(12) PATENT APPLICATION PUBLICATION
(19) INDIA
(22) Date of filing of Application :11/04/2022

(21) Application No.202211021458 A
(43) Publication Date : 22/04/2022

(54) Title of the invention : PHARMACEUTICAL COMPOSITIONS COMPRISING EPA AND A CARDIOVASCULAR AGENT AND METHODS OF USING THE SAME

(51) International classification :A61K0031505000, A61K0031366000, A61K0009480000, A61K0009200000, A61K0031400000
(86) International Application No :NA
Filing Date :NA
(87) International Publication No : NA
(61) Patent of Addition to Application Number :NA
Filing Date :NA
(62) Divisional to Application Number :NA
Filing Date :NA

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(57) Abstract :
According to the invention, pharmaceutical compositions of the present invention contain one or more cardiovascular drugs that can be utilised to treat various diseases and disorders. A statin, such as rosuvastatin, is a cardiovascular medication that is highly effective. The current invention also provides a method for treating or preventing cardiovascular diseases, such as administering an EPA-containing pharmaceutical composition or compositions to a subject that needs treatment or prevention. EPA and additional cardiovascular medications can be added to any formulations listed above in a single dosage unit or many dosage units to provide an integrated dose administered in a coordinated, combined, or concurrent manner.

No. of Pages : 12 No. of Claims : 7

BRIEF DESCRIPTION OF THE DRAWINGS

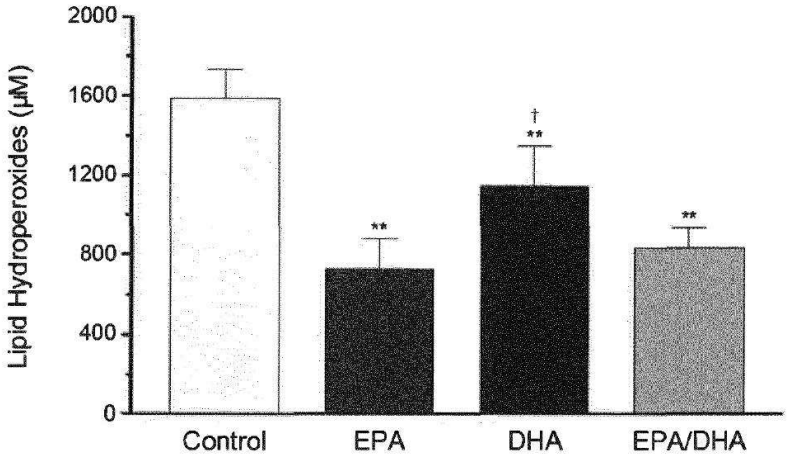


Fig.1 depcts the $p<0.01$ versus control; $p<0.01$ versus EPA alone or EPA/DHA combination treatment (student-Newman-keuls- multiple comparisons post-hoc test; overall ANOVA: $p<0.01$, $F=36.214$).
Values = mean± S.D (n=5-6). C/P= 1.0:1

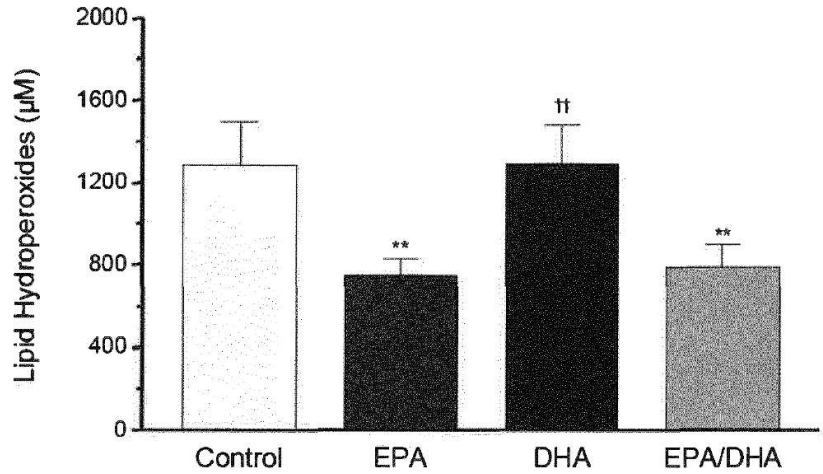


Fig.2 depcts the $p<0.01$ versus control; $p<0.01$ versus EPA alone or EPA/DHA combination treatment (student-Newman-keuls- multiple comparisons post-hoc test; overall ANOVA: $p<0.0001$, $F=27.650$).
Values = mean± S.D (n=6). C/P= 0.5:1

