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KRILL OIL - A NOVEL FOOD SUPPLEMENT FOR HUMAN HEALTH

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ABSTRACT

Krill- a marine zooplankton, constitute the most populous oceanic animal species. It is a small sized crustacean of the order Euphausiacea that inhabit cold water oceans globally as large surface swarms. The oil extracted from Antarctic *Euphausia superba* and Pacific *Euphausia pacifica* are the richest source of *n*-3 polyunsaturated essential fatty acids i.e. Eicosapentaenoic acid (EPA, 20:5*n*-3) and Docosahexaenoic acid (DHA, 22:6*n*-3) in their phospholipid form. The other important constituents include Astaxanthin (a potent antioxidant) and high-quality proteins containing essential amino acids. Krill oil has achieved novel food status (NFS) of European Union and generally recognized as safe (GRAS) by American Food and Drug Administration (FDA) for human consumption. Dietary supplementation of krill oil is well tolerated without adverse effects and reported to be useful against rheumatoid arthritis, obesity, premenstrual syndrome, neuronal as well as cardio-vascular disorders and keep blood lipid profile healthy. Representing its high nutritional value, krill is categorized as innovative marine raw material. Recently, krill harvest has increased from 1.2×10^5 to 2.0×10^5 ton in last five years owing to its scientific findings and utilization. These shrimp-like tiny organisms have enormous health applications and information in this article is an attempt to create awareness among mankind to achieve multitude of benefits from this natural resource.

Keywords: *Euphausia superba*, Eicosapentaenoic acid, Docosahexaenoic acid, Astaxanthin.

INTRODUCTION

Earth defines its name ‘Blue Planet’ from its oceans that occupy more than 70 percent of surface area and contain about 97 percent of global water. Oceans are unexplored treasure of natural resources and accounts for 80 percent of life on the planet. The expected rise in mariculture by year 2020 is 54-70 million metric tons (Delgado *et al.,* 2003) making marine sources as major component of global food production. In developing countries of Asia, fisheries and aquaculture generate 97 percent of the livelihoods (FAO, 2010). Fish as food contributes 17 percent of the total animal protein consumed by humans worldwide (FAO, 2012).

‘Krill’ is the most common generic name given to family Euphausidae. Antarctic Ocean is a substantial source of species *Euphausia superba* (Fig. 1A) called as Antarctic krill playing an important role in Antarctic marine ecosystems (Hureau 1985). Six species of Euphausidae are numerously found in southern waters of the Antarctic Polar Front (APF), (Gibbons *et al.,* 1999). *Euphausia frigida*, *E. triacantha*, *Thysanoessa macrura*, *T. vicina* (Nishikawa *et al.,* 2009), *E. crystallorophias* are smaller krill species (Atkinson *et al.,* 2012) whereas *E. superba* is the largest one (approx. 5 cm) that comprise the largest total biomass. Average life span of *E. superba* ranges from 5 to 7 years (Siegel, 1987). Krill inhabit phytoplankton-rich areas (Smetacek *et al.,* 2004) and are particularly important in the productive Southern Ocean systems (Hunt *et al.,* 2011; Parker *et al.,* 2011).

Antarctic Krill has been consumed as food in Japan, Russia, Ukraine and France since 1970. In the decade of 1980, out of 30,000 tons of total krill catch, 6000 tons were utilized as human food annually in Japan (Suzuki and Shibata, 1990; Nicol and Endo, 1997). European Commission has recognized the lipid extract from *Euphausia superba* as a safe novel food ingredient to be used under specified conditions (EFSA, 2009). FDA enlisted Krill oil in GRAS category for human consumption (Ramprasath *et al.,* 2013). Lipids of krill are rich in unsaturated fatty acids and phospholipids (Yamaguchi *et al.,* 1986). The influence of dietary omega-3 fatty acids on human health is widely recognized (Jordan, 2010). Present article describes the importance of this newly recognized natural marine species as resource of essential lipids for health benefits.

