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(54) Title: OMEGA-3 PENTAENOIC ACID COMPOSITIONS AND METHODS OF USE

(57) Abstract: Orally administrable composition comprising fatty acids copmrisingomega-3-fatty acids, salts or derivatives thereof are provided. These compositions can be used for the treatment or prophylaxis of dyslipidemic, cardiovascular, CNS, inflammatory, and other diseases/conditions or risk factors therefore. The present invention relates to omega-3 fatty acid compositions, and methods of treating, preventing, reducing the occurrence of, and improving symptoms associated with inflammatory conditions.

# OMEGA-3 PENTAENOIC ACID COMPOSITIONS AND METHODS OF USE

## RELATED APPLICATIONS

**[0001]** This application claims the benefit of U.S. Provisional Patent Application No. 61/780,948, filed March 13, 2013, the contents of which are incorporated herein by reference.

## FIELD OF INVENTION

**[0002]** The present invention relates to omega-3 fatty acid compositions, and methods of treating, preventing, reducing the occurrence of, and improving symptoms associated with inflammatory conditions.

## BACKGROUND OF THE INVENTION

**[0003]** Marine oils, also commonly referred to as fish oils, are a good source of the two main omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which have been found to regulate lipid metabolism. Omega-3 fatty acids have been found to have beneficial effects on the risk factors for cardiovascular diseases, especially mild hypertension, hypertriglyceridemia and on the coagulation factor VII phospholipid complex activity. Omega-3 fatty acids lower serum triglycerides (TG), increase serum HDL-cholesterol, lower systolic and diastolic blood pressure and the pulse rate, and lower the activity of the blood coagulation factor VII-phospholipid complex. Further, omega-3 fatty acids seem to be well tolerated, without giving rise to any severe side effects.

**[0004]** The table directly below lists the most common omega-3 fatty acids, including their 3-letter abbreviation code. In this application, the use of any of the 3-letter abbreviations shall refer to the omega-3 fatty acid, unless otherwise indicated (e.g. DPA or DPA 22:5 (n-3) or DPA 22:5-n3 or DPA 22:5n3 or DPA-n3, which all refer to the omega-3 isomer of docosapentaenoic acid).

| Common Name for Omega-3 Fatty Acid (+abbreviation) | Codified Lipid Name | Chemical Name |
|---|---|---|
| Hexadecatrienoic acid (HTA) | 16:3 (n–3) | all-cis-7,10,13-hexadecatrienoic acid |
| α-Linolenic acid (ALA) | 18:3 (n–3) | all-cis-9,12,15-octadecatrienoic acid |
| Stearidonic acid (SDA) | 18:4 (n–3) | all-cis-6,9,12,15-octadecatetraenoic acid |
| Eicosatrienoic acid (ETE) | 20:3 (n–3) | all-cis-11,14,17-eicosatrienoic acid |
| Eicosatetraenoic acid (ETA) | 20:4 (n–3) | all-cis-8,11,14,17-eicosatetraenoic acid |
| Eicosapentaenoic acid (EPA) | 20:5 (n–3) | all-cis-5,8,11,14,17-eicosapentaenoic acid |
| Heneicosapentaenoic acid (HPA) | 21:5 (n–3) | all-cis-6,9,12,15,18-heneicosapentaenoic acid |
| Docosapentaenoic acid (DPA) or Clupanodonic acid | 22:5 (n–3) | all-cis-7,10,13,16,19-docosapentaenoic acid |
| Docosahexaenoic acid (DHA) | 22:6 (n–3) | all-cis-4,7,10,13,16,19-docosahexaenoic acid |
| Tetracosapentaenoic acid (TPA) | 24:5 (n–3) | all-cis-9,12,15,18,21-tetracosapentaenoic acid |
| Tetracosahexaenoic acid (THA) or Nisinic acid | 24:6 (n–3) | all-cis-6,9,12,15,18,21-tetracosahexaenoic acid |

**[0005]** One form of omega-3 fatty acids is a concentrate of omega-3, long chain, polyunsaturated fatty acids from fish oil containing DHA ethyl esters, EPA ethyl esters as well as ethyl esters of other omega-3 fatty acids (described in USP35 for LOVAZA®) and is sold under the trademarks OMACOR® and LOVAZA®. Such a form of omega-3 fatty acid comprises at least 90% omega-3 fatty acids of which at least 80% EPA+DHA (in a ratio of 1.2:1) and is described, for example, in U.S. Pat. Nos.. 5,502,077, 5,656,667 and 5,698,594. LOVAZA® (omega-3-acid ethyl esters) is indicated for the treatment of patients with hypertriglyceridemia with TG levels of 500mg/dL or higher.

**[0006]** Another form of omega-3 fatty acid concentrate is sold under the trademark EPADEL® ® for the treatment of dyslipidemia. This product is described as 98% EPA ethyl ester in Lancet (Vol.369; March 31, 2007; 1090-1098) reporting on a large outcome study with EPADEL®. EPADEL® is known to contain less than 1% of any fatty acid other than EPA.

**[0007]** Similar to EPADEL®, another form of omega-3 fatty acid concentrate also consists almost entirely of EPA ethyl ester and is known under its developmental stage name AMR101 or its trade name VASCEPA®. This product is described in US patent application 2010/0278879 as comprising at least 95% EPA (typically referred to as 97% or at least 96% in company releases and references) and less than 1% of any other fatty acid. AMR101 was previously under development for the treatment of Huntingdon's Disease but failed in phase III clinical development. Subsequently, AMR101 was entered in a development program for hypertriglyceridemia and mixed dyslipidemia.

**[0008]** Yet another concentrate of omega-3, long chain, polyunsaturated fatty acids from fish oil containing approximately 75% DHA and EPA as free fatty acids is known under its developmental stage name EPANOVA™. This product is described as comprising approximately 55% EPA and 20% DHA. EPANOVA™ was previously under development for the treatment of Crohn's Disease but failed in phase III clinical development. Subsequently, EPANOVA™ was entered in a development program for hypertriglyceridemia and mixed dyslipidemia.

**[0009]** Generally, the bioavailability and therapeutic effect of omega-3 fatty acid compositions is dose dependent, i.e., the higher the dose, the greater the therapeutic affect and bioavailability. However, the effect of each specific omega-3 fatty acid composition may be different, and therefore the level of therapeutic effect of one composition at a given dose cannot necessarily be inferred from the level of therapeutic effects of other omega-3 fatty acid compositions at the same or similar dose.

**[0010]** Omega-3 fatty acids are known to be "essential fatty acids". There are two series of essential fatty acids (EFAs) in humans. They are termed "essential" because they cannot be synthesized de novo in mammals. These fatty acids can be interconverted within a series, but the omega-6 (n-6) series cannot be converted to the omega-3 series nor can the omega-3 (n-3) series be converted to the omega-6 series in humans. The main EFAs in the diet are linoleic acid of the omega-6 series and alpha-linolenic acid of the omega-3 series. However, to fulfill most of their biological effects these "parent" EFAs must be metabolised to the other longer chain fatty acids. Each fatty acid probably has a specific role in the body. The scientific literature suggests that particularly important in the n-6 series are dihomo-gammalinolenic acid (DGLA, 20:3-n6) and arachidonic acid (ARA, 20:4-n6), while particularly important in the n-3 series are eicosapentaenoic acid (EPA, 20:5-n3) and docosahexaenoic acid (DHA, 22:6-n3).

**[0011]** U.S. Patent No. 6,479,544 describes an invention in which it is found that ARA is highly desirable rather than undesirable and it may be helpful to administer ARA in association with EPA. This invention provides pharmaceutical formulations containing eicosapentaenoic acid or any appropriate derivative (hereinafter collectively referred to as EPA) and arachidonic acid (ARA), as set out in the granted

claims for this patent. ARA may be replaced by one or more of its precursors, DGLA or GLA. In this reference, the ratio of EPA to ARA is preferably between 1:1 and 20:1.

**[0012]** Patent application PCT/GB 2004/000242 describes the treatment or prevention of psoriasis with a formulation comprising more than 95% EPA and less than 2% DHA. In another embodiment of this invention the EPA is replaced with DPA.

**[0013]** Patent application PCT/NL 2006/050291 (WO/2007/058538, GB 0301701.9) describes combinations of idigestible oligosaccharides and long chain poly-unsaturated fatty acids such as ARA, EPA, DA, and combinations thereof to improve intestinal barrier integrity, improving barrier function, stimulating gut maturation and/or reducing intestinal barrier permeability.

**[0014]** Lindeborg et al. (*Prostag Leukotr Ess*, 2013, 88:313-319) discloses a study evaluating postprandial metabolism of docosapentaenoic acid (DPA) and eicosapentaenoic acid (EPA) in humans.

**[0015]** Holub et al. (*Lipids*, 2011, 46:399-407) discloses a study assessing the effect of oral supplementation with docosapentaenoic acid (DPA) on levels of serum and tissue lipid classes and their fatty acid compositions in rat liver, heart, and kidney.

**[0016]** Inflammatory conditions are commonly experienced by patients, and can affect multiple organ systems, including but not limited to the skin, musculoskeletal system, kidneys, lungs, GI tract, central nervous system, peripheral nervous system, cardiovascular system, lymphatic system, ocular system, spleen, liver, gallbladder, nasal, oropharynx, reproductive systems, endrocrine system and hematological systems, including bone marrow. Examples of such conditions include but are not limited to osteoarthritis, rheumatoid arthritis, asthma, COPD (chronic obstructive pulmonary disease), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, and allergic ocular reactions; post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia; diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae (ie, shingles),

neuropathic pain, solid tumors, enlarged prostate, macular degeneration, lupus; diseases specifically affecting female patients such as mittlesmerchz (pain associated with ovulation) , premature (preterm) labor, dysmenorrhea (both primary and secondary), endometriosis, and PCOS (polycystic ovarian syndrome).

**[0017]** There is a high unmet need in the area of menstrual disorders and it is estimated that up to 90% of all menstruating women are affected to some degree. Up to 42% of women miss work or other activities due to menstrual pain and it has been estimated that around 600 million work hours a year are lost in the Unites States as a result.

**[0018]** Menstrual pain in the lower abdomen is thought to be caused by myometrial hyperactivity and reduced uterine blood flow. These pathophysiological changes result in abdominal pain that radiates out to the back and legs. Primary dysmenorrhea is a condition associated with the state of the most extreme sensation of severe pain and cramping during menses. Clinical and experimental research has shown that the over production of uterine prostaglandins is a key contributing factor to the development of dysmenorrhea. During menstruation the degeneration and loss of the endometrium causes the release of prostaglandins, which in turn cause uterine ischemia through myometrial contraction and vasoconstriction. This may result in women feeling nauseous, having headaches, suffering from insomnia and being incapacitated for a period of 1-4 days every month, resulting in a lower quality of life. Primary dysmenorrhea afflicts between 30- 50% of the female population.

**[0019]** Where an underlying gynecological disorder is present, such as endometriosis, pelvic inflammatory disease (PID), fibroids, or cancers, secondary dysmenorrhea will be diagnosed. Secondary dysmenorrhea is diagnosed in approximately 12% of women, and can occur in conjunction with menorrhagia, which accounts for around 12% of referrals to gynecology outpatients departments.

**[0020]** The primary objectives in the treatment of dysmenorrhea are to provide symptomatic relief, while limiting or preventing the underlying pathology that results in symptoms. Non-steroidal anti-inflammatory drugs (NSAIDs), which inhibit the cyclooxygenase (COX) enzymes, are commonly used to control the pain and inflammation. Long term NSAID use may, however, be associated with significant side effects included nausea, dyspepsia, peptic ulcer and diarrhea, and may also

increase the risk of cardiovascular events, such as myocardial infarcts and/or cardiac death. The oral contraceptive steroids (OCP) that inhibit ovulation and decrease menstrual flow, also have the propensity to reduce symptoms of dysmenorrhea. However, use of OCPs for dysmennorrhea has been associated with an increased risk of breast cancer upon long-term use. In cases of secondary dysmenorrhea surgery may be undertaken to correct the underlying gynecological disorder. Due to the poor adverse effects profile of these medical treatments, many women seek alternative and complimentary therapies to manage their dysmenorrhea.

**[0021]** Osteoarthritis is the most common type of joint disease, affecting more than 20 million individuals in the United States. It is a degenerative disorder arising from the biochemical breakdown of the cartilage found in the synovial joints. However, the current view holds that osteoarthritis involves not only the articular cartilage but also the entire joint organ, including the subchondral bone and synovium. The progression of osteoarthritis is characteristically slow, occurring over several years or decades. Over this period, the patient can become less and less active and thus more susceptible to morbidities related to decreasing physical activity. Symptoms of osteoarthritis include deep, achy joint pain exacerbated by extensive use, reduced range of motion and crepitus, stiffness during rest (gelling) associated with morning joint stiffness usually lasting for less than 30 minutes. The severity of damage and disease impact can be measured readily, in most instance using plain radiography, that can aid in visualizing the narrowing of the joint space in the affected area, loss of cartilage, and the extent and degree of damage to bone structures. Most common regions of the body that are afflicted include the knee, hands, shoulder and hips.

**[0022]** Current management of osteoarthritis is dependent on the severity of the disease and symptoms. A weight loss regimen may also be employed, as the incidence of osteoarthritis of the knee increases with an increase in weight. In severe instances, joint replacement surgery may be performed. Pharmacological treatment is commonly employed, using anti-inflammatory agents and analgesics, to reduce swelling, prevent the degenerative aspects associated with mediators of inflammation, and to impact on pain. Common classes of agents employed include oral and topical non-steroidal anti-inflammatory drugs (NSAIDs), selective COX-2

inhibitors, topical capsaicin, topical corticosteroids, intra-articular corticosteroids, tramadol, acetaminophen, intra-articular hyaluronins and intra-articular cartilage.

**[0023]** Despite the number of therapeutic options available, there is still an unmet need for the treatment of osteoarthritis, due to suboptimal efficacy and side-effects. Upon chronic use with NSAIDs, there is a propensity for increased risk of developing peptic ulcers. The selective COX-2 inhibitors increase the risk of cardiovascular events, including myocardial infarcts and cardiac death. Tramadol and related opioid-like analgesics may elicit neurological effects including addiction resulting in chronic substance abuse.

**[0024]** All references cited herein are incorporated by reference in their entirety.

## SUMMARY OF THE INVENTION

**[0025]** The present invention provides omega-3 fatty acid compositions and methods of administering these compositions.

**[0026]** The present invention provides a pharmaceutical composition comprising fatty acids, wherein at least 50% by weight of the fatty acids comprise omega-3 fatty acids, salts, esters, or derivatives thereof, wherein the omega-3 fatty acids comprise eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA) and wherein the ratio of docosahexaenoic acid to DHA to EPA (DHA:EPA) is less than 1:10, and wherein the ratio of DHA to DPA (DHA:DPA) is less than 2:1.

**[0027]** The present invention provides a pharmaceutical composition comprising eicosapentaenoic acid (EPA) in an amount between about 70% to about 95% of the total amount of fatty acids and docosapentaenoic acid (DPA) , wherein the composition comprises no more than 5% docosahexaenoic acid (DHA) of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower.

**[0028]** The present invention provides a pharmaceutical composition comprising pharmaceutical composition comprising eicosapentaenoic acid (EPA) in an amount between about 750 mg/g to about 950 mg/g, and docosapentaenoic acid (DPA), wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower.

**[0029]** The present invention provides a pharmaceutical composition comprising eicosapentaenoic acid (EPA) in a daily dosage amount of between about 1000 mg to about 5000 mg, and further comprising docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA), wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower.

**[0030]** The present invention provides a pharmaceutical composition comprising eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA), wherein the amount of EPA and DPA is about 55% or more by weight of the total amount of fatty acids, and wherein the ratio of DHA:DPA is no more than 1:1.

**[0031]** The present invention provides a pharmaceutical composition comprising: docosapentaenoic acid (DPA) in an amount between about 50% to about 80% of the total amount of fatty acids, docosahexaenoic acid (DHA) in an amount between

about 25% to about 40% of the total amount of fatty acids, and optionally eicosapentaenoic acid (EPA) in an amount less than about 10% of the total amount of fatty acids.

**[0032]** In some embodiments, the compositions of the present invention comprise additional fatty acids, such as heneicosapentaenoic acid (HPA), arachidonic acid (ARA), and omega-6-docosapentaenoic acid (n-6 DPA), tetracosapentaenoic acid (TPA), and/or gamma-linoleic acid (GLA).

**[0033]** The present invention provides methods comprising administering the compositions. The present invention provides a method of treating, preventing, reducing the occurrence of, and improving symptoms associated with inflammatory conditions. Examples of inflammatory conditions include, but are not limited to primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS).

## DETAILED DESCRIPTION OF THE INVENTION

**[0034]** The present invention provides an orally administrable composition comprising fatty acids, wherein at least 50% by weight of the fatty acids comprise omega-3-fatty acids, salts, esters, or derivatives thereof, wherein the omega-3 fatty acids comprise eicosapentaenoic acid (EPA; C20:5-n3), docosapentaenoic acid (DPA; C22:5-n3), and docosahexaenoic acid (DHA; C22:6-n3), wherein the ratio of DHA to EPA (DHA:EPA) is less than 1:20, and wherein the ratio of DHA to DPA (DHA:DPA) is less than 2:1.

**[0035]** The present invention provides a pharmaceutical composition comprising fatty acids, wherein at least 50% by weight of the fatty acids comprise omega-3 fatty acids, salts, esters, or derivatives thereof, wherein the omega-3 fatty acids comprise eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA) and wherein the ratio of docosahexaenoic acid to DHA to EPA (DHA:EPA) is less than 1:10, and

wherein the ratio of DHA to DPA (DHA:DPA) is less than 2:1, and methods of using this composition. In some embodiments the composition comprises EPA in an amount between about 70% and about 95% of the total amount of fatty acids. In some embodiments, the composition comprises less than about 5% of DHA of the total amount of fatty acids. In some embodiments, the composition comprises DPA in an amount of between about 5% and about 15% of the total amount of fatty acids. In some embodiments, the ratio of EPA to DPA (EPA:DPA) is less than about 1:1. In some embodiments, the composition further comprises heneicosapentaenoic acid (HPA) in an amount of at least 1% of the total amount of fatty acids

**[0036]** The present invention provides a pharmaceutical composition comprising eicosapentaenoic acid (EPA) in an amount between about 70% to about 95% of the total amount of fatty acids and docosapentaenoic acid (DPA), wherein the composition comprises no more than 5% docosahexaenoic acid (DHA) of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower, and methods of using the composition. In some embodiments, the composition comprises DPA in an amount of between about 5% and about 15% of the total amount of fatty acids. In some embodiments, the composition further comprises heneicosapentaenoic acid (HPA) in an amount of at least 1% of the total amount of fatty acids. In some embodiments, the ratio of EPA to DPA (EPA:DPA) is less than about 1:1. In some embodiments, the ratio of DHA:EPA is less than about 1:10.

