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Omega-3 in linseed and its role in human diet

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Linseed oil is well-known for its health benefits mainly attributed to its high content of omega-3 alpha linolenic acid (55-57%). Linseed oil is composed of five main fatty acids, namely palmitic (C16:0;~6%) (PAL), stearic (C18:0;~2.5%) (STE), oleic (C18:1cisΔ^9; ~19%) (OLE), linoleic (C18:2 cisΔ^9; □ 6 fatty acid; ~24%) (LIO) and linolenic (C18:3 cis$\Delta^{9\ 12,\ 15}$; □ 3 fatty acid; ~55 57%) (LIN) acid The nutritional significance of flax seed oil is due to the presence of higher level of α-linolenic acid (ALA) of omega-3 fatty acid (O3FA) family. ALA, an essential fatty acid, acts as precursor of biological active longer chain polyunsaturated fatty acid (PUFA) of omega-3 class, mainly eicosapentaeonic acid (EPA) and Docosahexanoic acid (DHA). The positive impact of LC omega-3 on heart health includes: protection against heart attacks by reducing the risk of abnormal heart rhythms; maintaining healthy blood vessels. At present Western diet is "deficient" in omega-3 fatty acids with a ratio of omega-6 to omega-3 of 15/1 to 16.7/1, instead of 1/1 as is the case with wild animals and presumably human beings.A land plant source of LC omega-3, if achieved and assuming their cultivation will be permitted will be cheaper than using yeast or microalgae. The omega-3 desaturase obtained from the roundworm *Caenorhabditis elegans* efficiently and quickly converted the omega-6 fatty acids.

Key words : Omega-3, Omega-6, α-linolenic acid (ALA), Eicosapentaeonic acid (EPA), Docosahexanoic acid (DHA), Linseed

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INTRODUCTION

Linseed oil is well-known for its health benefits mainly attributed to its high content of omega-3 alpha linolenic acid (55-57%). Linseed oil has been used for centuries in paints and varnishes because of its unique drying properties attributable to its distinctive fatty acid composition (Przybylski, 2001). Consumption of ground seeds adds nutritional benefits because flax seeds are also a rich source of lignans, compounds that have anticancer properties (Westcott and Muir, 2003). Linseed oil is composed of five main fatty acids, namely palmitic (C16:0;~6%) (PAL), stearic (C18:0;~2.5%) (STE), oleic (C18:1cis Δ^9; ~19%) (OLE), linoleic (C18:2 cis Δ^9; □ 6 fatty acid; ~24%) (LIO) and linolenic (C18:3 cis $\Delta^{9\ 12,\ 15}$; □ 3 fatty acid; ~55-57%) (LIN) acid (Westcott and Muir, 2003). The iodine value (IOD), which refers to the mass of iodine in grams that is consumed by 100 g of a chemical substance, is used to determine the saturation of fatty acids and, therefore, is used as a selection parameter in flax breeding. A higher IOD value represents a higher degree of unsaturation. A high proportion of LIN and consequent oxidative instability, resulting in a soft and flexible film, makes linseed oil valuable in dry oil industries such as paints, linoleum flooring, inks, soaps and varnishes (Cullis, 2007). Reduced LIN levels (~3%) have been achieved by mutation breeding (Green, 1986; Rowland, 1991) and the modified oil (LinolaTM), which solidifies at a higher temperature, has been found to be suitable for the fabrication of margarines (Dribnenki and Green, 1995; Dribnenki *et al.*, 2007). Also, a few high linolenic acid (high-LIN) lines with as much as ~65-70 per cent α-linolenic acid have been developed by flax breeders (Friedt *et al.,* 1995; Kenaschuk, 2005). Recently, NuLinTM 50, the first high-LIN flax variety, was registered in Canada (*www.viterra.ca*).

