



Cancer: Possible Prevention and Chemotherapy by Fatty Materials: (A Review)

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Abstract

Dietary factors are well known to play an important role in cancer. About 55% of all cancers have been related to nutritional habits. Good nutrition is especially important for people with cancer. That is because the illness itself, as well as its treatments, may affect our appetite. It is now popular, to use diet or natural dietary supplement against cancers. This review highlights the possible prevention of cancer by including fatty materials in our diet.

Key words: fats, polyunsaturated fatty acids, anti tumor agents, phytochemicals, functional foods.

Introduction

Cancer is the leading cause of death among the global population including United States. A recent American Cancer Society statistical survey has concluded that cancer now exceeds heart disease as the top cause of death among Americans below the age of 85 years, responsible for about 47600 fatalities compared with 450,600 deaths yearly from heart disease. Cancer refers to a large number of diseases categorized by unregulated replication (proliferation) and spread (metastasis) of abnormal cells.

All the time scientific community are making strides in developing therapeutic strategies--ranging from nutritional and herbal to body and mind practices--that may one day become universally acceptable treatments. While no one is claiming to have found an outright remedy, several leading oncologists have had such positive experiences with complementary and alternative methods that they have started integrating them into their practices.

The good news is that scientific validation for the protective power of food is accumulating and empowering people to preserve their health through daily choices puts responsibility in the hands of cancer patients. A dizzying amount of information exists on cancer-preventive food and supplements. It is a perfect opportunity to discuss diet and supplements for cancer prevention.

We are exposed to oxidizing and cancer-producing chemicals in our daily life, but the natural compounds found in vegetables help limit the free radical initiation and DNA damage caused by these carcinogens and therefore appear to lower the incidence of various types of cancer. Recently, functional foodstuffs are known that possess disease preventing and/or health enhancing characteristics together their nutritive or processing values. A food can be regarded as “functional” if it satisfactorily offers beneficial affect on one or more target functions in a human body system, beyond adequate nutritional effects. A natural food can act as a functional food if required in that a certain desired constituent has been added, or from which an undesired component has been removed either by technological or biotechnological methodology.

Mostly a variety of fatty acids present in lipids of fatty oils are great nutritional beneficial compounds and have recently being recognized as candidates of potential advantages of their incorporation into human diets as essential functional ingredients. Functional foodstuffs must be safe according to all standards assessing food risk. However, the concept of risk versus potential benefits cannot be treated in such a straightforward fashion as it is for drugs. Finally, long term consequences of interactions between various ingredients of functional food and functions in a human body and interactions between components must be carefully monitored.

Fat is always treated and considered as a worst word in current nutritional world and particularly women are more attracted to eat food consisting of a low-fat diet to help prevent breast cancer, as well as several other ailments, including different kinds of other cancers. Animal fats such as butter have taken a harsh bashing in the media over the past few decades and have been blamed for horrific crimes, including obesity, cancer and heart disease and so on. Accordingly, Western populations have been virtually brainwashed into seriously considering that butter and other predominantly saturated fats like tallow and coconut oil are unhealthy. So-called safe substitutes like margarine and various vegetable oils have been heavily promoted and advertised with the result being that the public associates these things with health and well being. When it comes to breast cancer prevention, and in some cases treatment, the so-called ‘bad fats’ are actually the ‘good fats’, and the ‘safe substitutes’ are increasingly being shown up for what they really are: fabricated foods that cause disease, including breast cancer. Whole-grain foods, rather than those derived from processed grains, are also worth emphasizing. Whole grains contain essential fatty acids (EFAs), which serve as precursors to prostaglandins and are important components of cell membranes.

American Institute for Cancer research (AICR) has always recommended a diet for cancer survivors that is low in fat; is high in fruits, vegetables, and whole-grain products; and has adequate levels of the major macronutrients as well as the various vitamins and minerals necessary to maintain good health [1]. Dietary supplements include macronutrients, vitamins, and minerals that are essential to human health as well as a wide variety of nonessential nutrients, such as certain phytochemicals, hormones, and herbs. The recommendation for cancer patients is to take only moderate doses of supplements because evidence from human clinical studies that confirm their safety and benefits is limited [2]. AICR and the World Cancer Research Fund advised that five or more servings of fruits and vegetables be consumed daily to reduce the risk of certain cancers [1]. The beneficial effects of fruits and vegetables for both healthy people and cancer survivors have sometimes been associated with the presence of various antioxidant micronutrients. It has been claimed that oxidative processes are involved in various stages of carcinogenesis, that excessive antioxidants

interfere with the cytotoxic effects of antineoplastic agents on cancer cells, and that certain micronutrients affect cancer prevention and treatment through their antioxidant properties. These micronutrients include vitamin E, vitamin C, β -carotene, and other carotenoids, which are available singly or combined. The trace element selenium has an important role in antioxidant defenses as a crucial component of selenoproteins, such as glutathione peroxidase. Phytochemicals with antioxidant properties also include some flavonoids, such as quercetin, and some polyphenols.

Overall, there is no convincing evidence that antioxidant nutrients in the amounts obtained from fruits and vegetables in the diet have any deleterious effects on human health [1]. However, trials in which selected antioxidants are taken in amounts or combinations much higher than those normally found in foods have yielded conflicting data regarding cancer risk [3, 4]. Cancer patients should try to eat sufficient fruits and vegetables daily to provide adequate levels of antioxidants, with the addition of a daily multivitamin-multi-mineral pill. The benefits of eating fruits and vegetables may be much greater than are the effects of any of the individual antioxidants they contain because the various vitamins, minerals, and phytochemicals in these whole foods may act synergistically [1, 5].

Phytochemicals and Zoo chemicals: Phytochemicals are a group of nutritive components found in herbs, fruits, vegetables, grains, legumes, nuts and spices. Animal foods contain a similar group of disease preventing nutrients- the term zoo chemical has been suggested for them. Several disease preventing benefits have been proposed for phytochemicals and zoo chemicals.

1. Facilitate cell- to –cell communication,
2. Mortify cellular receptor uptake of hormones,
3. Convert to vitamin A,
4. Repair DNA damage from toxic enzymes.
5. Detoxify carcinogens through the activation of the cytochrome P450 and phase 2 liver enzyme systems,
6. Cause apoptosis (cell death) in cancer cells,
7. Enhance immune response,
8. Help prevent cardio vascular diseases, osteoporosis etc.

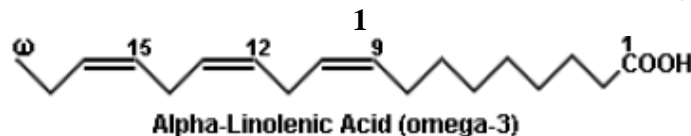
Phytochemicals and zoo chemicals can be grouped into five families based on their chemical structure and biological activity. The families include terpenes, organosulfur compounds, phenols, organic acids and polysaccharides, and lipids (by Marcia Zimmerman, M. Ed., C.N.). Phytochemicals like resveratrol, curcumin, capsaicin, genistein and ginseng, marine foods (omega-3-polyunsaturated fatty acids) and minerals (Zn^{2+}) would appear to support the CELEX hypothesis. These include lycopene a potent antioxidant carotenoid, mostly found in tomatoes, which has been shown to inhibit tumor cell growth [6]. In combination with vitamin E and selenium, lycopene suppressed metastasis tendency in human prostate cancer [7]. Catechins are the active ingredients of green tea for which there are substantial anti-cancer effects with a range of modes of action [8]. A particularly important such effect appears to involve angiogenesis [9]. It would be of interest to determine if such effects of catechins might involve ion channels including VGSCs, known to be expressed in human endothelial cells [10]. “Kava Kava” is another dietary supplement which is a strong ‘calming agent’, associated with low incidence of cancer [11]. In conclusion, several dietary compounds could have anti-cancer effects via action upon ion channels and reduction of membrane excitability.