**[0037]** The present invention provides a pharmaceutical composition comprising pharmaceutical composition comprising eicosapentaenoic acid (EPA) in an amount between about 750 mg/g to about 950 mg/g, and docosapentaenoic acid (DPA), wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower, and methods of using the composition. In some embodiments, the composition comprises about 60 mg/g to about 120 mg/g of DPA. In some embodiments, the ratio of DHA:EPA is less than 1:10. In some embodiments, the ratio of EPA:DPA is less than about 1:1. In some embodiments, the composition further comprises heneicosapentaenoic acid (HPA) in an amount of at least 1% of the total amount of fatty acids.

**[0038]** The present invention provides a pharmaceutical composition comprising eicosapentaenoic acid (EPA) in a daily dosage amount of between about 1000 mg to

about 5000 mg, and further comprising docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA), wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower, and methods of using the composition. In some embodiments, the ratio of DHA:EPA is less than about 1:10. In some embodiments, the ratio of EPA:DPA is less than about 1:1. In some embodiments, the composition further comprises heneicosapentaenoic acid (HPA) in an amount of at least 1% of the total amount of fatty acids.

**[0039]** The present invention provides a pharmaceutical composition comprising eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA), wherein the amount of EPA and DPA is about 55% or more by weight of the total amount of fatty acids, and wherein the ratio of DHA:DPA is no more than 1:1, and methods of using the composition. In some embodiments, the composition comprises docosahexaenoic acid (DHA) in an amount of less than about 30% of the total amount of fatty acids. In some embodiments, the composition comprises a daily dosage of DPA of greater than about 120 mg/day. In some embodiments, the composition comprises omega-6 fatty acids in an amount of no more than 6% of total amount of fatty acids. In some embodiments, the composition comprises DPA in an amount of at least 6% of the total amount of fatty acids.

**[0040]** The present invention provides a pharmaceutical composition comprising: docosapentaenoic acid (DPA) in an amount between about 50% to about 80% of the total amount of fatty acids, docosahexaenoic acid (DHA) in an amount between about 25% to about 40% of the total amount of fatty acids, and optionally eicosapentaenoic acid (EPA) in an amount less than about 10% of the total amount of fatty acids, and methods of using the composition. In some embodiments, the composition comprises docosapentaenoic acid (DPA) in an amount between about 50% to 75%, alternatively about 50% to about 70%, alternatively about 50% to about 65%, or alternatively about 50% to about 60%, of the total amount of fatty acids. In some embodiments, the composition comprises docosahexaenoic acid (DHA) in an amount between about 25% to about 38%, alternatively about 25% to about 35%, alternatively about 30% to about 35% of the total amount of fatty acids. In some embodiments, the composition comprises eicosapentaenoic acid (EPA) in an amount

less than about 9%, alternatively less than about 8%, alternatively less than about 7%, alternatively less than about 6%, alternatively less than about 5%, of the total amount of fatty acids.

**[0041]** In some embodiments, the compositions of the present invention comprise at least 50% omega-3 fatty acids, alternatively at least 55%, alternatively at least 60%, alternatively at least 65%, alternatively at least 70%, alternatively at least 75%, alternatively at least 80%, alternatively at least 85%, alternatively at least 95%, most preferably at least 90% omega-3 fatty acids of the total amount of fatty acids. In some embodiments, the composition comprises at least about 92% to about 99%, alteratively about 93% to about 98%, alternatively about 94% to about 98%, omega-3 fatty acids of the total amount of fatty acids.

**[0042]** In other embodiments, EPA and DPA are jointly present in the compositions of the present invention at between about 55% and about 100% of total fatty acids, alternatively between about 60% and about 100%, alternatively between about 65% and about 100%, alternatively between about 70% and about 100%, alternatively between about 75% and about 100%, alternatively between about 80% and about 100%, alternatively between about 85% and about 95%, alternatively about 85% to about 100%, alternatively between about 85% and about 97%, alternatively between about 88% and about 95%, alternatively between about 88% and about 97%, alternatively about 88% to about 100%, alternatively between about 90% and about 95%, alternatively between about 90% and about 97%, alternatively about 90% to about 100%, alternatively about 95% to about 100%, alternatively about 97% to about 100% of the total amount of fatty acids.

**[0043]** On a EPA+DPA daily dose basis, the compositions of the present invention may be provided in a dose of between 100 mg and 10,100 mg/day, alternatively between 200 mg and 8,100 mg/day, alternatively between 300 mg and 6,100 mg/day, alternatively between 400 mg and 5,100 mg/day, alternatively between 500 mg and 4,100 mg/day. In some embodiments, on a EPA+HPA+DPA daily dose basis, the compositions and methods of the present invention may be provided in a dose of between 100 mg and 10,100 mg/day, alternatively between 200 mg and 8,100 mg/day, alternatively between 300 mg and 6,100 mg/day, alternatively between 400 mg and 5,100 mg/day, alternatively between 500 mg and 4,100

mg/day. In some embodiments, on an omega-3-pentaenoic acid daily dose basis, the methods and compositions of the present invention may be provided in a dose of between 100 mg and 10,100 mg/day, alternatively between 200 mg and 8,100 mg/day, alternatively between 300 mg and 6,100 mg/day, alternatively between 400 mg and 5,100 mg/day, alternatively between 500 mg and 4,100 mg/day.

**[0044]** The fatty acids, such as EPA and DPA, may be present in free fatty acid form, or as a salt, ester, or derivative. The fatty acids are preferably composed as a triglyceride, an ester (such as an ethyl ester) or free fatty acid. Other forms of the fatty acids which may be useful include salts, esters of any type, amides, mono-, di- or triglycerides, phospholipids or any other form which can lead to metabolization of the fatty acids (such as EPA and/or DPA), or the incorporation of the fatty acids (such as EPA and/or DPA) into body fluids, tissues or organs.

**[0045]** Omega-3 fatty acids may be grouped by the number of double bonds contained in the fatty acid chain. For instance, hexadecatrienoic acid (HTA), alpha-linolenic acid (ALA) and eicosatrienoic acid (ETE) are omega-3-trienoic acids; stearidonic acid (SDA) and eicosatetraenoic acid (ETA) are omega-3-tetraenoic acids; EPA, heneicosapentaenoic acid (HPA), DPA and tetracosapentaenoic acid (TPA) are omega-3-pentaenoic acids; and DHA and tetracosahexaenoic acid (THA) are omega-3-hexaenoic acids. In some preferred embodiments, the term omega-3-pentaenoic acids will refer to a mixture of at least two omega-3 pentaenoic acids in a ratio of at least 1:25, more preferably in a ratio of at least 1:50, more preferably in a ratio of at least 1:75, more preferably in a ratio of at least 1:100, more preferably in a ratio of at least 1:125, more preferably in a ratio of at least 1:150, more preferably in a ratio of at least 1:200. In some embodiments, the ratio refers to the ratio of the least prevalent omega-3 pentaenoic acid in the mixture to the most prevalent omega-3 pentaenoic acid in the mixture.

**[0046]** In some embodiments, the compositions of the present invention comprise EPA, HPA, DPA and TPA, alternatively EPA and DPA, and alternatively the compositions of the present invention comprise EPA, HPA and DPA.

**[0047]** In some embodiments, the omega-3-pentaenoic acids in the compositions of the present invention comprise no more than 99.5% of a single omega-3-pentaenoic acid, alternatively no more than 99%; alternatively no more than 98.5%;

alternatively no more than 98%; alternatively no more than 97.5%; alternatively no more than 96%; alternatively no more than 95%; alternatively no more than 94%; alternatively no more than 93%; alternatively no more than 92%; alternatively no more than 91%; alternatively no more than 90%; alternatively no more than 88%; alternatively no more than 85%; alternatively no more than 80%; alternatively no more than 75%; alternatively no more than 70%; alternatively no more than 65%; alternatively no more than 60%; alternatively no more than 55%; alternatively no more than 50%; alternatively no more than 45%; alternatively no more than 40%; alternatively no more than 30%.

**[0048]** In some embodiments, the compositions of the present invention wherein at least 10%, alternatively at least 20%, alternatively at least 25%, alternatively at least 35%, alternatively at least 50%, alternatively at least 60%, alternatively at least 65%, alternatively at least 70%, alternatively at least 75%, by weight of the fatty acids comprise omega-3-pentaenoic acids, salts, esters, or derivatives thereof.

**[0049]** In some embodiments, compositions and methods comprise significant amounts of omega-3-pentaenoic acids or their glycerol or ethyl esters may be used in the methods of the present invention. In some embodiments, the compositions and methods comprise at least 100 mg omega-3-pentaenoic acids per day, alternatively at least 200mg omega-3-pentaenoic acids per day, alternatively at least 300mg omega-3-pentaenoic acids per day, alternatively at least 500mg omega-3-pentaenoic acids per day, alternatively at least 700mg omega-3-pentaenoic acids per day, alternatively at least 900mg omega-3-pentaenoic acids per day, alternatively at least 1000mg omega-3-pentaenoic acids per day, alternatively at least 1500mg omega-3-pentaenoic acids per day, alternatively at least 1900mg omega-3-pentaenoic acids per day, alternatively at least 2000mg omega-3-pentaenoic acids per day, alternatively at least 2500mg omega-3-pentaenoic acids per day, alternatively at least 2900mg omega-3-pentaenoic acids per day, alternatively at least 3000mg omega-3-pentaenoic acids per day, alternatively at least 3500mg omega-3-pentaenoic acids per day, alternatively at least 3900mg omega-3-pentaenoic acids per day, alternatively at least 4000mg omega-3-pentaenoic acids per day, alternatively at least 4100mg omega-3-pentaenoic acids per day, alternatively at least 4500mg omega-3-pentaenoic acids per day,

alternatively at least 5000mg omega-3-pentaenoic acids per day, alternatively at least 5500mg omega-3-pentaenoic acids per day, alternatively at least 6000mg omega-3-pentaenoic acids per day, alternatively at least 6100mg omega-3-pentaenoic acids per day or their glycerol or ethyl esters.

**[0050]** In some embodiments, the compositions provide a DHA as compared to the amount of omega-3-pentaenoic acids (N3-5enoicFA) such that the DHA:N3-5enoicFA ratio is no more than 15:1 of DHA:N3-5enoicFA, alternatively no more than 12:1 of DHA:N3-5enoicFA, alternatively no more than 10:1 of DHA:N3-5enoicFA, alternatively no more than 8:1 of DHA:N3-5enoicFA, alternatively no more than 5:1 of DHA:N3-5enoicFA, alternatively no more than 3:1 of DHA:N3-5enoicFA, alternatively no more than 2:1 of DHA:N3-5enoicFA, alternatively no more than 1:1 of DHA:N3-5enoicFA, alternatively no more than 1:2 of DHA:N3-5enoicFA, alternatively no more than 1:3 of DHA:N3-5enoicFA, alternatively no more than 1:5 of DHA:N3-5enoicFA, alternatively no more than 1:8 of DHA:N3-5enoicFA, alternatively no more than 1:10 of DHA:N3-5enoicFA, alternatively no more than 1:15 of DHA:N3-5enoicFA, alternatively a relative amount of no more than 1:20 of DHA:N3-5enoicFA.

**[0051]** In some embodiments, the compositions of the present invention comprise at least 0.01% HPA of total fatty acids in the composition, alternatively at least 0.05% HPA, alternatively at least 0.10% HPA, alternatively at least 0.15% HPA, alternatively at least 0.2% HPA, alternatively at least 0.3% HPA, alternatively at least 0.4% HPA, alternatively at least 0.5% HPA, alternatively at least 0.75% HPA, alternatively at least 1% HPA, alternatively at least 1.5% HPA, alternatively at least 2% HPA, alternatively at least 2.5% HPA, alternatively at least 3% HPA, alternatively at least 3.5% HPA, alternatively at least 4% HPA, alternatively at least 4.5% HPA, alternatively at least 5% HPA, alternatively at least 6% HPA, alternatively at least 7% HPA, alternatively the compositions of the present invention comprise at least 9% HPA of total fatty acids in the composition.In some embodiments, the compositions of the present invention comprise no more than 20% HPA of total fatty acids in the composition, alternatively no more than 15% HPA, alternatively no more than 12% HPA, alternatively no more than 10% HPA, alternatively no more than 8% HPA, alternatively no more than 7% HPA, alternatively no more than 6% HPA, alternatively

no more than 5% HPA, alternatively no more than 4% HPA, alternatively no more than 3% HPA, alternatively no more than 2% HPA, alternatively no more than 1.5% HPA, alternatively the compositions of the present invention comprise at least 1% HPA of total fatty acids in the composition. In some embodiments, the compositions of the present invention comprise 1% to 20% HPA of the total fatty acids in the composition. In some embodiments, the compositions of the present invention comprise about 1% to about 6% HPA, alternatively about 2% to about 5% HPA, alternatively about 3% to about 4% HPA, relative to the total amount of fatty acids in the composition. In some embodiments, the compositions of the present invention comprise about 10 mg/g to about 50 mg/g HPA, alternatively about 15 mg/g to about 45 mg/g, alternatively about 20 mg/g to about 40 mg/g, alternatively about 25 mg/g to about 35 mg/g, alternatively about 30 mg/g HPA.

**[0052]** In some embodiments, the present invention provides compositions and methods which comprise significant amounts of omega-3 heneicosapentaenoic acid (HPA) or its glycerol or ethyl esters. In some embodiments, the methods of treatment may provide to a subject in need thereof a dose of at least 10 mg HPA per day, alternatively at least 15 mg HPA per day, alternatively at least 20 mg HPA per day, alternatively at least 25 mg HPA per day, alternatively at least 30mg HPA per day, alternatively at least 40mg HPA per day, alternatively at least 50mg HPA per day, alternatively at least 60mg HPA per day, alternatively at least 70mg HPA per day, alternatively at least 80mg HPA per day, alternatively at least 90mg HPA per day, alternatively at least 100mg HPA per day, alternatively at least 120mg HPA per day, alternatively at least 150mg HPA per day, alternatively at least 160mg HPA per day, alternatively at least 180mg HPA per day, alternatively at least 200mg HPA per day, alternatively at least 250mg HPA per day, alternatively at least 300mg HPA per day, alternatively at least 350mg HPA per day, alternatively at least 400mg HPA per day, alternatively at least 500mg HPA per day, alternatively at least 600mg HPA per day, alternatively at least 800mg HPA or its glycerol or ethyl esters per day.

**[0053]** In some embodiments, the compositions of the present invention comprise no more than 10% omega-3 fatty acids that are not omega-3-pentaenoic acids, alternatively no more than 9%, alternatively no more than 8%, alternatively no more than 7%, alternatively no more than 6%, alternatively no more than 5%, alternatively

no more than 4.5%, alternatively no more than 4%, alternatively no more than 3.5%, alternatively no more than 3%, alternatively no more than 2.5%, alternatively no more than 2%, alternatively no more than 1.5%, alternatively no more than 1.25%, alternatively no more than 1%, alternatively no more than 0.75%, alternatively no more than 0.5%, alternatively no more than 0.4%, alternatively no more than 0.3%, alternatively no more than 0.2%, alternatively the compositions of the present invention comprise no more than 0.1% omega-3 fatty acids that are not omega-3-pentaenoic acids.

**[0054]** In the embodiments of the present invention, the compositions comprise EPA and DPA in an EPA:DPA ratio between 99:1 and 1:99 EPA:DPA, alternatively between 90:1 and 1:90, alternatively between 60:1 and 1:60, alternatively between 60:1 and 1:20, alternatively between 60:1 and 1:4, alternatively between 40:1 and 1:20, alternatively between 30:1 and 1:20, alternatively between 30:1 and 1:10, alternatively between 30:1 and 1:5, alternatively between 40:1 and 1:4, alternatively between 30:1 and 1:4, alternatively between 30:1 and 1:2, alternatively between 30:1 and 1:1, alternatively between 30:1 and 2:1, alternatively between 30:1 and 5:1, alternatively between 20:1 and 1:20, alternatively between 20:1 and 1:10, alternatively between 20:1 and 1:5, alternatively between 20:1 and 1:2, alternatively between 20:1 and 1:1, alternatively between 20:1 and 2:1, alternatively between 20:1 and 5:1, alternatively between 20:1 and 10:1, alternatively between 20:1 and 10:1, alternatively between 30:1 and 10:1, alternatively between 60:1 and 10:1, alternatively comprise EPA and DPA in an EPA:DPA ratio between 40:1 and 10:1. In some embodiments, the ratio of EPA:DPA is greater than 1:1, preferably greater than 2:1, and more preferably greater than 5:1. In some embodiments, the ratio of EPA:DPA is 1:1 to 25:1, preferably 5:1 to 20:1, more preferably 8:1 to 15:1, even more preferably 9:1 to 13:1, even more most preferably about 10:1 to 11:1, and most preferably about 10:1.

