physician Enlarged has half a page about it, 'The fresh leaves dipped in a batter of flour, eggs, and a little milk, and fried in butter, and served to the table.

In the Sturtevant's Edible Plants of the World said that the leaves of it are used in omelets, made with Eggs and so must be in a garden. There is also evidence of using Salvia Sclarea for seasoning soups in Sicily.

Salvia Sclarea oil safeness and evidence of edibility

According to the U.S. food and drug administration, department of health and human services code of federal regulations, title 21, and part 182, Salvia Sclarea include as substances generally recognized as safe. In general provisions sec. 182.10 Salvia Sclarea include as spices and other natural seasonings and flavorings that are generally recognized as safe for their intended use.

Salvia Sclarea seed oil is been used in the Israeli functional food industry since 2006. Tara Milko industries (part of the Coca Cola group in Israel) used Salvia Sclarea seed oil to enrich chocolate milk drinks for kids with Omega 3. The inventive and innovative of this product give rise to place it as product of the year (2006) in Israel. Israeli food companies Elit and B&D are using Salvia Sclarea seed oil to fortify their original products with Omega 3.

Salvia Sclarea oil fatty acids profile

Salvia Sclarea seed oil has high content of omega 3 ALA fatty acid in it, as can be seen in table number 1. Fatty acid profiling was carried out by Miluda Ltd. Laboratories using a standard method (ISO 5508 & 5509 – Fatty Acid profile) Fatty acid profile was carried out for 3 different batches of Salvia Sclarea seed oil (oil samples were delivered by Magnetika Interactive LTD who is responsible for growing Salvia Sclarea in Israel).

As it specified in table number 1 the sum of omega 3 fatty acids is reaching above 50 percent, again, mainly dew to hi content of alfa linolenic acid. Additional important findings are the close to no presence of saturated fatty acids and Trans fatty acids.

The major fatty acids found in Salvia Sclarea seed oil are as follows:

- Palmitic acid – is the most widely occurring saturated fatty acid and is present in most commercial oils (Gunstone et al., 1986). It is found in large quantities in fish oils (10 to 30%) and tropical fats such as coconut (6.9%), palm kernel (6.5 to 11%) and palm (32 to 59%) oils (Gunstone et al., 1986; Horrobin, 1990a,b). Salvia Sclarea seed oil contains on average 6.5% palmitic acid.

- Stearic acid – is found in abundance in tallow (5 to 30%), cocoa butter (30 to 36%) and shea nut butter (44%) (Gunstone et al., 1986; Erasmus, 1993). Salvia Sclarea seed oil contains on average 2.5% stearic acid.

- Oleic acid – Oleic acid is the most widely occurring natural fatty acid and is found in practically all lipids (Gunstone et al., 1986). It is found in large quantities in olive (43.7 to 83%), almond (65 to 70%) and peanut (37.9%) oils (Erasmus, 1993). Oleic acid is also produced by mammalians metabolism (Gunstone et al., 1986; Erasmus, 1993). Salvia Sclarea seed oil contains on contains on average 24% oleic acid.

- Linoleic acid – is found in safflower (75.3%), sunflower (68.5%), soybean (53%) and sesame (45%) oils (Gunstone et al., 1986; Erasmus, 1993). Salvia Sclarea seed oil contains on contains on average 14 Linoleic acid.

- Alpha linolenic acid – is the major fatty acid found in plant leaves, stems and roots and other photosynthetic organisms (Gunstone et al., 1986). Flax seed is the richest source of ALA with over 50%; Chia and kukui (candlenut) contain about 30%, and hemp seed around 20% (Erasmus, 1993). Pumpkin seed oil may have up to 15%, canola up to 10% and walnut between 3 to 11% (Erasmus, 1993). Soybean oil normally contains 5 to 7% (Erasmus, 1993). Salvia Sclarea seed oil contains on average 51% ALA.

Table Number 1
Salvia Sclarea Seed Oil Fatty acid profile

Formula	Fatty Acid Name	(%) Fatty Acid Composition		
		Batch number 1	Batch number 2	Batch number 3
C 14:0	Myristic Acid	0.03	0.035	0.037
C 14:1	Myristoleic Acid	----	----	----
C 15:0	Pentadecanoic Acid	0.01	0.014	----
C 16:0	Palmitic Acid	6.44	6.47	6.524
C 16:1	Palmitoleic Acid	0.07	0.068	0.07
C 17:0	Heptadecanoic Acid	0.05	0.049	0.046
C 17:1	Heptadecenoic Acid	0.08	0.099	0.093
C 18:0	Stearic Acid	2.49	2.567	2.518
C 19:0		0.166	0.168	0.157
C18:1n9t	Elaidic Acid	----	----	----
C18:1n9c	Oleic Acid	23.89	25.756	23.213
C18:2n6t	Linolelaidic Acid	----	----	----
C 18:2	Linoleic Acid	13.84	13.817	14.009
C 20:0	arachidic Acid	0.12	0.119	0.112
C 18:3 n6	γ-Linolenic Acid	0.26	0.255	0.263
C 20:1	Eicosenoic Acid	0.61	0.632	0.6
C 18:3 n3	α-Linolenic Acid	51.12	49.212	51.727
C21:0	Heneicosanoic Acid	----	----	----
C 20:2 n6	Eicosadienoic Acid	0.05	0.046	0.041
C 22:0	Behenic Acid	0.05	0.056	0.046
C 20:3 n6	Eicosatrienoic Acid	----	----	0.033
C22:1n9	Erucic Acid	0.12	0.128	0.112
C 20:3 n3	Eicosatrienoic Acid	0.03	0.034	0.032
C 20:4 n6	Arachidonic Acid	----	----	----
C 23:0	Tricosanoic Acid	0.01	0.016	0.014
C 22:2 n6	Docosadienoic Acid	----	----	----
C 24:0	Lignoceric Acid	0.04	0.039	0.036
C 20:5 n3	Eicosapentaenoic Acid	----	----	----
C 24:1	Nervonic Acid	0.14	0.152	0.138
C 22:6 n3	Docosahexaenoic Acid	----	----	----

Nutritional value of Salvia Sclarea oil

Nutrition values were measured using standardized methods for three different batches;
nutrition value analysis was carried out by Miluda laboratories detailing the following results (table number 3):

Table Number 2
Nutritional value Parameters of Salvia Sclarea Seed Oil

Parameter	Batch number 1	Batch number 2	Batch number 3
Energy, Kcal/100 g	891	892	895
Moisture, g/100 g	Not found	0.03	Not found
Fat (calculated) g/100 g	98.97	99.11	99.4
Saturated fat, g/100 g	10.07	9.21	10.17
Insoluble matter (hexane), g/100 g	0.07	0.1	0.04
Ash, g/100 g	Not found	Not detected	Not found
Sodium, mg/100 g	<1	Not detected	<1

Microbiology lab test

Microbial findings in 3 different batches of Salvia Sclarea seed oil are represented in table number 4.
Microbiology testing for three different batches was carried out by the Bactochem laboratories.
All results were in the allowed standard.

Table Number 2
Microbiology Test of Salvia Sclarea Seed Oil

Test	Units	Batch number 1	Batch number 2	Batch number 3
Total aerobic mesophilic count	In 1gr	< 10	< 10	< 10
Coliforms	In 1gr	< 10	< 10	< 10
.Salmonella spp	In 20gr	Negative	Negative	Negative
Yeasts/ Molds	In 1gr	< 10	< 10	< 10
E. coli	In 1gr	< 10	< 10	< 10
Aerobic mesophilic spore bearers	In 1gr	< 10	< 10	< 10
Anaerobic mesophilic spore bearers	In 1gr	< 3	< 3	< 10

Active Ingredients in Salvia Sclarea oil

Salvia Sclarea oil present a natural vegetable oil formula of unique and rare active ingredients present in the oil. The presence of those ingredients suggest that the oil may provide an Anti-bacterial, Anti-oxidant Antiseptic, Antiviral, Anti-mutagenic Anti - inflammation, Antifungal and Astringent qualities.
One of those ingredients is Sclareol; Sclareol is a rare substance which used to be produced from whales. Sclareol has many unique medical properties and its presence in the Salvia Sclarea oil differentiate the oil from any known vegetable oil today.

Substance	Benefits
Alpha Linolenic Acid (ALA) Omega 3	Omega-3 fatty acids are PUFA required for the structure and function of the body's cells and are important in maintaining our health Salvia Sclarea Oil contain 50% Omega 3 ALA
Oleic Acid Omega 9	• Oleic acid may hinder the progression of ALD, or Adrenoleukodystrophy, a fatal disease that affects the Brain and adrenal glands. • Oleic acid may help boost memory. • Oleic acid may be responsible for the hypotensive (Blood pressure reducing) effects of olive oil. • Salvia Sclarea Oil contain 25% Omega 9
Lectin extracted from the seeds of Salvia sclarea	The lectin extracted from the seeds of Salvia sclarea (SSL) recognizes the Tn antigen (GalNAc alpha1-->Ser/Thr) expressed in certain human carcinomas. (J Biomed Sci. 2005;12(1):167-84. LinksLectinochemical studies on the glyco-recognition factors of a Tn (GalNAcalpha1-->Ser/Thr) specific lectin isolated from the seeds of Salvia sclarea).
Omega 3 to Omega 6 Ratio	Salvia Sclarea seed oil has an excellent 3:1 Omega 3 to Omega 6 ratio
Tannic Acid	Tannic acid has Anti-bacterial, Anti-oxidant Antiseptic, Antiviral, Anti-mutagenic and Astringent properties (The effects of resveratrol and tannic acid on apoptosis in colon adenocarcinoma cell line.Department of Medical Biology, Eskisehir Osmangazi University, Medical Faculty, Eskisehir, Turkey)

Substance	Benefits
Sclareol	• Sclareol has Antioxidant, Antibacterial and Antifungal properties. • Sclareol posses cyto-toxic and cyto-static activity: Induced Apoptosis in human leukemic cells. • Sclareol enhanced the activity of known Anticancer Drugs, doxorubicin, etoposide and cisplatinum, against MDD2 breast cancer cell line. Sclareol demonstrated a good Antibacterial activity against: • Staphylococcus aureus ATCC 25923, • Pseudomonas aeruginosa ATCC 27950, • Escherichia coli ATCC 25922 • Enterococcus faecalis ATCC 29212. • Sclareol demonstrated significant cytotoxic activity against Hep-2 cells. (*J Pharm Sci. 2007 Apr;20(2):146-8. Links*) • Antibacterial and cytotoxic activity of the acetone extract of the flowers of Salvia sclarea and some natural products
Linalool and Linalyl acetate	Found to be effective as Anti - inflammation, Antibacterial, Antifungal. Behave as synergistic and strengthening other bioactive materials. (Anti-inflammatory activity of linalool and linalyl acetate constituents of essential oils *Dipartimento di Scienze del Farmaco, Università degli Studi di Sassari, Sassari, Italy*)
Manool	Have proved as platelet aggregation inhibitors and effective Antimicrobial with: Staphylococcus Aureus, Candida Albicans and Proteus mirabilis (Synthesis of manool-related labdane diterpenes as platelet aggregation inhibitors Shionogi Research Laboratories, Shionogi & Co., Ltd., Osaka, Japan), (Transformations of manool. tri- and tetracyclic norditerpenoids with in vitro activity against Plasmodium falciparum *Department of Chemistry, Rhodes University, Grahamstown, South Africa*).
Caryophyllene oxide	Caryophyllene oxide, an oxygenated terpenoid, well known as preservative in food, drugs and cosmetics, Found to be effective as an Antifungal against dermatophytes (Use of caryophyllene oxide as an antifungal agent in an in vitro experimental model of onychomycosis Authors: *Yang, Depo 1; Michel, Laura 1; Chaumont, Jean-Pierre2; Millet-Clerc, Joëlle 1)*

