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Research Article

The Efficacy and Safety of Using Omega-3 Fatty Acid to Reduce the Risk of Breast Cancer

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Abstract

Omega-3 fatty acids are essential fatty acids though our bodies cannot make them. The main source of Omega-3 fatty acids is fish especially Tuna, Salmon and Halibut species. Omega -3 fatty acids also play a vital role in the brain function. It is very important to have the right ratios of Omega-3 fatty acids in the diet. This study has established that consumed in the right quantities fish oil supplements containing high levels of Omega-3 fats mainly DHA and EPA had a 30 percent reduced risk of developing breast cancer. However, this reduction in the risk seemed to be limited mainly to invasive ductal breast cancer, the most widespread type of the disease. The deficiency of Omega-3 fatty acids has always been underlying factor for different types of cancers. The aim of the project is to investigate and seek from many of the numerous studies that have linked Omega-3 supplementation with a decreased risk of invasive ductal breast cancer and it adds to growing research that have highlighted the health benefits of omega-3 fats. Omega -3 fats have been known to influence some genes responsible for the prevention of breast cancer. From this study it is evident Omega-3 fatty acids intake slowed the growth of cancer cells in some forms of cancer strains. On the other hand, the intake of high amounts of Omega-6 fatty acids is known to enhance tumor growth and metastasis. No doubt EPA and DHA, long-chain(n-3) PUFA mostly obtained from fish aid to restrain the propagation of breast tumors. Nevertheless, there have been safety concerns in the use of Omega 3 fatty acid intake therapy. Adult stem cells exist in various tissues of the body. They play a role in tissue growth, substitution and repair. Confirmation shows that breast stem cells are multi potent and can renew themselves. Countless groups have endorsed the cancer stem cell hypothesis from the hematopoietic system to hard cancers, where using *in vitro* culture techniques and *in vivo* transplant models have documented confirmation of cancer stem cells in prostate, brain, Prostate and breast cancers. In the report, we can deduce that cell surface makers such as CD44+/CD24- could be used for the enrichment of stem cells among women with non-recurrent breast cancer. However, current improvements in immunotherapy have aimed at breast cancer stem cells and this could eventually guide to more significant clinical remissions.

Keywords: *Omega-3; Fatty Acids; Fish Oil; DHA; EPA and Breast Cancer*

Abbreviations

n-3: Omega 3; n-6: Omega 6; n-3 FAs: Omega 3 Fatty Acids; n-6 FAs: Omega 6 Fatty Acids; FA: Fatty Acid; EFAs: Essential Fatty Acids; PUFA: Poly-unsaturated Fatty Acids; EPA: Eicosapentaenoic Acid; ALA: Alpha-linolenic Acid; DHA: Docosahexaenoic Acid; LA: linoleic Acid; CLA: Conjugated Linoleic Acid; EPEA: Eiccosapentaenoyl Ethanolamides; DHEA: Docosahexaenoyl Ethanolamide; 2-AG: 2- Arachydonoylglyceral; EPA: Environmental Protection Agency; FDA: Food and Drug Administration; PCB: Polychlorinated Biphenyl; LCPUFA Omega-3: Long-chain Polyunsaturated Fatty Acids; HSC: Hematopoietic Stem Cells; MSC: Mesenchymal Stem Cells

Introduction

Despite the opinion that omega-3fatty acids defend against breast cancer, epidemiologic studies have come up with inconsis-

tent results. Though, preclinical data heavily support the protective effect, contradictions persist, which impede definite suppositions despite 30 years of research in this area. Role of diet in breast cancer progress remains controversial. The contribution to mammary carcinogenesis of the specific fatty acid (FA) composition of the diet has received considerable attention in the literature [24]. Among the FAs, omega-6 and omega-3 fatty acids have been suggested to increase and decrease breast cancer risk respectively [1].

Omega−3 fatty acids widely known as n-3 fatty acids are prevalent in plant oils and marine. They are poly-unsaturated fatty acids (PUFA) which have a double bond (C=C) that begins after the third carbon atom. The n-3 fatty acids consist of the methyl (CH3) end and the acid (COOH) carbon end. Omega-3 fatty acids have inherent health benefits hence are regarded as essential fatty acids, which mean that they are not formed by the human body, rather they are necessary for normal body metabolism [5]. Even though mammals cannot manufacture omega−3 fatty acids, they still have a minor ability to build up the long chain fatty acids, such as α-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Regular sources of the fatty acids are algal oil, fish oils and other plant oils, for example, echium and flaxseed oil [7].

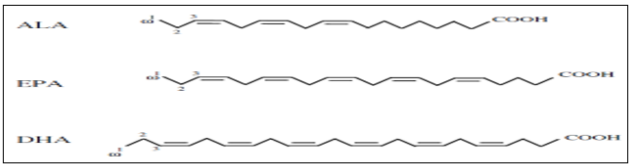

Figure 1: Chemical structures of omega-3 PUFAs. ALA: α-Linolenic Acid; EPA: Eicosapentaenoic Acid; DHA: Docosahexaenoic Acid.

Sources of n-3 fatty acids consist of fresh water fish that encompasses eicosapentaenoic acid, and (DHA), certain seeds (flax) and nuts (walnuts), and some vegetable oils (soy bean). Plant sources of n-3 FA contain a-linolenic acids (ALA). Supplies of n-6 FA include vegetable oils, for example corn or sunflower oil [containing linoleic acid (LA). After extensive researches carried out in Japan, USA, and France on the overall fat consumption, it was concluded that fats have no link to breast cancer; the amounts of fat could be [18]. The researchers studied the linkage that exists between the amounts of PUFA in adipose tissue in breast tumor incidence and postmenopausal females. Almost 291 breast cancer victims and approximately 351 controls were applied during the research which took place in five European health centers. All victims had segments of adipose tissue taken and scanned for the amounts of the key polyunsaturated fatty acids: i.e. omega-6 acids (LA), docosahexaenoic acid (DHA), omega-3 acids - eicosapentaenoic acid (EPA) and alpha-linolenic acid (ALA) [10].

The research found a tendency to accumulative incidence with cumulating stages of omega-6 in the adipose muscle trials even though they did find no important relationship between levels omega-3 fatty acid and breast cancer. Secondly, researchers found an important connection between the level of DHA and EPA to levels of LA and occurrence of breast cancer in 4 out of every 5 patients of the medical centers, who participated in the study. They discovered that women with high levels of adipose tissue of both DHA and EPA and low levels of LA and its metabolites are at less risk of cancer [1]. The scientists further noted that LA is the initiator of some eicosanoids that may then cause cancer development. EPA and DHA hinder formation of these dangerous compounds and may hinder tumor growth [19].

Several epidemiological researchers have found a contrary connection between depletion of fish and prevalence of breast cancer cases and desire for more research to ascertain the connection between dietary consumption of fish and breast cancer occurrences [8]. The studies indicate the following: Consumption of omega 3 has enhanced less spread and slowed the growth of the tumor [2,21]. Another study of approximately 12, 866 men in the U.S showed that those consuming large quantities of omega-3 and less quantities of omega-6 exhibited a lower risk level of 33% of suffering from cancer [3,7].

