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RESEARCH NOTES

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Essential Fatty Acids, Minerals, and Desaturase

The dietary supplement industry has produced a great deal of wonderful fatty acid (FA) products. There are omega-3 and omega-6, and combinations of the two. These all started with the initial products such as fish oil, evening primrose oil, and a few others. Over time, other sources of these have been developed. The fatty acids and their metabolism are clearly connected to the maintenance of the health and performance of a great deal of biological systems. There are two essential fatty acids: α -linolenic acid (omega-3 fatty acid) and linoleic acid (omega-6 fatty acid). These two fatty acids cannot be synthesized by the human body. The body cannot convert an omega-3 fatty acid into an omega-6 fatty acid, and vice versa. In nonscientific writing, common usage is that the term essential fatty acid comprises all of the omega-3 and the omega-6 fatty acids.

Omega-3 fatty acids:

- Eicosapentaenoic acid or EPA
- Docosahexaenoic acid or DHA

Omega-6 fatty acids:

- Gamma-linolenic acid or GLA
- Dihomo-gamma-linolenic acid or DGLA
- Arachidonic acid or AA

These fatty acids serve multiple functions, and they are the precursors to prostaglandins,

thromboxanes, prostacyclins, and leukotrienes, and they have a very wide ranging impact on body functions, including, but not limited to: mood, behavior, inflammation and inflammatory response (including white cell response), neuronal, as well as CNS activity.

However, the fatty acids have to be converted from their starting point via a series of enzymatic actions to become their bioactive form, whether it be prostaglandins or thromboxanes. The enzymes most commonly involved in the cascade of reactions surrounding the metabolism of the fatty acids are various desaturase enzymes. There are two desaturase enzymes that have been seen to be most often impaired in certain conditions. They are the delta-5-desaturase and the delta-6-desaturase enzymes. Without proper activity levels of these two enzymes, a wide range of health problems can ensue.

The following abstracts will point out some of the pitfalls resulting from the deficient activity of these two desaturase enzymes.

DIETARY FAT AND INSULIN ACTION IN HUMANS

VESBY B.

BR J NUTR, 2000;83 SUPPL 1:S91-6.

A high intake of fat may increase the risk of obesity. Obesity, especially abdominal obesity, is an important determinant of the risk of developing insulin resistance and non insulin-dependent diabetes mellitus. It is suggested that a high proportion of

fat in the diet is associated with impaired insulin sensitivity and an increased risk of developing diabetes, independent of obesity and body fat localization, and that this risk may be influenced by the type of fatty acids in the diet. Cross-sectional studies show significant relationships between the serum lipid fatty acid composition, which at least partly mirrors the quality of the fatty acids in the diet, and insulin sensitivity. Insulin resistance, and disorders characterized by insulin resistance are associated with a specific fatty acid pattern of the serum lipids with increased proportions of palmitic (16:0) and palmitoleic acids (16:1 n-7) and reduced levels of linoleic acid (18:2 n-6). The metabolism of linoleic acid seems to be disturbed with increased proportions of dihomo-gamma linolenic acid (20:3 n-6) and a reduced activity of the delta-5-desaturase, while the activities of the delta-9 and delta-6-desaturases appear to be increased. The skeletal muscle is the main determinant of insulin sensitivity. Several studies have shown that the fatty acid composition of the phospholipids of the skeletal muscle cell membranes is closely related to insulin sensitivity. **An increase saturation of the membrane fatty acids and a reduced activity of delta-5-desaturase have been associated with insulin resistance.** There are several possible mechanisms which could explain this relationship. The fatty acid composition of the lipids in serum and muscle is influenced by diet, but also by the degree of physical activity, genetic disposition, and possibly fetal undernutrition. However, controlled dietary intervention studies in humans investigating the effects of different types of fatty acids on insulin sensitivity have so far been negative.

A DEFECT IN THE ACTIVITY OF DELTA6 AND DELTA5 DESATURASES MAY BE A FACTOR IN THE INITIATION AND PROGRESSION OF ATHEROSCLEROSIS

DAS UN.

PROSTAGLANDINS LEUKOT ESSENT FATTY ACIDS, 2007 MAY;76(5):251-68.