**[0055]** In some embodiments of the present invention, the compositions comprise EPA in an amount between 55% and 95% relative to the total amount of fatty acids present in the composition, alternatively between 60% and 95%, alternatively between 65% and 95%, alternatively between 70% and 95%, alternatively between 75% and 95%, alternatively between 90% and 95%, alternatively between 80%

and 95%, alternatively between 90% and 95%, alternatively between 55% and 90%, alternatively between 60% and 90%, alternatively between 65% and 90%, alternatively between 70% and 90%, alternatively between 75% and 90%, alternatively between 80% and 90%, alternatively between 85% and 90%, alternatively between 55% and 92%, alternatively between 60% and 92%, alternatively between 65% and 92%, alternatively between 70% and 92%, alternatively between 75% and 92%, alternatively between 80% and 92%, alternatively between 85% and 92%, alternatively between 55% and 93%, alternatively between 60% and 93%, alternatively between 65% and 93%, alternatively between 70% and 93%, alternatively between 75% and 93%, alternatively between 80% and 93%, alternatively between 85% and 93%,alternatively more than 85%, alternatively more than 85%, alternatively between 85% and 95% EPA relative to the total amount of fatty acids present in the composition. In some embodiments, the compositions comprise about 70% to about 95%, 80% to about 90%, alternatively about 81% to about 88%, alternatively about 82% to about 88%, alternatively about 83% to about 87%, alternatively about 84% to about 86%, alternatively about 85% EPA relative to the total amount of fatty acids present in the composition. In some embodiments, the compositions comprise about 750 mg/g to about 950 mg/g, alternatively about 800 mg/g to about 900 mg/g, alternatively about 830 mg/g to about 870 mg/g, alternatively about 840 mg/g to about 870 mg/g, alternatively 845 mg/g to about 865 mg/g, alternatively 846 mg/g to about 860 mg/g, alternatively 847 mg/g to about 859 mg/g, alternatively about 848 mg/g to about 858 mg/g, alternatively about 849 mg/g to about 857 mg/g, alternatively about 850 mg/g to about 856 mg/g, alternatively about 851 mg/g to about 855 mg/g, alternatively about 852 mg/g to about 854 mg/g, alternatively about 853 mg/g EPA.

**[0056]** On a EPA daily dose basis, the compositions of the present invention are preferably provided in a dose of between 100 mg and 10,000 mg/day, alternatively between 200 mg and 8,000 mg/day, alternatively between 300 mg and 6,000 mg/day, alternatively between 400 mg and 5,000 mg/day, alternatively between 500 mg and 4,000 mg/day. In some embodiments, the compositions and methods of the present invention are provided in a dose of between about 1000 mg/day to about

5000 mg/day, alternatively about 1200 mg/day to about 3000 mg/day, alternatively about 1500 mg/day to about 2500 mg/day, alternatively 1600 mg/day to about 1950 mg/day, alternatively about 1735 mg/day to about 1855 mg/day, alternatively about 1740 mg/day to about 1840 mg/day, alternatively about 1745 mg/day to about 1820 mg/day, alternatively about 1750 mg/day to about 1800 mg/day, alternatively about 1755 mg/day to about 1790 mg/day, alternatively about 1760 mg/day to about 1780 mg/day, alternatively about 1770 mg/day of EPA. In some embodiments, the compostiions of the present invention are provided in a dose of between about 2300 mg/day to about 3000 mg/day, alternatively about 2400 mg/day to about 2800 mg/day, alternatively about 2520 mg/day to about 2780 mg/day, alternatively about 2600 mg/day to about 2700 mg/day, alternatively about 2610 mg/day to about 2680 mg/day, alternatively about 2620 mg/day to about 2670 mg/day, alternatively about 2630 mg/day to about 2665 mg/day, alternatively about 2640 mg/day to about 2660 mg/day, alternatively about 2650 mg/day of EPA. In some embodiments, the compostions of the present invention are provided in a dose of between about 3200 mg/day to about 3900 mg/day, alternatively 3300 mg/day to about 3800 mg/day, alternatively 3360 mg/day to about 3710 mg/day, alternatively about 3400 mg/day to about 3700 mg/day, alternatively about 3450 mg/day to about 3650 mg/day, alternatively about 3500 mg/day to about 3600 mg/day, alternatively about 3530 mg/day to about 3580 mg/day, alternatively about 3540 mg/day to about 3560 mg/day, alternatively about 3550 mg/day of EPA.

**[0057]** In some embodiments, the compositions of the present invention are provided in a dose of between about about 1650 mg/day to about 2050 mg/day, alternatively about 1700 mg/day to about 2000 mg/day, alternatively about 1750 mg/day to about 1950 mg/day, alternatively about 1775 mg/day to about 1925 mg/day, alternatively about 1800 mg/day to about 1900 mg/day, alternatively about 1800 mg/day to about 2000 mg/day, alternatively about 1820 mg/day to about 1880 mg/day, alternatively about 1830 mg/day to about 1870 mg/day, alternatively about 1840 mg/day to about 1860 mg/day, alternatively about 1850 mg/day of EPA. In some embodiments, the compostions of the present invention are provided in a dose of between about about 2500 mg/day to about 3100 mg/day, alternatively about 2600 mg/day to about 2000 mg/day, alternatively about 2650 mg/day to about 2950

mg/day, alternatively about 2700 mg/day to about 2900 mg/day, alternatively about 2725 mg/day to about 2875 mg/day, alternatively about 2750 mg/day to about 2850 mg/day, alternatively about 2780 mg/day to about 2820 mg/day, alternatively about 2790 mg/day to about 2810 mg/day, alternatively about 2800 mg/day of EPA. In some embodiments, the compostions of the present invention are provided in a dose of between about 3300 mg/day to about 4000 mg/day, alternatively about 3400 mg/day to about 3900 mg/day, alternatively about 3500 mg/day to about 3900 mg/day, alternatively about 3550 mg/day to about 3850 mg/day, alternatively about 3600 mg/day to about 3800 mg/day, alternatively about 3650 mg/day to about 3750 mg/day, alternatively about 3680 mg/day to about 3725 mg/day, alternatively about 3690 mg/day to about 3710 mg/day, alternatively about 3700 mg/day of EPA.

**[0058]** In some embodiments, the compositions of the present invention are provided in a dose of between about 1500 mg/day to about 2500 mg/day, alternatively about 1750 mg/day to about 2300 mg/day, alternatively about 1800 mg/day to about 2200 mg/day, alternatively about 1900 mg/day to about 2100 mg/day, alternatively about 1950 mg/day to about 2050 mg/day, alternatively about 1975 mg/day to about 2025 mg/day, alternatively about 2000 mg/day of EPA. In some embodiments, the compositions of the present invention are provided in a dose of between about 2500 mg/day to about 3500 mg/day, alternatively about 2700 mg/day to about 3300 mg/day alternatively about 2750 mg/day to about 3300 mg/day, alternatively about 2800 mg/day to about 3200 mg/day, alternatively about 2900 mg/day to about 3100 mg/day, alternatively about 2950 mg/day to about 3050 mg/day, alternatively about 2975 mg/day to about 3025 mg/day, alternatively about 3000 mg/day of EPA. In some embodiments, the compositions of the present invention are provided in a dose of between about 3500 mg/day to about 4500 mg/day, alternatively about 3700 mg/day to about 4300 mg/day, alternatively about 3750 mg/day to about 4300 mg/day, alternatively about 3800 mg/day to about 4200 mg/day, alternatively about 3900 mg/day to about 4100 mg/day, alternatively about 3950 mg/day to about 4050 mg/day, alternatively about 3975 mg/day to about 4025 mg/day, alternatively about 4000 mg/day of EPA.

**[0059]** In other embodiments of the present invention, the compositions comprise DPA in an amount between 1% and 99% relative to the total amount of fatty acids

present in the composition, alternatively between 1% and 95%, alternatively alternativelybetween 1% and 90%, alternatively between 1% and 85%, alternatively between 1% and 80%, alternatively between 1% and 75%, alternatively between 1% and 70%, alternatively between 1% and 65%, alternatively between 1% and 60%, alternatively between 1% and 55%, alternatively between 1% and 50%, alternatively between 1% and 45%, alternatively between 1% and 40%, alternatively between 1% and 35%, alternatively between 1% and 30%, alternatively between 1% and 25%, alternatively between 1% and 20%, alternatively between 1% and 15%, alternatively between 1% and 10%, alternatively between 1% and 5%, alternatively between 2% and 99%, alternatively between 2% and 95%, alternatively between 2% and 90%, alternatively between 2% and 85%, alternatively between 2% and 80%, alternatively between 2% and 75%, alternatively between 2% and 70%, alternatively between 2% and 65%, alternatively between 2% and 60%, alternatively between 2% and 55%, alternatively between 2% and 50%, alternatively between 2% and 45%, alternatively between 2% and 40%, alternatively between 2% and 35%, alternatively between 2% and 30%, alternatively between 2% and 25%, alternatively between 2% and 20%, alternatively between 2% and 15%, alternatively between 2% and 10%, alternatively between 2% and 5%, alternatively between 3% and 99%, alternatively between 3% and 95%, alternatively between 3% and 90%, alternatively between 3% and 85%, alternatively between 3% and 80%, alternatively between 3% and 75%, alternatively between 3% and 70%, alternatively between 3% and 65%, alternatively between 3% and 60%, alternatively between 3% and 55%, alternatively between 3% and 50%, alternatively between 3% and 45%, alternatively between 3% and 40%, alternatively between 3% and 35%, alternatively between 3% and 30%, alternatively between 3% and 25%, alternatively between 3% and 20%, alternatively between 3% and 15%, alternatively between 3% and 10%, alternatively between 3% and 5%, alternatively between 4% and 99%, alternatively between 4% and 95%, alternatively between 4% and 90%, alternatively between 4% and 85%, alternatively between 4% and 80%, alternatively between 4% and 75%, alternatively between 4% and 70%, alternatively between 4% and 65%,

alternatively between 4% and 60%, alternatively between 4% and 55%, alternatively between 4% and 50%, alternatively between 4% and 45%, alternatively between 4% and 40%, alternatively between 4% and 35%, alternatively between 4% and 30%, alternatively between 4% and 25%, alternatively between 4% and 20%, alternatively between 4% and 15%, alternatively between 4% and 10%, alternatively between 4% and 5%, alternatively between 5% and 99%, alternatively between 5% and 95%, alternatively between 5% and 90%, alternatively between 5% and 85%, alternatively between 5% and 80%, alternatively between 5% and 75%, alternatively between 5% and 70%, alternatively between 5% and 65%, alternatively between 5% and 60%, alternatively between 5% and 55%, alternatively between 5% and 50%, alternatively between 5% and 45%, alternatively between 5% and 40%, alternatively between 5% and 35%, alternatively between 5% and 30%, alternatively between 5% and 25%, alternatively between 5% and 20%, alternatively between 5% and 15%, alternatively between 5% and 12%, alternatively between 5% and 10%, alternatively between 6% and 99%, alternatively between 6% and 95%, alternatively between 6% and 90%, alternatively between 6% and 85%, alternatively between 6% and 80%, alternatively between 6% and 75%, alternatively between 6% and 70%, alternatively between 6% and 65%, alternatively between 6% and 60%, alternatively between 6% and 55%, alternatively between 6% and 50%, alternatively between 6% and 45%, alternatively between 6% and 40%, alternatively between 6% and 35%, alternatively between 6% and 30%, alternatively between 6% and 25%, alternatively between 6% and 20%, alternatively between 6% and 15%, alternatively between 6% and 12%, alternatively between 6% and 11%, alternatively between 6% and 10%, alternatively between 7% and 99%, alternatively between 7% and 95%, alternatively between 7% and 90%, alternatively between 7% and 85%, alternatively between 7% and 80%, alternatively between 7% and 75%, alternatively between 7% and 70%, alternatively between 7% and 65%, alternatively between 7% and 60%, alternatively between 7% and 55%, alternatively between 7% and 50%, alternatively between 7% and 45%, alternatively between 7% and 40%, alternatively between 7% and 35%,

alternatively between 7% and 30%, alternatively between 7% and 25%, alternatively between 7% and 20%, alternatively between 7% and 15%, alternatively between 7% and 12%, alternatively between 7% and 11%, alternatively between 7% and 10%, alternatively between 8% and 99%, alternatively between 8% and 95%, alternatively between 8% and 90%, alternatively between 8% and 85%, alternatively between 8% and 80%, alternatively between 8% and 75%, alternatively between 8% and 70%, alternatively between 8% and 65%, alternatively between 8% and 60%, alternatively between 8% and 55%, alternatively between 8% and 50%, alternatively between 8% and 45%, alternatively between 8% and 40%, alternatively between 8% and 35%, alternatively between 8% and 30%, alternatively between 8% and 25%, alternatively between 8% and 20%, alternatively between 8% and 15%, alternatively between 8% and 12%, alternatively between 9% and 95%, alternatively between 9% and 90%, alternatively between 9% and 85%, alternatively between 9% and 80%, alternatively between 9% and 75%, alternatively between 9% and 70%, alternatively between 9% and 65%, alternatively between 9% and 60%, alternatively between 9% and 55%, alternatively between 9% and 50%, alternatively between 9% and 45%, alternatively between 9% and 40%, alternatively between 9% and 35%, alternatively between 9% and 30%, alternatively between 9% and 25%, alternatively between 9% and 20%, alternatively between 9% and 15%, alternatively between 9% and 12%, relative to the total amount of fatty acids present in the composition. In some embodiments, the compositions comprise docosapentaenoic acid (DPA) in an amount between about 5% to about 15%, alternatively about 6% to about 12%, alternatively about 7% to about 11%, alternatively about 8% to about 10% relative to the total amount of fatty acids present in the composition. In some alternative embodiments, the composition comprises at least about 4% or at least about 5% or at least about 6% or at least about 7% or at least about 8% or at least about 9% or at least about 10% or at least about 15% or at least about 20% or at least about 25% or at least about 30% or at least about 35% or at least about 40% or at least about 45% or at least about 50% or at least about 55% or at least about 60% or at least about 65% or at least about 70% or at least about

75% or at least about 80% or at least about 85% or at least about 90% or at least about 95% of docosapentaenoic acid (DPA).

**[0060]** In some embodiments, the compositions comprise docosapentaenoic acid (DPA) in an amount of about 60 mg/g to about 120 mg/g, alternatively about 70 mg/g to about 100 mg/g, 75 mg/g to about 90 mg/g, alternatively about 77 mg/g to about 85 mg/g, alternatively about 78 mg/g to about 84 mg/g, alternatively about 79 mg/g to about 83 mg/g, alternatively about 80 mg/g to about 82 mg/g, alternatively about 81 mg/g to about 82 mg/g. In some embodiments, the compositions comprise docosapentaenoic acid (DPA) in an daily dosage amount of at least about 20 mg/day, alternatively at least about 25 mg/day, alternatively at least about 30 mg/day, alternatively at least about 40 mg/day, alternatively at least about 50 mg/day, alternatively at least about 60 mg/day alternatively, at least about 70 mg/day alternatively at least about 75 mg/day, alternatively at least about 80 mg/day, alternatively at least about 90 mg/day, alternatively at least about 100 mg/day, alternatively at least about 120 mg/day, alternatively at least about 150 mg/day, alternatively at least about 160 mg/day, alternatively at least about 180 mg/day, alternatively at least about 200 mg/day, alternatively at least about 250 mg/day, alternatively at least about 300 mg/day, alternatively at least about 350 mg/day, or alternatively at least about 400 mg/day, alternatively at least about 500 mg/day, alternatively at least about 600 mg/day, alternatively at least about 800 mg/day, or alternatively at least about 1000 mg/day, alternatively at least about 1200 mg/day, alternatively at least about 1500 mg/day, or alternatively at least about 2000 mg/day, or alternatively at least about 3000 mg/day, or alternatively at least about 3500 mg/day, or alternatively at least about 4000 mg/day, or alternatively at least about 4250 mg/day. In some embodiments, the composition comprises DPA in a daily dosage of about 120 mg/day to about 150 mg/day, alternatively about 150 mg/day to about 200 mg/day, alternatively about 200 mg/day to about 250 mg/day, alternatively about 250 mg/day to about 300 mg/day, alternatively about 300 mg/day to about 400 mg/day, alternatively about 400 mg/day to about 600 mg/day, alternatively about 600 mg/day to about 1000 mg/day. In some embodiments, the method of treatment provides a dose of at least about 1 mg/kg of docosapentaenoic acid (DPA) per day, alternatively about 2 mg/kg of DPA per day, alternatively about 3 mg/kg of DPA per

day, alternatively about 4 mg/kg of DPA per day, alternatively about 6 mg/kg of DPA per day, alternatively about 8 mg/kg of DPA per day, alternatively about 10 mg/kg of DPA per day, alternatively about 20 mg/kg of DPA per day, alternatively about 30 mg/kg of DPA per day, and alternatively about 40 mg/kg of DPA per day, alternatively about 50 mg/kg of DPA per day, alternatively about 75 mg/kg of DPA per day, and alternatively about 100 mg/kg of DPA per day.

**[0061]** In some embodiments, a relatively small amount of docosahexaenoic acid (DHA) as compared to EPA is present. In some embodiments, the compositions of the present invention comprise no more than 1:1 of DHA:EPA, alternatively no more than 1:2, alternatively no more than 1:3, alternatively no more than 1:3, alternatively no more than 1:4, alternatively no more than 1:5 of DHA:EPA, alternatively no more than 1:6 of DHA:EPA, alternatively no more than 1:7 of DHA:EPA, alternatively no more than 1:8 of DHA:EPA, alternatively no more than 1:9 of DHA:EPA, alternatively no more than 1:10 of DHA:EPA, alternatively no more than 1:12 of DHA:EPA, alternatively no more than 1:15 of DHA:EPA, alternatively no more than 1:20 of DHA:EPA, alternatively no more than 1:25 of DHA:EPA, alternatively no more than 1:30 of DHA:EPA, alternatively no more than 1:40 of DHA:EPA, alternatively no more than 1:50 of DHA:EPA, alternatively no more than 1:75 of DHA:EPA, alternatively no more than 1:90 of DHA:EPA, alternatively no more than 1:99 of DHA:EPA. Alternatively, DHA may be present in the compositions of this invention at a relative amount of ratio less than 1% than the amount of EPA. Alternatively, docosahexaenoic acid (DHA) may be present in the compositions of this invention at a DHA:EPA ratio of less than 1:99.

**[0062]** In some embodiments, a relatively small amount of docosahexaenoic acid (DHA) relative to the total amount of fatty acids present in the composition is present. In some embodiments, the compositions of the present invention comprise no more than 30% DHA, alternatively no more than 20% DHA, alternatively no more than 15% DHA, alternatively no more than 12% DHA, alternatively no more than 10% DHA, alternatively no more than 9% DHA, alternatively no more than 8% DHA, alternatively no more than 7% DHA, alternatively no more than 6% DHA, alternatively no more than 5% DHA, alternatively no more than 4% DHA, alternatively no more than 3% DHA, alternatively no more than 2% DHA,

alternatively no more than 1% DHA relative to the total amount of fatty acids present in the composition. In some embodiments, the compositions and methods comprise less than 1500mg of DHA, alternatively less than 1200mg of DHA, alternatively less than 1000mg of DHA, alternatively less than 800mg of DHA, alternatively less than 700mg of DHA, alternatively less than 600mg of DHA, alternatively less than 500mg of DHA, alternatively less than 400mg of DHA, alternatively less than 350mg of DHA, alternatively less than 300mg of DHA, alternatively less than 250mg of DHA, alternatively less than 200mg of DHA alternatively less than 150mg of DHA, alternatively less than 120mg of DHA, alternatively less than 100 mg of DHA, alternatively less than 80 mg of DHA, alternatively less than 60 mg of DHA, alternatively less than 40 mg of DHA, alternatively less than 30 mg of DHA, alternatively less than 25 mg of DHA, alternatively less than 20 mg of DHA or its glycerol or ethyl esters as a totally daily dose.