KRILL PREVALENCE AND CATCH

There are 85 species of krill found in oceanic waters throughout the world. Euphausiids dominate in terms of number and weight in Antarctic waters. *E. Superba* alone constitutes 50% of the total herbivorous zooplankton biomass in the Indian Ocean sector (Ingole and Parulekar, 1993). Atlantic sector alone accounts for 75 percent of the total stock of *E. superba* species, making it a key Antarctic species (Atkinson *et al.*, 2008). *E. superba* dominate in Antarctic Indian Ocean (Area 58), while another species *Euphausia crystallorophias* is abundant in Antarctic Pacific Ocean (Area 88). *Euphausia crystallorophias* also called 'ice krill', is the most common euphausiid in Antarctic shelf waters of the southeastern Weddell Sea (Siegel, 1987; Boysen-Ennen *et al.*, 1991).

Living resource harvesting in Southern Ocean has been reported since 1790. But large scale fishing started in late 1960s. Variable amount of krill fishing has been reported since 1978. Though Antarctic krill is fished for over 35 years, Krill fishery is under-exploited (Garcia and Rosenberg, 2010). The Commission for the Conservation of Antarctic Marine Living Resources (CCAMLR), established in 1982, is responsible for the management of fisheries in the Southern Ocean. The global biomass estimates of krill are 133×10^6 tons (Atkinson *et al.*, 2009) and the current annual catch is 2.1×10^5 tons. The annual catch limits set by CCAMLR is 8.6×10^6 tons, which is 40 times more than the current annual catch. Antarctic krill still remained as an untapped marine resource. In 2009, Russian Federation, Norway, Korea and Japan were major fishing countries. Now a days, Norway and Korea dominate in krill catch. China, the largest aquaculture producer, has recently emphasized on krill fishery (Olsen *et al.*, 2008). Average density of krill swarm (Fig. 1B) in the Indian sector of Antarctic Ocean varies between 5×10^3 individuals per 1×10^3 m^3 of water (Ingole and Parulekar, 1993).

COMPOSITION

Lipids are the major energy store for many marine animals in Polar Regions. Lipid contents of polar herbivorous zooplankton are generally high (Clarke and Peck, 1991). Antarctic zooplanktons accumulate lipids more than proteins which lead to high lipid/protein ratio, (Ingole and Parulekar, 1995). Eicosapentanoic acid (EPA) is being the second most abundant and Oleic acid the predominant fatty acids present (Kattner and Hagen, 1998). Moreover, Polyunsaturated fatty acids namely; Docosapentaenoic acid (DPA) and Docosahexaenoic acid (DHA) are present in their phospholipid derivative forms.

The increasing interests in marine organisms resulted in biochemical analysis of zooplanktons (Clarke A., 1984). Reinhardt and Van Vleet (1986), started investigations on the lipid contents of Antarctic plankton communities for the first time and found high lipid reserves in Crustaceans. Later, Hagen and Van Vleet (1988), described the presence of higher degree of unsaturation in phospholipids of zooplankton comprising herbivorous species i.e. krill, copepods etc. Polyunsaturated lipids help in sustaining fluidity and proper functioning of bio membranes at extremely low underwater temperatures (-2^{o}C). Krill oil is low in triglycerides (37%) and high in phospholipids (39.5%) as its characteristic feature. The phospholipid fraction includes - Phosphatidylcholine (72%), Phosphatidylethanolamine (22%), Cardiolipin (5%) and Phosphatidylinositol (1%). EPA and DHA being the major polyunsaturated fatty acids present in phospholipids with no *trans-* fatty acid (EFSA, 2009). The approximate compositional profile of krill oil is represented in the Tables 1, 2 & 3.

Polyunsaturated fatty acids are highly susceptible to oxidative rancidity, resulting in the generation of potentially toxic end-products, imparting undesirable chemical and sensory properties (Frankel, 1984). In contrast, studies based upon peroxide and anisidine value determination indicate high oxidative stability of krill oil. Krill oil contains a powerful antioxidant namely; Astaxanthin (Fig. 3) that provides superior antioxidative protection against lipid peroxidation and free radical damage. Astaxanthin is a fat soluble carotenoid responsible for red color of krill oil (Lu *et al.*, 2014). Additionally, strecker degradation compounds and pyrroles generated as secondary products generated during oxidation process reported to have antioxidative effects.