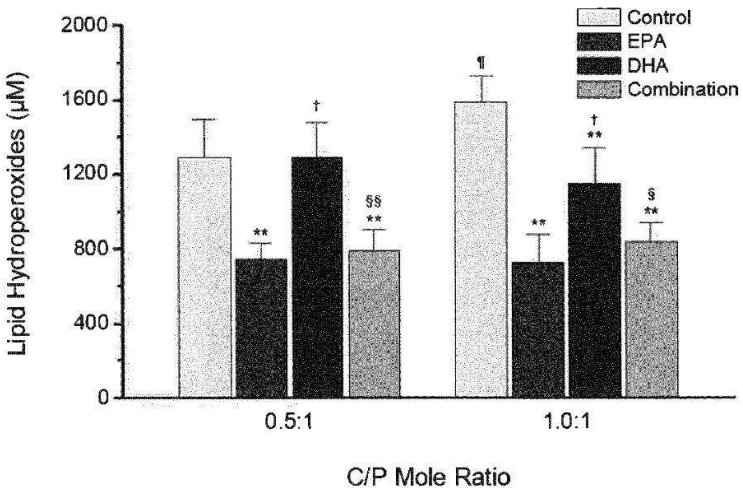


Fig.3 depcts the p<0.001 versus control at same C/P ; p<0.001 versus EPA alone at same C/P; 5p<0.001 Versus DHA alone at same C/P; p<0.01 versus control at 0.5 C/P (student-Newman-keuls- multiple comparisons post-hoc test; overall ANOVA: p<0.0001, F=25.260). Values = mean± S.D (n=5-6).

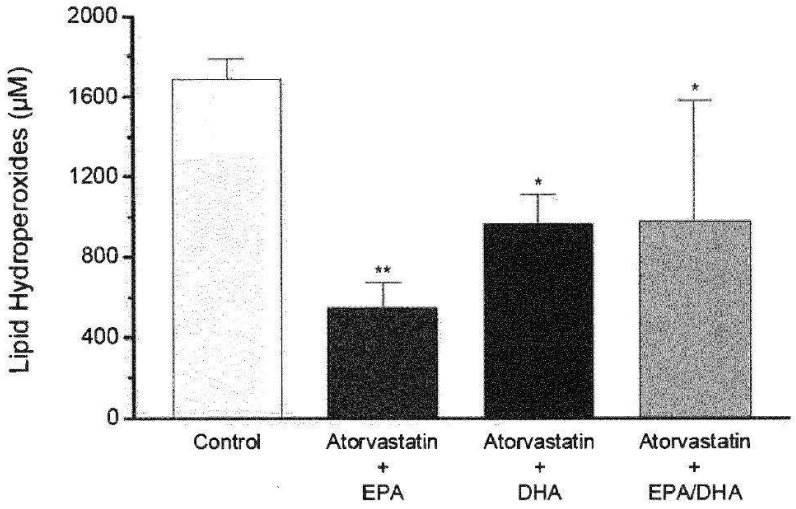


Fig.4 depcts the p<0.01 versus control (student-Newman-keuls- multiple comparisons post-hoc test; overall ANOVA: p<0.0001, F=11.226).

PHARMACEUTICAL COMPOSITIONS COMPRISING EPA AND A CARDIOVASCULAR AGENT AND METHODS OF USING THE SAME

FIELD OF THE INVENTION

The current invention relates to pharmaceutical compositions containing the EPA and one or more cardiovascular drugs and therapeutic procedures for treating various diseases and disorders. The cardiovascular agent is, in particular, a statin such as rosuvastatin.

BACKGROUND OF THE INVENTION

The leading cause of death globally is cardiovascular disease (CVD). CVDs include a wide range of conditions affecting the heart and blood vessels. Included are: Cardiovascular diseases have: coronary heart disease (heart disease of the ship), cerebrovascular disease (brain vessel disease), peripheral artery disease (arms and legs vessel disease), rheumatic heart disease (heart muscle and valve damage from rheumatic fever caused by streptococcal bacteria), congenital heart disease (congenital disabilities affecting normal heart development), and peripheral arterial disease These are blood clots that can travel to the heart and lungs via the deep vein thrombosis (DVT) or pulmonary embolism (PE). A blockage that prevents blood from reaching the heart or brain is the primary cause of heart attacks and strokes, which usually occur suddenly. Fat deposits on the walls of blood arteries that supply the heart and brain are the most typical cause of this. A blood clot can trigger strokes in the brain or a blood clot bursting a blood artery.

