Introduction
Introduction:

Human body needs fats to function properly. Nearly half of the dry weight of the brain is fat, and a quarter of this is cholesterol. Cholesterol is an essential part of sex hormones, bile acids, D vitamins and steroid hormones from the cortex of the adrenal gland — among other important substances. Cholesterol does not need to be eaten, however, because the liver and other tissues can manufacture cholesterol from saturated fats. But too many saturated fats result in excessively high blood levels of cholesterol that end up being deposited in atherosclerotic plaques on blood vessels, leading to cardiovascular disease. High blood cholesterol also depresses the immune system and thereby increases the incidence of cancer (4).

Up until about 200 years ago, the human diet contained much higher levels of n-3 fatty acids. The meat of wild animals that forage for food is rich in EPA, unlike the meat of domesticated animals that have been fattened with grains. High levels of dietary n-6 vegetable oils are a modern phenomenon. EPA competes with arachidonic acid for the cyclo-oxygenase enzyme, reducing the production of thromboxane A2, the most powerful platelet aggregating agent known. Some people feel that restoration of the historic n-3/n-6 ratios is a more "natural" way of preventing heart attack than using aspirin to irreversibly inactivate cyclo-oxygenase (15). Aspirin, even in normal therapeutic doses, can produce dizziness, migraine headaches, depression, anxiety, and stomach irritation or stomach bleeding (87).

The high levels of n-6 fatty acids in modern diets may even adversely affect n-3 utilization by cellular mechanisms that reduce desaturase formation (88). Rats on a perilla oil diet which results in n-6 to n-3 ratios of approximately 1-to-4 showed the longest life spans. Eskimos have low heart and autoimmune disease on a fish oil diet that gives a 1-to-3 ratio (6). Concerns that the anti-clotting effect of fish oil might lead to increased incidence of stroke are apparently unfounded, since stroke is primarily the result of high blood pressure and weakened blood vessels.

Aside from cholesterol, most other fat in the body is constructed from what is known as fatty acids. A fatty acid is a long straight chain of carbon atoms (studded with hydrogen
atoms) that has an acid group (carboxylic acid) at one end (the water-soluble end). The rest of the fatty acid is oil-soluble, with a methyl group at the other end. Fatty acids in the body usually exist unattached to any other molecule (free fatty acids), attached to glycerol in groups of three (triglycerides), or attached to phosphatidic acid molecules (phospholipids [PL]).

Polyunsaturated fats have often been recommended to reduce coronary heart disease (9). But all saturated fats do not have the same effect on cholesterol synthesis in the liver. Only the saturated fats of chain-length 12, 14 and 16 (lauric acid, myristic acid and palmitic acid) have been shown to elevate blood cholesterol. Of these, myristic acid (high in coconut and palm oil) elevates cholesterol the most (10). Stearic acid (18-carbon, saturated) has been shown to lower cholesterol by 21% -- even more than oleic acid (18-carbon, mono-unsaturated), which lowers LDL by 15% (11).

Polyunsaturated fatty acids can be a health hazard because carbon-carbon double bonds can lead to free-radical formation and reactions with oxygen to form unstable lipid peroxide compounds containing the same unstable oxygen-oxygen bond found in hydrogen peroxide. Lipid peroxidation and free radicals can cause cancer and may accelerate aging. High rates of lung cancer among women in China have been associated with lipid-peroxidized oils in fumes from cooking polyunsaturated vegetable oils in a wok (12).

Polyunsaturated "cis" fatty acids can be beneficial in cell membranes by preventing the tight packing of fatty acids in membranes -- thereby making the membranes more "fluid". Membrane fluidity is important for optimal function of most cells in the body. But membrane fluidity is especially important on portions of cells that act as receptors for hormones or neurotransmitters. The typical North American eats three times as much saturated fat as unsaturated fat, yet animal experiments show that insulin receptor responsiveness is substantially improved when dietary unsaturated fat is greater than saturated fat (13).