Prevalence of breast cancer maximized as Icelandic and Greenland women discarded their usual diets of sea food [4]. Omega-3 fatty acids are acquired by consuming food, thus making external sources of these fats "vital." Fish that are wealthy in essential oils also referred to as omega-3 comprise of tuna mackerel, mullet, salmon, sturgeon, sardines, bluefish, menhaden, herring and trout [9,13]. Although not all specialists approve this, women who feed on diets with omega-3 fatty acids in many years are unlikely to acquire breast cancer. Thus additional findings are required show omega-3

Oil	Omega-6 Content	Omega-3 Content
Safflower	75%	0%
Sunflower	65%	0%
Corn	54%	0%
Cottonseed	50%	0%
Sesame	42%	0%
Peanut	32%	0%
Soybean	51%	7%
Canola	20%	9%
Walnut	52%	10%
Flaxseed	14%	57%
Fish*	0%	100%

Figure 2: Percentage of omega 3 and omega 6 in dietary intake.

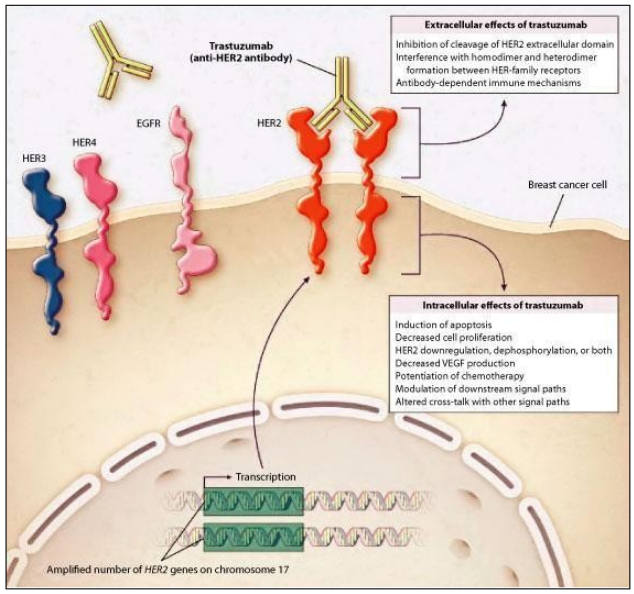

Figure 3: Shows the mechanism of HE2R test on breast cancer.

fatty acids activity on breast cancer. Previous studies have revealed an entirely natural prescription, that not only defends against the growth of cancer, but also those patients who have been identified with inveterate cancer and discharged to die, have managed to live normal lives [5,6]. It's also likely that the omega-3 diet may help in treatment of depression, according to scientist who premeditates the effects of omega-3s on the disease [7,8].

Mechanism of action

The protective role played by omega-3 fatty acids in managing breast cancer could stem from many hypothesized mechanisms. One common mechanism where omega-3 fats exert physiologic effects thus could influence carcinogenesis is a basic modulation of eicosanoid metabolism [8]. A common polyunsaturated in many diets is linoleic acid. This acid is a member of the omega-6 group. The acid mostly converted to arachidonic acid that acts as a parent compound for many eicosanoids, which can affect cell function. Cells with tumor produce large quantities of arachidonate-derived eicosanoids like prostaglandin E2 that may cause immunosuppressive effects [9,11].

High levels of omega-3 reduce the delta-5 and 6 desaturase avenues that cause the production of arachidonic. These fatty acids battle with arachidonic acid to be incorporated into human cell membranes figure 3. Moreover, they struggle for enzyme pathways that result into eicosanoids, which consequently yield metabolites that different from those related to arachidonate [7].

Omega-3 fatty acids could hence inhibit tumor development or growth by both inhibiting metabolism of arachidonic acid competitively and the effects of the omega-3's own metabolites. Other anticarcinogenic effects of omega-3 acids include: modification of hepatic phases (I,II) detoxification processes affecting carcinogen activation and/or detoxification, minimizing estradiol hydroxylase and system circulation of estrogen levels associated with dietary intake of fish oil could inhibit tumor promotion, lipid peroxidation products associated with highly unsaturated fats production have a direct cytotoxic effects on tumor cells. Omega-3 fatty acids in carcinogenesis also suppress fatty acid syntheses process and selected effects on gene expression [5,7,10].

Anticarcinogenity through inhibition of omega-3 fats metabolism shows that the amount of omega-3 fats taken should be less significant compared to the balance between it and omega-6 intake. If an individual's intake of omega-6 is high, large quantities of omega-3 are required offset the balance [6,17].

HER2 antibody

HER2/neu (ERBB2), an oncogene expressed in approximately 20% of all breast cancer cases, encodes for transmembrane recep-

tors of the critical growth factors that activate subcellular signal transduction pathways responsible for epithelial cell growth and differentiation.HER2-positive breast cancers usually have an aggressive course and relatively short disease-free intervals.

The ERBB2 gene is a member of a family of genes that encode for transmembrane receptors of growth factors, including the epidermal growth factor receptors (-EGFRs) HER1, HER2, HER3, and HER4. The HER2 receptor has both an intracellular and an extracellular domain; the intracellular domain has tyrosine kinase activity, which regulates important aspects of cellular physiology, growth, and differentiation. The HER2 extracellular domain facilitates signal transduction after ligand binding. There is no known ligand for HER2 itself; thus, the primary role of HER2 may be to modulate signals after ligand binding to other HER-family receptors.

Amplification of the ERBB2 oncogene and related genetic elements causes a marked increase (up to 100 times the usual level) in the expression of HER2 on the surface of breast tumor cells. Although the mechanism of the selective amplification of ERBB2 is unknown, overexpression of the HER2 protein may transform cultured cells into a malignant phenotype, accelerate tumorigenesis, and encourage the formation of receptor homo- and heterodimers that possess different signaling properties than seen normally. In fact, results of population-based studies and retrospective analyses suggest that HER2 overexpression is an adverse prognostic factor that is linked to poorly differentiated, high-grade tumors; high rates of cell proliferation; lymph-node involvement, and relative resistance to certain types of chemotherapy.

Anthracycline-based adjuvant chemotherapy is particularly effective against HER2-positive tumors. Roughly half of HER2-positive breast cancers also express the steroid hormone receptors for estrogen and/or progesterone. However, the levels of steroid hormone receptors in such tumors typically are lower than those in HER2-negative, hormone receptor–positive tumors; thus, HER2-positive breast cancer is relatively resistant to tamoxifen. All of these factors contribute to the greater risk of recurrence noted among women with HER2-positive breast cancer, as compared with those having HER2-negative breast cancer.

In view of these facts, the tremendous need for new ways to attack HER2- positive breast cancer becomes clear. The information summarized in this article is based on an educational session, entitled “Management of HER2-Positive Breast Cancer”, which was presented during the 42nd annual meeting of the American Society of Clinical Oncology in Atlanta, Georgia. Speakers discussed the role of trastuzumab, used both alone and with other oncolytic agents, in treating selected patients with advanced breast cancer. These experts addressed the use of trastuzumab in preoperative, postoperative, and metastatic settings and discussed the emerging problem of trastuzumab resistance.

