

New FLAX FACTS

METABOLISM OF ALPHA-LINOLENIC ACID

by Dr. Diane H. Morris

Alpha-linolenic acid (ALA) is the true essential omega-3 fatty acid, being required in our diets because our bodies do not make it. ALA has important roles in human health. It dampens inflammation, which is a feature of many chronic diseases like heart disease, stroke and cancer. It is incorporated into cell membranes, promotes the health of blood vessels and is converted to long-chain omega-3 fatty acids. Young women appear to convert more ALA to long-chain omega-3 fatty acids than men do, possibly because of their greater need for omega-3 fats during pregnancy and lactation. The efficiency of ALA conversion by both women and men is affected by diet. Our bodies use ALA to make energy for work and play and to form ketone bodies, which may help preserve cognition in elderly adults. Excess ALA is stored in adipose tissue to meet future energy needs.

Alpha-linolenic acid (ALA) constitutes about 57% of the total fatty acids in flax, making flax one of the richest sources of ALA in the diet.¹ The sections below describe the metabolism of ALA and its roles in human health.

ALA Is the True Essential Omega-3 Fatty Acid

ALA is the parent compound of the omega-3 fatty acid family. It must be obtained from our diets because our bodies do not make it.² In this regard, ALA is an essential nutrient just like vitamin C and calcium.

ALA Is Needed for Good Health

ALA has important biologic effects and helps prevent and manage chronic diseases like heart disease, stroke, type 2 diabetes, kidney disease and certain types of cancer.¹ ALA dampens inflammation, which is a feature of many chronic diseases,³ and it helps promote the proper functioning of blood vessels, which reduces the risk of heart attacks and stroke.⁴

ALA constitutes 75-80% of total omega-3 fatty acids in breast milk, underscoring its importance for infant growth and development.^{5,6} ALA is also required for maintaining the nervous system. A deficiency of ALA in humans causes poor growth, numbness, pain in the legs, difficulty walking and blurred vision.⁷ These deficiency symptoms can be alleviated by adding ALA to the diet.¹

Metabolic Fates of ALA

Dietary ALA has several metabolic fates. The list below describes how ALA is used by the human body.

- **Increases the omega-3 fat content of cell membranes.** ALA is incorporated into the triacylglycerols (triglycerides) and phospholipids of cell membranes, where it affects how nutrients are transferred into and out of the cell and how cells communicate with one another. In one study, healthy men who consumed about 2 tbsps of flax oil daily for 12 weeks showed a 225% increase in the ALA content

and a 150% increase in the eicosapentaenoic acid (EPA) content of red blood cell membranes.⁸ Increasing the omega-3 content of cell membranes makes them more flexible and decreases inflammation.⁹

- **Is converted to long-chain omega-3 fatty acids.** ALA is converted to the long-chain omega-3 fatty acids, particularly EPA and docosapentaenoic acid (DPA).¹⁰
- **Produces energy.** ALA undergoes β -oxidation to produce energy for the work of muscles, the digestion of food, breathing, and the like. About 24-33% of an ingested dose of ALA undergoes β -oxidation in men; in women, the figure is 19-22%.^{1,10}
- **Is used to make ketone bodies.** ALA appears to be preferred over linoleic acid (an omega-6 fatty acid) as a substrate for ketogenesis – the process of making ketone bodies. Ketone bodies serve as an alternate energy source for the brain during starvation or fasting. This function of ALA may be important in maintaining healthy cognition in elderly adults.¹¹
- **Is stored for future energy needs.** ALA is stored in adipose tissue, where it serves as a reserve supply of energy. Women store more ALA in their adipose tissue than men because of their greater fat mass.¹²

ALA Metabolism

The metabolic pathways of the omega-3 and omega-6 fatty acids are shown in the figure below. The discussion that follows focuses on the metabolism of the omega-3 family of fatty acids.

Desaturation and elongation. ALA is converted to long-chain fatty acids by a series of alternating desaturations and elongations. The desaturations add a double bond by removing hydrogen, while the elongations add two carbon atoms.