Essential fatty acids (EFAs), linoleic acid (LA), and α -linolenic acid (ALA) are essential for humans, and are freely available in the diet. Hence, EFA deficiency is extremely rare in humans. To derive the full benefits of EFAs, they need to be metabolized to their respective long-chain metabolites, i.e., dibromo- γ -linolenic acid (DGLA), and arachidonic acid (AA) from LA; and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from ALA. Some of these long-chain metabolites not only form precursors to respective prostaglandins (PGs), thromboxanes (TXs), and leukotrienes (LTs), but also give rise to lipoxins (LXs) and resolvins that have potent anti-inflammatory actions. Furthermore, EFAs and their metabolites may function as endogenous angiotensin-converting enzyme and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, nitric oxide (NO) enhancers, anti-hypertensive, and anti-atherosclerotic molecules. Recent studies revealed that EFAs react with NO to yield respective nitroalkene derivatives that exert cell-signaling actions via ligation and activation of peroxisome proliferator-activated receptors. The metabolism of EFAs is altered in several diseases such as obesity, hypertension, diabetes mellitus, coronary heart disease, schizophrenia, Alzheimer's disease, atherosclerosis, and cancer. Thus, EFAs and their derivatives have varied biological actions and seem to be involved in several physiological and pathological processes [12].

Vitamin E: Vitamin E is a lipid-soluble antioxidant. It is naturally synthesized only by plants, and its various forms occur in different proportions. The main sources of vitamin E are edible polyunsaturated vegetable oils. Vitamin E is the most important nutrient for preventing polyunsaturated fatty acid peroxidation. α -Tocopherol is the form of the vitamin most commonly used as a supplement, but vitamin E succinate is also used. The RDA for vitamin E is 15 mg/d; the UL is 1000 mg/d [13]. Vitamin E may prove to be an important nutrient for enhancing antineoplastic activity because of its role in preventing the peroxidation of lipids. This property maintains the rapid proliferation of cancer cells, which is essential to chemotherapy, while preventing damage to normal cells and having beneficial effects on immune function. Some evidence shows that in cancer cells vitamin E has a synergistic effect with chemotherapy and radiation [14]. In animal studies, combinations of high doses of vitamin E and chemotherapy have had beneficial effects, detrimental effects, and no effect [14]. Vitamin E may be useful in the management of treatment for some cancer patients because it has been shown to reduce pain [15] prolong survival in conjunction with (n-3) polyunsaturated fatty acids [16], reduce fibrosis from radiation treatment [17], and decrease oral mucositis associated with chemotherapy [18]. Vitamin E, although reported to reduce somewhat the cardio toxicity of doxorubicin, had no striking effect otherwise [19, 20]. Treatment of oral leukoplakia with vitamin E was successful and well tolerated [21]. Intensive topical treatment with vitamin E may facilitate the healing of chemotherapy-induced stomatitis [22]. In considering the possible use of supplementary vitamin E, it is essential to remember that vitamin E may act as a prooxidant in cigarette smokers, particularly if they are following a diet with high amounts of (n-6) fatty acids [23]. In addition, vitamin E acting as a prooxidant in high concentrations was shown to directly inhibit human prostate tumor growth via induction of tumor cell apoptosis without affecting surrounding tissues [24]. 5-Fluorouracil is possibly the single most effective treatment for advanced colorectal cancer; vitamin E was shown to induce cell death in colorectal cancer cells and to enhance growth inhibition of these cells by 5-fluorouracil [25], suggesting an adjuvant therapy for colorectal cancer.

Poly unsaturated fatty acids: Two families of polyunsaturated fatty acids are essential: the (n-6) and the (n-3) families, which are grouped according to their chemical structures.

Although plants can synthesize both the basic (n-6) and (n-3) structures, animals (including humans) cannot and must obtain them from dietary sources. Linoleic acid is the parent fatty acid of the (n-6) family and α -linolenic acid is the parent of the (n-3) family (fig. 1 and 2)



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The Western diet is rich in (n-6) fatty acids and poor in (n-3) fatty acids because of the large amounts of vegetable oils and meats and relatively low amounts of fish in the diet. Both (n-6) and (n-3) polyunsaturated fatty acids are important components of animal and plant cell membranes. α -Linolenic acid comes from green leafy vegetables, flaxseed, rapeseed, and walnuts. Humans can form eicosapentaenoic acid and docosahexaenoic acid from α -linolenic acid or get them from eating fish. Most liquid vegetable oils, including corn, are rich in linoleic acid. Humans can form arachidonic acid from linoleic acid or get it from eating meat. Eicosapentaenoic acid and arachidonic acid are precursors of prostaglandins and leukotrienes. Indications are that dietary (n-3) fatty acids can significantly retard the growth of tumors whereas (n-6) fatty acids potentially can increase tumor development [26]. However, the data are largely derived from animal experiments [27], and regulation of the growth of human cancers is still a controversial issue. Mechanisms of fatty acid effects on tumor genesis and tumor growth are not well defined, but evidence exists that high levels of prostaglandin E₂, derived from (n-6) fatty acids, promote tumor growth. Fish oil-enriched diets containing eicosapentaenoic acid and docosahexaenoic acid decrease the formation of prostaglandin E₂, which coincides with retarded growth of tumor cells. An alternative mechanism proposed is that oxidative damage of the polyunsaturated fatty acids in fish oil enhances lipid peroxidation in the tumor to toxic levels.

Fish oil supplementation enhanced the efficacy of the cancer chemotherapeutic agent CPT-11 (irinotecan) against MCF7 breast carcinoma xenografts and ameliorated intestinal side effects in MCF-7-bearing mice [28]. The explanation given is that the combination of fish oil and CPT-11 leads to the selective accumulation of lipid peroxidation products to cytotoxic levels in the MCF7 xenografts.

Experimental studies indicate that very-long-chain polyunsaturated fatty acids, in particular docosahexaenoic acid, may increase the sensitivity of mammary tumors to several cytotoxic drugs, including doxorubicin [29]. Omega-3 (n-3) fatty acid supplementation for breast cancer chemoprevention is strongly supported by epidemiologic and experimental studies. Experimental data and data from a case-control study conducted on a homogeneous population in France suggest that α -linolenic acid may have a protective effect in breast cancer [30]. The association between levels of fatty acids stored in breast adipose tissue and the response of the tumor to chemotherapy in patients with an initially localized carcinoma was studied [31]; primary chemotherapy combined mitoxantrone, vindesine, cyclophosphamide, and 5-fluorouracil. The results suggested that docosahexaenoic acid could increase the response of the tumor to the cytotoxic agents used. Dietary supplementation with (n-3) fatty acids was evaluated in several clinical trials, and the results suggest some benefits to cancer patients [16, 32].

Omega-3-fatty acids and Cancer: The “Cellular and Molecular Aspects of omega-3 fatty acids and Cancer” workshop was held on June 28-30, 2001 at the Beaver Run Resort, Brackenridge, CO, U.S.A. The conference organizing committee consisted of Laura Jenks, William Stillwell, Arthur Specters, and Robert Katz.

It is now well established that dietary omega-3 polyunsaturated fatty acids (omega-3 PUFAs) can reduce the incidence and/or severity of many cancers. The purpose of “Cellular and Molecular Aspects of omega-3 fatty acids and Cancer” workshop was to bring together investigators from diverse backgrounds who would not normally have the opportunity to interact to discuss the relationship between omega-3 PUFAs and cancer.