SUMMARY OF THE INVENTION

EPA and one or more other cardiovascular medicines can be included in the pharmaceutical composition of the present invention. IN SOME CASES, the EPA can also be found in eicosapentaenoic acid ethyl ester. Docosahexaenoic acid or a derivative thereof may not be present in the composition in another embodiment (e.g. ethyl-DHA). Additionally, the present invention provides methods for treating and preventing cardiovascular-related disease, such as administering a pharmaceutical composition or compositions that contain EPA and optionally one or more additional cardiovascular agents to a subject in need of the treatment or prevention of the disease to the topic. Any preceding embodiments can be co-formulated with the EPA and additional cardiovascular agent(s) in a single dosage unit or several dosage units for coordinated, combined, or concurrent administration.

BRIEF DESCRIPTION OF THE DRAWINGS

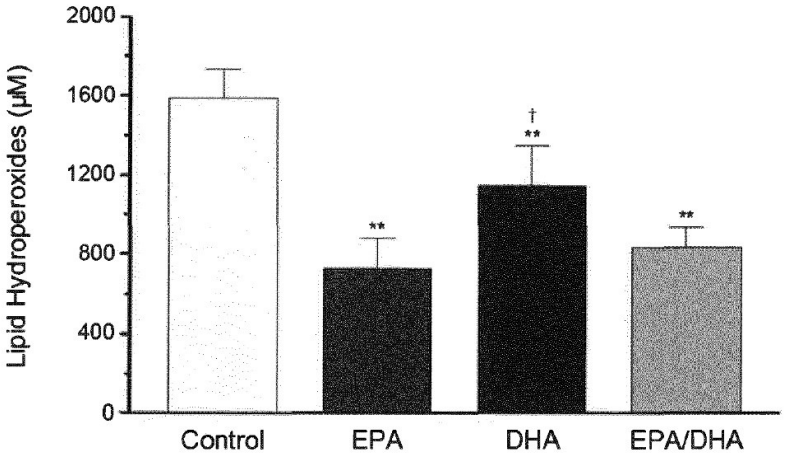


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Values = mean± S.D (n=5-6). C/P= 1.0:1

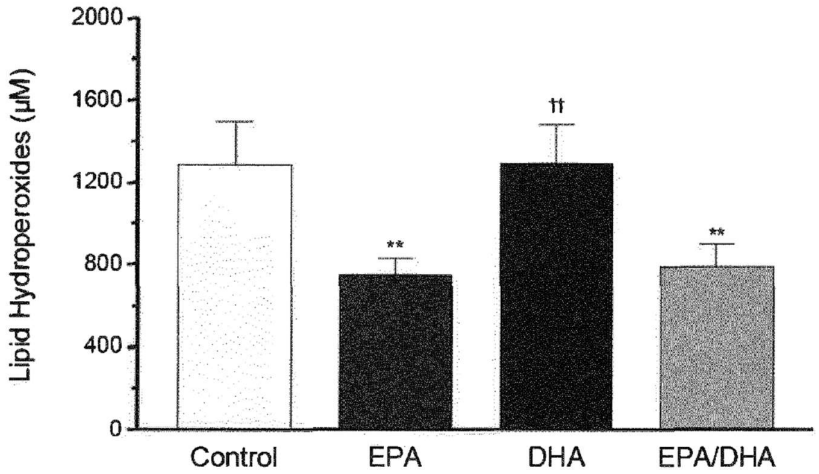


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Values = mean± S.D (n=6). C/P= 0.5:1

