(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 November 2014 (06.11.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/179341 A1

(51) International Patent Classification:
A61K 31/20 (2006.01) *A61K 35/60* (2006.01)
A61K 31/21 (2006.01)

(21) International Application Number:
PCT/US2014/035922

(22) International Filing Date:
29 April 2014 (29.04.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/817,285 29 April 2013 (29.04.2013) US

(71) Applicant: **MATINAS BIOPHARMA, INC.** [US/US]; 1545 Route 206, Suite 302, Bedminster, NJ 07921 (US).

(72) Inventors: **BOBOTAS, George**; 1245 N. Florida Avenue, Tarpon Springs, FL 34689 (US). **FAWZY, Abdel, A.**; 12525 Colony Preserve Drive, Boynton Beach, FL 33436 (US).

(74) Agents: **KIM, Yelee, Y.** et al.; Arent Fox, LLP, 1717 K Street, N.W., Washington, DC 20036-5342 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2014/179341 A1

(54) Title: TREATMENT WITH OMEGA-3 FATTY ACID COMPOSITIONS

(57) Abstract: Fatty acid compositions comprising at least 81% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids. The compositions can be used for the treatment or prophylaxis of dyslipidemic, cardiovascular, CNS, inflammatory, and other diseases/conditions or risk factors therefore.

TREATMENT WITH OMEGA-3 FATTY ACID COMPOSITIONS

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Provisional Patent Application No. 61/817,285, filed on April 29, 2013.

FIELD OF INVENTION

[0002] The present invention relates to a method utilizing formulations comprising omega-3 fatty acids for the treatment of patients by administering an effective amount of a pharmaceutical formulation of the present invention to a subject prone to or afflicted with such disease, and wherein the disease is an amenable disease selected from the group consisting of: hypertriglyceridemia; hypercholesterolemia; mixed dyslipidemia; coronary heart disease (CHD); vascular disease; atherosclerotic disease and related conditions; heart failure; cardiac arrhythmias; ischemic dementia; hypertension; coagulation related disorders; nephropathy; kidney or urinary tract disease; retinopathy; cognitive and other CNS disorders; autoimmune diseases; inflammatory diseases; asthma or other respiratory disease; dermatological disease; metabolic syndrome; diabetes or other form of metabolic disease; liver disease; disease of the gastrointestinal tract; disease of the male or female reproductive system or related secondary sexual organs; a cancer; an infection caused by a virus, bacterium, fungus, protozoa or other organism; and the treatment and/or prevention and/or reduction of cardiac events and/or cardiovascular events and/or vascular events and/or symptoms. The present invention also relates to treatment of such conditions in with concomitant treatments regimes or combination products with other active pharmaceutical ingredients.

BACKGROUND OF THE INVENTION

[0003] In humans, cholesterol and triglycerides are part of lipoprotein complexes in the bloodstream, and can be separated via ultracentrifugation into high-density lipoprotein (HDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) fractions. Cholesterol and triglycerides are synthesized in the liver, incorporated into VLDL, and released into the plasma.

High levels of total cholesterol (total-C), LDL-cholesterol, and apolipoprotein B (a membrane complex for LDL-cholesterol and VLDL-cholesterol, as well as IDL-cholesterol in rare individuals suffering from a disorder resulting in significant IDL-cholesterol levels) promote human atherosclerosis; these elevated levels are often referred to as hypercholesterolemia. Decreased levels of HDL-cholesterol and its transport complex, apolipoprotein A, as well as elevated levels of apolipoprotein C-III and serum triglycerides (TG) are also associated with the development of atherosclerosis. Further, cardiovascular morbidity and mortality in humans can vary directly with the level of total-C, LDL-cholesterol and TG and inversely with the level of HDL- cholesterol. In addition, researchers have found that non-HDL-cholesterol is an important indicator of hypertriglyceridemia (elevated triglycerides), vascular disease, atherosclerotic disease and related conditions. Therefore, non-HDL-cholesterol and fasting TG reduction has also been specified as a treatment objective in NCEP ATP III. Fasting TG is commonly used as a key measure for TG in lipid management, because it minimizes the confounding factor of TG recently absorbed from meals, including the high variability of the content of meals and high variability of post-meal (post-prandial) spikes in TG. In some preferred embodiments, we refer to fasting TG levels when we refer to triglycerides or TG.

[0004] The NCEP ATPIII treatment guidelines identify HMG-CoA reductase inhibitors ("statins") as the primary treatment option for hypercholesterolemia. In patients with TG<500mg/dL, LDL-cholesterol is the primary treatment parameter. Many patients, however, have increased LDL-cholesterol combined with high TG and low HDL-cholesterol, a condition also known as mixed dyslipidemia. Patients with hypercholesteremia or mixed dyslipidemia often present with high blood levels of LDL-cholesterol (i.e. greater than 190 mg/dl) and TG (i.e. levels of 200 mg/dl or higher). The use of diet and single-drug therapy does not always decrease LDL-cholesterol and TG adequately enough to reach targeted values in patients with mixed dyslipidemia with or without a concomitant increase in triglycerides. In these patients, a combined therapy regimen of a statin and a second anti-dyslipidemic agent is often desired. This second agent has historically been a fibrate (i.e. gemfibrozil, bezafibrate, or fenofibrate) or extended release niacin. Over the few years, the use omega-3 fatty acid concentrates in combination with a statin has been

growing rapidly due to concerns about the lack of outcome benefits with fibrates (i.e. the FIELD study) or extended release niacin (i.e. the AIM-HIGH study). In patients with isolated hypertriglyceridemia, the use of omega-3 fatty acid concentrates has also grown versus fibrates and extended release niacin.

[0005] 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.

[0006] 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

[0007] 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.

[0008] 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.

[0009] 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.

[0010] 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.

[0011] 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.

[0012] For instance, in the MARINE study, it was found that four 1-gram capsules of AMR101/VASCEPA® significantly reduced fasting TG in patients with very high triglycerides (TG>500mg/dL) (March 2011, ACC poster reporting top-line results of the MARINE study), similar to four 1-gram capsules of LOVAZA® but in a less potent manner (LOVAZA® prescribing information, December 2010). In this same study, AMR101 slightly and non-significantly changed LDL-C while LOVAZA® shows a large significant increase in this same population, putting the latter at a disadvantage. Table A directly below compares these profiles.

Table A. Comparison of therapeutic profile of Lovaza and Vascepa in patients with very high triglycerides (>500 mg/dL)

	LOVAZA - 4 gram/day		Vascepa - 4 gram/day		Vascepa - 2 gram/day	
	% change vs. Placebo	p-value	% change vs. Placebo	p-value	% change vs. Placebo	p-value
TG	-51.6	p<0.05	-33.1	p<0.05	-19.7	p<0.05
Total-C	-8.0	p<0.05	-16.3	p<0.0001	-6.8	p=0.0148
LDL-C	49.3	p<0.05	-2.3	NS	5.2	NS
VLDL-C	-40.8	p<0.05	-28.6	p=0.0002	-15.3	p=.038
Non-HDL-C	-10.2	p<0.05	-17.7	p<0.0001	-8.1	p=.0182
Apo-B	NR		-8.5	p=0.0019	-2.6	NS
HDL-C	9.1	p<0.05	-3.6	NS	1.5	NS

NR = Not Reported; NS = Not Significant

[0013] In another study with AMR101/VASCEPA®, the ANCHOR study, it was found that four 1-gram capsules of AMR101 significantly reduced fasting TG in patients on statin therapy with high triglycerides (TG 200-499 mg/dL), similar to four 1-gram capsules of LOVAZA® but in a less potent manner (Study in table 3, LOVAZA® prescribing information, December 2010). In this same study, AMR101 decreased LDL-C at 4 gr/day while LOVAZA® shows a significant LDL-C increase in this same population. AMR101 is also more potent than LOVAZA® in reducing non-HDL-cholesterol in this population. Table B directly below compares these profiles.

