

# (12) United States Patent

Bruheim et al.

#### (54) **BIOEFFECTIVE KRILL OIL COMPOSITIONS**

(71) Applicant: AKER BIOMARINE ANTARCTIC

**AS**, Stamsund (NO)

(72) Inventors: Inge Bruheim, Volda (NO); Snorre

Tilseth, Bergen (NO); Daniele Mancinelli, Orsta (NO)

(73) Assignee: AKER BIOMARINE ANTARCTIC

AS, Stamsund (NO)

(\*) Notice: Subject to any disclaimer, the term of this

patent is extended or adjusted under 35

U.S.C. 154(b) by 0 days.

This patent is subject to a terminal dis-

claimer.

(21) Appl. No.: 15/589,572

(22)Filed: May 8, 2017

(65)**Prior Publication Data** 

> US 2017/0240842 A1 Aug. 24, 2017

#### Related U.S. Application Data

(63) Continuation of application No. 15/180,431, filed on Jun. 13, 2016, now Pat. No. 9,644,169, which is a continuation of application No. 14/020,162, filed on Sep. 6, 2013, now Pat. No. 9,375,453, which is a (Continued)

(51) Int. Cl. C11B 3/00 (2006.01)A61K 31/202 (2006.01)

(52) U.S. Cl. CPC ............. C11B 3/006 (2013.01); A61K 31/202

(2013.01)

#### US 9.816.046 B2 (10) **Patent No.:**

(45) Date of Patent: \*Nov. 14, 2017

#### (58) Field of Classification Search

None

See application file for complete search history.

#### (56)References Cited

#### U.S. PATENT DOCUMENTS

2,652,235 A 9/1953 Samuelsen 4,036,993 A 7/1977 Ikeda 4,038,722 A 8/1977 Terase et al. (Continued)

#### FOREIGN PATENT DOCUMENTS

2002322233 2/2003 BR8701265 3/1987 (Continued)

#### OTHER PUBLICATIONS

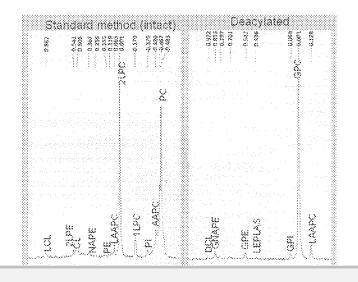
Action Closing Prosecution, 348 Patent, mailed May 14, 2013. (Continued)

Primary Examiner — Yate K Cutliff (74) Attorney, Agent, or Firm — Casimir Jones S.C.

#### ABSTRACT

This invention discloses new krill oil compositions characterized by having high amounts of phospholipids, astaxanthin esters and/or omega-3 contents. The krill oils are obtained from krill meal using supercritical fluid extraction in a two stage process. Stage 1 removes the neutral lipid by extracting with neat supercritical CO2 or CO2 plus approximately 5% of a co-solvent. Stage 2 extracts the actual krill oils by using supercritical CO<sub>2</sub> in combination with approximately 20% ethanol. The krill oil materials obtained are compared with commercially available krill oil and found to be more bioeffective in a number of areas such as antiinflammation, anti-oxidant effects, improving insulin resistances and improving blood lipid profile.

