Future of Omega 3 in Nutrition

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ABSTRACT

In this article we review the international recommendations for n-3 fatty acid (omega 3) oral supplement and their rule in enteral nutrition formulas. The metabolic action of omega3 depends on its metabolism to DHA and EPA. Also the activity of desaturases that stimulate this process increases with insulin, exercise, peroxisome proliferators and oestrogens in the fertile women, While it reduce with oligoelements and protein deficiencies, fasting, sedentary lifestyle, age <30 years, cigarette smoking, cholesterol, alcohol, trans and saturated fatty acids, stress hormones (adrenaline and glucocorticoids) and insulin deficiency. Most of strategy recommends 20-30% of general energy must come from fat, 8-11% come from saturated fat, 7-9 % polyunsaturated and 15-20 come from monosaturated fat. The recommended daily intake of n-3 fatty acid is 0.5-2 gram or 0.5-2 % of entire caloric ingestion with a maximum limit of 3 grams daily. While for n-6 fatty acid the recommendation is 2.5-8 % of entire caloric ingestion. The DHA and EPA content should be minimum 500/Day and the EPA/DHA ratio is 2:1 in the majority of them. The formulas of nutrition standard present a suitable content in fats, but the majority of products containing EPA and DHA exceed the limit of 3 g/day. Some of formulas that are designed for the weak elderly people did not include EPA or DHA, and if include them, their concentration either too much or with a percent that different from the percentage which is found in oil of fish.

Keywords: Omega 3 fatty acids. EPA. DHA.

Introduction

The fatty acid (FA) is natural lipid molecules having a terminal carboxyl group bound to a hydrocarbon chain. They can be classified in different ways depending on the number of carbon atoms in the chain or by the number of double bonds present. Of all these, it is well known that the polyunsaturated Fatty Acid (PUFA)(Goodnight, Harris, Connor, & Illingworth, 1982), i.e. those containing two or more double bonds in the chain and play an
important role in our body. There are two main families of PUFA: omega-3 (n-3) and omega 6 (n-6). Although it is structurally and functionally different families, both are very interrelated metabolic pathways, as we will review later. In this review we focus on n-3 FA. The human body synthesizes many nonessential called Fatty Acid, but another to be incorporated through the diet, since the body is unable to synthesize, for what are known as essential, George and Mildred Burr, in 1929, found that feeding rats a diet lacking in fat produced very poor growth of the animals, severe dermatitis, and loss of fur, wasting and sometimes death. It was not clear until 1963 when Hansen and his colleagues demonstrated the clear need for the contribution of certain fatty acid in diet in human (A Valenzuela & Uauy, 2005).

The FA n-6 and n-3 are very important to maintain the structure of cell membranes, facilitating the absorption of fat soluble vitamins and regulate cholesterol metabolism, which makes them play a major role in the development of the nervous system and vision. Moreover, in recent years has increased scientific interest in relation to its ability to produce eicosanoids (prostaglandins, prostacyclins, leukotrienes, and thromboxanes) and the regulation of many cellular processes including control of vascular homeostasis, blood coagulation and inflammatory phenomenon (Kelley, 2001). The interest in the study of n-3 FA emerged from the 70 after observing Dyberg Bang and those detected in the Greenland Eskimo population low mortality from cardiovascular disease despite a diet rich in fats. The authors proposed a diet rich in n-3 from a marine source (fish, seals and whales) as a cause of this finding (Bang, Dyerberg, & Nielsen, 1971). Since then, numerous experimental studies, epidemiological and interventional studies have shown that eating a diet rich in n-3 FA reduce coronary mortality and sudden cardiac death, and in the geographical areas where they predominate in the n-3 FA diet incidence cardiovascular disease decreases. It has been shown that n-3 FA have antiarrhythmic properties, antiatherogenic, antithrombotic and anti-inflammatory (Bang et al., 1971; Caballero et al., 2006).

Certain underlying chronic inflammatory diseases could then be amenable to treatment with n-3 FA. Pathologies would emphasize as Crohn's disease, ulcerative colitis, acute pancreatitis, rheumatoid arthritis, asthma, cystic fibrosis and Alzheimer's disease (Mesa Garcia, Aguilera Garcia, & Hernández, 2006). Moreover, the importance of increased ratio n-6/n-3 repeatedly been studied in recent years. In industrialized society is an increase in the consumption of refined carbohydrates, saturated fats, n-6 FA and trans fats, while decreasing that of n-3 FA, slow absorption’s carbohydrates and fibre. This has meant that while the n-6/n-3 ratio in industrialized countries is 15-20/1, the wild animals and we assume of prehistoric man is 1/1 (Nutrition, 1985).

