



US008030348B2

(12) **United States Patent**
Sampalis

(10) **Patent No.:** **US 8,030,348 B2**
(45) **Date of Patent:** **Oct. 4, 2011**

(54) **NATURAL MARINE SOURCE
PHOSPHOLIPIDS COMPRISING
POLYUNSATURATED FATTY ACIDS AND
THEIR APPLICATIONS**

(75) Inventor: **Fotini Sampalis, Laval (CA)**

(73) Assignee: **Neptune Technologies &
Bioresources, Inc., Laval (CA)**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 871 days.

(21) Appl. No.: **10/485,094**

(22) PCT Filed: **Jul. 29, 2002**

(86) PCT No.: **PCT/CA02/01185**

§ 371 (c)(1),

(2), (4) Date: **Jul. 13, 2004**

(87) PCT Pub. No.: **WO03/011873**

PCT Pub. Date: **Feb. 13, 2003**

(65) **Prior Publication Data**

US 2004/0234587 A1 Nov. 25, 2004

Related U.S. Application Data

(60) Provisional application No. 60/307,842, filed on Jul. 27, 2001.

(51) **Int. Cl.**

A61K 31/215 (2006.01)

A61K 31/661 (2006.01)

(52) **U.S. Cl.** **514/506; 514/75**

(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2003/0083238 A1* 5/2003 Toda et al. 514/9

FOREIGN PATENT DOCUMENTS

EP 0 609 078 A1 8/1994
WO 92 21335 A 12/1992
WO 97 39759 A 10/1997
WO 00 23546 A 4/2000

OTHER PUBLICATIONS

ACS Chemical Registry, "4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-6,8-di-β-D-glucopyranosyl-5,7-dihydroxy-", Nov. 16, 1984, 1 page.*

Aureli, M. et al. Aging brain: effect of acetyl-L-carnitine treatment on rat brain energy and phospholipid metabolism. A study by ³¹P and ¹H NMR spectroscopy. *Brain Research*. 1990; 526(1): 108-112.

Barak, Y. et al. Inositol treatment of Alzheimer's disease : a double blind, cross-over placebo controlled trial. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 1996; 20: 729-735.

Bast, A. et al. Interlay between lipoic acid and glutathione in the protection against microsomal lipid peroxidation. *Biochem. Biophys. Acta*. 1988; 963: 558-561.

Bell, M.V. et al. Molecular Species Composition of the Major Diacyl Glycerophospholipids from Muscle, Liver, Retina and Brain of Cod (*Gadus morhua*). *Lipids* 1991; 26(8): 563-73.

Benjamin, J. et al. Double-blind, placebo-controlled, crossover trial of inositol treatment for panic disorders. *Am. J. Psychiatry* 1995; 15: 1084-1086.

Birchall, J. et al. Aluminum, chemical physiology, and Alzheimer's disease. *Lancet* 1988; 29:1008-1010.

Caprioli, A. et al. Age-dependent deficits in radial maze performance in the rats: effect of chronic treatment with acetyl L-carnitine. *Prog. In Neuropsychopharmacol. Biol. Psychiatr.* 1990; 14(3): 3 59-369.

Cheng, D. et al. A novel promising acetylcholinesterase inhibitor. *Neuroreport* 1996; 8: 97-101.

Devasagayam, T.P. et al., Prevention of Singlet Oxygen-Induced DNA Damage by Lipoate. *Chemical Biological Interactions* 1993; 86 : 79-92.

Ghirardi, O. et al. Effects of acetyl L-carnitine chronic treatment on discrimination models in aged rats. *Physiol. Behav.* 1988; 44(6): 769-773.

Gill, D.L. et al. Calcium signalling mechanisms in endoplasmic reticulum activated by inositol 1, 4, 5 triphosphate and GTP. *Cell Calcium* 1989; 10: 363-374.

