



US009644170B2

(12) **United States Patent**
Bruheim et al.

(10) **Patent No.:** **US 9,644,170 B2**

(45) **Date of Patent:** ***May 9, 2017**

(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 disclaimer.

(21) Appl. No.: **15/180,439**

(22) Filed: **Jun. 13, 2016**

(65) **Prior Publication Data**

US 2016/0279173 A1 Sep. 29, 2016

Related U.S. Application Data

(63) Continuation of application No. 14/020,162, filed on Sep. 6, 2013, now Pat. No. 9,375,453, which is a continuation of application No. 12/057,775, filed on Mar. 28, 2008, now Pat. No. 9,034,388.

(60) Provisional application No. 60/920,483, filed on Mar. 28, 2007, provisional application No. 60/975,058, filed on Sep. 25, 2007, provisional application No. 60/983,446, filed on Oct. 29, 2007, provisional application No. 61/024,072, filed on Jan. 28, 2008.

(51) **Int. Cl.**

C11B 3/00 (2006.01)
A61K 9/48 (2006.01)
A61K 31/20 (2006.01)
A61K 31/122 (2006.01)
A61K 31/23 (2006.01)
A61K 31/683 (2006.01)
A61K 31/685 (2006.01)
A61K 35/612 (2015.01)
A61K 45/06 (2006.01)
A61K 31/202 (2006.01)
A61K 31/235 (2006.01)
A61K 9/00 (2006.01)

(52) **U.S. Cl.**

CPC **C11B 3/006** (2013.01); **A61K 9/0053** (2013.01); **A61K 9/48** (2013.01); **A61K 9/4825** (2013.01); **A61K 9/4858** (2013.01); **A61K 31/122** (2013.01); **A61K 31/20** (2013.01); **A61K 31/202** (2013.01); **A61K 31/23** (2013.01); **A61K 31/235** (2013.01); **A61K 31/683** (2013.01); **A61K 31/685** (2013.01); **A61K 35/612** (2013.01); **A61K 45/06** (2013.01)

31/122; A61K 31/685; A61K 31/133; A61K 31/198; A61K 31/202; A61K 31/575; A61K 38/1767; A61K 9/2009; A61K 9/2054; A61K 9/2866; A61K 31/23; A61K 31/683; A61K 31/20; A61K 31/235; A61K 45/06; A61K 9/0053; A61K 9/48; A61K 9/4825; A61K 9/4858; A61K 31/201; A23L 1/3006; A23L 1/33; A23L 1/305; C11B 3/006

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 Terasa et al.
4,119,619 A 10/1978 Rogozhin et al.
4,133,077 A 1/1979 Jasniewicz et al.
4,251,557 A 2/1981 Shimose et al.
4,505,936 A 3/1985 Meyers et al.
4,714,571 A 12/1987 Kearns et al.
4,749,522 A 6/1988 Kamarei
4,814,111 A 3/1989 Kearns et al.
5,006,281 A 4/1991 Rubin et al.
5,266,564 A 11/1993 Modolell
5,434,183 A 7/1995 Larsson-Backstrom

(Continued)

FOREIGN PATENT DOCUMENTS

AU 2002322233 2/2003
BR 8701265 3/1987

(Continued)

OTHER PUBLICATIONS

Declaration of Bjorn Ole Haugsgjerd submitted during inter partes reexamination of parent patent U.S. 8,030,348 ("Haugsgjerd '348 Decl.").

(Continued)

Primary Examiner — Debbie K Ware

(74) Attorney, Agent, or Firm — Casimir Jones, S.C.

(57)

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 CO₂ 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 anti-inflammation, anti-oxidant effects, improving insulin resistances and improving blood lipid profile.

