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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
TINA	SAMPALIS	Laval, Quebec, Canada

☐ *Additional inventors are being named on the____ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (280 characters max)

NATURAL MARINE SOURCE PHOSPHOLIPIDS COMPRISING FLAVONOIDS, POLYUNSATURATED FATTY ACIDS AND THEIR APPLICATIONS

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☒ Specification *Number of Pages* 21 ☐ CD(s), Number

☒ Drawing(s) *Number of Sheets* 13 ☐ Other (specify)

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☒ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check or money order is enclosed to cover the filing fees

☒ The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number 19-2550

☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE AMOUNT ($): $75.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are: ____________

Respectfully submitted,

SIGNATURE [signature] Date 07/27/01

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USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

NATURAL MARINE SOURCE PHOSPHOLIPIDS COMPRISING FLAVONOIDS, POLYUNSATURATED FATTY ACIDS AND THEIR APPLICATIONS

Field of the Invention

The present invention is directed to nutraceutical, pharmaceutical or cosmetic compositions, particularly to phospholipid compositions derived from natural marine or aquatic sources.

Background of the Invention

Phospholipids are complex lipids containing phosphorus. The phosphatides, known as phospholipids, are usually divided into groups on the basis of compounds from which they are derived. In addition to two chains of fatty acids they contain phosphoric acid, glycerol and nitrogenous bases such as choline. The phospholipids considered most important are phosphatidyicholine, phosphatidylethanolamine and phosphatidylinositol. Their nature as amphophilic molecules provides them with unique physicochemical properties. Their function as the principle components of cell membranes makes phospholipids essential for all vital cell processes. They are widespread as secretory and structural components of the body and can mimic or enhance natural physiological processes.

Phospholipid production may be either synthetic or through extraction from natural tissues. The chief source of commercial natural phospholipids is soybean, egg yolk and cows (brain and liver). Since an individual phospholipid may contain a variety of fatty acid residues, it may be described as pure only with this limitation in mind. Naturally occurring essential polyunsaturated fatty acids, can contribute to the activation of cellular metabolism. The main fatty acid found in phospholipid products is linoleic acid, present in soybean at more than 65%. The longest chain polyunsaturated fatty acids found in commercial available phospholipids either as preparations or individually are 20:4 among the eicosanoids, known as arachidonic acid and 22:6 known as docosahexanoic acid.

Arachidonic acid is a fatty acid that is found as part of the phospholipid membrane, generally as part of phosphatidylcholine and phosphatidylinositol. Adverse cellular stimuli will activate enzymes (phospholipase) that cleave arachidonic acid from the phospholipid backbone in the cell membrane. Arachidonic acid, which serves as the precursor for prostaglandins and prostacyclin (PGs, PGI_2) and thromboxane (TXs) can then be metabolized by one of two major pathways: the cyclooxygenase (COX) pathway or the lipoxygenase pathway. The COX pathway products, PGG_2 and PGH_2 can then be acted upon by thromboxane synthase (in platelets) or prostacyclin synthase (in endothelium) to form TXs or PGI_2, respectively. Arachidonic acid can also be acted upon by 5-lipoxygenase, primarily in leukocytes, to form leukotrienes (LTs). One or more of these metabolites can mediate all the signs and symptoms associated with arachidonic acid, i.e. inflammatory disease and pain.

Platelets, leukocytes, smooth muscle, and endothelium can produce vasoactive substances, products of arachidonic acid metabolism such as prostaglandins (PGs), prostacyclin (PGI_2), leukotrienes (LTs), and thromboxanes (TXs). These substances can either act as vasodilators or as vasoconstrictors. PGI_2 is essential in vascular function since it inhibits platelet adhesion to the vascular endothelium and has significant vasodilatation qualities. Damaged endothelial cells cannot produce PGI_2, making the vessel more susceptible to thrombosis and vasospasm. Thromboxanes and leukotrienes serve a vascular function during inflammation, generally producing vasoconstriction. Prostaglandins have a vascular role during inflammation, and also play a more subtle role in normal flow regulation, most notably as modulators of other control mechanisms. Prostaglandins have both vasoconstrictor and vasodilator activities. Leukotrienes and prostaglandins can also increase the endothelial membrane permeability thus promoting edema during inflammation. Arachidonic acid is naturally present in most phospholipid mixtures or emulsions available today.

Nervonic acid (C24:1) is also called selacholeic acid or tertracosenic acid. Nervonic acid is the symbol of white matter in glucoside, which is quantitatively contained in nerve tissue and white matter. The absence of nervonic acid may result in cerebral lesion, fatigue, hypodynamia, amentia, and senile dementia.

Nervonic acid, tertracosenic acid in another name, is monounsaturated, non-oxidable/decomposed and absorptive. It is called a rare tonic as it is rare existent in nature, may be micro-obtained by compounded in cerebral chondriosome. Therefore, the substance is far below the demand of human body. In foreign countries, nervonic acid mainly comes from shark brain and oil.

Flavonoids are polyphenolic compounds ubiquitous in nature. They are categorized into isoflavones, anthocyanidins, flavans, flavonols, flavones, citrus flavonoids, hesperidin, chalcones, catechins, rutin, and flavanones. Essential flavonoids, such as quercetin in onions and genistein in soy are actually considered subcategories rather than independent categories. Over 4,000 flavonoids have been identified in fruits, vegetables and beverages (tea, coffee, beer, wine and fruit drinks). Even though they have a similar molecular structure between them, their functions are different from each other. Flavonoids have been shown to have antibacterial, anti-inflammatory, antiallergic, antimutagenic, antiviral, antineoplastic, anti-thrombotic, and vasodilatory activity. Quercetin has been proven to block the "sorbitol pathway" which is directly associated with diabetes as well as to prevent LDL-cholesterol oxidative damage, which is essential for the maintenance of a healthy cardiovascular system.

Flavonoids are found in a wide range of fruits and vegetables. For example, Quercetin (a flavonol in vegetables, fruit and onions), Xanthohumol (a prenylated chalcone in beer). Isoxanthohumol (a prenylated flavanone in beer), Genistein (an isoflavone in soy), Chalconaringenin (a non-prenylated chalcone in citrus fruits) and Naringenin (a non-prenylated flavanone in citrus fruits).

In plants flavonoids have very well defined functions. First, the accumulation of pigment in flower petals, seeds and leafs. Flowers, as pollinators, must attract pollen carriers. Second, they protect plants from UV damage, by absorbing UV at the epidermal layer. Third, they protect the plants against insects and pathogens.

The flavonoid biosynthetic pathway is one of the best understood plant secondary metabolism pathways (1992, Gerats). The key enzymes are phenylalanine-ammonia lyase and chalcone synthase. Phenylalanine-ammonia lyase converts phenylalanine into cinnamic acid as it controls the total flow of carbons into phenolics which is shown to be the limiting step in this pathway (1974, Cressy). Another key enzyme of the flavonoid pathway is the chalcone synthase. It condenses three molecules of

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