Henderson, R.J. et al. Lipid Composition fo the Pineal Organ from Rainbow Trout (*Oncorhynchus mykiss*). *Lipids* 1994; 29(5): 311-17.

Hosokawa, M. et al., Conversion to Docosahexaenoic Acid-Containing Phosphatidylserine from Squid Skin Lecithin by Phospholipase D-Mediated Transphosphatidylation. *Journal of Agricultural and Food Chemistry* 20000; 48(10): 4550-54.

Imperato, A. et al. L-carnitine enhances acetylcholine release in the striatum and hippocampus of awake freely moving rats. *Neuroscience Letters*. 1989; 107(1-3): 251-255.

Kagan, V.E. et al. Dihydrolipoic acid: A universal antioxidant both in the membrane and in the aqueous phase. *Biochem. Pharmacol.* 1992; 44: 1637-1649.

Kawakami, Y. et al. The rationale for E2020 as a potent acetylcholinesterase inhibitor. *Bioorg. Med. Chem.* 1996; 4: 1429-1446.

Kitamura, H. et al. Inhibition of myo-inositol transport causes acute renal failure with selective medullary injury in the rat. *Kidney Int.* 1998; 53: 146-153.

Knopman, D. et al. Long term tacrine (Cognex) treatment: effects on nursing home placement and mortality, tacrine study group. *Neurology* 1996; 47: 166-167.

Levine, J. et al. Double-blind, controlled trial of inositol treatment of depression. *Am. J. Psychiatry* 1995; 152: 792-794 (Abstract Only).

Levine, J. et al. Inositol treatment raises CSF inositol levels. *Brain Research* 1993; 627 : 168-169.

Levine, J. Controlled trials of inositol in psychiatry. *Eur. Neuropsychopharmacol.* 1997; 7: 147-155.

Colodny, L. et al. *Altern. Med. Rev.* 1998; 3(6): 432-447.

Mohr, E. et al. Treatment of Alzheimer's disease with sabelzole : functional and structural correlates. *Clin. Neuropharmacol.* 1997; 20: 338-345 (Abstract Only).

Paradies, G. et al. Carnitine-acylcarnitine translocase activity in cardiac mitochondria from aged rats: the effect of acetyl-L-carnitine. *Mech. of Aging and Develop.* 1995; 84(2): 103-112.

Parthasarathy, L. et al. Biochemical and molecular properties of lithium-sensitive myo-inositol monophosphatase. *Life Sci.* 1994; 54: 1127-1142.

(Continued)

Primary Examiner — James Anderson

Assistant Examiner — Gregg Polansky

(57) **ABSTRACT**

A phospholipid extract from a marine or aquatic biomass possesses therapeutic properties. The phospholipid extract comprises a variety of phospholipids, fatty acid, metals and a novel flavonoid.

21 Claims, 4 Drawing Sheets

Petition for Inter Partes Review
Of U.S. Patent 8,278,351
Exhibit

000001

OTHER PUBLICATIONS

Rogers, S. et al. The efficacy and safety of donepezil in patients with Alzheimer's disease: results of a US multicentre, randomized, double-blind, placebo-controlled trial. The donepezil study group. *Dementia* 1996; 7: 293-303 (Abstract Only).

Schneider, L. et al. Potential role for estrogen replacement in the treatment of Alzheimer's dementia. *Am. J. Med.* 1997; 103: 46S-50S.

Seidman, M. Polyunsaturated Phosphatidylcholine in NT Factor™ Improves Mitochondrial Function, Auditory Sensitivity and May Slow Some Aspects of the Aging Processes. *Anti-Aging Medical News*, Winter 2001.

Suzuki, Y.J. et al. Alpha-lipoic acid is a potent inhibitor of NFkB activation in human Tcells. *Biochem. Biophys. Res. Commun.* 1992; 189: 1709-1715 (Abstract Only).

Van Dyck, C. et al. The acetylcholine releaser linopiridine increases parietal regional cerebral blood flow in Alzheimer's disease. *Psychopharmacology* 1997; 132: 217-226.