Efficacy

Evidence accumulated from numerous experimental systems indicates that n-3 FAs may exert an antitumor action by altering the cell-membrane phospholipids composition and consequently, affecting the expression and function of numerous receptors, proteins, and lipid-derived signaling molecules [6,8,22]. This process eventually leads to amplified cell death and the inhibition of cell propagation i.e. inhibitory effect [2]. Alpha-linolenic acid (ALA) is transformed to DHA and EPA, which is structural phospholipids of cell membranes that alter membrane fluidity, cellular interaction, and cellular signaling. They are omega-3 polyunsaturated fatty acids that have growth-inhibitory effects on different types of cancers and tumors, including breast cancer by lessen the function of proteins that prevent apoptosis, thus restraining tumor growth [18]. DHA and EPA also function in the parameter of the immune system by acting as predecessors for the building of eicosanoids, which are immune-regulatory metabolites [7].

The increasing prevalence of breast tumor may be described in light of the finding of absence of oxygen in cells; breasts have an extremely high quantity of fatty tissue [8]. A distinctive cell membrane in tissues contains about one- third EFAs (oxygen transferors) and is half-fat constituted. However, fatty tissue, such as the breast, encompasses almost 80-95% fats amounts [5,6]. These fatty constituents of breast tissue necessitate and must consist of high levels of EFA; nonetheless due to modern methods of food processing they do not have those high levels of EPA. Since central organs like the heart brain, heart, kidneys and lungs need EFAs regularly, there is sufficient level remaining to guarantee that breast tissue get an enough quantity of EFAs [10,20].

Therefore, lack of oxygen in tissues of the breast is very crucial. This evidence shows that breast tissue is the prevalent area of can-

cer in women globally. This observation is a reality in elaborating the great increase in levels of breast cancer. In a previous study of the consumption of maternal omega-6 revealed that the group of women with less consumption of LA had uppermost frequency of breast cancer [9].

Some scientists have discovered and clearly specified the major reason for cancer is small amounts of oxygen entering the cell membrane. They concluded through demonstration, about 35% prevention of oxygen respiration serves to cause such a change during cell growth [10]. Treatment using fish oil products can be restricted to the quantity of DHA and EPA rather than basing it on the entire quantity of fish oil. The ratios and quantity of DHA and EPA vary in supplements. Most common amounts of omega-3 in fish oil capsules include 120 mg of docosahexaenoic acid and 180 mg of EPA. Various fish species have different quantities of omega-3 fatty acids [5].

Long chain PUFA, for example, docosahexaenoic acid or EPA, facilitates the process of cytotoxicity of numerous anti-cancer drugs that fit in various classes. These are 5-fluorouracil; anthracyclines e.g. epirubicin and doxorubicin; mitomycin; vinorelbine; taxanes, such as docetaxel and paclitaxel. These drugs help in providing defenses against many human cancerous cell, such as breast, bladder colon, glioblastoma and neuroblastoma cells [11,12,25]. Numerous putative methods that account for tumors induced by DHA chemo-sensitization have been associated with the function of docosahexaenoic acid in lines of breast cancer cells. The changes stimulated by uptake of drugs and oxidative form of tumor cells are some major means involved [13,14,19].

Polyunsaturated fats are vital nutrients that cannot be synthesized hence they are obtained from the diet. As mentioned earlier, polyunsaturated are classified into two main families, omega-3 and omega-6, with the latter predominant in most diets. Laboratory research shows the involvement of polyunsaturated in metastasis and tumor growth [5,8]. Mammary tumors often produce omega-6 metabolites that may have immune function and help in tumor growth. On the other hand, omega-3 metabolites have been studied and shown to block tumor growth. Therefore, an increase in omega-3 rather than omega-6 fat could inhibit production of metabolites of omega-6 and subsequently maximize production of omega-3 metabolites, thus causing anticarcinogenic effects. Increasing omega-3 as opposed to omega-6 fatty acid in tumor cell cultures of mammary glands minimizes the production of prostaglandin E2 [6,10].

Oxidative stress

Apart from their main influence on topoisomerases, some drugs in the anthracycline group are associated with stimulating death of cancerous cells by inducing the development of reactive oxygen cells in some cancer-affected areas that later aggravate cell damage that is irreversible [15].

Studies conducted with breast cancer cell line indicated that DHA fortification of the culture medium amplified the cytotoxic reaction to doxorubicin. The action was practical with polyunsaturated fatty acid, but the degree remained relative to the unsaturation level [22]. The chemo-sensitizing impact of polyunsaturated fatty acid was related to be the quantity of double bonds, lessening from docosahexaenoic acid [11]. Parallel results had previously been detailed by a different experimental group system [16]. Since re-oxidation of lipid relies on the degree of fatty acid un-saturation, this shows that the fundamental process of chemo-sensitization could be associated to the sensitive nature of omega fatty acids the process of oxidation [17]. Moreover, a correlation is drawn from the degree of hydroperoxides of the cell and cytotoxicity occurring due to doxorubicin stimulation. Research has shown that DHA can deteriorate tumor cells whilst incorporating phospholipids. This occurs since its peroxidation effect that would follow the process of oxidative stress is stimulated by anthracyclines [18].

Mechanism by which PRL

The model which conceptualizes the mechanism by which PRL confers resistance against cisplatin is presented in figure 4. After diffusing into the cell, cisplatin enters the nucleus and binds to DNA, with the ensuing cell cycle arrests leading to apoptosis. Binding of PRL to its receptor induces the activation of Jak-Stat and MAPK pathways, which separately or in concert increase the expression and activity of GST. GST conjugates cisplatin to glutathione, leading to its extrusion from the cell. Consequently, less cisplatin is available for entering the nucleus and inflicting DNA damage. The overall effect of PRL is a marked reduction in cisplatin-induced cell death. In addition to cisplatin, GST confers resistance to doxorubicin but not to the microtubule-altering drugs). Thus, the mechanism by which PRL antagonizes drugs which are not substrates for GST may involve alterations in Bcl-2 family proteins.

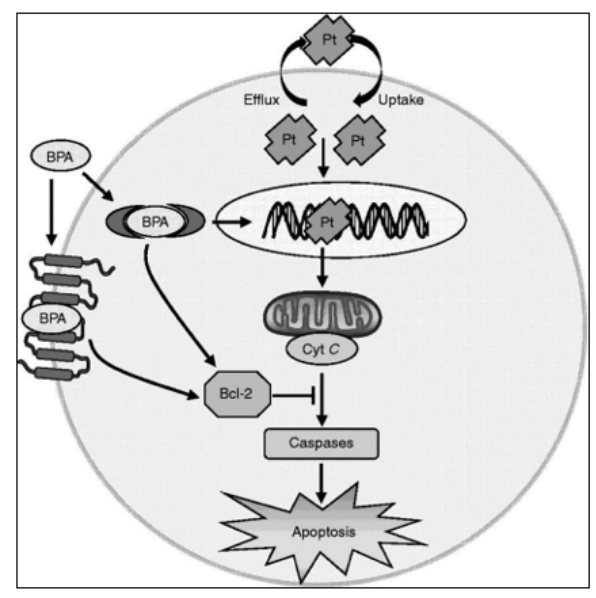

Figure 4: The mechanism by which PRL confers resistance against cisplatin.

