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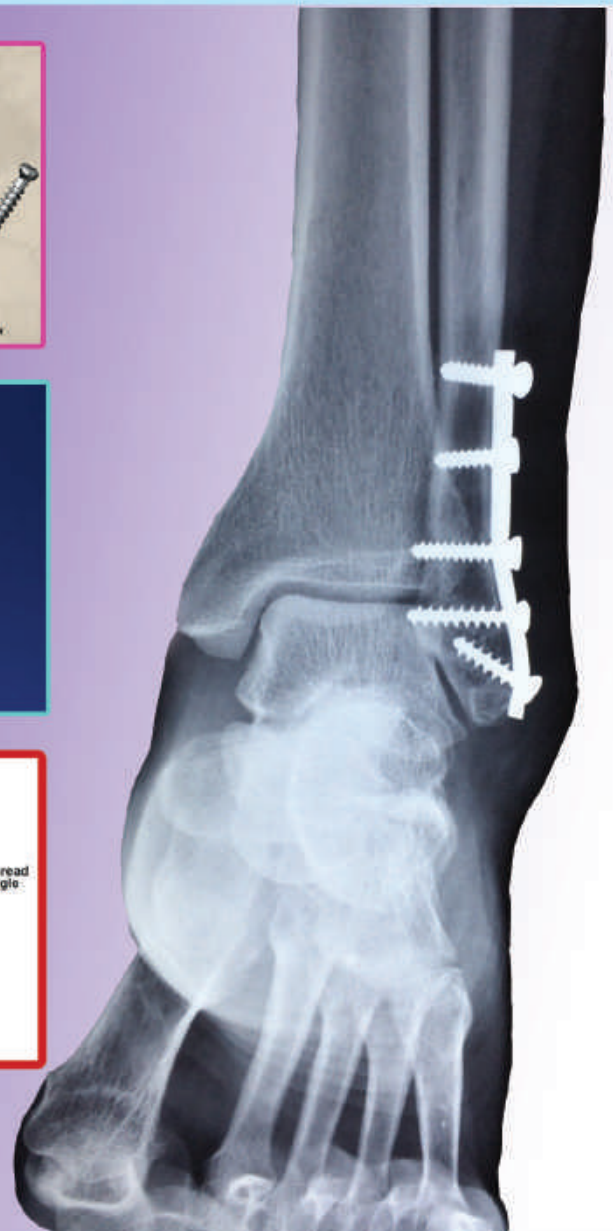
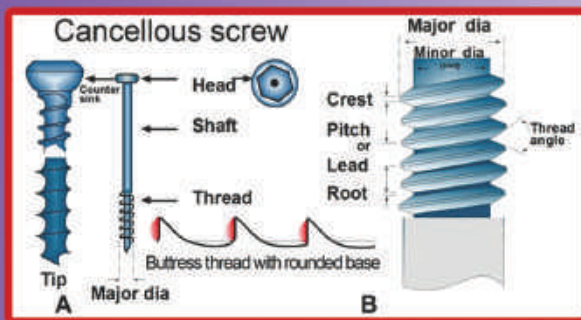
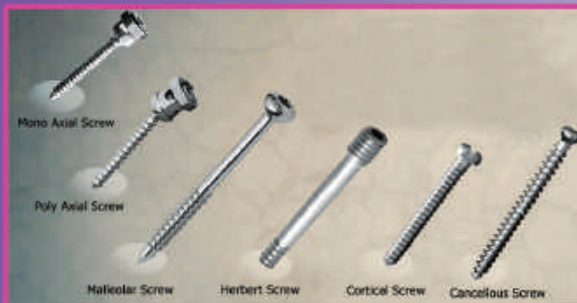
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## Biodegradable Bone Screws

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# Omega 3 fatty acids as GRAS!

**SANJAY AGRAWAL, SHANAZ KHAN**

They belong to poly-unsaturated fatty acids. The important among them are n-3 fatty acids (or omega-3 fatty acids) and n-6 fatty acids (or omega-6 fatty acids). The word Omega refers to the methyl end of the molecule, and the number following indicates the position of the double-bond closest to that end of the chain.