Substance	Benefits
Sterols	Plant sterols reduce the uptake of cholesterol into the body. The cholesterol that is not absorbed or taken up is removed from the body. As a result blood total and bad (LDL) cholesterol decrease, while good (HDL) cholesterol is not affected. (Extensive research shows that functional foods fortified with plant sterols and plant sterol supplements, can effectively reduce cholesterol up to 15% (*Katan MB et al. 2003, Mayo Clin Proc. 2003 Aug;78(8):965-78. Review*)
Sterols present in Salvia Sclarea seed oil	• Campestanol • Stigmasterol D-7-Campesterol • D-5, 23-Stigmastadienol • Chlerosterol • B-Sitosterol • Sitostanol • D-5-Avenasterol • D-5,24-Stigmastadienol • D-7-Stigmastenol • D-7-Avenasterol
Tocopherols (Vitamin E)	• Vitamin E may help prevent or delay coronary heart disease by limiting the oxidation of LDL-cholesterol. • Vitamin E also may help prevent the formation of blood clots, which could lead to a heart attack. • Observational studies have associated lower rates of heart disease with higher vitamin E intake
Tocopherols in Salvia Sclarea seed oil	Tocopherols occur in Salvia Sclarea are Alpha, Beta, Gamma and Delta forms, determined by the number of methyl groups on the chromanol ring all of them
Substance	Benefits
Coenzyme Q10	Coenzyme Q10, also referred to as Co Q10 is a vitamin-like compound which is present in all cells. Q10 has several different actions in the body. Its most notable effects are: • Antioxidant - it scavenges free radicals • Improves the efficiency of cellular energy production in the • mitochondria of the cell • Regulates genes concerned with energy production • Stabilizes membranes

Salvia Sclarea seed oil affect on lipid profile

Table Number 3
Results after the intake of Salvia Sclarea capsules for 2 months

Test preformed	Intake of 0 sage capsules per day	Intake of 4 sage capsules per day
Cholesterol	224	181
Triglycerides	228	126
Cholesterol HDL	47.1	57
Cholesterol LDL	132	98.8

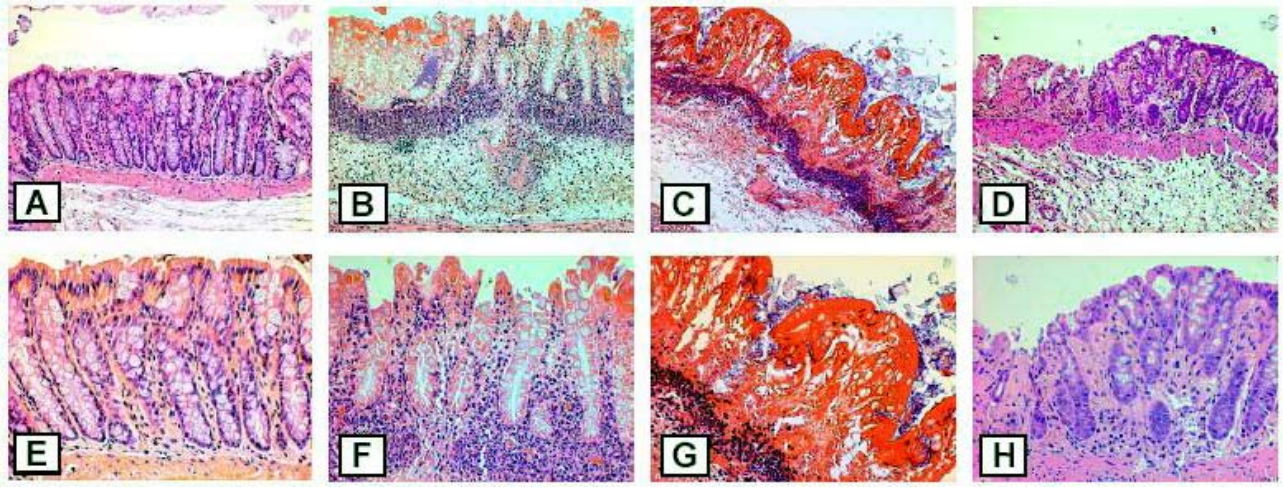
Pre clinical experiments done with Salvia Sclarea

Salvia Sclarea effect on inflammation

Two pre clinical experiments on Salvia Sclarea health benefits were conducted by the Hebrew University of Jerusalem. The experiments focused on areas were Salvia Sclarea's health benefits were examined comparing to other Omega 3 oils (fish oil, pure ALA oil, flax seed oil etc) with the progress of the experiments the researches found that Salvia Sclarea oil has it's unique health properties which are not 100% relaying on the high concentration of Omega 3 in the oil but on the natural health promoting ingredients in the oil per se.
The pre clinical experiments were focused on the following research areas:

An in vivo study was designed to examine the effect of Salvia Sclarea on the course of inflammation using two models of colitis. The purpose of the experiment is to study and compare the affects of two different sources (Fish Oil and Sage oil) of Polly unsaturated fatty acids Omega 3 on 2 in-vivo models of colitis (TBNS, DSS) From the research finding we can determine that the intake of sage oil reduces the level of inflammation and reduces the damage for the colon tissue in rats, infected with Colitis

Histology results



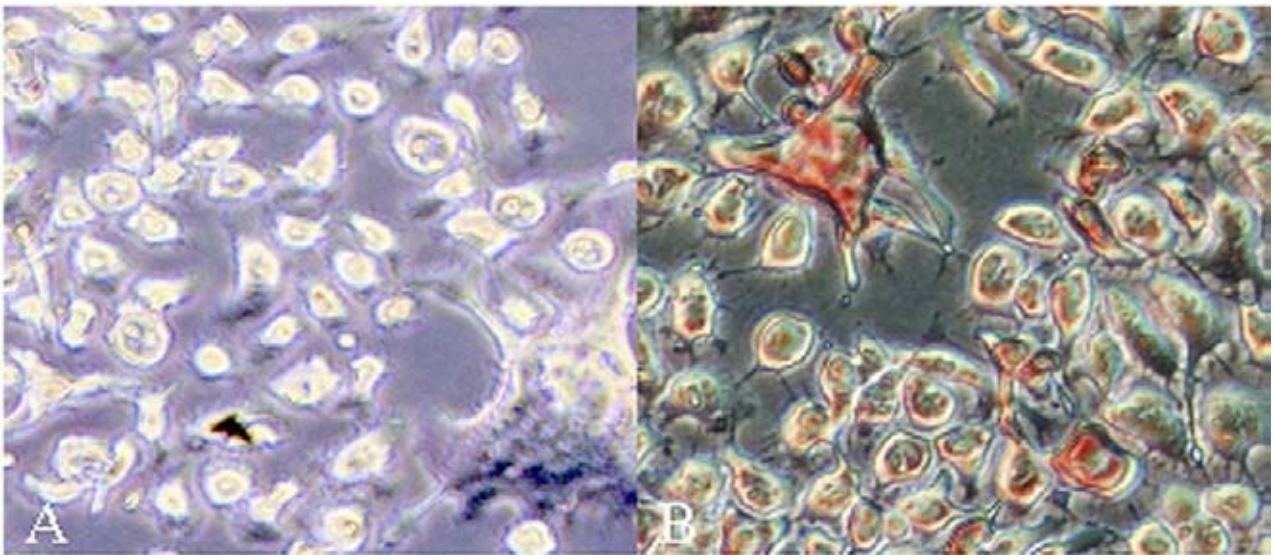
Level of Necrosis in mucosa 0 – level of inflammation in colon – SO+A.0–A,E
Level of Necrosis in mucosa 3 – level of inflammation in colon – CO.3– B,F
Level of Necrosis in mucosa 4 – level of inflammation in colon – FO.3–C,G
Level of Necrosis in mucosa 2 – level of inflammation in colon – SO.2–D,H

Salvia Sclarea effect on Hair & skin

The Effects of Salvia Sclarea on skin cells, anti-aging, sebum production and hair follicles where tested at the, Dept. of Biological Chemistry, Hebrew University of Jerusalem, Israel, Myers Laboratory of Skin Biochemistry and Biology, the following attributes were related to Salvia Sclarea:

- Increases keratinocyte viability
- Prevents UV damage when applied before and after UV irradiation
- Decreases sebum production
- Anti-oxidant activity

Uptake by skin cells



Before Salvia Sclarea oil addition

After Salvia Sclarea oil addition

Flaxseeds and Flax seeds oil a source for Omega 3

Flaxseed and Flax seed oil, today Flaxseed (lean seed) is one of the known vegetable sources for ALA Omega 3 to the functional food industry.
Despite the fact that there are many known health hazard related to Flax seeds and Flax seeds oil, Flax seed products are still sold to the functional food industry (especially in the US), 90% of the use of Flax seeds and oil products is in the ground seeds form, or plain seeds spread on the final products.
As Omega 3 functional food products are evolving to become a main stream product line, enterprise food companies who will check the option of using Flax seeds products will not overlook the potential health hazard related to Flax seeds products and will actively look for another source of Omega 3 like Salvia Sclarea which introduce health hazard "risk free" solution.