This change in the pattern of FA consumed has led to the increased prevalence of chronic diseases such as atherosclerosis, essential hypertension, obesity, diabetes mellitus, arthritis and some autoimmune diseases as well as different types of cancers, including breast, colon and prostate (Gómez Candela, Bermejo López, & Loria Kohen, 2011).

The potential clinical benefit of this type of FA in a large amount of pathologies has led to increased interest in the composition of these nutrients in the specific enteral nutrition formulas (Abilés, 2006). The next part will assess the n-6/n-3 ratio rather than the total
composition of n-3 FA in the recent studies. And finally, in the last part we reviewed the contribution of EPA and DHA in these enteral nutrition products.

**Enzymes and factors affecting the metabolism of LA and ALA**

Both linoleic acid (LA) and α-linolenic acid (ALA) are essential FA, i.e., humans cannot synthesize by itself. Once ingested, can metabolize leading to other fatty acids with a higher degree of unsaturation and chain larger and because of that it's called long-chain PUFA. Thus, the LA is the precursor of arachidonic acid (AA) while ALA is the eicosapentaenoic acid (EPA). FA competes for these enzymes responsible for the desaturation process (D5 and D6 desaturase) and lengthen the charge of the hydrocarbon chain (elongases). The highest level of competition enzyme occurs in AA and EPA. Although the two synthetic routes long chain PUFA use the same enzyme, no cross-reactions between them. It is known that this enzyme is quite an inefficient conversion, particularly in regard to the production of DHA (Qi, Hall, & Deckelbaum, 2002). Specifically, it is estimated that the efficiency of conversion of ALA to EPA is 0.2%, DPA n-3 0.13% and DHA 0.05% (Pawlosky, Hibbeln, Novotny, & Salem, 2001).

LA, through D6 desaturase leads to γ-linolenic acid, which through an elongase produced dihomo-γ-linolenic acid (DHGL). This is desaturated by the action of the D5 desaturase to form AA. AA by different enzymatic reactions elongation and desaturation β last step oxidation becomes docosapentaenoic acid (DPA n-6). Meanwhile, ALA, through D6 desaturase leads to stearidonic acid, which by the action of the elongase is transformed into eicosatetraenoic acid. This, in turn, by the action of D5 desaturase produce EPA. The EPA, by an elongase, becomes docosapentaenoic acid (DPA), which by various enzymatic reactions gives rise to docosahexaenoic acid (DHA). DHA peroxosomal oxidation is reduced again to EPA. All of these enzymatic reactions take place in the endoplasmic reticulum with the exception of the final DHA forming reaction that occurs in the peroxisome. ALA intake increases the levels of EPA and DPA n-3. However, minimally influences the DHA. Besides, if this is ALA intake chronically raised, there is an increased conversion to EPA, with an increase in plasma levels of EPA and cellular deposits. However, the degree of conversion to DHA is insufficient to increase the concentration of the FA and DHA levels decrease can reach (Burdge & Calder, 2005a). The Figure 1 summarizes the metabolism of LA and ALA.
These n-3 FA mainly DHA, are incorporated into the phospholipids of cell membranes as structural components, such as the brain or the sperm and as part of retinal tissues so that it is essential in the development of optimal visual function, reproduction and brain. The amount of PUFA in cell membranes (primarily AA and DHA) is maintained by a feedback mechanism which has its own pathway (Mesa Garcia et al., 2006). EPA is produced as a results metabolite of ALA, DHA. However, when the applicable EPA diet, ends up producing eicosanoids. These eicosanoids antagonize the action of the AA-derived eicosanoids. In addition, also have an effect in lowering triglyceride levels, cholesterol, vasodilation and antithrombotic effects.

The D6 desaturase is the first rate-limiting step in the metabolic pathway (Sprecher, 1981). Its activity, coupled with the D5 desaturase and producing long chain PUFA, is regulated by multiple factors (M. Nakamura & Nara, 2003) is interesting to study these factors and has been described that the desaturase activity was associated with the development of cardiometabolic disease, such as myocardial infarction (Öhrvall et al., 1996) or metabolic syndrome (Warensjö, Risérus, & Vessby, 2005).