Precautions

It's advisable anyone at risk of cancer to take omega3 fish oil dietary supplements with physician approval only due to high interaction with other medication. Omega-3 fatty acids causes a bleeding disorder hence should be used carefully by the individual who easily bruises or takes blood thinning medicines, such as, clopidogrel (Plavix), warfarin or aspirin. Over-doses of omega-3 can upsurge the risk factor of hemorrhage, even in persons deprived of a history of bleeding condition [13].

Persons suffering from schizophrenic attacks or diabetes mostly are deficient in the ability to change alpha-linolenic acid and EPA that are the types more willingly uptake in the body [22]. Individuals under these circumstances should be sure to get sufficient DHA and EPA from their food. In addition, patients with type 2 diabetes mellitus may exhibit rises in levels of blood-sugar when consuming fish oil products [16,22].

Though research findings advocate that intake of fish may lessen the threat of macular degeneration [15,16], some present research, consisting of two groups of male and female participants showed that foods with ALA is likely to upsurge the danger of macular degeneration. Unless research offers new findings, it is advisable that individual with macular deterioration they are supposed to get omega-3 from supplies of DHA and EPA instead of ALA [4].

Some fish species may have potentially dangerous pollutants, for example, heavy metals that consist of mercury and polychlorinated biphenyls (PCBs). In fish caught through sport fishing, the United States Environmental Protection Agency (EPA) advices all pregnant women to have less than a single 6 ounce food every week while children should consume less than two ounces every week [15]. On fish raised on farms, imported, or sea fish, the United States department of Food and Drug Administration (FDA) advices that young children under the age of 10 years and pregnant mothers to avoid feeding on fish species with higher amounts of mercury e.g. sharks, swordfish and mackerel. In addition, they should eat at least 12 ounces on a weekly basis of other type fish or seafood. Individuals that present some forms of allergy to marine food might be allergic to fish oil enhancements. However, there is no dependable data displaying how possible individuals with marine food allergy are to also allergic to fish oil. Therefore, until reliable information is available, patients that are allergic to seafood are recommended to stay away from fish oil supplements [18].

Some studies findings suggest that fish oil upsurges the risk of arrhythmia heartbeat in the individual who have an implanted defibrillator [9]. It is recommended that, for the victims to be safe they should avoid fish oil supplements. Moreover, there have been some mild concerns that fish oil might upsurge the risk of acquiring cancer in individuals with Familial adenomatous polyposis condition [8]. Previous studies, have found that taking fish oil increases some of the Bipolar disorder symptoms [25].

Prevention of breast cancer by LC-PUFA

It seems clear that there exists an inhibition of INa in cardiac cells which can account for anti-arrhythmic properties of EPA and DHA, similar to class I anti- arrhythmic drugs. The same applies to the cancer line MDA-MB-231 but some questions still remain to be answered: 1) In cancer cells, chronic exposure to DHA induced a reduction of NaV1.5 density in the plasma membrane subsequent to a reduction of mRNA expression [23]. Is it the case in cardiac cells? 2) it has been published that the inhibition of cardiac ion channels by DHA is due to the activity of some peroxidized form of this ω-3

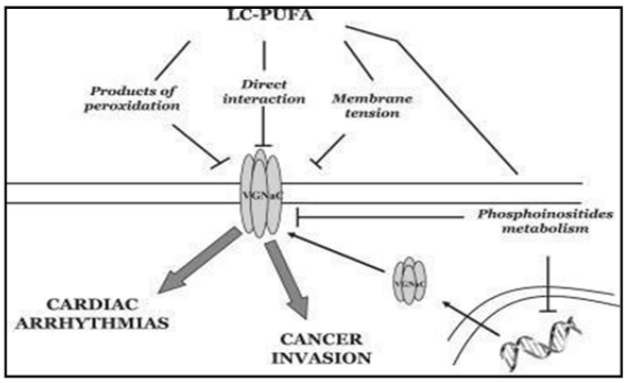

Figure 5: Prevention of cardiac arrhythmias and breast cancer by LC-PUFA: hypothetic mechanisms of action.

LC- PUFA. Is it also the case in breast cancer cells? in situ, is it the production of lipoperoxides (associated with the production of ROS due to the disease) which explains some of the beneficial effects or is there a need for a reduction in protein synthesis? In the same vein, it would be of interest to check if the neo-adjuvant effect of ω-3 LC-PUFA in patients treated with doxorubicin is mediated, at least partly, through an inhibition of NaV1.5 by lipoperoxides.

Since altered regulation of the phosphoinositide pathways with ω-3 LC-PUFA can participate in the beneficial effects it would be of interest to evaluate if these effects are also responsible for the effects on INa.

Another interesting point to consider is the influence of ω-3 LC-PUFA contained in the phospholipids of membrane lipid rafts. Indeed, it is known that the DHA content of lipid rafts can affect cell signalling through different pathways (see [26] for review). In cardiac cells, most ion channels, including NaV, are located in lipid rafts, which can affect their function the situation in cancer cells has not been studied to the best of our knowledge. However, in these cells, it has been shown that the lipid composition in rafts can be influenced by the presence of ω-3 LC- PUFA in the culture medium [28]. These researchers showed that culturing cells in the presence of 100 µM ω-3 LC-PUFA decreases epidermal growth factor receptor levels in the rafts, which can explain some anti-proliferative and pro-apoptotic effects of DHA. The translocation of proteins, such as ion channels, from the raft to the non-raft membrane fraction can also participate in the anti-invasive effects of ω-3 LC-PUFA. However, it must be underlined that the inhibition of migration and invasion by ω-3 LC-PUFA is observed at concentrations in the range of the micromolar, not 100 µM.

Whatever the mechanisms involved, it appears more obvious now that the beneficial effects of ω-3 LC-PUFA on chronic diseases, beside their well-known anti-inflammatory action, are supported by molecular determinants, such as NaV1.5 and probably other channels, involved in the different diseases.

Medications interactions

Individual on some specific medications should avoid uptake of omega-3 fatty acid enhancements, such as docosahexaenoic acid, eicosapentaenoic acid and alpha-linolenic acid. Omega-3 fatty acid maximizes the actions of blood thinning drugs, such as aspirin, clopidogrel (Plavix) and warfarin [19]. Taking omega-3 fatty acids and aspirin can be supportive in some conditions, for instance, heart complications. However, they should be used alongside a physician's directions and orders [14]. Consuming food reach in omega-3 fatty acid enhancement increases blood sugar intensities. It is advisable to for patients to take the medications with caution in order to reduce levels of blood sugar, Glucotrol [20].