(56)

References Cited

U.S. PATENT DOCUMENTS

6,214,396 B1 4/2001 Barrier
 6,346,276 B1 2/2002 Tanouchi et al.
 6,537,787 B1 3/2003 Breton
 6,800,299 B1 10/2004 Beaudoin
 7,488,503 B1 2/2009 Porzio et al.
 7,666,447 B2 2/2010 Rockway
 8,030,348 B2 10/2011 Sampalis
 8,057,825 B2 11/2011 Sampalis
 8,278,351 B2 10/2012 Sampalis
 8,372,812 B2 2/2013 Tilseth et al.
 8,383,675 B2 2/2013 Sampalis
 8,697,138 B2 4/2014 Bruheim et al.
 9,028,877 B2 5/2015 Bruheim et al.
 9,034,388 B2 5/2015 Bruheim et al.
 9,072,752 B1 7/2015 Bruheim et al.
 9,078,905 B2 7/2015 Bruheim et al.
 9,119,864 B2 9/2015 Bruheim et al.
 2002/0076468 A1 6/2002 Saxby
 2003/0044495 A1 3/2003 Kagan
 2003/0113432 A1 6/2003 Yoshitomi
 2004/0241249 A1 12/2004 Sampalis
 2005/0003073 A1 1/2005 Pivovarov et al.
 2006/0078625 A1 4/2006 Rockway
 2006/0193962 A1 8/2006 Kamiya et al.
 2008/0166419 A1 7/2008 Sones
 2008/0166420 A1 7/2008 Sones
 2009/0061067 A1 3/2009 Tilseth et al.
 2010/0143571 A1 6/2010 Breivik
 2010/0160659 A1 6/2010 Catchpole
 2010/0226977 A1 9/2010 Tilseth et al.
 2011/0130458 A1 6/2011 Breivik
 2014/0005421 A1 1/2014 Bruheim et al.
 2014/0010888 A1 1/2014 Bruheim et al.
 2014/0080791 A1 3/2014 Berge et al.
 2014/0088043 A1 3/2014 Hoem et al.
 2014/0088047 A1 3/2014 Hoem et al.
 2014/0107072 A1 4/2014 Tilseth et al.
 2014/0274968 A1 9/2014 Berge et al.
 2014/0363517 A1 12/2014 Bruheim et al.
 2014/0370115 A1 12/2014 Hoem et al.
 2015/0030718 A1 1/2015 Saebo
 2015/0050403 A1 2/2015 Tilseth et al.
 2015/0164841 A1 6/2015 Hoem et al.

FOREIGN PATENT DOCUMENTS

CA 1098900 4/1981
 CA 2251265 4/2000
 CL 40348 7/1997
 CN 102746941 1/2014
 EP 0609078 8/1994
 EP 0670306 6/1995
 EP 1127497 8/2001
 EP 1392623 3/2004
 EP 1406641 4/2004
 EP 1631280 4/2004
 EP 1542670 6/2005
 EP 0973532 9/2005
 EP 1689413 8/2006
 EP 1660071 1/2007
 EP 1743531 1/2007
 EP 1123368 4/2008
 EP 1419768 1/2009
 EP 1292294 3/2009
 EP 1706106 7/2009
 EP 1385500 7/2010
 GB 2097014 10/1982
 GB 921537 6/1999
 JP S51-125774 11/1976
 JP S52-114046 9/1977
 JP 60-153779 8/1985
 JP 61281159 12/1986
 JP 02049091 2/1990