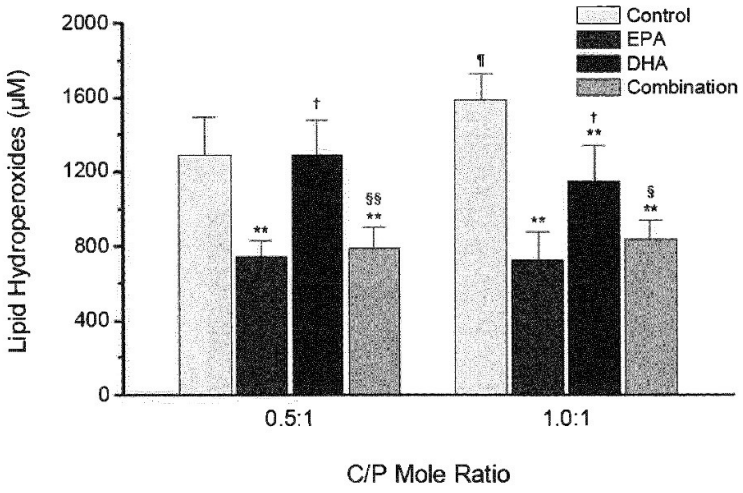


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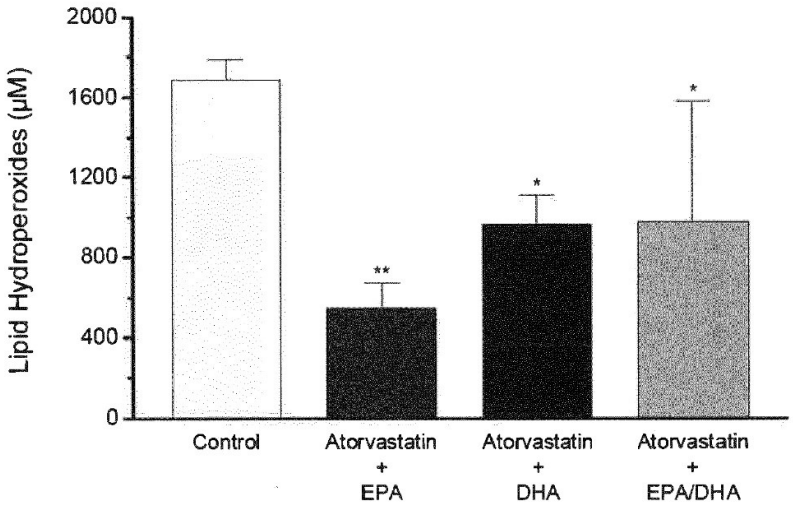


Fig.4 depcts the p<0.01 versus control (student-Newman-keuls- multiple comparisons post-hoc test; overall ANOVA: p<0.0001, F=11.226).

BRIEF DESCRIPTION OF THE INVENTION

The leading cause of death globally is cardiovascular disease (CVD).In 2019, an estimated 17.9 million people will die from cardiovascular disease(CVD), accounting for 32% of all fatalities worldwide. A heart attack or a stroke was responsible for 85% of the deaths. More than three-quarters of all deaths from cardiovascular disease occur in nations with a low or middle income. In 2019, CVDs were responsible for 38 per cent of the 17 million premature deaths (before the age of 70) caused by noncommunicable diseases. It can prevent most cardiovascular illnesses by making lifestyle changes to reduce risk factors such as tobacco use, a sedentary lifestyle, an unhealthy diet, and excessive alcohol consumption. Early detection of cardiovascular illness is critical for effective treatment, including counselling and medication.

While the current invention can take many forms, the following description of numerous embodiments is meant to serve as an example of the design and not limit it to those depicted. The headings are supplied just for convenience and are not intended to limit the invention. Any embodiment may be paired with any other image.

Unless otherwise mentioned, all numerical values in this application are approximations, with the minimum and maximum values preceded by the word "approximately." In this way, modest changes from a given value can have similar consequences. Also, the disclosure of ranges includes all matters between the minimum and maximum values and any ranges produced by such issues. Also given are all ratios (and ranges of ratios) that can be made by dividing one number by another. Derivations from numerical values are unambiguous in many cases. These derivations reflect various embodiments of the current invention.

Eicosapentaenoic acid

Compositions of the invention may contain EPA as an active component in one embodiment. A pharmaceutically approved ester, derivative, conjugation, or salt of EPA (eicosapentaenoic acid) or any preceding combination is referred to herein as "EPA." To be considered "pharmaceutically acceptable," a chemical must not cause unacceptable toxicity to the individual or interfere with other components of the mixture.

All-cis Nicosia-5,8,11,14,17-pentanoic acid is one example of the EPA. The EPA can also be found in the form of an ester of eicosapentaenoic acid (also referred to herein as E-EPA or ethyl-EPA). According to another embodiment, the EPA is an alkyl ester of EPA from C1 to C5. For example, the EPA can be composed of eicosapentaenoic acid methyl ester, propyl ester, or butyl ester. All-cis eicosa-5,8,11,14,17-pentanoic acid ethyl ester may also be used to make EPA.

Lithium EPA, mono, di, or triacylglyceride EPA, or any other ester of EPA and the free acid form of EPA can also be included in the EPA. A 2-substituted derivative or another derivative of EPA may also be used, which slows down the EPA's oxidation rate but does not fundamentally alter its biological effect.

Another form of EPA is an EPA-Fatty Acid Conjugate, in which EPA is linked to another EPA molecule or another fatty acid. This is another embodiment of EPA. Diesters between EPA and

EPA or between EPA and second fatty acid, as illustrated in structures (I) and (II), are one example of EPA-Fatty Acid conjugates (II). H, a 12- to 30-carbon-atom-long 12-carbon-atom-long acyl group with cis or trans double bonds, and 12- to 30-carbon-atom-long acyl groups are examples of R1 and R2 in one embodiment. Both R1 and R2 can come from EPA (EPA-EPA), or one can come from EPA, and the other from another fatty acid (EPA-Fatty acid), for example, gamma-linolenic acid dihomo-gamma-linolenic acid, arachidonic acid, adrenic acid, stearidonic acid, docosapentaenoic acid n-3, etc. A C1-C4 alkyl group is one example of R3 that can be either hydrogen, a hydrocarbon or contain heteroatoms.

