liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) are the most common causes of chronic liver disease in the adult population and represents a crucial risk factor for progression to liver failure, cirrhosis and hepatocellular carcinoma. While steatosis affects approximately 30% of the population, 80% of obese patients have NAFLD and 50% of patients undergoing bariatric surgery have steatohepatitis. NAFLD also represents the most common cause of liver disease in children. It is estimated that NAFLD affects up to 20 percent of adults and nearly 5 percent of children. Some experts estimate that about two thirds of obese adults and half of obese children may have fatty liver. In the past ten years, as the rates of obesity in have doubled in adults and tripled in children and teenagers, NAFLD and NASH are becoming more common. NASH can cause scarring and hardening of the liver, leading to cirrhosis, a very serious disease that may require a liver transplant, and eventually to hepatocellular carcinoma.

There is no single established medical treatment for fatty liver. Presently, treatment of NAFLD is limited to 1) treatment of associated metabolic disorders such as diabetes and hyperlipidemia; 2) the management of insulin resistance focusing on weight loss, exercise and/or a pharmacological approach; and 3) the use of antioxidants as hepatic protection agents. Despite the use of many different therapeutic modalities, no clear treatment is currently available to address NAFLD. Because it is clinically important to resolve NAFLD and its sequelae, new approaches aimed at preventing and reversing fat accumulation in the liver are necessary.

We have surprisingly found that 15-OHEPA, a metabolite of EPA, is more potent than EPA in the treatment of FLD. In one ~~aspect~~example, ~~the present invention refers~~disclosed herein is ~~to~~ the use of 15-OHEPA in the manufacture of a medicament for treating a fatty liver disorder. In one aspect, the present invention refers to use of 15-Hydroxy-eicosa-5,8,11,13,17-pentaenoic acid or a pharmaceutically acceptable ester, derivative, conjugate, salt, or mixture thereof ("15-HEPE") 15-OHEPA in the manufacture of a medicament for treating a fatty liver disorder.

DETAILED DESCRIPTION

The present invention relates to compositions and methods for treating fatty liver disorders, including non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), by administration of a composition comprising 15-OHEPA in a subject in need thereof.

As used herein, "15-OHEPA" is 15-Hydroxy-eicosa-5,8,11,13,17-pentaenoic acid. 15-OHEPA can be synthesized from eicosapentaenoic acid, EPA according to methods known in the art. As used herein, the term "15-OHEPA" refers to 15-OHEPA in its free acid form (*e.g,* 15-hydroxy-eicosa-5,8,11,13,17-pentaenoic acid) and/or a pharmaceutically acceptable ester, conjugate or salt thereof, or mixtures of any of the foregoing. A derviative of 15-OHEPA may be used

Claims

1. Use of 15-Hydroxy-eicosa-5,8,11,13,17-pentaenoic acid or a pharmaceutically acceptable ester, derivative, conjugate, salt, or mixture thereof ("15-HEPE") ~~15-OHEPA~~ in the manufacture of a medicament for treating a fatty liver disorder.

2. The use of 15-HEPE ~~15-OHEPA~~ according to claim 1, in which the fatty liver disorder is selected from non-alcoholic fatty liver disease and non-alcoholic steatohepatitis.

3. The use of 15-HEPE ~~15-OHEPA~~ according to claim 1 or claim 2, in which the 15-HEPE ~~15-OHEPA~~ comprises a $C_1 - C_5$ alkyl ester.

4. The use of 15-HEPE ~~15-OHEPA~~ according to any preceding claim, in which the 15-OHEPA is in the form of a pharmaceutical composition.

5. The use of 15-HEPE ~~15-OHEPA~~ according to claim 4, in which the pharmaceutical composition further comprises a pharmaceutically acceptable excipient.

6. The use of 15-HEPE ~~15-OHEPA~~ according to claim 4 or claim 5, in which the pharmaceutical composition is an oral pharmaceutical composition.

7. The use of 15-HEPE ~~15-OHEPA~~ according to any preceding claim, in which the 15-HEPE ~~15-OHEPA~~ represents at least about 90%, by weight, of all fatty acids present.

8. The use of 15-HEPE ~~15-OHEPA~~ according to any preceding claim, in which there are substantially no such ~~are no substantial amounts of any~~ other omega-3 fatty acids present.

9. The use of 15-HEPE ~~15-OHEPA~~ according to any preceding claim, in which there is no other omega-3 fatty acid present.

10. The use of 15-HEPE ~~15-OHEPA~~ according to any preceding claim, in which the 15-HEPE~~15-OHEPA~~ is present from about 50 mg to about 3000 mg.