Omega-3 oils can act as a blood thinner and also on the other increase blood hemorrhage [19]. Individual taking anti-coagulant medications and have a hemorrhage disorder should consult their health provider physician before using Omega-3 supplements because it can affect treatment of breast cancer. In addition, some evidence shows that birth contraceptives might affect the triglyceride-lowering functions of fish oil. Such medications include levonorgestrel (triphase) and ethinyl estradiol [1,20].

When fish oil is consumed in large amounts, it can hinder the immune system's function subsequently reducing the body's capability to fight infection. It should be a big worry for persons taking these medications to lessen the action of their immune system and ageing [24].

Mixing fish oil with blood pressure lowering drugs can upsurge the consequences of these medications and can reduce blood pressure to considerable amounts [23]. Certain drugs for hypertension comprise enalapril (Vasotec), captopril (Capoten), losartan

(Cozaar, diltiazem (Cardizem), amlodipine (Norvasc), furosemide (Lasix). Orlistat might retain the helpful fatty acids from being engrossed by the body. Consuming fish oil and Xenical and Alli two hours duration can prevent this from occurring. This means that fish oil combined with certain drugs and medications can affect its effect on treatment of breast cancer [7].

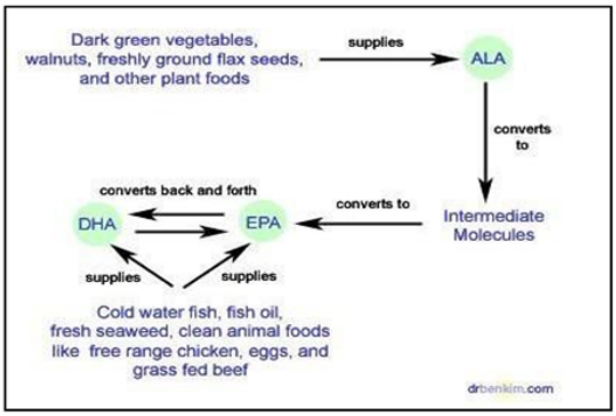

Figure 6: Omega-3 make from DHA and EPA.

Omega-3 fatty acids come in three varieties

- ALA (Alpha-Linolenic Acid) - found primarily in dark green leafy vegetables, flax seeds, hemp seeds, walnuts, and a variety of vegetable oils. Dark green vegetables, freshly ground flax seeds, and raw walnuts are the healthiest sources of ALA.
- EPA (Eicosa-Pentaenoic Acid) - found primarily in cold water fish like salmon, cod, mackerel, and tuna, as well as in fresh seaweed. Also found in smaller amounts in organically raised animal products like free-range eggs, chickens, and grass-fed beef.
- DHA (Docosa-Hexaenoic Acid) - found in the same foods that EPA is found in.

Your body is able to convert ALA into EPA and DHA. So theoretically, if you are in excellent health and eat lots of dark green leafy vegetables, ground flax seeds, and walnuts, your body should be able to produce enough EPA and DHA from ALA to provide all of the health benefits listed above.

People who support the use of fish oil as a direct source of EPA and DHA will sometimes cite studies that claim that some groups of people are not able to convert ALA to DHA, at least not very efficiently.

People who support exclusive use of plant foods tend to point to studies that suggest that humans don't have a problem converting ALA found in plant foods to EPA and DHA, thereby suggesting that it is not essential to eat animal foods that contain EPA and DHA.

Ultimately, the only way to know with absolute certainty that you are getting enough ALA, EPA, and DHA from your diet is to analyze your fatty acid profile with a specialized blood test.

Rather than spend money and time getting an expensive fatty acid profile test, I prefer to rely on a well balanced diet that includes lots of dark green leafy vegetables, some walnuts, and a small amount of clean animal foods like wild salmon, organic eggs, and cod liver oil to ensure that my family and I are getting enough ALA, EPA, and DHA to support our best health.

Some people who support eating only plant foods raise objections to using fish oil, such as the possibility of omega-3 fatty acids in fish oil turning rancid, as well as the possibility of fish oil containing environmental pollutants like mercury. These objections are valid, as independent studies performed by organizations like consumerlabs.com have found that some brands of fish oil contain rancid fatty acids that can harm your health. And there's no question that fish from all parts of the world stand a chance of being contaminated to some degree by mercury and other industrial pollutants.

These are reasons why I use and recommend cod liver oil made by Carlson Labs in Arlington Heights, Illinois. Carlson goes to great lengths to protect the fatty acids in their cod liver oil against rancidity. They also have their cod liver oil tested on a regular basis by an independent, FDA-approved laboratory to ensure that it is not contaminated by mercury and dozens of other environmental pollutants.

Do you need to use a high quality fish oil on a regular basis to get enough EPA and DHA to support your best health? Not necessarily. If you regularly eat foods that are listed beside each of the omega-3 fatty acids listed above, chances are that you will get enough omega-3 fatty acids to support your best health.

What if you want to be strict vegan? Then I recommend that you eat lots of dark green leafy vegetables, some walnuts, some freshly ground flax seeds, and take a DHA supplement made from a plant source.

Suggestions for supplements and omega-3

The safe, daily basis dosage intake recommended by the health providers for a 70-kg human is a total of 3g/day of DHA and EPA omega-3 fatty acids from conventional and food sources. Increasing an individual's nutritional intake of fish is highly commendable. There are some worries over the amounts of impurities like mercury and Polychlorinated biphenyl (PCB) in fish. The highest amounts of impurities have been discovered in cultivated fish and the lowest amounts in marine reaped fish [3,6]. The mercury content in fish oil is not a worry because mercury is deposited in the tissue, and not in the oil. Most toxins, including dioxin, PCB, pesticides, etc. however, are deposited in the fat and are a thoughtful apprehension [3]. From this, it is advisable traders of fish oil subject the oil to molecular purification to eliminate these contaminants. This treatment becomes costly, but it's more worth it. Some side effects of Fish oil include belching, heartburn, bad breath, and nausea. Intake of fish oil supplements in every meal can reduce the related side effects [7].

Significance

The aim of this paper is to investigate if the omega-3 fatty acid effective to reduce the risk and prevention of breast cancer. Omega-3 fatty acids (EPA and DHA being the major components) are safe and effective in reducing the risk and prevent breast cancer because they inhibit tumor growth and development, inhibit metabolism of arachidonic acid, modify the hepatic phases (1 and 2) of the detoxifying process hence affect carcinogen activation and have cytotoxic effects on tumor cells. The big question that the paper seeks to answer is; how efficient is the use of fatty acids in the actual reduction of the risk and prevention of breast cancer?

Materials and Methods

The data in this study was collected via Royal Melbourne Institute of Technology (RMIT) University Library as electronic database by accessing other database such as, Web of Science, ProQuest, PubMed, Medline, and Science Direct databases.

Key words which used in this study were: Omega-3, fatty acids, fish oil, DHA, EPA and breast cancer. The searches were limited to English articles which were written in recent years those articles might be trials, reports, review and original articles which recovered from reference lists of identified studies to expand the search. The Endnote program from RMIT Library was used to organize the references for this study by using the Vancouver style in writing.