Possible modes of action for omega-3 fatty acids discussed at the workshop are briefly summarized below.

Effect on membrane structure and function: The focus on the structural effects of omega-3 fatty acids on membranes was on docosahexaenoic acid (DHA), the longest (22 carbons) and most unsaturated (six double bonds) of the omega-3s. This fatty acid is rapidly incorporated into membrane phospholipids, phosphatidylethanolamines (PE), and cholines (PC) in tumor cells and phosphatidylserines (PS) in neuronal cells. Once incorporated, DHA has a profound effect on many membranes physical properties, including permeability, lateral diffusion, lipid packing, and domain formation. Alterations in basic membrane properties in turn affect the activity of resident proteins. The effect of omega-3 fatty acids on the G-protein coupled metarhodopsin, Raf-1 kinase, ion channels, tyrosine kinases, adeny cyclase, and class 1 major histocompatibility complex protein.

Effect on cell biology: DHA (fig.3) was reported to be involved in programmed cell-death, increasing apoptosis in tumor cells, yet preventing apoptosis in neuronal cells. Perhaps this discrepancy is due to DHA accumulate primarily into PE and PC in the tumor cells and PS in neuronal cells. Another suggesting role for DHA was a competitor of arachidonic acid (fig.4) for cyclooxygenase (COX-2) and 5-lipoxygenase, reducing eicosonoid synthesis and depressing the growth of some cancers. Over expression of COX-2 was anti-apoptotic and therefore tumorigenic.



3

4, 7, 10, 13, 16, 19-docosahexaenoic acid (DHA)



4

Arachidonic acid

Effect on transcription/ translation: The effect of DHA on endothelial cells was attributed to reduction of COX-2 protein expression and enzyme activity by transcriptional regulation likely to involve NF-kB activation.

As source of lipid peroxidation products: The long chain PUFAs were shown to be highly susceptible to lipid peroxidation. In breast cancer cell lines, it was reported that DHA increased toxicity of anthracyclins (agents that generate oxidative stress) and increased lipid peroxides and that both were inhibited by the antioxidant vitamin E. Anti-cancer agents that

have high peroxide generating potential(e.g., doxorubicin and epirubicin)were shown to enhance cytotoxicity with DHA but not with oleic acid. Tumor growth was related to the generation of 13-hydroxy octadecadienoic acid (13-HODE) and was reversed by a lipoxygenase inhibitor.

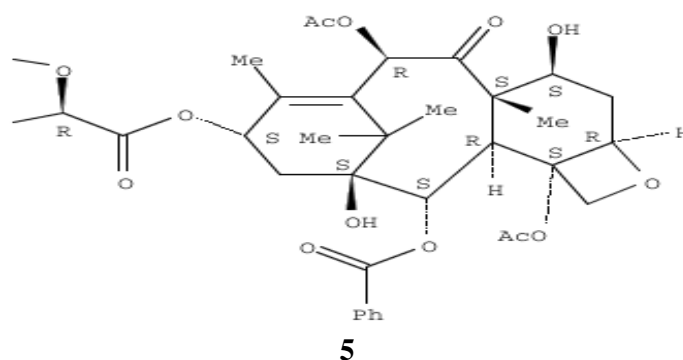
Effect on metabolism: PUFAs regulate the abundance and activities of PPAR (peroxisome proliferation activated receptor) and SREBP (sterol response element binding protein), both involved in the balance between hepatic fatty synthesis/ storage and oxidation. The importance of fatty acid binding proteins (FABPs) in regulating cellular processes, perhaps through transporting the omega-3 fatty acids to the nucleus was also discussed.

As components of novel anti-cancer drugs: It was reported that dietary fish oils improve responsiveness of human mammary carcinoma to chemotherapy with doxorubicin, mitomycin, and cyclophosphamide, probably by enhancing membrane permeability to the drugs. It was predicted that nutritional omega-3s improve the therapeutic index of these three drugs by enhancing pharmacological effects but also by lowering host toxicity. It was demonstrated that omega-3 fatty acids may play a role in treatment of cachexia associated with cancer and AIDS.

Recommendations made by AICR and other official organizations are that energy from dietary fat should be $\leq 30\%$ of the total energy intake. Research indicates that the type of dietary fat is also important for normal growth and development and for treatment of cancer and other diseases. The ratio of (n-6) to (n-3) fatty acids seems to be critical in some cases. It is recommended that cancer patients and healthy people should consume the recommended AI for polyunsaturated fatty acids [26].

Webb et al [33] tested Taxoprexin (a covalent conjugate of cis-docosahexaenoic acid and paclitaxel, fig.5) against lung carcinoma in mice and rats.

$C_{69}H_{81}NO_{15}$



Mochida et al [34], studied Capsanthin (derived from *Capsicum annum*, fig.6) derivatives as anti cancer agents in health food.

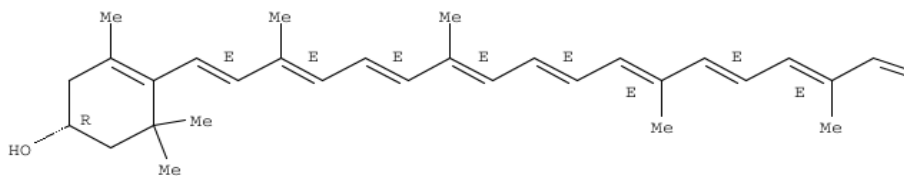
CAS Registry Number: 465-42-9

$C_{40}H_{56}O_3$

β , κ -Caroten-6'-one, 3, 3'-dihydroxy-, (3R, 3'S, 5'R)-

2,4,6,8,10,12,14,16,18-Nonadecanonaen-1-one, 19-(4-hydroxy-2,6,6-trimethyl-1-cyclohexen-1-yl)-1-(4-hydroxy-1,2,2-trimethylcyclopentyl)-4,8,13,17-tetramethyl-, (all-E)- (8CI) ; 2,4,6,8,10,12,14,16,18-Nonadecanonaen-1-one, 19-(4-hydroxy-2,6,6-trimethyl-1-cyclohexen-

1-yl)-1-(5-hydroxy-1,2,2-trimethylcyclopentyl)-4,8,13,17-tetramethyl- (6CI) ; Capsanthin (7CI) ; all-trans-Capsanthin



6

Kubota et al [35] suggested ketol-type unsaturated fatty acids as anti cancer agents and studied their enzymic manufacture. The enzymes used were lipoxygenase and hydro peroxide isomerase. Linoleic acid (2.5g) was treated with pulverized corn in water at 20-30% for one hour to manufacture 0.3g of 13-hydroxy-10-oxo-trans -11-octadecenoic acid and 0.5g of 9-hydroxy-10-oxo-cis-12-octadecenoic acid. 13-hydroxy-10-oxo-trans-11-octadecenoic acid at 20mg/day p.o. showed strong anti cancer activity in S180-bearing mice.

Nakamura et al, [36] reported higher fatty acids as anticancer agents and anticancer agent enhancers.

Anticancer agents contain MeCHR (CH₂) NCO₂H (R=C1-5 alkyl; n=4-22) as active ingredients. The fatty acids are also useful as enhancers for other anticancer agents. Ehrlich ascetic tumor-bearing mice treated i.p. with 12-methyltridecanoic acid at 10mg/kg/day for 5 days had mean survival days \geq 50 days, vs. 14.0 days, for controls. IC₉₀ of bleomycin and 12-methyltetradecanoic acid against Ehrlich ascetic tumor cells was 7.0 μ g/mL, for bleomycin alone.