A more in-depth discussion of the metabolism of omega-3 and omega-6 fatty acids, along with information about their roles in human health, can be found in the Flax Council of Canada's book, *Flax—A Health and Nutrition Primer*. The book is available on the Council's website at www.flaxcouncil.ca

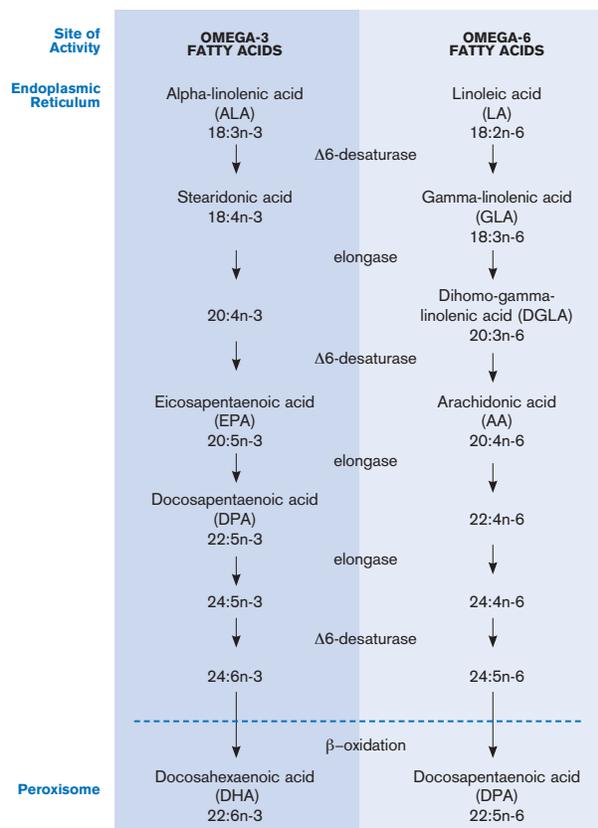
The first step in ALA metabolism is desaturation, catalysed by delta-6-desaturase. This step is considered rate-limiting, as it is most affected by nutritional, hormonal and metabolic factors.¹³

The desaturation and elongation steps occur in the endoplasmic reticulum of the cell. The desaturation steps tend to be slow, while the elongation steps are rapid. For this reason, the tissue concentration of stearidonic acid tends to be low, because it is formed slowly by desaturation and then quickly elongated to other metabolites.¹⁴

Competition between fatty acid families. Mammals cannot interconvert the omega-3 and omega-6 fatty acids. That is, omega-3 fatty acids cannot be changed into omega-6



Metabolic Pathways of the Omega-3 and Omega-6 Fatty Acids*



* The conversion pathway shown is the "Sprecher pathway", which is believed to be the major route. Conversion of DPA to DHA via $\Delta 4$ -desaturase occurs in bacteria and some microorganisms. The exact method by which DHA is moved out of the peroxisome is not known, and the factors that affect its translocation have not been identified. New research suggests that regulation of DHA synthesis may be independent of the other steps in the omega-3 pathway (10).

fatty acids, or vice versa. Furthermore, there is competition between the two families. An excess of one family of fatty acids can interfere with the metabolism of the other, changing their concentrations in tissues and their biological effects.¹⁴

Efficiency of Conversion of ALA. Estimates of the conversion of ALA to EPA range from 0.2% to 8%,^{12,15} with young women showing a conversion rate as high as 21%.¹⁶ Conversion of ALA to DPA is estimated at 0.13% to 6%,¹⁰ with women showing a conversion rate on the higher end (6%).¹⁶

ALA conversion to DHA appears to be limited in humans, with most studies showing a conversion rate of about 0.05%,^{10,17} although one study reported a figure of 4%.¹⁸ Here again, young women appear to convert more ALA to DHA than men do – as much as 9% of ingested ALA may be converted to DHA in young women.¹⁶

Factors Affecting ALA Conversion

Various factors affect ALA's conversion rate. One innovative test tube study of human breast cells found less ALA converted to EPA and DHA when cigarette smoke was bubbled into the growth medium; the enzyme most affected by the concentration of cigarette smoke was delta-5-desaturase.¹⁹ Two other factors affecting ALA conversion – gender and diet – are described below.

Gender. Young women convert more ALA to the long-chain omega-3 fatty acids, possibly because their unique hormonal profile makes them more sensitive to diet than men are. Their greater ability to convert ALA to DHA may be important during pregnancy and lactation.^{20,21}

Diet. A diet rich in linoleic acid decreases ALA conversion by as much as 40%.¹⁸ A high maternal intake of linoleic acid lowers EPA and DHA levels in umbilical plasma, suggesting reduced ALA conversion and availability of omega-3 fatty acids to the developing fetus.²² Saturated fat, oleic acid, *trans* fatty acids, and dietary cholesterol interfere with ALA desaturation and elongation. High intakes of EPA and DHA – and even of ALA itself – can decrease the conversion rate.¹³

ALA Metabolism: What's Needed Now

The fact that ALA conversion to EPA, DPA, and DHA is affected by gender, smoking, and diet suggests that people differ in their metabolic capacity for ALA conversion. Clearly, ALA conversion is more complex than was originally thought. Studies are needed to identify other roles of ALA in human health and determine the diet and lifestyle patterns that enhance ALA conversion to the long-chain omega-3 fatty acids.

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