Wiegand, R. et al. Phospholipid Molecular Species of Frog Rod Outer Segment Membranes. *Exp. Eye Res.* 1983; 37(2): 159-73.

* cited by examiner

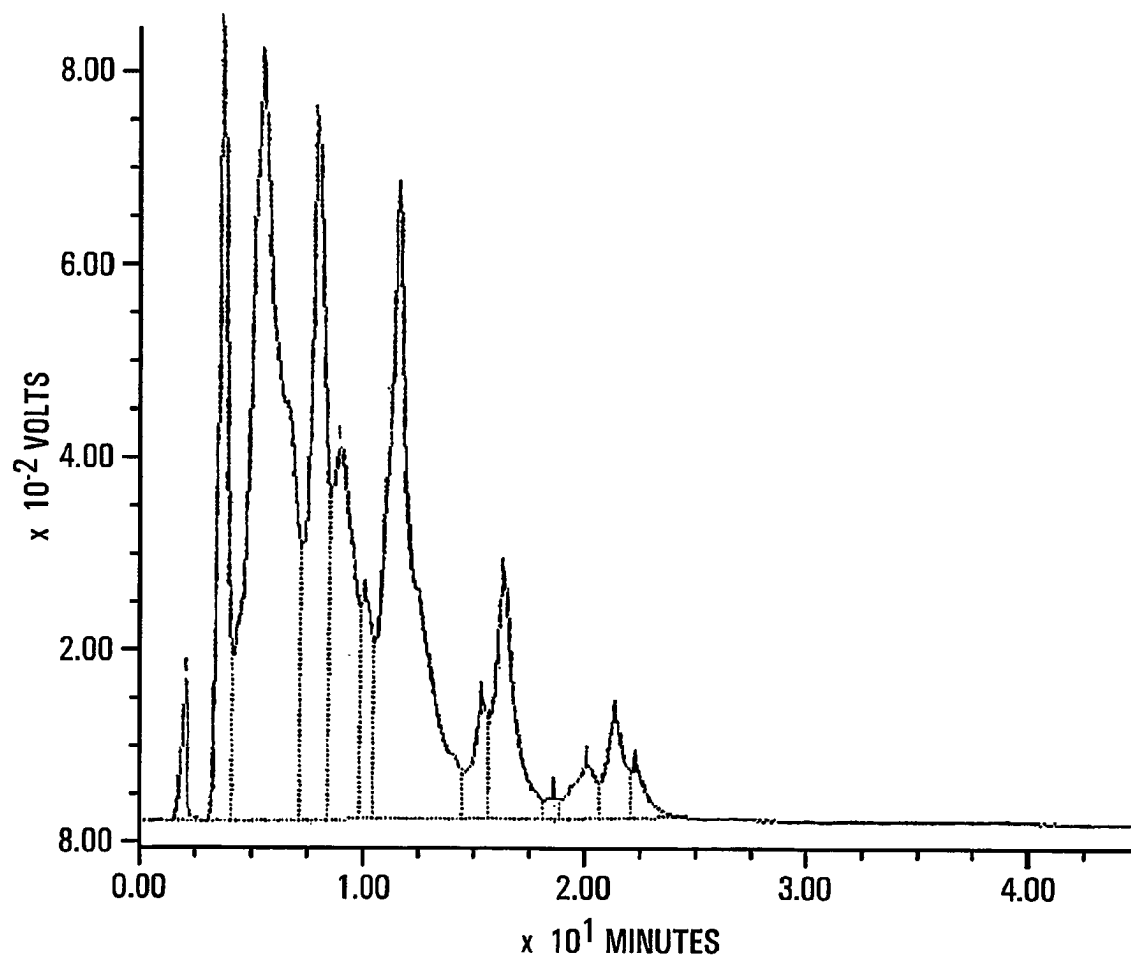


Fig. 1

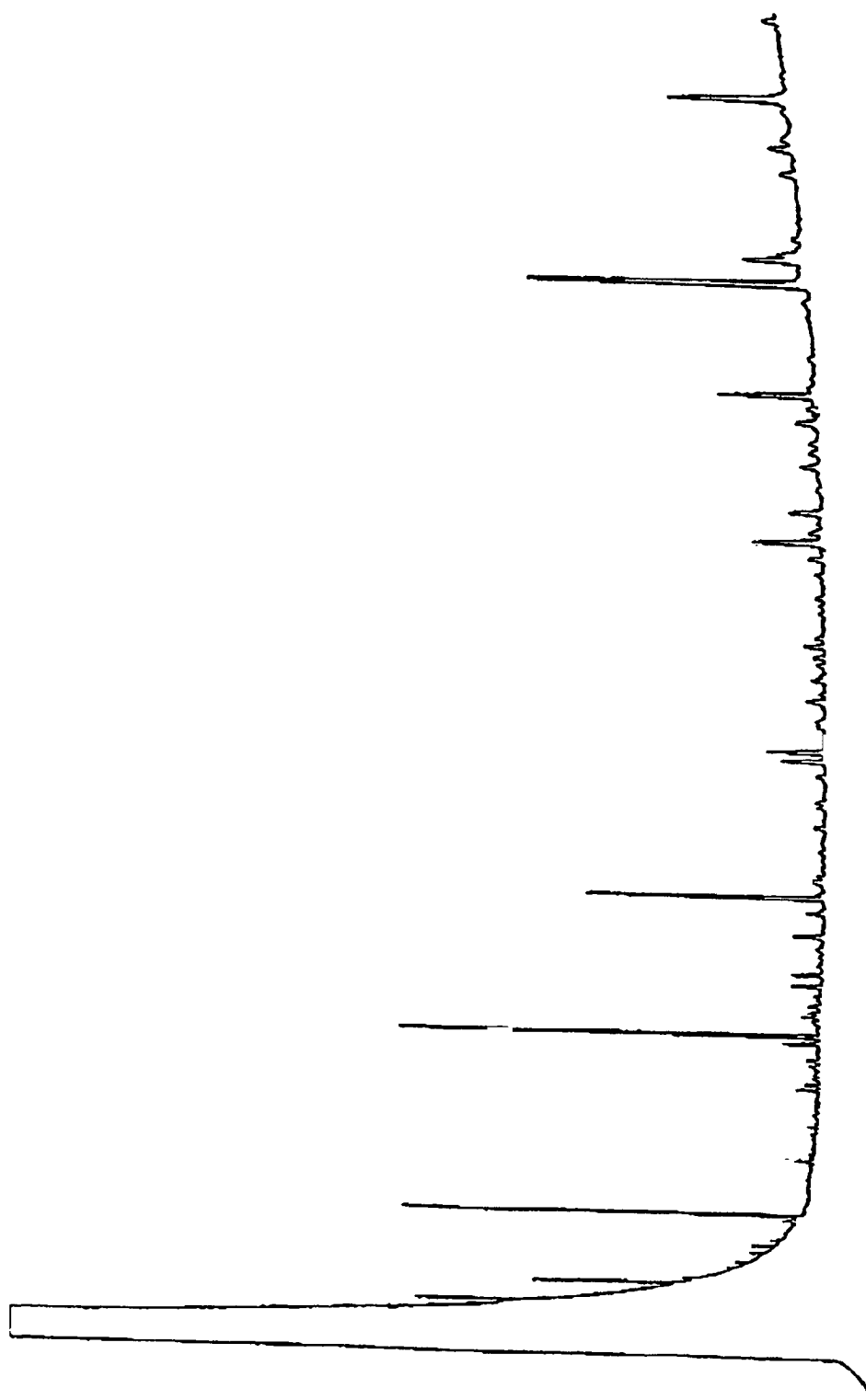


