International Journal of Biological Chemistry

ISSN 1819-155X

Academic Journals Inc.

www.academicjournals.com

OPEN ACCESS International Journal of Biological Chemistry

ISSN 1819-155X
DOI: 10.3923/ijbc.2016.1.6

Review Article
Significance of Ratio of Omega-3 and Omega-6 in Human Health with Special Reference to Flaxseed Oil

[1]Kshitij Bhardwaj, [2]Narsingh Verma, [2]R.K. Trivedi, [2]Shipra Bhardwaj and [3]Neha Shukla

[1]Department of Chemical Technology, Harcourt Butler Technological Institute, Kanpur, India
[2]Department of Physiology, King George Medical University, Lucknow, India
[3]Department of Biotechnology, Jaipur National University, Jaipur, India

Abstract
It is known from the past that the quantity of n-6 in the diet directly affects the conversion of n-3 ALA (α-linolenic acid), found in plant foods, to long-chain n-3 icosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which protect us from disease consumption of omega-6 fats increased at the expense of n-3 fats. This change was due to both the advent of the modern vegetable oil industry and the increased use of cereal grains as food for domestic livestock which in turn altered the fatty acid profile of meat that humans consumed. Study suggests that our ancestors consumed omega-6 and omega-3 fats in a ratio of roughly 1:1. It also indicates that both ancient and modern hunter-gatherers were free of the modern inflammatory diseases, like heart disease, cancer and diabetes, that are the primary causes of death and morbidity today. At the onset of the industrial revolution (about 140 years ago), there was a marked shift in the ratio of n-6 to n-3 fatty acids in the diet. From this, it is concluded that it's all about balance this balance affects things on a cellular level with your omega-3 and omega-6 ratio. Average intake of n-6 fatty acids is between 10 and 25 times higher than evolutionary norms. In this review, the importance of flaxseed and ratio of omega-3 and omega-6 in health balance are discussed.

Key words: Omega-3, omega-6, flaxseed oil, ratio, palm oil, blending, oxidation stability

Received: January 04, 2016 Accepted: March 29, 2016 Published: June 15, 2016

Citation: Kshitij Bhardwaj, Narsingh Verma, R.K. Trivedi, Shipra Bhardwaj and Neha Shukla, 2016. Significance of ratio of omega-3 and omega-6 in human health with special reference to flaxseed oil. Int. J. Biol. Chem., 10: 1-6.

Corresponding Author: Kshitij Bhardwaj, Department of Chemical Technology, Harcourt Butler Technological Institute, Kanpur, India

Copyright: © 2016 Kshitij Bhardwaj *et al.* This is an open access article distributed under the terms of the creative commons attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Amount of omega-3 to eat depends largely on how much omega-6 we eat. Over the course of human evolution there has been a dramatic change in the ratio of omega-6 and omega-3 fats consumed in the diet. This change, perhaps more than any other dietary factor, has contributed to the epidemic of modern disease[1].

In the human body, Linolenic Acid (LA) and ALA compete for metabolism by the enzyme Δ6-desaturase. It has been suggested that this is important to health, as too high an intake of LA would reduce the amount of Δ6-desaturase available for the metabolism of ALA, which may increase the risk of heart disease. This was supported by data showing that over the last 150 years, intakes of omega-6 have increased and intakes of omega-3 have decreased in parallel with the increase in heart disease. Thus, the concept of a balanced ratio of omega-6 to omega-3 fatty acids in the diet was developed[2].

It is simply suggested that balancing the amount of ALA, EPA and DHA in the diet would achieve the desired increase in levels of these fatty acids in the body's tissues and that decreasing the intake of LA and ALA was not necessary[3]. But their use in food applications is limited due to their susceptibility to lipid oxidation; higher fish oil addition (as source of omega-3) in formulated fats resulted in increasingly fishy flavor and decreased sensory quality[4,5]. Flaxseed oil is a potentially vegetable important source of omega-3 as it is relatively stable to oxidation compared to fish oils[6].

Omega-6 Compete with omega-3 vice versa: Omega-6 and omega-3 fatty acids compete for the same conversion enzymes. This means that the quantity of n-6 in the diet directly affects the conversion of n-3 ALA, found in plant foods, to long-chain n-3 EPA and DHA, which protect us from disease[7]. Several studies have shown that the biological availability and activity of n-6 fatty acids are inversely related to the concentration of of n-3 fatty acids in tissue. Studies have also shown composition of EPA and DHA in membranes reduces the availability of AA for eicosanoid production[8].