Table 1. **Fatty acid profile of krill oil**

S. No.	Fatty acid	% age (approx.)
1.	Polyunsaturated fatty acids	36.7
A)	*n*-3 Fatty acids (total)	33.6
	(i) *n*-3 Eicosapentaenoic acid (EPA)	17.2
	(ii) *n*-3 Docosahexaenoic acid (DHA)	11.3
	(iii) *n*-3 Docosapentaenoic acid (DPA)	0.6
B)	*n*-6 Fatty acids (total)	1.6
	(i) *n*-6 Linoleic acid	1.4
C)	*n*-9 fatty acids (total)	9.6
2.	Monounsaturated fatty acids (total)	22.1
	(i) Oleic acid	8.6
3.	Saturated fatty acids (total)	29.8
4.	*trans-* fatty acids (total)	0.01

Table 2. Biochemical profile of krill oil

S.No.	Parameter	Amount
1	Saponification value	175 mg /g
2	Iodine value	138 g /100 g
3	Peroxide value	0.1
4	*p*-Anisidine value	1.0

Table 3. Other important constituents in krill oil

Constituent	Content
Vitamin A	260 IU/g
Vitamin E	0.65 IU/g
Astaxanthin (esterified)	163 mg/100 g
Protein	3.0 g/100 g

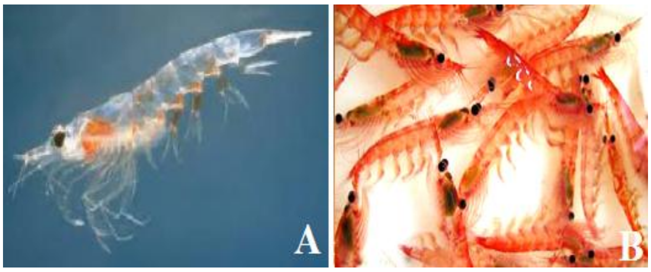

Figure 1: (A) Krill (*Euphausia superba*) and (B) Krill swarm

TOXICOLOGICAL ASSAY

Krill oil passed the subchronic and genotoxicity tests recommended by Joint Expert Committee on food additives and supplements. Thirteen weeks toxicity study performed (Robertson *et al.*, 2014) on both sexes of Han-Wistar rats fed with diet comprising 5% krill oil demonstrated the lack of toxicologically significant adverse effects and confirmed krill oil as non-toxic, safe dietary supplement. Quantitative studies revealed no significant changes in organ weight (adrenal glands, brain, heart, kidneys, liver, lung, ovaries, pituitary gland, prostate, spleen, testes, thymus and thyroid), clinical chemistry profile (urea, glucose, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total protein, albumin, Globulin, cholesterol, total bilirubin, calcium and phosphate), urine analysis (colour, pH, protein, glucose, ketones, urobilinogen, bilirubin, pigments), histopathological examinations (respiratory tract, cranial, thoracic and abdominal cavities, adrenal glands, aortic arch, blood smear, brain, eyes, epididymis, gastro-intestinal tract, heart, implant, kidney, ureter, liver, lung, mesenteric lymph node, nasal cavity, oesophagus, optic nerve, ovaries, pancreas, pituitary, prostate, rib, salivary glands, sciatic nerve, seminal vesicles, spinal cord, skin, mammary gland, spleen, sternum, submandibular lymph node, testis, thigh muscle, thyroid with parathyroid, tongue, trachea, urinary bladder, thymus, uterus and vagina) and motor activity measurements.

Krill oil was also assayed for the mutagenic activity using the five bacterial strains comprising four of *Salmonella typhimurium* (*his-*) and one of *Escherichia coli* (*trp-*). Two mutation experiments (AMES assay) performed by direct plate incorporation and pre-incubation methods using krill oil at doses range up to 5000 μg per plate reported no mutagenic activity. Both tests clinically and genetically confirmed that krill oil is non-toxic and safe for use in food as well as pharmaceutical supplements.