Table B. Therapeutic profile comparison of Lovaza and Vascepa in patients on statin with high triglycerides (TG 200-499 mg/dL)

	LOVAZA - 4 gram/day		Vascepa - 4 gram/day		Vascepa - 2 gram/day	
	% change vs. Placebo	p-value	% change vs. Placebo	p-value	% change vs. Placebo	p-value
TG	-23.2	p<0.0001	-21.5	p<0.0001	-10.1	p=0.0005
Total-C	-3.1	p<0.05	NR	p<0.0001	NR	p=0.0019
LDL-C	3.5	p=0.05	-6.3	p=0.0067	-3.6	NS
VLDL-C	-20.3	p<0.05	-24.4	p<0.0001	-10.5	p=0.0093
Non-HDL-C	-6.8	p<0.0001	-13.6	p<0.0001	-5.5	p=0.0054
Apo-B	-2.3	p<0.05	-9.3	p<0.0001	-3.8	p=0.0170
HDL-C	4.6	p<0.05	-4.5	p=0.0013	-2.2	NS

NS = Not Significant

[0014] The resulting lipid profile of AMR101 versus LOVAZA® in highly similar patient populations indicates that there are significant benefits of using an almost pure EPA oil composition as opposed to an omega-3 mixture as in LOVAZA®. These benefits translate into better non-HDL- and LDL-Cholesterol reduction with the pure EPA form, where these benefits are less or, in the case of the LDL-C effect, the opposite.

The recently released results from Omthera's EVOLVE trial with EPANOVA™, in patients with very high triglycerides (TG ≥ 500 mg/dL), described a TG reduction of 31% versus baseline for the 4 gram per day dose and 26% versus baseline for the 2 gram per day dose, with 10% and 8% non-HDL reduction respectively. It appears that the TG-reducing potency of EPANOVA™ is similar to the potency of AMR101. No data were reported by Omthera on the LDL-C effect in the EVOLVE trial.

[0015] The recently released results from Omthera's ESPRIT trial with EPANOVA™, in patients with high triglycerides (TG 200-499 mg/dL) while on statin therapy, described a TG reduction of 21% versus baseline for the 4 gram per day dose and 15% versus baseline for the 2 gram per day dose, with 7% and 4% non-HDL reduction respectively. It appears that the TG-reducing potency of EPANOVA™ is similar to the potency of AMR101. No data were reported by Omthera on the LDL-C effect in the ESPRIT trial.

From the comparison of LOVAZA® versus AMR101 data, there appears to be a benefit of using pure EPA concentrates for dyslipidemia treatment over omega-3 mixtures with regard to LDL-Cholesterol and non-HDL-cholesterol effects. With the NCEP ATP III guidelines placing LDL-cholesterol and non-HDL-cholesterol reduction at the top of the treatment hierarchy for patients with TG<500 mg/dL, AMR101 is clearly superior to LOVAZA® in this patient category.

[0016] In the ECLIPSE study it is found that EPANOVA™ is significantly more bioavailable than LOVAZA® after single dose administration (four capsules of 1 gram for both products), both by Cmax (maximum concentration) and AUC (area under curve) measures (see Table C below, where Cmax and AUC are estimated from the data points in Figures 1 and 2). Relative to LOVAZA® under high fat meal conditions, EPANOVA™ is 1.17 x more bioavailable by Cmax and 1.27 by AUC comparison. Under low fat meal conditions, LOVAZA® has only 15% AUC and 12%

Cmax of the bioavailability versus LOVAZA® under high fat meal conditions, whereas EPANOVA™ under low fat meal conditions has 78% AUC and 53% Cmax of the bioavailability versus LOVAZA® under high fat meal conditions. EPANOVA™ under low fat meal conditions has 62% AUC and 46% Cmax of the bioavailability versus EPANOVA™ under high fat meal conditions.

Table C. Comparison of bioavailability of EPA+DHA in Plasma for Lovaza (4g) and Epanova (4g) under high-fat and low-fat meal dosing conditions

	LOVAZA - High Fat	LOVAZA - Low Fat	Epanova - High Fat	Epanova - Low Fat
Cmax EPA+DHA	385 nmol/ml	45 nmol/ml	450 nmol/ml	205 nmol/ml
Est. AUC,0-24 EPA+DHA	3080 nmol*hr/ml	465 nmol*hr/ml	3920 nmol*hr/ml	2415 nmol*hr/ml
Tmax EPA+DHA	5 hrs	10 hrs	5 hrs	5 hrs
Multiple of Lovaza-HF AUC	1.00 x	0.15 x	1.27 x	0.78 x
Multiple of LF vs. HF AUC	NA	0.15 x Lovaza-HF AUC	NA x	0.62 x Epanova-HF AUC
Multiple of Lovaza-HF Cmax	1.00 x	0.12 x	1.17 x	0.53 x
Multiple of LF vs. HF Cmax	NA	0.12 x Lovaza-HF Cmax	NA x	0.46 x Epanova-HF Cmax
Low fat meal - AUC vs. Lov.	NA	1.00 x	NA	5.19 x
Low fat meal - Cmax vs. Lov.	NA	1.00 x	NA	4.56 x
High fat meal - AUC vs. Lov.	1.00 x	NA	1.27 x	NA
High fat meal - Cmax vs. Lov.	1.00 x	NA	1.17 x	NA

[0017] 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).

[0018] 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.

[0019] 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.

[0020] 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.

[0021] 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.

[0022] 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.

[0023] Given the highly beneficial efficacy and side-effect profile of omega-3 fatty acid concentrates, these compositions are increasingly popular for the treatment of patients with dyslipidemias. However, with the increased popularity of omega-3 fatty acid concentrates, there is an unmet medical need for omega-3 fatty acid containing compositions with improved bioavailability and absorption and a more optimal ratio of potency in reducing TG versus the resulting cholesterol profile. Specifically, agents with both a higher potency than AMR101/EPADEL® and lesser increase in LDL-C or further decrease in LDL-C and non-HDL-C than LOVAZA® are required.

SUMMARY OF THE INVENTION

[0024] The present invention provides fatty acid compositions comprising at least 81% of omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of total fatty acids and

docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of total fatty acids, while comprising no more than 6% omega-6 fatty acids. The compositions can be used for the treatment or prophylaxis of cardiovascular, CNS, inflammatory, and other diseases/conditions or risk factors therefore. These compositions have an improved profile versus pure EPA compositions which are almost free of DHA and omega-6 fatty acids. These compositions also have an improved profile versus compositions containing EPA:DHA in ratios less than 8:1 and compositions which have omega-3:omega-6 fatty acid ratios of less than 20:1.

DETAILED DESCRIPTION OF THE INVENTION

[0025] The present invention provides fatty acid compositions comprising at least 81% of omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.

[0026] The EPA is preferably composed as a triglyceride, ethyl ester or free fatty acid which is present at 80% and 95% of total fatty acids. Other forms of the fatty acids which may be useful include the free acids, salts, esters of any type (including ethyl ester), amides, mono-, di- or triglycerides, phospholipids or any other form which can lead to metabolization of EPA or the incorporation of EPA into body fluids, tissues or organs.

[0027] The DHA is preferably composed as a triglyceride, ethyl ester or free fatty acid which is present at a relative amount between 1% and 10% of total fatty acids. Other forms of the fatty acids which may be useful include the free acids, salts, esters of any type (including ethyl ester), amides, mono-, di- or triglycerides, phospholipids or any other form which can lead to metabolization of DHA or the incorporation of DHA into body fluids, tissues or organs.

[0028] In some embodiments, the compositions of the present invention comprise no more than 6% omega-6 fatty acids relative to total fatty acids, more preferably no more than 5%, more preferably no more than 4.5%, more preferably no more than 4%, more preferably no more than 3.5%, more preferably no more than 3%, more

preferably no more than 2.5%, most preferably no more than 2% omega-6 fatty acids.