Atherosclerosis is a dynamic process. Dyslipidemia, diabetes mellitus, hypertension, obesity, and shear stress of blood flow, the risk factors for the development of atherosclerosis, are characterized by abnormalities in the metabolism of essential fatty acids (EFAs). Gene expression profiling studies revealed that at the sites of atherosclerosis-prone

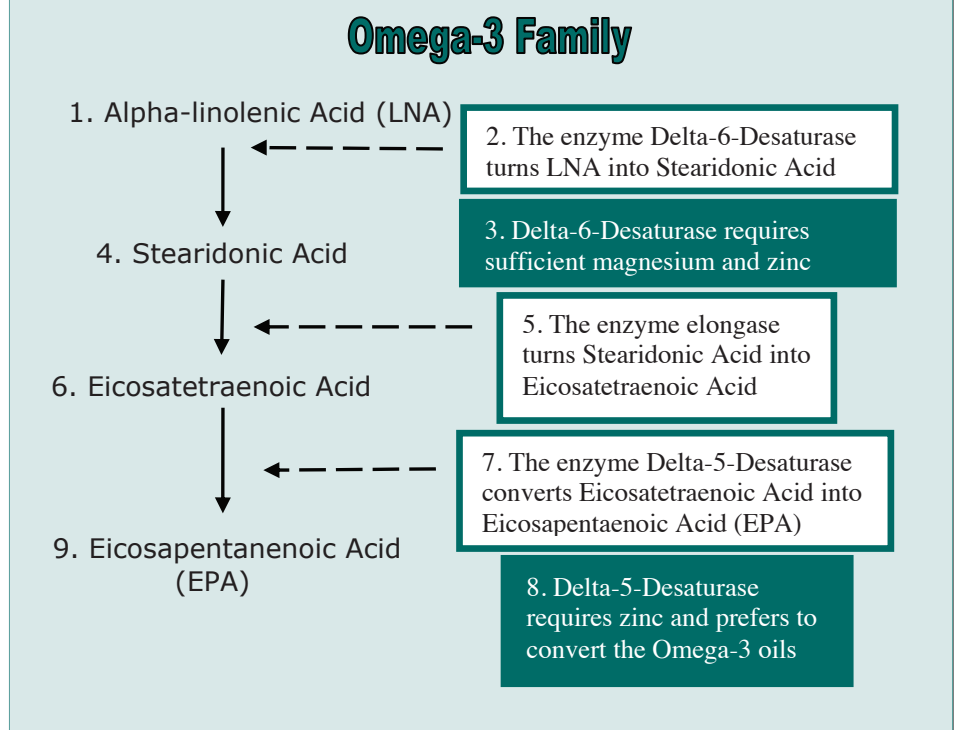
regions, endothelial cells showed upregulation of pro-inflammatory genes as well as antioxidant genes, and endothelial cells themselves showed changes in cell shape and proliferation. Uncoupled respiration (UCP-1) precedes atherosclerosis at lesion-prone sites but not at the sites that are resistant to atherosclerosis. UCP-1 expression in aortic smooth muscle cells causes hypertension, enhanced superoxide anion production and decreased the availability of NO, suggesting that inefficient metabolism in blood vessels causes atherosclerosis without affecting cholesterol levels. Thus, mitochondrial dysfunction triggers atherosclerosis. Atherosclerosis-free aortae have abundant concentrations of the EFA-linoleate, whereas fatty streaks (an early stage of atherosclerosis) are deficient in EFAs. EFA deficiency promotes respiratory uncoupling and atherosclerosis. I propose that a defect in the activity of Delta6 and Delta5 desaturases decreases the formation of gamma-linolenic acid (GLA), dihomog-DGLA (DGLA), arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) from dietary linoleic acid (LA) and alpha-linolenic acid (ALA). This, in turn, leads to inadequate formation of prostaglandin E1 (PGE1), prostacyclin (PGI2), PGI3, lipoxins (LXs), resolvins, neuroprotection D1 (NPD1), NO, and nitrolipids that have anti-inflammatory and platelet anti-aggregatory actions, inhibit leukocyte activation and augment wound healing and resolve inflammation and thus, lead to the initiation and progression of atherosclerosis. In view of this, it is suggested that Delta6 and Delta5 desaturases could serve as biological target(s) for the discovery and development of pharmaceuticals to treat atherosclerosis.

CHANGES OF LINOLEIC ACID METABOLISM AND CELLULAR PHOSPHOLIPID FATTY ACID COMPOSITION IN LLC-PK CELLS CULTURED AT LOW MAGNESIUM CONCENTRATIONS

MAHFOUZ MM, SMITH TL, KUMMEROW FA. *BIOCHIM BIOPHYS ACTA*, 1989 NOV 6;1006(1):70-4.

LLC-PK cells grown on media containing normal (480 microM) or reduced magnesium levels (25, 6.3 or 2.5 microM) were used to study the effect of magnesium deficiency on linoleic acid metabolism and cellular membrane fatty acids. The fatty acid composition of the cellular phospholipids showed a significant decrease in 20:4(n-6) and 22:4(n-6) acids and a significant increase in 18:2(n-6), 18:3(n-6) and 20:3(n-6) fatty acids in magnesium-deficient cells compared to magnesium-sufficient cells. When [1-14C] linoleic acid was incubated with control (480 microM Mg²⁺) or magnesium deficient cells (2.6 microM Mg²⁺) the rate of tetraenoic acid synthesis (20:4(n-6) + 22:4(n-6)) was significantly reduced in magnesium-deficient cells, indicating that the metabolic conversion of 18:2(n-6) to 20:4(n-6) is impaired in magnesium deficiency. This reduction in conversion may be due to the impairment of either the delta5- or the delta6-desaturase, or both. This study shows that magnesium deficiency perturbs essential fatty acid (EFA) metabolism and decreases

Figure 1.



the cellular membrane polyunsaturated fatty acid (PUFA) content. These alterations are likely to have adverse effects on cellular membrane properties and functions.