**[0063]** In some embodiments, the composition comprises about 5 mg/g to about 20 mg/g, alternatively about 8 mg/g to about 18 mg/g, alternatively about 9 mg/g to about 15 mg/g, alternatively about 10 mg/g to about 14 mg/g, alternatively about 11 mg/g to about 13 mg/g, alternatively about 12 mg/g to about 13 mg/g of docosahexaenoic acid (DHA).

**[0064]** In some embodiments, the ratio of EPA:HPA is about 1500:1 to 25:1, alternatively 1000:1 to 50:1, alternatively 800:1 to 60:1, alternatively 500:1 to 60:1, alternatively 250:1 to 75:1, and alternatively 100:1 to 80:1. In some preferred embodiments, the ratio of EPA:HPA is about 85:1. In some preferred embodiments, the ratio of EPA:HPA is about 30:1. In some embodiments, the ratio of DPA:HPA is about 250:1 to 1:1, alternatively 200:1 to 2:1, alternatively 150:1 to 3:1, alternatively 100:1 to 4:1, alternatively 50:1 to 5:1, alternatively 25:1 to 6:1, and alternatively 10:1 to 7:1. In some preferred embodiments, the ratio of DPA:HPA is about 8:1. In some embodiments, the ratio of DPA:HPA is about 3:0.

**[0065]** In other embodiments, a relatively small amount of DHA as compared to DPA is present. In these embodiments, the compositions of the present invention comprise no more than 15:1 of DHA:DPA, alternatively no more than 12:1 of DHA:DPA, alternatively no more than 10:1 of DHA:DPA, alternatively no more than 8:1 of DHA:DPA, alternatively no more than 5:1 of DHA:DPA, alternatively no more

than 4:1 of DHA:DPA, alternatively no more than 3:1 of DHA:DPA, alternatively no more than 2:1 of DHA:DPA, alternatively no more than 1:1 of DHA:DPA, alternatively no more than 1:2 of DHA:DPA, alternatively no more than 1:3 of DHA:DPA, alternatively no more than 1:4 of DHA:DPA, alternatively no more than 1:5 of DHA:DPA, alternatively no more than 1:6 of DHA:DPA, alternatively no more than 1:7 of DHA:DPA, alternatively no more than 1:8 of DHA:DPA, alternatively no more than 1:10 of DHA:DPA, alternatively no more than 1:12 of DHA:DPA, alternatively no more than 1:15 of DHA:DPA, alternatively no more than 1:20 of DHA:DPA, alternatively no more than 1:25 of DHA:DPA, alternatively no more than 1:50 of DHA:DPA, alternatively no more than 1:75 of DHA:DPA, alternatively no more than 1:90 of DHA:DPA, alternatively no more than 1:95 of DHA:DPA, alternatively no more than 1:100 of DHA:DPA. In some embodiments, the ratio of DHA:DPA is preferably less than 2:1.

**[0066]** In other embodiments, a relatively small amount of DHA as compared to HPA is present. In these embodiments, the compositions of the present invention comprise no more than 15:1 of DHA:HPA, alternatively no more than 12:1 of DHA:HPA, alternatively no more than 10:1 of DHA:HPA, alternatively no more than 8:1 of DHA:HPA, alternatively no more than 5:1 of DHA:HPA, alternatively no more than 3:1 of DHA:HPA, alternatively no more than 2:1 of DHA:HPA, alternatively no more than 1:1 of DHA:HPA, alternatively no more than 1:2 of DHA:HPA, alternatively no more than 1:3 of DHA:HPA, alternatively no more than 1:5 of DHA:HPA, alternatively no more than 1:8 of DHA:HPA, alternatively no more than 1:10 of DHA:HPA, alternatively no more than 1:15 of DHA:HPA, alternatively no more than 1:20 of DHA:HPA, alternatively no more than 1:25 of DHA:HPA, alternatively no more than 1:50 of DHA:HPA, alternatively no more than 1:75 of DHA:HPA, alternatively no more than 1:90 of DHA:HPA, alternatively no more than 1:95 of DHA:HPA, alternatively no more than 1:100 of DHA:HPA.

**[0067]** In yet other embodiments, the compositions of the present invention comprise no more than 10% omega-6 fatty acids relative to the total amount of fatty acids, alternatively no more than 9%, alternatively no more than 8%, alternatively no more than 7%, alternatively no more than 6%,alternatively no more than 5%, alternatively no more than 4.5%, alternatively no more than 4%, alternatively no

more than 3.5%, alternatively no more than 3%, alternatively no more than 2.5%, alternatively no more than 2%, alternatively no more than 1.7%, alternatively no more than 1.5%, alternatively no more than 1.2%, alternatively no more than 1%, alternatively no more than 0.5% omega-6 fatty acids versus the total amount of fatty acids comprised by the compositions of the present invention.

**[0068]** Omega-6 fatty acids include, but are not limited to: linoleic acid (LA; C18:2-n6); gamma-linoleic acid (GLA; C18:3-n6); eicosadienoic acid (C20:2-n6); dihomo-gamma-linoleic acid (DGLA; C20:3-n6); arachiconic acid (ARA; C20:4-n6); and omega-6 docosapentaenoic acid (DPA; C22:5-n6).

**[0069]** In further embodiments, the compositions of the present invention comprise no more than 10% omega-6 fatty acids relative to the total amount of omega-3 fatty acids plus omega-6 fatty acids, alternatively no more than 9%, alternatively no more than 8%, alternatively no more than 7%, alternatively no more than 6%, alternatively no more than 5%, alternatively no more than 4.5%, alternatively no more than 4%, alternatively no more than 3.5%, alternatively no more than 3%, alternatively no more than 2.5%, alternatively no more than 2%, alternatively no more than 1.7%, alternatively no more than 1.5%, alternatively no more than 1.2%, alternatively no more than 1%, alternatively no more than 0.5% omega-6 fatty acids versus the total amount of omega-3 fatty acids plus omega-6 fatty acids comprised by the compositions of the present invention.

**[0070]** In yet other embodiments, the compositions of the present invention comprise no more than 8% arachidonic acid (ARA; C20:4-n6) relative to the total amount of omega-3 fatty acids plus omega-6 fatty acids, alternatively no more than 7%, alternatively no more than 6%, alternatively no more than 5%, alternatively no more than 4.5%, alternatively no more than 4%, alternatively no more than 3.5%, alternatively no more than 3%, alternatively no more than 2.5%, alternatively no more than 2%, alternatively no more than 1.7%, alternatively no more than 1.5%, alternatively no more than 1.2%, alternatively no more than 1%, alternatively no more than 0.5% arachidonic acid (ARA; C20:4-n6) versus the total amount of omega-3 fatty acids plus omega-6 fatty acids comprised by the compositions of the present invention.

**[0071]** In some embodiments, a relatively small amount of omega-3 fatty acids in aggregate other than EPA, ETA, HPA and DPA (alternatively indicated as non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids in aggregate) relative to the total amount of fatty acids present in the composition is present. In some embodiments, the compositions of the present invention comprise no more than 20% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 15% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 12% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 10% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 8% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 7% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 6% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 5% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 4% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 3% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 2% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids, alternatively no more than 1% non-EPA, non-ETA, non-HPA and non-DPA omega-3 fatty acids in aggregate relative to the total amount of fatty acids present in the composition.

**[0072]** In some embodiments, a relatively small amount of the sum of ALA, SDA and DHA relative to the total amount of fatty acids present in the composition is present, while at the same time large amounts of the sum of EPA, DPA-n3, HPA and ETA are present. In some embodiments, the compositions of the present invention comprise no more than 20% of the sum of ALA, SDA and DHA, alternatively no more than 15% of the sum of ALA, SDA and DHA, alternatively no more than 12% of the sum of ALA, SDA and DHA, alternatively no more than 10% of the sum of ALA, SDA and DHA, alternatively no more than 8% of the sum of ALA, SDA and DHA, alternatively no more than 7% of the sum of ALA, SDA and DHA, alternatively no more than 6% of the sum of ALA, SDA and DHA, alternatively no more than 5% of the sum of ALA, SDA and DHA, alternatively no more than 4% of the sum of ALA, SDA and DHA, alternatively no more than 3% of the sum of ALA, SDA and DHA,

alternatively no more than 2% of the sum of ALA, SDA and DHA, alternatively no more than 1% of the sum of ALA, SDA and DHA relative to the total amount of fatty acids present in the composition, while at the same time contain more than 40% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 50% the sum of EPA, DPAn-3, HPA and ETA, , alternatively more than 60% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 70% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 75% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 80% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 85% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 90% the sum of EPA, DPAn-3, HPA and ETA, alternatively more than 95% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 80% and 98% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 80% and 96% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 85% and 98% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 85% and 96% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 90% and 98% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 90% and 97% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 90% and 96% the sum of EPA, DPAn-3, HPA and ETA, alternatively between 90% and 95% the sum of EPA, DPAn-3, HPA and ETA, relative to the total amount of fatty acids present in the composition is present.

**[0073]** In further embodiments, the compositions of the present invention comprise no more than 8% arachidonic acid (ARA; C20:4-n6) relative to the total amount of fatty acids, alternatively no more than 7%, alternatively no more than 6%, alternatively no more than 5%, alternatively no more than 4.5%, alternatively no more than 4%, alternatively no more than 3.5%, alternatively no more than 3%, alternatively no more than 2.5%, alternatively no more than 2%, alternatively no more than 1.7%, alternatively no more than 1.5%, alternatively no more than 1.2%, alternatively no more than 1%, alternatively no more than 0.5% arachidonic acid (ARA; C20:4-n6) relative the total amount of fatty acids comprised by the compositions of the present invention.

**[0074]** In other embodiments, the compositions of the present invention comprise no more than 2.5% arachidonic acid (ARA; C20:4-n6), no more than 0.4% omega-6-docosapentaenoic acid (DPA; C22:5-n6) and no more than 0.2% gamma-linoleic

acid (GLA; C18:3-n6) relative the total amount of fatty acids comprised by the compositions of the present invention.

**[0075]** Further embodiments provide fatty acid compositions comprising no more than 2.5% arachidonic acid (ARA; C20:4-n6), no more than 0.3% omega-6 docosapentaenoic acid (DPA; C22:5-n6) and no more than 0.1% gamma-linoleic acid (GLA; C18:3-n6) relative the total amount of fatty acids comprised by the compositions of the present invention.

**[0076]** In some embodiments, the composition of the present invention further comprises TPA at concentration of at least 0.05%. In some embodiments, the TPA concentration is about 0.01% to about 5%, alternatively about 0.05% to about 2%, alternatively about 0.1% to about 1%, alternatively about 0.2% to about 0.8%, alternatively about 0.4% to about 0.6%, alternatively about 0.5%.

**[0077]** The compositions of the present invention may also be taken as a general nutritional supplement.

**[0078]** In yet other embodiments, the active ingredient of the formulations of the present invention consists essentially wholly of the EPA and DPA or precursors thereof (ethyl ester, triglyceride, or any other pharmaceutically acceptable salt or derivative thereof). In that case, no large amounts (preferably less than 15%, alternatively less than 12%, alternatively less than 10%, alternatively less than 9%, alternatively less than 8%, alternatively less than 7%, alternatively less than 6%, alternatively less than 5%, alternatively less than 4%, alternatively less than 3%, alternatively less than 2%, alternatively less than 1%, alternatively less than 0.5%, alternatively less than 0.25%) of any other fatty acids are present.

**[0079]** In further embodiments, the active ingredient of the formulations of the present invention consists essentially wholly of omega-3-pentaenoic acids or precursors thereof (ethyl ester, triglyceride, or any other pharmaceutically acceptable salt or derivative thereof). In that case, no large amounts (preferably less than 15%, alternatively less than 12%, alternatively less than 10%, alternatively less than 9%, alternatively less than 4%, alternatively less than 4%, alternatively less than 4%, alternatively less than 4%, alternatively less than 4%, alternatively less than 3%, alternatively less than 2%, alternatively less than 1%, alternatively less than 0.5%, alternatively less than 0.25%) of any other fatty acids are present.

**[0080]** The fatty acid percentage is determined on a weight/weight, mol/mol, or chromatography area percent basis relative to all fatty acids present in the composition as determined by methods such as disclosed in the European Pharmacopeia monograph for omega-3 fatty acid concentrates, European Pharmacopeia monograph for omega-3-acid ethyl esters 90%, or European Pharmacopeia monograph method 2.4.29, USP monograph for fish oil dietary supplements, USP 35 omega-3-acid ethyl esters (LOVAZA®) monograph, or any essentially equivalent methods (whether by gas chromatography, HPLC, FPLC or any other chromatographic method).

**[0081]** In some embodiments, the fatty acid percentage is determined not as a percentage of all fatty acids present in the composition but as a specific type of fatty acid ethyl esters as percentage of all fatty acid ethyl esters present in the composition, thus excluding from the fatty acid percentage determination such fatty acids present as, for instance: free fatty acids; mono-, di-, and tri-glycerides; or fatty acids present in phospholipids (such as phosphatidylserine or phosphatidylcholine) or polysorbates (such as Tween 80, Tween 20, or polysorbate 40).

**[0082]** In other embodiments, the fatty acid percentage is determined not as a percentage of all fatty acids present in the composition but as a specific type of free fatty acid as percentage of all free fatty acids present in the composition, thus excluding from the fatty acid percentage determination such fatty acids present as, for instance: fatty acid ethyl esters; mono-, di-, and tri-glycerides; or fatty acids present in phospholipids (such as phosphatidylserine or phosphatidylcholine) or polysorbates (such as Tween 80, Tween 20, or polysorbate 40).

**[0083]** In yet other embodiments, the fatty acid percentage is determined not as a percentage of all fatty acids present in the composition but as a specific type of glycerol fatty acid ester as percentage of all glycerol fatty acid esters present in the composition, thus excluding from the fatty acid percentage determination such fatty acids present as, for instance: fatty acid ethyl esters; free fatty acids; or fatty acids present in phospholipids (such as phosphatidylserine or phosphatidylcholine) or polysorbates (such as Tween 80, Tween 20, or polysorbate 40).

**[0084]** In further embodiments, the fatty acid percentage is determined not as a percentage of all fatty acids present in the composition but as di- or tri-fatty acid

esters with glycerol as percentage of all glycerol di- and tri-fatty acid esters present in the composition, thus excluding from the fatty acid percentage determination such fatty acids present as, for instance: glycerol-mono-fatty acid esters; fatty acid ethyl esters; free fatty acids; or fatty acids present in phospholipids (such as phosphatidylserine or phosphatidylcholine) or polysorbates (such as Tween 80, Tween 20, or polysorbate 40).

**[0085]** In yet other embodiments, the fatty acid percentage is determined not as a percentage of all fatty acids present in the composition but as a tri-fatty acid esters with glycerol as percentage of all glycerol tri-fatty acid esters present in the composition, thus excluding from the fatty acid percentage determination such fatty acids present as, for instance: mono- and di-fatty acid esters of glycerol; fatty acid ethyl esters; free fatty acids; or fatty acids present in phospholipids (such as phosphatidylserine or phosphatidylcholine) or polysorbates (such as Tween 80, Tween 20, or polysorbate 40).

**[0086]** The EPA, HPA, DPA, or omega-3-pentaenoic acids may be derived from any appropriate source including plant seed oils, microbial oils from algae or fungal or marine oils from fish or other marine animals. Certain species are a particular good source of oils containing DPA, for example seal oil. They may be used in the form of the natural oil, if that oil meets the required purity requirements of the present invention, or may be purified to give products containing the fatty acid composition of the present invention.

**[0087]** The compositions of the present invention may be produced through a range of the methods. Such methods may include: distillation, including short path distillation; urea precipitation; enzymatic conversion concentration; conventional chromatography; HPLC/FPLC; supercritical carbondioxide extraction; supercritical carbondioxide chromatography; simulated moving bed chromatography; supercritical carbondioxide simulated moving bed chromatography; or chemical conversion methods such as iodolactonization. Such methods are generally known to those skilled in the art of purifying and isolating omega-3 fatty acids.

**[0088]** Typically, the omega-3 fatty acid concentration/purification process is initiated by esterifying the fatty acids comprised by the marine oil raw material (such as crude fish oil) with ethanol (to form fatty acid ethyl esters) in order to separate

omega-3 fatty acids from other fatty acids covalently bound together in the natural triglyceride molecules of the source oil. Subsequently, the material may be distilled once or several times to achieve omega-3-acid ethyl ester concentrations above 60%-70%. Alternatively, enzymatic concentration, urea precipitation or supercritical extraction may be used alone or in conjunction with distillation to reach omega-3 levels above 70%-90%. In order to prepare a highly pure concentrate of a single omega-3 fatty acid, methods such as chromatography, supercritical chromatography, simulated moving bed chromatography, supercritical simulated moving bed chromatography, or chemical conversion methods such as iodolactolization are typically most practical to reach levels above 50%, alternatively above 60%, alternatively above 70%, alternatively above 80%, alternatively above 90%, alternatively above 95%, of a single omega-3 fatty acid such as ETA, EPA, HPA, DPA, TPA, or DHA.

**[0089]** Those skilled in the art will be able to design processes suited to prepare a certain omega-3 fatty acid composition as desired, based on the methods described above. Such processes are flexible enough to affect the relative proportions between the long chain C18, C20, C21 and C22 fatty acids which occur naturally in available fish oil raw materials and other marine oils. It provides not only for the concentration of the individual omega-3 fatty acids, but the ratio between them will remain within a pattern of variation caused by variations in nature. However, suitable methods compensate for sometimes extreme variations which may occur naturally. Thus, for those skilled in the art, it will be possible to make a product with a constant and predetermined composition.