[0029] 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 (AA; C20:4-n6); and docosapentaenoic acid (DPA; C22:5-n6).

[0030] In other embodiments, the present invention provides fatty acid compositions comprising at least 81% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of total fatty acids, while preferably comprising no more than 4.5% arachidonic acid (AA; C20:4-n6), more preferably no more than 4%, more preferably no more than 3.5%, more preferably no more than 3%, more preferably no more than 2.5%, more preferably no more than 2.25%, most preferably no more than 2% arachidonic acid (AA; C20:4-n6).

[0031] Further embodiments provide fatty acid compositions comprising at least 81% of omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of total fatty acids, while comprising no more than 2.5% arachidonic acid (AA; 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).

[0032] Yet other embodiments provide fatty acid compositions comprising at least 81% of omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of total fatty acids, while comprising no more than 2.5% arachidonic acid (AA; 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).

[0033] In some embodiments, the compositions of the present invention comprise at least 80% eicosapentaenoic acid (EPA; C20:5-n3), more preferably more than

85%, more preferably more than 88%, more preferably 80% to 95%, more preferably 85% to 95%, more preferably 88% to 95%, more preferably 89% to 94%, more preferably 89% to 95%, more preferably 90% to 94%, more preferably 90% to 95%, most preferably more than 90% eicosapentaenoic acid (EPA; C20:5-n3).

[0034] In other embodiments, the compositions of the present invention comprise between 1% and 10% docosahexaenoic acid (DHA; C22:6-n3), more preferably between 2% and 10%, more preferably between 3% and 10%, more preferably between 4% and 8%, more preferably between 5% and 10%, more preferably between 5% and 8%, more preferably between 1% and 8%, more preferably between 2% and 8%, more preferably between 3% and 8%, more preferably between 4% and 8%, more preferably between 5% and 8%, more preferably between 1% and 7%, more preferably between 2% and 7%, more preferably between 3% and 7%, more preferably between 4% and 7%, more preferably between 1% and 6%, more preferably between 2% and 6%, more preferably between 3% and 6%, more preferably between 1% and 5%, more preferably between 2% and 5%, more preferably between 3% and 5%, more preferably between 1% and 4%, more preferably between 2% and 4%, more preferably between 1% and 3%, most preferably between 2% and 3% docosahexaenoic acid (DHA; C22:6-n3).

[0035] Still preferably, the active ingredient of the formulations of the present invention consists essentially wholly of the EPA and DHA or precursors thereof (ethyl ester, triglyceride, or any other pharmaceutically acceptable salt or derivative thereof). In that case, no significant amounts (preferably any amount above 1%, more preferably above 0.5%, most preferably 0.25%) of other omega-3 or omega-6 fatty acids are present.

[0036] The fatty acid percentage is determined on a weight/weight, mol/mol, or 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, or any

essentially equivalent methods (whether by gas chromatography, HPLC, FPLC or any other chromatographic method).

[0037] 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).

[0038] 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).

[0039] 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).

[0040] 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).

[0041] 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).

[0042] The compositions of the present invention is 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.

[0043] Typically, the omega-3 fatty acid concentration/purification process is initiated by esterifying the marine oil raw material (such as crude fish oil) in order to separate omega-3 fatty acids from other fatty acids 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 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 80% of a single omega-3 fatty acid such as EPA or DHA.

[0044] 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 upgrading of the individual 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 it will be possible to make a product with a constant and predetermined composition.

[0045] Fish oils may also contain by-products and contaminants such as pesticides, chlorinated 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.

[0046] Triglycerides comprising more than 60% omega-3 fatty acids may be produced from ethyl esters and glycerol by well known 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.

[0047] The compositions of the present invention have an improved profile versus pure EPA compositions which are almost free of DHA (EPA:DHA ratios more than 50:1, more preferably more than 100:1) and omega-6 fatty acids (omega-3:omega-6 fatty acid ratios more than 100:1, more preferably more than 200:1).

[0048] The compositions of the present invention also have an improved profile versus compositions containing EPA:DHA in ratios less than 8:1 (or EPA:DHA ratios less than 15:1 in alternative embodiments) and compositions which have omega-3:omega-6 fatty acid ratios of less than 20:1(omega-3:omega-6 fatty acid ratios of less than 30:1 in alternative embodiments).

[0049] In some embodiments, the compositions of the present invention have improved pharmacological features as demonstrated by improved bioavailability in a mammal of EPA, DHA, or EPA+DHA combined. 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. When comparing Tmax, Cmax, and AUC for embodiments of the present invention to LOVAZA®, EPANOVA®, and VASCEPA® (also known as AMR101) throughout this application, such comparison will be on the basis of an equal dose of 4 capsules of 1 gram each for each of these products. The comparative parameters, however, do apply to all essentially equivalent dosing modes comparing embodiments of the present invention to LOVAZA®, EPANOVA®, and VASCEPA®.

[0050] Meal conditions during administration to a subject of omega-3 fatty acid compositions or omega-3 fatty acid formulations are 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 6-8 hours prior to administration and 2-3 hours post administration of the treatment); a low fat meat (a meal containing 5 gram to 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).

[0051] 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, DHA, EPA+DHA, 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, more preferably less than 6 hours, more preferably approximately 5 hours, most preferably 4 hours or less. In other preferred embodiments of the present invention, Tmax under low fat meal administration conditions is less than 8 hours, more preferably less than 6 hours, more preferably approximately 5 hours, most preferably 4 hours or less. In yet

other preferred embodiments of the present invention, Tmax under fasting administration conditions is less than 8 hours, more preferably less than 6 hours, more preferably approximately 5 hours, most preferably 4 hours or less. In further embodiments of the present invention, Tmax for EPA+DHA and total omega-3 fatty acids are equal or less than than Tmax for LOVAZA® for EPA+DHA and total omega-3 fatty acids under high fat meat, low fat meal, and fasting administration conditions. In other embodiments of the present invention, Tmax for EPA+DHA and total omega-3 fatty acids are less than Tmax for LOVAZA®for EPA+DHA and total omega-3 fatty acids under either low fat meal, fasting, or both administration conditions.

[0052] In yet other embodiments of the present invention, Tmax for EPA+DHA and total omega-3 fatty acids are equal or less than Tmax for VASCEPA® for EPA+DHA and 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+DHA and total omega-3 fatty acids are less than Tmax for VASCEPA® for EPA+DHA and total omega-3 fatty acids under either low fat meal, fasting, or both administration conditions.

[0053] In other embodiments of the present invention, compositions of the present invention are better absorbed than LOVAZA® as measured by the maximum concentration (Cmax) in blood, serum or plasma of EPA, DHA, EPA+DHA, or total omega-3 fatty acids.

[0054] In preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under high fat meal administration conditions are preferably at least 1.1 x (110% of) Cmax for EPA+DHA and total omega-3 fatty acids for LOVAZA®, more preferably at least 1.2 x (120% of), more preferably at least 1.3 x (130% of), more preferably at least 1.4 x (140% of), most preferably at least 1.5 x (150% of) Cmax for EPA+DHA and total omega-3 fatty acids for LOVAZA®.

[0055] In other preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under low fat meal administration conditions are preferably at least 1.5 x (150% of) Cmax for EPA+DHA and total omega-3 fatty acids for LOVAZA®, more preferably at least 2 x (200% of), more preferably at least

3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), most preferably at least 6 x (600% of) Cmax for EPA+DHA and total omega-3 fatty acids for LOVAZA®.

[0056] In other preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under fasting administration conditions are preferably at least 1.5 x (150% of) Cmax for EPA+DHA and total omega-3 fatty acids for LOVAZA®, more preferably at least 2 x (200% of), more preferably at least 3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), more preferably at least 6 x (600% of), most preferably at least 7 x (700% of) Cmax for EPA+DHA and total omega-3 fatty acids for LOVAZA®.

