TITLE OF THE INVENTION

METHODS OF TREATING HYPERTRIGLYCERIDEMIA

PRIORITY CLAIM

[0001] This application claims priority to U.S. provisional application Serial No. 61/151,291 filed February 10, 2009 and U.S. provisional application Serial No. 61/173,755 filed April 29, 2009, each of which are incorporated by reference herein in their entireties.

BACKGROUND

[0002] Cardiovascular disease is one of the leading causes of death in the United States and most European countries. It is estimated that over 70 million people in the United States alone suffer from a cardiovascular disease or disorder including but not limited to high blood pressure, coronary heart disease, dislipidemia, congestive heart failure and stroke. A need exists for improved treatments for cardiovascular diseases and disorders.

SUMMARY

[0002a]In one aspect, the present disclosure refers to use of a composition comprising 4 g of ethyl eicosapentaenoate and substantially no docosahexaenoic acid, in the manufacture of a medicament for treating moderate to severe hypertriglyceridemia in a subject having a fasting baseline triglyceride level of 500 mg/dl to 1500 mg/dl, wherein the composition is to be administered to the subject twice per day.

[0002b] In another aspect, the present disclosure refers to use of a composition comprising at least 96%, by weight, of all fatty acids present in the composition, ethyl eicosapentaenoate and the composition comprises not more than 4%, by weight, of total fatty acids other than ethyl eicosapentaenoate, and the composition contains 0.1% to 0.6% of at least one fatty acid other than ethyl eicosapentaenoate, and the composition contains substantially no docosahexaenoic acid in the manufacture of a medicament for treating moderate to severe hypertriglyceridemia in a subject having a fasting baseline triglyceride level of 500 mg/dl to 1500 mg/dl, and wherein 4 capsules, each containing 1g of the composition, are to be administered to the subject daily.

[0003] In various examples, the present disclosure describes methods of treating and/or preventing cardiovascular-related diseases and, in particular, a method of blood lipid therapy comprising administering to a subject in need thereof a pharmaceutical composition

comprising eicosapentaenoic acid or a derivative thereof. In one example, the composition contains not more than 10%, by weight, docosahexaenoic acid or derivative thereof, substantially no docosahexaenoic acid or derivative thereof, or no docosahexaenoic acid or derivative thereof. In another example, eicosapentaenoic acid ethyl ester comprises at least 96%, by weight, of all fatty acids present in the composition; the composition contains not more than 4%, by weight, of total fatty acids other than eicosapentaenoic acid ethyl ester; and/or the composition contains about 0.1% to about 0.6% of at least one fatty acid other than eicosapentaenoic acid ethyl ester and docosahexaenoic acid (or derivative thereof).

[0004] In one example, a pharmaceutical composition useful in accordance with the disclosure comprises, consists of or consists essentially of at least 95% by weight ethyl eicosapentaenoate (EPA-E), about 0.2% to about 0.5% by weight ethyl octadecatetraenoate (ODTA-E), about 0.05% to about 0.25% by weight ethyl nonaecapentaenoate (NDPA-E), about 0.2% to about 0.45% by weight ethyl arachidonate (AA-E), about 0.3% to about 0.5%

by weight ethyl eicosatetraenoate (ETA-E), and about 0.05% to about 0.32% ethyl heneicosapentaenoate (HPA-E). In another example, the composition is present in a capsule shell. In another example, the composition contains substantially no or no amount of docosahexaenoic acid (DHA) or derivative thereof such as ethyl-DHA (DHA-E).

[0005] In another example, the invention provides a method of treating moderate to severe hypertriglyceridemia comprising administering a composition as described herein to a subject in need thereof one to about four times per day.

[0006] These and other embodiments of the present invention will be disclosed in further detail herein below.

DETAILED DESCRIPTION

[0007] While the present invention is capable of being embodied in various forms, the description below of several embodiments is made with the understanding that the present disclosure is to be considered as an exemplification of the invention, and is not intended to limit the invention to the specific embodiments illustrated. Headings are provided for convenience only and are not to be construed to limit the invention in any manner. Embodiments illustrated under any heading may be combined with embodiments illustrated under any other heading.