- 10-Methylundecanoic acid
- 12-Methyltridecanoic acid
- 14-Methylpentadecanoic acid
- 12-Methyltetradecanoic acid
- 14-Methylhexadecanoic acid

Wendel et al [37] reviewed anti cancer actions of omega 3 fatty acids. Omega-3 fatty acids (ω 3-FA) were shown to attenuate growth and induce apoptosis in a variety of human cancer cell lines derived from colonic, pancreatic, prostate, and breast cancer. In addition, recent findings indicate that ω 3-FA act synergistically with chemotherapeutic agents and may also be used to enhance tumor radio sensitivity. The mechanisms underlying the antitumor effects of ω 3-FA are complex. Incorporation of ω 3-FA in biological membranes alters the profile of lipid mediators generated during inflammatory reactions. Furthermore, ω 3-FA act as ligands of nuclear peroxisome proliferators activated receptors that attenuate transcription of NF- κ B-dependent genes. Thereby, the cyclooxygenase-2/prostaglandin E₂-dependent production of pro-angiogenic vascular endothelial growth factor and levels of anti-apoptotic bcl-2 and bcl-XL are decreased. Eicosanoid-independent pro-apoptotic pathways include enhanced lipid peroxidation, modulation of mitochondrial calcium homeostasis and enhanced production of reactive oxygen species as well as activation of p53. This review article will give a comprehensive overview over the pleiotropic actions of ω 3-FA and will discuss the potential of ω 3-FA and derivatives like conjugated eicosapentaenoic acid as important nutritional adjuvant therapeutics in the management of various human cancer diseases and the impact of nutritional ω -3 FA on cancer prevention

Pohl et al [38] examined the role of hydroxyl group-containing fatty acids in anti-inflammatory action, neuroprotection, bactericide and anticancer defense. However, the mechanism of long-chain hydroxyl fatty acids (HFA) transport across plasma membranes is still disputed. Two main hypotheses have been formulated: firstly, that protonated HFAs traverse across the membranes spontaneously and, secondly, that the transport is facilitated by proteinaceous carriers. Here, we demonstrate that the protonated HFA are able to move across planar lipid bilayers without protein assistance. This transport step is accompanied by the acidification of the buffer in receiving compartment and the pH augmentation in the donating compartment. The latter contained liposome's doped with HFA. As revealed by scanning pH-sensitive microelectrodes, the pH shift occurred only in the immediate vicinity of the membrane, while bulk pH remained unchanged. In concurrence with the theoretical model of weak acid transport, the pH value at maximum proton flux was almost equal to the pK of the studied HFA. Intrinsic pK_i values were calculated from the electrophoretic mobilities of HFA-containing liposome's and were 5.4, 6.5, 6.9 and 6.3 for 2-hydroxyhexadecanoic, 16-hydroxyhexadecanoic, 12-hydroxydodecanoic, and 9, 10, 16-trihydroxyhexadecanoic acid, respectively.

12-Hydroxydodecanoic acid

16-Hydroxyhexadecanoic acid

2-Hydroxyhexadecanoic acid

9, 10, 16-Trihydroxyhexadecanoic acid

Hydrogen ion, biological studies

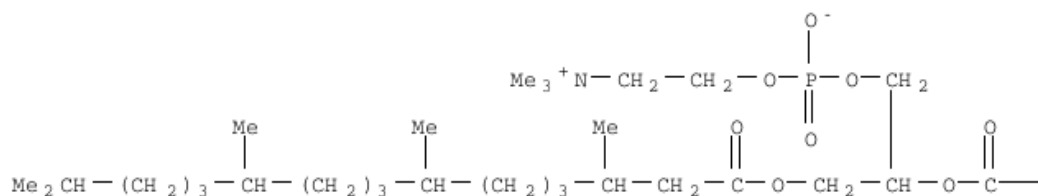
Diphytanoylphosphatidyl choline (fig.7)

CAS Registry Number: 64626-70-6

C₄₈ H₉₆ N O₈ P

3,5,9-Trioxa-4-phosphapentacosan-1-aminium,4-hydroxy-N,N,N,12,16,20,24-heptamethyl-10-oxo-7-[(3,7,11,15-tetramethyl-1-oxohexadecyl)oxy]-, inner salt, 4-oxide

1,2-Diphytanoylphosphatidylcholine;Diphytanoyllecithin; Diphytanoylphosphatidylcholine



7

Kuhnt et al [39] reviewed Tran's fatty acids in human nutrition. This review comprises the impact of Tran's fatty acids (tFA) and conjugated linoleic acids (CLA) in the human nutrition. The knowledge of the impact of the relation between dietary tFA and the risk of cardiovascular diseases, diabetes mellitus type-2, and cancer increased in the last years. There is increasing evidence that the effects of tFA on human health differ among positional trans-isomers. CLA show various metabolic properties, mainly anti-carcinogenic, anti-inflammatory, and anti-atherogenic, with potent impact in humans.

Fukuzawa et al [40] examined the inhibitory effects of an ethanolic extract of the spores of *Ganoderma lucidum* (Reishi Houshi) as the spore extract, on the proliferation of various human cancer cell lines by comparison with several authentic long chain fatty acids.

Of the fatty acids examined, nonadecanoic acid (C19:0) showed the highest inhibitory activity for HL-60 cell proliferation with IC₅₀ values of $68 \pm 7 \mu\text{M}$ followed by heptadecanoic acid (C17:0, $120 \pm 23 \mu\text{M}$), octa- (C18:0, $127 \pm 4 \mu\text{M}$) and hexadecanoic acids (C16:0, $132 \pm 25 \mu\text{M}$), respectively. The corresponding unsaturated fatty acids containing one double bond such as cis-10-nonadecenoic acid (C19:1), cis-9-octadecenoic acid (C18:1), cis-10-heptadecenoic acid (C17:1) and cis-9-hexadecenoic acid (C16:1) were less effective. The ethanolic extract of spores of *G. lucidum* were shown by annexin-V FITC/PI double staining to induce apoptosis of HL-60 cells in a similar way to cis-10-nonadecenoic acid (C19:1). These unsaturated fatty acids probably inhibit tumor necrosis factor production induced by lip polysaccharide in a mouse macrophage preparation.

Yoo et al, [41] reported the isolation of fatty acids with anti cancer activity from *Protaetia brevitarsis* larva.

In this study, biological active compounds were isolated from *Protaetia brevitarsis* larva (PBL) by dichloromethane extraction. The dichloromethane extract from PBL was highly cytotoxic to various cancer cells. From a silica gel column chromatography of this extract, they obtained four fractions (F-2, F-4, F-5 and F-7) having apoptosis-inducing activity. These fractions induced DNA ladder and caspase-3 activation during apoptosis in colon 26 tumor cells. In ¹H and ¹³C NMR and mass spectral analysis of the fraction F-2 showing the highest apoptosis-inducing activity, it was found that the fraction was composed of three free fatty acids such as palmitic acid, (Z)-9-octadecenoic acid and octadecenoic acid. These results indicate that the dichloromethane extract of PBL includes anti cancer components composed of at least three fatty acids, and apoptosis-inducing activity of the ext. was mediated by caspase-3 activation in tumor cells.