Consequences of n-6: n-3 on human health: Elevated n-6 intakes are associated with an increase in all inflammatory diseases, which is to say virtually all diseases. The list includes (but isn't limited to): Cardiovascular disease, type 2 diabetes, obesity, metabolic syndrome, irritable bowel syndrome and inflammatory bowel disease, macular degeneration, rheumatoid arthritis, asthma, cancer, psychiatric disorders, autoimmune diseases. Several clinical studies have shown that decreasing the n-6: n-3 ratio protects against chronic, degenerative diseases. One study showed that replacing corn oil with olive oil and canola oil to reach an n-6: n-3 ratio of 4:1 led to a 70% decrease in total mortality. That is no small difference[9-11].

The increases in world LA consumption over the past century may be considered a very large uncontrolled experiment that may have contributed to increased societal burdens of aggression, depression and cardiovascular mortality and those are just the conditions which have the strongest evidence for. It's likely that the increase in n-6 consumption has played an equally significant role in the rise of nearly every inflammatory disease. Since, it is now known that inflammation is involved in nearly all diseases, including obesity and metabolic syndrome, it's hard to overstate the negative effects of too much omega-6 fat. Vegetable oils are dangerous for many reasons, including that they can easily go rancid, they are processed with chemicals and they can turn in to trans fats when heated. Vegetable oils are also high in omega-6 fats and proportionately low in omega-3 fats[12].

Ratio matters: Omega-3s and omega-6s compete for the enzymes needed for digestion and that: This means that the more omega-3 fat you eat, the less omega-6 will be available to the tissues to produce inflammation. Table 1 indicated that Omega-6 is pro-inflammatory, while omega-3 is neutral. A diet with a lot of omega-6 and not much omega-3 will increase inflammation. A diet of a lot of omega-3 and not much omega-6 will reduce inflammation[8,9]. As rates of vegetable oil and sugar consumption have risen, so have rates of heart disease and many other health problems (in fact, the graphs look almost identical). During this same time, consumption of foods that contain saturated fats and omega-3 fats has decreased. Essential Fatty Acids (EFAs) are required in the diet as they cannot be made by humans. The two established EFAs are linoleic acid (C18:2n-6, LA) and ALA. The ALA can be converted in the body into EPA and DHA. The LA is converted in the body to another long chain fatty acid, Arachidonic Acid (AA)-both LA and AA are omega-6s[13]. Figure 1 shows the pathway of conversion of LA and ALA to their longer chain omega families.

The AA and EPA are further metabolized to produce very powerful hormone-like substances (called 'Eicosanoids') that effect physiological functions such as cell growth and division, inflammatory responses, muscle activity, blood pressure and immune function. Eicosanoids formed from AA are released in the body in response to injury, infection, stress or certain diseases. The EPA forms eicosanoids that behave in opposition to those derived from AA and may help protect against heart attacks and strokes, as well as certain inflammatory diseases such as arthritis, lupus and asthma.

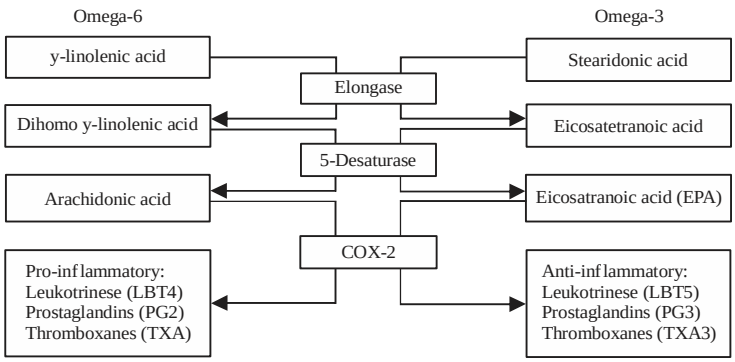

Fig. 1: Mechanism of omega-3 and omega-6. Source: APS knowledge center

Table 1: Most common omega-3 and omega-6 fatty acids and their dietary sources (Source: Susanallport)

		Polyunsaturated fat		
Dietary fat	Saturated fat	Linoleic acid (an omega-6 fatty acid)	α-linoleic acid (an omega-3 fatty acid)	Monounsaturated fat Oleic acid (an omega-9 fatty acid)
Canola oil	7	21	11	61
Safflower oil	8	14	1	77
Flaxseed oil	9	16	57	18
Sunflower oi	12	71	1	16
Corn oil	13	57	1	29
Olive oil	15	9	1	75
Soybean oil	15	54	8	23
Peanut oil	19	33	*	48
Cottonseed oil	27	54	*	19
Lard	43	9	1	47
Palm oil	51	10	*	39
Butter	68	3	1	28
Coconut oil	91	2		7