The human body can manufacture most of the fats it needs, including cholesterol, saturated fatty acids and unsaturated fatty acids. But there are two fatty acids which
cannot be manufactured in the body, and which must be obtained from dietary sources: linoleic acid (LA) and alpha-linolenic acid (ALA). These are the essential fatty acids (EFAs). Linoleic acid (omega-6 FA) is an 18-carbon chain with 2 double-bonds, whereas alpha-linolenic acid (omega-3 FA) is an 18-carbon chain with 3 double-bonds. **Omega-6 & omega-3 FAs are also designated as n-6 and n-3 FA respectively.** The position of double bonds in a fatty acid is critical to function, and this is especially true of double-bonds close to the methyl end. For long-chain fatty acids, the body’s enzymes cannot add double-bonds near the methyl end.

The body cannot make an n-3 or n-6 fatty acid because human metabolism cannot add a double bond to a fatty acid that is more than 9 carbons away from the delta end. For the same reason, the body cannot convert an n-3 to an n-6 fatty acid, or vice-versa. But the body can make n-9 fatty acids. And the body can add more double-bonds closer to the delta end of n-3 and n-6 fatty acids.

Two distinct families of essential fatty acids exist in the human body: the n-3 family and n-6 family. The n-3 family comes from alpha-linolenic acid, and the n-6 family comes from linoleic acid. Each family is the result of increasing chain length and of forming double bonds from one of these two essential fatty acids. The two families compete for the same enzymes for forming double bonds (desaturase enzymes) and enzymes for lengthening the carbon chain (elongase enzymes). Elongase enzymes always add carbon atoms (in pairs) to the delta end of the fatty acid.

Noteworthy members of the n-3 family of fatty acids manufactured from alpha-linolenic acid are EicosaPentaenoic Acid (EPA) and DocasaHexaenoic Acid (DHA). A pentaenoic acid has 5 double-bonds. A hexaenoic acid has 6 double-bonds. EPA is a 20-carbon chain fatty acid, whereas DHA is a 22-carbon chain fatty acid. Like arachidonic acid, EPA gives rise to its own class of eicosanoids. The EPA-generated eicosanoids are in the n-3 family, as distinct from the n-6 eicosanoids derived from arachidonic acid.

The primary source of n-6 fatty acid in the diet is linoleic acid from the oils of seeds and grains. Sunflower, safflower and corn oil are particularly rich sources of linoleic acid, which is at the root of the n-6 fatty-acid family. Evening primrose oil and borage oil are
high not only in linoleic acid, but the n-6 derivative gamma-linolenic acid (GLA). Avocado is 15-20% oil — mainly monosaturated, but also high in linoleic acid. (Avocado has the highest fat content and the highest fiber content — soluble as well as insoluble — of any fruit.)

N-3 fatty acids, on the other hand, are more frequently found in green leaves. The leaves and seeds of the perilla plant (widely eaten in Japan, Korea and India) are the richest plant source of alpha-linolenic acid, although linseed oil is also a rich source. Fish oil contains very little alpha-linolenic acid, but is rich in the n-3 derivatives EPA and DHA. Fish are at the top of a food chain based on phytoplankton (algae) that manufactures large amounts of EPA and DHA. Nonetheless, fish can be high in toxic methylmercury.

It has been estimated that thousands of years ago the diet of human hunter-gatherers consisted of approximately equal parts of n-3 and n-6 essential fatty acids [*15]. Since the beginning of agriculture ten thousand years ago there has been a steady increase in n-6 at the expense of n-3 fat in the human diet. This process accelerated about 50 years ago as cattle began to be fed increasingly on grains rather than grass. Recommendations by nutritionists to eat margarine rather than butter (polyunsaturated rather than saturated fats) only increased the trend toward n-6 consumption. Currently, the ratio of n-6 to n-3 fatty acids in the American diet is 7-to-1 or more. There are good reasons to believe that this imbalanced essential fatty acid ratio has led to increased cancer, heart disease, allergies, diabetes and other afflictions. Much of the reason for this lies in the membranes of our cells.

**Essential fatty acids in cell membranes:**

Phospholipids and cholesterol are the principal components of nearly all cell membranes. The backbone of a phospholipid is the same glycerol molecule that forms the backbone of triglycerides. But instead of 3 fatty acids attached to glycerol, a phospholipid consists of 2 fatty acids, a phosphate group and an alcohol.