JP 2963152 2/1992
 JP 04057853 2/1992
 JP 3081692 7/1994
 JP 2524217 8/1996
 JP H08-231391 8/1996
 JP 3344887 7/1997
 JP 3611222 8/1997
 JP 2909508 6/1999
 JP 2001-158736 6/2001
 JP 2003-003192 1/2003
 JP 2003-048831 2/2003
 JP 2003-146883 5/2003
 JP 3467794 9/2003
 JP 2003-530448 10/2003
 JP 3486778 10/2003
 JP 2004-534800 11/2004
 JP 3678317 5/2005
 JP 2005-245379 9/2005
 JP 2006-069948 3/2006
 JP 2006-083136 3/2006
 JP 2006-290784 10/2006
 JP 2006-316073 11/2006
 JP 2006-328014 12/2006
 JP 2007-126455 5/2007
 JP 2007-246404 9/2007
 SU 220741 1/1971
 WO 82/02819 9/1982
 WO 86/06082 10/1986
 WO 89/01031 2/1989
 WO 89/10960 11/1989
 WO 90/05765 5/1990
 WO 93/24142 12/1993
 WO 97/38585 10/1997
 WO 97/39759 10/1997
 WO 98/34498 8/1998
 WO 99/39589 8/1999
 WO 00/23546 4/2000
 WO 00/25608 5/2000
 WO 00/38708 7/2000
 WO 01/28526 4/2001
 WO 01/82928 11/2001
 WO 02-083122 10/2002
 WO 02/083122 10/2002
 WO 02/092540 11/2002
 WO 02/102394 12/2002
 WO 03/011873 2/2003
 WO 03/013497 2/2003
 WO 2004/028529 4/2004
 WO 2004/047554 6/2004
 WO 2004/112767 12/2004
 WO 2005/004593 1/2005
 WO 2005-018632 3/2005
 WO 2005/037848 4/2005
 WO 2005/038037 4/2005
 WO 2005/070411 8/2005
 WO 2006/030552 3/2006
 WO 2004-100943 5/2006
 WO 2006/111633 10/2006
 WO 2007/080514 7/2007
 WO 2007/080515 7/2007
 WO 2007/108702 9/2007
 WO 2007/123424 11/2007
 WO 2008/006607 1/2008
 WO 2008/072563 6/2008
 WO 2008/117062 10/2008
 WO 2009/027692 3/2009
 WO 2010/097701 9/2010
 WO 2011/050474 5/2011
 WO 2013/102792 7/2013
 WO 2014/013335 1/2014

OTHER PUBLICATIONS

Declaration of Dr. Albert Lee in Support of Inter Partes Review of U.S. Pat. No. 8,278,351 ("Lee").