*Trace fatty acid content normalized to 100%

Table 2: Effects of omega-3 and omega-6 fatty acids on chronic diseases

Chronic diseases	Risk factors	Comments	Omega-3	Omega-6
Cardiovascular diseases	Arrhythmias (irregular heart beat)	Causes sudden cardiac death	Lowers	Increases
	Thrombosis (clot)	Leads to myocardial infarction or stroke	Lowers	Increases
	Atherosclerotic plaque	Leads to atherosclerosis	Lowers	Increases
	HDL	Good cholesterol	Increases	Lowers
	LDL	Bad cholesterol	Lowers	Increases
	Triglycerides	Cardiovascular risk factor	Lowers	Increases
Inflammatory responses	IL-1 (Interleukin 1)	Inflammation response	Lowers	Increases
	IL-6 (Interleukin 6)	Inflammation response	Lowers	Increases
	CRP (C-reactive protein)	Inflammation response	Lowers	Increases

Long-chain omega-3 fatty acids (EPA and DHA) provide many health benefits with regard to their cardiovascular disease prevention properties and anti-inflammatory effects. This overwhelming intake of omega-6 leads to hyper immune responses and interferes with the proper function of omega-3 fatty acids, causing detrimental effects associated with chronic cardiovascular diseases and inflammatory responses (Table 2).

Ratio recommdations: Due to the opposing effects of omega-3 and omega-6 fatty acids, a healthy diet should contain a balanced omega-6: omega-3 ratio. Human beings evolved eating a diet with an omega-6: omega-3 ratio of about 1:1. Modern Western diets exhibit omega-6: Omega-3 ratios ranging between 15:1 to 17:1. Epidemiology and dietary intervention studies have concluded that while an exceptionally high omega-6: Omega-3 ratio promotes the development of many chronic diseases, a reduced omega-6: omega-3 ratio can prevent or reverse these diseases. For example, a ratio of 4:1 was associated with a 70% reduction in mortality in secondary coronary heart disease prevention and a ratio of 2.5:1 reduced rectal cell proliferation in patients with colorectal cancer. A lower omega-6: omega-3 ratio in women was associated with decreased risk for breast cancer. A ratio of 2:1-3:1 suppressed inflammation in patients with

rheumatoid arthritis and a ratio of 5:1 had a beneficial effect on patients with asthma, whereas a ratio of 10:1 had adverse consequences.

Furthermore, a high omega-6: omega-3 ratio is especially detrimental to carriers of certain genetic variations. For example, minor allele carriers of the APOA5 gene have elevated triglycerides levels and minor allele carriers of 5-lipoxygenase polymorphism in the gene promoter region exhibit increased risk for atherosclerosis. Other gene polymorphisms that are affected by this ratio include CD36 (a cell surface scavenger receptor) and TCF7L2 (a transcription factor). Lowering the omega-6: omega-3 ratio is particularly important for these variant carriers to prevent chronic diseases[7,13,14].

It is important to get omega-3 fats and omega-6 fats in a healthy balance and as close to a 1:1 ratio as possible.

Some other steps that can help this ratio and overall health:

- **Optimize vitamin D and fat soluble vitamins:** Fat soluble vitamins in proper amounts in the body have a protective effect on tissues and organs (including the heart). If you've been on a law-fat diet or used sunscreen all your life, you could be seriously deficient in vitamin D, so consider getting your blood levels tested
- **Get enough omega-3s:** These help balance out the omega-6 to omega-3 ratio in the body and prevent inflammation. Omega-3s also can thin the blood and keep it from clotting too regularly, a risk factor in heart disease. Having a proper omega-3 balance also helps keep triglyceride levels in check
- **Reduce stress and get enough sleep:** High stress levels and lack of sleep can both increase inflammation and stress hormones in the body. Both are also linked to higher levels of many diseases, including heart disease and increased overall mortality

Most Americans, young and old are highly deficient in omega-3 and one of the best things you can do for yourself and your children is routinely consume fish oil in warm months and cod liver oil in cool months[9], as they are high in the best kind of omega-3.