**Fats for immunity:**

The eicosanoids produced from arachidonic acid cause a stronger inflammatory response than the eicosanoids from EPA or DGLA. The arachidonic acid products
Leukotrienes B4 (LTB4) and Prostaglandin E2 (PGE2) are powerful promoters of inflammation. LTB4 is only formed in granulocytes subject to stimuli favoring action by 5-lipoxygenase activating protein (17).

Gamma-Linolenic Acid (GLA) has been shown to be effective against the inflammation of rheumatoid arthritis in a number of studies. Although one might expect that GLA could lead to the formation of arachidonic acid's pro-inflammatory eicosanoids, there is instead a production of the anti-inflammatory prostaglandin PGE1 of the 1-series (19,20). It may be that rheumatoid arthritis patients suffer from impaired function of desaturase enzymes, preventing arachidonic acid formation. In ulcerative colitis, an inflammatory condition in which desaturase enzymes are normal, both n-3 oils from fish and perilla have been used for treatment (21).

Feeding laboratory animals diets rich in n-3 fatty acids (linseed or fish oil) reduces Natural Killer cell and cytotoxic T-lymphocyte activity (22), but stimulates the more antigen-specific immunoglobulins IgM and IgG (17). Innate immune response, although closely tied to inflammation can be separated from inflammation to some extent.

**Fats against cancer:**

High fat diets are well known to be associated with certain kinds of cancers, including breast cancer, in particular (31). Although butterfat stimulates breast cancer when compared with a fat-free diet, safflower oil margarine (linoleic acid, an n-6) has been shown to induce breast cancer much more strongly (6). Linoleic acid is the fat that most frequently is associated with cancer, whereas n-3 fatty acids like DHA and perilla-oil suppress cancer (32,33). It has been theorized that linoleic acid causes cancer by chronic overproduction of the inflammatory arachidonic acid eicosanoids, which stimulate the proliferation of mutated cells (6).

**Fats against diabetes and the effects of alcoholism:**

Alcoholics suffer from disturbances of fat metabolism, notably in the liver. The liver is the most active site of delta-6-desaturase activity in the body. In fact, many (if not most) cells in the body have no delta-6-desaturase enzymes and are dependent upon the liver for n-3/n-6 desaturase / elongase products. Neuropathy and other conditions resulting from
desaturase dysfunction in alcoholics are benefitted by both evening primrose oil and fish oil in combination (43). Arachidonic acid deficiency is the most serious problem for alcoholics, however, so evening primrose oil seems to be the best therapy (44).

**Fats in pregnancy:**

In the last third of pregnancy, and in the first four months after birth, rapid brain growth in the human infant requires large amounts of n-3 and n-6 essential fatty acids. Human milk contains (in total fatty acids by weight) 12% linoleic acid, 0.5% alpha-linolenic acid, 0.6% arachidonic acid and 0.3% DHA (45).

Optimum dietary benefit from fat for most people would come from a program of reduced total fat, reduced saturated and unessential fat, and increased proportions of n-3 (relative to n-6) essential fats. High n-3 oil like perilla oil might be a simple remedy for young people and the best remedy for smokers. But as most people age, they will benefit most from CLA, GLA, and DHA supplementation combined with antioxidants (especially vitamin E) to protect these polyunsaturated essential fats from oxidation.

Fats are an important component of membranes in our hearts, brains, immune cells and most of the other tissues of our bodies. Since we need these fats, it is important to ensure that we have the right kind of fats that we have enough of them and that we protect them with antioxidants.

**Dietary modification of inflammation with lipids:**

The n-3 polyunsaturated fatty acids (PUFA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are found in high proportions in oily fish and fish oils. The n-3 PUFA are structurally and functionally distinct from the n-6 PUFA. Typically, human inflammatory cells contain high proportions of the n-6 PUFA arachidonic acid and low proportions of n-3 PUFA. The significance of this difference is that arachidonic acid is the precursor of 2-series prostaglandins and 4-series leukotrienes, which are highly active mediators of inflammation. Feeding fish oil results in partial replacement of arachidonic acid in inflammatory cell membranes by EPA. This change leads to decreased production of arachidonic acid-derived mediators. This response alone is a potentially beneficial anti-inflammatory effect of n-3 PUFA.
Several well-conducted randomized controlled trials report that in people with a history of heart attack, regular consumption of oily fish (200-400 grams of fish each week equal to 500-800mg of daily n-3 fatty acids) or n-3 fatty acids/n-3 supplements (containing 850-1800mg of EPA + DHA) reduces the risk of non-fatal heart attack, fatal heart attack, sudden death, and all-cause mortality (death due to any cause) (107; 110-115). Most patients in these studies were also using conventional heart drugs, suggesting that the benefits of n-3 fatty acids may add to the effects of other therapies. There is strong scientific evidence from human trials that n-3 fatty acids from fish or n-3 fatty acids supplements (EPA + DHA) significantly reduce blood triglyceride levels (97-102). Benefits appear to be dose-dependent, with effects at doses as low as 2 grams of n-3 fatty acids per day. Higher doses have greater effects, and 4 grams per day can lower triglyceride levels by 25-40%. Effects appear to be additive with HMG-CoA reductase inhibitor ("statin") drugs such as simvastatin (103), pravastatin (104; 105), and atorvastatin (106).