DIETARY AND BIOMEDICAL IMPORTANCE

Polyunsaturated fatty acids (PUFAs) of krillare categorized into two main categories (Venegas-Caleron *et al.*, 2010) ie. *n*-6 and *n*-3 series (ω-6 and ω-3) as mentioned in Table 4. The *n*-3 and *n*-6 designate the position of unsaturation at the third and sixth carbon resp. from the methyl terminus of the hydrocarbon chain of fatty acids (Fig. 2). Both LA and ALA are the parent fatty acids of *n*-6 series and *n*-3 series resp. (Abozid and Ayimba 2014). Humans are unable to synthesize Linoleic acid (LA; C18:2 *n*-6) and alpha-linolenic acid (ALA; C18:3*n*-3) from the common precursor Oleic acid ($18{:}1\Delta^9$) (Brian, 2007). Mammals are unable to create unsaturation beyond Δ^9 position in the fatty acid chain (De Lorgeril and Salen, 2004) due to lack of Δ^{12} and Δ^{15}-desaturase activities (Nakamura and Nara, 2004). Therefore, both LA and ALA are essential amino acids; so must be present in the diet (Wayne *et al.*, 2000).

ALA is the principal *n*-3 fatty acid required for the biosynthesis of EPA, which in turn get converted to DHA (Charles et al., 2006 and Julius, 2006). LA and ALA are enzymatically metabolized to long chain polyunsaturated fatty acids (LC-PUFAs) by D6 and D5-desaturases (Holman, 1998). But the activities of both desaturases are slow in humans (Undurti, 2007). Conversion rate of ALA to EPA is less than 5% and EPA to DHA less than 15% under optimal conditions (Gregory *et al.*, 2011). The conversion efficiency is further reduced during vitamin (B3, B6, C) and mineral (Zn, Mg) deficiency (Brenna et al., 2009). Due to low conversion efficiency, direct uptake of EPA and DHA from dietary sources becomes more effective (Horrocks and Yeo, 1999). In a healthy adult, dietary fat should provide 20% to 35% of Total Energy Intake (TEI) (Vannice and Rasmussen, 2014). With the follow up of Westernized lifestyle, the increased consumption of saturated fat over unsaturated fat has led to raised dietary fat-TEI from 25% to 40% (Kremmyda *et al.*, 2011). This dietary misappropriation must be balance with increased consumption of n-3 series PUFAs. PUFA reduces triglyceride content of body. Nutritional studies indicate the importance of both *n*-3 and *n*-6 series PUFAs in dispersing the low-density lipoproteins (LDL) in liver and increasing the high density lipoproteins (HDL) in plasma (Asadpour, 2014). PUFAs activate β-oxidation of fatty acids and inhibit triglyceride biosynthesis in liver; thereby, reduce serum triglyceride levels by 25–30% (Harris, 1997).

n-3 series PUFAs are essential nutrients that promote human health and growth (Schmidt *et al.*, 2001). The original source of *n*-3 series PUFAs present in fish oils is marine microorganisms (Marai and Massalha, 2014). DHA and EPA are the most abundant *n*-3 essential fatty acids from marine source (Ackman and Ratnayake, 1990). Both are the precursors of eicosanoids that act as anti-inflammatory, anti-thrombotic, anti-arrhythmic and vasodilating agents (Kapoor and Patil, 2011). *n*-3 series fatty acids added to infant formula results in the improved respiratory health during infancy and childhood (Lapillonne *et al.*, 2014). *n*-3 series PUFAs are also beneficial in the primary prevention of age related cognitive decline and dementia i.e. Alzheimer's disease (Cole *et al.*, 2009; Morris *et al.*, 2009). The high dietary intake of *n*-3 PUFAs protective role against Chronic Obstructive Pulmonary Disease (COPD) and deterioration of lung functions in cigarette smokers (Sahar *et al.*, 1994). *n*-3 PUFAs may also act as anticoagulant and antihypertensive agents (Corrêa *et al.*, 2008). Dietary supplementation with *n*-3 PUFAs influence the acute inflammatory response in critically ill patients (Martin and Stapleton, 2010).