(56) **References Cited**

OTHER PUBLICATIONS

- Declaration of Dr. Chong Lee submitted during inter partes reexamination of parent patent U.S. 8,030,348 ("Yeboah Reexam Decl.").
- Declaration of Dr. Earl White submitted during prosecution of parent patent U.S. 8,030,348 ("2011 White Decl.").
- Declaration of Dr. Ivar Storø in support of Inter Partes Review of U.S. Pat. No. 8,278,351 ("Storø").
- Declaration of Dr. Ivar Storø in support of Inter Partes Review of U.S. Pat. No. 8,383,675 ("Storø").
- Declaration of Dr. Jacek Jaczynski from inter partes reexamination of the parent patent U.S. Pat. No. 8,030,348 ("Jaczynski Reexam. Decl.").
- Declaration of Dr. Jaczynski submitted during prosecution of parent patent U.S. 8,278,351 (Jaczynski '351 Decl.).
- Declaration of Dr. Jeff Moore in Support of Inter Partes Review of U.S. Pat. No. 8,278,351 ("Moore").
- Declaration of Dr. Jeff Moore in Support of Inter Partes Review of U.S. Pat. No. 8,383,675 ("Moore").
- Declaration of Dr. Richard van Breemen in Support of Inter Partes Review of U.S. Pat. No. 8,278,351 ("Van Breemen").
- Declaration of Dr. Richard van Breemen in Support of Inter Partes Review of U.S. Pat. No. 8,383,675 ("Van Breemen").
- Declaration of Dr. Shahidi submitted during inter partes reexamination of parent patent U.S. 8,030,348 (Shahidi Reexam. Decl.).
- Declaration of Dr. Shahidi submitted during prosecution of parent patent U.S. 8,278,351 (Shahidi '351 Decl.).
- Declaration of Dr. Suzanne Budge in Support of Inter Partes Review of U.S. 8,278,351 ("Budge").
- Declaration of Dr. Suzanne Budge in Support of Inter Partes Review of U.S. 8,383,675 ("Budge").
- Declaration of Dr. Thomas Brenna in support of Inter Partes Review of U.S. 8,278,351.
- Declaration of Dr. Thomas Brenna in support of Inter Partes Review of U.S. 8,383,675.
- Declaration of Dr. Thomas Gundersen submitted during inter partes reexamination of parent patent U.S. 8,030,348 ("Gundersen Decl.>").
- Declaration of Dr. Tina Sampalis submitted during inter partes reexamination of parent patent U.S. 8,030,348 ("Sampalis").
- Declaration of Dr. Van Breemen submitted during Ex parte Reexamination of the '351 patent (Van Breemen '351 Reexam. Decl. Decl.).
- Declaration of Dr. Van Breemen submitted during Inter partes Reexamination of the '348 patent (Van Breemen '348 Reexam Decl. Decl.).
- Declaration of Dr. Yeboah submitted during inter partes reexamination of parent patent U.S. 8,030,348 ("Yeboah Reexam Decl.>").
- Declaration of Dr. Yeboah submitted during prosecution of parent patent U.S. 8,278,351 ("Yeboah '351 Decl.>").
- Eichberg, "Lecithin—It Manufacture and Use in the Fat and Oil Industry," Oils and Soap 51-54, 1939 ("Eichberg").
- Expert Witness Report of Dr. Theodore Welch submitted in relation to ITC Investigation No. 337-TA-877 ("Welch").
- Farkas, Composition and Physical State of Phospholipids in Calanoid Copepods from India and Norway, LIPIDS, vol. 23, No. 6 (1988).
- Final Prospectus dated May 11, 2001 ("Final Prospectus").
- Folch, et al., A Simple Method for the Isolation and Purification of Total Lipids from Animal Tissues. J. Biol. Chem., 226, 497-509 (1957).
- Grant of Request for Ex parte Reexamination of the '351 patent.
- Grit et al., Hydrolysis of phosphatidylcholine in aqueous liposome dispersions, Int. J. Pharmaceutics 50:1-6 (1989).
- 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).
- Itano Refrigerated Food Co., Ltd., Bio & High Technology Johnson and Lucas, Comparison of Alternative Solvents for Oils Extraction, JAOCS 60(2):229-242 (1983).
- Le Grandois et al., Investigation of Natural Phosphatidylholone 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").
- 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.
- 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).
- Oct. 24, 2012 Office Action, '675 patent.
- Office Action dated Jan. 5, 2012, '351 patent.
- U.S. Appl. No. 60/307,842 (Priority document for the '351 patent), available in PAIR.
- Supplemental Declaration of Bjorn Ole Haugsgjerd submitted during inter partes reexamination of parent patent U.S. Pat. No. 3,030,348 ("Haugsgjerd '348 Supp. Decl.>").
- Supplemental Declaration of Dr. Earl White submitted during inter partes reexamination of parent patent U.S. Pat. No. 3,030,348 ("White Supp. Reexam. Decl.>").
- Supplemental Declaration of Dr. Earl White submitted during prosecution of parent patent U.S. Pat. No. 8,278,351 ("White Supp. Decl.>").
- Supplemental Declaration of Dr. Thomas Gundersen submitted during inter partes reexamination of parent patent 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").
- 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).
- 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.
- Todoric et al., 2006, "Adipose tissue inflammation induced by high-fat diet in obese diabetic mice is prevented by n-3 polyunsaturated 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.
- Treble 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.
- Ukkola et al., 2002, "Adiponectin: a link between excess adiposity and associated comorbidities?", J. Mol. Med., 80 (11): 696-702.
- Van Der Veen et al., 1971 "The Lipids of Krill (*Euphausia Species*) and Red Crab (*Pleuroncodes Planipes*)", Lipids, 6(7): 481-485.
- Virtue, et al. 1996, Reproductive trade-off in male Antarctic krill, *Euphausia superba*, Marine Biology, vol. 126, No. 3, pp. 521-527.
- Yamaguchi et al., 1983, "The Composition of Carotenoid Pigments in the Antarctic Krill *Euphausia superba*", Bulletin of the Japanese Society of Scientific Fisheries, 49(9): 1411-1415.
- Yamaguchi et al., 1986, "Supercritical Carbon Dioxide Extraction