[0057] In other embodiments of the present invention, compositions of the present invention are better absorbed than LOVAZA®as measured by the area under the concentration curve over time (AUC) in blood, serum or plasma of EPA, DHA, EPA+DHA, or total omega-3 fatty acids.

[0058] In preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under high fat meal administration conditions are preferably at least 1.1 x (110% of) AUC for EPA+DHA and total omega-3 fatty acids for LOVAZA®, more preferably at least 1.2 x (120% of), more preferably at least 1.3 x (130% of), more preferably at least 1.4 x (140% of), most preferably at least 1.5 x (150% of) AUC for EPA+DHA and total omega-3 fatty acids for LOVAZA®.

[0059] In other preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under low fat meal administration conditions are preferably at least 1.5 x (150% of) AUC for EPA+DHA and total omega-3 fatty acids for LOVAZA®, more preferably at least 2 x (200% of), more preferably at least 3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), most preferably at least 6 x (600% of) AUC for EPA+DHA and total omega-3 fatty acids for LOVAZA®.

[0060] In other preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under fasting administration conditions are preferably at least 1.5 x (150% of) AUC for EPA+DHA and total omega-3 fatty acids for LOVAZA®, more preferably at least 2 x (200% of), more preferably at least 3 x

(300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), more preferably at least 6 x (600% of), most preferably at least 7 x (700% of) AUC for EPA+DHA and total omega-3 fatty acids for LOVAZA®.

[0061] In other embodiments of the present invention, compositions of the present invention are better absorbed than VASCEPA® as measured by the maximum concentration (Cmax) in blood, serum or plasma of EPA, DHA, EPA+DHA, or total omega-3 fatty acids.

[0062] In preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under high fat meal administration conditions are preferably at least 1.1 x (110% of) Cmax for EPA+DHA and total omega-3 fatty acids for AMR101, more preferably at least 1.2 x (120% of), more preferably at least 1.3 x (130% of), more preferably at least 1.4 x (140% of), most preferably at least 1.5 x (150% of) Cmax for EPA+DHA and total omega-3 fatty acids for VASCEPA®.

[0063] In other preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under low fat meal administration conditions are preferably at least 1.5 x (150% of) Cmax for EPA+DHA and total omega-3 fatty acids for AMR101, more preferably at least 2 x (200% of), more preferably at least 3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), most preferably at least 6 x (600% of) Cmax for EPA+DHA and total omega-3 fatty acids for AMR101.

[0064] In other preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under fasting administration conditions are preferably at least 1.5 x (150% of) Cmax for EPA+DHA and total omega-3 fatty acids for VASCEPA®, more preferably at least 2 x (200% of), more preferably at least 3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), more preferably at least 6 x (600% of), most preferably at least 7 x (700% of) Cmax for EPA+DHA and total omega-3 fatty acids for VASCEPA®.

[0065] In other embodiments of the present invention, compositions of the present invention are better absorbed than VASCEPA® as measured by the area under the concentration curve over time (AUC) in blood, serum or plasma of EPA, DHA, EPA+DHA, or total omega-3 fatty acids.

[0066] In preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under high fat meal administration conditions are preferably at least 1.1 x (110% of) AUC for EPA+DHA and total omega-3 fatty acids for VASCEPA®, more preferably at least 1.2 x (120% of), more preferably at least 1.3 x (130% of), more preferably at least 1.4 x (140% of), most preferably at least 1.5 x (150% of) AUC for EPA+DHA and total omega-3 fatty acids for VASCEPA®.

[0067] In other preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under low fat meal administration conditions are preferably at least 1.5 x (150% of) AUC for EPA+DHA and total omega-3 fatty acids for VASCEPA®, more preferably at least 2 x (200% of), more preferably at least 3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), most preferably at least 6 x (600% of) AUC for EPA+DHA and total omega-3 fatty acids for VASCEPA®.

[0068] In other preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under fasting administration conditions are preferably at least 1.5 x (150% of) AUC for EPA+DHA and total omega-3 fatty acids for VASCEPA®, more preferably at least 2 x (200% of), more preferably at least 3 x (300% of), more preferably at least 4 x (400% of), more preferably at least 5 x (500% of), more preferably at least 6 x (600% of), most preferably at least 7 x (700% of) AUC for EPA+DHA and total omega-3 fatty acids for VASCEPA®.

[0069] In other embodiments of the present invention, compositions of the present invention are better absorbed than EPANOVA® as measured by the maximum concentration (Cmax) in blood, serum or plasma of EPA, DHA, EPA+DHA, or total omega-3 fatty acids.

[0070] In preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under high fat meal administration conditions are preferably approximately 1.0 x (100% of) Cmax (or non-significant difference) for EPA+DHA and total omega-3 fatty acids for EPANOVA®, more preferably at least 1.05 x (105% of), more preferably at least 1.1 x (110% of), more preferably at least 1.2 x (120% of), most preferably at least 1.3 x (130% of) Cmax for EPA+DHA and total omega-3 fatty acids for EPANOVA®. In other preferred embodiments of the present invention,

Cmax for EPA+DHA and total omega-3 fatty acids under low fat meal administration conditions are preferably approximately 1.0 x (100% of) Cmax (or non-significant difference) for EPA+DHA and total omega-3 fatty acids for EPANOVA®, more preferably at least 1.05 x (105% of), more preferably at least 1.1 x (110% of), more preferably at least 1.2 x (120% of), most preferably at least 1.3 x (130% of) Cmax for EPA+DHA and total omega-3 fatty acids for EPANOVA®.

[0071] In other preferred embodiments of the present invention, Cmax for EPA+DHA and total omega-3 fatty acids under fasting administration conditions are preferably approximately 1.0 x (100% of) Cmax (or non-significant difference) for EPA+DHA and total omega-3 fatty acids for EPANOVA®, more preferably at least 1.05 x (105% of), more preferably at least 1.1 x (110% of), more preferably at least 1.2 x (120% of), most preferably at least 1.3 x (130% of) Cmax for EPA+DHA and total omega-3 fatty acids for EPANOVA®.

[0072] In other embodiments of the present invention, compositions of the present invention are better absorbed than EPANOVA® as measured by the area under the concentration curve over time (AUC) in blood, serum or plasma of EPA, DHA, EPA+DHA, or total omega-3 fatty acids.

[0073] In preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under high fat meal administration conditions are preferably approximately 1.0 x (100% of) AUC (or non- significant difference) for EPA+DHA and total omega-3 fatty acids for EPANOVA®, more preferably at least 1.05 x (105% of), more preferably at least 1.1 x (110% of), more preferably at least 1.2 x (120% of), most preferably at least 1.3 x (130% of) AUC for EPA+DHA and total omega-3 fatty acids for EPANOVA®.

[0074] In other preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under low fat meal administration conditions are preferably approximately 1.0 x (100% of) AUC (or non-significant difference) for EPA+DHA and total omega-3 fatty acids for EPANOVA®, more preferably at least 1.05 x (105% of), more preferably at least 1.1 x (110% of), more preferably at least 1.2 x (120% of), most preferably at least 1.3 x (130% of) AUC for EPA+DHA and total omega-3 fatty acids for EPANOVA®.

[0075] In other preferred embodiments of the present invention, AUC for EPA+DHA and total omega-3 fatty acids under fasting administration conditions are preferably approximately 1.0 x (100% of) AUC (or non- significant difference) for EPA+DHA and total omega-3 fatty acids for EPANOVA®, more preferably at least 1.05 x (105% of), more preferably at least 1.1 x (110% of), more preferably at least 1.2 x (120% of), most preferably at least 1.3 x (130% of) AUC for EPA+DHA and total omega-3 fatty acids for EPANOVA®.

[0076] 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.