**[0090]** EPA is relatively abundant in fish oils or other marine oils and can be relatively easy obtained through the application of concentration and purification technologies from such fish or marine oils. DPA and HPA are present at much lower concentrations. In order to prepare the compositions of the present invention, DPA or HPA may be concentrated and purified from fish or other marine oils according to the methods referred to above, either alone or DPA combined with EPA and/or HPA. Alternatively, the DPA or HPA may be chemically prepared from a high purity EPA concentrate by elongation of the EPA fatty-acid chain with two or one hydrogen-saturated carbons (C2-elongation or C1-elongation) on the carboxyl side of the

molecule (for instance with a method similar to or alternate methods with equivalent results such as described by Kuklev DV and Smith WL in Chem Phys Lipids, 2006; 144(2): 172-177). In another alternative approach, a high purity EPA concentrate may be partially converted to DPA (or HPA) using a method for C2-elongation (or C1-elongation) of EPA similar to those described above, thus directly yielding compositions of the present invention or intermediates therefore.

**[0091]** Once the oils containing one or more of the desired fatty acids have been obtained, and purified as necessary, these oils may be blended to give the desirable relative amounts of EPA, DPA, HPA, DHA, TPA, other omega-3 fatty acids and omega-6 fatty acids to obtain the compositions of the present invention described in detail above.

**[0092]** Fish oils may also contain by-products and contaminants such as pesticides, chlorinated or brominated hydrocarbons, heavy metals, cholesterol and vitamins. During the production of the concentrate, the concentrations of these components are significantly reduced compared to untreated fish oils. Such reduction is inherent due to the nature of purification methods and their ability to concentrate of several or specific omega-3 fatty acids, thus removing other compounds.

**[0093]** Triglycerides comprising more than 60% of the omega-3 fatty acids in the composition may be produced from ethyl esters and glycerol by well known, published, or alternative chemical synthetic or enzymatic procedures. The free acids may be produced from ethyl esters by well known hydrolization or saponification procedures. Methods for converting ethyl esters to triglycerides, free fatty acids, and other molecular forms comprising fatty acids, are generally known to those skilled in the art chemically or enzymatically converting omega-3 fatty acids from one form to another.

**[0094]** In some embodiments, the compositions of the present invention have improved pharmacological features as demonstrated by improved bioavailability in a mammal of EPA, HPA, DPA, DHA, EPA+DHA, EPA+DPA or EPA+HPA+DPA combined, total omega-3-pentaenoic acids, or of total omega-3 fatty acids. Key parameters for determining bioavailability are maximum concentration of a therapeutic compound or a metabolite thereof (Cmax); the time from administration to maximum concentration (Tmax); and the area under the concentration curve over

time (AUC). Such parameters may be determined under single dose or multiple dose administration regimens. Methods to determine comparative bioavailability in mammals are generally known to those skilled in the art.

**[0095]** Meal conditions during administration to a subject of omega-3 fatty acid compositions or omega-3 fatty acid formulations can be of special significance for absorption and bioavailability of omega-3 fatty acids. The meal conditions typically considered are: fasting (no food at all prior for 8-12 hours prior to administration and 2-3 hours post administration of the treatment); a low fat meat (a meal typically containing less than 25 gram of fat [350-600 Kcal] consumed just before or after the administration of the treatment; typically within a 15-30 minute range); or a high fat meat (a meal containing 40 gram to 75 gram of fat [700-1000 Kcal] consumed just before or after the administration of the treatment; typically within a 15-30 minute range).

**[0096]** In some embodiments of the present invention, compositions of the present invention are more rapidly absorbed as measured by the time to reach the maximum concentration (Tmax) in blood, serum or plasma of EPA, DPA, DHA , EPA+DPA, EPA+DHA, total omega-3-pentaenoic acids, or total omega-3 fatty acids. In preferred embodiments of the present invention, Tmax under high fat meal administration conditions is less than 8 hours, alternatively less than 6 hours, alternatively approximately 5 hours, alternatively 4 hours or less. In other preferred embodiments of the present invention, Tmax under low fat meal administration conditions is less than 8 hours, alternatively less than 6 hours, alternatively approximately 5 hours, alternatively 4 hours or less. In yet other preferred embodiments of the present invention, Tmax under fasting administration conditions is less than 8 hours, alternatively less than 6 hours, alternatively approximately 5 hours, alternatively 4 hours or less.

**[0097]** In yet other embodiments of the present invention, Tmax for EPA, DPA, DHA , EPA+DPA, EPA+DHA, or total omega-3 fatty acids are equal or less than than Tmax for AMR101 for EPA, DPA, DHA , EPA+DPA, EPA+DHA, total omega-3-pentaenoic acids, or total omega-3 fatty acids under high fat meat, low fat meal, and fasting administration conditions. Finally, in other embodiments of the present invention, Tmax for EPA, DPA, DHA , EPA+DPA, EPA+DHA, or total omega-3 fatty

acids are less than Tmax for AMR101 for EPA+DHA and to EPA, DPA, DHA , EPA+DPA, EPA+DHA, or total omega-3 fatty acids under either low fat meal, fasting, or both administration conditions.

**[0098]** In some embodiments, the improved bioavailability features described above are apparent upon single dose administration, while in other embodiments the improved bioavailability features described above are apparent after multiple dose administration of formulations according to the present invention as compared to referenced comparator products above or substantial equivalent forms thereof.

**[0099]** In another embodiment, the compositions of the present invention are more potent and effective than other omega-3 compositions known in the prior art (such as LOVAZA®, EPANOVA™ or VASCEPA®).

**[0100]** The formulation may be a single daily dose preparation to give in one dose the above intakes, or may be in convenient divided doses, for example, a daily dose formed of two to four soft gelatin or other dosage forms, each containing 300-1500 mg of EPA, EPA+DPA, EPA+DPA+HPA, or omega-3-pentaenoic acids in any form embodied in the present invention.

**[0101]** Flavourants or emulsifiers may be included, for instance, to make the preparation palatable. Other conventional additives, diluents and excipients may be present. The preparation for ingestion may be in the form of a capsule, a dry powder, a tablet, a solution, an oil, an emulsion or any other appropriate form. The capsules may be hard or soft gelatin capsules, agar capsules, or any other appropriate capsule.

**[0102]** Use of the formulations of the invention in the manufacture of a medicament for the treatment or prevention of any disease or disorder, including those mentioned above, is included in the present invention.

**[0103]** The omega-3 fatty acid composition optionally includes chemical antioxidants, such as alpha tocopherol, which are administered in pure form or suspended in a vegetable oil, such as soybean oil or corn oil.

**[0104]** The blended fatty acid compositions may then be incorporated into any appropriate dosage form for oral, enteral, parenteral, rectal, vaginal, dermal or other route of administration. Soft or hard gelatin capsules, flavoured oil blends,

emulsifiers or other liquid forms, and microencapsulate powders or other dry form vehicles are all appropriate ways of administering the products.

**[0105]** The formulated final drug product containing the omega-3 fatty acid composition may be administered to a mammal or patient in need thereof in a capsule, a tablet, a powder that can be dispersed in a beverage, or another solid oral dosage form, a liquid, a soft gel capsule or other convenient dosage form such as oral liquid in a capsule, as known in the art. In some embodiments, the capsule comprises a hard gelatin. The combination product may also be contained in a liquid suitable for injection or infusion.

**[0106]** Example pharmaceutical grade finished dosage forms: (a) Soft or hard gelatin capsules each containing 500 mg or 1000 mg of a mix 20 parts of EPA as a free fatty acid to 1 parts of DPA as a free fatty acid; (b) As in (a) but where the EPA and DPA free fatty acids are replaced with the fatty acids in any other appropriate bioassimilable form such as the ethyl esters; (c) As in (a)-(b) but where the material is in the form of a microencapsulated powder which can be used as a powder or compressed into tablets. Such powders may be prepared by a variety of technologies known to those skilled in the art; (d) As in (a)-(b) but where the formulation is a liquid or emulsion, appropriately flavoured for palatable oral administration; (e) As in (a)-(b) but where the material is formulated into a pharmaceutically acceptable vehicle appropriate for topical application such as a cream or ointment.

**[0107]** The omega-3 compositions of the present invention may also be administered with a combination of one or more non-active pharmaceutical ingredients (also known generally herein as "excipients"). Non-active ingredients, for example, serve to solubilize, suspend, thicken, dilute, emulsify, stabilize, preserve, protect, color, flavor, and fashion the active ingredients into an applicable and efficacious preparation that is safe, convenient, and otherwise acceptable for use. Thus, the non-active ingredients may include colloidal silicon dioxide, crospovidone, lactose monohydrate, lecithin, microcrystalline cellulose, polyvinyl alcohol, povidone, sodium lauryl sulfate, sodium stearyl fumarate, talc, titanium dioxide and xanthum gum.

**[0108]** The term "pharmaceutically acceptable vehicle," as used herein, includes any of the following: a solution where the first API and optional other ingredients are wholly dissolved in a solubilizer (e.g., a pharmaceutically acceptable solvent or mixture of solvents), wherein the solution remains in clear liquid form at about room temperature; a suspension; an oil; or a semi-solid, wherein the first API and optionally other ingredients are dissolved wholly or partially in a solubilizer (an emulsion, cream, etc.).

**[0109]** A "pharmaceutical grade finished dosage form" as used herein may be construed as a unit dose form suitable for administration to, for example, human or animal subjects, and having content uniformity acceptable to regulatory authorities. For example, under the USP requirements for content uniformity, a pharmaceutical grade finished dosage form should have an amount of API within the range of 85% to 115% of the desired dosage and an RSD less than or equal to 6.0%. In addition, a pharmaceutical grade finished dosage form must be stable (i.e., have a "shelf life") for a pharmaceutically acceptable duration of time, preferably at least six months, alternatively at least one year,or at least two years, when stored at room temperature (about 23 degree Celcius to 27 degree Celcius , preferably about 25 degree Celcius) and 60% relative humidity. Typically, stability is determined by physical appearance and/or chemical modification of the ingredients, in accordance with standards well-known in the pharmaceutical arts, including those documented in ICH guidelines.

**[0110]** The omega-3 fatty acid dosage form optionally includes chemical antioxidants, such as alpha tocopherol, oils, such as soybean oil and partially hydrogenated vegetable oil, and lubricants such as fractionated coconut oil, lecithin and a mixture of the same.

**[0111]** The compositions of the present invention may be used for the treatment of patients by administering an effective amount of such compositions to a subject in need thereof, such as a subject prone to or afflicted with a disease or condition or in need of treatment for a disease or condition. The present invention provides methods of treating, preventing, and reducing the symptoms, pathology or events associated with a disease or condition comprising administration of any of the compositions of the present invention. The present invention provides a method of treating, preventing, reducing the occurrence of, and improving symptoms

associated with inflammatory conditions. Inflammatory conditions are commonly experienced by patients, and can affect multiple organ systems, including but not limited to the skin, musculoskeletal system, kidneys, lungs, GI tract, central nervous system, peripheral nervous system, cardiovascular system, lymphatic system, ocular system, spleen, liver, gallbladder, nasal, oropharynx, reproductive systems, endrocrine system and hematological systems, including bone marrow. Examples of inflammatory conditions include, but are not limited to primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS).

**[0112]** The effectiveness of the compositions of the present invention may be attributed in part to its activity in modulating prostanoids involved in decreasing inflammation, decreasing the release or effect of proinflammatory mediators such as but not limited to prostaglandins (such as prostaglandin $E_2$), arachidonic acid and interleukins (such as interleukin-6). As such, the compositions of the present invention would have particular utility for the treatment of the following inflammatory diseases, disorders or conditions, that may or may not also have an associated pathophysiological component of fibrosis.

**[0113]** The compositions of the present invention may be useful for any subjects, including those with and without comorbidities. In some embodiments, the subjects to be treated with or administered the compositions of the present invention, are selected based on the presence of certain comorbidities. Such comorbidities may include, but are not limited to the following: hypertriglyceridemia, dyslipidemia, hypercholesteremia, inflammatory conditions, renal disease, nephropathy, IgA nephropathy, renal impairment, renal failure (also kidney failure or renal insufficiency) chronic analgesic nephritis, polycystic kidney disease, proteinuria, hypertension, thrombotic microangiopathy, renal failure (acute renal failure, chronic renal failure), uremic pericarditis, uremia, renal artery stenosis, renal ischemia,

hypertensive nephropathy, renovascular hypertension, renal osteodystrophy, nephroptosis, renal cortical necrosis, glomerulitis, metabolic syndrome, diabetes, or pre-diabetes. In some embodiments, the methods of administering the compositions of the present invention are useful in subjects having cardiopathy, coronary ischemia, cardiac decompensation, or diabetic pathology with cardiopathy, and subjects with previous myocardial infarction, stroke, or any other major cardiovascular event.

**[0114]** In some embodiments, treatment with the compositions of the present invention results in clinical improvement of such comorbidities. In some embodiments, administration with the compositions of the present invention may reduce the time necessary to achieve clinical improvement and/or attain treatment goals. In some embodiments, the administration of compositions can result in clinical improvements in clinical markers. For example, in patients with dysmenorrhea, clinical improvement can be measured in a number of ways, including but not limited to the decrease in the intensity and duration of pain using pain scales, such as but not limited to the Total Pain Relief Score Over the First 6 Hours (TOPAR6), Global Evaluation of Pain at 6 Hours After the Initial Dose (GLOBAL6), Global Evaluation of Pain at 24 Hours After the Initial Dose (GLOBAL24), and measuring the change between baseline evaluation period and treatment evaluation period in the number of days with dysmenorrheic pain. In some embodiments, in patients with osteoarthritis, clinical improvement can be measured in a number of ways, including but not limited to measurring the decrease in the intensity and duration of pain using various scales, such as but not limited to the visual analog scale (VAS) that measures the intensity of pain, or the WOMAC (Western Ontario and McMaster Universities) osteoarthritis index, which is a composite of pain, stiffness, and functional measures of osteoarthritis. Another method would be to measure the impact on disease progression by utilizing radiographic techniques assessing the joint space over the time course of treatment.

**[0115]** The compositions of the present invention can be administered by a multitude of routes, including oral, intravenous, topical, rectal and direct injection to the site of action.

**[0116]** The compositions of the present invention may be co-administered with one or more other therapeutic agents. In some embodiments, clinical benefits resulting from the administration or treatment of subjects with the compositions of the present invention may be improved with concomitant use or in combination with other therapeutic agents, such as any therapeutic agents which impact the inflammatory processes, provide analgesia, and/or target the myometrium . The co-administration may result in a synergistic, more potent and efficacious course of treatment. In addition, it may be possible to use lower doses of these agents to elicit the synergistic effect, which may reduce the number and severity of adverse effects that are associated when they are used alone. Examples of such concomitant or fixed combination treatments may include coadministration with one or more of the following: NSAIDS (such as naproxen and ibuprofen), COX-2 selective inhibitors (such as celecoxib and rofecoxib), acetaminophen, caffeine, isopropylantipyrine, 5-HT receptor antagonists (or "triptans" such as sumatriptan), lidocaine, anti-inflammatory steroids (such as cortisone), oral contraceptives (such as ethinyl estradiol), vasopressin and oxytocin agents (such as atosiban), capsaicin, glucosamine, chondroitin, hyaluronic acid, opioids, and opioid-like analgesics (such as tramadol).

EXAMPLES

**[0117]** Example 1

**[0118]** A composition according to the present invention is prepared by mixing and homogenizing in a ratio of 98:2 the intermediates MEGAPEX E90D00EE (90% EPA ethyl ester,) and MAXOMEGA DPA95 FFA (≥95% DPA synthetic fatty acid produced from EPA ethyl ester concentrate) converted to ethyl ester, respectively. These intermediates were prepared and commercially offered for sale by Chemport Korea (MEGAPEX) and Equateq Ltd from Scotland, UK (MAXOMEGA). The relative amounts of fatty acids present in the starting intermediates and in the resulting novel composition are listed in Table 1 below. The resulting novel composition comprises 89.10% EPA, 1.95% DPA, 0.19% HPA, 91.24% omega-3-pentaenoic acids, less than 0.01% DHA, 91.24% omega-3-pentaenoic acids, 93.09% total omega-3 fatty acids, 3.15% ARA and 3. 57% omega-6 fatty acids (all Area%).

**Table 1. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 1**

| | 98.0% | 2.0% | |
|---|---|---|---|
| Fatty Acid | Megapex E90D00EE | Maxomega DPA95FFA => EE | Novel Composition |
| c18:0 | 0.05 | 0 | 0.05 |
| c18:1n9 | 0.06 | 0 | 0.06 |
| c18:1n7 | 0.02 | 0 | 0.02 |
| c18:2n6 | 0.01 | 0 | 0.01 |
| c18:3n6 | 0.02 | 0 | 0.02 |
| c18:3n3 | 0.03 | 0 | 0.03 |
| c18:4n3 | 0.42 | 0 | 0.41 |
| c18:4n1 | 0.07 | 0 | 0.07 |
| c20:0 | 0 | 0 | 0.00 |
| c20:1n11 | 0 | 0 | 0.00 |
| c20:1n9 | 0 | 0 | 0.00 |
| c20:1n7 | 0 | 0 | 0.00 |
| c20:2n6 | 0.25 | 0 | 0.25 |
| c20:3n9 | 0 | 0 | 0.00 |
| c20:3n6 | 0.15 | 0 | 0.15 |
| c21:0 | 0 | 0 | 0.00 |
| c20:4n6 | 3.21 | 0 | 3.15 |
| c20:3n3 | 0 | 0 | 0.00 |
| c20:4n3 | 1.44 | 0 | 1.41 |
| **c20:5n3** | 90.92 | 0 | 89.10 |
| c22:0 | 0.3 | 0 | 0.29 |
| c22:1n11 | 0.07 | 0 | 0.07 |
| c22:1n9 | 0.18 | 0 | 0.18 |
| c22:1n7 | 0.19 | 0 | 0.19 |
| **c21:5n3** | 0.19 | 0 | 0.19 |
| c22:5n6 | 0 | 0 | 0.00 |
| **c22:5n3** | 0 | 97.27 | 1.95 |
| c22:6n3 | 0 | 0 | 0.00 |
| c24:0 | 0 | 0.33 | 0.01 |
| OTHER | 2.42 | 2.4 | 2.42 |
| | **100** | **100** | **100** |

**[0119]** Example 2

**[0120]** A composition according to the present prevention is prepared by mixing and homogenizing in a ratio of 96:4 the intermediates MEGAPEX E90D00EE (90% EPA ethyl ester,) and MAXOMEGA DPA95 FFA (≥95% DPA synthetic fatty acid produced from EPA ethyl ester concentrate), converted to ethyl ester, respectively. These intermediates were prepared and commercially offered for sale by Chemport Korea (MEGAPEX) and Equateq Ltd from Scotland, UK (MAXOMEGA). The relative amounts of fatty acids present in the starting intermediates and in the resulting novel

composition is listed in Table 2 below. The resulting novel composition comprises 87.28% EPA, 3.89% DPA, 0.18% HPA, 91.35% omega-3-pentaenoic acids, less than 0.01% DHA, 93.17% total omega-3 fatty acids and 3.49% omega-6 fatty acids (all Area%).