Ghazala et al [42] studied the phytochemistry and bioactivity of ten freshwater algae from Pakistan. Seven blue-green and three green algae were collected from various freshwater habitats of Sindh (Pakistan) during Jan. 1997 - Dec. 1999 and investigated. Their methanol extracts revealed 17 saturated, 2 monoynoic, 12 monoenoic, 5 di-unsaturated, 5 tri-unsaturated and 6 polyunsaturated fatty acids (FAs), β -sitosterol and trans-phytol, which were identified by GC-MS and NMR spectroscopy. Palmitoleic acid was the most commonly occurring FA, while C15:0, C16:0, C14:1 and C18:1 was the next commonly occurring acids. The unsaturated acids were found in larger proportion (46.50-70.46%) than saturated FAs (16.82-39.20%). The blue-green algae did not differ much from green algae of Pakistan in their FA-components. Their methanol extracts exhibited poor antibacterial activity but strong antifungal activities. They showed a significant phytotoxic activity but non-significant cytotoxic and insecticidal activities. The extract of *Lyngbya hieronymusii* enhanced anti tumor activity from 20 to 45% with an increase in the concentration of extract. Algae belonging to three phyla (Cyanophyta, Chlorophyta, and Charophyta) revealed differences in their FA-, sterol- and terpene-components as well as their bioactivities.

Shen et al [43] isolated the essential oils and fatty acids from fly larva and studied their anti tumor compositions. The title method comprises the steps of: (1) washing fly larva, vacuum-drying at 30-40° and 0.01 MPa, pulverizing, and extracting at 0-50° with 1-10 wt. times organic solvent for 1-5 h, (2) separating solid and liquid phase, and evaporating the liquid phase at 20-40° and 0.01 Mpa to obtain fly larva oil, (3) mixing neutral lipase solution (dissolving in pH 6.0-8.0 sodium hydrogen phosphate and sodium dihydrogen phosphate buffer solution) and fly larva oil at a volume ratio of 1: 0.5-1.5), stirring and reacting for 1.5-

3.5 h at 38-40°, and (4) separating oil phase, washing with water for 2-5 times, and rotary-evaporating at 30-40° and 0.01 Mpa to obtain fly larva fatty acid. The fly larva oil and fatty acid can be used for treating hepatic carcinoma, pulmonary carcinoma, gastric cancer, leukemia, mammary cancer, ovarian cancer and cervical carcinoma.

Shuto et al [44], studied antitumor agents containing phospholipids nucleoside derivatives. Antitumor agents containing R₁OCH₂CH (OR₂) CH₂OP (O) (OH) ONs (I; R₁, R₂ = long-chain fatty acid residue; Ns = 5-fluorouridin-5'-yl) or their salts as active ingredients. 5-Fluorouridine was treated with Phospholipase D-P (phospholipase D) and dipalmitoylphosphatidylcholine in an acetate buffer containing CaCl₂ at 45° for 3 h with stirring to manufacture 50.5% I (R₁, R₂ = palmitoyl, Ns = 5-fluorouridin-5'-yl) (II). II was administered to mice bearing leukemia P-388 carcinoma at 30 mg/kg i.p. 5 times a day for 3-5 days to show antitumor activity resulting in 206.3% increase in life span. II at 150 mg/kg showed no acute toxicity.

Acyl derivatives of epigallocatechin gallate as antitumor agents: The epigallocatechin gallate derivatives were prepared by introducing C12-20 fatty acid group with lipase from *Alcaligenes* in organic solvents. The Antitumor effects of the derivatives were tested against human tumors in vitro and in mice. For example, such an epigallocatechin-gallate palmitate (Epalm) showed the outstanding anti cancer effect. [45].

Dietary flaxseed has been shown to prevent azoxymethane (AOM)-induced colorectal cancers in male Fisher rats. The present study was designed to investigate the chemo preventive effects of dietary flaxseed on the development of intestinal tumors in Apc^{Min} mice. Apc^{Min} mice were divided into five different groups, fed with control (AIN-93M meal), corn meal, and flaxseed meal, corn oil, and flaxseed oil supplemented diets. Results showed that dietary flaxseed significantly decreased (P < 0.05) tumor multiplicity and size in the small intestine and colon as compared to control, corn-treated groups. Intestine, colon, and serum samples of corn-treated groups showed higher levels of ω -6 fatty acids, whereas the flaxseed treated groups exhibited higher levels of ω -3 fatty acids. Lignans were detected in the serum, intestine, and colon samples for flaxseed meal group. COX-1 and COX-2 expression in the colon samples from the flaxseed meal group were significantly lower (P < 0.05) as compared to the corn meal group. Dietary flaxseed may be chemo preventive for intestinal tumor development in Apc^{Min} mice possibly by increasing ω -3 fatty acid levels, lignans, and decreasing COX-1 and COX-2 levels. [46]

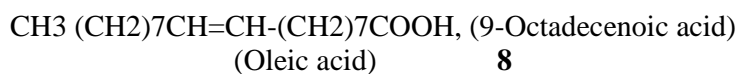
Olive oil:

Scientists have discovered why eating a Mediterranean diet rich in fruits, vegetables and particularly olive oil can help to protect women from developing breast cancer. The key is oleic acid, the main component of olive oil.

Dr Javier Menendez, of Northwestern University Feinberg School of Medicine in Chicago, said oleic acid blocks the action of a cancer-causing oncogene called HER-2/neu which is found in about 30 percent of breast cancer patients.

Doctors and researchers had been aware that eating a Mediterranean diet reduced the risk of breast cancer and other illnesses such as heart disease. But until now they did not know how. Menendez and his colleagues in the United States and Spain studied the impact of oleic acid in laboratory studies of breast cancer cells.

"We are able to demonstrate that the main component of olive oil, oleic acid (fig.8), is able to down-regulate the most important oncogene in breast cancer," Menendez explained.



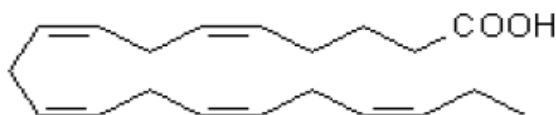
"The most important source of oleic acid is olive oil." They found that oleic acid not only suppressed the action of the oncogene, it also improved the effectiveness of the breast cancer drug Herceptin, a targeted therapy made by Swiss drug maker Roche Holding AG that works against the HER-2/neu gene. Breast cancer patients with HER-2/neu positive tumors suffer from an aggressive form of the disease and have a poor prognosis.

"There is no evidence at all that olive oil is toxic," said Menendez, who reported his findings in the journal *Annals of Oncology*, explained.

Olive oil contains alpha-tocopherol, (vitamin E), in appreciable amounts. Vitamin E is non toxic, fat soluble vitamin. A large number of recent animal and human studies, both in vivo and in vitro, have shown that vitamin E effectively protects against the development of a number of cancers, such as oral, colon, skin, lung and breast cancer. A study published in the January 2005 issue of *Annals of Oncology* has identified oleic acid, a monounsaturated fatty acid found in olive oil, as having the ability to reduce the affect of an oncogene (a gene that will turn a host cell into a cancer cell). This particular oncogene is associated with the rapid growth of breast cancer tumors. The conclusion of the researchers was that oleic acid when combined with drug therapy encouraged the self-destruction of aggressive, treatment-resistant cancer cells thus destroying the cancer. Olive oil has been positively indicated in studies on prostate and endometrial cancers as well. Unlike other fats, which are associated with a higher risk of colon cancer, olive oil helps protect the cells of the colon from carcinogens. A study published in the November 2003 issue of *Food Chemistry Toxicology* suggests that the antioxidants in olive oil reduce the amount carcinogens formed when meat is cooked.

Fish oil beneficial for human body: Fish oil has a sound influence on body health of human being and it has also the capability to resist as well as ameliorate various conditions of disease occurring on the human body. The traditional techniques regarding treatment of human diseases by fish is now-a-days a subject of research.