Historic use of Flax seeds and Flax seeds oil

Flax seed is one of the known plants to humans, trough human history flax seed was never used as a source for food, on the contrary flax seed and flax seed oil was mainly used in for industrial uses including:

- Preparation of Varnish
- Preparation of paint
- Preparation of linoleum
- Preparation of soap

The only medical use (last millennium) known for Flax seed was:

- Is used as a laxative (linseed oil)
- Is used as an expectorant and demulcent

Flax contain potent allergens

There is much evidence on the allergic properties of Flax seeds and Flax seeds oil:

- Five different allergens have been detected in flax seed and flax oil (Alonso L, Marcos ML, Blanco JG, Navarro JA, Juste S, del Mar Garces M, Perez R, Carretero PJ. Anaphylaxis caused by linseed (flaxseed) intake. J Allergy Clin Immunol 1996;98(2):469-70)

- In another study, allergens with a higher molecular weight intensely bound with IgE, were found, (Lezaun A, Fraj J, Colas C, Duce F, Dominguez MA,
- Cuevas M, Eiras P. Anaphylaxis from linseed. Allergy 1998;53(1):105-6)

- Anaphylaxis reaction to Linseed products was reported in 3 cases; (Leon F, Rodriguez M, Cuevas M. The major allergen of linseed. Allergy. 2002;57(10):968) (Alonso L, Marcos ML, Blanco JG, Navarro JA, Juste S, del Mar Garces M, Perez R, Carretero PJ. Anaphylaxis caused by linseed (flaxseed) intake. J Allergy Clin Immunol 1996;98(2):469-70) Stricker WE, Anorve-Lopez E, Reed CE. Food skin testing in patients with idiopathic anaphylaxis. J Allergy Clin Immunol 1986;77(3):516-9)

- Allergic symptoms may increase because of the increased use of Linseed in bread and laxatives, and in a range of products from health food shops (Leon F, Rodriguez M, Cuevas M. Anaphylaxis to Linum. Allergol Immunopathol (Madr)

- The flaxseed components 30 g of seed or 6 g of ALA in the oil (equal to 12 capsules per day) were deliver over a 3 month test period in healthy male and female subjects.

- **There were no changes in plasma cholesterol or triglycerides or in platelet aggregation at any time point in any of the groups**. (Bioavailability of alpha-linolenic acid in subjects after ingestion of three different forms of flaxseed 2008 Apr Cell Biology Laboratory, St Boniface Hospital Research Centre, Winnipeg, Manitoba, R2H 2A6, Canada)

Sensory panel done on Flax seed and Salvia Sclarea oil

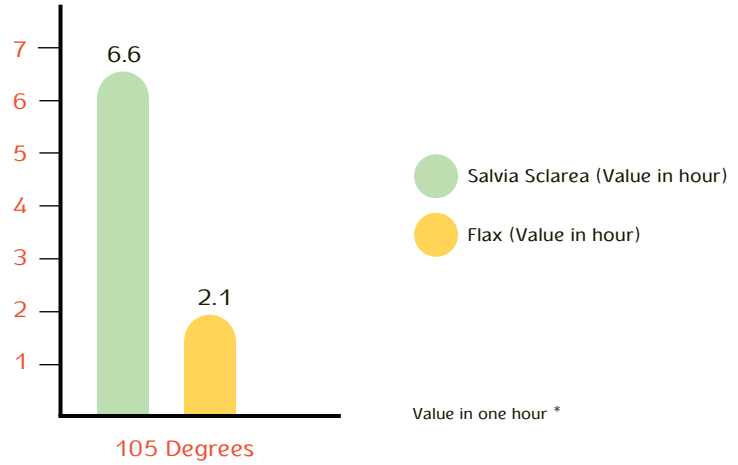
In addition to the above known hazards related to Flax seeds and Flax seeds oil, in 2006 the company conducted an independent sensory panel between Salvia Sclarea oil and Flax seed oil focusing only on the sensory properties of both oils: The sensory research of the oils was performed in 12/2006 on two Omega 3 source oils – "Salvia Sclarea" Sage oil & flaxseed oil. It was executed at a central location in Israel on a population of 240 adult respondents selected randomly. The respondents were interviewed face to face and asked to sample either the "Salvia Sclarea" oil or the flaxseed oil. Both oils were extracted at the same facility by a "cold press" process at proximate dates. Afterwards they were asked to evaluate the sensory characteristics of the oils using the Blind Test method.

Summary "Salvia Sclarea" oil was found to be superior to flaxseed oil in all sensorial parameters that were evaluated and to have a similar and in some cases an even better sensorial profile than many popular edible oils.

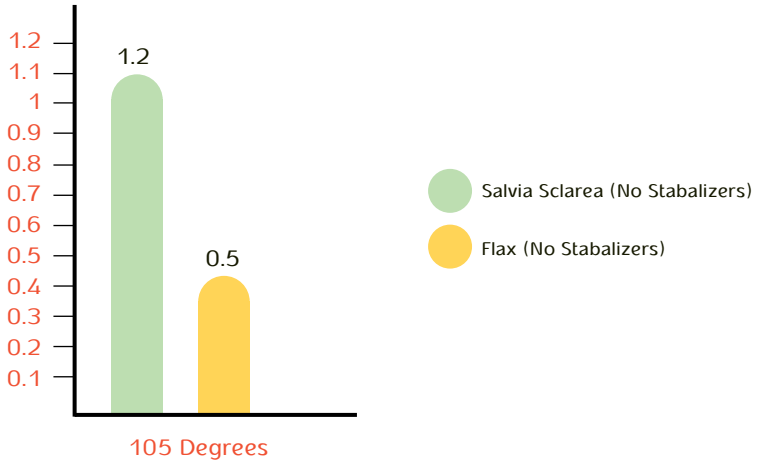
Stability of Flax seed oil comparing to Salvia Sclarea oil

Stability lab tests were preformed on Flax seed oil comparing its rancidity reaction to Salvia Sclarea seed oil, the rancidity testes were preformed on different batches compositions using different temperatures.

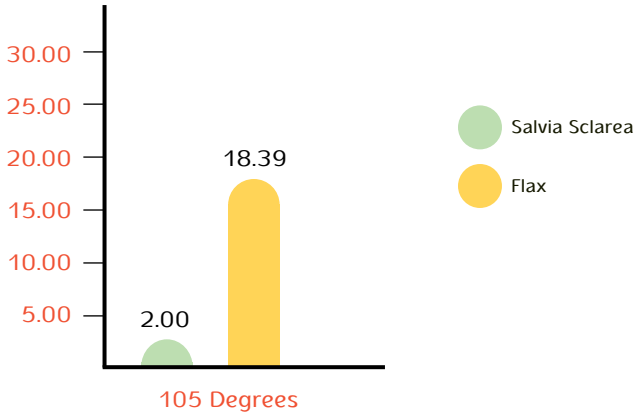
Rancidity test Salvia Sclarea vs. Flax (plus the addition of stabilizers)



Rancidity test Salvia Sclarea vs. Flax (Without the addition of stabilizers)



Peroxide value in Salvia Sclarea Oil vs. Flax oil (after 3 months)



Fish oil vs. Salvia Sclarea oil – detailed analysis

Different production process – cold pressed natural oil (sage oil) versus refined oil (fish oil).
Refined oil undergoes a number of processes in order to achieve uniformity in the texture, color, and purity of the oil, and in order to lengthen its shelf life as much as possible.
Refined oil undergoes a process in whic h the oil is extracted from its source, usually with the help of an oil-based solvent. At the cleaning stage, phospholipids and oil compounds are removed, including lecithin. Various minerals, such as iron and magnesium, are also removed. After the cleaning stage, the refining stage begins, and the oil is mixed with sodium hydroxide to remove additional materials liable to shorten its shelf life. Following this stage, the whitening stage begins, and beta carotene is removed by heating the oil to a temperature of 110 degrees. The next stage is reducing the odor, during which aromatic oils and surviving free fatty acid remnants are removed. This stage continues for 30-60 minutes at temperatures of 240-270 degrees Celsius. At the end of the refining process, the oil is left odorless and tasteless, with none of the natural qualities of the materials that were in the oil, such as vitamins, minerals, and other materials. Not only are all the good supplements removed from the oil – the oil is also damaged by the high temperatures it underwent in the course of its refining. The fish oil also undergoes refining processes.
Sage oil produced in a cold pressing process is 100% natural.

Fish oil altered to an ester structure

Fish oil is produced from deep-sea fish liver, and its Omega 3 content varies according to the kind of fish. Some manufacturers sell highly concentrated fish oil capsules, but it is important to note that this oil is synthetic, and has undergone chemical softening processes. In order to concentrate the oil, its chemical structure is altered to an ester structure. Some assert that the usefulness of Omega 3 in this structure is questionable (Omega 3 does not exist in nature in this chemical structure). Furthermore, it become oxidized easily, and includes Trans fats.

Conversion of ALA to EPA and DHA the Omega 3 metabolic pathway

Sage oil includes a 50% concentration of Omega 3 alpha-linolenic acid (ALA) - a fatty acid that is the source of all the other Omega3-type fatty acids, making it essential.
The body must consume Omega 3, which it is unable to produce; it must obtain Omega 3 from food. The human body breaks down ALA into other long Omega 3-type fatty acids, including Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA).

A new scientific study, known as the firefighters study, proved that ALA is converted into long acids in the same concentrations as fish oil. The purpose of the study was to clarify whether this assumption was really true. A clinical trial was conducted on 62 healthy firefighters. It is known that this profession involves risk factors for heart disease. The firefighters were divided into six groups, which received supplements of either 1.2, 2.4, or 3.6 grams daily of ALA-rich oil, 0.6 or 1.2 grams daily of fish oils, or 1.0 grams daily of sunflower oil for 12 weeks.

Blood samples were taken every two weeks for analysis of acids in red blood cells. As expected, the findings showed that giving fish oil increased the DHA level. However, it was also found that daily consumption of 2.4 grams and 3.6 grams of ALA raised the DHA level, thereby also increasing the concentration of ALA and EPA. The researchers concluded that consuming an ALA-rich nutritional supplement in the concentrations examined for 12 weeks was sufficient to increase the DHA levels, and of course the EPA levels, to the desirable values. This clinical study in effect proved that the doubts as to whether alpha-linolenic acid could contribute to proper creation of DHA were unfounded. "Flaxseed Oil and Fish-Oil Capsule Consumption Alters Human Composition: A Red Blood Cell n-3 Fatty Acid Trial Comparing 2 Sources of Multiple-Dosing n-3 Fatty Acid," American Journal of Clinical Nutrition, 2008, 88:801.

In addition, the US Food and Drug Administration (FDA) recommends against daily consumption of more than 3 grams of EPA and DHA *the Food and Drug Administrations report 2 1 CFR Part 184 (Docket)

Presence of Toxins and Heavy Metals

Fish oil includes toxins, such as heavy metals (mercury, for example), dioxins, and toxins of the PCB family. Many companies state that their fish oil capsules include no toxins or heavy metals, according to the required standard. The FDA restricts consumption of fish by children, pregnant women, and breast-feeding women because of the presence of toxins and heavy metals in fish (Center for Food Safety and Applied Nutrition, "Mercury Levels in Seafood Species," FDA, www.cfsan.fda.gov/~frf/sea-mehg.html, May 11, 2001).