In another article in Warensjo et al. (Warensjö, Öhrvall, & Vessby, 2006) quantifies the risk of developing overweight by changes in enzyme activity: it was found that for each standard deviation increase in the activity of D9 and D6, the risk of developing overweight increased by 60%. By contrast, each standard deviation increase D5 activity reduced the risk of a 30% overweight. Significantly, the difficulty of calculating desaturase activity in humans, so that multiple studies have estimated the activity of these enzymes estimated using a product ratio FA / and its precursor. Estimated activity D5 desaturase is usually expressed as the ratio AA / DHGL while D6 estimated activity of desaturase is expressed as acido-γ-linoleic /LA (Metz,
Among the factors that affect the activity of these enzymes include the following:

**Dietary fat intake**

It is well known that both the quantity and the quality (especially the quality) of the fats we eat daily have an effect on the development of cardiovascular, endocrine and metabolic diseases. But in turn, this affects dietary fat significantly in enzyme activity. Already Garg et al. (Garg, Snoswell, & Sabine, 1986) in the 80 pointed to the decline of this activity in high-fat diets and later Huang et al. (Huang, Mills, Ward, Simmons, & Horrobin, 1990) with cholesterol intake. Various studies indicate that the Δ6 desaturase activity is induced by diets low in essential fatty acids while decreasing with diets rich in vegetable or marine oils (M. T. Nakamura & Nara, 2004). Moreover, the increased intake of trans fatty acids and higher n-6 FA also reduce this activity, as does the DHA itself. However, when n-3 FA is supplied, a reduction in the activity of Δ6 desaturase and Δ5 increased associated with increased plasma EPA and DHA (Vessby, GUSTAFSSON, Tengblad, Boberg, & Andersson, 2002). In an intervention study published by Waren sjö E. et al. (Warensjö et al., 2008) observed an increase in the estimated activity of Δ6 desaturase and a low estimate of Δ5 desaturase activity in this group of individuals following a diet rich in saturated fatty acids compared to those who ate a diet rich in unsaturated FA. This change in enzyme activity has been linked to the development of metabolic syndrome (Warensjö et al., 2006). The synthesis of n-3 FA from ALA is more effective when the intake is rich in saturated fatty acids and low in LA. This author was the first to show the change in desaturase activity estimated by the quality of the fat eaten. Overall inhibit the action of both desaturases saturated fats, cholesterol and trans fats (Brenner, 1981; Mozaffarian et al., 2004). Intake of n-3 and n-6 FA produce a counter-regulatory mechanism of liver desaturases (M. T. Nakamura & Nara, 2004).

**Nutritional factors**

The deficits of some trace elements such as iron, zinc, copper and magnesium, which can be observed in situations of malnutrition, reduce the activity of the Δ6 desaturase and secondly the formation of long-chain PUFA (Seiliez, Panserat, Kaushik, & Bergot, 2001). Pyridoxine, zinc, nicotinic acid and magnesium are co-factors for the action of Δ6 desaturase, so deficits are associated with a decreased activity. The total fast, the deficient protein intake and glucose diet reduce the activity of desaturase, while the partial caloric restriction stimulates its activity. (Brenner, 1981).

**Endocrine factors**

In diabetic patients has detected a decrease in Δ5 desaturase activity (M. T. Nakamura & Nara, 2004) and Δ6 desaturase (M. T. Nakamura & Nara, 2004). In particular, several authors have detected this decrease in enzyme activity (particularly the 5Δ desaturase) in type 1 diabetic patients and the restoration of this activity with the onset of insulin therapy (El Boustan et al., 1989; TILVIS & MIETTINEN, 1985). Also in those patients with poor control, such as when the patient is in a state of ketosis, this decrease is continued (Bassi et al., 1996). However, these findings described in patients with type 1 diabetes mellitus are
opposite to those found in patients with type 2 diabetes. In these patients, this desaturase activity increases (Sartore et al., 2008) and following the start of the insulinization not altered its activity (Vessby et al., 2002). Also another study have been reported that 5 desaturase activity correlates positively with the values of glycated haemoglobin in situations of poor metabolic control, but is not correlated if there is a good metabolic control (Sartore et al., 2008). The interest in studying the activity of this distress is defined by its possible role in the development of insulin resistance in both human studies and animal (Das, 2005). Other hormones involved in controlling stress such as adrenaline and glucocorticoids have been shown to inhibit the action of both desaturases (Mozaffarian et al., 2004).

Toxic factors
In vitro studies conducted in rat liver microsomes fed ethanol, they reported a decreased in the activity of Δ6 and Δ5 desaturase (Nervi, Peluffo, Brenner, & Leikin, 1980; Wang & Reitz, 1983). Subsequently Nakamura et al. (M. T. Nakamura & Nara, 2004) also corroborated these in vitro results for months in pigs fed with a diet rich in fat and alcohol. Additionally, Narce et al. (Narce, Poisson, Bellenger, & Bellenger, 2001) described enzymatic activity in vivo in rat liver cell cultures at different concentrations of ethanol: a higher concentration of alcohol decreased enzyme activity, but increased with minimal alcohol concentrations. In addition to altering the action of desaturases, alcohol consumption decreases tissue concentrations of long hip PUFA (Pawlosky & Salem, 2004). Another factor that influences this enzymatic activity is tobacco (Agostoni et al., 2008). In the study of Marangonni et al. (Marangonni et al., 2004) performed in vitro with epithelial cells of the mammary gland that were exposed to smoke was detected tobacco inhibiting the conversion of ALA to n-3 FA and a block enzymatic action of desaturase 5Δ.

