University of Ferrara

UNIFE PATENTS

biotechnologies

TREATMENT AND PROPHYLAXIS OF CARDIOVASCULAR DISORDERS WITH ERUCIC ACID AND RELATED DIAGNOSTIC METHODS

Erucic acid | Liposomes | Thrombotic risk | Cardiovascular diseases



OBIETTIVI PER LO SVILUPPO SOSTENIBILE

3 SALUTE E BENESSERE

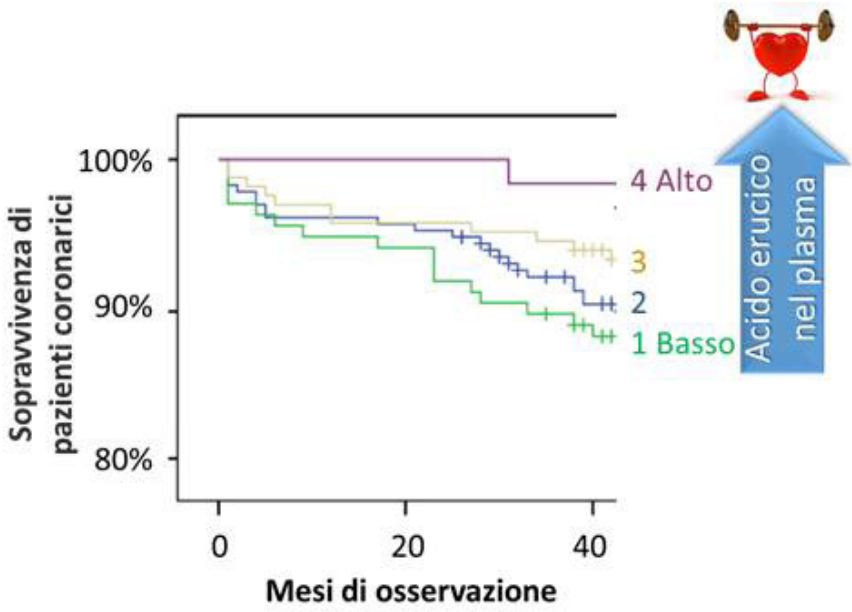
TECHNOLOGY AREA

Health and Pharmacology

RELEVANT MARKETS

Pharmacological, Food

PATENT OWNER: University of Ferrara
PRIORITY NUMBER: 102018000008940
FILING DATE: 26/09/2018



The present invention relates to the use of erucic acid for the treatment and prevention of thrombotic disorders and cardiovascular diseases, and the methods related diagnostics with the determination of blood levels erucic acid as diagnostic-prognostic framing tool for patients with disorders thrombotics and/or cardiovascular diseases. More particularly, the invention relates to the use of erucic acid (or cis-13-docosenoic acid) as a pharmaceutical supplement or dietary, to be administered for example delivered in liposomes or other formulations pharmaceuticals, for the prevention and treatment of coronary heart disease, and for the prevention of thrombotic disorders associated with them. The invention concerns in addition diagnostic methods involving the assessment of concentrations erucic acid blood as a diagnostic and prognostic biomarker in diseases cardiovascular and thrombotic disorders.

According to the present invention, the maintenance of physiologically elevated blood levels of erucic acid has favorable cardiovascular effects thanks to its anticoagulant properties of this acid, which is able to reduce the generation of thrombin. For these reasons it is proposed, for the prevention and treatment of cardiovascular diseases and for prevention of thrombotic disorders, erucic acid supplementation in the diet, or as a dietary or nutraceutical supplement, in addition to normal lifestyle measures and possibly to drugs indicated for coronary artery disease.

CHARACTERISTICS OF THE INVENTION

Specific object of the present invention is a preparation for administration erucic acid (cis-13-docosenoic acid) based systemics for use as anticoagulant and antithrombotic agent. This preparation is proposed for use in the prevention and treatment of cardiovascular disease and thrombotic disorders, and in a particular way it is proposed in the case in which the said cardiovascular diseases they are coronary artery disease. According to preferred embodiments of the invention, the prepared for use according to the invention is formulated in a vehicle also suitable for the oral administration.