Table number 4
Mercury Content of Five Preparations of Fish Oil

Fish Oil Brand Name	Mercury Level, μg/L
CVS	10
Kirkland	<6
Nordic Ultimate	<6
Omega Brite	12
Sundown	<6

Reprints: *Kent B. Lewandrowski*
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02114

Problems Linked to Digestion and Taking Capsule Fish Oil

Fish oil generates a fishy aftertaste after swallowing the capsules, and bad breath.
Fish oil causes problems in the digestive system, such as incomplete digestion of food, heartburn, abdominal pains, and gas.
Fish oil is liable to cause oily stool, and even diarrhea.
Fish oil detracts from the absorption of vitamins that are soluble in oil.

Damage to the Activity of White Blood Cells and Weakening of the Immune System

ALA Omega 3 does not affect the differentiation of T white blood cells, while cases are documented in which fish oil, and especially EPA, does have a harmful effect. (*"Dietary supplementation with gamma linolenic acid or fish oil decreases T lymphocyte proliferation in healthy older humans," Department of Biochemistry, University of Oxford, UK).*

Fish oil weakens the immune system, among other things by increasing self-destruction of white blood cells. Taking fish oil supplements for 12 weeks caused a marked decrease in creation of Interleukin 2 (IL-2), a chemical produced by T cells that is involved in suppressing tumors. In the same study, ALA-rich oil supplements were also taken, but did not cause the same response.

Fish oil is rich in vitamins A and D, and taking it for long periods is liable to cause toxicity

Fish oil produced from fish liver includes very high concentrations of vitamins A and D. High consumption of these vitamins is liable to cause toxicity. These high concentrations are absent from sage oil.

Fish oil increases bad cholesterol values

Fish oil has been demonstrated to lower triglyceride value but also to increase bad cholesterol (LDL) values. It is therefore recommended to consume fish oil together with drugs from the statin family in order to lower the cholesterol levels that fish oil raises. A more extreme manifestation of this phenomenon has been observed among diabetes patients (*"Fish Oil in People with Type 2 Diabetes Mellitus," Department of Primary Health Care, Institute of Health Sciences, University of Oxford*). It is recommended that patients taking Omega 3 from fish oil regularly monitor their cholesterol values because of the rise in LDL values, and because of the concentration of cholesterol and Trans fats in fish oil. Not only is sage oil free from this phenomenon; sage oil has been documented as reducing values of bad cholesterol and triglycerides and increasing values of good cholesterol.

Fish Oil Oxidizes Quickly

In a rancidity test performed at Miluda Labs in Israel, different oil mixtures were tested (rancidity test at 105 degrees Celsius). Test results showed that fish oil stability is poor, and the oil oxidizes almost immediately, compared to sage oil.

Table number 5 - Fish oil and Sage oil Rancidity tests (105 Celsius degrees)

Serial Number	Oil Type
011	Sage oil + Fish oil
012	Sage oil + Fish oil
013	Fish oil
014	Sage oil
C18:1n9	Omega 9
C18:2n6	Omega 6
C18:3n3	Omega 3

MILOUDA
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דואר נע אשרת 25201
טלפון 04-9853292, פקסימילה 04-9853291

CHEMICAL ANALYSIS

Laboratory Number 11851

Test Matter: Different Oils

Parameter Tested	011	012	013	014
Oil Stability 105°C	< 10 min	< 10 min	< 10 min	60 min
Fatty acid profile	See attached Table			

Authorized Signature

1/3

Remarks:

1. The laboratory operates in accordance with recognized standards of the International ISO/IEC 17025 in all tests where recognition has been granted.
2. The microbiological tests are recognized and published by the Israel Board of health.
3. The results relate to the sample tested only.
4. Laboratory results are to be used in their entirety and no part may be quoted or copied to other documents.
5. Sampling was provided by and is the sole responsibility of the customer.
6. The Israel Laboratory Accreditation Authority is not responsible for the test results.

Comparison table
Salvia Sclarea vs. other oils

Table number 4
comparison between Salvia Sclarea oil, Fish Oil, Flax seed oil

Benefit	Salvia Sclarea Oil	Fish Oil	Flax Seeds oil
Excellent taste and odor	Yes	Fishy taste	Bitter after taste
Allergens free	Yes	Sea products are Known Allergen	Flax is a known Allergen
No toxic matters	No presence of toxic matters	Potential exposure to heavy metals due to ocean pollutions	Contain toxic Cynic glycoside in the seeds
upper limit" due to a" risk of internal bleeding	No upper limit	Recommended dosage is up to 3 Grams a day Or two portions of fish a week	Unknown
High amount of Omega 3	Up to 55% ALA in the Oil	Between 20%-30% of EPA and DHA	Up to 55% ALA in Flax
Stability	Excellent stability	Non stable source - oxidize quickly	Non stable source - oxidize quickly
Can be sold to the wide population including vegans and vegetarians Nursing women and children	Yes	Not Suitable for vegans and vegetarians and for some Kosher requirements	There are warning on the consumption of Flax for Nursing women and children - due to the high amount of phytoestrogens in Flax products
Essential fatty Acid	Yes	Only ALA is considered an essential fatty acid	Yes

List of scientific Articles

DHA formation from ALA in mammals

ALA is metabolized in mammals to EPA and EPA is being further metabolized to DHA.
Studies carried out on the rates of these conversions report 10-15% conversion of ALA to EPA and 1-5% conversion of EPA to DHA.
Accordingly ALA supplementation was criticized by some for the low formation of DHA being insufficient to meet the requirement of the main target organ, the brain.
However the main issue in the evaluation of low formation rate of DHA versus target organ function is the half-life of DHA in brain tissue.
In a study that measured the half-life of DHA in the brain of rat pups it has been shown that the half-life is prolonged by 15 weeks when the pups were deprived of n-3 polyunsaturated fatty acids.
The authors conclude that a mechanism must exist in the adult rat brain to minimize DHA metabolic loss (J.Neurobiochm.91:1125, 2004)
In a very recent publication (J.Lipid Res. July 1, 2009) the incorporation of circulating DHA into human brain was evaluated using positron emission tomography.

Tow very important findings came out of this study:

- The half-life of DHA in the human brain is two and a half years!
- The daily incorporation of DHA into the human brain is 3.8 mg!
  Thus, with two and a half years of DHA half-life in the human brain the reported small formation of DHA when supplementing with ALA is meaningless!
  Moreover the unofficial RDA of ALA is 2gram. Accordingly if only 1% DHA is formed this means formation of 20mg DHA that easily meets the daily incorporation of 3.8mg into the human brain!

In summary when considering the half-life of DHA in human brain ALA supplementation meets all requirements for optimal function of the brain that are DHA-dependent.

Omega-3 deficiency causes 96,000 US deaths per year, say researchers.
Omega-3 deficiency is the sixth biggest killer of Americans and more deadly than excess Trans fat intake, according to a new study.
The Harvard University researchers looked at 12 dietary, lifestyle and metabolic risk factors such as tobacco smoking and high blood pressure and used a mathematical model to determine how many fatalities could have been prevented if better practices had been observed.

The study, jointly funded by the Centers for Disease Control and Prevention (CDC) through the Association of Schools of Public Health, drew on 2005 data from the US National Health Center for Health Statistics. They determined that there were 72,000-96,000 preventable deaths each year due to omega-3 deficiency, compared to 63,000-97,000 for high trans fat intake.

Power of diet

"This is a very interesting analysis," said Andrew Shao, PhD, vice president of scientific and regulatory affairs at the Council for Responsible Nutrition (CRN).

"I think this analysis reinforces the long-held notion that the diet has a tremendously powerful impact on health and longevity and that the consumption of omega-3's (along with fruits and veggies) by Americans is far from adequate."

But he questioned the precision of the study findings due to complicating factors that had not been addressed.
"It is hard to say how definitive their findings are as far as the numbers are concerned, since chronic diseases and associated deaths are multifactorial," he told NutraIngredients-USA.com this morning.

"As far as diet goes, is it the lack of fruits and veggies or the excess animal and processed foods that is the culprit? It is hard to say."
He added that the study did not consider other key nutrients such as vitamin D.

Shao's counterpart at the Natural Products Association, Dan Fabricant, PhD, emphasized the potential public health care savings that could be derived from better nutrition, especially in tight economic times, but called for further study.
"We need more clinical research that nails down why omega-3 is so effective," Fabricant said. *"This seems to be the last missing piece for omega-3s in terms of clarifying the picture for governmental/regulatory bodies of its efficacy."*

Shao added the study highlighted the importance of establishing a dietary reference intake (DRI) for omega-3 forms, EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid).

"Once these requirements are established, the government can undertake initiatives to improved Americans' intake of these critical nutrients," he observed. "But until that happens, Americans are likely to continue to fall short in their omega-3 intake, and we see a glimpse of what the consequence can be from this study."

Shocking

The study will do no harm to the omega-3 industry, with the world's leading supplier, Ocean Nutrition Canada, calling the results "shocking".

"...this new study validates that Omega-3 EPA/DHA is more than just part of a healthy diet...it's a matter of life and death," said Ocean Nutrition Canada's vice president of marketing and communications, Lori Covert.

"We know that daily doses of Omega-3 EPA/DHA can help with many conditions, such as cardiovascular disease, and we're committed to increasing consumer awareness about the drastic Omega-3 EPA/DHA deficiency in the Western diet," Covert said.

Tobacco smoking ranked as the highest risk factor with 436,000 to 500,000 attributed preventable deaths, followed by high blood pressure (372,000 to 414,000), obesity (188,000 to 237,000), physical inactivity (164,000 to 222,000), high blood glucose (163,000 to 217,000), high LDL cholesterol (94,000 to 124,000) and high salt intake (97,000 to 107,000).

The other risk factors were alcohol use; low polyunsaturated fatty acids; low fruits and vegetables intake and alcohol use.

Source: Public Library of Science Medicine Journal
Vol. 6, April, 2009
'The Preventable Causes of Death in the United States: Comparative Risk Assessment of Dietary, Lifestyle, and Metabolic Risk Factors'
http://www.nutraingredients-usa.com/Research/Omega-3-deficiency-causes-96-000-US-deaths-per-year-say-researchers

Linolenic acid in health and disease

William E Connor

There are 2 series of polyunsaturated fatty acids that are deemed essential: the n-6 and n-3 series. Although plants can synthesize both the basic n-6 and n-3 structures, animals lack this capacity and must obtain them from dietary sources. Deficiency of the n-6 fatty acid linoleic acid leads to poor growth, fatty liver, skin lesions, and reproductive failure. In contrast, the symptoms of n-3 -linolenic acid deficiency are more obscure and have only been well demarcated in experimental animals and human infants. n-3 Fatty acid deficiency causes reduced vision, abnormal electroretinogram results, and, perhaps, impaired cognition and behavior. The metabolism of -linolenic acid in humans has been well characterized.