Constitutional factors
The age can also affect desaturases, in fact it is known that this activity decreases from the third decade of life keeping this decline in old age. Hence the importance of incorporating into the diet of our older fatty fish intake as a source of PUFA. Furthermore, the enzymatic action decreases during the first 6 months of life. For example, in babies born preterm or with low weight at birth, this low activity of the Δ6 desaturase can lead to a defect in the synthesis of FA, with the consequent defect in the development of an optimum neurological function. Hence the importance of breastfeeding that brings these FA or the intake of milk formulations for premature babies enriched in these FA. In terms of sex we can also find differences both in the path of desaturation/elongation and in the proportion of ALA that is directed to be oxidized. It seems that estrogens increase the activity of this path and can also produce an increase in conversion of ALA with the consequent increase of EPA and DHA. A higher rate of conversion of DPA n-3 DHA is also detected in women (Purohit, Williams, Roberts, Potter, & Reed, 1995). The concentration of DHA is known to be higher in women compared with men. It seems that the reason for this finding is due to an increase in the hepatic expression of 5Δ and 6Δ desaturase in women of childbearing age, which gives them a greater ability to synthesize DHA from dietary ALA (Extier et al., 2010). This study supports the hypothesis about the hormonal regulation of the synthesis of PUFA. Another difference between men and women is the lowest proportion of ALA destined to oxidation in women.
compared to men of the same age (Burdge & Calder, 2005a; Burdge, Jones, & Scholz-Ahrens, 2002).

Other factors
It’s already known that oncogenic viruses and radiation inhibit Δ6 desaturase. This situation has a special interest in oncology patients. Notably, since these enzymatic reactions taking place in the liver (which is the organ most Δ5 and Δ6 desaturase activity), all diseases involving impaired hepatic function may affect enzyme activity. In fact, in cirrhotic patients there has been a decrease in the levels of EPA and AA (Burdge et al., 2002). Finally, we should mention the influence of physical activity on the enzyme activity. Andersson et al described how more physically active patients showed increased Δ5 desaturase activity more than inactive patients. Among all subjects studied no difference was found in terms of fat intake in their diet (Andersson, Sjödin, Hedman, Olsson, & Vessby, 2000). Under physiological conditions, the Δ6 desaturase has more affinity for the ALA to that in LA. But, as in our diet are more LA than ALA (Lands, 2008), ALA pathway is activated shortly and therefore the production of EPA and DHA is limited. This causes the plasma and tissue concentrations of long chain PUFA of the n-6 family is greater than those of the n-3 family. In fact, the percentage of ALA tissue lipids present in plasma and represent about 0.5% of all the FA (Burdge & Calder, 2005b). In conclusion, we find different situations in which there seems to be a decrease in desaturase activity. As much ALA we manage, its metabolism to EPA and DHA is limited, because the conversion is inefficient, and because chronic elevation of ALA lowers levels of DHA. Fish consumption provides the omega 3, but also rich in EPA and DHA, so it does not depend on its transformation from the precursor. Additionally, anti-inflammatory, antithrombotic and reducing cholesterol level, i.e. cardiovascular protection, come from dietary EPA and EPA produced from ALA, which will lead to DHA.

The intake of n-3 FA decreases Δ6 desaturase activity (the first rate-limiting enzyme) so you would think that increasing the intake of n-3 FA not get increased levels of EPA and DHA. However, this intake of n-3 FA stimulates the activity of the Δ5 desaturase (the second enzyme), so that the final effect appears to be an enhanced production of EPA and DHA. Burdge is the author who has best studied these effects and indicates that ALA intake increases the levels of EPA and DPA n-3, but minimally affects the DHA (Burdge & Calder, 2005a).