**Table 2. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 2**

| | **96.0%** | 4.0% | |
|---|---|---|---|
| Fatty Acid | Megapex E90D00EE | Maxomega DPA95FFA => EE | Novel Composition |
| c18:0 | 0.05 | 0 | 0.05 |
| c18:1n9 | 0.06 | 0 | 0.06 |
| c18:1n7 | 0.02 | 0 | 0.02 |
| c18:2n6 | 0.01 | 0 | 0.01 |
| c18:3n6 | 0.02 | 0 | 0.02 |
| c18:3n3 | 0.03 | 0 | 0.03 |
| c18:4n3 | 0.42 | 0 | 0.40 |
| c18:4n1 | 0.07 | 0 | 0.07 |
| c20:0 | 0 | 0 | 0.00 |
| c20:1n11 | 0 | 0 | 0.00 |
| c20:1n9 | 0 | 0 | 0.00 |
| c20:1n7 | 0 | 0 | 0.00 |
| c20:2n6 | 0.25 | 0 | 0.24 |
| c20:3n9 | 0 | 0 | 0.00 |
| c20:3n6 | 0.15 | 0 | 0.14 |
| c21:0 | 0 | 0 | 0.00 |
| c20:4n6 | 3.21 | 0 | 3.08 |
| c20:3n3 | 0 | 0 | 0.00 |
| c20:4n3 | 1.44 | 0 | 1.38 |
| **c20:5n3** | 90.92 | 0 | 87.28 |
| c22:0 | 0.3 | 0 | 0.29 |
| c22:1n11 | 0.07 | 0 | 0.07 |
| c22:1n9 | 0.18 | 0 | 0.17 |
| c22:1n7 | 0.19 | 0 | 0.18 |
| **c21:5n3** | 0.19 | 0 | 0.18 |
| c22:5n6 | 0 | 0 | 0.00 |
| **c22:5n3** | 0 | 97.27 | 3.89 |
| c22:6n3 | 0 | 0 | 0.00 |
| c24:0 | 0 | 0.33 | 0.01 |
| OTHER | 2.42 | 2.4 | 2.42 |
| | **100** | **100** | **100** |

**[0121]** Example 3

**[0122]** A composition according to the present invention is prepared by mixing and homogenizing in a ratio of 94:6 the intermediates MEGAPEX E90D00EE (90% EPA ethyl ester,) and MAXOMEGA DPA95 FFA (≥95% DPA synthetic fatty acid produced from EPA ethyl ester concentrate) converted to ethyl ester, respectively. These intermediates were prepared and commercially offered for sale by Chemport Korea (MEGAPEX) and Equateq Ltd from Scotland, UK (MAXOMEGA). The relative amounts of fatty acids present in the starting intermediates and in the resulting novel composition are listed in table 3 below. The resulting novel composition comprises 85.46% EPA, 5.84% DPA, 0.18% HPA, 91.48% omega-3-pentaenoic acids, less than 0.01% DHA, 93.26% total omega-3 fatty acids, 3.02% ARA, and 3.42% omega-6 fatty acids (all Area%).

**Table 3. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 3**

| | **94.0%** | 6.0% | |
|---|---|---|---|
| Fatty Acid | Megapex E90D00EE | Maxomega DPA95FFA => EE | Novel Composition |
| c18:0 | 0.05 | 0 | 0.05 |
| c18:1n9 | 0.06 | 0 | 0.06 |
| c18:1n7 | 0.02 | 0 | 0.02 |
| c18:2n6 | 0.01 | 0 | 0.01 |
| c18:3n6 | 0.02 | 0 | 0.02 |
| c18:3n3 | 0.03 | 0 | 0.03 |
| c18:4n3 | 0.42 | 0 | 0.39 |
| c18:4n1 | 0.07 | 0 | 0.07 |
| c20:0 | 0 | 0 | 0.00 |
| c20:1n11 | 0 | 0 | 0.00 |
| c20:1n9 | 0 | 0 | 0.00 |
| c20:1n7 | 0 | 0 | 0.00 |
| c20:2n6 | 0.25 | 0 | 0.24 |
| c20:3n9 | 0 | 0 | 0.00 |
| c20:3n6 | 0.15 | 0 | 0.14 |
| c21:0 | 0 | 0 | 0.00 |
| c20:4n6 | 3.21 | 0 | 3.02 |
| c20:3n3 | 0 | 0 | 0.00 |
| c20:4n3 | 1.44 | 0 | 1.35 |
| **c20:5n3** | 90.92 | 0 | 85.46 |
| c22:0 | 0.3 | 0 | 0.28 |
| c22:1n11 | 0.07 | 0 | 0.07 |
| c22:1n9 | 0.18 | 0 | 0.17 |
| c22:1n7 | 0.19 | 0 | 0.18 |
| **c21:5n3** | 0.19 | 0 | 0.18 |
| c22:5n6 | 0 | 0 | 0.00 |
| **c22:5n3** | 0 | 97.27 | 5.84 |
| c22:6n3 | 0 | 0 | 0.00 |
| c24:0 | 0 | 0.33 | 0.02 |
| OTHER | 2.42 | 2.4 | 2.42 |
| | **100** | **100** | **100** |

**[0123]** Example 4

**[0124]** A composition according to the present invention is prepared by mixing and homogenizing in a ratio of 75:25 the intermediates MEGAPEX E90D00EE (90% EPA ethyl ester,) and MAXOMEGA DPA95 FFA (≥95% DPA synthetic fatty acid produced from EPA ethyl ester concentrate, converted to ethyl ester, respectively. These intermediates were prepared and commercially offered for sale by Chemport Korea (MEGAPEX) and Equateq Ltd from Scotland, UK (MAXOMEGA). The relative amounts of fatty acids present in the starting intermediates and in the resulting novel composition is listed in table 4 below. The resulting novel composition comprises 68.10% EPA, 24.32% DPA, 0.19% HPA, 92.65% omega-3-pentaenoic acids, less than 0.01% DHA, 94.07% total omega-3 fatty acids, 2.41% ARA and 2.73% omega-6 fatty acids (all Area%).

**Table 4. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 4**

| | **75.0%** | 25.0% | |
|---|---|---|---|
| Fatty Acid | Megapex E90D00EE | Maxomega DPA95FFA => EE | Novel Composition |
| c18:0 | 0.05 | 0 | 0.04 |
| c18:1n9 | 0.06 | 0 | 0.05 |
| c18:1n7 | 0.02 | 0 | 0.02 |
| c18:2n6 | 0.01 | 0 | 0.01 |
| c18:3n6 | 0.02 | 0 | 0.02 |
| c18:3n3 | 0.03 | 0 | 0.02 |
| c18:4n3 | 0.42 | 0 | 0.32 |
| c18:4n1 | 0.07 | 0 | 0.05 |
| c20:0 | 0 | 0 | 0.00 |
| c20:1n11 | 0 | 0 | 0.00 |
| c20:1n9 | 0 | 0 | 0.00 |
| c20:1n7 | 0 | 0 | 0.00 |
| c20:2n6 | 0.25 | 0 | 0.19 |
| c20:3n9 | 0 | 0 | 0.00 |
| c20:3n6 | 0.15 | 0 | 0.11 |
| c21:0 | 0 | 0 | 0.00 |
| c20:4n6 | 3.21 | 0 | 2.41 |
| c20:3n3 | 0 | 0 | 0.00 |
| c20:4n3 | 1.44 | 0 | 1.08 |
| **c20:5n3** | 90.92 | 0 | 68.19 |
| c22:0 | 0.3 | 0 | 0.23 |
| c22:1n11 | 0.07 | 0 | 0.05 |
| c22:1n9 | 0.18 | 0 | 0.14 |
| c22:1n7 | 0.19 | 0 | 0.14 |
| **c21:5n3** | 0.19 | 0 | 0.14 |
| c22:5n6 | 0 | 0 | 0.00 |
| **c22:5n3** | 0 | 97.27 | 24.32 |
| c22:6n3 | 0 | 0 | 0.00 |
| c24:0 | 0 | 0.33 | 0.08 |
| OTHER | 2.42 | 2.4 | 2.42 |
| | **100** | **100** | **100** |

**[0125]** Example 5

**[0126]** A composition according to the present invention isprepared by mixing and homogenizing in a ratio of 60:40 the intermediates KD-PharmaKD-PUR 900EE and MAXOMEGA DPA95 FFA converted to ethyl ester, respectively. These intermediates were prepared and commercially offered for sale by KD-Pharma Germany (KD-Pharma) and Equateq Ltd from Scotland, UK (MAXOMEGA). The relative amounts of fatty acids present in the starting intermediates and in the

resulting novel composition is listed in table 5 below. The resulting novel composition comprises 55.74% EPA, 39.26% DPA, 2.39% HPA, 97.44% omega-3-pentaenoic acids, and 98.06% total omega-3 fatty acids (all Area%).

**Table 5. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 5**

| | **60.0%** | 40.0% | |
|---|---|---|---|
| Fatty Acid | KD-Pur 900EE | Maxomega DPA95FFA => EE | Novel Composition |
| c18:0 | 0 | 0 | 0.00 |
| c18:1n9 | 0 | 0 | 0.00 |
| c18:1n7 | 0 | 0 | 0.00 |
| c18:2n6 | 0 | 0 | 0.00 |
| c18:3n6 | 0 | 0 | 0.00 |
| c18:3n3 | 0 | 0 | 0.00 |
| c18:4n3 | 0 | 0 | 0.00 |
| c18:4n1 | 0 | 0 | 0.00 |
| c20:0 | 0 | 0 | 0.00 |
| c20:1n11 | 0 | 0 | 0.00 |
| c20:1n9 | 0 | 0 | 0.00 |
| c20:1n7 | 0 | 0 | 0.00 |
| c20:2n6 | 0 | 0 | 0.00 |
| c20:3n9 | 0 | 0 | 0.00 |
| c20:3n6 | 0 | 0 | 0.00 |
| c21:0 | 0 | 0 | 0.00 |
| c20:4n6 | 0 | 0 | 0.00 |
| c20:3n3 | 0 | 0 | 0.00 |
| c20:4n3 | 1.04 | 0 | 0.62 |
| **c20:5n3** | 92.99 | 0 | 55.79 |
| c22:0 | 0 | 0 | 0.00 |
| c22:1n11 | 0 | 0 | 0.00 |
| c22:1n9 | 0 | 0 | 0.00 |
| c22:1n7 | 0 | 0 | 0.00 |
| **c21:5n3** | 3.98 | 0 | 2.39 |
| c22:5n6 | 0 | 0 | 0.00 |
| **c22:5n3** | 0.58 | 97.27 | 39.26 |
| c22:6n3 | 0 | 0 | 0.00 |
| c24:0 | 0 | 0.33 | 0.13 |
| OTHER | 1.41 | 2.4 | 1.81 |
| | **100.00** | **100** | **100.00** |

**[0127]** Example 6

**[0128]** A composition according to the present invention is prepared by mixing and homogenizing in a ratio of 96:4 the intermediates KD-PUR 900EE KD-Pharma and MAXOMEGA DPA95 FFA converted to ethyl ester, respectively. These

intermediates were prepared and commercially offered for sale by KD-Pharma Germany (KD-Pharma) and Equateq Ltd from Scotland, UK (MAXOMEGA). The relative amounts of fatty acids present in the starting intermediates and in the resulting novel composition is listed in table 6 below. The resulting novel composition comprises 89.27% EPA, 4.45% DPA, 3.82% HPA, 97.54% omega-3-pentaenoic acids, and 98.54% total omega-3 fatty acids (all Area%).

**Table 6. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 6**

| | **96.0%** | 4.0% | |
|---|---|---|---|
| Fatty Acid | KD-Pur 900EE | Maxomega DPA95FFA => EE | Novel Composition |
| c18:0 | 0 | 0 | 0.00 |
| c18:1n9 | 0 | 0 | 0.00 |
| c18:1n7 | 0 | 0 | 0.00 |
| c18:2n6 | 0 | 0 | 0.00 |
| c18:3n6 | 0 | 0 | 0.00 |
| c18:3n3 | 0 | 0 | 0.00 |
| c18:4n3 | 0 | 0 | 0.00 |
| c18:4n1 | 0 | 0 | 0.00 |
| c20:0 | 0 | 0 | 0.00 |
| c20:1n11 | 0 | 0 | 0.00 |
| c20:1n9 | 0 | 0 | 0.00 |
| c20:1n7 | 0 | 0 | 0.00 |
| c20:2n6 | 0 | 0 | 0.00 |
| c20:3n9 | 0 | 0 | 0.00 |
| c20:3n6 | 0 | 0 | 0.00 |
| c21:0 | 0 | 0 | 0.00 |
| c20:4n6 | 0 | 0 | 0.00 |
| c20:3n3 | 0 | 0 | 0.00 |
| c20:4n3 | 1.04 | 0 | 1.00 |
| **c20:5n3** | 92.99 | 0 | 89.27 |
| c22:0 | 0 | 0 | 0.00 |
| c22:1n11 | 0 | 0 | 0.00 |
| c22:1n9 | 0 | 0 | 0.00 |
| c22:1n7 | 0 | 0 | 0.00 |
| **c21:5n3** | 3.98 | 0 | 3.82 |
| c22:5n6 | 0 | 0 | 0.00 |
| **c22:5n3** | 0.58 | 97.27 | 4.45 |
| c22:6n3 | 0 | 0 | 0.00 |
| c24:0 | 0 | 0.33 | 0.01 |
| OTHER | 1.41 | 2.4 | 1.45 |
| | **100.00** | **100** | **100.00** |

**[0129]** Example 7

**[0130]** A composition according to the present invention is prepared by mixing and homogenizing in a ratio of 91.8:8.2 the intermediates KD-PUR 910EE KD-Pharma and DPA95 FFA converted to ethyl ester, respectively. The relative amounts of fatty acids present in the starting intermediates and in the resulting novel composition is listed in table 7 below.

**Table 7. Fatty acid Composition (Area %) of intermediates and novel composition according to Example 7**

| | **91.8%** | 8.2% | | | |
|---|---|---|---|---|---|
| Fatty Acid | KD-Pur EPA910EE | DPA - 95% Est | Novel compositio | N6 | N3 |
| c18:0 | 0 | 0 | 0.00 | | |
| c18:1n9 | 0 | 0 | 0.00 | | |
| c18:1n7 | 0 | 0 | 0.00 | | |
| c18:2n6 | 0 | 0 | 0.00 | 0.00 | |
| c18:3n6 | 0 | 0 | 0.00 | 0.00 | |
| c18:3n3 | 0 | 0 | 0.00 | | 0.00 |
| c18:4n3 | 0 | 0 | 0.00 | | 0.00 |
| c18:4n1 | 0 | 0 | 0.00 | | |
| c20:0 | 0 | 0 | 0.00 | | |
| c20:1n11 | 0.1 | 0 | 0.09 | | |
| c20:1n9 | 0 | 0 | 0.00 | | |
| c20:1n7 | 0 | 0 | 0.00 | | |
| c20:2n6 | 0 | 0 | 0.00 | 0.00 | |
| c20:2n9 | 0 | 0.2 | 0.02 | | |
| c20:3n9 | 0 | 0 | 0.00 | | |
| c20:3n6 | 0 | 0 | 0.00 | 0.00 | |
| c21:0 | 0 | 0 | 0.00 | | |
| c20:4n6 | 0.3 | 0 | 0.28 | 0.28 | |
| c20:3n3 | 0 | 0 | 0.00 | | 0.00 |
| c20:4n3 | 1.2 | 0.3 | 1.13 | | 1.13 |
| **c20:5n3** | 92.5 | 0 | **85.34** | | 85.34 |
| c22:0 | 0.2 | 0 | 0.18 | | |
| c22:1n11 | 0 | 0 | 0.00 | | |
| c22:1n9 | 0 | 0 | 0.00 | | |
| c22:1n7 | 0 | 0 | 0.00 | | |
| c22:4n3 | 0 | 1.9 | 0.16 | | 0.16 |
| **c21:5n3** | 3.3 | 0.1 | **3.08** | | 3.08 |
| c22:5n6 | 0 | 0 | 0.00 | 0.00 | |
| **c22:5n3** | 0.2 | 97 | **8.16** | | 8.16 |
| c22:6n3 | 1.5 | 0 | **1.25** | | 1.25 |
| c24:0 | 0 | 0 | 0.00 | | |
| OTHER | 0.7 | 0.5 | 0.68 | | |
| | **100.00** | **100** | **100.36** | **0.28** | **99.11** |

**[0131]** Example 8

**[0132]** The ethyl ester composition of Example 4 may be converted into a free fatty acid composition with essentially the same fatty acid composition according to "Conversion Method EE to FFA" below. This method is indiscriminate with respect to the type, degree of saturation or length of fatty acid if performed for an adequate amount of time under the described conditions.