Synthesis of a diester conjugate can be accomplished according to methods well known in the art, including, for example, using metals, metal-chlorides, or organic acids as catalysts; using fatty acid chlorides such as EPA-chloride, γ-linolenic acid chloride (GLA-chloride), dihomo-γ-linolenic acid chloride (DGLA-chloride), linoleic acid chloride (LA-chloride), arachidonic acid chloride (AA-chloride), conjugated linoleic acid chloride (cLA-chloride), ALA-chloride, STA-chloride, ETA-chloride, DPA-chloride, etc.; and the use of immobilised enzymes as catalysts.

Cardiovascular Agents

Additional cardiovascular medicines may be included in an innovation composition (or co-administration regimen) in one or more versions. It can be used with one or more cardiovascular drugs or combined with EPA. There are several interchangeable words for "cardiovascular agent" or "cardiovascular drug" here that refer to a drug or agent that can treat, prevent, or lessen a person's risk of acquiring any cardiovascular disease or problem. Agents that modulate cholesterol and triglyceride levels and those that treat coronary artery disease, hypertension, and arrhythmias are all examples of cardiovascular drugs included in this section. Those that treat ischemia and thrombosis are also included.

ACAT inhibitors, including selective inhibitors of ACAT-1 and ACAT-2 as well as dual inhibitors of ACAT-1 and ACAT-2, acyl-coenzyme A: cholesterol acyltransferase (ACAT) inhibitors, alpha-blockers, alpha/beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and aldosterone antagonists are just a few classes from which cardiovascular agents suitable for use according to the present invention.

ACAT inhibitors

"ACAT" is an enzyme that transfers acyl-CoA cholesteryl acyl groups to other acyltransferase enzymes. ACAT is involved in the intracellular synthesis of cholesterol esters from cholesterol in bile acid biosynthesis. Cholesterol esters are accumulated in the vascular tissues due to ACAT treatment. Atherosclerosis can be prevented or treated with the use of ACAT inhibitors. CI-1011 (Avasimibe, Pfizer), CS-505 (Pactimibe sulphate, Sankyo Pharma), or combinations thereof, are non-limiting examples of acceptable ACAT inhibitors.

It is typical for one or more ACAT inhibitors, if desired, to be present in a composition of the invention (or co-administered with EPA according to other embodiments of the invention) in an amount of between about 1 mg and around 1000 milligrammes (mg), for example, a single

ACAT inhibitor can be present in a composition of the invention (or co-administered with the EPA according to other embodiments of the invention) in an amount of between one and ten milligrammes (mg).

One or more ACAT inhibitors, if desired, are typically present in a composition of the invention (or co-administered with EPA according to other embodiments of the invention) in an amount of about 1 mg to about 1000 mg, for example, about 1 mg, about 5 mg, about 10 mg, about 20 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 225 mg, about 250 mg, about 266 mg, about 275 mg, about 300 mg, about 324 mg, about 325 mg, about 330 mg, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, about 500 mg, about 525 mg, about 550 mg, about 575 mg, about 600 mg, about 625 mg, about 650 mg, about 675 mg, about 700 mg, about 725 mg, about 750 mg, about 775 mg, about 800 mg, about 825 mg, about 850 mg, about 875 mg, about 900 mg, about 925 mg, about 950 mg, about 975 mg, about 1000 mg.

Aldosterone antagonists

Inhibition of renal function by aldosterone contributes to hypertension. Hypertension can be prevented or treated with agents that compete with aldosterone for mineralocorticoid receptors. Suitable aldosterone medications include eplerenone and Aldactone and mixtures of the two.

Alpha-blockers

Adrenergic alpha-antagonists, also known as alpha-blockers, compete with adrenaline binding at -adrenoreceptors to reduce the effects of stress. When adrenaline binds to these receptors, it results in hypertension. Hypertension can be prevented or treated with drugs that inhibit or compete with adrenaline or its receptors, the -adrenoreceptors. Doxazosin, methyldopa, clonidine, prazosin, terazosin, and clonidine are all non-limiting examples of alpha-blockers.

Beta-blockers

Beta-blockers block responses to the beta nerve receptor, which tends to slow heart rate and lower blood pressure. Non-limiting examples of suitable beta blockers include acebutolol, atenolol, metoprolol, nadolol, nebivolol, pindolol, propranolol, or combinations thereof.