#### 19 Claims, 19 Drawing Sheets





	Related U.S. Application Data	EP EP	1292294 1706106	3/2009 7/2009
	continuation of application No. 12/057,775, filed on	$\mathbf{EP}$	1385500	7/2010
	Mar. 28, 2008, now Pat. No. 9,034,388.	GB GB	2097014 921537	10/1982 6/1999
		JР	A-S51-125774	11/1976
(60)	Provisional application No. 60/920,483, filed on Mar.	JP	A-S52-114046	9/1977
	28, 2007, provisional application No. 60/975,058,	JP JP	60-153779 61281159	8/1985 12/1986
	filed on Sep. 25, 2007, provisional application No. 60/983,446, filed on Oct. 29, 2007, provisional	JP	S6323819	2/1988
	application No. 61/024,072, filed on Jan. 28, 2008.	JP JP	02049091 2215351	2/1990 8/1990
	11	JP	4012665	1/1992
(56)	References Cited	JР JР	2963152 04057853	2/1992 2/1992
	U.S. PATENT DOCUMENTS	JP	3081692	7/1994
		JP	2524217	8/1996
	4,119,619 A 10/1978 Rogozhin et al. 4,133,077 A 1/1979 Jasniewicz	JP JP	H08-231391 3344887	9/1996 7/1997
	4,251,557 A 2/1981 Shimose et al.	JP	3611222	8/1997
	4,505,936 A 3/1985 Meyers et al.	JP JP	2909508 A-2001-158736	6/1999 6/2001
	4,714,571 A 12/1987 Kearns et al. 4,749,522 A 6/1988 Kamarei	JP	A-2003-003192	1/2003
	4,814,111 A 3/1989 Kearns et al.	JP JP	A-2003-048831 A-2003-146883	2/2003 5/2003
	5,006,281 A 4/1991 Rubin et al. 5,266,564 A 11/1993 Modolell	JP	A-2003-140883 3467794	9/2003
	5,434,183 A 7/1995 Larsson-Backstrom	JP	2003-530448	10/2003
	6,214,396 B1 4/2001 Barrier 6,346,276 B1 2/2002 Tanouchi et al.	JP JP	3486778 2004-534800	10/2003 11/2004
	6,346,276 B1 2/2002 Tanouchi et al. 6,537,787 B1 3/2003 Breton	JP	3678317	5/2005
	6,800,299 B1 10/2004 Beaudoin	JP JP	A-2005-245379 A-2006-069948	9/2005 3/2006
	7,488,503 B1 2/2009 Porzio et al. 7,666,447 B2 2/2010 Rockway	JP	A-2006-083136	3/2006
	8,030,348 B2 10/2011 Sampalis	JP	A-2006-290784	10/2006
	8,278,351 B2 10/2012 Sampalis 8,383,675 B2 2/2013 Sampalis	JP JP	A-2006-316073 A-2006-328014	11/2006 12/2006
	8,586,567 B2 11/2013 Sampalis	JP	A-2007-126455	5/2007
200	8,697,138 B2 4/2014 Bruheim et al.	JP SU	A-2007-246404 220741	9/2007 1/1971
	2/0076468 A1 6/2002 Saxby 3/0044495 A1 3/2003 Kagan	wo	WO 82/02819	9/1982
200	3/0113432 A1 6/2003 Yoshitomi	WO WO	WO 1986/06082 WO 89/01031	10/1986 2/1989
	4/0241249 A1 12/2004 Sampalis 5/0003073 A1 1/2005 Pivovarov et al.	wo	WO 89/01031 WO 89/10960	11/1989
200	6/0078625 A1 4/2006 Rockway	WO	WO 1990/05765	5/1990
	6/0193962 A1 8/2006 Kamiya et al. 8/0166419 A1 7/2008 Sones	WO WO	WO 1993/24142 WO 97/38585	12/1993 10/1997
	8/0166420 A1 7/2008 Sones	WO	WO 1997/38585	10/1997
	8/0268117 A1 10/2008 Rubin et al. 8/0274203 A1 11/2008 Bruheim et al.	WO WO	WO 1997/39759 WO 98/34498	10/1997 8/1998
	8/0274203 A1 11/2008 Bruheim et al. 0/0143571 A1 6/2010 Breivik	WO	WO 1998/34498	8/1998
201	0/0160659 A1 6/2010 Catchpole	WO WO	WO 99/39589 WO 1999/39589	8/1999 8/1999
	0/0226977 A1 9/2010 Tilseth et al. 1/0130458 A1 6/2011 Breivik	WO	WO 2000/23546	4/2000
	1/0160161 A1 6/2011 Sampalis	WO	WO 2000/25608	5/2000
	1/0223246 A1 9/2011 Opheim et al. 1/0224450 A1 9/2011 Sclabos et al.	WO WO	WO 2000/38708 WO 2001/028526	7/2000 4/2001
	1/0256216 A1 10/2011 Lefkowitz	WO	WO 01/76385	10/2001
	4/0274968 A1 9/2014 Berge et al.	WO WO	WO 2001/082928 WO 2002/083122	11/2001 10/2002
2014	4/0370115 A1 12/2014 Hoem et al.	wo	WO 2002-083122	10/2002
	FOREIGN PATENT DOCUMENTS	WO	WO 2002/092540 WO 02/102394	11/2002
		WO WO	WO 02/102394 WO 2002/102394	12/2002 12/2002
CA CA	1098900 4/1981 2251265 4/2000	WO	WO 2003/011873	2/2003
CL	40348 7/1997	WO WO	WO 2003/013497 WO 2004/028529	2/2003 4/2004
CN	102746941 1/2014 0609078 8/1994	WO	WO 2004/047554	6/2004
EP EP	0609078 8/1994 0670306 6/1995	WO WO	WO 2004/112767	12/2004
EP	1127497 8/2001	WO	WO 05/004593 WO 2005-018632	1/2005 3/2005
EP EP	1392623 3/2004 1406641 4/2004	WO	WO 2005/037848	4/2005
EP	1631280 4/2004	WO WO	WO 2005/038037 WO 2005/070411	4/2005 8/2005
EP EP	1542670 6/2005 0973532 9/2005	WO	WO 2006/030552	3/2005
EP	1689413 8/2006	WO	WO 2004-100943	5/2006
EP	1660071 1/2007	WO WO	WO 06/111633 WO 07/080515	10/2006 7/2007
EP	1743531 1/2007	WO	M O 01/080313	772007