***Conversion Method EE to FFA***

1. *Fatty Acid Ethyl Ester (FAEE GMP, approx. 3mmol/g) oil is brought into a closed heated/cooled reaction chamber under nitrogen atmosphere (preferably with pressure control), and heated to 50-60 degree Celcius under stirring.*
2. *2M NaOH solution in water is added under firm stirring to ensure phase mixing (est. 2-3 x FAEE w/w) and stir until no ethyl ester is presence (est. 2-4 hrs). Test ethyl ester presence at lab scale/in process with TLC (hexanes/EtOAc 9:1) and with EP GC method to confirm reaction completion under GMP.*
3. *Under cooling (keep mixture below 70 degree Celcius), add 6M HCl in water (est. <1 hr) until slightly acid (~pH3-4). It may be necessary to control pressure to prevent excessive foaming. Then halt stirring, give time to let phases separate, and remove water phase from bottom (keep oil protected from oxygen, apply nitrogen atmosphere blanket).*
4. *Add demineralized water (est. 2-3 x FAEE w/w) and wash out NaCl and ethanol from oil under firm stirring (est. ~1hr). Halt stirring, give time to let phases separate, and remove water phase from bottom (keep oil protected from oxygen, apply nitrogen atmosphere blanket).*
5. *Repeat Step 4 several times (~2x) to remove ethanol and NaCl.*
6. *Remove water and remaining ethanol [determine in-process controls], confirm under GMP with USP residual solvent method (target: ethanol < 100ppm) by stirring oil while applying vacuum 10-50 mbar (with solvent trap) and heat oil (70-80 degree celcius) until water/ethanol target is met (est. 2-4 hrs).*

7. *Add anti-oxidants (i.e. alpha-D-tocopherol, USP, target 4 mg/g) and/or other excipients.*
8. *All reagents and excipients USP grade.*

**[0133]** Example 9

**[0134]** The ethyl ester composition of Example 3 is converted into a free fatty acid composition with essentially the same fatty acid composition according to "Conversion Method EE to FFA" above. This method is indiscriminate with respect to the type, degree of saturation or length of fatty acid if performed for an adequate amount of time under the described conditions.

**[0135]** Example 10

**[0136]** The ethyl ester composition of Example 6 is converted into a free fatty acid composition with essentially the same fatty acid composition according to "Conversion Method EE to FFA" above. This method is indiscriminate with respect to the type, degree of saturation or length of fatty acid if performed for an adequate amount of time under the described conditions.

**[0137]** Example 11

**[0138]** The composition of Example 4 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti-oxidant preparation (composed of 4000 mg alpha-D-tocopherol in one liter of corn oil; corn oil is a triglyceride low in omega-3) is added to the composition of Example 4, by mixing and homogenizing 100mL of this anti-oxidant preparation into 100 liters of the oil composition of Example 4 followed by thorough homogenization. The resulting pre-encapsulation formulated oil contains approximately 4mg/gram alpha-D-tocopherol. Subsequently, the formulated oil is encapsulated into soft gelatin capsules with printed logo according to general methods typically used by Accucaps in Canada for fish oils or by any other documented and operational encapsulation method. The fill mass of the oil is approximately 1.08 gram/capsule, providing a dose of approximately 1000mg omega-3-pentaenoic-acids ethyl esters per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

**[0139]** Example 12

**[0140]** The composition of Example 9 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti-oxidant preparation (composed of 4000 mg alpha-D-tocopherol in one liter of corn oil; corn oil is a triglyceride low in omega-3) is added to the composition of Example 4, by mixing and homogenizing 100mL of this anti-oxidant preparation into 100 liters of the oil composition of Example 4 followed by thorough homogenization. The resulting pre-encapsulation formulated oil contains approximately 4mg/gram alpha-D-tocopherol. Subsequently, the formulated oil is encapsulated into soft gelatin capsules with printed logo according to general methods typically used by Banner in High Point, NC, for fish oils or by any other documented and operational encapsulation method. The fill mass of the oil is approximately 1.09 gram/capsule, providing a dose of approximately 1000mg omega-3-pentaenoic-acids per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

**[0141]** Example 13

**[0142]** The composition of Example 5 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti-oxidant preparation (composed of 4000 mg alpha-D-tocopherol in one liter of corn oil; corn oil is a triglyceride low in omega-3) is added to the composition of Example 4, by mixing and homogenizing 100mL of this anti-oxidant preparation into 100 liters of the oil composition of Example 4 followed by thorough homogenization. The resulting pre-encapsulation formulated oil contains approximately 4mg/gram alpha-D-tocopherol. Subsequently, the formulated oil is encapsulated into soft gelatin capsules with printed logo according to general methods typically used by Catalent in St.Petersburg, FL, for fish oils or by any other documented and operational encapsulation method. The fill mass of the oil is approximately 1.05 gram/capsule, providing a dose of approximately 1000mg omega-3-pentaenoic-acids ethyl esters per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

**[0143]** Example 14

**[0144]** The composition of Example 10 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti-oxidant preparation (composed of 4000 mg alpha-D-tocopherol in one liter of corn oil; corn oil is a triglyceride low in omega-3) is added to the composition of Example 4, by mixing and homogenizing 100mL of this anti-oxidant preparation into 100 liters of the oil composition of Example 4 followed by thorough homogenization. The resulting pre-encapsulation formulated oil contains approximately 4mg/gram alpha-D-tocopherol. Subsequently, the formulated oil is encapsulated into soft gelatin capsules with printed logo according to general methods typically used by Banner in High Point, NC, for fish oils or by any other documented and operational encapsulation method. The fill mass of the oil is 1.06 gram/capsule, providing a dose of approximately 1000mg omega-3-pentaenoic-acids per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

**[0145]** Example 15

**[0146]** A patient is diagnosed with primary dysmenorrhea. Thereupon, the patient may be initiated on daily treatment with one of the encapsulated compositions according to Examples 10, 11, 12 or 13. Four capsules per day are administered to this patient (4g/d).

**[0147]** Example 16

**[0148]** A patient is treated as per Example 15. The treatment results in significant reduction of pain.

**[0149]** Example 17

**[0150]** The following are examples of preferred embodiments of the present invention.

| **COMPOSITION 1a** | | | |
|---|---|---|---|
| Composition | Minimum (mg/g) | Maximum (mg/g) | Target (mg/g) |
| Omega-3 pentaenoic acid | 880 | 980 | 930 |
| Eicosapentaenoic acid (EPA) | 800 | 950 | 850 |

| | | | |
|---|---|---|---|
| Heneicosapentaenoic acid (HPA) | 5 | 60 | 30 |
| Docosapentaenoic acid (DPA) | 60 | 100 | 80 |
| Docosahexaenoic acid (DHA) | | 25 | <10 |

| COMPOSITION 1b | | | |
|---|---|---|---|
| Composition | Minimum (mg/g) | Maximum (mg/g) | Target (mg/g) |
| Omega-3 pentaenoic acid | 870 | 990 | 920 |
| Eicosapentaenoic acid (EPA) | 750 | 950 | 830 |
| Heneicosapentaenoic acid (HPA) | 5 | 70 | 40 |
| Docosapentaenoic acid (DPA) | 50 | 130 | 90 |
| Docosahexaenoic acid (DHA) | | 40 | 20 |

In COMPOSITIONS 1a and 1b, the EPA:HPA ratio is between 13 and 190, the EPA:DPA ratio is between 8 and 15, the HPA:DPA ration between 0.05 and 1, the DPA:DHA ratio more than 2.4, preferably more than 4, more preferably more than 6, most preferably more than 10, and the EPA:DHA ratio more than 32, preferably more than 38, more preferably more than 80, most preferably more than 95. The EPA, HPA, DPA and DHA may be composed as a glyceride (such as triglyceride), an ester (such as ethyl ester), or a free fatty acid.

**[0151]** Example 18

**[0152]** The following is an example of a preferred embodiment of the present invention.

| COMPOSITION 2 | | | |
|---|---|---|---|
| Composition | Minimum (mg/g) | Maximum (mg/g) | Target (mg/g) |
| Omega-3 pentaenoic acid | 900 | 980 | 940 |
| Eicosapentaenoic acid (EPA) | 15 | 60 | 30 |
| Heneicosapentaenoic acid (HPA) | 5 | 60 | 30 |
| Docosapentaenoic acid (DPA) | 800 | 950 | 880 |
| Docosahexaenoic acid (DHA) | | 25 | <10 |

In COMPOSITION 2, the EPA:HPA ratio is between 0.25 and 12, the DPA:EPA ratio is between 13 and 63, the DPA:HPA ration between 13 and 190, the DPA:DHA ratio more than 32, preferably more than 38, more preferably more than 80, most preferably more than 95, and the EPA:DHA ratio more than 00.6, preferably more than 1.5, more preferably more than 2.4, most preferably more than 6. The EPA, HPA, DPA and DHA may be composed as a glyceride (such as triglyceride), an ester (such as ethyl ester), or a free fatty acid.

**[0153]** Example 19

**[0154]** The following is an example of an embodiment of the present invention.

| **COMPOSITION 3** | | | |
|---|---|---|---|
| Composition | Minimum (mg/g) | Maximum (mg/g) | Target (mg/g) |
| Docosapentaenoic acid (DPA n-3) | 800 | 990 | 920 |

The DPA may be composed as a glyceride (such as triglyceride), an ester (such as ethyl ester), or a free fatty acid.

**[0155]** Example 20

**[0156]** The following is an example of an embodiment of the present invention.

| COMPOSITION 4 | | | |
|---|---|---|---|
| Composition | Minimum (mg/g) | Maximum (mg/g) | Target (mg/g) |
| Omega-3 pentaenoic acid | 930 | 1000 | 966 |
| Eicosapentaenoic acid (EPA) | 840 | 870 | 853 |
| Heneicosapentaenoic acid (HPA) | 20 | 40 | 30 |
| Docosapentaenoic acid (DPA) | 60 | 100 | 81 |
| Docosahexaenoic acid (DHA) | 5 | 20 | 12 |

**[0157]** Example 21

**[0158]** A mixture of DPA and EPA was prepared by combining 1g DPA Ethyl Ester (SE-133-III) with 10g EPA Ethyl Ester, 914 mg/g (KD Pharma FM13001) in 150ml of 95% ethanol/water containing 35ml of 2M sodium hydroxide. This reaction mixture was stirred overnight at ambient temperature. Tlc analysis showed complete conversion of the ethyl esters to the corresponding acids. The reaction mixture was cooled in an ice bath, acidified with 6N hydrochloric acid and concentrated on a rotavap under reduced pressure. Water and ethyl acetate were added, the phases separated and the aqueous residue extracted with ethyl acetate. The ethyl acetate extracts were combined, dried over sodium sulfate and concentrated to dryness on a rotavap under reduced pressure. Yield: 9.83 g . The ethyl ester mixture was then converted to the free fatty acids as described in Example 8.

**[0159]** A representative sample of this ethyl ester composition was analysed using split inject by capillary gas chromatography by a 30 meter x 0.25 mm Restek Stabil wax column using temperature programming.

**[0160]** DESCRIPTION OF EMBODIMENTS OF THE PRESENT INVENTION

1. A fatty acid composition comprising at least 50% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
2. A fatty acid composition comprising at least 60% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
3. A fatty acid composition comprising at least 70% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
4. A fatty acid composition comprising at least 75% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
5. A fatty acid composition comprising at least 80% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
6. A fatty acid composition comprising at least 85% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
7. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.
8. A fatty acid composition comprising at least 95% omega-3-fatty acids, salts or derivatives thereof, while comprising eicosapentaenoic acid (EPA; C20:5-n3) and

docosapentaenoic acid (DPA; C22:5-n3) and wherein the EPA:DHA ratio is higher than 20:1.

9. A composition according to one of the preferred embodiments 1 through 8, comprising at least 2% docosapentaenoic acid (DPA; C22:5-n3).
10. A composition according to one of the preferred embodiments 1 through 8, comprising at least 4% docosapentaenoic acid (DPA; C22:5-n3).
11. A composition according to one of the preferred embodiments 1 through 8, comprising at least 5% docosapentaenoic acid (DPA; C22:5-n3).
12. A composition according to one of the preferred embodiments 1 through 8, comprising at least 6% docosapentaenoic acid (DPA; C22:5-n3).
13. A composition according to one of the preferred embodiments 1 through 8, comprising at least 7% docosapentaenoic acid (DPA; C22:5-n3).
14. A composition according to one of the preferred embodiments 1 through 8, comprising at least 8% docosapentaenoic acid (DPA; C22:5-n3).
15. A composition according to one of the preferred embodiments 1 through 8, comprising at least 10% docosapentaenoic acid (DPA; C22:5-n3).
16. A composition according to one of the preferred embodiments 1 through 8, comprising at least 12% docosapentaenoic acid (DPA; C22:5-n3).
17. A composition according to one of the preferred embodiments 1 through 8, comprising at least 15% docosapentaenoic acid (DPA; C22:5-n3).
18. A composition according to one of the preferred embodiments 1 through 17, comprising no more than 95% EPA.
19. A composition according to one of the preferred embodiments 1 through 17, comprising no more than 10% omega-6 fatty acids.
20. A composition according to one of the preferred embodiments 1 through 17, comprising no more than 7% omega-6 fatty acids.
21. A composition according to one of the preferred embodiments 1 through 17, comprising no more than 5% omega-6 fatty acids.
22. A composition according to one of the preferred embodiments 1 through 17, comprising no more than 3% omega-6 fatty acids.
23. A composition according to one of the preferred embodiments 1 through 22, comprising no more than 5% arachidonic acid (C22:4-n6).

24. A composition according to one of the preferred embodiments 1 through 22, comprising no more than 4% arachidonic acid (C22:4-n6).
25. A composition according to one of the preferred embodiments 1 through 22, comprising no more than 3% arachidonic acid (C22:4-n6).
26. A composition according to one of the preferred embodiments 1 through 22, comprising no more than 2% arachidonic acid (C22:4-n6).
27. A composition according to one of the preferred embodiments 1 through 22, comprising no more than 1% arachidonic acid (C22:4-n6).
28. A composition according to one of the preferred embodiments 1 through 27, also comprising heneicosapentaenoic acid (C21:5-n3).
29. A composition according to one of the preferred embodiments 1 through 27, comprising at least 0.01% heneicosapentaenoic acid (C21:5-n3).
30. A composition according to one of the preferred embodiments 1 through 27, comprising at least 0.1% heneicosapentaenoic acid (C21:5-n3).
31. A composition according to one of the preferred embodiments 1 through 27, comprising at least 0.3% heneicosapentaenoic acid (C21:5-n3).
32. A composition according to one of the preferred embodiments 1 through 27, comprising at least 0.5% heneicosapentaenoic acid (C21:5-n3).
33. A composition according to one of the preferred embodiments 1 through 27, comprising at least 1% heneicosapentaenoic acid (C21:5-n3).
34. A composition according to one of the preferred embodiments 1 through 27, comprising at least 2% heneicosapentaenoic acid (C21:5-n3).
35. A composition according to one of the preferred embodiments 1 through 27, comprising at least 3% heneicosapentaenoic acid (C21:5-n3).
36. A composition according to one of the preferred embodiments 1 through 27, comprising at least 4% heneicosapentaenoic acid (C21:5-n3).
37. A composition according to one of the preferred embodiments 1 through 27, comprising at least 5% heneicosapentaenoic acid (C21:5-n3).
38. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 5% omega-3 fatty acids that are not omega-3-pentaenoic acids.

39. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 4% omega-3 fatty acids that are not omega-3-pentaenoic acids.
40. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 3% omega-3 fatty acids that are not omega-3-pentaenoic acids.
41. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 2% omega-3 fatty acids that are not omega-3-pentaenoic acids.
42. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 1.5% omega-3 fatty acids that are not omega-3-pentaenoic acids.
43. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 1.25% omega-3 fatty acids that are not omega-3-pentaenoic acids.
44. A composition according to one of the preferred embodiments 1 through 37, comprising no more than 1% omega-3 fatty acids that are not omega-3-pentaenoic acids.
45. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 99:1 and 1:99.
46. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 60:1 and 1:60.
47. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 50:1 and 1:10.
48. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 1:3.
49. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 1:2.
50. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 1:1.
51. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 30:1 and 1:1.

52. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 20:1 and 1:1.
53. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 10:1 and 1:1.
54. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 5:1 and 1:1.
55. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 10:1 and 2:1.
56. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 20:1 and 2:1.
57. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 30:1 and 2:1.
58. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 2:1.
59. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 50:1 and 2:1.
60. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 10:1 and 3:1.
61. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 20:1 and 3:1.
62. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 30:1 and 3:1.
63. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 3:1.
64. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 50:1 and 3:1.
65. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 60:1 and 3:1.
66. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 10:1 and 5:1.
67. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 20:1 and 5:1.

68. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 30:1 and 5:1.
69. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 5:1.
70. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 50:1 and 5:1.
71. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 60:1 and 5:1.
72. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 20:1 and 10:1.
73. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 30:1 and 10:1.
74. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 40:1 and 10:1.
75. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 50:1 and 10:1.
76. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 60:1 and 10:1.
77. A composition according to one of the preferred embodiments 1 through 44, wherein the EPA:DPA ratio is between 100:1 and 10:1.
78. A composition according to one of the preferred embodiments 1 through 44, comprising between 55% and 95% EPA.
79. A composition according to one of the preferred embodiments 1 through 44, comprising between 60% and 95% EPA.
80. A composition according to one of the preferred embodiments 1 through 44, comprising between 65% and 95% EPA.
81. A composition according to one of the preferred embodiments 1 through 44, comprising between 70% and 95% EPA.
82. A composition according to one of the preferred embodiments 1 through 44, comprising between 75% and 95% EPA.
83. A composition according to one of the preferred embodiments 1 through 44, comprising between 80% and 95% EPA.

84. A composition according to one of the preferred embodiments 1 through 44, comprising between 85% and 95% EPA.
85. A composition according to one of the preferred embodiments 1 through 44, comprising between 90% and 95% EPA.
86. A composition according to one of the preferred embodiments 1 through 44, comprising between 1% and 3% DPA.
87. A composition according to one of the preferred embodiments 1 through 44, comprising between 1% and 5% DPA.
88. A composition according to one of the preferred embodiments 1 through 44, comprising between 2% and 10% DPA.
89. A composition according to one of the preferred embodiments 1 through 44, comprising between 3% and 20% DPA.
90. A composition according to one of the preferred embodiments 1 through 44, comprising between 3% and 30% DPA.
91. A composition according to one of the preferred embodiments 1 through 44, comprising between 3% and 50% DPA.
92. A composition according to one of the preferred embodiments 1 through 44, comprising between 3% and 75% DPA.
93. A composition according to one of the preferred embodiments 1 through 44, comprising between 3% and 90% DPA.
94. A fatty acid composition according to one of the preferred embodiments 1 through 93, in which the fatty acids are present as ethyl esters.
95. A fatty acid composition according to one of the preferred embodiments 1 through 93, in which the fatty acids are present as free fatty acids.
96. A fatty acid composition according to one of the preferred embodiments 1 through 93, in which the fatty acids are present as esters in di-glyceride form.
97. A fatty acid composition according to one of the preferred embodiments 1 through 93, in which the fatty acids are present as esters in triglyceride form.
98. A fatty acid composition according to one of the preferred embodiments 94 through 97, also comprising a suitable anti-oxidant in a concentration sufficient to protect the fatty acids of the composition from oxidation.