One or more beta-blockers, if desired, are typically present in a composition of the invention (or co-administered with EPA according to other embodiments of the invention) in an amount of about 1 mg to about 1000 mg, about 1 mg to about 750 mg, or about 1 mg to about 500 mg, for example about 1 mg, about 2 mg, about 2.5 mg, about 3 mg, about 4 mg, about 5 mg, about 10 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 120 mg, about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 225 mg, about 250 mg, about 275 mg, about 300 mg, about 325 mg, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, or about 500 mg.

Bile acid sequestrants.

Bile acid sequestrants interrupt the enterohepatic circulation of bile acids by binding bile acid components in the gastrointestinal tract, rendering them unabsorbable. Bile acid sequestrants are thus helpful in preventing or treating hyperlipidemia, among other diseases and disorders. Non-limiting examples of bile acid sequestrants include colesevelam Hcl, colestipol, locholest and cholestyramine.

Calcium channel blockers.

Calcium channel blockers help prevent or treat hypertension through their vasodilating action. Non-limiting calcium channel blockers include nicardipine, diltiazem, clevidipine butyrate, isradipine, nimodipine, nisoldipine, verapamil, etc., amlodipine besylate, or combinations thereof. Non-limiting examples of combination calcium channel blockers include amlodipine, olmesartan, valsartan, or combinations thereof.

One or more calcium channel blockers, if desired, are typically present in a composition of the invention (or co-administered with EPA according to other embodiments of the invention) in an amount of about 1 mg to about 10 mg, for example about 1 mg, about 2 mg, about 2.5 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 9 mg, or about 10 mg; in an amount of about 5 mg to about 34 mg, for example about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 8.5 mg, about 9 mg, about 10 mg, about 15 mg, about 17.5 mg, about 20 mg, about 22.5 mg, about 25 mg, about 25.5 mg, about 27.5 mg, about 30 mg, about 32.5, or about 34 mg; in an amount of about 10 mg to about 60 mg, for example about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, or about 60 mg; in an amount of about 20 mg to about 120 mg, for example about 20 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110, or about 120 mg; in an amount of about 60 mg to about 420 mg, for example about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 140 mg, about 160 mg, about 180 mg, about 200 mg, about 220 mg, about 240 mg, about 260 mg, about 280 mg, about 300 mg, about 320 mg, about 340 mg, about 360 mg, about 380 mg, about 400, or about 420 mg.

CETP inhibitors

Cholesteryl ester transfer protein ("CETP") plays a vital role in transferring cholesteryl esters and triglycerides. Inhibition of CETP, also called plasma lipid transfer protein, helps prevent or treat atherosclerosis and other cardiovascular diseases and disorders. Non-limiting examples of CETP inhibitors include torcetrapib, anacetrapib, JTT-705, BAY-60-5521, PF-3185043, and CP-800569, or combinations thereof.

One or more CETP inhibitors, if desired, are present in a composition of the invention (or co-administered with EPA according to other embodiments of the invention) in an amount sufficient to provide the subject with a dose of about 25 mg per kg body weight ("mg per kg") to about 100 mg per kg, for example about 25 mg per kg, about 30 mg per kg, about 35 mg per kg, about 40 mg per kg, about 45 mg per kg, about 50 mg per kg, about 55 mg per kg, about

60 mg per kg, about 65 mg per kg, about 70 mg per kg, about 75 mg per kg, about 80 mg per kg, about 85 mg per kg, about 90 mg per kg, about 95 mg per kg, or about 100 mg per kg.

Antiretroviral Therapy

In one embodiment, the present invention provides a method of treating a cardiovascular-related disease as defined herein, for example, dyslipidemia or hyperlipidemia, in an HIV positive subject. In another embodiment, the method comprises co-administration, or concomitant administration, of a composition or composition with one or more HIV-1 protease inhibitors. Non-limiting HIV-1 protease inhibitors include amprenavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir.

One or more HIV-1 protease inhibitors, if desired, are typically present in a composition of the invention (or co-administered with EPA according to other embodiments of the invention) in an amount of about 100 mg to about 2500 mg, for example about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 225 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 625 mg, about 650 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1250 mg, about 1300 mg, about 1400 mg, about 1500 mg, about 1600 mg, about 1700 mg, about 1800 mg, about 1825 mg, about 1900 mg, about 2000 mg, about 2100 mg, about 2200 mg, about 2300 mg, about 2400 mg, or about 2500 mg; in an amount of about 200 mg to about 1000 mg, for example about 200 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, or about 1000 mg; in an amount of about 50 mg to about 400 mg, for example about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, or about 400 mg; in an amount of about 200 mg to about 1066 mg, for example about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 533 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, about 1000 mg, or about 1066 mg; in an amount of about 50 mg to about 1200 mg, for example about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, about 1000 mg, about 1050 mg, about 1100 mg, about 1150 mg, or about 1200 mg; or in an amount of about 15 mg per kg body weight to about 40 mg per kg body weight, for example about 15 mg per kg, about 20 mg per kg, about 25 mg per kg, about 30 mg per kg, about 35 mg per kg, about mg per kg, or about 40 mg per kg.