Health benefit due to Omega-3 :

The health benefits of LC omega-3 were first reported some three decades ago. Scientists observed that Greenland Eskimos had lower amounts of heart disease than other groups despite the fact their traditional diet is actually high in fat (Bang and Dyerberg, 1980). Associated with this finding was that Eskimo blood took longer to clot. The nutritional significance of flax seed oil is due to the presence of higher level of α-linolenic acid (ALA) of omega-3 fatty acid (O3FA) family. ALA, an essential fatty acid, act as precursor of biological active longer chain polyunsaturated fatty acid (PUFA) of omega-3 class, mainly eicosapentaeonic acid (EPA) and docosahexanoic acid (DHA). The shorter bleeding times common in Western countries can increase the risk of forming a blood clot which may trigger a heart attack. Investigations found that the traditional, seafood rich diet of the Eskimos was responsible both for the thinner blood and the healthier hearts (Bang *et al.*, 1976). The key ingredient of this diet was found to be LC omega-3. The human body needs fats of different types to grow and function properly and LC omega-3 oils are particularly relevant for foetal and infant growth since without LC omega-3, infant and children's vision and growth can be impaired (Carson, 1995 ; Heird *et al.*, 1997). The human body cannot produce short chain omega-3 on its own, and does not convert the short chain omega-3 to the long-chain versions, especially DHA, efficiently. The issue of the poor conversion efficiency of 18:3ω3 (α-linolenic acid, ALA) to EPA and DHA in humans is also crucial to the debate on sustainable sources, with fish oil or other sources of LC omega-3 clearly the preferred and benefitting nutrient required (Burdge and Calder, 2005; Wang *et al.*, 2006). When the diet does not supply sufficient omega-3, growth can be impaired and vulnerability to a number of diseases can increase. The positive impact of LC omega-3 on heart health includes: protection against heart attacks by reducing the risk of abnormal heart rhythms; maintaining healthy blood vessels; lowering of high blood pressure; influencing the narrowing of arteries; and making the blood less likely to clot. LC omega-3 also lower high blood fats by reducing their production in the liver and purified LC omega-3 is available as a treatment for patients with very high blood fat levels (Bays, 2006). LC omega-3 oils help to combat certain inflammatory conditions such as rheumatoid arthritis (Cleland and James, 1997) and it has been suggested that they may also have a positive impact on kidney function. In addition to these purely physical health benefits, it has been suggested that LC omega-3 may have benefits for neuropsychiatric disorders including depression and dementia (Parker *et al.*, 2006; Schaefer *et al.*, 2006; Freeman *et al.*, 2006).

Available source of omega-3 :

In an alternative approach to the use of micro-organisms, a number of international teams are now using genetic engineering technology to allow land plant crops to produce the health-benefitting LC omega-3 oils; several reviews are available and provide summaries of the considerable progress to date towards this goal (Graham *et al.*, 2004; Venegas *et al.*, 2010). This alternative approach to obtaining LC omega-3 oils has resulted from concerns on over-fishing and about pollution of the marine environment (Miller *et al.*, 2008; Naylor *et al.*, 2009; Venegas *et al.*, 2010), in addition to the increasing recognition of the enormous health and socio-economic benefits of these oils and the expanding global population and finally the clear need for new sustainable sources. LC omega-3 oil and increased levels of DHA in particular are still required. It is interesting to point out, that as little as one tablespoon (10 ml) of soybean oil containing 20 per cent of EPA could make a significant contribution to the recommended dietary intake of the beneficial omega-3 LC-PUFA. Considerable effort is now being focused on increasing the levels of DHA and it is not unrealistic to hope that DHA levels of 20 per cent can be achieved in transgenic plants in the next few years. Future novel land-based plants will likely provide the most economically viable source LC omega-3 oil for aquaculture and other applications (Fig. 1). A land plant source of LC omega-3, if achieved and assuming their cultivation will be permitted, will be cheaper than using yeast or microalgae and could be used in fish feeds and other feed and food products to help deliver increased human health benefits (Miller *et al.*, 2008; Ratledge, 2005). Research involving the use of microbial genes in land plants has so far led to increases the production of LC omega-3 in a number of land plant species.

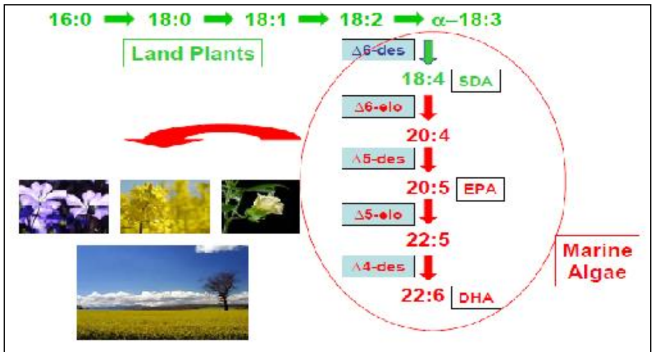

Fig. 1 : Schematic representation of fatty acid pathway for new land plants containing EPA and DHA, with incorporation on selected microalgae-derived genes. Although the a6 route is shown here, another pathway for LC omega-3 biosynthesis (a9, from ALA) also exists