Multiple human trials report small reductions in blood pressure with intake of n-3 fatty acids (118-124). Reductions of 2-5 mmHg have been observed, and benefits may be greater in those with higher blood pressures. Effects appear to be dose-responsive (higher doses have greater effects) (119). DHA may have greater benefits than EPA (125). However, intakes of greater than 3 grams of n-3 fatty acids per day may be necessary to obtain clinically relevant effects, and at this dose level, there is an increased risk of bleeding.

Multiple randomized controlled trials report improvements in morning stiffness and joint tenderness with the regular intake of n-3 fatty acids supplements for up to three months (143-157). Benefits have been reported as additive with anti-inflammatory medications such as NSAIDs (like ibuprofen or aspirin). However, because of weaknesses in study designs and reporting, better research is necessary before a strong favorable recommendation can be made. Some research reports that regular intake of fish or n-3 fatty acids supplements reduces the risk of developing atherosclerotic plaques in the arteries of the heart (190; 191), while
other research reports no effects (192). Additional evidence is necessary before a firm conclusion can be drawn in this area.

**Osteoarthritis** is a type of arthritis that is caused by the breakdown and eventual loss of the cartilage of one or more joints. Cartilage is a protein substance that serves as a "cushion" between the bones of the joints. Osteoarthritis is also known as degenerative arthritis. Among the over 100 different types of arthritis conditions, osteoarthritis is the most common, affecting over 20 million people in the United States. Osteoarthritis occurs more frequently as we age. Before age 45, osteoarthritis occurs more frequently in males. After age 55 years, it occurs more frequently in females. In the United States, all races appear equally affected. A higher incidence of osteoarthritis exists in the Japanese population, while South African blacks, East Indians and Southern Chinese have lower rates.

Aside from weight reduction and avoiding activities that exert excessive stress on the joint cartilage, there is no specific treatment to halt cartilage degeneration or to repair damaged cartilage in osteoarthritis. The goal of treatment in osteoarthritis is to reduce joint pain and inflammation while improving and maintaining joint function.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are medications that are used to reduce pain and inflammation in the joints. Examples of NSAIDs include aspirin (Ecotrin), ibuprofen (Motrin), nabumetone (Relafen), and naproxen (Naprosyn). It is sometimes possible to use NSAIDs for a while and then discontinue them for periods of time without recurrent symptoms, thereby decreasing side effect risks.

The most common side effects of NSAIDs involve gastrointestinal distress, such as stomach upset, cramping diarrhea, ulcer and even bleeding. The risk of these and other side effects increases in the elderly. Newer NSAIDs called Cox-2 Inhibitors have been designed that have less toxicity to the stomach and bowels. Because osteoarthritis symptoms vary and can be intermittent, these medicines might be given only when joint pains occur or prior to activities that have traditionally brought on symptoms.

N-3 fatty acids are found in coldwater fatty fish (such as salmon, mackerel, and herring), flaxseed, rapeseed, and walnuts. Research regarding the use of n-3 fatty acid supplements
for inflammatory joint conditions has focused almost entirely on rheumatoid arthritis. Based on laboratory studies, however, many researchers suggest that diets rich in n-3 fatty acids (and low in n-6 fatty acids) may benefit people with other inflammatory disorders, such as OA. In fact, several laboratory studies of cartilage-containing cells have found that n-3 fatty acids decrease inflammation and reduce the activity of enzymes that break down cartilage.