Mediators in the immune system
Eicosanoids are molecules with 20 carbon atoms that act by modulating the renal function (Van Der Meij, 2011), the vascular inflammation (Féléto, Huang, & Vanhoutte, 2010; Imig, 2006) of autocrine or paracrine forms. Prostacyclins, Leukotrienes, prostaglandins and thromboxanes among other molecules are included in this group. Prostaglandins are produced in most tissues, the vascular endothelium prostacyclins, leukotrienes primarily in leukocytes and finally thromboxane in platelets. These mediators of the immune response mainly derived from metabolism of AA and EPA. In fact, the main function of AA is to be a precursor for the synthesis of these molecules. Human inflammatory cells have large amounts
of AA and small FA of n-3 family. The proportion of both families varies according to cell type. The presence of higher amount of AA in cell membranes can be metabolized leading to potentially inflammatory substances. However, this ratio can be altered through oral administration of EPA and DHA. Meaning that increasing dietary intake of EPA, will reduce the proportion of AA of the cellular membranes and increase of EPA, thus decreasing the production of the harmful lipid metabolites (Dobrian et al., 2010). This is known as the immunomodulatory function of omega3 fatty acid, given that the change in the fat composition in the inflammatory cells modifies its function.

**Eicosanoids derived from AA metabolism**

The AA cell membrane, through the activation of phospholipase and in particular phospholipase A2, is capable of being released to plasma. So, it becomes a substrate for enzymatic pathways, among which are three: Cyclooxygenase (COX), Lipoxygenase (LOX) and Cytochrome P450 (CYP). The Eicosanoids derived from the COX route have greater biological activity than those who make the LOX.

**Eicosanoids derived from EPA**

*The COX-2 enzyme*

The COX2 converts the EPA in the PG and TX series 1 and 3. Also COX2 act on prostacyclin 1 in endothelial cells which is vasodilator and antiplatelet agent.

*By the action of LOX*

The 5 series of LT are formed in the leukocytes. Among them we should mention the LT-B5, which has anti-inflammatory and inhibitor of cell adhesion. All these mediators are significantly less inflammatory, i.e. have less biological activity.

*The epoxygenation*

The epoxygenation of EPA results in substances called resolvins, in particular resolvin E1, with antiinflammatory properties.

**Eicosanoids derived from other PUFA**

Besides eicosanoids derived from AA and EPA also other lipid mediators may be produced from the other PUFAs such as DHA or DHGL. The DHGL, which is an intermediate substance in the metabolism of AA, is a source of production of substances with anti-inflammatory properties. There are some PG and TX Series 1 that inhibit the production of clots. Also the DHA produce a molecule with anti-inflammatory properties called resolvinas or docosanoides and present in the blood, leukocytes, and brain tissue. We emphasize the resolvin D1 and protectin D1 and these substances have been involved in the protection of some tissues such as the nervous system, lung, and liver as well as in the resolution of the inflammatory process.

**International dietary recommendations of essential fatty acids**

The shortage of studies and lack of concurrence on the ideal levels of these nutrients in the enteral nutrition formulas, forces us to rely on oral dietary recommendations. In the next section we will review the dietary recommendations of various scientific societies. These we may serve as reference for enteral nutrition formulas. The dietary recommendations of PUFA is still a topic that need to be discussed, because haven’t yet established the maximum levels
of intake of n-6 and n-3 FA. In addition, recommending the amounts will depend on the type of diseases. There is also no agreement on the best contribution ratio of DHA and EPA, and whether if it is better to give them separately or combined, and if there are other n-3 FA long chain that they may have a beneficial effect. Other reasons that make it difficult to establish clear guidelines regarding the recommendations of the n-3 FAs are the great variability in their metabolism, based on genetic, sex, age and underlying disease. Therefore the requirements for their physiological effects need to be adjusted individually (Calder, 2002). The recommendations of the scientific societies on the intake of fat and FAs in particular has been both for healthy people and for the prevention and treatment of chronic diseases. It is generally recommended a reduction in the intake of saturated fat and trans FA, with a total intake of fat that range between 20-25% to 35% of the total energy intake (Molendi-Coste, Legry, & Leclercq, 2010). Although in a recent review of Aranceta et al. (Aranceta & Pérez-Rodrigo, 2012; Kris-Etherton, Innis, & American, 2007) is considered that there is no standard recommendation, which varies from country to country and only the most recent recommendations establish the importance of an adequate contribution of n-3 FAs (Kris-Etherton et al., 2007).

The first recommendations were based on studies that linked the beneficial effects of n-3 FAs with fish consumption, but not with n-3 directly by its own (Aranceta & Pérez-Rodrigo, 2012). In subsequent studies used only n-3 FA, they showed that these FAs are most important nutrients that provided by the fish and it's the main preventer of cardiovascular diseases (Burr et al., 1989; Jialal et al., 1999). Another way to approach the intake recommendations n-3 FA is the ratio n-6/n-3. FA's contributions through the diet have been developed, and the n-6/n-3 ratio today compared to the first humans. The diet of the hunter-gatherers of the Paleolithic diet was rich in lean meats, fish, green vegetables and fruits, with low total fat intake (20%) and saturated fat (<6%), and virtually no saturated fat and the relationship between the n-6 and n-3 FA consumed was 1/1. The meat of fish and other marine products are supplied n-3 FA and green vegetables supplied LA and ALA.