[0008] The use of numerical values in the various quantitative values specified in this application, unless expressly indicated otherwise, are stated as approximations as though the minimum and maximum values within the stated ranges were both preceded by the word "about." Also, the disclosure of ranges is intended as a continuous range including every value between the minimum and maximum values recited as well as any ranges that can be formed by such values. Also disclosed herein are any and all ratios (and ranges of any such ratios) that can be formed by dividing a disclosed numeric value into any other disclosed numeric value. Accordingly, the skilled person will appreciate that many such ratios, ranges, and ranges of ratios can be unambiguously derived from the numerical values presented herein and in all instances such ratios, ranges, and ranges of ratios represent various embodiments of the present invention.

[0009] In one embodiment, the invention provides a method for treatment and/or 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. Non-limiting examples of cardiovascular-related disease and disorders

CLAIMS

What is claimed is:

1. Use of a composition comprising 4 g of ethyl eicosapentaenoate and substantially no docosahexaenoic acid, in the manufacture of a medicament for treating moderate to severe hypertriglyceridemia in a subject having a fasting baseline triglyceride level of 500 mg/dl to 1500 mg/dl, wherein the composition is to be administered to the subject twice per day.

2. Use of a composition comprising at least 96%, by weight, of all fatty acids present in the composition, ethyl eicosapentaenoate and the composition comprises not more than 4%, by weight, of total fatty acids other than ethyl eicosapentaenoate, and the composition contains 0.1% to 0.6% of at least one fatty acid other than ethyl eicosapentaenoate, and the composition contains substantially no docosahexaenoic acid in the manufacture of a medicament for treating moderate to severe hypertriglyceridemia in a subject having a fasting baseline triglyceride level of 500 mg/dl to 1500 mg/dl, and wherein 4 capsules, each containing 1g of the composition, are to be administered to the subject daily.

3. The use of claim 1 or claim 2, wherein the composition is useful for reducing triglycerides in the subject compared to placebo.

4. The use of claim 1 or claim 2, wherein the composition is useful for reducing triglycerides in the subject compared to baseline.

5. The use of claim 4, wherein the composition is useful for reducing triglycerides in the subject by at least 25% compared to baseline.

6. The use of claim 1 or claim 2, wherein the composition is useful for reducing triglycerides in the subject compared to a second subject having a fasting baseline triglyceride level of 500 mg/dl to 1500 mg/dl who has not been administered the composition.

7. The use of claim 6, wherein the composition is useful for reducing triglycerides in the subject by at least 20% compared to the second subject.

8. The use of any one of claims 1 to 6, wherein the composition is useful for reducing an apolipoprotein B level in the subject.

9. The use of any one of claims 1 to 6, wherein the composition is useful for not substantially increasing an LDL-C level in the subject.

10. The use of claim 9, wherein the composition is useful for reducing the LDL-C level in the subject.

11. The use of claim 4 or claim 5, wherein the composition is useful for increasing an LDL-C level in the subject by no more than 5%.

12. The use of any one of claims 1 to 6, wherein the composition is useful for reducing a VLDL-C level in the subject.

13. The use of any one of claims 1 to 6, wherein the composition is useful for reducing a high-sensitivity C-reactive protein level in the subject.

14. The use of any one of claims 1 to 6, wherein the subject is to be administered the composition daily for a period of at least 12 weeks.

15. The use of claim 1, wherein the composition comprises at least 90%, by weight, of all fatty acids present, ethyl eicosapentaenoate.

16. The use of claim 15, wherein the composition comprises at least 95%, by weight, of all fatty acids present, ethyl eicosapentaenoate.

17. The use of claim 15, wherein the composition comprises at least 96%, by weight, of all fatty acids present, ethyl eicosapentaenoate.

18. The use of any one of claims 1 to 17, wherein the subject is not to be administered an additional lipid lowering drug.

19. The use of any one of claims 1 to 17, wherein the subject is to be further administered an additional lipid lowering drug.

20. The use of claim 19, wherein the additional lipid lowering drug is a statin.

21. The use of any one of claims 1 to 20, wherein the subject is diabetic.