EFFECT OF MAGNESIUM DEFICIENCY ON DELTA6 DESATURASE ACTIVITY AND FATTY ACID COMPOSITION OF RAT LIVER MICROSOMES

MAHFOUZ MM, KUMMEROW FA. *LIPIDS*, 1989 AUG;24(8):727-32.

Experimental Mg²⁺ deficiency was induced in a group of rats by feeding them a Mg²⁺ deficient diet for 23 days. They were pair-fed to compare with a control group of rats fed a Mg²⁺-sufficient diet. In the Mg²⁺-deficient group the plasma total cholesterol and triglyceride levels were increased while HDL-cholesterol was decreased. In the Mg²⁺-deficient group the plasma level of thiobarbituric acid reacting substances (TBARS) used as a measure for lipid peroxidation was increased. The increase was attributed to the increased cytosolic (Ca²⁺ in Mg²⁺-deficiency which can cause: 1) increase of hydro and endoperoxide levels as a consequence of the increase of arachidonic acid release and eicosanoid synthesis in Mg²⁺-deficiency, and 2) inhibition of the mitochondrial respiratory activity and activation of Ca²⁺-dependent proteases which may activate the conversion of xanthine dehydrogenase to xanthine oxidase which generates active O₂ species. In the Mg²⁺-deficient group, the fatty acid composition of the liver microsomes indicated a slower rate of conversion of linoleic acid to arachidonic acid which was consistent with the decrease of delta6 desaturase activity in liver microsomes

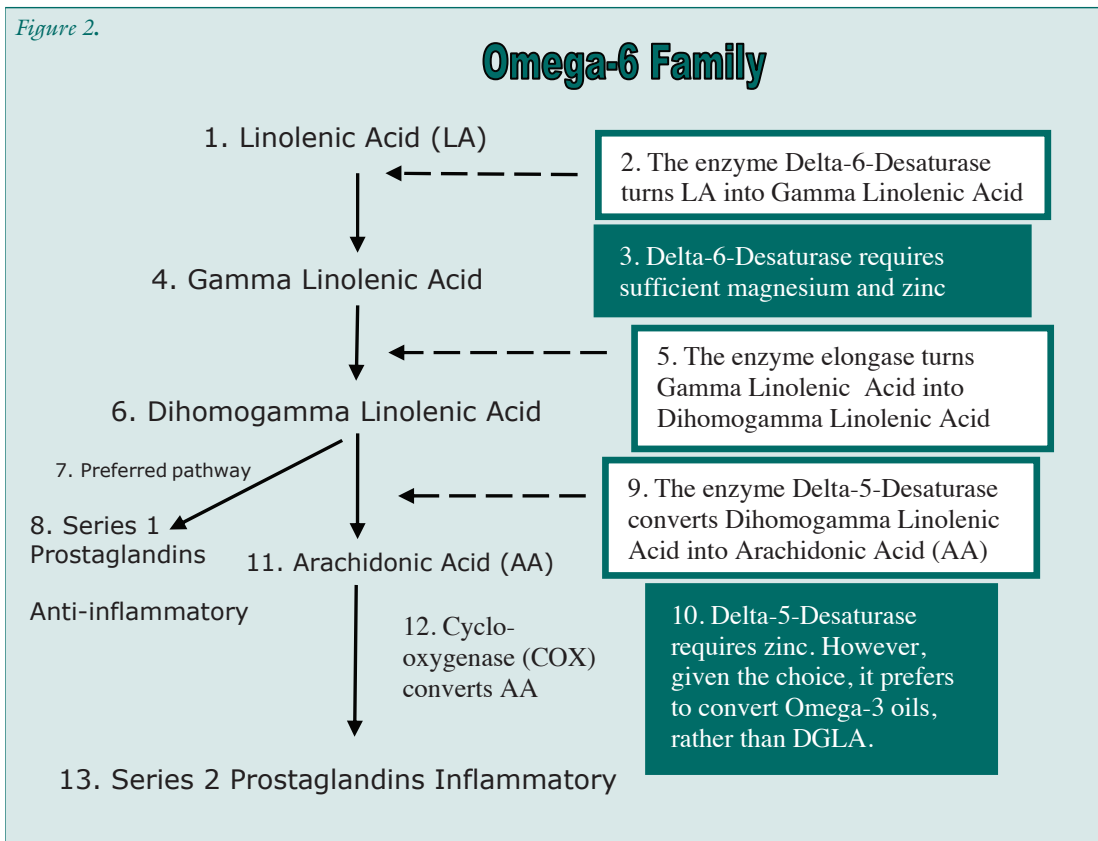
of Mg²⁺-deficient rats as measured in vitro. The decrease of delta6 desaturase activity was attributed to the lower concentration of actual enzyme molecules as a result of the decreased rate of protein synthesis in Mg²⁺-deficiency. The possible effects of the increased catecholamine release in Mg²⁺-deficiency are discussed.