### (56) References Cited

#### FOREIGN PATENT DOCUMENTS

WO	WO 2007/108702	9/2007
WO	WO 07/123424	11/2007
WO	WO 2008/006607	1/2008
WO	WO 08/072563	6/2008
WO	WO 08/117062	10/2008
WO	WO 2008/117062	10/2008
WO	WO 2009/027692	3/2009
WO	WO 2010/097701	9/2010
WO	WO 2011/050474	5/2011
WO	WO 2012/139588	10/2012
WO	WO 2013/102792	7/2013
WO	WO 2014/013335	1/2014

#### OTHER PUBLICATIONS

Ali-Nehari et al., "Characterization of purified phospholipids from krill () residues deoiled by supercritical carbon dioxide", Korean Journal of Chemical Engineering, 2012, vol. 29, No. 7.

Allahpichay et al., "Extraction of Growth Promoting Fractions from Non-muscle Krill Meal of Euphausia superba and its Effect on Fish Growth," Bulletin of the Japanese Society of Scientific Fisheries, 1984, 50(5): 821-826.

Ando and Hatano, 1988, "Isolation of apolipoproteins from carotenoid-carrying lipoprotein in the serum of chum salmon, *Oncorhynchus keta*", J. Lipid Research, 29: 1264-1271.

Aoi et al., 2003, "Astaxanthin limits exercise-induced skeletal and cardiac muscle damage in mice", Antioxidants & Redox Signaling, 5(1): 139-44.

Apr. 2, 2012 Response to Office Action, '351 patent.

Balassa et al., Microencapsulation in the Food Industry, Critical Reviews in Food Technology, 2:2, 245-265 (1971)("Balassa").

Bell and Dick, Molecular Species Composition of the Major Diacyl Glycerophospholipids from Muscle, Liver, Retina and Brain of Cod (*Gadus morhua*), Lipids, vol. 26, No. 8, pp. 565-573 (1991) ("Bell and Dick").

Bell, Molecular Species Analysis of Phosphoglycerides from the Ripe Roes of Cod, Lipids, vol. 24, No. 7 (1989).

Bell, Molecular Species Composition of Phosphatidylcholine from Crypthecodinium cohnii in Relation to Growth Temperature Lipids 25, 115-118 (1990).

Bergelson (ed.), *Lipid Biochemical Preparations*, Chapter 1.1, pp. 1-13 (1980) ("Bergelson").

Bottino N.R., "Lipid Composition of Two Species of Antarctic Krill: *Euphausia superba* and *E. crystallorophias*," Comp. Biochem. Physiol., 1975, vol. 50B, pp. 479-484.

Britton, 1985, "General Carotenoid Methods", Methods in Enzymology, vol. 111, pp. 113-149.

Brzustowicz, Michael R., et al., "Controlling Membrane Cholesterol Content. A Role for Polyunsaturated (Docosahexaenoate) Phospholipids," Biochemistry (2002), 41, pp. 12509-12519.

Buchi R-220 Rotovapor® Manual, dated Nov. 16, 2009, pp. 1-50. BUDA, Structural order of membranes and composition of phospholipids in fish brain cells during thermal acclimatization, Proc. Natl. Acad. Sci. USA vol. 91, pp. 8234-8238, Aug. 1994.

Budzinskli, E., et al., "Possibilities of processing and marketing of products made from Antarctic Krill", FAO Fish. Tech. Pap. (268) 46 pages (1985) (Budzinski).

Bunea R., et al., "Evaluation of the Effects of Neptune Krill Oil on the Clinical Course of Hyperlipidemia," Alternative Medicine Review, Thorne Research Inc., Sandpoint, US, vol. 9, No. 4, Jan. 1, 2004

Calder, 2006, "n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases", Am. J. Clin. Nutr., 83: 1505S.