Lipophilic substances such as erucic acid often present a difficulty of administration precisely because of the intrinsic characteristics that limit its solubility in water and, consequently, limit its relative absorbability and bioavailability. Such lipophilic substances are good candidates for the use of advanced technologies of solubilization: In particular, a potential vehicle to ensure effective release of erucic acid in the bloodstream is also in the form of lipid micelles or liposomes containing erucic acid in their composition.

POSSIBLE APPLICATIONS

According to the invention, erucic acid proposed for use as an antithrombotic and anticoagulant in patients with heart disease, and in particular in patients with pathologies coronary arteries and those subject to thrombotic disorders should be administered to a daily dosage such as to restore physiological blood concentrations medium-high of this acid, i.e. above 0.30% with regard to the plasma or erythrocyte dosage (and in any case less than ’1.00%). Therefore, according to the invention, erucic acid should be administered at a dosage including between 50 mg/day and 500 mg/day per day, preferably between 200 mg/day and 400 mg/day until restoration of the above blood levels.

According to a further aspect of the present invention, as already noted, it is proposed a prognostic diagnostic evaluation procedure in subjects with cardiovascular disease, ischaemic heart disease and thrombotic disorders, which includes the execution of the following operations:

- perform a dosage of blood erucic acid levels in a subject, typically by gas chromatographic method, and
- classify said subject as having an increased thrombophilic diathesis and a increased cardiovascular risk, and therefore likely to benefit from a selective supplementation with erucic acid, if blood levels of erucic acid are less than 0.30% by weight.

The dosage of blood levels of erucic acid preferably includes both the level plasma than erythrocyte.

From clinical studies carried out so far, it has emerged that erucic acid is inversely related to thrombin generation and is an independent predictor of endogenous thrombin potential.

It also emerged that high levels of erucic acid are associated with a reduced risk of atherosclerotic coronary artery disease. Not only that: high levels of erucic acid are