Omega-3 and Omega-6 in balance diet :

It has been estimated that the present Western diet is "deficient" in omega-3 fatty acids with a ratio of omega-6 to omega-3 of 15/1 to 16.7/1, instead of 1/1 as is the case with wild animals and presumably human beings (Simopoulos and Childs, 1990 ; Eaton and Konner, 1985 ; Simopoulos, 1991; Simopoulos, 1995 ; Simopoulos, 1994). An absolute and relative change of omega-6/omega-3 in the food supply of Western societies has occurred over the last 100 years. Examples of plant components with suggested functionality (Table 1).

Mammalian cells cannot convert omega-6 to omega-3 fatty acids because they lack the converting enzyme, omega-3 desaturase. Linoleic acid (LA) and α-linolenic acid (ALA) and their long-chain derivatives are important components of animal and plant cell membranes. Because of the increased amounts of omega-6 fatty acids in the Western diet, the eicosanoid metabolic products from AA, specifically

Table 1 : Fatty acids

Class/components	Source[b]	Potential health benefit
Omega-3 fatty acids – DHA/EPA	Tuna; fish and marine oils	May reduce risk of CVD and improve mental, visual functions.
Conjugated linoleic acid (CLA)	Cheese, meat products	May improve body composition, may decrease risk of certain cancers
Gamma linolenic acid	Borage, evening primrose	May reduce inflammation risk of cancer, CVD disease and improve body composition.

Modified from Ref. (Chassy *et al.*, 2004)
(a) Examples are not an all-inclusive list.
(b) U.S. Food and Drug Administration approved health claim established for component.

prostaglandins, thromboxanes, leukotrienes, hydroxy fatty acids, and lipoxins, are formed in larger quantities than those formed from omega-3 fatty acids, specifically EPA (Simopoulos, 1991). Thus, a diet rich in omega- 6 fatty acids shifts the physiological state to one that is prothrombotic and proaggregatory, with increases in blood viscosity, vasospasm, and vasoconstriction and decreases in bleeding time. Bleeding time is decreased in groups of patients with hypercholesterolemia, hyperlipoproteinemia, myocardial infarction, other forms of atherosclerotic disease, and diabetes (obesity and hypertriglyceridemia).

The higher the ratio of omega-6/omega-3 fatty acids in platelet phospholipids, the higher the death rate from cardio-vascular disease. Excessive amounts of omega-6 PUFA and a very high omega-6/omega-3 ratio, as is found in today's Western diets, promote the pathogenesis of many diseases, including cardio-vascular disease, cancer, and inflammatory and autoimmune diseases, whereas increased levels of omega-3 PUFA (a lower omega-6/omega-3 ratio), exert suppressive effects (Simopoulos, 2003). Ferruci *et al.* (2006) concluded, omega-3 fatty acids are beneficial in patients affected by diseases characterized by active inflammation. The omega-3 desaturase obtained from the roundworm *Caenorhabditis elegans* efficiently and quickly converted the omega-6 fatty acids that were fed to the cardiomyocytes in culture to the corresponding omega-3 fatty acids. Thus, omega-6 LA was converted to omega-3 ALA and AA was converted to EPA, so that at equilibrium, the ratio of omega-6 to omega-3 PUFA was close to 1/1. Further studies demonstrated that the cancer cells expressing the omega-3 desaturase underwent apoptotic death whereas the control cancer cells with a high omega-6/omega-3 ratio continued to proliferate (Kang, 2003). More recently, Kang *et al.* (2004) showed that transgenic mice expressing the *C. elegans* fat-1 gene encoding an omega-3 fatty acid desaturase are capable of producing omega-3 from omega-6 fatty acids, leading to enrichment of omega-3 fatty acids with reduced levels of omega-6 fatty acids in almost all organs and tissues, including muscles and milk, with no need of dietary omega-3 fatty acid supply. This discovery provides a unique tool and new opportunities for omega-3 research, and raises the potential of production of fat-1 transgenic livestock as a new and ideal source of omega-3 fatty acids to meet the human nutritional needs (Kang, 2003; Lai *et al.*, 2006).