Recent research shows that fish oil containing omega-3-fatty acid can reduce the risk of occurrence of various deadly diseases which are none devastating drastically the human health. Human body needs polyunsaturated fatty acids (PUFA) of the n-6 and n-3 configurations but they are not synthesized by the humans and so must be obtained from the diet. The most common PUFAs are linoleic acid, eicosapentaenoic acid (EPA, fig.9) and docosahexaenoic acid (DHA). Fish oil contains all these acids. Fish oil have been found to aid in preventing or ameliorating coronary heart disease, stroke, lupus, nephropathy (kidney disorders), Crohn's disease, breast cancer, prostate cancer, colon cancer, hypertension and rheumatoid arthritis.



Eicosapentaenoic acid (EPA)

9

Fish consumption helps prevent prostate cancer: (STOCKHOLM, SWEDEN). Several studies have shown an inverse relationship between blood levels of fish oils (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) and the risk of prostate cancer. A study just completed by medical researchers at the Karolinska Institute confirms this association. The Swedish study involved 3136 pairs of male twins born between 1886 and 1925. The participants completed food frequency questionnaires in 1961 and 1967 and were then followed up for 30 years. By December 31, 1997 the researchers had recorded 466 diagnoses of prostate cancer (340 fatal ones). The average age of diagnosis was 76.7 years. After adjusting for other known risk factors the researchers conclude that men who never eat fish have a two- to three-fold higher risk of prostate cancer than do men who eat moderate to high amounts. The researchers emphasize that only fatty fish such as salmon, herring and mackerel, which contain high amounts of omega-3 fatty acids (EPA and DHA), would be expected to be beneficial [47].

Fish oils help prevent prostate cancer: (Auckland, New Zealand). Medical researchers in New Zealand provide convincing evidence that an increased consumption of fish oils helps reduce the risk of developing prostate cancer. Their study involved 317 men who had been diagnosed with prostate cancer during 1996-97 and 480 age-matched controls. Blood samples were obtained from all participants and the erythrocyte (red blood cell) phosphatidylcholine fraction of the plasma was analyzed for EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), the two main components of fish oils.

Evaluation of the collected data showed a clear correlation between blood level of EPA and DHA and the presence of prostate cancer. Study participants with levels in the highest quartile were found to have a 40 per cent lower incidence than participants with levels in the lowest quartile. This relationship held true even when adjusted for age, height, use of NSAIDs (non-steroidal anti-inflammatory drugs), socio-economic status, and estimated intake of lycopene and polyunsaturated fats.

The researchers also found that men with low socio-economic status, a low intake of lycopene, and non-regular use of NSAIDs were more likely to develop prostate cancer. They did not, however, find any correlation between self-reported intake of EPA and DHA indicating that food frequency questionnaires are not an accurate method for estimating fish oil intake. The researchers speculate that fish oils may prevent the progression of prostate cancer by inhibiting the biosynthesis of eicosanoids from arachidonic acid [48].

Fish oil recommended for Colon cancer patients: A highly dietary fat intake increases the risk of colon cancer. The correlation is particularly strong in the case of animal fats. It has been concluded that the consumption of fish and fish oil helps protect colon cancer in its later stages, but doesn't affect the initiation stage. Fish oils exert their protective effect by inhibiting the formation of prostaglandin PGE₂ which has been associated with the development and progression of colon cancer. A high intake of fish oil counteracts the detrimental effects of a high animal fat consumption.

Fish oil lowers lung cancer risk: Lung cancer is one of the leading causes of cancer death in many developing countries. It is seen that consumption of cooked or raw fish decrease to half the probability of occurrence of lung adenocarcinoma. It is now believed that a high intake of

omega-6 fatty acids stimulate the growth of lung cancer where as omega-3 fatty acid suppress the growth of cancer cell. It has been experimentally justified that DHA, a main component of fish oil, is highly effective in inhibiting the growth of human melanoma cells. Optimistic scientists are even of the opinion of warranting a clinical trial of DHA as an adjuvant to current surgical and chemotherapeutic intervention.

Fish oils in cancer prevention (Stockholm, Sweden). Several test tube (in vitro) and animal experiments have clearly shown that the long-chain omega-3 polyunsaturated fatty acids (PUFAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the main components of fish oil, help inhibit the promotion and progression of cancer. Their beneficial effect is particularly pronounced in hormone-dependent cancers such as breast and prostate cancer. Some, but not all, epidemiologic studies have also found a beneficial effect.

Researchers at Sweden's famous Karolinska Institute have just published a comprehensive review of the current knowledge regarding the role of PUFAs in carcinogenesis. They conclude that omega-3 PUFAs are protective against cancer progression, while omega-6 PUFAs, notably arachidonic acid and its derivatives, help promote the growth of cancer. They believe the n-3 PUFAs exert their beneficial effects in several different ways: They suppress the synthesis of pro-inflammatory eicosanoids from arachidonic acid and thus produce an overall anti-inflammatory effect.

They positively affect gene expression or the activities of signal transduction molecules involved in the control of cell growth, differentiation apoptosis, angiogenesis and metastasis. They suppress excessive production of nitrogen oxide (NO) during chronic inflammation and thereby help prevent DNA damage and impaired DNA repair. They decrease estrogen production and thus reduce the estrogen-stimulated growth of hormone- dependent cancer cells.

Fish oils improve insulin sensitivity and cell membrane fluidity and may help prevent metastasis through these effects.

Free radicals and reactive oxygen species produced in cells may attack PUFAs resulting in the formation of more free radicals, specifically hydro peroxides. The hydro peroxides, in turn, may damage DNA ultimately leading to cancer. These effects have indeed been observed in some in vitro experiments, but not in actual human beings. Many studies have shown that fish oils actually retard aging and suppress so- called free radical diseases such as atherosclerosis and cancer. Other studies have shown that a daily EPA + DHA intake in excess of 2.3 grams decreases the production of super oxide, a potent cancer promoter. At least one in vitro and one animal experiment have observed that EPA + DHA kill human breast cancer cells via the formation of hydro peroxides, but that this effect is strongly inhibited by vitamin E. Thus, at this point, it is not entirely clear whether EPA + DHA exert part of their beneficial effect through an increase or a decrease in the production of free radicals and reactive oxygen species. The researchers recommend more work in this area, but emphasize that the major benefits of fish oils probably are associated with their ability to inhibit the synthesis of arachidonic acid-derived, pro-inflammatory eicosanoids. The Swedish researchers also confirm that fatty, cold-water fish are the best sources of EPA and DHA and that the conversion rate of alpha-linolenic acid (flaxseed oil) to EPA is very low, even in healthy humans-probably in the order of 2-5% [49]. There is now also considerable evidence that fish oil consumption can delay or reduce tumor development in breast cancer. Studies have also shown that a high blood level of omega-3 fatty acids combined with a low level of

omega-6 acids reduces the risk of developing breast cancer. Daily supplementation with as little as 2.5 grams of fish oils has been found effective in preventing the progression from benign polyps to colon cancer and Korean researchers recently reported that prostate cancer patients have low blood levels of omega-3 fatty acids.

Bathen et al, [50] reported that omega-3 fatty acids suppress growth of SW620 human colon cancer xenografts in nude mice.

The purpose of this study was to examine the influence of fish oil on growth of colon cancer in nude mice. **Materials and Methods:** Xenografts were initiated in mice receiving a standard diet or diets modified with corn or fish oil. After 3 weeks, mice were sacrificed; tumors were removed and processed for lipid analysis, histopathology and high resolution magic angle spinning magnetic resonance spectroscopy. **Results:** Diet modified with fish oil suppressed tumor growth. Xenografts from mice receiving fish oil had higher levels of omega-3 polyunsaturated fatty acids (PUFAs) with concomitant reduced levels of omega-6 PUFAs. Furthermore, these xenografts had significantly lower levels of phosphocholine. Overall the results indicated less aggressive tumor growth in mice receiving a fish oil diet.