Another potential source of n-3 fatty acids is the New Zealand green lipped mussel (*Perna canaliculus*), used for centuries by the Maori people for good health. In a trial involving 38 people with OA, nearly 40% of those who received *P. canaliculus* extracts experienced the following:

- Decreased joint stiffness and pain
- Increased grip strength
- Enhanced walking pace

While chronic pain often necessitates medical therapy, particularly in extreme cases, an integrative approach that combines simple dietary modifications, regular exercise, and nutritional supplements can dramatically improve quality of life and reduce the requirement for non-steroidal anti-inflammatory drugs (NSAIDs) to control pain.

Unfortunately, physicians rarely recommend alternative therapies to patients, either because they are unaware of their potential benefits, or for fear of criticism from their colleagues and peers.

**EPA/DHA**

More than 25 years ago, epidemiological data on Greenland Eskimos triggered a spate of research into the role of essential fatty acids contained in fish oils. Today, the benefits of eating fish rich in n-3 fatty acids are well established. Additionally, a large body of research suggests that consuming fish oil capsules can aid in reducing the symptoms of systemic lupus (303) and rheumatoid arthritis (304). Supplementing with the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) also works in much
the same way as the dietary modifications discussed at the outset of this article.

The EPA and DHA contained in fish oils compete favorably with AA, and are processed by COX enzymes. The family of eicosanoids produced from n-3 fatty acids are far less inflammatory than those produced by AA, which is an n-6 fatty acid. Supplementing with fish oil capsules should be considered in addition to the dietary changes suggested above. Although the clinical benefits of dietary supplementation with n-3 polyunsaturated fatty acids (PUFA) has been recognised for a number of years, the molecular mechanisms by which particular PUFA affect metabolism of cells within the synovial joint tissues are not understood. This study by Curtis CL et al set out to investigate how n-3 PUFA and other classes of fatty acids affect both degenerative and inflammatory aspects of metabolism of articular cartilage chondrocytes using an in vitro model of cartilage degradation. Using well-established culture models, cartilage explants from normal bovine and human osteoarthritic cartilage were supplemented with either n-3 or n-6 PUFA, and cultures were subsequently treated with interleukin 1 (IL-1) to initiate catabolic processes that mimic cartilage degradation in arthritis. Results show that supplementation specifically with n-3 PUFA, but not n-6 PUFA, causes a decrease in both degenerative and inflammatory aspects of chondrocyte metabolism, whilst having no effect on the normal tissue homeostasis. Dietary supplementation of n-3 PUFA, which in turn may have a beneficial effect of slowing and reducing inflammation in the pathogenesis of degenerative joint diseases in man.

Curtis CL, ReesSG, Little CB et al have also shown that supplementation with n-3 PUFA (but not other fatty acids) reduced, in a dose-dependent manner, the endogenous and IL-1-induced release of proteoglycan metabolites from articular cartilage explants and specifically abolished endogenous aggreganase and collagenase proteolytic activity. Similarly, expression of mRNA for ADAMTS-4, MMP-13, and MMP-3 (but not TIMP-1, -2, or -3) was also specifically abolished with n-3 PUFA supplementation. In addition, n-3 PUFA supplementation abolished the expression of mRNA for mediators of inflammation (cyclooxygenase 2, 5-lipoxygenase, 5-lipoxygenase-activating protein, tumor necrosis factor alpha, IL-1alpha, and IL-1beta) without affecting the expression of message for several other proteins involved in normal tissue homeostasis.
Rheumatoid arthritis is an autoimmune disease that causes chronic inflammation of the joints. Rheumatoid arthritis can also cause inflammation of the tissue around the joints, as well as other organs in the body. Autoimmune diseases are illnesses, which occur when the body tissues are mistakenly attacked by its own immune system. The immune system is a complex organization of cells and antibodies designed normally to "seek and destroy" invaders of the body, particularly infections. Patients with these diseases have antibodies in their blood, which target their own body tissues, where they can be associated with inflammation. Because it can affect multiple other organs of the body, rheumatoid arthritis is referred to as a systemic illness and is sometimes called rheumatoid disease.