After -linolenic acid is ingested, the body converts it to very-long-chain polyunsaturated fatty acids: readily to eicosapentaenoic acid (20:5n-3) and more slowly to docosahexaenoic acid (22:6n-3). A major consequence of -linolenic acid deficiency is that its chief synthetic end product, docosahexaenoic acid, is not adequately produced . Because docosahexaenoic acid is a major component of the phospholipid membranes of the brain and retina, its deficiency in these organs then leads to abnormal function . n-3 Fatty acid deficiency is accentuated when there is simultaneously a high content of linoleic acid in the diet, which tends to inhibit the synthesis of docosahexaenoic acid from linolenic acid. Thus, diets rich in corn, safflower, sunflower, and peanut oils, all of which are high in linoleic acid and low in -linolenic acid, can lead to n-3 fatty acid deficiency Thus; a high ratio of n-6 to n-3 fatty acids in the diet accentuates n-3 fatty acid deficiency.

http://www.ajcn.org/cgi/content/full/69/5/827

Alpha-Linolenic acid and long-chain omega-3 fatty acid

supplementation in three patients with omega-3 fatty acid deficiency: effect on lymphocyte function, plasma and red cell lipids, and prostanoid formation

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Trondheim Regional Hospital, Norway.

alpha-Linolenic acid deficiency is described in three patients. Observed clinical symptoms were hemorrhagic dermatitis, hemorrhagic folliculitis, skin atrophy, and scaly dermatitis. Supplementation with ethyl alpha-linolenate followed by a purified fish oil (EPA-oil) began to normalize symptoms within 10 d.

The mitogenic response in isolated lymphocytes was reduced whereas the number of T lymphocytes increased significantly. Serum thromboxanes, urinary excretion of 2,3-dinor-6- keto-prostaglandin F1 alpha (PGI2-M), and bleeding time were unaffected. The results indicate that omega-3 fatty acids are essential for normal accumulation of erythrocyte omega-6 acids. The dietary intake of long-chain omega-3 acids required to obtain midnormal concentrations of omega-3 acids in plasma and erythrocyte lipids was estimated to be 350-400 mg/d (0.4% of calories), whereas the corresponding mean intake of alpha-linolenic acid was 990 mg/d (1.0% of calories). It is suggested that essential fatty acid requirement should be stated as grams or milligrams per day, similarly to other essential nutrients.

http://www.ajcn.org/cgi/content/abstract/49/2/290

The Firefighters study

Flaxseed oil and fish-oil capsule consumption alters human red blood cell n-3 fatty acid composition: a multiple-dosing trial comparing 2 sources of n-3 fatty acid

Gwendolyn Barceló-Coblijn, Eric J Murphy, Rgia Othman, Mohammed H Moghadasian, Tarek Kashour and James K Friel -2008

From the Departments of Pharmacology, Physiology, and Therapeutics (GB-C and EM) and Chemistry (EJM), University of North Dakota, Grand Forks, ND, and the Departments of Human Nutritional Sciences (MHM, RO, and JKF) and of Medicine and Biochemistry and Medical Genetics (TK), University of Manitoba, Winnipeg, Canada

Background An increase in plasma n-3 fatty acid content, particularly eicosapentaenoic acid (20:5n-3; EPA) and docosahexaenoic acid (22:6n-3; DHA), is observed after consumption of fish oil-enriched supplements. Because -linolenic acid (18:3n-3; ALA) is the direct precursor of EPA and DHA, ALA-enriched supplements such as flax may have a similar effect, although this hypothesis has been challenged because of reported low conversion of ALA into DHA.

Objective To address this question, we designed a clinical trial in which flax oil, fish-oil, and sunflower oil (placebo group) capsules were given to firefighters (n = 62), a group traditionally exposed to cardiovascular disease risk factors.

Design Firefighters were randomly divided into 6 experimental groups receiving 1.2, 2.4, or 3.6 g flax oil/d; 0.6 or 1.2 g fish oil/d; or 1 g sunflower oil/d for 12 wk. Blood was drawn every 2 wk, and the total phospholipid fatty acid composition of red blood cells was determined.

Results As expected, fish oil produced a rapid increase in erythrocyte DHA and total n-3 fatty acids. The consumption of either 2.4 or 3.6 g flax oil/d (in capsules) was sufficient to significantly increase erythrocyte total phospholipid ALA, EPA, and docosapentaenoic acid (22:5n-3) fatty acid content. There were no differences among groups in plasma inflammatory markers or lipid profile.

Conclusions The consumption of ALA-enriched supplements for 12 wk was sufficient to elevate erythrocyte EPA and docosapentaeoic acid content, which shows the effectiveness of ALA conversion and accretion into erythrocytes. The amounts of ALA required to obtain these effects are amounts that are easily achieved in the general population by dietary modification.

http://www.ajcn.org/cgi/content/abstract/88/3/801

Dietary alpha-linolenic acid decreases c-reactive protein, serum amyloid a and interleukin-6 in dyslipidaemic patients

Rallidis, LS et al Atherosclerosis, 2003

Background Inflammation plays an important role in the pathogenesis of coronary artery disease. We examined whether dietary supplementation with alpha-linolenic acid (ALA, 18:3n-3) affects the levels of inflammatory markers in dyslipidaemic patients. METHODS: We recruited 76 male dyslipidaemic patients (mean age=51+/-8 years) following a typical Greek diet. They were randomly assigned either to 15 ml of linseed oil (rich in ALA) per day (n=50) or to 15 ml of safflower oil (rich in linoleic acid (LA, 18:2n-6)) per day (n=26). The ratio of n-6:n-3 in linseed oil supplemented group was 1.3:1 and in safflower oil supplemented group 13.2:1.

Dietary intervention lasted for 3 months. Blood lipids and C-reactive protein (CRP), serum amyloid A (SAA), and interleukin-6 (IL-6) levels were determined prior and after intervention. CRP and SAA were measured by nephelometry and IL-6 by immunoassay. RESULTS: Dietary supplementation with ALA decreased significantly CRP, SAA and IL-6 levels. The median decrease of CRP was 38% (1.24 vs. 0.93 mg/l, P=0.0008), of SAA 23.1% (3.24 vs. 2.39 mg/l, P=0.0001) and of IL-6 10.5% (2.18 vs. 1.7 pg/ml, P=0.01). The decrease of inflammatory markers was independent of lipid changes. Dietary supplementation with LA did not affect significantly CRP, SAA and IL-6 concentrations but decreased cholesterol levels.

Conclusions Dietary supplementation with ALA for 3 months decreases significantly CRP, SAA and IL-6 levels in dyslipidaemic patients. This anti-inflammatory effect may provide a possible additional mechanism for the beneficial effect of plant n-3 polyunsaturated fatty acids in primary and secondary prevention of coronary artery disease

http://www.ncbi.nlm.nih.gov/pubmed/12818406

Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States

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Objective To examine the association between fat intake and the incidence of coronary heart disease in men of middle age and older.

Design Cohort questionnaire study of men followed up for six years from 1986.

Setting The health professionals follow up study in the United States.

Subjects 43 757 health professionals aged 40 to 75 years free of diagnosed cardiovascular disease or diabetes in 1986.

Main Outcome Measure Incidence of acute myocardial infarction or coronary death.

Results During follow up 734 coronary events were documented, including 505 non-fatal myocardial infarctions and 229 deaths. After age and several coronary risk factors were controlled for significant positive associations were observed between intake of saturated fat and risk of coronary disease. For men in the top versus the lowest fifth of saturated fat intake (median = 14.8% v 5.7% of energy) the multivariate relative risk for myocardial infarction was 1.22 (95% confidence interval 0.96 to 1.56) and for fatal coronary heart disease was 2.21 (1.38 to 3.54). After adjustment for intake of fibre the risks were 0.96 (0.73 to 1.27) and 1.72 (1.01 to 2.90), respectively. Positive associations between intake of cholesterol and risk of coronary heart disease were similarly attenuated after adjustment for fibre intake. Intake of linolenic acid was inversely associated with risk of myocardial infarction; this association became significant only after adjustment for non-dietary risk factors and was strengthened after adjustment for total fat intake (relative risk 0.41 for a 1% increase in energy, P for trend < 0.01).

Conclusions These data do not support the strong association between intake of saturated fat and risk of coronary heart disease suggested by international comparisons. They are compatible, however, with the hypotheses that saturated fat and cholesterol intakes affect the risk of coronary heart disease as predicted by their effects on blood cholesterol concentration. They also support a specific preventive effect of linolenic acid intake

http://www.ncbi.nlm.nih.gov/pubmed/8688759

Dietary Fat Intake and the Risk of Coronary Heart Disease in Women

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Department of Nutrition, Harvard School of Public Health, Boston, USA.

Abstract Background The relation between dietary intake of specific types of fat, particularly trans unsaturated fat, and the risk of coronary disease remains unclear. We therefore studied this relation in women enrolled in the Nurses' Health Study.

Methods We prospectively studied 80,082 women who were 34 to 59 years of age and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabetes in 1980. Information on diet was obtained at base line and updated during follow-up by means of validated questionnaires. During 14 years of follow-up, we documented 939 cases of nonfatal myocardial infarction or death from coronary heart disease. Multivariate analyses included age, smoking status, total energy intake, dietary cholesterol intake, percentages of energy obtained from protein and specific types of fat, and other risk factors.

Results Each increase of 5 percent of energy intake from saturated fat, as compared with equivalent energy intake from carbohydrates, was associated with a 17 percent increase in the risk of coronary disease (relative risk, 1.17; 95 percent confidence interval, 0.97 to 1.41; P = 0.10). As compared with equivalent energy from carbohydrates, the relative risk for a 2 percent increment in energy intake from trans unsaturated fat was 1.93 (95 percent confidence interval, 1.43 to 2.61; P<0.001); that for a 5 percent increment in energy from monounsaturated fat was 0.81 (95 percent confidence interval, 0.65 to 1.00; P = 0.05); and that for a 5 percent increment in energy from polyunsaturated fat was 0.62 (95 percent confidence interval, 0.46 to 0.85; P = 0.003).

Total fat intake was not significantly related to the risk of coronary disease (for a 5 percent increase in energy from fat, the relative risk was 1.02; 95 percent confidence interval, 0.97 to 1.07; P = 0.55). We estimated that the replacement of 5 percent of energy from saturated fat with energy from unsaturated fats would reduce risk by 42 percent (95 percent confidence interval, 23 to 56; P<0.001) and that the replacement of 2 percent of energy from trans fat with energy from unhydrogenated, unsaturated fats would reduce risk by 53 percent (95 percent confidence interval, 34 to 67; P<0.001).