Genetic control in flax seed :

The genetic control of storage oil biosynthesis in flax seeds has been extensively studied (Green, 1986; Fofana *et al.*, 2004; Sorensen *et al.*, 2005; Vrinten *et al.*, 2005; Krasowska *et al.*, 2007; Khadake *et al.*, 2009). Ethyl methane sulphonate (EMS)-induced low-LIN mutants of flax were developed in 1984, following which two independent loci controlling LIN content in flax seed were identified (Green and Marshall, 1984; Green, 1986; Rowland, 1991). Furthermore, a stearoyl-ACP desaturase (SAD) gene was identified and cloned in flax varieties Glenelg and AC McDuff (Fofana *et al.*, 2004; Singh *et al.*, 1994). Two fad2 (D12 fatty acid desaturase/omega-6 desaturase) genes have been cloned from two flax cultivars, namely Nike and NL97 (Krasowska *et al.*, 2007; Khadake *et al.*, 2009). Similarly, two fad3 genes (fad3A and fad3B) were cloned from SolinTM line 593–708 (Vrinten *et al.*, 2005). Compared to their respective wild types, these two fad3 alleles carried point mutations, resulting in premature stop codons and predicting their non-functional FAD activity (Vrinten *et al.*, 2005). Low-LIN lines have 2–3 per cent LIN, a phenomenon that could be explained by the production of small amounts of FAD3A and/or FAD3B (Vrinten *et al.*, 2005) or by yet another not very efficient FAD3 enzyme.

LITERATURE CITED

Bang, H.O., Dyerberg, J. and Hjorne, N. (1976). The composition of food consumed by Greenland Eskimos. *Acta Med. Scand.*, **200** (1-2) : 69-73.

Bang, H.O. and Dyerberg, J.E. (1980). Lipid metabolism and ischaemic heart disease in Greenland Eskimos. *Adv. Nutr. Res.*, **3** : 1-22.

Bays, H. (2006). Clinical overview of Omacor a concentrated formulation of omega-3 polyunsaturated fatty acids. *Am. J. Cardiol.*, **98** (4) : 71-76.

Burdge, G.C. and Calder, P.C. (2005). Conversion of α-linolenic acid to longer-chain polyunsaturated fatty acids in human adults. *Reprod. Nutr. Dev.*, **45** (5) : 581-597.

Carson, S.E. (1995). The role of PUFA in infant nutrition. *INFORM.*, **6** : 940-946.

Chassy, B. (2004). Nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology an executive summary. *Compr. Rev. Food Sci. Food Saf.*, **3** (2) : 38–104.

Cleland, L.G. and James, M.J. (1997). Rheumatoid arthritis and the balance of dietary N-6 and N-3 essential fatty acids. *Br. J. Rheumatol.*, **36** : 513-514.

Cullis, C.A. (2007). Flax In : Kole C (ed) *Genome mapping and molecular breeding in plants*, *Springer, Berlin*. pp. 275–295.

Dribnenki, J.C.P. and Green, A.G. (1995). Linola low linolenic acid flax. *Can. J. Plant Sci*., **75** (1) : 201-202.

Dribnenki, J.C.P., McEachern, S.F., Chen, Y., Green, A.G. and Rashid, K.Y. (2007). 2149 Solin (low linolenic flax). *Can. J. Plant Sci*., **87** (2) : 297–299.

Eaton, S.B. and Konner, M. (1985). Paleolithic nutrition. A consideration of its nature and current implications. *N. Engl. J. Med*., **312** (5) : 283–289.

Ferruci, L., Cherubini, A., Bandinelli, S., Bartali, B., Corsi, A. and Lauretani, F. (2006). Relationship of plasma polyunsaturated fatty acids to circulating inflammatory markers. *J. Clin. Endocrinol. Metab*., **91** (2) : 439–446.

Fofana, B., Duguid, S. and Cloutier, S. (2004). Cloning of fatty acid biosynthetic genes b-ketoacyl CoA synthase, fatty acid elongase, stearoyl-ACP desaturase and fatty acid desaturasem and analysis of expression in the early developmental stages of flax (*Linum usitatissimum* L.) seeds. *Plant Sci.*, **166** (6) : 1487–1496.