Certificate of translation of Ex. 1072: Fisheries Agency, General Report on Research and Development of Techniques in Processing and Utilization of Marine Products, Chapter 6, Development of technology for recovery of valuable substances (astaxanthin) from

Certificate of translation of Ex. 1074: Japanese Patent No. 60-153779, entitled "Nutritional Supplement".

Certificate of translation of Ex. 1076: Japanese Patent Publication No. H08-231391, entitled "Medicine for Improvement of Dementia Symptoms".

Certification of translation of Ex. 1070: Japanese Unexamined Patent Application Publication No. 02-215351.

Certified translation of Ex. 1070: Japanese Unexamined Patent Application Publication No. 02-215351, titled Krill Phospholipids Fractioning Method ("Maruyama,"); Certificate of Translation provided as Ex. 1071; dated Jul. 9, 2013, 1 page.

Certified translation of Ex. 1072: Fisheries Agency, General Report on Research and Development of Techniques in Processing and Utilization of Marine Products, Chapter 6, Development of technology for recovery of valuable substances (astaxanthin) from krill, by Takao Fujita, pp. 273-307 (Mar. 1985) ("Fujita"); Certificate of Translation provided as Ex. 1073.

Certified translation of Ex. 1074: Japanese Patent No. 60-153779, entitled "Nutritional Supplement" ("Fukuoka"); Certificate of Translation provided as Ex. 1075, dated Aug. 16, 2013.

Certified translation of Ex. 1076: Japanese Patent Publication No. H08-231391, entitled "Medicine for Improvement of Dementia Symptoms" ("Yasawa"); Certificate of Translation provided as Ex. 1077, dated Aug. 16, 2013, 1 page.

Charest et al., 2001, "Astaxanthin Extraction from Crawfish Shells by Supercritical CO2 with Ethanol as Cosolvent", J. Aquatic Food Product Technology, 10(3): 79-93.

Chen and Meyers, 1982, "Extraction of Astaxanthin Pigment from Crawfish Waste Using a Soy Oil Process", J. Food Sci., 47: 892-896. Clarke, 1980, "The Biochemical Composition of Krill, Euphausia superba dana, from South Georgia", J. Exp. Mar. Biol. Ecol., 43: 221-236.

CN Office Action dated Apr. 27, 2012, JP Patent Application No. 200880112125.6 (and English translation).

CRC 2013-2014, 94th ed., pp. 6-231-6-235.

Czeczuga, 1974, "Comparative Studies of Carotenoids in the Fauna of the Gullmar Fjord (Bohuslan, Sweden). II. Crustacea: Eupagurus bernhardus, Hyas coarctatus and Upogebia deltaura", Marine Biology, 28: 95-98.

Database FSTA [Online] International Food Information Service, Frankfurt-Main; Shibata N. "Effect of fishing season on lipid content and composition of Antarctic krill (translated)" Database accession No. FS-1985-04-r-0091, abstract only.

Database WPI Week 200682, Thomson Scientific, London, GB, 2006

De Ritter and Purcell, 1981, "Carotenoid Analytical Methods", Carotenoids as Colorants and Vitamin A Precursors: Technological and Nutritional Applications, pp. 815-882.

Dec. 8, 2011 Office Action, KR Patent Application No. 10-2010-7006897 and its English translation.

Declaration of Bjorn Ole Haugsgjerd in support of Inter Partes Review of U.S. Pat. No. 8,278,351 ("Haugsgjerd"), dated Sep. 30, 2013, 12 pages.

Deutch, 1995, "Menstrual pain in Danish women correlated with low n-3 polyunsaturated fatty acid intake", Eur. J. Clin. Nutr., 49(7): 508-16.

Diez et al., 2003, "The role of the novel adipocyte-derived hormone adiponectin in human disease", Eur. J. Endocrinol., 148(3): 293-300

Eicherg, "Lecithin—It Manufacture and Use in the Fat and Oil Industry," Oils and Soap 51-54, 1939 ("Eichberg").

Ellingsen et al., 1987, "Biochemistry of the autolytic processes in Antarctic krill post mortem. Autoproteolysis." Biochem. J. 245, 295-305.

Emodi, 1978, "Carotenoids: Properties and Applications", Food Technology, 32(5): 38.

EP Opposition filed Feb. 13, 2014 by Olympic Seafood AS, EP Patent Application No. EP08718910I6.

