

(12) United States Patent

Bruheim et al.

(10) **Patent No.:**

US 9,375,453 B2

(45) **Date of Patent:**

*Jun. 28, 2016

(54) METHODS FOR PRODUCING 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 41 days.

This patent is subject to a terminal dis-

claimer.

(21) Appl. No.: 14/020,162

(22)Filed: Sep. 6, 2013

(65)**Prior Publication Data**

> US 2014/0005421 A1 Jan. 2, 2014

Related U.S. Application Data

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

(52) U.S. Cl.

CPC A61K 35/612 (2013.01); A61K 9/48 (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 45/06 (2013.01); C11B 3/006 (2013.01)

(58) Field of Classification Search

CPC A61K 2300/00; A61K 31/122; A61K 35/612; A61K 31/685; A61K 31/23; A61K 31/683; A61K 31/202; A61K 45/06; A61K 31/6615; A61K 8/553; A61K 2800/70;

A61K 31/355; A61K 31/663; A61K 35/74; A61K 9/4858; A61K 31/20; A61K 31/235 See application file for complete search history.

References Cited (56)

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.
4,119,619	A	10/1978	Rogozhin et al.
4,133,077	A	1/1979	Jasniewicz
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
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

(Continued)

FOREIGN PATENT DOCUMENTS

2002322233 2/2003 ΑU BR 8701265 3/1987

(Continued)

OTHER PUBLICATIONS

"Neptune Technologies & Bioressources 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").

(Continued)

Primary Examiner — Debbie K Ware

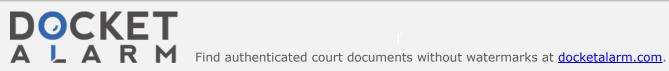
(74) Attorney, Agent, or Firm — Casimir Jones, S.C.