The balance between both the *n*-6 and *n*-3 series PUFAs directly influences the biosynthesis of Prostanoid (inflammatory mediator) (Watkins *et al.*, 2007). The dietry intake ratio of *n*-3/*n*-6 PUFAs is the key index for the balanced biosynthesis of Eicosanoids (Steffens, 1997); with an ideal ratio of 1/ (5-10). For infants, this ratio must not be higher than 10 (Gerster, 1998). In India, the *n*-3/n-6 PUFAs ratio is 1/(30-70). Whereas in Japan, this ratio is 1/(2-4), which is due to the more seafood consumption (Aleksandra *et al.*, 2009). Larger *n*-3/*n*-6 PUFAs ratios are correlated with the increased pathogenesis of Coronary Heart Disease (CHD) (Simopoulos, 2008). Reduction in *n*-3/*n*-6 PUFAs ratio in diet supports the joint health.

The dietary pattern of low *n*-3 PUFAs compared to *n*-6 PUFAs in United States resulted in the poor health of female populations. The adequate intake of DHA and EPA increase gestation length by reducing the incidence of preterm birth along with improved infant cognitive and visual activities. *n*-3 series PUFAs are found primarily in fish oils, yet fish is avoided because of contamination with mercury and polychlorinated-biphenyls. So, women must consume *n*-3 PUFAs between 200-300 mg daily during pregnancy from safe food sources (Jordan, 2010).

EPA acts as precursor of the Eicosanoids (Kinsella *et al.*, 1990). The positive effects of EPA are mainly associated with cardiovascular diseases (Nieto *et al.*, 1997). DHA is found mostly in phospholipids and is one of the most abundant components of structural lipids of the brain. DHA reduces the gastrointestinal inflammations (Teitelbaum and Walker, 2001). Food fortification with *n*-3 PUFAs lowers the incidence of diarrhea in infants and mild gastrointestinal symptoms like lack of appetite and abdominal pain in 6–10 years old children (Thomas *et al.*, 2012). The structural lipids of retina and non-myelin membranes of the nervous system are enriched with phospholipids containing DHA (Bradbury 2011; Tvrzicka *et al*. 2011). DHA supports the immune system acting as immunomodulatory nutrients (Gottrand, 2008). DHA plays an important role in preventing Neurodegenerative conditions like, Alzheimer's, Multiple Sclerosis and Parkinson's disease. DHA participates in development of the nervous system (Valenzuela *et al.*, 2012). DHA also promotes the retinal functions and preterm infants must be provided with the extra supplements of it (San-Giovanni *et al.*, 2000). DHA supplementation results in increased plasticity and functional flexibility of developing brain cells. It also reverses age-related neuronal changes and maintains memory performance (Su, 2010). Decline in the levels of DHA and EPA may contribute towards the development of aggression, anxiety, depression, schizophrenia, dementia (Morley, 2010; Amminger *et al.*, 2010).

Table 4. Important polyunsaturated fatty acids

PUFA	Abbrevation	Formula	Series
α-Linolenic acid	ALA	18:3 $\Delta^{9,12,15}$	*n*-3
Eicosapentanoic acid	EPA	20:5 $\Delta^{5,8,11,14,17}$	*n*-3
Docosapentanoic acid	DPA	22:5 $\Delta^{7,10,13,16,19}$	*n*-3
Docosahexanoic acid	DHA	22:6 $\Delta^{4,7,10,13,16,19}$	*n*-3
Linoleic acid	LA	18:2 $\Delta^{9,12}$	*n*-6

Marine *n*-3 PUFAs have evidently showed beneficial effects in various cardiac disorders and recommended for management of Myocardial Infarction (Saravanan *et al.*, 2010). The high PUFA contents of krill oil make it effective in the treatment of various medical conditions including arthritis, cardiovascular and liver diseases. EPA and DHA from krill oil are beneficial to the health of multiple organ systems, including cardiovascular, gastrointestinal, endocrine, renal, immune, visual and nervous systems (Lopez, 2012). Krill oil at dose of 1-3 g/day is effective for the reduction of glucose, total cholesterol, triglycerides, LDL and HDL; therefore, may be effective in the management of hyperlipidemia (Bunea *et al.*, 2004).