Noninvasive, pharmaceutical-based therapies for the treatment of arthritic diseases are primarily limited to oral administration of nonsteroidal antiinflammatory drugs, which inhibit cyclooxygenase (COX) \(^1\)-mediated production of inflammatory eicosanoids such as prostaglandins. Parenthetically, clinical studies on dietary supplementation with \(n-3\) (\(n-3\)) fatty acids (the principle long chain polyunsaturated fatty acids found in fish oils) have also demonstrated modulation of inflammatory symptoms involved in the pathogenesis of arthritis. Such epidemiological observations have been largely anecdotal, because they did not investigate the molecular mechanisms whereby dietary \(n-3\) fatty acid supplementation might affect the metabolism of cells within articular joint tissues and thereby provide relief to arthritic symptoms. Significantly, however, dietary supplementation with \(n-3\) fatty acids elicits antiinflammatory effects in neutrophils and monocytes by inhibiting the 5-lipoxygenase pathway responsible for metabolism of arachidonic acid to leukotrienes. Furthermore, \(n-3\) fatty acid supplementation can also suppress phospholipase C-mediated signal transduction, thus demonstrating additional molecular mechanisms whereby \(n-3\) fatty acids can specifically affect cell metabolism.

One of the key pathological features common to degenerative joint diseases (arthritis) is the loss of cartilage proteoglycan (aggrecan), which precedes subsequent cartilage erosion. Catabolism of aggrecan is mediated by the proteolytic activity of aggrecanases' two isoforms of which have recently been purified and cloned. Aggrecanase activity is up-regulated by cartilage exposure to pro-inflammatory cytokines such as IL-1 and TNF-\(\alpha\), and model cartilage explant and chondrocyte culture systems stimulated with IL-1 or TNF-\(\alpha\) mimic the degradative processes involving aggrecan catabolism which occur.
during arthritis In addition, exposure to these inflammatory mediators propogates the autocrine synthesis of cartilage cytokines, which contribute to the chronic progression of arthritis. Furthermore, cytokine-induced degradative activities in synovial joint tissues can be potentiated via the biosynthesis of inflammatory eicosanoids by the cyclooxygenases COX-1 and COX-2. COX-1, which is constitutively expressed in most tissues, is responsible for key aspects of eicosanoid biosynthesis, which are important in maintaining homeostasis during normal cellular metabolism. Conversely, COX-2 expression and activity is induced during inflammation, and it is this enzyme that is selectively involved in inflammatory aspects of arthritic disease. Consequently, modulation of COX-2 activity has been a major target of pharmaceutical companies for intervention in the pathogenesis of arthritis.

Rheumatoid arthritis (RA) is a debilitating disease and is associated with increased risk of cardiovascular disease and osteoporosis. Poor nutrient status in RA patients has been reported and some drug therapies, such as nonsteroidal anti-inflammatory drugs (NSAIDs), prescribed to alleviate RA symptoms, may increase the requirement for some nutrients and reduce their absorption. This paper reviews the scientific evidence for the role of diet and nutrient supplementation in the management of RA, by alleviating symptoms, decreasing progression of the disease or by reducing the reliance on, or combating the side-effects of, NSAIDs. Supplementation with long-chain n-3 polyunsaturated fatty acids (PUFA) consistently demonstrates an improvement in symptoms and a reduction in NSAID usage. Evidence relating to other fatty acids, antioxidants, zinc, iron, folate, other B vitamins, calcium, vitamin D and fluoride are also considered. The present evidence suggests that RA patients should consume a balanced diet rich in long-chain n-3 PUFA and antioxidants. More randomized long-term studies are needed to provide evidence for the benefits of specific nutritional supplementation and to determine optimum intake, particularly for n-3 PUFA and antioxidants.