99. A pharmaceutically suitable formulation comprising one of the compositions according to preferred embodiments 94 through 98, in which the amount of eicosapentaenoic acid plus docosapentaenoic acid is present in an amount between 100 and 10,000 mg.

100. A pharmaceutically suitable formulation or dosage form comprising one of the compositions according to preferred embodiments 94 through 98, in which the amount of eicosapentaenoic acid plus docosapentaenoic acid is present in an amount between 250 and 1,250 mg.

101. A pharmaceutically suitable formulation or dosage form comprising one of the compositions according to preferred embodiments 94 through 98, in which the amount of eicosapentaenoic acid plus docosapentaenoic acid is present in an amount between 500 and 1,100 mg.

102. A pharmaceutically suitable formulation or dosage form comprising one of the compositions according to preferred embodiments 94 through 98, in which the amount of eicosapentaenoic acid plus docosapentaenoic acid is present in an amount between 100 and 10,000 mg.

103. A method of administration or treatment to a subject of a formulation or dosage form according to one of the preferred embodiments 94 through 102 at a daily dose between 100 and 10,000 mg.

104. A method of administration or treatment to a subject of a formulation or dosage form according to one of the preferred embodiments 94 through 102 at a daily dose between 500 and 5,000 mg.

105. A method of administration or treatment to a subject of a formulation or dosage form according to one of the preferred embodiments 94 through 102 at a daily dose between 1,500 and 4,100 mg.

106. A method of treatment according to preferred e embodiments 103 through 105, in which the subject is a patient diagnosed with very high triglycerides (equal or more than 500 mg/dL).

107. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with high triglycerides (equal to or more than 200 mg/dL but less than 500 mg/dL).

108. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient already undergoing treatment with a statin and then diagnosed with high triglycerides (equal to or more than 200 mg/dL but less than 500 mg/dL).

109. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 200-499 mg/dL and LDL-cholesterol equal to or more than 190 mg/dL.

110. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 300-700 mg/dL and LDL-cholesterol equal to or more than 190 mg/dL.

111. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 200-499 mg/dL and non-HDL-cholesterol equal to or more than 200 mg/dL.

112. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 300-700 mg/dL and non-HDL-cholesterol equal to or more than 200 mg/dL.

113. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 200-499 mg/dL and LDL-cholesterol equal to or more than 160 mg/dL.

114. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 300-700 mg/dL and LDL-cholesterol equal to or more than 160 mg/dL.

115. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 200-499 mg/dL and non-HDL-cholesterol equal to or more than 160 mg/dL.

116. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 300-700 mg/dL and non-HDL-cholesterol equal to or more than 160 mg/dL.

117. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 200-499 mg/dL and LDL-cholesterol equal to or more than 130 mg/dL.

118. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 300-700 mg/dL and LDL-cholesterol equal to or more than 130 mg/dL.

119. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 200-499 mg/dL and non-HDL-cholesterol equal to or more than 130 mg/dL.

120. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with mixed dyslipidemia with TG 300-700 mg/dL and non-HDL-cholesterol equal to or more than 130 mg/dL.

121. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed/assessed to be at substantially elevated risk for cardiovascular events.

122. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with diabetes.

123. A method of treatment according to preferred embodiments 103 through 105, in which the subject is a patient diagnosed with pre-diabetes or metabolic syndrome.

124. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma triglyceride levels.

125. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma triglyceride levels while not significantly increasing blood, serum or plasma LDL-cholesterol levels.

126. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma total-cholesterol levels.

127. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma non-HDL-cholesterol levels.

128. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma LDL-cholesterol levels.

129. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma VLDL-cholesterol levels.

130. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma VLDL-cholesterol levels while not significantly increasing blood, serum or plasma LDL-cholesterol levels.

131. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma apo-B levels.

132. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma apo-C-III levels.

133. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma LP-PLA2 levels.

134. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of blood, serum or plasma hs-CRP levels.

135. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant increase of blood, serum or plasma HDL-cholesterol levels.

136. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant increase of blood, serum or plasma apo-A levels.

137. A method of treatment according to one of the preferred embodiments 103 through 123, in which the treatment results in significant reduction of the risk of suffering certain cardiovascular events.

138. The composition of claim 1, wherein the ratio of EPA to DPA (EPA:DPA) is between 15:1 to 8:1.

139. An orally administrable composition comprising fatty acids, wherein at least 50% by weight of the fatty acids comprise omega-3-pentaenoic acids, salts, esters, or derivatives thereof, wherein the composition comprises eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA), and wherein the ratio of DHA to EPA (DHA:EPA) is less than 1:20, and wherein the ratio of DHA to DPA (DHA:DPA) is less than 2:1.

WHAT IS CLAIMED:

Claim 1. A method of treating, preventing, reducing the occurrence of, and improving symptoms associated with an inflammatory disease or condition in a subject in need thereof, comprising administering to the subject a composition comprising fatty acids, wherein at least 50% by weight of the fatty acids comprise omega-3 fatty acids, salts, esters, or derivatives thereof, wherein the omega-3 fatty acids comprise eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA) and wherein the ratio of docosahexaenoic acid to DHA to EPA (DHA:EPA) is less than 1:10, and wherein the ratio of DHA to DPA (DHA:DPA) is less than 2:1.

Claim 2. The method of claim 1, wherein the inflammatory disease or condition is selected from the group consisting of: primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS), diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae, neuropathic pain, solid tumors, enlarged prostate, macular degeneration, and lupus.

Claim 3. The method of claim 1, wherein the ratio of DHA:EPA is less than 1:20.

Claim 4. The method of claim 1, wherein the ratio of DHA:DPA is less than 1:1.

Claim 5. The method of claim 1, wherein the ratio of EPA to DPA (EPA:DPA) is between 30:1 and 1:1.

Claim 6. The method of claim 1, wherein ratio of DHA:EPA is less than 1:10.

Claim 7. The method of claim 1, wherein the composition comprises DHA in an amount less than 5% of the total amount of fatty acids.

Claim 8. The method of claim 1, wherein the composition comprises EPA in an amount between about 80% and about 90% of the total amount of fatty acids.

Claim 9. The method of claim 1, wherein the composition comprises DPA in an amount between about 5% and about 15% of the total amount of fatty acids.

Claim 10. The method of claim 1, wherein the composition comprises DPA free fatty acid or a salt, ester or derivative of DPA.

Claim 11. The method of claim 1, wherein composition comprises EPA free fatty acid or a salt, ester or derivative of EPA.

Claim 12. A method of treating, preventing, reducing the occurrence of, and improving symptoms associated with an inflammatory disease or condition in a subject in need thereof, comprising administering to the subject a composition comprising eicosapentaenoic acid (EPA) in an amount between about 750 mg/g to about 950 mg/g,

and wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and

and wherein the ratio of DHA:DPA is 1:1 or lower.

Claim 13. The method of claim 12, wherein the inflammatory disease or condition is selected from the group consisting of: primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian

syndrome (PCOS), diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae, neuropathic pain, solid tumors, enlarged prostate, macular degeneration, and lupus.

Claim 14. The method of claim 12, wherein the composition comprises eicosapentaenoic acid (EPA) in an amount between about 800 mg/g to about 900 mg/g,

and wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and

and wherein the ratio of DHA:DPA is 1:1 or lower.

Claim 15. The method of claim 12, wherein the composition comprises eicosapentaenoic acid (EPA) in an amount between about 830 mg/g to about 870 mg/g,

and wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and

and wherein the ratio of DHA:DPA is 1:1 or lower.

Claim 16. The method of claim 12, wherein the composition comprises docosapentaenoic acid (DPA) is an amount between about 60 mg/g to about 120 mg/g.

Claim 17. The method of claim 1, wherein the composition comprises docosapentaenoic acid (DPA) is an amount between about 70 mg/g to about 100 mg/g.

Claim 18. A method of treating, preventing, reducing the occurrence of, and improving symptoms associated with an inflammatory disease or condition in a subject in need thereof, comprising administering to the subject a composition comprising:

- eicosapentaenoic acid (EPA) in an amount between about 70% to about 95% of the total amount of fatty acids and

- docosapentaenoic acid (DPA) ,

wherein the composition comprises no more than 5% docosahexaenoic acid (DHA) of the total amount of fatty acids, and

wherein the ratio of DHA:DPA is 1:1 or lower.

Claim 19. The method of claim 18, wherein the inflammatory disease or condition is selected from the group consisting of: primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS), diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae, neuropathic pain, solid tumors, enlarged prostate, macular degeneration, and lupus.

Claim 20. The method of claim 18, wherein the composition comprises eicosapentaenoic acid (EPA) in an amount between about 80% to about 90% of the total amount of fatty acids.

Claim 21. The method of 18, wherein the composition comprises eicosapentaenoic acid (EPA) in an amount between about 82% to about 88% of the total amount of fatty acids.

Claim 22. The method of 18, wherein the composition comprises docosapentaenoic acid (DPA) in amount between about 5% and about 15% of the total amount of fatty acids.

Claim 23. The method of 18, wherein the composition comprises docosapentaenoic acid (DPA) in an amount between about 6% to about 12% of the total amount of fatty acids.

Claim 24. The method of claim 18, wherein the composition comprises EPA free fatty acid or a salt, ester or derivative of EPA.

Claim 25. A method of treating, preventing, reducing the occurrence of, and improving symptoms associated with an inflammatory disease or condition in a subject in need thereof, comprising administering to the subject a composition comprising eicosapentaenoic acid (EPA) in a daily dosage amount of between about 1000 mg to about 5000 mg,

and further comprising docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA),

wherein the composition comprises no more than 5% DHA of the total amount of fatty acids, and wherein the ratio of DHA:DPA is 1:1 or lower.

Claim 26. The method of claim 25, wherein the inflammatory disease or condition is selected from the group consisting of: primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS), diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae, neuropathic pain, solid tumors, enlarged prostate, macular degeneration, and lupus.

Claim 27. The method of claim 25, wherein the composition comprises eicosapentaenoic acid (EPA) in a daily dosage amount selected from the group

consisting of: about 1735 mg to about 1855 mg, about 2520 mg to about 2780 mg, and about 3360 mg to about 3710 mg.

Claim 28. The method of claim 25, wherein the composition comprises eicosapentaenoic acid (EPA) in a daily dosage amount selected from the group consisting of: about 1750 mg to about 1950 mg, about 1800 mg to about 2000 mg about 2650 mg to about 2950 mg, and about 3500 mg to about 3900 mg.

Claim 29. The method of claim 25, wherein the composition comprises eicosapentaenoic acid (EPA) in daily dosage amount selected from the group consisting of: about 1900 mg to about 2100 mg, about 2700 mg to about 3300 mg, and about 3700 mg to about 4300 mg.

Claim 30. The method of claim 25, wherein the composition comprises EPA free fatty acid or a salt, ester or derivative of EPA.

Claim 31. The method of claim 25, wherein the composition comprises DPA free fatty acid or a salt, ester or derivative of DPA.

Claim 32. A method of treating, preventing, reducing the occurrence of, and improving symptoms associated with an inflammatory disease or condition in a subject in need thereof, comprising administering to the subject a composition comprising eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA), wherein the amount of EPA and DPA is about 55% or more by weight of the total amount of fatty acids, and wherein the ratio of DHA:DPA is no more than 1:1.

Claim 33. The method of claim 32, wherein the inflammatory disease or condition is selected from the group consisting of: primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome, dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders

including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS), diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae, neuropathic pain, solid tumors, enlarged prostate, macular degeneration, and lupus.

Claim 34. The method of claim 32, wherein the composition comprises a daily dosage of about 120 mg/day to about 150 mg/day.

Claim 35. The method of claim 32, wherein the composition comprises a daily dosage of DPA of about 150 mg/day to about 200 mg/day.

Claim 36. The method of claim 32, wherein the composition comprises a daily dosage of DPA of about 200 mg/day to about 250 mg/day.

Claim 37. The method of claim 32, wherein the composition comprises a daily dosage of DPA of about 250 mg/day to about 300 mg/day.

Claim 38. The method of claim 32, wherein the composition comprises a daily dosage of DPA of about 300 mg/day to about 400 mg/day.

Claim 39. The method of claim 32, wherein the composition comprises a daily dosage of DPA of about 400 mg/day to about 600 mg/day.

Claim 40. The method of claim 32, wherein the composition comprises a daily dosage of DPA of about 600 mg/day to about 1000 mg/day.

Claim 41. The method of claim 32, wherein the composition further comprises eicosapentaenoic acid (EPA) and, wherein the amount of EPA and DPA is about 55% or more by weight of the total amount of fatty acids, and wherein the ratio of DHA:DPA is no more than 1:1.

Claim 42. The method of claim 32, wherein the amount of EPA and DPA is selected from the group consisting of about 60% or more, about 65% or more, about 70% or more, about 75% or more, about 80% or more, about 85% or more, and about 90% or more by weight of the total amount of fatty acids.

Claim 43. The method of claim 32, wherein the composition comprises further omega-6 fatty acids in an amount of no more than 6% of total amount of fatty acids.

Claim 44. The method of claim 32, wherein the composition comprises no more than about 30% docosahexaenoic acid (DHA) by weight of fatty acids present in the composition.

Claim 45. The method of claim 32, wherein the composition comprises no more than about 10% docosahexaenoic acid (DHA) by weight of fatty acids present in the composition.

Claim 46. The method of claim 32, wherein the composition comprises no more than about 5% docosahexaenoic acid (DHA) by weight of fatty acids present in the composition.

Claim 47. The method of claim 32, wherein the composition comprises DPA in ethyl ester form.

Claim 48. The method of claim 32, wherein the composition comprises DPA in free fatty acid form.

Claim 49. The method of claim 32, wherein the composition further comprises docosahexaenoic acid (DHA), and the ratio of DHA:DPA is no more than 2:1.

Claim 50. The method of claim 32, wherein the composition further comprises docosahexaenoic acid (DHA), and the ratio of DHA:DPA is no more than 1:1.

Claim 51. The method of claim 32, wherein the composition further comprises docosahexaenoic acid (DHA), and the ratio of DHA:DPA is no more than 1:2.

Claim 52. The method of claim 32, wherein the composition further comprises docosahexaenoic acid (DHA), and the ratio of DHA:DPA is no more than 1:4.

Claim 53. The method of claim 32, wherein the composition comprises at least about 6% docosapentaenoic acid (DPA) by weight of fatty acids present in the composition.

Claim 54 The method of claim 32, wherein the composition comprises at least about 20% docosapentaenoic acid (DPA) by weight of fatty acids present in the composition.

Claim 55. The method of claim 32, wherein the composition comprises at least about 50% docosapentaenoic acid (DPA) by weight of fatty acids present in the composition.

Claim 56. A method of treating, preventing, reducing the occurrence of, and improving symptoms associated with an inflammatory disease or condition in a subject in need thereof, comprising administering to the subject a composition comprising comprising: docosapentaenoic acid (DPA) in an amount between about 50% to about 80% of the total amount of fatty acids, docosahexaenoic acid (DHA) in an amount between about 25% to about 40% of the total amount of fatty acids, and optionally eicosapentaenoic acid (EPA) in an amount less than about 10% of the total amount of fatty acids.

Claim 57. The method of claim 56, wherein the inflammatory disease or condition is selected from the group consisting of: primary dysmenorrhea, secondary dysmenorrhea, osteoarthritis, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), ulcerative colitis, psoriasis, irritable bowel syndrome,

dry eye, allergic ocular reactions, post-surgical pain, post-trauma pain due to strains, sprains and tears of the musculoskeletal system, connective tissue disorders including Raynaud's disease and fibromyalgia, mittlesmerchz (pain associated with ovulation), premature (preterm) labor, endometriosis, and polycystic ovarian syndrome (PCOS), diabetes, atherosclerosis, renal failure, kidney stones, toxemia, leukemia, encephalitis, respiratory syncytial virus, meningitis, Alzheimer's Disease, herpes simplex virus and sequalae, neuropathic pain, solid tumors, enlarged prostate, macular degeneration, and lupus.

Claim 58. The method of claim 56, wherein the composition comprises docosapentaenoic acid (DPA) in an amount between about 50% to 75% of the total amount of fatty acids.

Claim 59. The method of claim 56, wherein the composition comprises docosapentaenoic acid (DPA) in an amount between about 50% to 65% of the total amount of fatty acids.

Claim 60. The method of claim 56, wherein the composition comprises docosahexaenoic acid (DHA) in an amount between about 25% to about 35%, of the total amount of fatty acids.

Claim 61. The method of claim 56, wherein the composition comprises docosahexaenoic acid (DHA) in an amount between about 30% to about 35% of the total amount of fatty acids.

Claim 62. The method of claim 56, wherein the composition comprises eicosapentaenoic acid (EPA) in an amount less than about 8% of the total amount of fatty acids.

Claim 63. The method of claim 56, wherein the composition comprises eicosapentaenoic acid (EPA) in an amount less than about 5% of the total amount of fatty acids.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/075704

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K31/231 (2014.01)
USPC - 554/224
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61K 31/202, 225, 23, 231 (2014.01)
USPC - 514/549, 560 ; 554/224

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61K 31/202, 225, 23, 231 (2014.02)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Orbit, Google Patents, Google Scholar

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | US 2006/0241088 A1 (ARTERBURN et al) 26 October 2006 (26.10.2006) entire document | 1-63 |
| A | US 2012/0093922 A1 (MANKU et al) 19 April 2012 (19.04.2012) entire document | 1-63 |
| A | US 2008/0269330 A1 (STAHL et al) 30 October 2008 (30.10.2008) entire document | 1-63 |
| A | US 2012/0302639 A1 (JACKOWSKI et al) 29 November 2012 (29.11.2012) entire document | 1-63 |
| A | US 2009/0054329 A1 (WILLEMSEN et al) 26 February 2009 (26.02.2009) entire document | 1-63 |
| A | US 2007/0104856 A1 (STANDAL et al) 10 May 2007 (10.05.2007) entire document | 1-63 |

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 25 March 2014 | 18 APR 2014 |
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents<br>P.O. Box 1450, Alexandria, Virginia 22313-1450<br>Facsimile No. 571-273-3201 | Authorized officer:<br>Blaine R. Copenheaver<br>PCT Helpdesk: 571-272-4300<br>PCT OSP: 571-272-7774 |