Conclusions Our findings suggest that replacing saturated and trans unsaturated fats with unhydrogenated monounsaturated and polyunsaturated fats is more effective in preventing coronary heart disease in women than reducing overall fat intake.

http://www.ncbi.nlm.nih.gov/pubmed/9366580

Dietary linolenic acid and carotid atherosclerosis: the National Heart, Lung, and Blood Institute Family Heart Study

Luc Djoussé, Aaron R Folsom, Michael A Province, Steven C Hunt and R Curtis Ellison

From the Section of Preventive Medicine & Epidemiology, Evans Department of Medicine, Boston University School of Medicine (LD and RCE); the Division of Epidemiology, University of Minnesota, Minneapolis (ARF); the Division of Biostatistics, Washington University, St Louis (MAP); and the Department of Cardiovascular Genetics, University of Utah, Salt Lake City (SCH).

Background Dietary intake of linolenic acid is associated with a lower risk of cardiovascular disease mortality. However, it is unknown whether linolenic acid is associated with a lower risk of carotid atherosclerosis.

Objective The objective was to examine the association between dietary linolenic acid and the presence of atherosclerotic plaques and the intima-media thickness of the carotid arteries.

Design In a cross-sectional design, we studied 1575 white participants of the National Heart, Lung, and Blood Institute Family Heart Study who were free of coronary artery disease, stroke, hypertension, and diabetes mellitus. High-resolution ultrasound was used to assess intima-media thickness and the presence of carotid plaques beginning 1 cm below to 1 cm above the carotid bulb. We used logistic regression and a generalized linear model for the analyses.

Results From the lowest to the highest quartile of linolenic acid intake, the prevalence odds ratio (95% CI) of a carotid plaque was 1.0 (reference), 0.47 (0.30, 0.73), 0.38 (0.22, 0.66), and 0.49 (0.26, 0.94), respectively, in a model that adjusted for age, sex, energy intake, waist-to-hip ratio, education, field center, smoking, and the consumption of linoleic acid, saturated fat, fish, and vegetables. Linoleic acid, fish long-chain fatty acids, and fish consumption were not significantly related to carotid artery disease. Linolenic acid was inversely related to thickness of the internal and bifurcation segments of the carotid arteries but not to the common carotid artery.

Conclusion Higher consumption of total linolenic acid is associated with a lower prevalence odd of carotid plaques and with lesser thickness of segment-specific carotid intima-media thickness.

http://www.ajcn.org/cgi/content/abstract/77/4/819

Dietary omega-3 fatty acids for women

INSERM U 705, CNRS UMR 7157, Universités Paris 7 et 5, Hôpital Fernand Widal, 200 rue du Faubourg Saint Denis, Paris, France.

Abstract This review details the specific needs of women for omega-3 fatty acids, including alpha linoleic acid (ALA) and the very long chain fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Omega-3 fatty acid (dietary or in capsules) ensures that a woman's adipose tissue contains a reserve of these fatty acids for the developing fetus and the breast-fed newborn infant. This ensures the optimal cerebral and cognitive development of the infant. The presence of large quantities of EPA and DHA in the diet slightly lengthens pregnancy, and improves its quality. Human milk contains both ALA and DHA, unlike that of other mammals. Conditions such as diabetes can alter the fatty acid profile of mother's milk, while certain diets, like those of vegetarians, vegans, or even macrobiotic diets, can have the same effect, if they do not include seafood.

ALA, DHA and EPA, are important for preventing ischemic cardiovascular disease in women of all ages. Omega-3 fatty acids can help to prevent the development of certain cancers, particularly those of the breast and colon, and possibly of the uterus and the skin, and are likely to reduce the risk of postpartum depression, manic-depressive psychosis, dementias (Alzheimer's disease and others), hypertension, toxemia, diabetes and, to a certain extend, age-related macular degeneration. Omega-3 fatty acids could play a positive role in the prevention of menstrual syndrome and postmenopausal hot flushes.

The normal western diet contains little ALA (less than 50% of the RDA). The only adequate sources are rapeseed oil (canola), walnuts and so-called "omega-3" eggs (similar to wild-type or Cretan eggs). The amounts of EPA and DHA in the diet vary greatly from person to person. The only good sources are fish and seafood, together with "omega-3" eggs.

http://www.ncbi.nlm.nih.gov/pubmed/17254747?ordinalpos=&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.SmartSearch&log$=citationsensor

Dietary substitution with an alpha-linolenic acid-rich vegetable oil increases eicosapentaenoic acid concentrations in tissues

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Thirty healthy male volunteers were randomly allocated into two dietary treatment groups. The flaxseed group (n = 15) maintained a diet high in alpha-linolenic acid (alpha-LA; 18:3n-3) and low in linoleic acid (LA; 18:2n-6) by using a flaxseed oil and spread that are high in alpha-LA. The control group (n = 15) maintained a diet high in LA and low in alpha-LA, typifying a Western diet. Both groups maintained their diets for 4 wk, followed by another 4-wk period in which they supplemented the diets with fish oil [1.62 g eicosapentaenoic acid (EPA, 20:5n-3) daily and 1.08 g docosahexaenoic acid (DHA, 22:6n-3) daily] in a triglyceride form. The flaxseed oil-containing diet resulted in significant increases in alpha-LA concentrations in the plasma phospholipid, cholesteryl ester, and triglyceride fractions (eightfold increase) and neutrophil phospholipids (50% increase). EPA concentrations increased by 2.5-fold in the plasma lipid fractions and neutrophil phospholipids. After fish-oil supplementation EPA concentrations increased in parallel in both dietary groups, remaining higher in the flaxseed group for both the plasma lipid fractions and neutrophil phospholipids. The results indicate that alpha-LA-rich vegetable oils can be used in a domestic setting

(in conjunction with a background diet low in LA) to elevate EPA in tissues to concentrations comparable with those associated with fish-oil supplementation.

http://www.ncbi.nlm.nih.gov/sites/entrez

Dietary supplementation with gamma-linolenic acid or fish oil decreases T lymphocyte proliferation in healthy older humans

Thies, F. et al / J.Nutr. 131:1918, 2001

Animal and human studies have shown that greatly increasing the amounts of flax seed oil [rich in the (n-3) polyunsaturated fatty acid (PUFA) alpha-linolenic acid (ALNA)] or fish oil [FO; rich in the long chain (n-3) PUFA eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] in the diet can decrease mitogen-stimulated lymphocyte proliferation. The objective of this study was to determine the effect of dietary supplementation with moderate levels of ALNA, gamma-linolenic acid (GLA), arachidonic acid (ARA), DHA or FO on the proliferation of mitogen-stimulated human peripheral blood mononuclear cells (PBMC) and on the production of cytokines by those cells. The study was randomized, placebo-controlled, double-blinded and parallel. Healthy subjects ages 55-75 y consumed nine capsules/d for 12 wk; the capsules contained placebo oil (an 80:20 mix of palm and sunflower seed oils) or blends of placebo oil with oils rich in ALNA, GLA, ARA or DHA or FO. Subjects in these groups consumed 2 g of ALNA or 770 mg of GLA or 680 mg of ARA or 720 mg of DHA or 1 g of EPA plus DHA (720 mg of EPA + 280 mg of DHA) daily from the capsules. Total fat intake from the capsules was 4 g/d. The fatty acid composition of PBMC phospholipids was significantly changed in the GLA, ARA, DHA and FO groups. Lymphocyte proliferation was not significantly affected by the placebo, ALNA, ARA or DHA treatments. GLA and FO caused a significant decrease (up to 65%) in lymphocyte proliferation.

This decrease was partly reversed by 4 wk after stopping the supplementation. None of the treatments affected the production of interleukin-2 or interferon-gamma by PBMC and none of the treatments affected the number or proportion of T or B lymphocytes, helper or cytotoxic T lymphocytes or memory helper T lymphocytes in the circulation. We conclude that a moderate level GLA or EPA but not of other (n-6) or (n-3) PUFA can decrease lymphocyte proliferation but not production of interleukin-2 or interferon-gamma.

http://www.ncbi.nlm.nih.gov/pubmed/11435508

Effect of linolenic acid supplementation during pregnancy on maternal and neonatal polyunsaturated fatty acid status and pregnancy outcome

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Background Maternal essential fatty acid status declines during pregnancy, and as a result, neonatal concentrations of docosahexaenoic acid (DHA, 22:6n-3) and arachidonic acid (AA, 20:4n-6) may not be optimal. OBJECTIVE: Our objective was to improve maternal and neonatal fatty acid status by supplementing pregnant women with a combination of alpha-linolenic acid (ALA, 18:3n-3) and linoleic acid (LA, 18:2n-6), the ultimate dietary precursors of DHA and AA, respectively.

Design From week 14 of gestation until delivery, pregnant women consumed daily 25 g margarine supplying either 2.8 g ALA + 9.0 g LA (n = 29) or 10.9 g LA (n = 29). Venous blood was collected for plasma phospholipid fatty acid analyses at weeks 14, 26, and 36 of pregnancy, at delivery, and at 32 wk postpartum. Umbilical cord blood and vascular tissue samples were collected to study neonatal fatty acid status also. Pregnancy outcome variables were assessed.

Results ALA+LA supplementation did not prevent decreases in maternal DHA and AA concentrations during pregnancy and, compared with LA supplementation, did not increase maternal and neonatal DHA concentrations but significantly increased eicosapentaenoic acid (20:5n-3) and docosapentaenoic acid (22:5n-3) concentrations. In addition, ALA+LA supplementation lowered neonatal AA status. No significant differences in pregnancy outcome variables were found.

Conclusion Maternal ALA+LA supplementation did not promote neonatal DHA+AA status. The lower concentrations of Osbond acid (22:5n-6) in maternal plasma phospholipids and umbilical arterial wall phospholipids with ALA+LA supplementation than with LA supplementation suggest only that functional DHA status improves with ALA+LA supplementation.

http://www.ncbi.nlm.nih.gov/sites/entrez

Essential fatty acid requirements of vegetarians in pregnancy, lactation, and infancy

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Abstract Long-chain polyunsaturated fatty acids (LCPUFAs) derived from linoleic (18:2n-6) and -linolenic (18:3n-3) acids are required for the normal development of the retina and central nervous system, but the extent to which they can be synthesized from the parent fatty acids is debated. Consuming LCPUFAs markedly increases their proportions in tissue lipids compared with their parent fatty acids. Thus, it has been argued that LCPUFAs must be supplied in the diet. LCPUFAs are generally absent from plant foods, thus it is important find out how essential fatty acid requirements are met by vegetarians. A developing fetus obtains LCPUFAs via selective uptake from its mother's plasma and LCPUFAs are present in the breast milk of vegetarians. There is no evidence that the capacity to synthesize LCPUFAs is limited in vegetarians. However, there are greater proportions of n-6 LCPUFAs and lower proportions of n-3 LCPUFAs in vegetarians compared with omnivores. This difference is probably a consequence of the selection of foods by vegetarians with high amounts of linoleic acid. Although lower concentrations of docosahexaenoic acid (22:6n-3; DHA) have been observed in blood and artery phospholipids of infants of vegetarians, it is uncertain whether their brain lipids contain lower proportions of DHA than do those of infants of omnivores. On the basis of experiments in primates that showed altered visual function with a high ratio of linoleic acid to -linolenic acid, it would be prudent to recommend diets with a ratio between 4:1 and 10:1 in vegetarians and that excessive intakes of linoleic acid be avoided.

http://www.ajcn.org/cgi/content/full/70/3/555S

Fish oil in people with type 2 diabetes mellitus

Farmer, a et al / COCHRANE DATABASE Syst.Rev. 1, 2008
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Background People with type 2 diabetes mellitus are at increased risk from cardiovascular disease. Dietary fish oils are known to reduce triglyceride levels, but their impact on cholesterol levels, glycemic control and vascular outcomes are not well known.