EFFECTS OF ZINC DEFICIENCY AND CASTRATION ON FATTY ACID COMPOSITION AND DESATURATION IN RATS

CLEJAN S, CASTRO-MAGANA M, COLLIPP PJ, JONAS E, MADDAIAH VT. *LIPIDS*, 1982 MAR;17(3):129-35.

The effects of zinc deficiency and testosterone on fatty acid composition of plasma lipids and microsomes of liver, intestine and testes were studied. The activities of fatty acid desaturase (delta6 and delta5) in rat liver and testes were also measured. A significant decrease in the level of arachidonic acid was observed in plasma of normal rats fed the zinc-deficient diet. Castration significantly decreased arachidonic acid but increased 20:3 fatty acid, which is negligible in normal rats. Testosterone and zinc administration restored arachidonic acid to normal values. Zinc deficiency does not significantly change the fatty acid profile in liver, but castration decreased both arachidonic and 22:6 fatty acid. Intestinal mucosal microsomes showed that the predominant fatty acid in this tissue, palmitic acid, is independent of zinc status, whereas polyunsaturated fatty acids 18:2 and 20:4 were decreased by zinc-deficient diet or castration. Zinc deficiency sharply decreased 22:5 fatty acid and to some extent, other polyunsaturated fatty acids in testis microsome. These

Figure 2.



(2007) 61, 54-60) further supports the effect that magnesium glycinate chelate can have on the production of anti-inflammatory benefits for asthmatics. Magnesium glycinate chelate supported the production of the PGE 1 and PGE3 series, which are important in helping improve lung function in asthma. The Canadian Asthma Prevention Institute has stated on its website that magnesium and zinc are critical to the function of the desaturase enzymes, delta5 and delta-6. Specifically, magnesium and zinc are needed for proper delta-6 desaturase activity, and zinc is critical to delta-5 desaturase activity.

changes in fatty acids are in agreement with increased delta9 desaturation and decreased delta5 desaturase activity. In testes, both delta6 and delta5 desaturase activities are decreased in zinc deficiency. It appears that zinc influences the conversion of linoleic to arachidonic acid, whereas testosterone influences delta6 desaturase activity. The data suggest that zinc deficiency may be one of the important factors in the causation of polyunsaturated fatty acid deficiency, which, in turn, may induce serum hypertriglyceridemia.

acid metabolic pathways to flow in a healthy pattern: delta-5 desaturase and delta-6 desaturase. Figures 1 (omega-3 fatty acid family) and 2 (omega 6 fatty acid family) depict where in the metabolism of the essential fatty acids, these two enzymes exert their impact. As we have seen here as well, magnesium and zinc are key to the activity of these two desaturase enzymes. If one is deficient in either or both of these minerals, the desaturase enzyme activity level will come to a halt at stages in the metabolism far too early for there to be effective production of the prostaglandins, thromboxanes, prostacyclins, leukotrienes, and other bioactive factors. This disruption is what has caused a large increase in many diseases - the so-called diseases of civilization - that heavily involve the inflammatory processes. Inflammatory processes are involved in hypertension, atherosclerosis, diabetes mellitus, arthritis, inflammatory bowel disease, infectious diseases and others. A recent study (Gontijo-Amaral, et al, EJCN

The creation of supplements containing omega-3 and omega-6 fatty acids is a healthy idea, but to ensure that you get the full benefits possible with the supplementation of these fatty acid products, you must be sure that magnesium and zinc are part of the formula.

Recent studies on the bioavailability of different magnesium and zinc compounds have showed that Albion's magnesium and zinc TRAACS mineral ingredients are much better absorbed than the non-chelate forms.

Trends seen for EFA's, Desaturase Activity, and Minerals

The fluid or healthy cascade of reactions for the omega-3 and the omega-6 fatty acids is needed to maintain a large amount of bodily functions. A disruption of any of these can result in a health disorder or disease. As just evidenced in the abstracts rendered here, the disruption of the metabolism of the fatty acids can lead to insulin resistance (diabetes mellitus), atherosclerosis, and faulty cellular membrane functions. Two of the critical desaturase enzymes are needed for the fatty

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