You should cut out or reduce the oils and foods high in omega-6 fats, as Americans get far too much of them. This includes corn, sunflower, soy, canola and safflower oil, margarine, vegetable oil and shortening[10].

Role of flaxseed oil: Intake of omega-3 fats is much lower today because of the decrease in fish consumption and the industrial production of animal feeds rich in grains containing omega-3 fats, leading to production of meat rich in omega-6 and poor in omega-3 fats[15]. The same is true for cultured fish and eggs. Even cultivated vegetables contain fewer omega-3 fats than do plants in the wild. In summary, modern agriculture, with its emphasis on production, has decreased the omega-3 fat content in many foods: Green leafy vegetables, animal meats, eggs and even fish.

One advantage of the consumption of ALA over omega-3 fats from fish is that the problem of insufficient vitamin E intake does not exist with high intake of ALA from plant sources. ALA, found in flax seed oil is the precursor of omega-3 fats can be converted to long-chain omega-3 fats and can therefore be substituted for fish oils. However, ALA is not equivalent in its biological effects to the long-chain omega-3 fats found in marine oils. The EPA and DHA are more rapidly incorporated into plasma and membrane lipids and produce more rapid effects than does ALA. Experimental studies suggest that intake of 3-4 g of ALA per day is equivalent to 0.3 g (300 mg) EPA per day[16]. Relatively large reserves of LA in body fat, as are found in vegans or in the diet of omnivores in Western societies, would tend to slow down the formation of long-chain omega-3 fats like EPA and DHA from ALA[17]. It is known that, oils derived from animal fat are not good for our health due to their high levels of saturated fat and cholesterol and that oils derived from plants are generally good for our health due to their unsaturated fat content. However, not all unsaturated fats are healthy. Many plant seed oils such as flaxseed, sunflower, peanut and corn oil are rich in inflammatory polyunsaturated fatty acids (PUFAs) and devoid of anti-inflammatory PUFAs[14]. On the other hand, some plant seed oils such as canola and olive oil have balanced PUFAs and are considered healthier. Therefore, it is important to distinguish between the types of PUFAs in dietary oils for optimal health.

The problem with today's diet is that not only are people eating much less omega-3, but they are eating large amounts of processed seed and vegetable oils, which are loaded with omega-6 and balancing this ratio is become a challenge for the food industry animal foods are the best sources of the preformed omega-3 fatty acids, EPA and DHA. One more problem today is that animals are usually fed grain-based feeds with soy and corn. This reduces the omega-3 content, so the polyunsaturated fats[18,19] in the meat are mostly omega-6. Therefore, if you can afford it, grass-fed meat is definitely optimal. However, even conventionally raised meat is healthy, as long as it is not processed[16]. Currently omega-3 fatty acid can be found in fish, but unfortunately, many vegetarian consumers find it difficult or too expensive to incorporate fatty fish in the diet on a regular basis. Others are concerned about levels of heavy metals and overfishing. However, the

overwhelming majority of Indians did not take fish oil supplements. How to utilize maximum plant based sources of EPA and DHA and produce maximum amount of omega-3 fatty acids using different methods of fortification and extractions is a major issue. Flaxseed oil can be a better and economic alternate for balancing in omega-3 and omega-6 ratio. In this review, The Importance of flaxseed and Ratio of omega-3 and omega-6 in health balance is discussed. Regular intake of alternative supplementation with the n-3 PUFA recommendation is in all probability insufficiently realized, particularly in inland countries[20]. Plasma and erythrocyte membrane n-3 polyunsaturated fatty acid (PUFA) levels are an important parameter of diet composition as well as a marker of cardiovascular risk and effect of these fortified omega3 fatty acids is also very important to elucidate their potential benefit on health of humans.

CONCLUSION

Chronic diseases are multigenic and multifactorial. Along these lines, it is entirely conceivable that the remedial measurement of omega-3 unsaturated fats will rely on upon the level of seriousness of sickness coming about because of the hereditary inclination. Studies also indicate that the optimal ratio may vary with the disease. An optimized proportion of omega-3 and omega-6 unsaturated fats is more alluring in decreasing the danger of a number of the interminable sicknesses of high commonness in Western social orders and in addition in the creating nations, that are being sent out to whatever remains of the world. Seeking new stable oils and proper ratio of omega-3 and omega-6 blending should be a research point depending on the target oil as well as the application it will be used in. Accumulating evidences suggest that flaxseed is a rich source of natural antioxidants. Thus far, antioxidant potential of flaxseed and their phenolic constituents must have been studied in both *in vitro* and *in vivo* models.