Dosage Forms

In one embodiment, compositions of the invention are orally deliverable. The terms "orally deliverable" or "oral administration" herein include any form of delivery of a therapeutic agent or a composition thereof to a subject wherein the agent or composition is placed in the mouth of the issue, whether or not the agent or piece is swallowed. Thus "oral administration" includes buccal and sublingual and oesophagal administration. In some embodiments, compositions of

the invention are in the form of solid dosage forms. Non-limiting examples of suitable concrete dosage forms include tablets (e.g. suspension tablets, bite suspension tablets, rapid dispersion tablets, chewable tablets, melt tablets, effervescent tablets, bi-layer tablets, etc.), caplets, capsules (e.g. soft or hard gelatin capsule filled with solids and liquids), powder (e.g. a packaged powder, a dispensable powder or an effervescent powder), tablets, sachets, cachets, troches, pellets, granules, micro granules, encapsulated micro granules, aerosol powder formulations, or any other solid dosage form reasonably adapted for oral administration.

EPA and any desired cardiovascular agent(s) can be co-formulated in the same dosage unit or individually formulated in separate dosage units. The terms "dose unit" and "dosage unit" herein refer to a portion of a pharmaceutical composition that contains an amount of a therapeutic agent suitable for a single administration to provide a therapeutic effect. Such dosage units may be administered one to a plurality (i.e. 1 to about 10, 1 to 8, 1 to 6, 1 to 4 or 1 to 2) times per day or as many times as needed to elicit a therapeutic response. EPA is disseminated or suspended in one or more cardiovascular agents in a capsule (for example, gelatin or HPMC capsule), sachet, or other dosage form or carrier as defined herein in one embodiment of the invention. The dispersion or suspension can also be uniform in another embodiment. However, in a further embodiment, if co-administration of two or more dosage units is required, the cardiovascular agent is included in a second dosage unit, for example, a tablet. At the same time, the EPA is present in the first dosage unit. A third composition may optionally contain any extra cardiovascular medication.

Excipients

Pharmaceutically approved excipients may be included in the invention's compositions. When we talk about "pharmaceutically acceptable excipient," we mean a substance that is not a therapeutic agent but is added to a pharmaceutical composition to improve its handling or storage properties or make it easier to make an individual dose of the formulation and that does not produce toxic effects that are unacceptable or interact negatively with the composition's other components. A pharmaceutically acceptable diluent may be used as an excipient in the invention's compositions. Sucrose-based diluting substances include mannitol; sorbitol; xylitol; dextrose (e.g., CereloseTM 2000); dextrose monohydrate; dibasic calcium phosphate dihydrate; sucrose-based diluting substances such as confectioner's sugar, monobasic calcium sulphate monohydrate, and xylitol. Examples of suitable diluents include lac. If present, these diluents make up between 5% and 99% of the total weight of the composition, between 10% and 85%, or between 20% and 80% of the total weight. Compositions of the invention optionally comprise one or more pharmaceutically acceptable binding agents or adhesives as excipients. Such binding agents and adhesives can impart sufficient cohesion to a powder being tableted to allow for normal processing operations such as sizing, lubrication, compression and packaging but still allow the tablet to disintegrate and the composition to be absorbed upon ingestion. Suitable binding agents and adhesives include, either individually or in combination, acacia; tragacanth; sucrose; gelatin; glucose; starches such as but not limited to, pregelatinised starches (e.g., National™ 1511 and National™ 1500); celluloses such as but not limited to, methylcellulose and carmellose sodium (e.g., Tylose™); alginic acid and salts of alginic acid;

magnesium aluminium silicate; PEG; guar gum; polysaccharide acids; bentonites; povidone, for example, povidone K-15, K-30 and K-29/32; polymethacrylates; HPMC; hydroxypropyl cellulose (e.g., Klucel™); and ethylcellulose (e.g., Ethocel™). Such binding agents and adhesives, if present, constitute in total about 0.5% to about 25%, about 0.75% to about 15%, or about 1% to about 10%, of the total weight of the composition.