Important nutritionally-essential n-3 fatty acids are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). The human body cannot synthesize n-3 fatty acids de novo, but it can form 20- and usmical analogues that are derived from linoleic acid. Both the n-3  $\alpha$ -linolenic acid and n-6 linolenic acid are essential nutrients which must be obtained from food. Synthesis of the longer n-3 fatty acids from linolenic acid within the body is competitively slowed by the n-6 analogues.

## The n-6 to n-3 ratio:

Clinical studies indicate that the ratio of n-6 to n-3 fatty acids in diet is important to maintaining proper health. n-3 and n-6 compete for the same metabolic enzymes, thus the n-6:n-3 ratio will significantly influence the ratio of the ensuing eicosanoids (hormones), (e.g. prostaglandins, leukotrienes, thromboxanes etc.), and will alter the body's metabolic function. Metabolites of n-6 are

significantly more inflammatory (esp. arachidonic acid). In contrast eicosanoids made from n-3 fats are often anti-inflammatory rather than inflammatory. This necessitates that n-3 and n-6 be consumed in a balanced proportion. Healthy ratios of n-6:n-3 range from 1:1 to 4:1. Studies suggest that the evolutionary human diet, rich in nuts, seeds, grains, fruits and wild fish and meat may have provided such a ratio. In contrast typical Western diets provide ratios of between 10:1 and 30:1 - i.e., dramatically skewed toward n-6. This change in omega fatty acids consumption is one of the major contributors of many chronic diseases. This is important considering the balance of n-6 and n-3 in body tissues like the brain it is 1:1, in body fat it is 5:1 and in other body tissue it is 4:1.

Further, the conversion of ALA to EPA and then to DHA in humans is limited making the direct supplementation of EPA and DHA more important in deficiency states.

Omega-3 fatty acids are considered essentials as they are necessary for human health, but can't be synthesized by body itself. So we depend on external sources for it. Omega-3 fatty acids are found in fish, such as salmon, tuna, and halibut, other sea-foods including algae and krill, some plants, and nut oils. Also known as polyunsaturated fatty acids (PUFAs), omega-3 fatty acids play a crucial role in brain function, as well as normal growth and development. They are gaining popularity as they may reduce the risk of heart disease.

Research shows that omega-3 fatty acids reduce inflammation and may help lower risk of chronic diseases such as heart disease, cancer, and arthritis. Omega-3 fatty acids are highly concentrated in the brain and appear to be important for cognitive (brain memory and performance) and behavioral function. In fact, infants who do not get enough omega-3 fatty acids from their mothers during pregnancy are at risk for developing vision and nerve problems. Symptoms of omega-3 fatty acid deficiency include fatigue, poor memory, dry skin, heart problems, mood swings or depression, and poor circulation.

Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs) with a double bond at the third carbon atom from the end of the carbon chain. The three types of omega-3 fatty acids involved in human physiology are  $\alpha$ -linolenic acid (ALA) (found in plant oils), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) (both commonly found in fish oil that originally come from microalgae that is further consumed by phytoplankton, a source of diet for fish). Omega-3 fatty acids play a critical role in metabolism and cellular function and they are available as daily supplements.

## EPA and DHA: Health benefits-

Eicosapentaenoic acid and Docosahexaenoic are important omega-3 fatty acids in the body. They help balance the inflammatory omega-6 fatty acids and thus controls inflammation and limit the damages to the

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body. They are important in brain development, nervous system and retinal functions. They form the smooth lipid part of cell wall as organ wall structures and are important in maintaining proper elasticity of vascular structures. Their role in healthy lipid profile and atherosclerosis prevention has been proven clinically. They have positive effects on all parts of our body as they are important for formation of hormones and neurotransmitters in required amounts.