ACKNOWLEDGMENT

The authors are grateful to the HBTI Kanpur for technical help and King George Medical University for general enquiry.

SIGNIFICANT STATEMENT

The purpose of this study is to highlight a quantitative approach for establishing the correct omega- 3: omega-6 ratio that would enable reproducible formulations with oxidation stability.

REFERENCES

1. Lunn, J. and H.E. Theobald, 2006. The health effects of dietary unsaturated fatty acids. Nutr. Bull., 31: 178-224.
2. Simopoulos, A.P., 2008. The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. Exp. Biol. Med., 233: 674-688.
3. Stanley, J.C., R.L. Elsom, P.C. Calder, B.A. Griffin and W.A. Harris *et al*., 2007. UK food standards agency workshop report: The effects of the dietary *n*-6:*n*-3 fatty acid ratio on cardiovascular health. Br. J. Nutr., 98: 1305-1310.
4. Kolanowski, W., F. Swiderski, D. Jaworska and S. Berger, 2004. Stability, sensory quality, texture properties and nutritional value of fish oil-enriched spreadable fat. J. Sci. Food Agric., 84: 2135-2141.
5. Choo, W.S., J. Birch and J.P. Dufour, 2007. Physicochemical and quality characteristics of cold-pressed flaxseed oils. J. Food Compos. Anal., 20: 202-211.
6. Morris, D.H., 2006. Omega-3 fats in flax and fish are similar in many ways. Flaxseed Council of Canada, pp: 1-2. http://flaxcouncil.ca/wp-content/uploads/2015/03/ Fftsheet_ Fish_Flax_R2.pdf
7. Stephan Gyuvanet, 2008. The omega ratio. Whole Health Source Nutrition and Health Science, September, 2008. http://wholehealthsource.blogspot.com/2008/09/omega-ratio.html
8. Kresser, C., 2010. How much ω-3 is enough? That depends on ω-6. May 11, 2010. https://chriskresser.com/how-much-omega-3-is-enough-that-depends-on-omega-6/
9. Kresser, C., 2010. Why fish stomps flax as a source of ω-3. May 5, 2010. https://chriskresser.com/why-fish-stomps-flax-as-a-source-of-omega-3/
10. Angerer, P. and C. von Schacky, 2000. n-3 polyunsaturated fatty acids and the cardiovascular system. Curr. Opin. Lipidol., 11: 57-63.
11. Berbert, A.A., C.R. Kondo, C.L. Almendra, T. Matsuo and I. Dichi, 2005. Supplementation of fish oil and olive oil in patients with rheumatoid arthritis. Nutrition, 21: 131-136.
12. Goldberg, R.J. and J. Katz, 2007. A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. Pain, 129: 210-223.
13. Mori, T.A., 2010. Omega-3 fatty acids and blood pressure. Cell. Mol. Biol., 56: 83-92.
14. Simopoulos, A.P., 2002. The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed. Pharmacother., 56: 365-379.
15. Simopoulos, A.P., 1999. Health effects of omega-3 polyunsaturated fatty acids. http://www.helleniccomserve.com/omega3.html

16. Rohrmann, S., K. Overvad, H.B. Bueno-de-Mesquita, M.U. Jakobsen and R. Egeberg *et al*., 2013. Meat consumption and mortality-results from the European prospective investigation into cancer and nutrition. BMC Med., Vol. 11. 10.1186/1741-7015-11-63.
17. Simopoulos, A.P., 2004. Omega-3 fatty acids and antioxidants in edible wild plants. Biol. Res., 37: 263-277.
18. Ponnampalam, E.N., N.J. Mann and A.J. Sinclair, 2006. Effect of feeding systems on omega-3 fatty acids, conjugated linoleic acid and *trans* fatty acids in Australian beef cuts: Potential impact on human health. Asia Pac. J. Clin. Nutr., 15: 21-29.
19. Micha, R., S.K. Wallace and D. Mozaffarian, 2010. Red and processed meat consumption and risk of incident coronary heart disease, stroke and diabetes mellitus: A systematic review and meta-analysis. Circulation, 121: 2271-2283.
20. Galuszka, J., J. Vostalova, B. Cervena, D. Galuszkova and V. Simanek *et al*., 2015. Omega-3 fatty acid supplementation candidates can be selected using fatty acid profiling. Eur. J. Lipid Sci. Technol., 117: 601-607.