Freeman, M.P., Hibbeln, J.R., Wisner, K.L., Davis, J.M., Mischoulon, D., Peet, M., Keck, P.E., Marangell, L.B., Richardson, A.J., Lake, J. and Stoll, A.L. (2006). Omega-3 fatty acids: evidence basis for treatment and future research in psychiatry. *J. Clin. Psychiatry*, **67** (12) : 1954-1967.

Friedt, W., Bickert, C. and Schaub, H. (1995). *In vitro* breeding of high linolenic, doubled haploid lines of linseed (*Linum usitatissimum* L.) via androgenesis. *Plant Breed*., **114** (4) : 322–326.

Ge, Y.L., Chen, Z., Kang, Z.B., Cluette, B.J., Laposata, M. and Kang, J.X. (2002). Effects of adenoviral transfer of caenorhabditis elegans n-3 fatty acid desaturase on the lipid profile and growth of human breast cancer cells. *Anticancer Res.*, **22** (2A) : 537–544.

Graham, I.A., Cirpus, P., Rein, D. and Napier, J.A. (2004). The use of very long chain polyunsaturated fatty acids to ameliorate metabolic syndrome: transgenic plants as an alternative sustainable source to fish oils. *Nutr. Bull.*, **29** (3) : 228-233.

Green, A.G. (1986). Genetic control of polyunsaturated fatty acid biosynthesis in flax (*Linum usitatissimum* L.) seed oil. *Theor. Appl. Genet*., **72** (5) : 654–661.

Green, A.G. and Marshall, A.R. (1984). Isolation of induced mutants in linseed (*Linum usitatissimum* L.) having reduced linolenic acid content. *Euphytica*., **33** (2) : 321–328.

Heird, W.C., Prager, T.C. and Anderson, R.E. (1997). Docosahexaenoic acid and the development and function of the infant retina. *Curr. Opin. Lipidol.*, **8** (1) : 12-16.

Kang, J.X. (2003). The importance of omega-6/omega-3 fatty acid ratio in cell function. The gene transfer of omega-3 fatty acid desaturase. *World Rev. Nutr. Diet*., **92** : 23–36.

Kang, J.X. (2004). Balance of omega-6/omega-3 fatty acids is important for health: the evidence from gene transfer studies. *World Rev. Nutr. Diet.*, **95**: 93–102.

Kang, J.X., Wang, J., Wu, L., Kang, Z.B. (2004). Fat-1 mice convert n-6 to n-3 fatty acids. *Nature*, **427** : 504.

Khadake, R.M., Ranjekar, P.K. and Harsulkar, A.M. (2009). Cloning of a novel omega-6 desaturase from flax (*Linum usitatissimum* L.) and its functional analysis in Saccharomyces cerevisiae. *Mol. Biotechnol*., **42** (2) : 168–174.

Krasowska, A., Dziadkowiec, D., Polinceusz, A., Plonka. A. and Lukaszewicz, M. (2007). Cloning of flax oleic fatty acid desaturase and its expression in yeast. *J. Am. Oil Chem. Soc*., **84** (9) : 809–816.

Lai, L., Kang, J.X., Li. R., Wang, J., Witt, W.T. and Yong, H.Y. (2006). Generation of cloned transgenic pigs rich in omega-3 fatty acids. *Nat. Biotechnol*, **4** : 435–436.

McLennan, P.L., Bridle, T.M., Abeywardena, M.Y. and Charnock, J.S. (1992). Comparative efficacy of n-3 and n-6 polyunsaturated fatty acids in modulating ventricular fibrillation threshold in the marmoset monkey. *Am. J. Clin. Nutr*., **58** (5) : 666-669.

McLennan, P.L., Bridle, T.M., Abeywardena, M.Y. and Charnock, J.S. (1992). Dietary lipid modulation of ventricular fibrillation threshold in the marmoset monkey. *Am. Heart J.*, **123** (6) : 1555-1561.

Naylor, R.L., Hardy, R.W., Bureau, D.P., Chiu, A., Elliott, M., Farrell, A.P., Forster, I., Gatlin, D.M., Goldburg, R.J., Hua, K. and Nichols, P.D. (2009). Feeding aquaculture in an era of finite resources. *Proc. Natl. Acad. Sci.,* **106** : 15103-15110.