Fig. 2

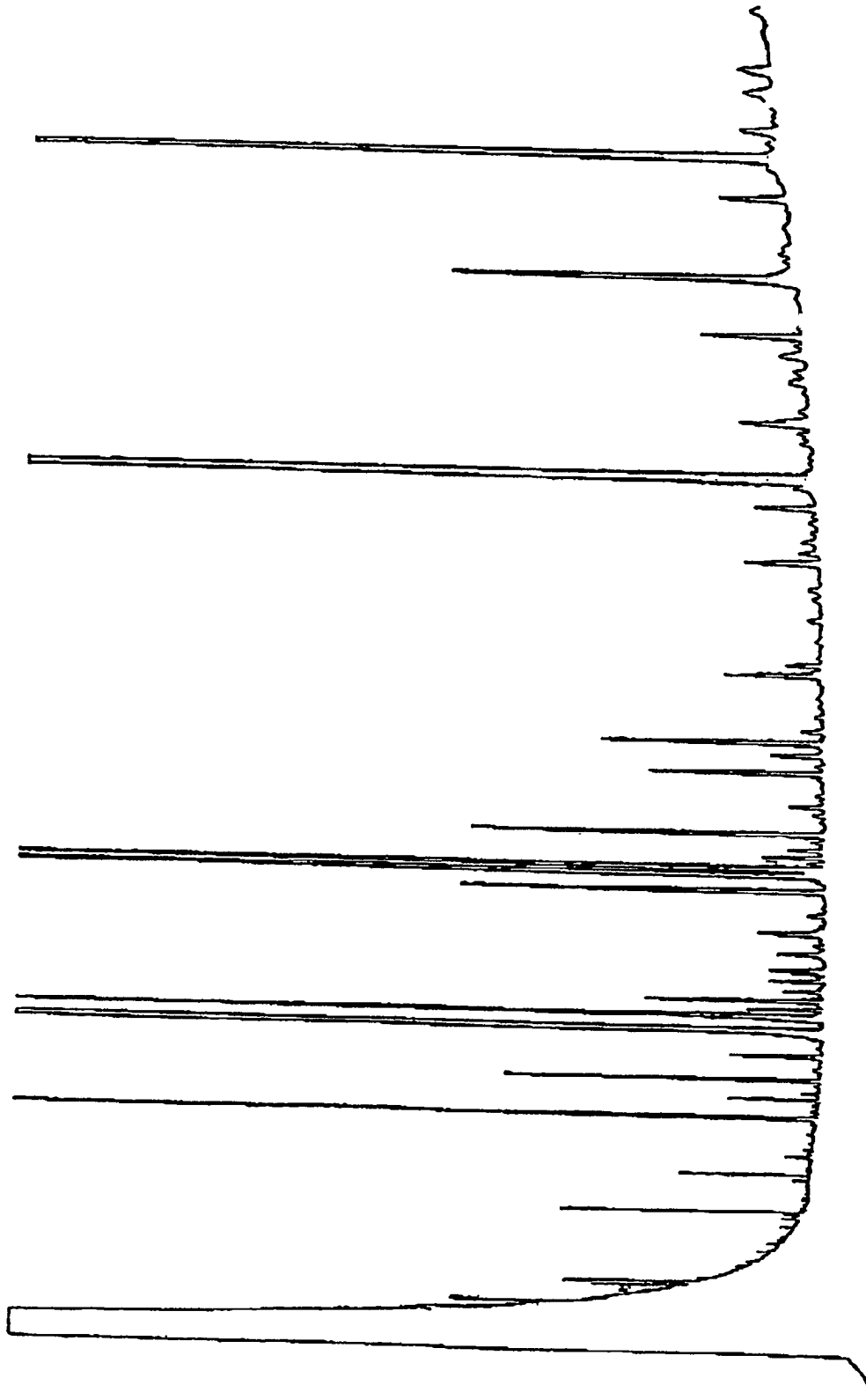


Fig. 3

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.