[0077] 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 prone to or afflicted with such disease (or in need of treatment for its disease or condition), and wherein the disease/condition is an amenable disease/condition selected from the group consisting of: hypertriglyceridemia; hypercholesterolemia; mixed dyslipidemia; coronary heart disease (CHD); vascular disease; atherosclerotic disease and related conditions; heart failure; cardiac arrhythmias; ischemic dementia; hypertension; coagulation related disorders; nephropathy; kidney or urinary tract disease; retinopathy; cognitive, psychiatric, neurological and other CNS disorders, including but not limited to schizophrenia, depression, bipolar disorder and any form of dementia; autoimmune diseases; inflammatory diseases; asthma, COPD or other respiratory disease; dermatological disease; metabolic syndrome; diabetes or other forms of metabolic disease; liver diseases including fatty liver disease; diseases affecting the senses, including those affecting vision and hearing; diseases of the gastrointestinal tract; diseases of the male or female reproductive system or related secondary sexual organs; a cancer; any infections caused by a virus, bacterium, fungus, protozoa or other organism; and the treatment and/or prevention and/or reduction of cardiac events and/or cardiovascular events and/or vascular events and/or symptoms.

[0078] Cardiovascular and/or cardiac events may include, but are not limited to: myocardial infarction, ischemic cardiac attack, ischemic attack, acute angina, hospitalization due to acute angina, stroke, transient ischemic cerebral attack, cardiac revascularization, cardiac revascularization with stent placement, carotid artery revascularization, carotid artery revascularization with stent placement, peripheral artery revascularization, peripheral artery revascularization with stent placement, plaque rupture, death due to cardiovascular event, and hospitalization due to cardiovascular event.

[0079] The improved profile of the compositions of the present invention may also be demonstrated by a differentiated impact on blood/serum/plasma lipid and lipoprotein levels in a mammal; these include, but are not limited to: TG, total-cholesterol, non-HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, Apolipoprotein B, Apolipoprotein A, HDL-cholesterol, and Lp-PLA2. Methods to determine comparative blood/serum/plasma lipid and lipoprotein levels and therapeutic effects on these levels in mammals are generally know to those skilled in the art. Differences of active treatment versus placebo are generally assessed on a group of subjects versus another group of subjects basis, with significant changes noted if the p-value for the appropriate statistical comparison is equal to or less than 0.05. P-values larger than 0.05 are generally considered not significant (NS).

[0080] In one embodiment, the compositions of the present invention as compared to placebo are more potent than other omega-3 compositions known in the prior art (such as LOVAZA®, EPANOVA®, or VASCEPA®) in reducing: TG levels, Total-cholesterol levels, non-HDL-cholesterol levels, VLDL-cholesterol levels, apolipoprotein-B levels, or combinations thereof.

[0081] In another embodiment, the compositions of the present invention as compared to placebo result in minor or non-significant changes in LDL-cholesterol levels in patients with baseline TG levels above 500 mg/dL. In yet another embodiment, the formulations of the present invention as compared to placebo result in significant reductions in LDL-cholesterol levels in patients with baseline TG levels of 200-499 mg/dL while on statin therapy.

[0082] In yet another embodiment, the compositions of the present invention as compared to placebo are more potent than other omega-3 compositions known in the prior art (such as LOVAZA®, EPANOVA®, or VASCEPA®) in increasing HDL-cholesterol levels, apolipoprotein-A levels, or a combination thereof.

[0083] In yet other embodiments, the compositions of the present invention as compared to placebo are more potent than other omega-3 compositions known in the prior art (such as LOVAZA®, EPANOVA®, or VASCEPA®) in reducing TG while causing a lesser increase in LDL-cholesterol, a lesser non-significant increase in LDL- cholesterol, or no increase in LDL-cholesterol at all in patients with baseline TG levels above 500 mg/dL.

[0084] The compositions of the present invention are also useful to treat coronary heart disease (CHD), vascular disease, atherosclerotic disease or related conditions. The compositions of the present invention may also be use for the treatment and/or prevention and/or reduction of cardiac events and/or cardiovascular events and/or vascular events and/or symptoms. Determination of such cardiovascular diseases/conditions and prevention of events/symptoms in mammals and methods to determine treatment and preventative/therapeutic effects therefore are generally know to those skilled in the art.

[0085] The present invention also relates to treatment of such conditions in with concomitant treatments regimes or combination products with other active pharmaceutical ingredients. Such concomitant or fixed combination treatments may include a statin, an anticoagulant (such as aspirin or clopidogrel), an anti hypertensive (such as a diuretic, beta-blocker, calcium channel blocker, ACE-inhibitor, angiotensin II receptor (ARB) antagonist, or other treatments for cardiovascular diseases.

[0086] The present invention also includes pharmaceutical compositions, for example, a unit dosage, comprising one or more statins and the omega-3 fatty acid composition of the present invention. The present invention may incorporate now known or future known statins in an amount generally recognized as safe. There are currently seven statins that are widely available: atorvastatin, rosuvastatin, fluvastatin, lovastatin, pravastatin, pitavastatin, and simvastatin. A eight statin,

cerivastatin, has been removed from the U.S. market at the time of this writing. However, it is conceivable to one skilled in the art that cerivastatin may be used in conjunction with some embodiments of the present invention if cerivastatin is ultimately determined to be safe and effective.

[0087] Generally, the effect of statins is dose dependent, i.e., the higher the dose, the greater the therapeutic effect. However, the effect of each statin is different, and therefore the level of therapeutic effect of one statin cannot be necessarily be directly correlated to the level of therapeutic effects of other statins. For example, bioavailability varies widely among the statins. Specifically, it has been shown that simvastatin is less than 5% bioavailable, while fluvastatin is approximately 24% bioavailable. Statins are absorbed at rates ranging from about 30% with lovastatin to 98% with fluvastatin. First-pass metabolism occurs in all statins except pravastatin. Pravastatin is also the least protein-bound of the statins (about 50%), compared with the others, which are more than 90% protein-bound. Accordingly, the statins possess distinct properties from one another. The combination products of this invention involving each statin or a plurality of statins are also distinct.

[0088] The compositions of the present invention may also be taken as a general nutritional supplement.

[0089] The EPA, as the most prevalent component of the omega-3 composition, is preferably provided in a dose of between 100 mg and 10,000 mg/day, more preferably between 200 mg and 8,000 mg/day, more preferably between 300 mg and 6,000 mg/day, more preferably between 400 mg and 5,000 mg/day, most preferably between 500 mg and 4,000 mg/day.

[0090] 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 300-1000 mg of EPA in an appropriate form

[0091] 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, 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.

[0092] 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.

[0093] The EPA and DHA 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. 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.

[0094] Once the oils containing one or more of the desired fatty acids have been obtained, and purified as necessary, the starting materials may be blended to give the desirable ratios of EPA to DHA and omega- 6 fatty acids described above.

[0095] 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.

[0096] 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.

[0097] 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.

[0098] 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 DHA as a free fatty acid; (b) As in (a) but where the EPA and DHA 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.

[0099] 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.

[0100] 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 (e.g., an emulsion, cream, etc.).

[0101] 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, more preferably at least one year, and most preferably 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.

[0102] 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.

[0103] EXAMPLES

[0104] Example 1

[0105] A composition according to the present prevention is prepared by mixing and homogenizing the intermediates Megapex E90D00EE and Megapex D80EE in a ratio of 88:12. Both intermediates were prepared and commercially offered for sale by Chemport Korea. The relative amounts of fatty acids present in the resulting novel composition is listed in table 1 below. This composition comprises 80.66% EPA, 9.97% DHA, 92.83% total omega-3 fatty acids and 3.95% omega-6 fatty acids (all Area%).