EP Opposition filed May 8, 2015 by Olympic Seafood AS, EP Patent No. 2144618 includes: ENGE, "Declaration" Mackenzie, "Certificate of Analysis"—Callahan Innovation.



#### (56) References Cited

#### OTHER PUBLICATIONS

Evidence in Support of Opposition, Rimfrost AS, Australian Patent Application No. 2013227998, filed Sep. 22, 2016, 22 pages.

Farkas, Composition and Physical State of Phospholipids in Calanoid Copepods from India and Norway, Lipids, vol. 23, No. 6 (1988).

Felix-Valenzuela et al., 2001, "Supercritical CO2/Ethanol Extraction of Astaxanthin from Blue Crab (*Callinectes sapidus*) Shell Waste", Journal of Food Process Engineering, 24: 101-112.

Final Prospectus dated May 11, 2001 ("Final Prospectus").

Fisheries Agency, General Report on Research and Development of Techniques in Processing and Utilization of Marine Products, Chapter 6, Development of technology for recovery of valuable substances (astaxanthin) from krill, by Takao Fujita, pp. 273-307 (Mar. 1985); Japanese language document.

Folch, et al., A Simple Method for the Isolation and Purification of Total Lipids from Animal Tissues. J. Biol. Chem., 226, 497-509 (1957).

Fox and Scheer, 1941, "Comparative Studies of the Pigments of Some Pacific Coast Echinoderms", The Biological Bulletin, 441-455.

Fricke, et al., 1-O-Alkylglycerolipids in Antarctic Krill (*Euphausia superba* Dana), Comp. Biochem. Physiol. (1986) 85B(1): 131-134. Fricke, et al., Lipid, Sterol and Fatty Acid Composition of Antarctic Krill (*Euphausia superba* Dana), Lipids (1984) 19(11): 821-827.

Geusens et al., 1994, "Long-term effect of omega-3 fatty acid supplementation in active rheumatoid arthritis. A 12-month, double-blind, controlled study", Arthritis Rheum., 37(6): 824-9.

Gigliotti et al., "Extraction and characterisation of lipids from Antarctic krill (*Euphausia superba*)", Food Chemistry, 2011, vol. 125, No. 3, pp. 1028-1036.

Gilchrist and Green, 1960, "The Pigments of Artemia", Proceedings of the Royal Society, Series B Biological Sciences, vol. 152 No. 946, pp. 118-136.

Goodwin and Srisukh, 1949, "Some Observations on Astaxanthin Distribution in Marine Crustacea", Department of Biochemistry, University of Liverpool, pp. 268-270.

Gordeev, K.Y., et al. "Fatty Acid Composition of the Main Phospholipids of the Antarctic Krill, *Euphausia superba*," Chem. Nat. Cmpds. (1990) 26(2), pp. 143-147.

Cmpds. (1990) 26(2), pp. 143-147. Gordeev, K.Y., et al. "Fatty Acid Composition of the Main Phospholipids of the Antarctic Krill, *Euphausia superba*," Khim. Prirod. Soed. 2 (1990), pp. 181-187.

Grant of Request for Ex parte Reexamination of the '351 patent. Grantham (1977) Southern Ocean Fisheries Survey Programme, FAO Rome, GLO/SO/77/3: 1-61.

Grit et al., Hydrolysis of phosphatidylcholine in aqueous liposome dispersions, Int. J. Pharmaceutics 50:1-6 (1989).

Gulyaev and Bugrova, 1976 Removing fats from the protein paste "Okean". Konservnaya I Ovoshchesushil'naya Promyshlennost, (4), 37-8.

Hardardottir and Kinsella, 1988, "Extraction of Lipid and Cholesterol from Fish Muscle with Supercritical Fluids" Journal of Food Science, 53(6): 1656-1658.

Henderson et al., Lipid Composition of the Pineal Organ from Rainbow Trout (*Oncorhynchus mykiss*), Lipids, vol. 29, No. 5, pp. 311-317 (1994) ("Henderson").

Herman and Groves, The Influence of Free Fatty Acid Formation on the pH of Phospholipid-Stabilized Triglyceride Emulsions, Pharmaceutical Research 10(5):774-776 (1993). Hvattum, Erlend, et al., "Effect of soybean oil and fish oil on

Hvattum, Erlend, et al., "Effect of soybean oil and fish oil on individual molecular species of Atlantic salmon . . . ", Journal of Chromatography B, 748 (2000) 137-149.