So, in today's world of consciousness of human health, one cannot underestimate the immense importance of consumption of fish oil by keeping a view regarding its role to combat and ameliorate various deadly disease. Physicians are also proscribing the inclusion of fish oil in the diet so as to form a perfect nutritionally balanced diet.

Shark oil: In the April 1996 issue of Life Extension Magazine, the benefits of shark liver oil and its primary ingredient, alkyl glycerols were reported. New findings validating the disease prevention and treatment effects of alkyl glycerol's, suggesting this Shark liver oil extract may soon be integrated into mainstream medicine. Alkyl glycerols were first isolated by a physician in Sweden named Dr. Artrid Brihult. She was treating children with leukemia, with little success. Because white blood cells are produced in the bone marrow, she started to feed the sick children bone marrow from calves. The result of the bone marrow feeding was a marked improvement in the children's immune systems and white blood cell counts. So Dr. Brohult set out to find out the active ingredient in bone marrow and isolate it. With the help of her husband Dr. Sven Brohult, it was determined that alkyl glycerol's were responsible for the immune system enhancing effects. These same compounds are found in the livers of cold-water Sharks, like the Greenland Shark. The Shark in general has gained a lot of popularity because cancer occurrence is very rare in Sharks. The existence of alkyl glycerol in their liver may be one reason for the natural immunity to cancers.

Alkyl glycerol's are glycerol ether lipids that are naturally occurring in hematopoietic (blood forming) organs such as bone marrow, spleen and liver.

The biologic effects of shark liver oil include stimulation of blood leukocyte and thrombocyte production as well as the activation of macrophage and anti-tumor activity. Other effects include the ability to protect against radiation damage during radiation therapy for various types of cancer. In a study published in the Journal of Cell Physiology (February 1999), researchers studied the cell differentiation-promoting potential of a particular type of alkylglycerols on human colon cancer cells. The scientists wanted to observe the ability of alkylglycerols to change the biological makeup of human colon cancer cells. Alkylglycerols were shown to "Promote a more benign or differentiated phenotype in colon cancer cells." Treatment of the cancer cells with alkylglycerols resulted in a reduction of cellular

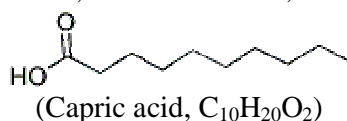
proliferation and a reduced capacity for cellular invasion. In other words, alkylglycerols led to lowered cancer cell reproduction and a reduced ability of the cancer cells to invade healthy cells. The authors concluded that alkylglycerols possess both cancer preventative properties, as well as cancer treatment effects. In a study published in the *Journal of Alternative & Complementary Medicine* (Spring 1998), researchers extolled the many biologic actions of shark liver oil alkylglycerols. It was pointed out that shark liver oil has been around for 40 years and has been used as both a preventative and therapeutic agent. Not only have alkylglycerols been used to treat leukemia, as in the case of the children in Sweden, they have also been used to prevent radiation sickness stemming from radiation cancer treatments. Furthermore, the high level of alkylglycerols that exist naturally within any given tumor cell has lead scientists to postulate that this is may be an apparent attempt of the body to control cell growth. In another study referred to in this paper, researchers found that the activation of protein kinase C, an essential step in cancer cell growth, can actually be stopped or inhibited by alkylglycerols. In addition, it's been suggested that alkylglycerols directly act on the macrophages (large immune cells that gobble up cancer cells). Overall, alkylglycerols are able to stimulate the macrophage to secrete over 50 substances concerned directly or indirectly with the immune system. Some of these substances, the interleukins, are powerful immune system fighters that interact with lymphocytes.

Coconut oil: Coconut oil is a colorless to pale brownish yellow oil with a melting point ranging from 23% to 26%. The glycerides of coconut oil are invariably a mixture of one, two, or three fatty acids. Though coconut oil is known as triglyceride or lipid, it also contains minor proportions of mono and diglycerides and has highest content of glycerol (upto 15%). Glycerol is a carbohydrate with chemical composition similar to that of simple sugar. So, now, it is clear that with coconut oil as a dietary fat, the actual intake of fatty substances is much less than that with same quantity of any other actual intake of any other oil.

A study done in a two groups of community living in New Zealand who consume a large number of coconut oil has proved that they have rare incidents of hypercholesterolemia and heart attack. According to Prior, Davidson et al. two groups of Polynesians from Cook Islands derive 35% and 27% of their calories from coconut oil but their mean cholesterol values are low, i.e. 153 mg% and 195 mg% respectively. Prevalence of heart attacks also is low in these groups compared to the usual New Zealand population.

In a study in the Philippines, 10 medical students tested diets consisting of different levels of animal fat and coconut oil. When the ratio of animal fat and coconut oil at ratio of 1:1, 1:2, 1:3 no significant change in cholesterol but when animal fat level increased total calories reached 40% and blood cholesterol increased. This study indicated that not only did coconut, had no effect on cholesterol levels, it even reduced the cholesterol elevating effect of animal fat.

Coconut oil has also, approximately 6-7% capric acid. Capric acid (fig.10) has a similar beneficial function when it is formed into monocaprin in the human or animal body. Monocaprin has also been shown to have antiviral effects against HIV and is being tested for antiviral effects against herpes simplex and antibacterial effects against Chlamydia and other sexually transmitted bacteria. (Reuters, London June 29, 1999).



10

Table 1. Estimated amounts of cholesterol in vegetable oils and animal fats

Oil/fat	Range (parts per million)
coconut	5-24
Palm kernel	9-40
sunflower	8-44
palm	13-19
Soy	20-35
Corn seed	28-108
Rape seed	25-80
corn	18-95
Beef tallow	800-1400
butter	2200-4100
Lard	3000-4000

(Source: Inform, Vol. 13, 2002)

To be diagnosed with cancer sounds more like a death sentence. So many people lose hope and spend their remaining life on earth in despair and regret. But some refuse to give up and seek all possible cures. Virgin coconut oil is one cure that can save the life of cancer patients. Every human being has cancer cells in their bodies but not all are diagnosed with the deadly disease. This is because people with a healthy immune system destroy these harmful cells before they spread and cause problems to various parts of the body. The white blood cells of the immune system defend the body against the attack of harmful microorganisms. However when too many microbes invade the body the WBCs and the immune system weakens and this triggers the development of cancer cells.

A study was done to a group of rats that were chemically induced with colon cancer. Various dietary oils like corn, safflower, olive and coconut oils were fed to the rats to determine their effect on the body. At the end of the study, the rats were fed with olive oil and coconut oil had the lowest incidence of tumor in the intestines. The medium chain fatty acids (MCFAs) component of coconut oil has antimicrobial properties so it effectively prevents the spread of cancer cells and enhances the immune system. In another study done by L. A. Cohen and his colleagues, animals were chemically induced with breast cancer. They found out that the animals that were given coconut oil did not develop tumors while those animals that were given other dietary oils develop tumors. Virgin coconut oil is probably the cure that will give hope to all cancer patients.

Soybean oil: Beans are classified as pulses where as soybeans are classified as oilseeds. It is a versatile bean having a diverse range of uses.