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

Fatty Acid	Megapex E90D00EE	Megapex D80EE	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	0.03
c18:4n3	0.42	0.06	0.38
c18:4n1	0.07	0	0.06
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	0.22
c20:3n9	0	0	0.00
c20:3n6	0.15	0	0.13
c21:0	0	0	0.00
c20:4n6	3.21	1.31	2.98
c20:3n3	0	0	0.00
c20:4n3	1.44	0.14	1.28
c20:5n3	90.92	5.44	80.66
c22:0	0.3	0	0.26
c22:1n11	0.07	0	0.06
c22:1n9	0.18	0	0.16
c22:1n7	0.19	0	0.17
c21:5n3	0.19	0.37	0.21
c22:5n6	0	4.89	0.59
c22:5n3	0	2.43	0.29
c22:6n3	0	83.12	9.97
OTHER	2.42	2.24	2.40
	100	**100**	**100**

[0106] Example 2

[0107] A composition according to the present prevention is prepared by mixing and homogenizing the intermediates Megapex E90D00EE and Megapex D80EE in a ratio of 97:3. Both intermediates were prepared and commercially offered for sale by Chemport Korea. The relative amounts of fatty acids present in the resulting novel composition is listed in table 2 below. This composition comprises 88.36% EPA, 2.49% DHA, 92.96% total omega-3 fatty acids and 3.72% omega-6 fatty acids (all Area%).

Table 2. Fatt y acid Compositi on (%) of intermediates and novel compositi on according to Examp

Fatt y Acid	Megapex E90D00EE	Megapex D80EE	Novel Compositi on
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	0.06	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	0.24
c20:3n9	0	0	0.00
c20:3n6	0.15	0	0.15
c21:0	0	0	0.00
c20:4n6	3.21	1.31	3.15
c20:3n3	0	0	0.00
c20:4n3	1.44	0.14	1.40
c20:5n3	90.92	5.44	88.36
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	0.37	0.20
c22:5n6	0	4.89	0.15
c22:5n3	0	2.43	0.07
c22:6n3	0	83.12	2.49
OTHER	2.42	2.24	2.41
	100	**100**	**100**

[0108] Example 3

[0109] A composition according to the present prevention is prepared by mixing and homogenizing the intermediates Megapex E90D00EE and Megapex D80EE in a ratio of 97:3. Both intermediates were prepared and commercially offered for sale by Chemport Korea. The relative amounts of fatty acids present in the resulting novel composition is listed in table 3 below. This composition comprises 88.78% EPA, 2.08% DHA, 92.96% total omega-3 fatty acids and 3.70% omega-6 fatty acids (all Area%).

Table 3. Fatt y acid Compositi on (%) of intermediates and novel compositi on according to Examp

Fatt y Acid	Megapex E90D00EE	Megapex D80EE	Novel Compositi on
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	0.06	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	0.24
c20:3n9	0	0	0.00
c20:3n6	0.15	0	0.15
c21:0	0	0	0.00
c20:4n6	3.21	1.31	3.16
c20:3n3	0	0	0.00
c20:4n3	1.44	0.14	1.41
c20:5n3	90.92	5.44	88.78
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	0.37	0.19
c22:5n6	0	4.89	0.12
c22:5n3	0	2.43	0.06
c22:6n3	0	83.12	2.08
OTHER	2.42	2.24	2.42
	100	**100**	**100**

[0110] Example 4

[0111] The ethyl ester composition of Example 1 is 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 maybe necessary to control pressure to event 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 (~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 other excipients.
8. All reagents and excipients USP grade.

[0112] Example 5

[0113] The ethyl ester composition of Example 2 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.

[0114] Example 6

[0115] 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.

[0116] Example 7

[0117] The composition of Example 4 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti- oxidant preparation (composed of 200 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 20mL of this anti-oxidant preparation into one liter 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. The fill mass of the oil is 1.28 gram/capsule, providing a dose of approximately 1000mg eicosapentaenoic acid per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

[0118] Example 8

[0119] The composition of Example 5 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti- oxidant preparation (composed of 200 mg

alpha-D-tocopherol in one liter of corn oil; corn oil is a triglyceride low in omega-3 fatty acids) is added to the composition of Example 5, by mixing and homogenizing 20mL of this anti-oxidant preparation into one liter of the oil composition of Example 5 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. The fill mass of the oil is 1.17 gram/capsule, providing a dose of approximately 1000mg eicosapentaenoic acid per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

[0120] Example 9

[0121] The composition of Example 3 is formulated into a soft gelatin capsule. Prior to encapsulation, an anti- oxidant preparation (composed of 200 mg alpha-D-tocopherol in one liter of corn oil; corn oil is a triglyceride low in omega-3 fatty acids) is added to the composition of Example 3, by mixing and homogenizing 20mL of this anti-oxidant preparation into one liter of the oil composition of Example 3 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. The fill mass of the oil is 1.16 gram/capsule, providing a dose of approximately 1000mg ethyl eicosapentaenoate per capsule. Finally, the capsules are bottled in HDPE bottles with induction seal and child resistant cap.

[0122] Example 10

[0123] A patient is diagnosed with severe hypertriglyceridemia (TG>500mg/dL). Thereupon, the patient is initiated on daily treatment with one of the encapsulated compositions according to Examples 7, 8 or 9 is. Four capsules per day are administered to this patient, resulting in a daily dose of 4000mg eicosapentaenoic acid (Examples 7 or 8) or ethyl eicosapentaenoate (Example 9).

[0124] Example 11

[0125] A patient is treated as per Example 10. The treatment results in significant reduction of TG as well as non-HDL- and VLDL-cholesterol levels while the LDL-cholesterol level changes insignificantly.

[0126] Example 12

[0127] A patient already undergoing treatment with a statin is diagnosed with high triglycerides (TG between 200 and 500mg/dL). Thereupon, the patient is initiated on daily treatment with one of the encapsulated compositions according to Examples 7, 8 or 9 is. Four capsules per day are administered to this patient, resulting in a daily dose of 4000mg eicosapentaenoic acid (Examples 7 or 8) or ethyl eicosapentaenoate (Example 9).

[0128] Example 13

[0129] A patient is treated as per Example 12. The treatment results in significant reduction of TG as well as non-HDL-, VLDL- and LDL-cholesterol levels.

[0130] Example 14

[0131] A patient is diagnosed with mixed dyslipidemia (TG between 200 and 500mg/dL and LDL-cholesterol above 190mg/d L). Thereupon, the patient is initiated on concomitant daily treatment with a statin and one of the encapsulated compositions according to Examples 7, 8 or 9 is. Four capsules per day are administered to this patient, resulting in a daily dose of 4000mg eicosapentaenoic acid (Examples 7 or 8) or ethyl eicosapentaenoate (Example 9).

[0132] Example 15

[0133] A patient is treated as per Example 12. The treatment results in significant reduction of TG as well as non-HDL-, VLDL- and LDL-cholesterol levels.

[0134] Example 16

[0135] A patient is diagnosed to be at high risk for a cardiovascular event according to the NCEP guidelines and has TG levels above 150mg/dL . Thereupon, the patient is initiated on daily treatment with one of the encapsulated compositions according to Examples 7, 8 or 9 is. Four capsules per day are administered to this patient, resulting in a daily dose of 4000mg eicosapentaenoic acid (Examples 7 or 8) or ethyl eicosapentaenoate (Example 9).

[0136] Example 17

[0137] A patient is treated as per Example 12. The treatment results in significant reduction of TG as well as non-HDL-, VLDL- and LDL-cholesterol levels.

[0138] Example 18

[0139] A patient diagnosed as per Example 10, 12, 14, or 16 is treated with 3 capsules per day (instead of 4) of one of the encapsulated compositions according to Examples 7, 8 or 9. The treatment results in significant reduction of TG as well as non-HDL- and VLDL-cholesterol levels.

[0140] Example 19

[0141] A patient diagnosed as per Example 10, 12, 14, or 16 is treated with 2 capsules per day (instead of 3 or 4) of one of the encapsulated compositions according to Examples 7, 8 or 9. The treatment results in significant reduction of TG as well as non-HDL- and VLDL-cholesterol levels.