Fish oils are a rich source of n-3 long chain polyunsaturated fatty acids (n-3 LC PUFA). The specific fatty acids, eicosapentaenoic acid and docosahexaenoic acid, are homologues of the n-6 fatty acid, arachidonic acid (AA). This chemistry provides for antagonism by n-3 LC PUFA of AA metabolism to pro-inflammatory and pro-thrombotic
n-6 eicosanoids, as well as production of less active n-3 eicosanoids. In addition, n-3 LC
PUFA can suppress production of pro-inflammatory cytokines and cartilage degradative
enzymes. In accordance with the biochemical effects, beneficial anti-inflammatory
effects of dietary fish oils have been demonstrated in randomised, double blind, placebo-
controlled trials in rheumatoid arthritis (RA). Also, fish oils have protective clinical
effects in occlusive cardiovascular disease, for which patients with RA are at increased
risk. Implementation of the clinical use of anti-inflammatory fish oil doses has been poor.
Since fish oils do not provide industry with the opportunities for substantial profit
associated with patented prescription items, they have not received the marketing inputs
that underpin the adoption of usual pharmacotherapies. Accordingly, many prescribers
remain ignorant of their biochemistry, therapeutic effects, formulations, principles of
application and complementary dietary modifications. Evidence is presented that
increased uptake of this approach can be achieved using bulk fish oils. This approach has
been used with good compliance in RA patients. In addition, an index of n-3 nutrition can
be used to provide helpful feedback messages to patients and to monitor the attainment of
target levels. Collectively, these issues highlight the challenges in advancing the use of
fish oil amid the complexities of modern management of RA, with its emphasis on
combination chemotherapy applied early.

Hepatitis means inflammation of the liver. Many illnesses and conditions can cause
inflammation of the liver, for example, drugs, alcohol, chemicals and autoimmune
diseases. Many viruses, for example, the virus of mononucleosis and the cytomegalovirus
can inflame the liver. Most viruses, however, do not primarily attack the liver; the liver is
just one of several organs that the viruses affect. When doctors speak of viral hepatitis,
ythey usually are referring to hepatitis caused by a few specific viruses that primarily
attack the liver. There are several hepatitis viruses; they have been named types A, B, C,
D, E, F (not confirmed), and G. As our knowledge of hepatitis viruses grows, it is likely
that this alphabetical list will become longer. The most common hepatitis viruses are
types A, B, and C.

It is theorized that the HC A virus has as some part of its structure a lipid or fat envelope.
Essential fatty acids such as omega 3 and omega 6 may play an important role in altering
the stability of this lipid envelope by either increasing or decreasing cellular membrane fluidity. It is theorized that the disruption or uncoating of the lipid envelope would make HCV more susceptible to destruction by the host’s immune system. Infants and children with chronic liver diseases have a high risk of EFAs deficiency correlated with progressive elevation of serum bilirubin and progressive deterioration of oxidant status. Polyunsaturated fatty acids suppress the development of acute hepatitis and prolong survival in females, regardless of whether they are of the n-6 or n-3 type, which are associated with altered gene expressions. Dietary supplementation with essential fatty acids and polyunsaturated lecithin may improve biochemical and histological parameters in liver disease.

Disorders of lipoprotein metabolism, in conjunction with the prevalence of high-fat diets, obesity, and physical inactivity, have resulted in an epidemic of atherosclerotic disease in the United States and other developed countries. The interaction of common genetic and acquired disorders of lipoproteins with these adverse environmental factors leads to the premature development of atherosclerosis. In the United States, mortality from coronary artery disease (CAD), particularly in persons younger than 60 years, has been declining since 1970; however, atherosclerotic cardiovascular disease remains the most common cause of death among both men and women.

There is consensus that elevated plasma LDL levels and reduced HDL levels are associated with an increased risk of atherosclerosis. The role of hypertriglyceridemia as a cardiovascular risk factor is more complex. Hypertriglyceridemia may be a marker for other lipoprotein abnormalities (e.g., increased levels of small, dense LDL particles; low levels of HDL; or remnant accumulation) that are part of the dyslipidemic pattern associated with FCHL, type 2 diabetes mellitus and the metabolic syndrome.

Of all known dietary factors, long-chain n-3 fatty acids may be the most protective against death from coronary heart disease. New evidence has confirmed and refined the cardio-protective role of these fatty acids.

**RECENT FINDINGS:**
n-3 fatty acid supplementation reduces the risk of sudden cardiac death and death from any cause within 4 months in post-myocardial infarction patients. Evidence continues to accrue for benefits in the primary prevention of coronary heart disease and stroke, and an anti-arrhythmogenic mechanism is emerging as the most likely explanation.