ABSTRACT

New krill oil compositions are disclosed as 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 obatined 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)	Referei	nces Cited	JP	2006-069948 A	3/2006	
U.S. PATENT DOCUMENTS			JP JP	2006-083136 A 2006-290784 A	3/2006 10/2006	
8,030,348 B2 10/2011 Sampalis			JP JP	2006-316073 A 2006-328014 A	11/2006 12/2006	
8,0:	57,825 B2 * 11/2011	Sampalis 424/522	JP	2006-528233 A	12/2006	
		Sampalis Sampalis	JP JP	2007-502805 A 2007-509131 A	2/2007 4/2007	
,		Sampalis	JP JP	2007-126455 A	5/2007	
		Bruheim et al.	JP	2007-518764 A 2007-246404 A	7/2007 9/2007	
		Saxby Kagan	SU	220741	1/1971	
2003/01	13432 A1 6/2003	Yoshitomi	WO WO	86/06082 89/01031	10/1986 2/1989	
		Sampalis Pivovarov et al.	WO	89/10960	11/1989	
		Rockway 424/538	WO WO	90/05765 93/24142	5/1990 12/1993	
		Kamiya et al 426/615	WO	97/38585	10/1997	
		Sones Sones	WO WO	97/39759 98/34498	10/1997 8/1998	
2010/01	43571 A1 6/2010	Breivik	WO	99/39589	8/1999	
		Catchpole Breivik	WO WO	00/23546 00/25608	4/2000 5/2000	
		Sampalis	wo	00/38708	7/2000	
		Lefkowitz	WO WO	01/28526	4/2001	
	EODEIGN DATE	NIT DOCUMENTS	wo	01/76385 01/82928	10/2001 11/2001	
	FOREIGN PALE	NT DOCUMENTS	WO	02/083122	10/2002	
CA	1098900	4/1981	WO WO	02/092540 02/102394	11/2002 12/2002	
CA CL	2251265 40348	4/2000 7/1997	WO	03/011873	2/2003	
EP	0609078	8/1994	WO WO	03/013497 2004/028529	2/2003 4/2004	
EP	670306	6/1995	wo	2004/028329	6/2004	
EP EP	1127497 1392623	8/2001 3/2004	WO	2004/100943	11/2004	
EP	1406641	4/2004	WO WO	2004/112767 2005/004393	12/2004 1/2005	
EP EP	1542670 0973532	6/2005 9/2005	WO	2005/018632	3/2005	
EP	1660071	5/2006	WO WO	2005/037848 2005/038037	4/2005 4/2005	
EP EP	1689413 1743531	8/2006 1/2007	WO	2005/070411	8/2005	
EP	1631280	3/2008	WO WO	2006/030552 2006/111633	3/2006 10/2006	
EP EP	1123368	4/2008	wo	2007/080514	7/2007	
EP EP	1406641 1419768	1/2009 1/2009	WO WO	2007/080515 2007/108702	7/2007 9/2007	
EP	1292294	3/2009	wo	2007/103702	11/2007	
EP EP	1706106 1385500	7/2009 7/2010	WO	2008/006607	1/2008	
GB	2097014	10/1982	WO WO	2008/072563 2008/117062	6/2008 10/2008	
GB JP	921537 A-S51-125774	6/1999 11/1976	WO	2009/027692	3/2009	
JР	A-S52-114046	9/1977	WO	2012/39588	10/2012	
JP JP	60-153779 61281159	8/1985 12/1986	D-11 A	OTHER PU	BLICATIONS	
JР	S6323819	2/1988		olecular Species Analy es of Cod, Lipids, vol. 2		cerides from the
JP JP	02049091 2215351	2/1990 8/1990	Bell, M	olecular Species Compo	sition of Phospha	
JР	4012665	1/1992		codinium cohnii in Rela ·118 (1990).	ition to Growth Te	emperature Lipids
JP	2963152	2/1992		on (ed.), Lipid Biochen	nical Preparations	, Chapter I.1, pp.
JP JP	04057853 3081692	2/1992 7/1994		980) ("Bergelson"). N.R., "Lipid Compositi	an af Twa Smaaiga	of Antonatio Viille
JР	2524217	8/1996		sia superba and E. ci		
JP JP	H08-231391 3344887	9/1996 7/1997	Physiol	, 1975, vol. 50B, pp. 479	9-484 ("Bottino")	
JР	3611222	8/1997		220 Rotovapor® Manu Structural order of		composition of
JP JP	2001-158736 A 2003-003192 A	6/2001 1/2003		olipids in fish brain cel		
JР	2003-048831 A	2/2003		atl. Acad. Sci. USA vol.		
JP JP	2003-146883 A	5/2003 9/2003		ate of translation of Ex on Research and Develo		
JP JP	3467794 2003-530448	9/2003 10/2003	and Util	ization of Marine Produ	cts, Chapter 6, Dev	elopment of tech-
JР	2003-531857 A	10/2003		for recovery of valuable o Fujita, pp. 273-307 (M		
JP JP	3486778 2004-525180 A	10/2003 8/2004	ment.	o i ajna, pp. 275-507 (N	1705), sapane	se language doed-
JР	2004-534800	11/2004		ate of translation of		nese Patent No.
JP JP	2004-536059 A 3678317	12/2004 5/2005		779, entitled "Nutritional ate of translation of Ex.		Patent Publication



(56) References Cited

OTHER PUBLICATIONS

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 ("Haugsgjerd").

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

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

Declaration of Dr. Albert Lee in Support of Inter Partes Review of U.S. Pat. No. 8,383,675 ("Lee").

Declaration of Dr. Chong Lee submitted during inter partes reexamination of parent patent U.S. Pat. No. 8,030,348 ("Yeboah Reexam Decl.").

Declaration of Dr. Earl White submitted during prosecution of parent patent U.S. Pat. No. 8,030,348 ("2011 White Decl.").

Declaration of Dr. Ivar Storm in support of Inter Partes Review of U.S. Pat. No. 8,278,351 ("Storrø").