Nichols, P.D., Virtue, P., Mooney, B.D., Elliott, N.G., Yearsley, G.K. Nichols, P.D. and Carter, C.G. (2008). Omega 3 oil sources for use in aquaculture–alternatives to the unsustainable harvest of wild fish. *Nutr. Res. Rev.*, **21** : 85-96.

Parker, G., Gibson, N.A., Brotchie, H., Heruc, G., Rees, A. and Hadzi, P.D. (2006). Omega-3 Fatty acids and mood disorders. *Am. J. Psychiatry.*, **163** : 969-978.

Przybylski, R. (2001). Flax oil and high linolenic oils. In : *Bailey's industrial oil and fat products*. 6th Ed. Edited by Shahidi F. Hoboken: John Wiley & Sons, Inc; pp. 281–301.

Ratledge, C. (2005). Single cell oils for the 21st century. In : *Single cell oils.* Cohen, Z., Ratledge, C., Eds. AOCS Press: Champaign, IL, USA, pp. 1-20.

Rowland, G.G. (1991). An EMS-induced low linolenic acid mutant in McGregor flax (*Linum usitatissimum* L.). *Can. J. Plant Sci*., **71** (2) : 393–396.

Schaefer, E.J., Bongard, V., Beiser, A.S., Lamon, S., Robins, S.J., Au, R., Tucker, K.L., Kyle, D.J., Wilson, P.W.F. and Wolf, P.A. (2006). Plasma phosphatidylcholine docosahexaenoic acid content and risk of dementia and Alzheimer disease: the Framingham Heart Study. *Arch. Neurol*., **63** (11) : 1545-1550.

Simopoulos, A.P. (1991). Omega-3 fatty acids in health and disease and in growth and development. *Am J. Clin. Nutr*., **54** (3) : 438–463.

Simopoulos, A.P. (1994). Is insulin resistance influenced by dietary linoleic acid and trans fatty acids? *Free Rad. Biol. Med.,* **17**(4) : 367–372.

Simopoulos, A.P. (1995). Plants in human nutrition, Basel Karger, *World Rev. Nutr. Diet.,* **77** : 160 p.

Simopoulos, A.P. and Childs, B. (1990). Genetic variation and nutrition. *World Rev. Nutr. Diet*., **63** : 25-28.

Simopoulos, A.P. and Cleland, L.G. (2003). Omega-6/omega-3 essential fatty acid ratio: the scientific evidence, Basel Karger. *World Rev. Nutr. Diet*., **92** : 174 p.

Simopoulos, A.P. and Ordovas, J. (2004). Nutrigenetics and nutrigenomics. *World Rev. Nutr. Diet.,* Basel Karger, **93** : 1-28 pp.

Simopoulos, A.P. and Robinson, J. (1999). The omega diet. The life saving nutritional program based on the diet of the Island of Crete. New York, Harper Collins.

Singh, S., McKinney, S. and Green, A. (1994). Sequence of a cDNA from *Linum usitatissimum* encoding the stearoyl-acyl carrier protein desaturase. *Plant Physiol.*, **104** (3) : 1075.

Sorensen, B.M., Furukawa, S.T.L., Marshall, K.S., Page, E.K., Mir, Z., Forster, R.J. and Weselake, R.J. (2005). Storage lipid accumulation and acyltransferase action in developing flaxseed. *Lipids*., **40** (10) : 1043–1049.

Venegas, C.M., Sayanova, O. and Napier, J.A. (2010). An alternative to fish oils metabolic engineering of oil-seed crops to produce omega-3 long chain polyunsaturated fatty acids. *Prog. Lipid Res.,* **49** (2) : 108-119.

Vrinten, P., Hu, Z., Munchinsky, M.A., Rowland, G. and Qiu, X. (2005). Two FAD3 desaturase genes control the level of linolenic acid in flax seed. *Plant Physiol*., **139** (1) : 79–87.

Wang, C., Harris, W.S., Chung, M., Lichtenstein, A.H., Balk, E.M., Kupelnick, B., Jordan, H.S. and Lau, J. (2006). n-3 Fatty acids from fish or fish oil supplements, but not α-linolenic acid, benefit cardio-vascular disease outcomes in primary-and secondary-prevention studies: a systematic review. *Am. J. Clin. Nutr.,* **84** (1) : 5-17.

Westcott, N.A. and Muir, A.D. (2003). Flax seed lignan in disease prevention and health promotion. *Phytochem Rev*., **2** (3) : 401–417.

9TH YEAR
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