USE OF EICOSAPENTAENOIC ACID ETHYL ESTER FOR 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

[0003] In one aspect, the present invention refers to a composition comprising about 4g of ethyl eicosapentaenoate, wherein the composition comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonadecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any. In another aspect, the present invention refers to use of ethyl eicosapentaenoate in the manufacture of a medicament for treating a cardiovascular-related disease in a subject having moderate to severe hypertriglyceridemia and on stable statin therapy, wherein the composition comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonaecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any. In one example, there is disclosed use of ethyl eicosapentaenoate in the manufacture of a medicament for treating a cardiovascular-

related disease in a subject on stable statin therapy, wherein the composition comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonaecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any. In yet another aspect, the present invention refers to use of 4 g/day of ethyl eicosapentaenoate in the manufacture of a medicament for treating a cardiovascular-related disease in a subject having a triglyceride level of at least 500 mg/dl serum triglyceride levels, wherein the medicament comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonaecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any. In another example, there is disclosed use of ethyl eicosapentaenoate in the manufacture of a medicament for treating a cardiovascular-related disease in a subject having a triglyceride level of at least 500 mg/dl serum triglyceride levels, wherein the medicament comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonaecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any. 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%

Claims

1. Use of ethyl eicosapentaenoate in the manufacture of a medicament for treating a cardiovascular-related disease in a subject having moderate to severe hypertriglyceridemia and on stable statin therapy, wherein the composition comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonaecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any.

2. The use of claim 1 wherein upon administration of 2 g of the composition to the subject daily for a period of at least 6 weeks, the subject exhibits an at least 200% increase in serum, plasma and/or red blood cell EPA compared to baseline.

3. The use of claim 1 wherein the composition is to be administered to the subject daily for a period of at least 6 weeks.

4. The use of claim 1 wherein serum, plasma and/or red blood cell EPA levels in the subject are increased by at least 400% compared to baseline.

5. The use of claim 4 wherein the composition is to be administered to the subject daily for a period of at least 6 weeks.

6. The use of any one of claims 3, 4 or 5 wherein the subject has a baseline serum, plasma and/or red blood cell EPA level of not greater than 50 μg/ml.

7. The use of claim 1 wherein upon daily administration of 4 g of the composition to the subject for a period of at least 6 weeks, the subject exhibits an at least 400% increase in plasma and/or serum EPA compared to baseline.

8. The use of claim 1 wherein upon daily administration of the composition to the subject, the subject exhibits an increase in serum phospholipid and/or red blood cell DPA levels and a decrease in serum phospholipid and/or red blood cell arachidonic acid (AA), and/or DHA levels.

9. The use of claim 8, wherein the composition is to be administered to the subject daily for a period of at least 6 weeks.

10. The use of claim 1 wherein upon daily administration of the composition to the subject for a period of at least 6 weeks, the subject exhibits a decrease in plasma phospholipid and/or serum DHA levels by at least 16% compared to baseline, a decrease in DGLA plasma and/or serum levels by at least 31% compared to baseline, a decrease in arachidonic acid (AA) plasma and/or serum levels by at least 20% compared to baseline, and/or an increase in plasma and/or serum DPA levels of at least 130% compared to baseline.

11. The use of claim 1 wherein the composition comprises at least 96% by weight ethyl eicosapentaenoate, 0.22% to 0.4% by weight ethyl octadecatetraenoate, 0.075% to 0.20% by weight ethyl nonaecapentaenoate, 0.25% to 0.40% by weight ethyl arachidonate, 0.3% to 0.4% by weight ethyl eicosatetraenoate and 0.075% to 0.25% ethyl heneicosapentaenoate.

12. The use of claim 1 wherein the composition comprises at least 98%, by weight, ethyl eicosapentaenoate, 0.25% to 0.38% by weight ethyl octadecatetraenoate, 0.10% to 0.15% by weight ethyl nonaecapentaenoate, 0.25% to 0.35% by weight ethyl arachidonate, 0.31% to 0.38% by weight ethyl eicosatetraenoate, and 0.08% to 0.20% ethyl heneicosapentaenoate.

13. The use of claim 1 wherein the composition further comprises tocopherol in an amount of 0.05% to 0.4%, by weight.

14. The use of claim 1 wherein the composition is present in a capsule shell.

15. Use of 4 g/day of ethyl eicosapentaenoate in the manufacture of a medicament for treating a cardiovascular-related disease in a subject having a triglyceride level of at least 500 mg/dl serum triglyceride levels, wherein the medicament comprises at least 96%, by weight, ethyl eicosapentaenoate, 0.2% to 0.5% by weight ethyl octadecatetraenoate, 0.05% to 0.25% by weight ethyl nonaecapentaenoate, 0.2% to 0.45% by weight ethyl arachidonate, 0.3% to 0.5% by weight ethyl

eicosatetraenoate, 0.05% to 0.32% ethyl heneicosapentaenoate and not more than 0.05% ethyl-DHA, if any.

16. The use of claim 1 or claim 15, wherein an LDL-C level in the subject is reduced by at least 5% compared to baseline.