(56)

References Cited

OTHER PUBLICATIONS

- Yanase M; 1974, "Modification of a Russian method for separation of heat-coagulated protein from Antarctic krill", Database FSTA (online); International Food Information Service (IFIS); Frankfurt-Main, DE.
- Yen et al., 1994, "Effect of dietary omega-3 and omega-6 fatty acid sources on PUVA-induced cutaneous toxicity and tumorigenesis in the hairless mouse", Arch. Dermatol. Res., 286(6): 331-6. Database WPI Week 200682, Thomson Scientific, London, GB, 2006.
- Yanase, M., "Modification of Russian Method for Separating Heat Coagulated Protein from Antarctic Krill," Bull. Tokai Reg. Fish. Res. Lab, 78: 79-84 (1974).
- Sikorski, E., "The Utilization of Krill for Food," Food Process Eng., 1:845-855 (1980).
- Budzinski, 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.
- 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.
- Dec. 8, 2011 Office Action, KR Patent Application No. 10-2010-7006897 and its English translation.
- JP Office Action mailed Feb. 23, 2012, JP Patent Application No. 2010-522444 (and English translation).
- CN Office Action mailed Apr. 27, 2012, JP Patent Application No. 200880112125.6 (and English translation).
- Fricke, et al., Lipid, Sterol and Fatty Acid Composition of Antarctic Krill (*Euphausia superba* Dana), Lipids (1984) 19 (11): 821-827.
- Fricke, et al., 1-O-Alkylglycerolipids in Antarctic Krill (*Euphausia Superba* Dana), Comp. Biochem. Physiol. (1986) 85B(1): 131-134.
- Gordeev, K.Y., et al. "Fatty Acid Composition of the Main Phospholipids of the Antarctic Krill, *Euphausia superba*," Chem. Nat. Compds. (1990) 26(2), pp. 143-147.
- Grantham (1977) Southern Ocean Fisheries Survey Programme, FAO Rome, GLO/SO/77/3: 1-61.
- Raventos et al., Application and Possibilities of Supercritical CO2 Extraction in Food Processing Industry: An Overview, Food Science and Technology International (2002) 8: 269-284.
- Tanaka, T., et al., Platelet-activating Factor (PAF)-like Phospholipids Formed during Peroxidation of Phosphatidylcholines from Different Foodstuffs, Biosci. Biotech. Biochem. (1995) 59 (8), pp. 1389-1393.
- Winther, et al., Elucidation of Phosphatidylcholine Composition in Krill Oil Extracted from *Euphausia superba*, Lipids (2011)46: 25-36.
- "Neptune Technologies & Bioresources Soon to Obtain a Major Patent in Over 30 Countries" ("2001 Press Release,").
- Action Closing Prosecution, '348 patent.
- 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 *Cryptocodinium cohnii* in Relation to Growth Temperature Lipids 25, 115-118 (1990).
- Bergelson (ed.), Lipid Biochemical Preparations, Chapter I.1, pp. 1-13 (1980).
- Bottino N.R., "Lipid Composition of Two Species of Antarctic Buchi R-220 Rotovapor® Manual.
- 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.
- 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 krill, by Takao Fujita, pp. 273-307 (Mar. 1985); Japanese language document.
- 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.
- 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.
- 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.
- Declaration of Bjorn Ole Haugsgjerd in support of Inter Partes Review of U.S. Pat. No. 8,278,351.
- 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.
- Britton, 1985, "General Carotenoid Methods", Methods in Enzymology, vol. 111, pp. 113-149.
- Calder, 2006, "n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases", Am. J. Clin. Nutr., 83: 1505S.
- 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.
- Czczuga, 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.
- De Ritter and Purcell, 1981, "Carotenoid Analytical Methods", Carotenoids as Colorants and Vitamin A Precursors: Technological and Nutritional Applications, pp. 815-882.
- 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.
- Ellingsen et al., 1987, "Biochemistry of the autolytic processes in Antarctic krill post mortem. Autoproteolysis." Biochem. J. 246, 295-305.