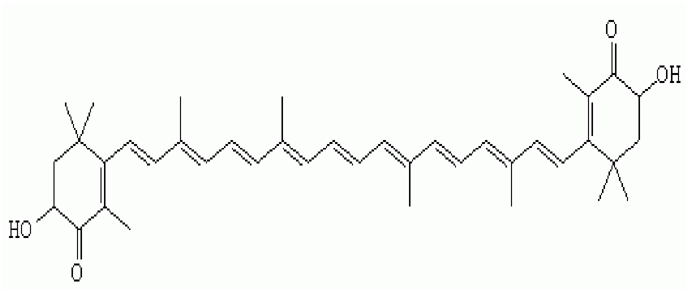

Figure 3: Astaxanthin ester

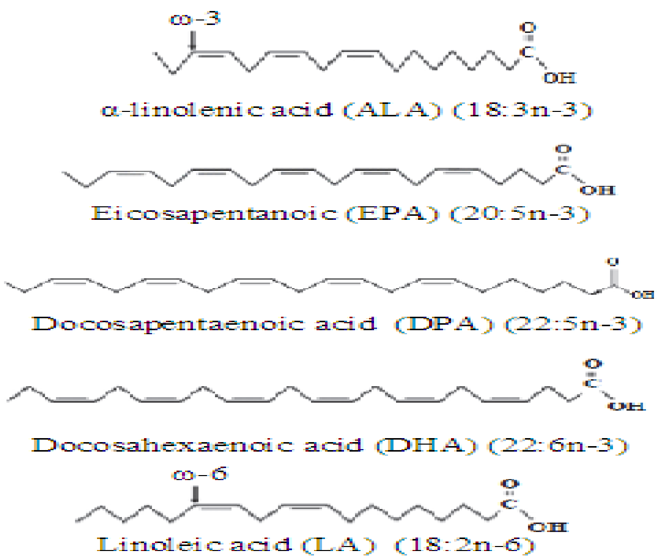

Figure 2: Structure of important polyunsaturated fatty acids

EXTRACTION

Extraction of oil from krill involves many conventional purification methods. Systematic approach towards krill oil extraction involves solvent extraction of crushed raw krill meal followed by evaporation of the filtrate. The common steps involved in the extraction of oil are mentioned in Fig. 4. However, with the implementation of advancements in extraction technology like low-temperature crystallization, silver-resin chromatography, acidolysis catalyzed by immobilized lipases and supercritical extraction produces 75–80% concentrates of krill oil (Ganga *et al.*, 1998).

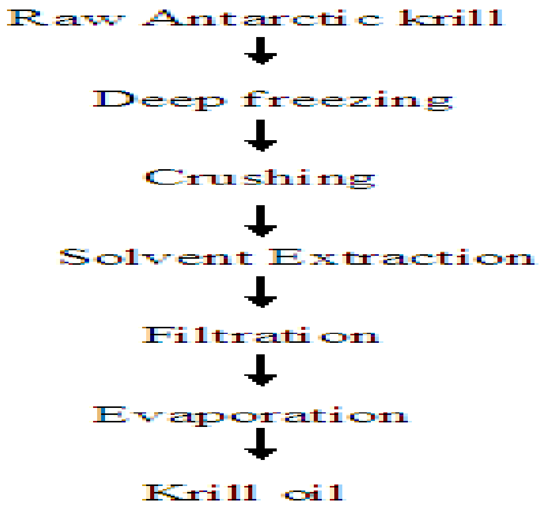

Figure 4: Krill oil extraction process

FUTURE PERSPECTIVES

Unsaturated oils from marine creatures are highly emphasized in the pharmaceutical, cosmetic and biotechnological industries. The marine n-3 PUFAs are now supplemented as concentrated formulations. Recent attentions have been focused on obtaining DHA and EPA at commercial levels from natural resources. Supplementation of nutritional formulas with krill oil is a recent area of research. The use of krill oil in pharma products and nutraceuticals drive the investments in the krill industry. Nutritional and pharmacological effects of n-3 PUFAs of marine origin have raised interest in developing laboratory techniques to prepare EPA and DHA concentrates. Krill oil from marine resources is under-utilized for industrial applications. The activities of various research scientists are now oriented towards studying its role in the field of food and medicine.

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