Igarashi, Daisuke, et al., "Positional Distribution of DHA and EPA in Phosphatidylcholine and Phosphatidylethanolamine from Different Tissues of Squids," J. Oleo Sci. vol. 50, No. 9 (2001). International Aqua Feed, 2006, vol. 9.

International Search Report and Written Opinion for PCT/IB2010/000512; dated Jun. 24, 2010.

International Search Report and Written Opinion, International Patent Application No. PCT/IB2014/002130, dated Feb. 3, 2015. International Search Report for PCT/IB2007/000098, dated: Jun. 26, 2007.

International Search Report, International Patent Application No. PCT/IB2016/000208, dated May 13, 2016.

Itano Refrigerated Food Co., Ltd., Bio & High Technology Announcement and Natural Astaxanthin & Krill Lecithin, pp. 1-16 (on or before Dec. 28, 1994) ("Itano").

Itoh et al., 2007; "Increased adiponectin secretion by highly purified eicosapentaenoic acid in rodent models of obesity and human obese subjects", Arteriosclerosis, Thrombosis, and Vascular Biology; 27(9): 1918-1925.

Johnson and Lucas, Comparison of Alternative Solvents for Oils Extraction, JAOCS 60(2):229-242 (1983).

Johnson et al., 1978, "Simple Method for the Isolation of Astaxanthin from the Basidiomycetous Yeast Phaffia rhodozyma", Applied and Environmental Microbiology, 35(6): 1155-1159.

Jong-Ho Lee, "A Review: Antioxygenic and Peroxide-decomposing Activities of Antarctic Krill Lipids," J. Korean Soc. Food Mutr. 13(3) pp. 326-333 (1984).

JP Office Action dated Feb. 23, 2012, JP Patent Application No. 2010-522444 (and English translation).

Ki Woong Cho, et al., "Lipid and Fatty Acid Composition of the Antarctic Krill *Euphausia superba*," Ocean Research 21(2): 109-116 (1999).

Kolakowska, 1989, "Krill lipids after frozen storage of about one year in relation to storage time before freezing", Die Nahrung Food, 33(3): 241-244.

Kolakowski and Gajowiecki, "Optimization of autoproteolysis to obtain and edible product 'precipitate' from Antarctic krill," Seafood Science and Technology, pp. 331-336.

Kris-Etherton et al., 2002, "Fish Consumption, Fish Oil, Omega-3 Fatty Acids, and Cardiovascular Disease", Circulation, 106:2747-2757

Kristensen et al., 1989, "Dietary supplementation with n-3 polyunsaturated fatty acids and human platelet function: a review with particular emphasis on implications for cardiovascular disease", J. Intern. Med. Suppl. 731:141-50.

Kunesova et al., 2006, "The influence of n-3 polyunsaturated fatty acids and very low calorie diet during a short-term weight reducing regimen on weight loss and serum fatty acid composition in severely obese women", Physiol Res.; 55(1):63-72.

Kyun-Ku Kim, et al., "Effects of Cooking and Drying Methods on the Polar Lipds Composition of Shrimp," Korean J. Food Sci. Technol. vol. 21, No. 1, pp. 25-30 (1989).

Laight et al., 1999, "F2-isoprostane evidence of oxidant stress in the insulin resistant, obese Zucker rat: effects of vitamin E", Eur. J. Pharmacol. 377(1): 89-92.

Lambertson and Braekkan, 1971, "Method of Analysis of Astaxanthin and its Occurrence in some Marine Products," J. Sci. Food. Agr., vol. 22(2): 99-101.

Le Grandois et al., Investigation of Natural Phosphatidylholine Sources: Separation and Identification by Liquid Chromatography—Electrospray Ionization-Tandem Mass Spectrometry (LC-ESI-MS2) of Molecular Species, J. Agric. Food Chem., 57, 6014-20 (2009) ("Le Grandois").

Libby et al., 2006, "Inflammation and Atherothrombosis: From Population Biology and Bench Research to Clinical Practice", J. Amer. Coll. Card., 48 (9, Suppl. A): A33-A46.

Lin et al., Effect of Dietary N-3 Fatty Acids Upon the PhospholipidMolecular Species of the Monkey Retina, Invest Ophthalmol Vis Sci. 1994;35:794-803.