(56)

References Cited

OTHER PUBLICATIONS

- 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.
- Fox and Scheer, 1941, "Comparative Studies of the Pigments of Some Pacific Coast Echinoderms", *The Biological Bulletin*, 441-455.
- 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.
- 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.
- 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.
- International Aqua Feed, 2006, vol. 9.
- International Search Report and Written Opinion for PCT/GB2008/002934, Dated Mar. 11, 2009.
- International Search Report and Written Opinion for PCT/IB2010/000512; dated Jun. 24, 2010.
- International Search Report for PCT/IB2007/000098, dated: Jun. 26, 2007.
- 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 et al., 1978, "Simple Method for the Isolation of Astaxanthin from the Basidiomycetous Yeast *Phaffia rhodozyma*", *Applied and Environmental Microbiology*, 35(6): 1155-1159.
- 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.
- 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.
- 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.
- Lamberton and Braekkan, 1971, "Method of Analysis of Astaxanthin and its Occurrence in some Marine roducts.", *J. Sci. Food. Agr.*, vol. 22(2): 99-101.
- 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.
- 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 Pigments, Lipids and Flavor Active Components from Raw Commercial Shrimp Waste", *Food Biotechnology*, 5(2): 185-195.
- Meyers and Bligh, 1981, "Characterization of Astaxanthin Pigments from Heat-Processed Crawfish Waste", *J. Agric. Food Chem.*, 29: 505-508.
- 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.
- Nikolaeva, 1967 "Amino acid composition of protein-coagulate in krill", *VNIRO*, 63:161-4.
- 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.
- 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.
- 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.
- Sidehu et al., 1970, "Biochemical Composition and Nutritive Value of Krill (*Euphausia superb dana*)", *J. Sci Food Agr.*, vol. 21, 293-296.
- 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.
- 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.
- Tanaka, Biosynthesis of 1,2-dieicosapentaenoyl-sn-glycero-3-phosphocholine in *Caenorhabditis elegans*, *Eur. J. Biochem.* 263, 189±194 (1999).
- Tocher, Chapter 6, Glycerophospholipid metabolism, *Biochemistry and molecular biology of fishes*, vol. 4, Hochachka and Mommsen (eds.)(1995).
- Watanabe et al., Effective Components in Cuttlefish Meal and Raw Krill for Improvement of Quality of Red Seabream *Pagrus major* Eggs, *Nippon Suisan Gakkaishi* 57(4):681-694 (1991)("Watanabe").
- WHO News and Activities, *Bulletin of the World Health Organization*, 73(4), pp. 547-51 (1995) ("WHO Bulletin").
- Valeri, D., et al., "Visocities of Fatty acids, triglycerides and their binary mixtures," *JAOCS* 74 (1997) pp. 1221-1226.
- CRC 2013-2014, 94th ed., pp. 6-231-6-235.
- EP Opposition filed Feb. 13, 2014 by Olympic Seafood AS, EP Patent Application No. EP0871891016.
- Brzustowicz, Michael R., et al., "Controlling Membrane Cholesterol Content. A Role for Polyunsaturated (Docosahexaenoate) Phospholipids," *Biochemistry* (2002), 41, pp. 12509-12519.
- Jong-Ho Lee, "A Review: Antioxygenic and Peroxide-decomposing Activities of Antarctic Krill Lipids," *J. Korean Soc. Food Nutr.* 13(3) pp. 326-333 (1984).
- Ki Woong Cho, et al., "Lipid and Fatty Acid Composition of the Antarctic Krill *Euphausia superba*," *Ocean Research* 21(2): 109-116 (1999).
- 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).
- Tochizawa, Kaoru, et al., "Effects of Phospholipids Containing Docosahexaenoic Acid on Differentiation and Growth of HL-60

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.