The oil and protein content together account for about 60% of dry soybeans by weight; protein at 40% and oil at 20%.The remainder consists of 35% carbohydrate and about 5% ash. The major unsaturated fatty acids in soy bean oil triglycerides are 7% linolenic acid; 51% linoleic acid; and 23% oleic acid. It also contains the saturated fatty acids 4% stearic acid and 10% palmitic acid. Soybeans also contain the isoflavones genistein and daidzein, types of phytoestrogen, that are considered by some nutritionists and physicians to be useful in the prevention of cancer and by others to be carcinogenic and endocrine disruptive. The dramatic increase in soy food sales is largely credited to the Food and Drug Administration's

(FDA) approval of health claims for soy in which studies are conflicting to their cholesterol lowering ability(Cornell University Food and Brand Lab Article)

Research has shown that soybean products contain five cancer preventive chemical agents.1)Protease inhibitors, which hold off activation of the specific oncogenes that cause cancer .,2) phytate, which binds iron in the intestines to prevent it from generating free radicals resulting in cancer;3) phytosterols, which neutralize the breakdown of cholesterol and reduce the development of colon tumors and skin cancer;4) saponins, which stop cellular mutations that could inevitably lead to cancer 5) isoflavones, which are plant estrogens with strong inhibiting effects in hormone related malignancies such as prostate, ovarian, cervical and breast cancers.

Cows' Milk Fat Components as Potential Anticarcinogenic Agents [51]. The considerable emphasis placed on cancer research during the past 25 y has resulted in remarkable insight into the molecular biology of the cell and improved treatment of cancer by surgery, radiation and chemotherapy. There have been pronounced declines in death from some cancers, notably Hodgkin's disease, Burkitt's lymphoma, lymphocytic leukemia, testicular cancer and a range of childhood carcinomas. However, there is little change in survival rates for patients with the most common types of invasive and metastatic carcinoma of the epithelia of the breast, lung, or pharynx, pancreas, colon, bladder and prostate [52]. A review of epidemiologic studies suggests that about 35% of cancer deaths are attributable to diet with a range of 20 to 60% for the various sites [53]. The food we eat contains components that may either help cause or help prevent cancer. The evaluation of natural components with cancer prevention properties in food is now an important element of overall cancer prevention strategy. Recent research shows that milk fat contains a number of potential anticarcinogenic components including conjugated linoleic acid, sphingomyelin, butyric acid and ether lipids.

Conjugated linoleic acid inhibited proliferation of human malignant melanoma, colorectal, breast and lung cancer cell lines. In animals, it reduced the incidence of chemically induced mouse epidermal tumors, mouse fore stomach neoplasia and aberrant crypt foci in the rat colon. In a number of studies, conjugated linoleic acid, at near-physiological concentrations, inhibited mammary tumor genesis independently of the amount and type of fat in the diet.

In cell culture studies, physiologic concentrations of CLA inhibited the proliferation of human malignant melanoma, colorectal and breast cancer cells [54], and three lung adenocarcinoma cell lines, but not a glioblastoma cell line [55]. Mechanisms by which CLA influences carcinogenesis, although well studied, are largely unresolved, and may vary for different sites, age, duration of exposure and stage of carcinogenesis. Various studies suggest that CLA may act by antioxidant mechanisms [56, 57], prooxidant cytotoxicity [55], inhibition of nucleotide synthesis [54], reduction of proliferative activity [58] and inhibition of both DNA-adduct formation [59, 54] and carcinogen activation [60].

In vitro studies showed that the milk phospholipids, sphingomyelin, through its biologically active metabolites ceramide and sphingosine, participates in three major antiproliferative pathways influencing on cogenesis, namely, inhibition of cell growth, and induction of differentiation and apoptosis. Mice fed sphingomyelin had fewer colon tumors and aberrant crypt foci than control animals. A unique feature of milk fat from ruminant animals is the presence of butyric acid. Butyrate is a potent inhibitor of proliferation and an inducer of differentiation and apoptosis in a number of cancer cell lines [61, 62 and 63]. At the molecular level, butyrate causes histone hyperacetylation and DNA hypermethylation. Both

of these events are associated with down-regulation or inactivation of oncogene expression. Butyrate may also play a role in the prevention of tumor invasiveness and metastasis by inhibiting urokinase, a facilitator of malignant cell penetration to the substratum [64]. About one third of all milk triacylglycerols contain one molecule of butyric acid, a potent inhibitor of proliferation and inducer of differentiation and apoptosis in a wide range of neoplastic cell lines. Although butyrate produced by colonic fermentation is considered important for colon cancer protection, an animal study suggests dietary butyrate may inhibit mammary tumor genesis [65].

The dairy cow also has the ability to extract other potential anticarcinogenic agents such as β -carotene, β -ionone and gossypol from its feed and transfer them to milk.

Although milk fat contains a number of potential anticarcinogenic compounds, is there any evidence to suggest that it has a restricting effect on cancer development? There are a few studies in which milk fat or butter was compared isocalorically with vegetable oils or margarines in animal models of carcinogenesis.

Yanagi *et al.* [66] fed female mice after weaning either a basal diet or that diet enriched with 20% butter, margarine (64 g linoleic acid/100 g fatty acids) or safflower oil. The incidence of spontaneous mammary tumor development, mainly adenocarcinomas, was significantly less in the butter-fed group (21%) than in the margarine- (43%) and safflower oil- (44%) fed groups. Similar diets were then fed to female rats from 1 wk before tumor induction with DMBA. The percentage of mammary tumor incidence was as follows: basal diet (which contained only 4.9% fat) 44%, butter 36%, margarine 63% and safflower oil 46%. To determine if the inhibitory effect of butter on mammary tumor development was due to milk lipids, Yanagi *et al.* [67] fed rats under similar conditions either a basal diet (4.6% fat) or the basal diet supplemented with dried whole milk (8.9% fat), skim milk (3.9% fat) or milk cream (20.8% fat). In this case, rats fed the high milk fat cream diet did not have enhanced tumor development (42.3%) compared with rats fed the basal diet (42.3%), dried whole milk diet (60%) or the skim milk diet (52%). Next, Yanagi *et al.* [68] fed rats a basal diet supplemented with margarine (60 g linoleic acid/100 g fatty acids) at the 5, 10 and 20% levels. This resulted in a mammary tumor incidence of 40, 70 and 80%, respectively. When 20% butter replaced 20% margarine in the diet, rats had a non-significantly lower tumor incidence of 70%. However, total tumor numbers (99 vs. 48), average tumor numbers (6.19 vs. 3.42) and average tumor diameter (11.6 vs. 9.6 mm) were significantly lower in the butter group. Cope and Reeve [69] recently demonstrated that, compared with butter and milk fat, polyunsaturated margarine and sunflower oil enhanced both ultraviolet (UV) light and UV light/DMBA-induced photo carcinogenesis in a hairless mouse model.

These animal models, in which high total fat intake itself is a risk factor for colon cancer [70] and mammary cancer [71], clearly demonstrate that milk fat-based diets produce fewer tumors than polyunsaturated vegetable oil-based diets.

Potential cancer chemo preventive agents from products of vegetable origin are actively being evaluated. It is feasible that some of these compounds may be transferred to milk by feeding products such as vegetable or cannery waste and spent brewers grains to dairy cows. These compounds, and those discussed above, may act synergistically to prevent cancer.

Conclusion

Good nutrition is especially important for people with cancer. Eating well means eating a variety of foods that provide the nutrients we need to maintain health while fighting cancer. These nutrients include protein, fat, carbohydrates, vitamins, water and minerals. Fat is an important nutrient in our diet and helps maintain many of our normal body functions. Without some fat in our diets the body cannot make all its necessary repairs and deficiencies of the fat-soluble vitamins A, D, E and K can develop. This review explains the possible prevention of cancer by including important fats in our diet and proves to be significant for further research on fats and cancer prevention.

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