Objectives To determine the effects of fish oil supplementation on cardiovascular outcomes, cholesterol levels and glycemic control in people with type 2 diabetes mellitus.

Search Strategy We carried out a comprehensive search of the Cochrane Controlled Trials Register, Medline, Embase, Lilacs, bibliographies of relevant papers and contacted experts for identifying additional trials. Date of last search: September 2000.

Selection Criteria All randomized placebo-controlled trials in which fish oil supplementation was the only intervention in people with type 2 diabetes were included. Authors were contacted for missing information.

Data Collection and Analysis Three investigators performed data extraction and quality scoring independently with discrepancies resolved by consensus.

Main Reasults Eighteen trials including 823 participants followed for a mean of 12 weeks were included. Doses of fish oil used ranged from 3 to 18 g/day. No trials with vascular event or mortality endpoints were identified. The outcomes studied were glycemic control and lipid levels. Meta-analysis of pooled data demonstrated a statistically significant effect of fish oil in lowering triglycerides by 0.56 mmol/l (95% CI -0.71 to -0.40 mmol/l) and raising LDL cholesterol by 0.21 mmol/l (95% CI 0.02 to 0.41 mmol/l). No statistically significant effect was observed for fasting glucose, HbA1c, total or HDL cholesterol. The triglyceride lowering effect and the elevation in LDL cholesterol were most marked in those trials that recruited people with hypertriglyceridemia and used oil.
No adverse effects of the intervention were reported.

Reviewers Conclusions Fish oil supplementation in type 2 diabetes lowers triglycerides, may raise LDL cholesterol (especially in hypertriglyceridemic patients on higher doses of fish oil) and has no statistically significant effect on glycemic control. Trials with vascular event or mortality defined endpoints are needed.

http://www.ncbi.nlm.nih.gov/pubmed/11687050

Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease.

De Lorgeril et al. / Lancet 18:345, 1995 de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, Guidollet J, Touboul P, Delaye J. INSERM
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In a prospective, randomised single-blinded secondary prevention trial we compared the effect of a Mediterranean alpha-linolenic acid-rich diet to the usual post-infarct prudent diet. After a first myocardial infarction, patients were randomly assigned to the experimental (n = 302) or control group (n = 303). Patients were seen again 8 weeks after randomisation, and each year for 5 years.

The experimental group consumed significantly less lipids, saturated fat, cholesterol, and linoleic acid but more oleic and alpha-linolenic acids confirmed by measurements in plasma. Serum lipids, blood pressure, and body mass index remained similar in the 2 groups. In the experimental group, plasma levels of albumin, vitamin E, and vitamin C were increased, and granulocyte count decreased. After a mean follow up of 27 months, there were 16 cardiac deaths in the control and 3 in the experimental group; 17 non-fatal myocardial infarction in the control and 5 in the experimental groups: a risk ratio for these two main endpoints combined of 0.27 (95% CI 0.12-0.59, p = 0.001) after adjustment for prognostic variables. Overall mortality was 20 in the control, 8 in the experimental group, an adjusted risk ratio of 0.30 (95% CI 0.11-0.82, p = 0.02).

An alpha-linolenic acid-rich Mediterranean diet seems to be more efficient than presently used diets in the secondary prevention of coronary events and death.

http://www.ncbi.nlm.nih.gov/pubmed/7911176

Prevention of insulin resistance by n-3 polyunsaturated fatty acids

Fedor, D and Kelley, DS /
Curr.Opin.Clin.Nutr.Metab.Care 12:138, 2009
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Purpose of Review Review results from recent human and animal studies regarding the effects of n-3 polyunsaturated fatty acid (PUFA) in the prevention of insulin resistance.

Recent Findings Overall, results from animal studies indicate that fish oil and individual n-3 PUFA [alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA)] prevented insulin resistance in animal models; results from two studies in mice showed that EPA increased insulin secretion. ALA, EPA, and DHA may act at different sites and involve different mechanisms. Fish oil or purified EPA reduced insulin resistance in some but not other human studies in normal weight and obese individuals. Discrepancies may be due to differences in health status of participants, macronutrient, fatty acid, and antioxidant nutrient composition of basal diet; amount, duration, and fatty acid composition of n-3 PUFA, and methods used to assess insulin resistance. Moderate amounts of n-3 PUFA did not improve or deteriorate glucose control in type 2 diabetics.

Summary n-3 PUFA supplementation has clinical significance in the prevention and reversal of insulin resistance. However, increased intake of n-3 PUFA should be part of an overall healthy lifestyle that includes weight control, exercise, and reduction in the intake of refined sugars, n-6, saturated, and trans fatty acids.

http://www.ncbi.nlm.nih.gov/pubmed/19202385

Quantitation of alpha-linolenic acid elongation to EPA and DHA as affected by the ratio of n6/n3 fatty acids

Hernack,K. et al / Nutr.Metab. 19: 2009

Background Conversion of linoleic acid (LA) and alpha-linolenic acid (ALA) to their higher chain homologues in humans depends on the ratio of ingested n6 and n3 fatty acids.

Design and Methods In order to determine the most effective ratio with regard to the conversion of ALA to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), human hepatoma cells were incubated with varying ratios of [13C] labeled linoleic acid ([13C]LA)- and alpha-linolenic acid ([13C]ALA)-methylesters. Regulative cellular signal transduction pathways involved were studied by determinations of transcript levels of the genes encoding delta-5 desaturase (D5D) and delta-6 desaturase (D6D), peroxisome proliferator-activated receptor alpha (PPARalpha) and sterol regulatory element binding protein 1c (SREBP-1c). Mitogen-activated protein kinase kinase 1 (MEK1) and mitogen-activated protein kinase kinase kinase 1 (MEKK1) were also examined.

Results Maximum conversion was observed in cells incubated with the mixture of [13C] LA/[13C]ALA at a ratio of 1:1, where 0.7% and 17% of the recovered [13C]ALA was converted to DHA and EPA, respectively. Furthermore, differential regulation of enzymes involved in the conversion at the transcript level, dependent on the ratio of administered n6 to n3 fatty acids in human hepatocytes was demonstrated.

Conclusion Formation of EPA and DHA was highest at an administered LA/ALA ratio of 1:1, although gene expression of PPARalpha, SREBP-1c and D5D involved in ALA elongation were higher in the presence of ALA solely. Also, our findings suggest that a diet-induced enhancement of the cell membrane content of highly unsaturated fatty acids is only possible up to a certain level.

http://www.ncbi.nlm.nih.gov/pubmed/19228394

Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian experiment of infarct survival - 4

In a randomized, placebo-controlled trial, the effects of treatment with fish oil (eicosapentaenoic acid, 1.08 g/day) and mustard oil (alpha-linolenic acid, 2.9 g/day) were compared for 1 year in the management of 122 patients (fish oil, group A), 120 patients (mustard oil, group B), and 118 patients (placebo, group C) with suspected acute myocardial infarction (AMI). Treatments were administered about (mean) 18 hours after the symptoms of AMI in all three groups.

The extent of cardiac disease, rise in cardiac enzymes, and lipid peroxides were comparable among the groups at entry into the study. After 1 year total cardiac events were significantly less in the fish oil and mustard oil groups compared with the placebo group (24.5% and 28% vs. 34.7%, $p < 0.01$). Nonfatal infarctions were also significantly less in the fish oil and mustard oil groups compared with the placebo group (13.0% and 15.0% vs. 25.4%, $p < 0.05$). Total cardiac deaths showed no significant reduction in the mustard oil group; however, the fish oil group had significantly less cardiac deaths compared with the placebo group (11.4% vs. 22.0%, $p < 0.05$). Apart from the decrease in the cardiac event rate, the fish oil and mustard oil groups also showed a significant reduction in total cardiac arrhythmias, left ventricular enlargement, and angina pectoris compared with the placebo group. Reductions in blood lipoproteins in the two intervention groups were modest and do not appear to be the cause of the benefit in the two groups. Diene conjugates showed a significant reduction in the fish oil and mustard oil groups, indicating that a part of the benefit may be caused by the reduction in oxidative stress. The findings of this study suggest that fish oil and mustard oil, possibly due to the presence of n-3 fatty acids, may provide rapid protective effects in patients with AMI. However, a large study is necessary to confirm this suggestion.

http://www.ncbi.nlm.nih.gov/pubmed/9310278

with increased consumption of oils rich in alpha linolenic acid

Europe are associated Cancer Epidemiology and Prevention Division, The Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, 5 Roentgen St., Warsaw, 02-781, Poland Department of Nutrition, Harvard School of Public Health, Boston, USA Zatonski et al / European Journal of Epidemiology, 23:3, 2008

Abstract During the 1980's, opposing time trends were observed in coronary heart disease (CHD) rates between Eastern and Western European countries. In all former socialistic economic countries, CHD was uniformly increasing or stable, but a steady decline in CHD was observed in Western European countries. Surprisingly, during the 1990's CHD mortality substantially decreased in some Eastern European countries but not in others. These changes were accompanied by major shifts in food consumption, including the type of vegetable oils used by the population. There are two major vegetable oils consumed in Eastern Europe (rapeseed and sunflower) that differ greatly in their content of n-3 fatty acids, specifically alpha-linolenic acid (ALA). Low ALA intake has been associated with risk of fatal CHD and sudden cardiac death. The purpose of this study was to examine trends in CHD in eleven Eastern European countries to identify whether national changes in vegetable oil consumption after 1990 were associated with changes in CHD mortality rates. Our data show that countries which experienced an increase in ALA consumption also experienced a substantial decline in CHD mortality. These results were consistent in men and women. We hypothesize that the decline in CHD mortality observed in Eastern Europe can be attributed, in part, to changes in ALA consumption.

http://www.springerlink.com/content/3702574u02uj742l/

Ratio of n-6 to n-3 fatty acids and bone mineral density in older adults: the rancho bernardo study

Weiss LA et al / Am.J.Clin.Nutr. 81:934, 2005
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Background Several lines of evidence suggest that n-3 fatty acids reduce the risk of some chronic diseases, including heart disease, diabetes, and cancer. Other research, mainly in animals, also suggests a role in bone health.
Objective: We aimed to investigate the association between the ratio of dietary n-6 to n-3 fatty acids and bone mineral density (BMD) in 1532 community-dwelling men and women aged 45-90 y.