In the beginning of agriculture, although modification of the nutritional profile of the man was occur, because they added the cereals to food, but this did not produce major changes in the availability of n-3 FA and the amount of total fat in the diet. The technological developments of the last 100-150 years have really contributed to a change in trends in consumption of fats and a radical change in the ratio of n-6/n-3 consumption. The current diet of the western countries is characterized by a high ratio n-6/n-3, which can be 15-20/1, due to the high consumption of n-6 and the decrease in the diet of n-3. This imbalance affects Western countries more than Eastern countries (n-6/n-3 ratio around 12/1) since in these countries the consumption of fish and seafood products rich in EPA and DHA is higher (Tavazzi et al., 2008). The ideal n6/n3 ratio is still need to be defined. In patients with asthma a 10/1 ratio associated with increased inflammation, while 5/1 ratio had beneficial effects. In the secondary prevention of cardiovascular disease, a ratio of 4/1 was associated with a 70% decrease in total mortality. This same ratio was not sufficient to reduce cell proliferation in colo-rectal cancer and needed a ratio 2.5 / 1. Patients with rheumatoid arthritis in a ratio of 2-3/1 reduced inflammatory component (Simopoulos, 2009). All these divergence indicate that the optimum ratio varies by disease to which we refer as they are chronic, multigenic and multifactorial. Furthermore, it is possible that the therapeutic dose of
n-3 FA depend on the severity of disease and the genetic susceptibility of the individual (Simopoulos, 2008a). In the last 70 years a processes have been developed such as hydrogenation of vegetable oils to preserve and better manage plant and animal oils. This however involves a decrease of the contribution of essential FA and increased production of trans fatty acids with very harmful effects on health. In addition, there was increasing in consuming more grain with n-6 FA and more vegetable oils (corn, sunflower, soy) rich in LA and hydrogenated products, while the consumption of sea products is becoming increasingly less (Gómez Candela et al., 2011).

Do not forget consensus reflections published in 2009 by the American Heart Association (AHA) (Simopoulos, 2008b). It recognizes that in many cases, is recommended to decrease the intake of n-6 in the diet as a strategy to improve the n-6/n-3 ratio and, consequently, reduce cardiovascular risk. However, according to scientific literature review conducted by the AHA, this strategy might not only be ineffective, but could also have effects contrary to those expected in cardiovascular health, as the intake of n-6 (5 - 10% of the total energy of the diet) was shown to have a cardiovascular protective effects. In conclusion, we could say that increased consumption of n-3 appears to be the best strategy for getting a proper n-6/n-3 ratio (Calder, 2002; Harris et al., 2009). To achieve this, it was necessary to increase the intake of fish to 2-3 servings a week, or in some cases recommend the use of supplements. Moreover, high intakes of n-3 FA can cause excessive bleeding in some individuals. The American Dietetic Society recommends that patients taking more than 3 g / day of n-3 fatty acids should be followed by a doctor (Rueda, Domingo, & Mach, 2011). The FDA (Harris, Kris-Etherton, & Harris, 2008; Skulas-Ray, West, Davidson, & Kris-Etherton, 2008) has established the levels of 3 g / day of long-chain PUFA is generally regarded as safe. They have established the same recommendations for other organizations such as the Australia and New Zealand National Health and Medical Research Council (Harris et al., 2008).

Regarding EPA's recommendations, until recent years, the daily recommended intake had focused on the ALA, with indirect references to the contribution of long-chain PUFA, EPA and DHA. In 2002 the Food and Nutrition Board of the American Institute of Medicine (FNB-IOM) (Mozaffarian & Rimm, 2006) issued a report announcing that there was no sufficient evidence to establish the adequate intakes or reference for intakes of EPA or DHA. Subsequently, new evidence has been emerged that justify the re-evaluation of the recommendations of EPA and DHA and its impact on health. The FAO/WHO establishes that there is no sufficient evidence to establish a minimum intake of EPA or DHA, and therefore recommend that both are consumed (Trumbo, Schlicker, Yates, & Poos, 2002). Furthermore, another problem is defining, what is the more beneficial ratio of EPA/DHA. Both metabolites are chemically different and may have different effects on cardiovascular risk (Tunstall-Pedoe, 2006). Nature shows us that the ratio in fish is tilted in favor of DHA. Ratios of EPA / DHA from 1/2 to 2/1 appear to be beneficial. In addition, the experience with other nutrients showed that the therapeutic effect is achieved using an isolated nutrient, so most international recommendations do not separate these two nutrients.