Therapeutic Methods

In various embodiments, compositions of the invention are valid for the treatment and prevention of a cardiovascular-related disease. The term "cardiovascular-related disease" herein refers to any disease or disorder of the heart or blood vessels (i.e. arteries and veins) or any symptom thereof, or any disease or condition that causes or contributes to cardiovascular disease." Non-limiting examples of cardiovascular-related diseases and disorders include acute cardiac ischemic events, acute myocardial infarction , angina, angina pectoris, arrhythmia, atrial fibrulation, atherosclerosis, arterial fibrillation, cardiac insufficiency, cardiovascular disease, chronic heart failure, chronic stable angina, congestive heart failure, coronary artery disease, coronary heart disease, deep vein thrombosis, diabetes, diabetes mellitus, diabetic neuropathy, diastolic dysfunction in subjects with diabetes mellitus, edema, essential hypertension , eventual pulmonary embolism, fatty liver disease, heart disease, heart failure, homozygous familial hypercholesterolemia (HoFH), homozygous familial sitosterolemia, hypercholesterolemia, hyperlipidemia, hyperlipidemia in HIV positive subjects, hypertension, hypertriglyceridemia, ischemic complications in unstable angina and myocardial infarction, low blood pressure, metabolic syndrome, mixed dyslipidemia, moderate to mild heart failure, myocardial infarction, obesity management, paroxysmal atrial/arterial fibrillation/fibrulation/flutter, paroxysmal supraventricular tachycardias (PSVT), particularly severe or rapid onset edema, platelet aggregation, primary hypercholesterolemia, primary hyperlipidemia, pulmonary arterial hypertension, pulmonary hypertension, recurrent hemodynamically unstable ventricular tachycardia (VT), recurrent ventricular arrhythmias, recurrent ventricular fibrillation (VF), ruptured aneurysm, sitisterolemia, stroke, supraventricular tachycardia, symptomatic atrial fibrillation/flutter, tachycardia, type-II diabetes, vascular disease, venous thromboembolism, ventricular arrhythmias, and other cardiovascular events.

The term "treatment" about a given disease or disorder includes, but is not limited to, inhibiting the disease or condition, for example, arresting the development of the disease or disorder; relieving the disease or illness, for example, causing regression of the disease or disorder; or relieving a condition caused by or resulting from the disease or disorder, for example, reducing, preventing or treating symptoms of the disease or illness. The term "prevention" about a given disease or condition means: preventing the onset of disease development if none had occurred, preventing the disease or condition from occurring in a subject that may be predisposed to the state or illness but has not yet been diagnosed as having the disorder or disease, and preventing further disease/disorder development if already present.

PHARMACEUTICAL COMPOSITIONS COMPRISING EPA AND A CARDIOVASCULAR AGENT AND METHODS OF USING THE SAME

ABSTRACT

According to the invention, pharmaceutical compositions of the present invention contain one or more cardiovascular drugs that can be utilised to treat various diseases and disorders. A statin, such as rosuvastatin, is a cardiovascular medication that is highly effective. The current invention also provides a method for treating or preventing cardiovascular diseases, such as administering an EPA-containing pharmaceutical composition or compositions to a subject that needs treatment or prevention. EPA and additional cardiovascular medications can be added to any formulations listed above in a single dosage unit or many dosage units to provide an integrated dose administered in a coordinated, combined, or concurrent manner.

CLAIMS

1. Ethyl eicosapentaenoic acid ("E-EPA") and rosuvastatin are combined to form a pharmaceutical composition containing no more than 10% by weight of DHA or ethyl-DHA if any. The pharmaceutical composition further comprises an additional cardiovascular agent.
2. ACAT inhibitor, ACE inhibitor, alpha/beta-blocker, angiotensin II receptor antagonist, anti-arrhythmic, antiplatelet, beta-blocker, calcium-channel blocker, HMG-CoA reductase inhibitor, apoA-1 mimetic, CETP inhibitor, bile acid sequestrant, cholesterol absorption inhibitor, diuretic, dyslipidemia agent, endothelin receptor antagonist.
3. The pharmaceutical composition contains less than 0.5% DHA or ethyl-DHA by weight of total fatty acids. The pharmaceutical composition contains substantially no DHA or ethyl-DHA. The weight ratio of E-EPA to other fatty acids is at least 96:4.
4. The Pharmaceutical composition contains less than 1% of tocopherols by weight. The pharmaceutical composition is in a dosage form comprising a capsule.
5. The composition, according to any preceding, comprises at least one surfactant—a composition according to any prior use in treating or preventing a cardiovascular-related disease. Composition wherein the E-EPA and rosuvastatin are administered as separate dosage units.
6. In a dosage of about 3000 to 5000 mg per day, a composition for use according to the composition provided to a subject. A composition for treating or preventing primary hypercholesterolemia and mixed dyslipidemia in a subject according to the composition
7. A composition for use according to any of the compositions, wherein the composition is for use in reducing triglyceride levels in a subject when treatment with a statin or niacin extended-release monotherapy is inadequate.