Results

The result part is composed of an analysis of five different studies conducted on the effects of fatty acids on breast cancer. The first sturdy was by Ruth., *et al*. on the prognosis of breast cancer with intake of fatty acids in drug and food supplements. The second result by Joann., *et al*. analyzes the effect of vitamin D and omega-3 fatty acids on the prevention of breast cancer. The third sturdy results by Isabelle., *et al*. show the results obtained from the clinical trials of fatty acid food supplements on the prevention of breast cancer. The forth study results by Kent and Neil show the role of stem cells and fatty acids in cancer prevention. The last results by Brown., *et al*. are about the level of detection of ethanolamides in patients after treatment with omega-3 fatty acids.

Prognosis of breast cancer with intake of marine fatty acids

The choice of patients for observation of the prognosis of breast cancer is limited to the women with no history of cancer recurrence. Ruth., *et al*. conducted the research on women who averaged 3088. The women were administered with fatty acids food sources and supplements in different doses. The occurrence or non-occurrence of breast cancer was observed among these women. Some of the obtained results are provided in details in table 1 below.

Ruth., *et al*. found out that there was a 25% risk reduction for additional events of breast cancer. A combination of marine fatty acids with dietary supplements produced the same effect. There was no sufficient evidence of additional events of breast cancer due to EPA and DHA supplements. Ruth., *et al*. collected information of the fatty acids intake from self-reports of subjects. The mean of the intake was calculated and found to be around 185 mg per day [12,36,40]. An average of 4.0 women reported using supplements with n-3 fatty acids such as fish oil supplements. The women who used fish oil supplements recorded a daily intake of the fatty acids that averaged a minimum of 350 mg. The study by Ruth., *et al*. recorded that several women who were using the fish oils to supplement their fatty acids content did not experience any additional events of breast cancer. A further examination of the reported in-

formation revealed that most of the women who did not take fish oil supplements recorded increased events of breast cancer.

The use of a time dependent multivariable covariate helped in the calculation of the events of breast cancer in these women. The model revealed a 25% reduction of the risks associated with breast cancer for the women who took fish oil supplements containing n-3 fatty acids [8].

Study population	Mode of fatty acid intake	No additional cancer events	Additional cancer events
3088 women with non -recurrent breast cancer	Food sources Baseline	n 2564	n 517
	6 mo	1214	195
	12 mo	2331	314
	24 mo	1129	115
	36 mo	1111	100
	48 mo	2189	144
	72 mo	2085	60
	Supplements Baseline	% of users 4.1	% of users 5.0
	6 mo	3.3	3.1
	12 mo	3.9	3.5
	24 mo	5.6	0.9
	36 mo	6.2	4.0
	48 mo	7.1	6.3
	72 mo	10.7	1.7

Table 1: Summary by Ruth., *et al.* on the association of marine fatty acid intake with a prognosis of breast cancer.

Effects of vitamin D and omega-3 fatty acids on cancer prevention

This study by Joann., *et al*. selected a group of 20,000 US women and men. The choice of these people was restricted to subjects with no history of cancer or cardiovascular disease. People from the African American origin were given special consideration due to the inability of their pigmented skin to synthesize vitamin D. The men and women were randomly administered with supplements of marine fatty acids at baseline and follow up procedures. They were observed for a period of 5 years. The observations are provided in detail in table 2 below. It has been found out that omega-3 fatty acids and vitamin D are helpful in the reduction of risks towards cancer and cardiovascular disease. Other than these, the omega-3 and vitamin D supplements also aided in prevention of secondary of these diseases as well as reducing the high risks [34].

Study population	10, 000 women aged over 55 years 10, 000 men aged over 50 years		
Cancer	Total cancer	Cancer	Breast in
	52.1	Mortality	Women
	86.3	-	-
	98.5	-	-
	99.9	42.3	32.8
	99.9	60.9	48.4
	99.9	77.7	64.7
	99.9	89.7	79.0
		96.2	89.4

Table 2: Summary by Joann*., et al*. on the vitamin D and n-3 trial (VITAL) on the prevention of cancer and cardiovascular disease (CDV).

Clinical trial for prevention of breast cancer

This study by Isabelle., *et al*. selected women who appear to be at a higher risk of developing breast cancer. As subjects for the assessment, 3,081 breast cancer survivors were used to assess whether a major increase in dietary fat intake reduces risk of recurrent and new primary breast cancer. Trained dietary assessors obtained detailed data on dietary intake and also probed participants on the consumption of dietary supplements. Even so, the use of double blind randomized control trial was applied to increase the efficiency of the survey as well as to do away with any possibility of biasness. 35,016 postmenopausal women between the ages of 50 and 76 took part in a ten year vitamins and lifestyle (VITAL) study. All participants were residents of Washington State and had no history of breast cancer [4].

Dietary foods such as flaxseed and drugs such as anastrozole were used as sources of omega-3 supplements. Isabelle., *et al*. used biomarkers for observational process. Details of the study are provided ion table 3 below.

These include the breast density and the progress of cancer. At the end of the clinical trial on the cancer survivors, with regard to the original tumor, 16.8% had additional invasive breast cancer events and 10.2% died. Breast cancer caused 83.1% of the deaths while 8.6% of the deaths were by other cancers [4]. Information on intake of marine fatty acids was also taken during the study.

Generally, intake of marine fatty acids increased overtime. Women who had increased intake of fatty acids from marine foods did not experience additional breast cancer events. For those who did not increase intake, they experienced additional events. 'This is the first study conducted on breast cancer survivors to indicate that consumption of marine fatty acids is associated with improved breast cancer prognosis; high intakes of EPA plus DHA from marine food was associated with a reduction in additional breast cancer events' [2,38].

The role of stem cells in cancer prevention

This study by Kent and Neil employed the services of experimental animals and tumor cells from human beings and found that high concentration of EPA, DHA and CLA is capable of altering cell tumorigenesis. However, dietary application of these agents in humans gives a very weak link to the prevention of breast tumor. By culturing tumor cells in dishes with low adherence, the effects of fatty acids on proliferation and cytotoxicity were observed for a period of two weeks. The cells causing tumors (stem cells) were significantly altered by the fatty acids. Fatty acids prevented both cancer tumor proliferation and cytotoxicity [39]. Detailed results are presented in table 4 below.

Ethanolamides detections after treatment with n-3 fatty acids

According to Brown., *et al*. the time during which eicosapentaenoyl ethanolamide retention (EPEA) occurred was approximately 6 minutes. On the other hand, the retention time for docosahexaenoyl ethanolamide (DHEA) in the human cell was observed to average about 7.0 minutes. The chromatography results on the retention of 2-arachidonoylglycerol (2-AG) recorded a peak result of 7.8 minutes.