A large number of countries have been published their recommendations and guides intake or adopted those suggested by international organizations or other countries. There is a great divergence between different countries and recommended intakes for total fat and FA. In addition, there is no standardized methodology to define these values. A systematic review
of dietary intakes recommended for fat and the FA has recently been published (Kris-Etherton et al., 2007). In the latest international recommendations in the general population appears to be some consensus with 400-500 mg / day, which would be the minimum levels of EPA + DHA intake. This is roughly equivalent to two servings a week of fish. Regarding the contribution of n-6 and n-3 FA, there is no consensus and recommendations both are very different. In general most opinions agree with the FAO / WHO in 2008 (Joint & Consultation, 2008) in recommending the 2.5-10% of total calories in the form of n-6 FA and 1-2% of n-3 FA, which would make a ratio of 5/1. The lower limit of 2.5% is set to prevent essential fatty acid deficiency, while the upper range would be indicated to reduce plasma levels of LDL and triglycerides. This ratio is far from the 12/1 or greater than the typical diets of nutrition in industrialized Western society. We must remember that the n-6/n-3 ratio was effective in diseases from 5/1 in asthma to 2.5 / 1 in colo-rectal cancer (Simopoulos, 2009).

In pregnant and lactating women, for optimal fetal development, the minimum intake of EPA + DHA should be 300 mg / day, of which at least 200 mg should be DHA. DHA plays an essential role in the development of brain and retina during fetal and the first two years of life. These findings support the need for adequate intake recommendations for pregnant women, breastfeeding women and children up to two years. The DHA should be considered conditionally essential during the initial stages of development, since the formation of DHA from ALA is very limited and highly variable (1-5%) (Kris-Etherton et al., 2007). Regarding patients with cardiovascular disease, in recent years there is a growing understanding of the relationship between intake of n-3 FA and cardiovascular risk reduction. The recommendations of the various companies agree that adults have to eat fish at least twice a week. For patients with coronary disease, consumer recommendations are 1 gram per day of EPA + DHA from oily fish or supplements. In case of patients with hypertriglyceridemia, the recommended supplement is 2 to 4 grams per day of EPA + DHA to decrease about 20-40% of triglycerides plasma levels.

**Dietary sources of n-3 and n-6 FA**

We know that the essential FA should be mandatory ingested through food for the production of long-chain PUFA of the n-6 and n-3. The n-6 FA from LA, widely distributed in plants, except coconut, cocoa and palm. They are mostly found in vegetable seed oils such as corn, sunflower, safflower, evening primrose, pumpkin, peanut, wheat germ and soy. AA precursor is synthesized in mammals, and therefore in foods of animal origin. The n-3 FA derived from ALA, which predominates in nuts, plant chloroplasts dark green leafy vegetable oils and soybean, flax, canola, flax, blackcurrant and other red fruits (Harris et al., 2009). Less than a 0.2 per cent of ALA is converted in the body in EPA and only 0.05 % in DHA. Therefore for these two FA achieve adequate concentrations must be provided on a regular basis and in sufficient quantities with a diet rich in marine products. The origin of these essential acids is of microscopic algae, plankton and planktonic crustaceans, which are at the base of the food chain.

There are significant differences in the content of EPA and DHA not only between different species (maximum in salmon and mackerel), but within the same species. The different lipid
composition will depend on their habitat, according to vary factors like temperature, depth and salinity of the water, from the moment of capture and if wild animals or come from fish farm. The total fat and n-3 FA content is greater in cold water fish. There are also differences in the concentrations of n-3 FA according to the form of preparation of fish. In fried fish (restaurants or fast food) reduces the content of n-3 FA and increases the ratio of n-6/n-3 and content in FA trans. Thus, in the majority of international recommendations insist on the intake of fish rather than a precise dose of n-3 FA (A Valenzuela & Uauy, 2005).