Fatty acids are an important source of energy, which can have an influence on serum lipids. N-3 and n-6 fatty acids, both polyunsaturated fatty acids, have been advocated as replacement for saturated fat. N-3 fatty acids, derived from fish and certain green plants, lower serum triglycerides, but they have also been shown to have a direct effect on myocardial contractility, blood pressure, platelet function, coagulation factors, cell-mediated immunity and markers of inflammation. Recently available clinical trial data, including those using the concentrated n-3 fatty acid preparation Omacor, indicate that n-3 fatty acids are valuable in preventing sudden death following myocardial infarction. Studies indicate that n-3 fatty acids are just as effective as, or have a benefit superior to, statins in secondary prevention. It is also useful in the treatment of hypertriglyceridaemia, both as monotherapy and in combination with statins.

Dietary triglycerides containing predominantly poly-unsaturated fatty acids (PUFAs) are known to reduce plasma total and low-density lipoprotein (LDL) cholesterol concentrations relative to triglycerides containing predominantly saturated fatty acids.

Thus fatty acids play an important role in human physiology and diseases and many clinical studies have shown that supplementation of essential fatty acids may have a beneficial role in treatment of these diseases.

The degenerative disease epidemic that wrecks around the globe came coincidently with the introduction of engineered fats and oils. It is the type of fats and oils that we consumed that is directly correlated to the rise of epidemic degenerative diseases; it is not the amount of fats and oils that we eat causes the problems.

The goal of modern medicine is no longer merely treatment of sickness but also prevention of diseases, promotion of health and improvement of quality of life of individual and group or community.
Epidemiological and clinical evidences supports that an imbalance in dietary consumption of EFAs (n-6 to n-3 FA) is one of the root causes for the genesis and progression of many degenerative chronic diseases around globe including Indians.

Medical knowledge is constantly changing, standard safety precaution must be followed but as now research and clinical experience broaden our knowledge, change in the treatment and drug therapy may become necessary or appropriate.

Americans leads the world in a lot of things and heart disease is one of them. For a long time, scientists did not understand why Greenland Eskimos and Costal Japanese have low levels of triglycerides (Tg) [blood-fat], cholesterol and correspondingly low incidences of heart diseases. These two groups of people consumed higher amount of fat in their diets than most Americans. The key to this paradox came when the research scientists discovered a big difference in the kind of fats Eskimos and Costal Japanese consumed to the rest of us. Cold-water fish consumption held the key to this paradox. Cold-water fish are high in the long-chain derivatives of n-3 fatty acids and low in n-6 fatty acids, which is unhealthy. The problem with cold-water fish in capsules is it can make our breath stink or leave a fishy after test and also acts as a source of entering of pesticides in human body. In addition, presence of high contents of methyl-mercury in fish may have great health hazards (Ben Best; http://www.scientificpychic.com/). Moreover, daily intake of fish or fish oil (gives direct EPA and DHA) in diet or used for long time as therapeutic supplementation can increases lipid peroxidation, thus additional supplementation of vitamin ‘E’ is necessary with fish or fish-oil. Supplementation of vitamin ‘E’ is not required with the plant derived (EFAs) ALA, a precursor of EPA and DHA (405).

Fortunately, linseed, also known as linseed oil or flaxseed oil is derived from the seeds of the plant “Linum usitatissimum.” Linseed oil is a very rich source of alpha-linolenic acid (ALA; n-3 FA). ALA concentration in linseed oil ranges from approximately 40 to 60 %. A lower amount of linoleic acid (LA; n-6 FA), approximately around 15 % is also present in linseed oil. Purified isolated LA and ALA provides 1:3 to 1:4 ratio of n-6 to n-3 fatty acid in linseed oil without odor thus create a healthy balance (near to normal levels) of EFAs in the body.
As most of the Indians are vegetarians and do not like to eat fish or to take animal source derived medicines. Furthermore, in our knowledge, short term or long-term studies using linseed derived EFAs (LA and ALA) as therapeutic agent in chronic degenerative diseases on Indian patients / subjects are lacking. Therefore, in view of the above facts and evidences the present study was designed to assess the therapeutic efficacy and tolerability of EFAs (Plant-derived [linseed-oil]) in human diseases. Therefore it was decided to investigate the role of essential fatty acids as hypolipidemic agent in dyslipidemia, as an anti-inflammatory agent in osteoarthritis & rheumatoid arthritis and as an anti-inflammatory and hepatoprotective agent in hepatitis in Indian patients / subjects.