Subject group	Trial tools	Outcomes that are measured
manipulation of hormones and the use of dietary supplements	n-3 dietary supplements such as lovaza Drug applications such as roloxifene	Density of breast, oxidase stress biomarkers, metabolites.
Use if flaxseed in cancer prevention for the premenopausal women	Diet supplement included flaxseed Drugs used was anastrozole	Primary cancer development, baseline changes to a period of 6 months
Treating women with stage 1 or stage 2 breast cancer	Flaxseed dietary supplement Drug called anastrozole	Transformations from the original biopsy of tumor to a resection tumor, The recurrence of mammastrate scores. Profiles of steroids and growth hormones
Women at a higher risk of developing cancer of the breast	The use of n-3 in the diet to preventing breast cancer	Mammographic density of the breast, Peroxidation of lipids, hormones.
Treating breast tumors using flaxseed and aromatase inhibitors	Dietary supplements of flaxseed, the anastrozole drug	Characteristic of the tumor, apoptosis as well as proliferation

Table 3: A summary by Isabelle et al on the clinical trials for the prevention of breast cancer.

Control element	Dead	1 cell	2-8 cells	Small cluster	Tumor-sphere
Control	0%	22%	35%	74%	100%
LA	5%	6%	15%	52%	100%
(t10.c12)-CLA	55%	58%	82%	98%	100%
C9.t11- CLA	55%	59%	72%	98%	100%
EPA	36%	0%	56%	87%	100%
DHA	48%	52%	67%	98%	100%

Table 4: Summary of Kent and Neil on the role of stem cells in fatty acids prevention of breast cancer.

This study by Brown., *et al*. used both human and animal cells. Human prostate and breast cancer cells were collected together with the cell culture of animals and tested with fatty acids. Several observations were made with different types of cells and cell compounds. Two peak retention times were observed for 2- AG as shown in table 4 below. According to Brown., *et al*. n-3 fatty acids aid in inhibiting the growth of prostate and cancer cells as shown in table 5. All the cells that were not treated had a greater level of the overall 2-AG as compared to endocannabinoids as demonstrated by Brown., *et al*. This is obtained to meet the mean of the value 135.63 pmol/mg, which confirmed that the breast related cancer cells attain a higher base line than that of prostate related cancer cells with respect to the 2-AG level. The EPEA was actually absent in the untreated breast cancer cells. After the administration of treatment, MDA-MB-231 cells increased significantly as well as the MCF-7 cells, which resulted in the production of both 0.99 pmol/mg of the overall cell protein and 0.93 pmol/mg of the total cell oriented protein. There was an increase in the DHEA related synthesis in cell lines following the treatment of cells with DHA. It is therefore correct to say that the actual treatment of the cancerous cells with DHA as well as EPA causes an increase in the level of the corresponding n-acylethanolamine endocannabinoid related derivatives in actual vitro [4]. This is so irrespective of the presence of FAAH. The CB receptors as well as the levels of FAAH, enables the actual treatment of cancer through dietary based intervention or perhaps the actual supplements of the available n-3 fatty acids [11,35].

Endocannabinoid Compounds	Peak retention time at 100 relative abundance (min)
EPEA	6.05
AEA	7.50
AEA-D4	7.50
DHEA	7.34
2-AG	7.89

Table 5: Summary by Brown., *et al*. showing that omega-3 N-acylethanolamines are synthesized endogenously from omega-3 fatty acids in different cancer and prostrate cell lines.

Discussion

From the research there is satisfactory evidence to suggest key involvement between omega 3 fatty acids and cancer incidences. According to the study, there was a 25% risk decline for extra events of breast cancer. A mixture of marine fatty acids with nutritional supplements created identical effect. There was little confirmation of extra events of breast cancer owing to EPA and DHA supplements. The study by Ruth., *et al*. established that some women who used the fish oils in supplement of their fatty acid content did not have recurrent events of breast cancer. An additional evaluation of the research revealed that the majority of the women who did not use fish oil supplements developed high events of breast cancer [26]. Nonetheless, the use of time reliant multivariable covariance assisted to approximate the events of breast cancer among women. The model confirmed a 25 percent decline in the risks linked with breast cancer for those women who had used fish oil supplements rich in n-3 fatty acids.

Thus, it was evident the consumption of marine fatty acids was connected to enhanced cancer prognosis in particular among the cohort of 3088 women with non-recurrent breast cancer (Table 1). Huge intakes of DHA and EPA in food also reduced the breast cancer recurrences. It is clear the models that used marine fatty acids as a constant variable were not considerable, and hence there were no indications of a linear association amid this experience and breast cancer result.

There is a brink effect with intakes of >72 months as the extra cancer events were negligible in relation to intakes of baseline and >6 months which amplified extra cancer events. The median intake was of >72 months and this were associated with a reduction in the risk. In line with our expectations, fish oil supplements gave huge amounts of marine fatty acids and were in no way associated to recurrent breast cancer events. The use of fish oil supplements in this cohort of 3088 women with non-recurrent breast cancer was small and therefore not adequate to examine its exposure.

In addition, the use of fish oil supplements contributed minimally to enhanced outcomes in this cohort is an indication that fatty acids from foods are usually indicative of other dietary and lifestyle factors. The modifications in our analysis have attempted to isolate an independent effect; unmeasured variables cannot be wholly evaluated in an observational study of this nature. It is now confirmed that results researching on the link between breast cancer risk and ω-3 fatty acids will vary based on the design of the study [27]. These results did confirm significant effects of ω-3 fatty acids from fish on breast cancer risk in women with non-recurrent

breast cancer. However, in respect to etiologies of recurrent breast cancer, various hypotheses will hold. Thus in most cases, the link between nutritional fat intakes and breast cancer risks will vary in women with recurrent breast cancer.

All cancer patients will differ from the controls in their dietary habits. The adding of other nutritional supplements has assisted us to know the impact of-3 fatty acids intake. From the study by Joann., *et al*. when a cohort of 10, 000 women aged over 55 years and 10, 000 men aged over 50 years were exposed to Vitamin D and consumed Omega-3 fatty acids, and their risk of cancer was lowered. Dietary DHA is known to be protective against aggressive prostate cancer in men and breast cancer in women. Furthermore, more research into nutritional intakes of Halogenated hydrocarbons or heavy metals and genetic factors will be imperative in expounding the protective effect of fish intake on breast cancer [30].

It is very evident that Omega- 3 fatty acids inhibit the tumour growth in breast cancer and high intakes reduced considerably the risk of cancer. There was almost a 50 per cent decline in the risk of cancer deaths and a 19 per cent reduction in mortality among the men and women taking Omega-3 fatty acids. Thus, there is a clear link between increased Omega 3 fatty acid intake and a favourable cancer prognosis in the cohort of 10, 000 women aged over 55 years and 10, 000 men aged over 50 years [29].

Advances in medicine in the past decades have enhanced diagnosis and treatment of breast cancer. In spite of this progress, breast cancer still remains the leading cause of mortality among women with majority relapsing with metastatic disease. The survival rates of the disease have remained minimal after close to 10 years. Joann's., *et al*. study raises the fact that the surveillance of tumours and other defensive mechanisms could have the ability to control the disease. This study by Joann., *et al*. researched on a cohort of 3081 women who at the time where at high risk of developing the disease. Omega-3 blocks the growth of breast cancer tumors even in women with recurrent breast cancer [29].