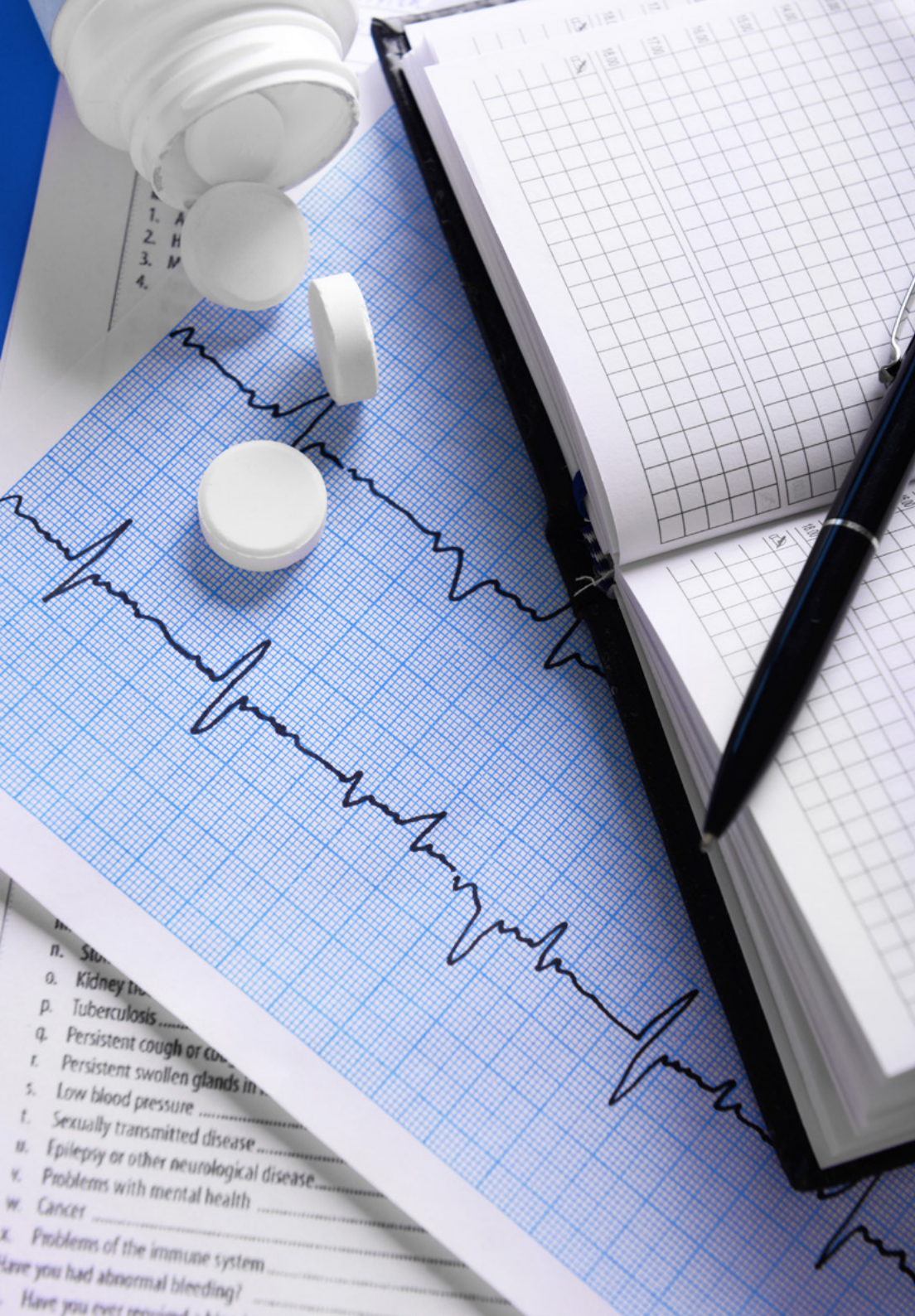
associated with a reduced risk of mortality total and cardiovascular in the context of secondary prevention of ischaemic heart diseases and laboratory results confirmed that erucic acid-enriched liposomes in plasma can reduce the generation of thrombin, the main enzyme. procoagulant.

ADVANTAGES

Liposomes are very frequently made up of natural lipids (such as acid erucic itself), which significantly limits its toxic effects and possible responses immune of the treated organism, but they can also be created with lipids of synthesis, in order to vary, even significantly, the basic characteristics of micelles, from charge to stability. Furthermore, by incorporating specific molecules, not only lipid, but also carbohydrate, or protein (such as antibodies), it is possible to confer high tissue-specificity to the liposome, making it a sophisticated, yet economical in large-scale synthesis, drug delivery system.

An additional advantage is that liposomes and molecules can be administered into them contained both orally, parenterally and finally also topically, which makes them a particularly versatile molecular tool. The main one limitation of liposomes lies in their poor stability and tendency to degrade oxidatively; however, it is possible, in order to also enormously increase its stability, coat liposomes with polyethylene glycol molecules, hydrogenate, also partially, the unsaturated fatty acids present in them, store the liposomes in the presence of antioxidants and finally freeze-dry the liposomes.

The geographical distribution of the reference market is of a global nature (merely by way of title informative the Centers for Disease Control and Prevention (CDC) estimates that they are affected from ischemic heart disease 20,000,000 Americans, or about 6% of the population total). Furthermore, erucic acid can be obtained at modest costs from easy vegetable oils discovery. In fact, the very high bioavailability in vegetable oils is accompanied by reduced complexity and purification cost of the molecule.



Università degli Studi di Ferrara

Settore
Innovazione tecnologica
e sociale

Via Saragat,1 Corpo B - II piano
44122 Ferrara
Tel 0532/293202
e-mail: utt@unife.it

www.unife.it