Many trials have correlated EPA and DHA deficiencies in different disorders. Several neurological/behavioral disorders have been suggested to be associated with depressed levels of DHA or DHA plus EPA combined. These include the neurological disorders of depression (including post-partum depression), Alzheimer's disease, behavioral disorders such as Attention Deficit Hyperactivity Disorder (ADHD) and hyperactivity, as well as developmental coordination disorder. Chronic inflammatory conditions such as rheumatoid arthritis, certain skin disorders, gastrointestinal disorders (Inflammatory Bowel Disease, Crohn's disease) have been found to be improved in a large number of studies to varying degrees with DHA plus EPA supplementation when added as a complementary intervention to standard pharmaceutical treatment regimens. Population studies have also revealed apparent benefits of consuming fish containing DHA plus EPA in a wide variety of conditions including chronic eye conditions (cataracts, dry eye), epilepsy, allergic sensitivity in very young children, pneumonia, lung/breathing capacity and chronic pulmonary disorders, plus other conditions recently

reported including bone health, fibromyalgia, etc.

Omega 3 Fatty acids can be used in High cholesterol, High blood pressure, Heart disease, Diabetes, Rheumatoid arthritis, Systemic lupus erythematosus (SLE), Osteoporosis, Depression, Bipolar disorder, Schizophrenia, Attention deficit/hyperactivity disorder (ADHD), Cognitive decline, Skin disorders, Inflammatory bowel disease (IBD), Asthma, Macular degeneration, Menstrual pain, Colon cancer, Breast cancer, Prostate cancer.

Omega-3 fatty acids broken down triglycerides into smaller fatty acid units. They act to reduce plasma triglyceride levels, however increase the cholesterol levels and are thought to possess potent anti-arrhythmic effects. Polyunsaturated fatty acids including eicosapentaenoic and docosahexaenoic acid mediate important cellular function such as inhibition of platelet function, prolongation of bleeding time, anti-inflammatory effects and reduction of plasma fibrinogen. Polyunsaturated fatty acids are components of the phospholipids that form the structures of the cell membranes and also serve as energy source. They form eicosanoids which are important signalling molecules with wide-ranging functions in the body's cardiovascular, pulmonary, immune and endocrine systems. Docosahexaenoic acid tends to exist in high concentrations in the retina, brain (via uptake by Mfsd2a as a transporter), and sperm.

Alpha Linoleic Acid, docosahexaenoic acid and eicosapentaenoic acid are metabolized and oxidized in the liver, which is the site of biosynthesis of n-3 fatty acid

intermediates, synthesizing Very low density lipoprotein (VLDL) that transport fatty acids in the plasma to tissues. Major enzymes that generate lipid signalling molecules from docosahexaenoic acid, eicosapentaenoic acid, Alpha Linoleic Acid are lipoxygenases and cyclooxygenase.

After ingestion, dietary lipids are hydrolyzed in the intestinal lumen. The hydrolysis products—monoglycerides and free fatty acids—are then incorporated into bile-salt-containing micelles and absorbed into enterocytes, largely by passive diffusion. The absorption rate is about 95%. Within intestinal cells, free fatty acids are primarily incorporated into chylomicrons and enter the circulation via the lymphatic system where they are delivered to various tissues for metabolism, oxidation and storage.

Omega-3 fatty acids mediate anti-inflammatory effects and increased levels of docosahexaenoic acid and eicosapentaenoic acid has shown to decrease the levels of ProstaglandinE2 and 4 series-LT. Eicosapentaenoic acids compete with constitutive levels of arachidonic acid in cell membranes for the same desaturation enzymes and produce 3-series prostaglandins and thromboxanes, and 5-series leukotrienes which have low pro-inflammatory potential. The alteration in leukotriene biosynthesis due to higher concentration of omega-3 fatty acids compared to arachidonic acid underlies the anti-inflammatory effects. Docosahexaenoic acid and eicosapentaenoic acid also give rise to resolvins and related lipid signalling molecules such as protectins via cyclooxygenase and lipoxygenase pathways, which have anti-inflammatory effects.