Declaration of Dr. Ivar Storm in support of Inter Partes Review of U.S. Pat. No. 8,383,675 ("Storrø").

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. Pat. No. 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. Pat. No. 8,030,348 ("Shahidi Reexam.

Declaration of Dr. Shahidi submitted during prosecution of parent patent U.S. Pat. No. 8,278,351 ("Shahidi '351 Decl.").

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

Declaration of Dr. Suzanne Budge in Support of Inter Partes Review of U.S. Pat. No. 8,383,675 ("Budge").

Declaration of Dr. Thomas Brenna in support of Inter Partes Review of U.S. Pat. No. 8,278,351.

Declaration of Dr. Thomas Brenna in support of Inter Partes Review of U.S. Pat. No. 8,383,675.

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

Declaration of Dr. Van Breemen submitted during Ex parte Reexamination of the '351 patent ("Van Breemen '351 Reexam. Decl."

Declaration of Dr. Van Breemen submitted during Inter partes Reexamination of the '348 patent ("Van Breemen '348 Reexam Decl."

Declaration of Dr. Yeboah submitted during inter partes reexamination of parent patent U.S. Pat. No. 8,030,348 ("Yeboah Reexam Decl.").

Declaration of Dr. Yeboah submitted during prosecution of parent patent U.S. Pat. No. 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").

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).

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 Announcement and Natural Astaxanthin & Krill Lecithin, pp. 1-16 (on or before Dec. 28, 1994) ("Itano").

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

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").

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). 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. Deck").

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

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



(56) References Cited

OTHER PUBLICATIONS

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. 547-551 (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.

European Search Report, EP Patent Application No. EP12187516, mailed Jun. 10, 2013.

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. Cmpds. (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 Posssibilities 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 Phospholoipds 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

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

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

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

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

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,

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.

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

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.

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.

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 of Oils From Antarctic Krill," Journal of Agricultural and Food Chemistry, vol. 34, pp. 904-907.

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 tumorogenesis in the hairless mouse", Arch. Dermatol. Res., 286(6): 331-6.

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

English Abstract; JP 2003-531857; See abstract from corresponding WO 2001/082928 filed herewith.

English Abstract; JP 2004-525180; See abstract from corresponding WO 2002/083122 filed herewith.

English Abstract; JP 2006-528233; See abstract from corresponding WO 2004/100943 filed herewith.

English Abstract; JP 2007-502805; See abstract from corresponding WO 2005/018632 filed herewith.

English Abstract; JP 2007-509131; See abstract from corresponding WO 2005/037848 filed herewith.

English Abstract; JP 2007-518764; See abstract from corresponding WO 2005/070411 filed herewith.

English Abstract; JP 2004-536059; See abstract from corresponding WO 2002/09254 filed herewith.

English Abstract; JP 2006-502196; See abstract from corresponding WO 2004/028529 filed herewith.

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.

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.

De Ritter and Purcell, 1981, "Carotenoid Analytical Methods",



(56) References Cited

OTHER PUBLICATIONS

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.

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

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

Fricke, et al., 1984, "Lipid, Sterol and Fatty Acid Composition of Antarctic Krill (*Euphausia superba Dana*)", Lipids, 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.

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.

Lambertson and Braekkan, 1971, "Method of Analysis of

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, 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.

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, "Biochmical 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.

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

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

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

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.

International Search Report and Written Opinion, International Patent Application No. PCT/IB2014/002130, mailed Feb. 3, 2015. EP Opposition filed May 8, 2015 by Olympic Seafood AS, EP Patent

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.

Third Party Submission, AU Patent Application No. 2014256345, filed Oct. 12, 2015.

Third Party Submission, AU Patent Application No. 2014256345, filed Dec. 22, 2015.

EP Opposition filed Feb. 13, 2014 by Olympic Seafood AS, EP Patent Application No. EP0871891016.

Brzustowicz, Michael R., et al., "Controlling Membrane Cholesterol



No. 2144618.

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.