Advances in medicine in the past decade have enhanced diagnosis and treatment of breast cancer. In spite of this progress, breast cancer still remains the leading cause of mortality among women with majority relapsing with metastatic disease. The survival rates of the disease have remained minimal after close to 10 years. The fact that the surveillance of tumors and other defensive mechanisms could have the ability to control the disease. The Joann's., *et al*. study researched on a cohort of 3081 women who at the time where at high risk of developing the disease.

Thus, the clinical trials by Isabelle., *et al*. in the cohort of women at high risk of developing cancer established that with the consumption of omega-3 supplements, just about 16 percent had additional breast cancer events and close to 10 percent succumbed to the disease. Many of the deaths were due to breast cancer and just about 8.5 percent was attributed to other cancers. During the research, the intake of marine fatty acids increased over time and those women who had increased their consumption of marine fatty acids did not have extra breast cancer events. The women who did not increase their consumption of marine fatty acids however developed additional breast cancer events. This is the first study to be done on breast cancer survivors that has established a link between the intake of marine fatty acids and flaxseeds improved breast cancer diagnosis. Thus from the cohort of the cancer survivors it was established that huge intakes of DHA, EPA and Flaxseeds as treatment reduced the occurrence of breast cancer events [31].

Kent and Neil, in the research they used experimental human and animal tumor cells and established that cells with high concentrations of DHA, CLA and EPA had the ability to modify tumorigenesis of the cell. Nutritional applications to these agents yielded a weak link in the prevention of breast cancer tumor growth. It is clearly evident fatty acids altered the tumor causing cells and hence prevented the growth of additional cancer events. Our present paradigm in respect to cancer prevention was introduced when many cancers were perceived as homogenous collections of many transformed cells [28]. This study by Kent and Neil has noted the mixed nature of solid tumors and the role played by stem cells.

We cannot deny the fact that stem cancer therapy theory has significant implications in relation to cancer treatment as most of the chemotherapy regimens used have been able to shrink tumors by killing the non-stem cells and hence eliminating the cancer stem cells. Epithelial models of cancer have given hope for the use of epithelial stem cell as a main candidate to be used as a predecessor of the cancer stem cells. So what unique features does the stem cell have to offer such prospects in cancer treatment? Stem cells are known to have unique properties of self-renewal, prolonged existence and pluripotentiality. Though most adult stem cells are tissue based, more attention has been given to the circulating adult stem

cells such as HSC (hematopoietic stem cells) and MSC mesenchymal stem cells. Key aspects of the stem cells are controlled by the stem cell niche.

A vital step in tumor development is the angiogenesis process as it includes the recruitment of endothelial progenitor cells from the blood to produce new blood vessels. In our model system, solid tumors could also arise from BMBDs instead of the epithelial stem cells as in the majority of cases they have been brought to the site by the chronic injury and inflammation of tissues. Inflammation promotes and some cases are known to induce cancer and this study established that T cells and macrophages are vital when it comes to sustaining the progression of tumor. On the other hand, the modifications in the stem cells could even result to the conversion of normal stem cells into cancerous stems cells. Nevertheless, more comprehension on the nature of stem cells could provide new approaches for inhibiting the formation of cancer at the initial stages when it is easily controllable [33]. There is a need to understand the role that maintenance of cell division and differentiation of stem cells play, as this could result in to a new approach that will give indications of the pathways that are involved in the progression of cancer, and this could eventually produce new approaches for the treatment of cancer.

The notion that the existence of transformed population's cells with characteristic of stem cells is responsible for the growth of tumors is very dominant in the breast cancer field. Any novel treatments targeting the population of the cancer stem cell can be used to treat both metastatic and primary breast cancer tumors. Most of the therapies using cancer stem cells have been proven to be clinically relevant when it comes to the inducing the long term clinical remissions of cancer. We should not also ignore that cancer stem cells have cell antigens that give new targets for the immune therapy of cancer. Dendritic cell (DC)-based therapies and adoptive T-cell transfer are known to treat putative cells with tumor origin and they are many times used with present treatments [29]. To ensure our treatments are effective, researchers will need to define the cancer stem cells in terms of antigenicity and the distinctions between stem cells and the cancer stem cells. Thus, it is imperative to assess the function of stem cells in mammopoiesis, their role in tumor development and the prospect of using cancer stem cells for therapy with a spotlight on breast cancer.

In the study by Brown., *et al*. it was established that eicosapentaenoyl ethanolamide retention (EPEA) occurred in around 6 minutes while the retention time for docosahexaenoyl ethanolamide (DHEA) in the human cell was close to 7 minutes. Thus, the Endogenous synthesis of omega-3 N-acylethanolamines by omega-3 fatty acids in prostate and cancer cells in the cohort of human and animal cells showed that n-3 fatty acids helped in the prevention of the growth of cancer and prostate cells as illustrated in table 5. The cells that had not been treated with n-3 fatty acids showed high levels of the overall 2-AG in relation to endocannabinoids in the study [32].

Thus, it is evident that the treatment of cancer cells by the use of EPA and DHA results in the increase of n-acylethanolamine endocannabinoid in actual vitro. DHA and EPA have been known to activate the CB1 and CB2 receptors in both LNCaP and PC3 cells. The ethanolamides DHEA and EPEA can be detected *in vivo* after the intakes of nutritional diets rich in DHA and EPA. The mechanisms responsible for such inhibitions are so far unclear as they differ between DHEA and EPEA and also in the prostate cancer cells used in the study [31]. There are no doubt a statistical difference between the potency of ethanolamides in relation to their fatty acid parent molecules.

DHEA is known to cause apoptosis in PC3 and LNCaP cells. Results from Brown., *et al*. study show that omega-3 long-chain polyunsaturated fatty acids (LCPUFA) can actually induce apoptosis [31] independently of the p53 activation that could modify the expression of the mutant p53 to establish the wild type role in brain cancer cells. It is still vague whether omega-3 ethanolamides can affect apoptosis in a similar reactivation approach in either breast or prostate cancer cells. Finally, it is now confirmed that EPEA, DHEA, and omega-3 ethanolamides are more patent than their parent fatty acids DHA and EPA in inhibiting prostate cancer growth [30]. Thus as a proposal DHEA and EPEA should be classified as endocannabinoids as omega-3 ethanolamides are produced *in vivo* after intake of their parent fatty acids, EPA and DHA.

Conclusion

This study concludes that Omega-3 fatty acids do fight against breast cancer especially among women who have been diagnosed with the disease. Omega-3 fatty acids have the ability to shrink the breast cancer cells preventing metastasizing. Thus, women who consume high levels of omega-3 in their diets or food supple-

ments have minimum incidences of metastasis that is very common among women with low levels of Omega-3 fatty acids in their bodies. Suggested areas for further study are imperative to assess the function of stem cells in mammopoiesis, their role in tumor development and the prospect of using cancer stem cells for therapy with a spotlight on breast cancer. In the future, further research is also needed on Omega -3 and breast cancer prevention especially focusing on the optimal Omega-3 doses that benefits the body.

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