Lopez et al., 2004, "Selective extraction of astaxanthin from crustaceans by use of supercritical carbon dioxide", Talanta, 64: 726-731

Mandeville, 1991, "Isolation and Identification of Carotenoid Pig-



#### (56) References Cited

#### OTHER PUBLICATIONS

Medina et al., C Nuclear Magnetic Resonance Monitoring of Free Fatty Acid Release After Fish Thermal Processing, J. Amer. Oil Chem. Soc. 71(5):479-82 (1994).

Meyers and Bligh, 1981, "Characterization of Astaxanthin Pigments from Heat-Processed Crawfish Waste", J. Agric. Food Chem., 29: 505-508

Meyers, 1977, "Using Crustacean Meals and Carotenoid-Fortified Diets", Feedstuffs, vol. 49(19).

Meyers, 1994, "Developments in world aquaculture, feed formulations, and role of carotenoids", Pure & Appl. Chem, vol. 66(5): 1069-1076.

Mills et al., 1989, "Dietary N-6 and N-3 fatty acids and salt-induced hypertension in the borderline hypertensive rat", Lipids, 24(1): 17-24

Moates and Van Bentem, 1990, "Separating out the value", Food Science and Technology Today, 4(4): 213-214.

Neptune krill Oil's Unique Properties, Internet Citation, 2011, URL:http://www.nowfoods.com/Products/ProductFAQs/081008/htm.

Neptune Technologies & Bioressources Soon to Obtain a Major Patent in Over 30 Countries ("2001 Press Release,").

Nikolaeva, 1967 "Amino acid composition of protein-coagulate in krill", VNIRO, 63:161-4.

Notice of Acceptance of Application, Australian Patent Application No. 2013227998, dated Oct. 5, 2016, 2 pages.

Oct. 24, 2012 Office Action, '675 patent.

Office Action dated Jan. 5, 2012, '351 patent.

Phleger, et al. (2002) "Interannual and between species comparison in the lipids, fatty acids, and sterols of Antarctic krill from the US AMLR Elephant Island survey area: 1997 and 1998". Comp Biochem Physiol 131B:733-747.

Takahashi et al., Compositional Changes in Molecular Species of Fish Muscle Phosphatidylcholine During Storage, Bull. Fac. Fish. Hokkaido Univ. 37(1), 80-84 1986.

Takahashi et al., Molecular Species of Fish Muscle Lecithin, Bulletin of the Japanese Society of Scientific Fisheries 48(12), 1803-1814 (1982).

Takahashi et al., Prediction of Relative Retention Value of the Individual Molecular Species of Diacyl Glycerolipid on High Performance Liquid Chromatography, Bull. Fac. Fish. Hokkaido Univ. 38(4), 398-404. 1987.

Takaichi et al., 2003, "Fatty Acids of astaxanthin esters in krill determined by mild mass spectrometry", Comparative Biochemistry and Physiology Part B, Biochemistry and Molecular Biology, Elsevier, Oxford, vol. 136, Jan. 1, 2003, p. 317-322.

Tanaka et al., 2004, "Extraction of Phospholipids from Salmon Roe with Supercritical Carbon Dioxide and an Entrainer", J. Oleo Sci, 53(9): 417-424.

Tanaka et al., 2005, "Extraction of Phospholipids from Unused Natrual Resources with Supercritical Carbon Dioxide and an Entrainer", Journal of Oleo Science, vol. 54(11): 569-576.

Tanaka, Biosynthesis of 1,2-dieicosapentaenoyl-sn-glycero-3-phosphocholine in Caenorhabditis elegans, Eur. J. Biochem. 263, 189±194 (1999).

Tanaka, T., et al., Platelet-activating Factor (PAF)-like Phospholoipds Formed during Peroxidation of Phosphatidylcholines from Different Foodstuffs, Biosci. Biotech. Biochem. (1995) 59 (8), pp. 1389-1393.

Third Party Observation against corresponding AU Patent Application No. 2013227998, filed Jul. 15, 2016, 6 pages.

Third Party Observation against corresponding AU Patent Application No. 2014256345, filed May 23, 2016, 50 pages.

Tocher, Chapter 6, Glycerophospholipid metabolism, Biochemistry and molecular biology of fishes, vol. 4, Hochachka and Mommsen (eds.)(1995).

Tochizawa, Kaoru, et al., "Effects of Phospholipds Containing Docosahexaenoic Acid on Differentiation and Growth of HL-60 Todoric et al., 2006, "Adipose tissue inflammation induced by high-fat diet in obese diabetic mice is prevented by n-3 polyun-saturated fatty acids", Diabetologia, 49(9): 2109-2119.