[0142] Throughout this application, various patents and publications have been cited. The disclosures of these patents and publications in their entireties are hereby incorporated by reference into this application, in order to more fully describe the state of the art to which this invention pertains.

[0143] The invention is capable of considerable modification, alteration, and equivalents in form and function, as will occur to those ordinarily skilled in the pertinent arts having the benefit of this disclosure.

[0144] While the present invention has been described for what are presently considered the preferred embodiments, the invention is not so limited. To the contrary, the invention is intended to cover various modifications and equivalent arrangements included within the spirit and scope of the detailed description provided above. Therefore, the scope of the appended claims should be accorded the broadest interpretation so as to encompass all such modification.

[0145] DESCRIPTION OF THE EXEMPLARY EMBODIMENTS

1. A fatty acid composition comprising at least 81% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at least 80% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.

2. A fatty acid composition comprising at least 82% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at least 80% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 10% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
3. A fatty acid composition comprising at least 81% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 10% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
4. A fatty acid composition comprising at least 82% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 80% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 10% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
5. A fatty acid composition comprising at least 86% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 85% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 8% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
6. A fatty acid composition comprising at least 87% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 85% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 8% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
7. A fatty acid composition comprising at least 89% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 8% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.

8. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 8% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
9. A fatty acid composition comprising at least 91% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 90% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 8% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
10. A fatty acid composition comprising at least 92% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 90% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 8% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
11. A fatty acid composition comprising at least 89% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 6% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
12. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 6% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
13. A fatty acid composition comprising at least 89% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 4% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.
14. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at

between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 4% of the total fatty acids, while comprising no more than 6% omega-6 fatty acids.

15. A fatty acid composition comprising at least 89% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 6% of the total fatty acids, while comprising no more than 4% omega-6 fatty acids.
16. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 6% of the total fatty acids, while comprising no more than 4% omega-6 fatty acids.
17. A fatty acid composition comprising at least 89% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 6% of the total fatty acids, while comprising no more than 2.5% arachidonic acid (AA; C20:4-n6).
18. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 2% and 6% of the total fatty acids, while comprising no more than 2.5% arachidonic acid (AA; C20:4-n6).
19. A fatty acid composition comprising at least 89% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA; C22:6-n3) comprises between 1% and 6% of the total fatty acids, while comprising no more than 2.0% arachidonic acid (AA; C20:4-n6).
20. A fatty acid composition comprising at least 90% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA; C20:5-n3) comprises at between 88% and 95% of the total fatty acids and docosahexaenoic acid (DHA;

C22:6-n3) comprises between 2% and 6% of the total fatty acids, while comprising no more than 2.0% arachidonic acid (AA; C20:4-n6).

21. A fatty acid composition according to one of the preferred embodiments 1 through 20, in which the fatty acids are present as ethyl esters.
22. A fatty acid composition according to one of the preferred embodiments 1 through 20, in which the fatty acids are present as free fatty acids.
23. A fatty acid composition according to one of the preferred embodiments 1 through 20, in which the fatty acids are present as esters in di-glyceride form.
24. A fatty acid composition according to one of the preferred embodiments 1 through 20, in which the fatty acids are present as esters in triglyceride form.
25. A fatty acid composition according to one of the preferred embodiments 21 through 24, also comprising a suitable anti-oxidant in a concentration sufficient to protect the fatty acids of the composition from oxidation.
26. A pharmaceutically suitable formulation comprising one of the compositions according to preferred embodiments 1 through 25, in which the amount of eicosapentaenoic acid (as ethyl ester, free fatty acid, or triglyceride) is present in an amount between 250 and 10,000 mg.
27. A pharmaceutically suitable dosage form comprising one of the compositions according to preferred embodiments 1 through 25, in which the amount of eicosapentaenoic acid (as ethyl ester, free fatty acid, or triglyceride) is present in an amount between 250 and 1,250 mg.
28. A pharmaceutically suitable dosage form comprising one of the compositions according to preferred embodiments 1 through 25, in which the amount of eicosapentaenoic acid (as ethyl ester, free fatty acid, or triglyceride) is present in an amount between 500 and 1,100 mg.
29. A method of administration or treatment to a subject of a formulation according to one of the preferred embodiments 26 through 28 at a daily dose between 100 and 10,000 mg.
30. A method of administration or treatment to a subject of a formulation according to one of the preferred embodiments 26 through 28 at a daily dose between 500 and 5,000 mg.

31. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient diagnosed with very high triglycerides (equal or more than 500 mg/dL).
32. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient diagnosed with high triglycerides (equal or more than 200 mg/dL but less than 500 mg/dL).
33. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient already undergoing treatment with a statin and then diagnosed with high triglycerides (equal or more than 200 mg/dL but less than 500 mg/dL).
34. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient diagnosed with mixed dyslipidemia (TG equal or more than 200 mg/dL and LDL-cholesterol equal or more than 190 mg/dL).
35. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient diagnosed/assessed to be at substantially elevated risk for cardiovascular events.
36. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient diagnosed with diabetes.
37. A method of treatment according to preferred embodiments 29 or 30, in which the subject is a patient diagnosed with pre-diabetes or metabolic syndrome.
38. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma triglyceride levels.
39. A method of treatment according to one of the preferred embodiments 29 through 37, 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.
40. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma total-cholesterol levels.

41. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma non-HDL-cholesterol levels.
42. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma LDL-cholesterol levels.
43. A method of treatment according to one of the preferred embodiments 177 through 182, in which the treatment results in significant reduction of blood, serum or plasma VLDL-cholesterol levels.
44. A method of treatment according to one of the preferred embodiments 29 through 37, 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.
45. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma apo-B levels.
46. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma LP-PLA2 levels.
47. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of blood, serum or plasma hs-CRP levels.
48. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant increase of blood, serum or plasma HDL-cholesterol levels.
49. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant increase of blood, serum or plasma apo-A levels.
50. A method of treatment according to one of the preferred embodiments 29 through 37, in which the treatment results in significant reduction of the risk of suffering certain cardiovascular events.

51. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 8 hours or less
52. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 6 hours or less
53. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 5 hours or less
54. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 4 hours or less
55. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 8 hours or less
56. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 6 hours or less
57. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 5 hours or less
58. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in a Tmax of 4 hours or less
59. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+DHA Tmax less than the EPA+DHA Tmax for LOVAZA® under the same administration conditions
60. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+DHA Tmax less than the EPA+DHA Tmax for LOVAZA® under the same administration conditions
61. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+DHA Tmax less than the EPA+DHA Tmax for AMR101 under the same administration conditions

62. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+DHA Tmax less than the EPA+DHA Tmax for AMR101 under the same administration conditions
63. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an Total Omega-3 FA Tmax less than the Total Omega-3 FA Tmax for LOVAZA® under the same administration conditions
64. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an Total Omega□3 FA Tmax less than the Total Omega-3 FA Tmax for LOVAZA® under the same administration conditions
65. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an Total Omega-3 FA Tmax less than the Total Omega-3 FA Tmax for AMR101 under the same administration conditions
66. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an Total Omega-3 FA Tmax less than the Total Omega-3 FA Tmax for VASCEPA® under the same administration conditions
67. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 110% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
68. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 120% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
69. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 130% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions

70. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 140% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
71. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
72. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
73. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 200% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
74. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 300% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
75. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 400% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
76. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 500% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
77. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 600% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions

78. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
79. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 200% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
80. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 300% of the EPA+ DHA Cmax or Total Omega-3FA Cmax for LOVAZA® under the same administration conditions
81. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 400% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
82. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 500% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
83. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 600% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
84. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 700% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for LOVAZA® under the same administration conditions
85. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 110% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions

86. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 120% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
87. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 130% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
88. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 140% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
89. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
90. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
91. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 200% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
92. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 300% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
93. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 400% of the EPA+ DHA AUC or Total Omega-3FA AUC for LOVAZA® under the same administration conditions

94. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 500% of the EPA+ DHA AUC or Total Omega-3FA AUC for LOVAZA® under the same administration conditions
95. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 600% of the EPA+ DHA AUC or Total Omega-3FA AUC for LOVAZA® under the same administration conditions
96. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
97. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 200% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
98. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 300% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
99. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 400% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
100. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 500% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions
101. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 600% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions

102. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 700% of the EPA+ DHA AUC or Total Omega-3 FA AUC for LOVAZA® under the same administration conditions

103. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 110% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

104. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 120% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

105. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 130% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

106. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 140% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

107. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

108. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax

or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

109. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 200% of the EPA+ DHA Cmax or Total Omega-3FA Cmax for VASCEPA® under the same administration conditions

110. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 300% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

111. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 400% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

112. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 500% of the EPA+ DHA Cmax or Total Omega-3FA Cmax for VASCEPA® under the same administration conditions

113. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 600% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

114. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

115. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 200% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

116. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 300% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

117. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3FA Cmax of at least 400% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

118. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 500% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

119. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 600% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

120. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 700% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for VASCEPA® under the same administration conditions

121. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 110% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

122. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 120% of the EPA+ DHA AUC or

Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

123. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 130% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

124. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 140% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

125. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

126. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

127. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 200% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

128. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 300% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

129. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 400% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

130. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 500% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

131. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 600% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

132. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

133. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 200% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

134. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 300% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

135. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 400% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

136. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 500% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

137. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 600% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

138. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 700% of the EPA+ DHA AUC or Total Omega-3 FA AUC for VASCEPA® under the same administration conditions

139. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 100% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

140. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 105% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

141. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 110% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

142. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 120% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

143. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 130% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

144. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 140% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

145. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 100% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

146. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 105% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

147. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 110% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

148. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 120% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

149. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+

DHA Cmax or Total Omega-3 FA Cmax of at least 130% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

150. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 140% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

151. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 100% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

152. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 105% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

153. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 110% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

154. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3FA Cmax of at least 120% of the EPA+ DHA Cmax or Total Omega-3FA Cmax for EPANOVA® under the same administration conditions

155. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 130% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

156. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 140% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

157. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA Cmax or Total Omega-3 FA Cmax of at least 150% of the EPA+ DHA Cmax or Total Omega-3 FA Cmax for EPANOVA® under the same administration conditions

158. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 100% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

159. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 105% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

160. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 110% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

161. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 120% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

162. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 130% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

163. A method of administration or treatment under high fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 140% of the EPA+ DHA AUC or

Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

164. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 100% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

165. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 105% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

166. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 110% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

167. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 120% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

168. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 130% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

169. A method of administration or treatment under low fat meal conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 140% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

170. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 100% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

171. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 105% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

172. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 110% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

173. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 120% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

174. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 130% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

175. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 140% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

176. A method of administration or treatment under fasting conditions according to one of the preferred embodiments 29 or 30 resulting in an EPA+ DHA AUC or Total Omega-3 FA AUC of at least 150% of the EPA+ DHA AUC or Total Omega-3 FA AUC for EPANOVA® under the same administration conditions

WHAT IS CLAIMED:

Claim 1. A fatty acid composition comprising at least 81% omega-3-fatty acids, salts or derivatives thereof, wherein eicosapentaenoic acid (EPA) comprises at least 80% of the total fatty acids and docosahexaenoic acid (DHA) comprises between 1% and 10% of the total fatty acids, and wherein the composition comprises no more than 6% omega-6 fatty acids.

Claim 2. The fatty acid composition of claim 1, wherein the composition comprises at least 82% omega-3 fatty acids, salts or derivatives thereof.

Claim 3. The fatty acid composition of claim 1, wherein the composition comprises at least 86% omega-3 fatty acids, salts or derivatives thereof.

Claim 4. The fatty acid composition of claim 1, wherein the composition comprises at least 87% omega-3 fatty acids, salts or derivatives thereof.

Claim 5. The fatty acid composition of claim 1, wherein the composition comprises at least 89% omega-3 fatty acids, salts or derivatives thereof.

Claim 6. The fatty acid composition of claim 1, wherein the composition comprises at least 90% omega-3 fatty acids, salts or derivatives thereof.

Claim 7. The fatty acid composition of claim 1, wherein the EPA comprises 80 to 95% of the total fatty acids in the composition.

Claim 8. The fatty acid composition of claim 1, wherein EPA comprises 85 to 95% of the total fatty acids in the composition.

Claim 9. The fatty acid composition of claim 1, wherein EPA comprises 88 to 95% of the total fatty acids in the composition.

Claim 10. The fatty acid composition of claim 1, wherein EPA comprises 90 to 95% of the total fatty acids in the composition.

Claim 11. The fatty acid composition of claim 1, wherein DHA comprises between 2% and 10% of the total fatty acids.

Claim 12. The fatty acid composition of claim 1, wherein DHA comprises between 2% and 8% of the total fatty acids.

Claim 13. The fatty acid composition of claim 1, wherein DHA comprises between 1% and 6% of the total fatty acids.

Claim 14. The fatty acid composition of claim 1, wherein DHA comprises between 1% and 4% of the total fatty acids.

Claim 15. The fatty acid composition of claim 1, wherein the composition further comprises arachidonic acid (AA).

Claim 16. The fatty acid composition of claim 1, wherein the EPA is in free fatty acid, ethyl ester, diglyceride, or triglyceride form.

Claim 17. The fatty acid composition of claim 1, wherein the DHA is in free fatty acid, ethyl ester, diglyceride, or triglyceride form.

Claim 18. The fatty acid composition of claim 1, wherein the composition comprises EPA in an amount between 250 mg and 10,000 mg.

Claim 19. The fatty acid composition of claim 1, wherein the composition comprises EPA in an amount between 250 mg and 1,250 mg.

Claim 20. The fatty acid composition of claim 1, wherein the composition comprises EPA in an amount between 500 mg and 1,100 mg.

Claim 21. A method of treating a condition in a subject in need thereof, comprising administering to the subject the fatty acid composition of claim 1, wherein the condition is selected from the group consisting of: disease/condition is an amenable disease/condition selected from the group consisting of: hypertriglyceridemia; hypercholesterolemia; mixed dyslipidemia; coronary heart disease (CHD); vascular disease; atherosclerotic disease and related conditions; heart failure; cardiac arrhythmias; ischemic dementia; hypertension; coagulation related disorders; nephropathy; kidney or urinary tract disease; retinopathy; cognitive, psychiatric, neurological and other CNS disorders, including but not limited to schizophrenia, depression, bipolar disorder and any form of dementia; autoimmune diseases; inflammatory diseases; asthma, COPD or other respiratory disease; dermatological disease; metabolic syndrome; diabetes or other forms of metabolic disease; liver diseases including fatty liver disease; diseases affecting the senses, including those affecting vision and hearing; diseases of the gastrointestinal tract; diseases of the male or female reproductive system or related secondary sexual organs; a cancer; any infections caused by a virus, bacterium, fungus, protozoa or other organism; and the treatment and/or prevention and/or reduction of cardiac events and/or cardiovascular events and/or vascular events and/or symptoms.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US14/35922

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/20, 31/21, 35/60 (2014.01)
CPC - A61K 31/201, 31/202, 31/232
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 31/20, 31/21, 35/60, 31/202, 31/232 (2014.01)
CPC: A61K 31/201, 31/202, 31/232

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 514/506, 560, 578

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google Scholar; Google; ProQuest; omega-3 fatty acid, eicosapentaenoic acid, docosahexaenoic acid, linoleic acid, eicosadienoic acid, arachiconic acid, docosapentaenoic acid

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 8,298,554 B2 (MANKU, M) October 30, 2012; column 1, lines 27-34; column 3, lines 4-67; column 4, lines 1-6	1-21

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 August 2014 (19.08.2014)	11 SEP 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774