**New sources of n-3 FA**

A recent epidemiological study placed low intake of n-3 FA in the eighth position of preventable causes of death in the United States (Carrero et al., 2005). Therefore, there is increasing interest in finding new sources of n-3 long chain especially. This is due to the problem of supply of fish, the appearance of pollutants, loss of species biodiversity in the future will affect the entire world population, etc. (Danaei et al., 2009). Biotechnology is developing new oils rich in n-3 FA that can be used in food or as supplements. From several bacterial and algae that are in the intestinal microbiota of saltwater fish oils are obtained especially rich in EPA and DHA (Danaei et al., 2009). They have also fed chickens and pigs and marine oils to increase the DHA content of meat and eggs. Genetic manipulation has also helped to increase the supply of n-3 in different foods, such as new strains of seeds that can synthesize DHA from ALA (Garg, Wood, Singh, & Moughan, 2006). Another option to increase the consumption of n-3 FA in the diet is incorporated in commonly consumed foods, developing functional foods rich in n-3. These products enriched in n-3 makes it easier to achieve these recommendations FA. The modern food technology today makes it possible that a large amount of food can be enriched in n-3 FA and, indeed, around the world there is a wide range of fortified food products. Some examples of these foods that are sold in almost all countries are the bread and bakery products, margarine, fat spreads, eggs and products, pastas, sauces, juices and soft drinks, meats, dairy products and milk (Alfonso Valenzuela, Julio Sanhueza, & Nieto, 2006). However, this contribution may be only 30%, there are great differences between products. These FA are very susceptible to oxidation and react very quickly when exposed to conditions or oxidizers such as oxygen from the air. For this reason, fish oils are added to foods with vitamin E and other antioxidants to prevent rusting which, otherwise, would cause Rancidity, odors and instability. In addition, the production of foods fortified with n-3 FA is technically difficult and requires special methods to produce fish oil suitable, appropriate for addition to food, without smell or taste fishy (Harris et al., 2009). Due to the difficulties to meet recommended intakes of n-3 FA, nutritional supplements have been appeared which attempt to satisfy the nutritional requirements of these FA. As is the case with certain foods, in supplementation there is wide variation in terms of its composition and concentration of EPA and DHA. In recent years the administration of n-3 FA as management oral drug has been approved. In Europe there is a galenic formulation providing 840 mg of n-3 FA (465 mg EPA and 375 mg of DHA). It is authorized for use in secondary prevention after myocardial infarction in combination with reference treatments and endogenous hypertriglyceridermia as Supplement to diet when there is an inadequate response to dietary measures (Caballero et al., 2006). The n-3 FA can then be considered both as essential nutrients, dietary supplements or
drugs active ingredients, depending on the level of intake and the reason being administered (Trautwein, 2001).

**Composition of n-3 FA enteral nutrition formulas marketed in Europe**
The composition of these n-3 FA, as well as their ratio n-6/n-3 is very variable from formulas of enteral nutrition to others. The classification of these formulas is based on whether they are complete or not, if they are polymeric, peptide or elementary, its richness and quality of proteins, their caloric concentration and content in fiber, but not in the quantity and quality of fats that contain (Gillies, Harris, & Kris-Etherton, 2011). Standard formulas provide a 15-16% of the caloric total value in form of protein, 48-55% carbohydrate, and 30-35% fat. The composition of these fats is very heterogeneous, being even more irregular n-3, n-6, EPA and DHA content much more. Most of these guides recommend the intake of 20-35% of the total fat as energy, although some increase to 40% in people with normal weight. The contribution of saturated fat tends to be reduced to 10% or even 7% of the total energy for the American Heart Association. In 100 cc of standard nutrition get 100 kcal, making it 7-10% of these calories would correspond to 0.77-1.1 g of saturated fat. In 100 cc of standard would be 20 kcal, corresponding to 2.2 g of MonoSaturated Fatty Acid (MSFA). Finally, the recommended intake of fat PUFA is 6-10% (0.66 to 1.1 g of PUFA in 100 cc's standard formula). The main objective of our study is to evaluate the effect of omega3 on the health and disease also to analyze the content of n-3 FA, n-6 FA, as well as EPA and DHA of enteral nutrition formulas and establish possible recommendations. So we've calculated for an average consumption of 1,500 cc / day, as is the usual dose. Regarding the recommended intake of n-6 FA, most agree with the guidelines of the FAO / WHO, 2008 (Joint & Consultation, 2008) recommending the 2.5-10% of total caloric intake in the form of n-6 FA. For a contribution of 1,500 kcal / day, this corresponds to 37.5 to 150 kcal FA as n-6, or what is the same, from 4.16 to 16.6 g / day. For this nutrient, all products are within the recommended range.

**Conclusion**
Most of studies and researches report a lot of benefit of Omega3 and showed its effect in prevention and correction some of cardiovascular and other systemic diseases, and because its found mainly in fishes and sea food, so its highly recommended to take at least 2-3 meal of sea food per week or use the omega 3 supplements ass alternative solution. Standard nutrition formulas have a proper fat content, but in the majority of products containing EPA and DHA exceed the limit of 3 g / day, Instead, the contents of n-6 FA is within the recommended range. Finally, the ratio EPA / DHA in most is 2/1, as recommended in the diet from food, but in some the contribution of DHA is very limited or nonexistent.
References