Design Between 1988 and 1992, dietary data were obtained through self-administered food-frequency questionnaires, and BMD was measured at the hip and spine with the use of dual-energy X-ray absorptiometry. A medical history was obtained and current medication use was validated. Age- and multiple-adjusted linear regression analyses were performed.

Results There was a significant inverse association between the ratio of dietary linoleic acid to -linolenic acid and BMD at the hip in 642 men, 564 women not using hormone therapy, and 326 women using hormone therapy; these results were independent of age, body mass index, and lifestyle factors. An increasing ratio of total dietary n-6 to n-3 fatty acids was also significantly and independently associated with lower BMD at the hip in all women and at the spine in women not using hormone therapy.

Conclusion A higher ratio of n-6 to n-3 fatty acids is associated with lower BMD at the hip in both sexes. These findings suggest that the relative amounts of dietary polyunsaturated fatty acids may play a vital role in preserving skeletal integrity in older age.

http://www.ajcn.org/cgi/content/abstract/81/4/934

Relation between dietary linolenic acid and coronary artery disease in the National Heart, Lung, and Blood Institute Family Heart Study

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Background Epidemiologic studies suggest that a higher consumption of eicosapentaenoic acid and docosahexaenoic acid is associated with a reduced risk of cardiovascular disease. Studies in humans and animals also reported an inverse association between -linolenic acid and cardiovascular disease morbidity and mortality. Objective: We examined the relation between dietary linolenic acid and prevalent coronary artery disease (CAD).

Design We studied 4584 participants with a mean (±SD) age of 52.1 ± 13.7 y in the National Heart, Lung, and Blood Institute Family Heart Study in a cross-sectional design. Participants' diets were assessed with a semiquantitative food-frequency questionnaire. For each sex, we created age- and energy-adjusted quintiles of linolenic acid, and we used logistic regression to estimate prevalent odds ratios for CAD.

Results From the lowest to the highest quintile of linolenic acid, the prevalence odds ratios of CAD were 1.0, 0.77, 0.61, 0.58, and 0.60 for the men (P for trend = 0.012) and 1.0, 0.57, 0.52, 0.30, and 0.42 for the women (P for trend = 0.014) after adjustment for age, linoleic acid, and anthropometric, lifestyle, and metabolic factors. Linoleic acid was also inversely related to the prevalence odds ratios of CAD in the multivariate model (0.60 and 0.61 in the second and third tertiles, respectively) after adjustment for linolenic acid. The combined effect of linoleic and linolenic acids was stronger than the individual effects of either fatty acid.

Conclusion A higher intake of either linolenic or linoleic acid was inversely related to the prevalence odds ratio of CAD. The 2 fatty acids had synergistic effects on the prevalence odds ratio of CAD.

http://www.ajcn.org/cgi/content/abstract/74/5/612

The beneficial effect of linolenic acid in coronary artery disease is not questionable

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In a recent prospective study of 667 men in Zutphen (Netherlands) and of 98 cases of coronary artery disease (CAD), Oomen et al concluded that the protective effect of dietary -linolenic acid (ALA) against CAD is questionable. However, recently confirmed positive effects of ALA were reported in several large studies. The first prospective study showing a beneficial effect of ALA on CAD was conducted in 6250 middle-aged men of the usual care group of the Multiple Risk Factor Intervention Trial. After 10.5 y of follow-up, 175 deaths from CAD occurred in that group. ALA intake, as evaluated by dietary recall interviews at 5 different periods, was significantly inversely related to mortality from CAD ($P < 0.04$) and from all causes ($P < 0.02$). The intake of ALA in the highest quintile was 3.2-fold that in the lowest quintile.

More recently, 2 large prospective studies in 76 283 nurses and 43 757 health professionals showed that ALA was the only fatty acid that protected against cardiac death and against nonfatal myocardial infarction , independently of other dietary or nondietary factors. In both studies, the intake of ALA in the highest quintile was 1.9-fold that in the lowest quintile.
In the Lyon intervention trial in 600 patients with coronary heart disease , both fatal and nonfatal myocardial infarctions were lowered by > 70%. Statistical analysis has indicated that most of the beneficial effects are attributable to plasma ALA concentrations. The experimental group had an ALA intake 2.9-fold that of the control group.

In a double-blind, placebo-controlled study in India, the effects of ALA (supplied by mustard oil) in 120 patients with suspected acute myocardial infarction were compared with those of a placebo in 98 control subjects.
After 1 y of follow-up, both cardiac death and nonfatal myocardial infarction were significantly lower in the group treated with mustard oil. ALA intake in the treated patients was 3.6-fold that in the placebo group.
Finally, the most recent results of the effects of linolenic acid (mostly ALA) on CAD are from a cross-sectional study in 4406 participants of the National Heart, Lung, and Blood Institute Family Heart Study. The intake of ALA was significantly inversely related to the prevalence (485 cases) of CAD, in both women and men.
Concordant with the results mentioned above are those of a dietary intervention study conducted in the entire country of Finland over the past 25 y. During that period, CAD mortality was reduced overall by > 65% and by 80% in 40-50-y-old men. Canola oil rich in ALA is now the main oil used for cooking and to make margarines in Finland.

Thus, 7 human studies (3 prospective, 1 cross-sectional, and 3 intervention studies) have reported significant protective effects of a diet enriched in ALA on CAD morbidity, mortality, or both, whereas negative results have only been reported in the Zutphen Elderly Study. Because of the suspected key role of ALA in the prevention of CAD, it may be important to unravel the possible explanation (other than the small sample size) for the discrepant results of the Zutphen Elderly Study.

Possible confounding factors in the Zutphen Elderly Study include the following. First, the intake of ALA was strongly associated with that of trans fatty acids, which are known for their positive association with CAD (10). When the statistical analysis was performed only with ALA sources without trans fatty acids, the positive association between the intake of ALA and CAD was no longer observed. In the Nurses Health Study, the intake of trans fatty acids also inhibited the inverse relation between ALA and fatal CAD, but not to the extent of the Zutphen Elderly Study. The ratio of trans fatty acids to ALA in the group with the highest intake of ALA in the Nurses Health Study was 2.86 and in the Zutphen Elderly Study was 8.65. Thus, the high intake of trans fatty acids may be the main reason for the discrepant results of the Zutphen Elderly Study. Even when the relation of food without trans fatty acids was evaluated, a residual confounding was probably not totally excluded. Second, an additional factor may be the difference in the intake of ALA between the experimental group or the highest tertile (or quintile) and the control group or the lowest tertile (or quintile). In the Indian intervention trial , the intake of ALA in the experimental group was 3.6-fold that in the control group; it was 2.9-fold that in the Lyon study . The intake of ALA in the highest quintile or tertile was 3.2-fold that in the lowest quintile or tertile in the prospective Multiple Risk Factor Intervention Trial, 2.15-fold that in the men and 2.05-fold that in the women in the Family Heart Study , 1.9-fold that in the Nurses Health Study and the Health Professionals Follow-up Study , and 1.68-fold that in the Zutphen Elderly Study . Thus, it seems that an intake 1.9-fold that of the control group may be required to observe a positive effect of ALA.

http://www.ajcn.org/cgi/content/full/76/4/903

The role of nutritional factors on the structure of the brain: an update on dietary requirements

Unité de recherches en Neuro - Pharmaco - Nutrition, INSERM U26, Hôpital Fernand Widal, Paris. Bourre, JM / Rev. Neutol (PARIS) 160:767, 2004.

The brain is an organ elaborated and functioning from substances present in the diet. Dietary regulation of blood glucose level (via ingestion of food with a low glycemic index ensuring a low insulin level) improves the quality and duration of intellectual performance, if only because at rest the adult brain consumes 50 p. 100 of dietary carbohydrates, 80 p.100 of them for energy purposes. The nature of the amino acid composition of dietary proteins contributes to good cerebral function; tryptophan plays a special role. Many indispensable amino acids present in dietary proteins help to elaborate neurotransmitters and neuromodulators. Omega-3 fatty acids provided the first coherent experimental demonstration of the effect of dietary nutrients on the structure and function of the brain. First it was shown that the differentiation and functioning of cultured brain cells requires omega-3 fatty acids. It was then demonstrated that alpha-linolenic acid (ALA) deficiency alters the course of brain development, perturbs the composition and physicochemical properties of brain cell membranes, neurones, oligodendrocytes, and astrocytes (ALA). This leads to physicochemical modifications, induces biochemical and physiological perturbations, and results in neurosensory and behavioral upset. Consequently, the nature of polyunsaturated fatty acids (in particular omega-3) present in formula milks for infants (premature and term) conditions the visual and cerebral abilities, including intellectual abilities. Moreover, dietary omega-3 fatty acids are certainly involved in the prevention of some aspects of cardiovascular disease (including at the level of cerebral vascularization), and in some neuropsychiatric disorders, particularly depression, as well as in dementia, notably Alzheimer's disease. Their deficiency can prevent the satisfactory renewal of membranes and thus accelerate cerebral aging.

Iron is necessary to ensure oxygenation, to produce energy in the cerebral parenchyma, and for the synthesis of neurotransmitters. The iodine provided by the thyroid hormone ensures the energy metabolism of the cerebral cells. The absence of iodine during pregnancy induces severe cerebral dysfunction, leading to cretinism. Manganese, copper, and zinc participate in enzymatic mechanisms that protect against free radicals, toxic derivatives of oxygen. The use of glucose by nervous tissue implies the presence of vitamin B1. Vitamin B9 preserves memory during aging, and with vitamin B12 delays the onset of signs of dementia, provided it is administered in a precise clinical window, at the onset of the first symptoms. Vitamins B6 and B12, among others, are directly involved in the synthesis of neurotransmitters. Nerve endings contain the highest concentrations of vitamin C in the human body. Among various vitamin E components, only alpha-tocopherol is involved in nervous membranes. The objective of this update is to give an overview of the effects of dietary nutrients on the structure and certain functions of the brain.

http://www.ncbi.nlm.nih.gov/pubmed/15454864

Update on Alpha Linolenic Acid

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Consumption of omega 3 fatty acids is known to have health benefits. For many years, the importance of the only member of the omega 3 family considered to be essential, alpha-linolenic acid (ALA), has been overlooked. Current research indicates that ALA, along with its longer chain metabolites, may play an important role in many physiological functions. Potential benefits of ALA include cardioprotective effects, modulation of the inflammatory response, and a positive impact on both central nervous system function and behavior. Recommended levels for ALA intake have been set, yet the possible advantages of its consumption are just being revealed.

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