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Bruheim et al.

(54) BIOEFFECTIVE KRILL OIL COMPOSITIONS

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(56) **References Cited**

U.S. PATENT DOCUMENTS

2,652,235 A	9/1953	Samuelsen
4,036,993 A	7/1977	Ikeda
1,000,000 11	17 25 11	tinued)

FOREIGN PATENT DOCUMENTS

AU	2002322233	2/2003
BR	8701265	3/1987
	(Cor	ntinued)

OTHER PUBLICATIONS

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.

(Continued)

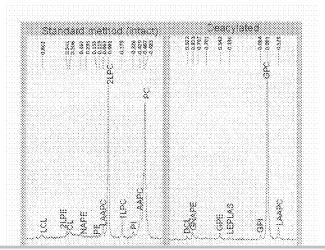
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(57) **ABSTRACT**

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 CO_2 or CO_2 plus approximately 5% of a co-solvent. Stage 2 extracts the actual krill oils by using supercritical CO_2 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.

20 Claims, 19 Drawing Sheets



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(56) **References** Cited

U.S. PATENT DOCUMENTS

U.S	. PATENT	DOCUMENTS	GB	2097014	10/198
			GB	921537	6/199
4,038,722 A	8/1977	Terase et al.	JP	S51-125774	11/197
4,119,619 A	10/1978	Rogozhin et al.	JP	S52-114046	9/197
4,133,077 A	1/1979	Jasniewicz	JP	60-153779	8/198
4,251,557 A	2/1981	Shimose et al.	JP	61281159	12/198
4,505,936 A	3/1985	Meyers et al.	JP	02049091	2/199
4,714,571 A	12/1987	Kearns et al.	JP	2215351	8/199
4,749,522 A	6/1988	Kamarei	JP	4012665	1/199
4,814,111 A		Kearns et al.	JP	2963152	2/199
5,006,281 A	4/1991	Rubin et al.	JP	04057853	2/199
5,266,564 A	11/1993	Modolell	JP	3081692	7/199
5,434,183 A		Larsson-Backstrom	JP	2524217	8/199
6,214,396 B1		Barrier	JP	H08-231391	8/199
6,346,276 B1		Tanouchi et al.	JP	3344887	7/199
6,537,787 B1		Breton	JP	3611222	8/199
6,800,299 B1		Beaudoin	JP	2909508	6/199
7,488,503 B1		Porzio et al.	JP	2001-158736	6/200
7,666,447 B2		Rockway	JP	2003-003192	1/200
8,030,348 B2	10/2011	Sampalis	JP	2003-048831	2/200
8,057,825 B2		Sampalis	JP	2003-146883	5/200
8,278,351 B2		Sampalis	JP	3467794	9/200
8,372,812 B2	2/2013	Tilseth et al.	JP	2003-530448	10/200
8,383,675 B2	2/2013		JP	3486778	10/200
8,697,138 B2		Bruheim et al.	JP	2004-534800	11/200
9,028,877 B2		Bruheim et al.	JP	3678317	5/200
9,034,388 B2		Bruheim et al.	JP	2005-245379	9/200
9,072,752 B1		Bruheim et al.	JP	2006-069948	3/200
9,078,905 B2		Bruheim et al.	JP	2006-083136	3/200
9,119,864 B2		Bruheim et al.	JP	2006-290784	10/200
2002/0076468 A1	6/2002		JP	2006-316073	11/200
2003/0044495 A1	3/2003		JP	2006-328014	12/200
2003/0113432 A1	6/2003	Yoshitomi	JP	2007-126455	5/200
2004/0241249 A1	12/2004	Sampalis	JP	2007-246404	9/200
2005/0003073 A1		Pivovarov et al.	\mathbf{SU}	220741	1/197
2006/0078625 A1		Rockway	WO	82/02819	9/198
2006/0193962 A1	8/2006	Kamiya et al.	WO	86/06082	10/198
2008/0166419 A1	7/2008		WO	89/01031	2/198
2008/0166420 A1	7/2008	Sones	WO	89/10960	11/198
2009/0061067 A1	3/2009	Tilseth et al.	WO	90/05765	5/199

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
\mathbf{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
$_{\rm JP}$	S51-125774	11/1976
JP	S52-114046	9/1977
JP	60-153779	8/1985
JP	61281159	12/1986
JP	02049091	2/1990
JP	2215351	8/1990
JP	4012665	1/1992
JP	2963152	2/1992
JP	04057853	2/1992
	3081692	7/1994
JP		
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

Find authenticated court documents without watermarks at docketalarm.com.

(56) References Cited

FOREIGN PATENT DOCUMENTS

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	2004-100943	11/2004
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	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

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 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.

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.

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

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 umorogenesis 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 Congulated 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).

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.

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. 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.

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

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).

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

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.

Find authenticated court documents without watermarks at docketalarm.com.

(56) **References** Cited

OTHER PUBLICATIONS

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

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.

International Search Report, International Patent Application No. PCT/IB2016/000208, mailed May 13, 2016, five pages.

Partial International Search Report, International Patent Application No. PCT/IB2016/000326, mailed Jun. 15, 2016, six pages.

Statement of Grounds and Particulars, Rimfrost AS, filed Jun. 10, 2016, Australian Patent Application No. 2014203179, 21 pages.

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-3phosphocholine 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 Organi-

zation, 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.

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

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 Mutr. 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 Phospholipds Containing Docosahexaenoic Acid on Differentiation and Growth of HL-60 Human Promyelocytic Leukemia Cells," J. Jpn. Oil Chem. Soc. vol. 46, No. 4 (1997)

Zerouga, Mustapha, et al., "Comparison of phosphatidylcholines containing one or two docosahexaenoic acyl chains on properties of phospholipid monolayers and bilayers," Biochimica et Biophysica Acta 1236 (1995) 266-272.

Eung-Ho Lee, et al., "Studies on the Processing of Krill Sauce," J. Korean Soc. Food Nutr. 13(1) 97-106 (1984).

Hyun-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).

Shon, Mi-Yae, et al., "Effects of Krill and Cadmium on Lipid

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

Yanase, M., "Innovations on the russian method for separating heat coagulated protein from antarctic krill, through autolysis," Bulletin of Tokai Regional Fisheries Research Laboratory, 1974, No. 78, p. 79-84

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

EP Opposition filed May 8, 2015 by Olympic Seafood AS, EP Patent No. 2144618, 150 pages.

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.

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 U.S. Pat. No. 8,030,348 ("2011 White Decl.")

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

Declaration of Dr. Ivar Storrø 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 U.S. Pat. No. 8,030,348 ("Jaczynski Reexam. Decl."). Declaration of Dr. Jaczynski submitted during prosecution of parent 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 U.S. Pat. No. 8,030,348 (Shahidi Reexam. Decl.). Declaration of Dr. Shahidi submitted during prosecution of parent 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 U.S. Pat. No. 8,030,348 ("Gundersen Decl.").

Declaration of Dr. Tina Sampalis submitted during inter partes reexamination of parent U.S. Pat. No. 8,030,348 (Sampalis)

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

(56) **References Cited**

OTHER PUBLICATIONS

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 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. 3,030,348 ("Haugsgjerd '348 Supp. Decl.").

Supplemental Declaration of Dr. Earl White submitted during inter partes reexamination of parent U.S. Pat. No. 3,030,348 ("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. 3,030,348 ("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).

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

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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", 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 modem. 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.

Geusens et al., 1994, "Long-term effect of omega-3 fatty acid supplementation in active rheumatoid arthritis. A 12-month, doubleblind, 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

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