They inhibit trans endothelial migration of neutrophils and inhibit TNF and IL-1 $\beta$  production. Omega-3 fatty acids also decrease adhesion molecule expression on leukocytes and on endothelial cells and decrease intercellular adhesive interactions. Omega-3 (or n-3) polyunsaturated fatty acids (PUFAs) and their metabolites are natural ligands for peroxisome proliferator-activated receptor (PPAR) gamma that regulates inflammatory gene expression and NF $\kappa$ B activation. Peroxisome proliferator-activated receptor alpha activation is also associated with induction of Cyclooxygenase-2 expression. The role of docosahexaenoic acid and eicosapentaenoic acid in reducing triglyceride levels include inhibition of acyl-CoA:1,2-diacylglycerol acyltransferase, increased mitochondrial and peroxisomal-beta-oxidation in the liver, decreased lipogenesis in the liver, and increased plasma lipoprotein lipase activity. They also may reduce triglyceride synthesis because they are poor substrates for the enzymes responsible for Triglyceride synthesis, and docosahexaenoic acid and eicosapentaenoic acid inhibit esterification of other fatty acids.

#### **EPA and DHA in pregnancy and lactation:**

Omega-3 fatty acids, particularly DHA are essential constituents of brain and retina of the new born baby. Omega-3 fatty acids make up 70% of the total brain mass. Omega-3 fatty acids supplements during pregnancy and nursing are brain food for baby. Further maternal supplementation of EPA and DHA has been shown to reduce complications like low birth weight, preterm delivery, postpartum depression and developmental problems in newborns.

In a study of nearly 9,000 pregnant women, researchers found women who ate fish once a week during their first trimester had 3.6 times less risk of low birth weight and premature birth than those who ate no fish. Low consumption of fish was a strong risk factor for preterm delivery and low birth weight.

The American Heart Association has recommended two fatty fish servings per week for people who are healthy individuals without cardiovascular disease. The DHA plus EPA (combined) equivalency of such fish consumption is approximately 250-300 mg/day. The NIH Workshop recommended a daily intake of 650 mg of DHA plus EPA for normal healthy individuals (for overall health and cardiovascular care)

#### **Conclusion:**

The industry players that as a whole the Indian omega-3 market is not performing upto expectations due to the lack of promotional activities to make consumers aware of health benefits associated with the intake of omega-3 fatty acids. Indian market for omega-3 polyunsaturated fatty

acid (PUFAs) ingredients is in growth stage of its lifecycle. Omega-3 fatty acids have been used in food fortification and dietary supplements from a long period in India. Consumer awareness of omega-3 health benefits and rising disposable income, especially in urban areas of the country, will lead the market growth in the future. Dietary supplements sector is the largest consumer of omega-3 ingredients in terms of volume and value, followed by food and beverage fortification sector. Pharma and clinical nutritional applications are yet to be developed in the Indian omega-3 market. There are no side effects, for example; do you think about side effects before eating a piece of salmon? I didn't think so. Taking a fish oil supplement is no different than just eating fish. So, for the average healthy person, it's completely safe.

**Generally recognized as safe (GRAS)** is a (FDA) designation that a chemical or substance added to food is considered safe by experts, and so is exempted from the usual (FFDCA) tolerance requirements. Omega-3 Fatty Acid is recognized as GRAS. ❖

Disorders that affect bone marrow can be divided into following categories: Reconversion due to hyperplasia, Marrow infiltration or replacement disorders, Depletion of hematopoietic marrow, Depletion of myeloid elements with fibrosis and Deposition of metabolic products.

#### **Journal of The Association of Physicians of India**

Levothyroxine taken at bedtime improved thyroid hormone level. Serum lipid levels showed no significant change with bedtime versus morning intake. Clinicians may consider prescribing levothyroxine at bedtime as an alternative to the conventional morning dose.

#### **Thyroid research & practice**