Tou et al., 2007, "Krill for human consumption: nutritional value and potential health benefits.", Nutrition Rev 65(2):63-77.

Trayhurn et al., 2004, "Adipokines: inflammation and the pleiotropic role of white adipose tissue", Br. J. Nutrition, 92(3): 347-355.

Popp-Snijders et al., 1987, "Dietary supplementation of omega-3 polyunsaturated fatty acids improves insulin sensitivity in non-insulin-dependent diabetes", Diabetes Res. 4(3): 141-7.

U.S. Appl. No. 60/307,842 (Priority document for the '351 patent). Raventos et al., Application and Posssibilities of Supercritical CO2 Extraction in Food Processing Industry: An Overview, Food Science and Technology International (2002)8: 269-284.

Sachindra, 2006, "Recovery of carotenoids from shrimp waste in organic solvents", Waste Management, 26: 1092-1098.

Saether et al., 1986, "Lipids of North Atlantic krill", J Lipid Res., 27(3):274-85.

Shahidi et al., 1998, "Carotenoid Pigments in Seafoods and Aquaculture" Critical Reviews in Food Science, 38(1): 1-67.

Shon, Mi-Yae, et al., "Effects of Krill and Cadmium on Lipid Composition of Plasma in Cholesterol-Fed Rats," J. Korean Soc. Food Nutr. 23(1), 38-43 (1994).

Sidehu et al., 1970, "Biochmical Composition and Nutritive Value of Krill (*Euphausia superb* dana)", J. Sci Food Agr., vol. 21, 293-296.

Sikorski, E., "The Utilization of Krill for Food," Food Process Eng., 1:845-855 (1980).

Simopoulos, 1991, "Omega-3 fatty acids in health and disease and in growth and development", Am. Clin. Nutr. 54:438-63.

Somiya, 1982, "'Yellow lens' eyes of a stomiatoid deep-sea fish, *Malacosteus niger*", Proc. R. Soc. Lond., 215: 481-489.

Statement of Grounds and Particulars, Rimfrost AS, filed Jun. 10, 2016, Australian Patent Application No. 2014203179, 22 pages.

Summons Materials downloaded from ESPACE on Dec. 16, 2014 for EP Patent Application No. 08 718 910.6.

Supplemental Declaration of Bjorn Ole Haugsgjerd submitted during inter partes reexamination of parent U.S. Pat. No. 8,030,348 ("Haugsgjerd '348 Supp. Decl.").

Supplemental Declaration of Dr. Earl White submitted during interpartes reexamination of parent U.S. Pat. No. 8,030,348 ("White Supp. Reexam. Decl.").

Supplemental Declaration of Dr. Earl White submitted during prosecution of parent U.S. Pat. No. 8,278,351 ("White Supp. Decl.").

Supplemental Declaration of Dr. Thomas Gundersen submitted during inter partes reexamination of parent U.S. Pat. No. 8,030,348 ("Gundersen Supp. Decl.").

Suzuki, T. and Shibata, N., "The utilization of Antarctic krill for human food," Food Rev. Int'l, 6:1, 119-147 (1990) ("Suzuki").

Petition for Inter Partes Review, U.S. Pat. No. 9,078,905, Case No. IPR2017-00747, filed Jan. 27, 2017.

Petition for Inter Partes Review, U.S. Pat. No. 9,028,877, Case No. IPR2017-00746, filed Feb. 3, 2017.

Petition for Inter Partes Review, U.S. Pat. No. 9,028,877, Case No. IPR2017-00748, filed Feb. 3, 2017.

Respondents' Notice of Prior Art, United States International Trade Commission, Investigation No. 337-TA-1019, dated Feb. 1, 2017. Notice of Opposition, Rimfrost AS, AU Patent Application No. 2014256345, filed Mar. 1, 2017.

Notice of Opposition, Enzymotec Ltd., AU Patent Application No. 2014256345, filed Mar. 1, 2017.

Respondents' Motion for Leave to Amend Their Response to the Complaint and Notice of Investigation, United States International Trade Commission, Investigation No. 337-TA-1019, dated Mar. 14, 2017.

Trebble et al., 2003, "Inhibition of tumour necrosis factor-alpha and interleukin 6 production by mononuclear cells following dietary fish-oil supplementation in healthy men and response to antioxidant co-supplementation", Br. J. Nutrition, 90(2): 405-412.



# DOCKET

# 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.

