Krill Oil

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Krill *(Euphausia superba)* is a small marine crustacean from the Antarctic Ocean that plays an important role in the marine ecosystem, serving as feed for most fish. It is a known source of highly bioavailable omega-3 polyunsaturated fatty acids (eicosapentaenoic acid and docosahexaenoic acid). In preclinical studies, krill oil showed metabolic, anti-inflammatory, neuroprotective and chemo preventive effects, while in clinical trials it showed significant metabolic, vascular and ergogenic actions. Solvent extraction is the most conventional method to obtain krill oil. However, different solvents must be used to extract all lipids from krill because of the diversity of the polarities of the lipid compounds in the biomass.

krill oil | omega-3 polyunsaturated fatty acids | bioavailability | nutraceuticals | dietary supplements

1. Introduction

Krill (Euphausia superba) is a small marine crustacean from the Antarctic Ocean that plays an important role in the marine ecosystem, serving as feed for most fish [1]. Although measuring krill biomass is difficult, it has been estimated at approximately 379 million metric tons. The Commission for the Conservation of Antarctic Marine Living Resources (CCAMLR) has set a catch limit of 620,000 tons per year to protect the marine ecosystem [2]. Nevertheless, the annual catch is around 250,000 tons, indicating use below the established limits, which is probably due to the difficulty in conserving krill and its fragility [3].

In fact, krill is commonly used in the sport fishing market as well as in the aquaculture industry. However, in recent years, krill has been successfully investigated for its role as a nutritional supplement to improve human health. This is because krill is rich in nutrients, including vitamins A and E, minerals, n-3 polyunsaturated fatty acids (n-3 PUFAs), phospholipids (PLs), astaxanthin and flavonoids [4].

Particular attention has been paid to lipid content (0.5% to 3.6%) [5], including phospholipids (30–65%) and triglycerides, while fish oil is only comprised of triglycerides. The main phospholipid in krill oil is phosphatidylcholine, with 40% of the total fatty acids bound to phosphatidylcholine being eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [6]. The EPA and DHA omega-3 fatty acids found in krill oil have shown several useful pharmacological properties in the management of numerous chronic dysfunctions, including cardiovascular, neurological and inflammatory diseases, as well as the prevention of cancer and promoting gut microbiota health [7][8][9][10]. In this regard, supplementation with krill polyunsaturated fatty acids may be a natural

way to relieve the symptoms of these conditions, potentially in combination with conventional therapies [11]. EPA and DHA from krill oil have also shown higher bioaccessibility than other forms of n-3 PUFAs (ethyl-ester and re-esterified omega 3), demonstrating similar benefits, but at smaller dosages [12].

Krill oil was authorized in 2008 by the U.S. Food and Drug Administration (FDA) as GRAS (Generally Recognized as Safe), was approved in Europe by EFSA as a novel food in 2009 and was also approved in China in 2014. Finally, krill oil was authorized by EFSA for pregnant and lactating women in 2014.

2. Highly Active Omega-3 Fatty Acids from Krill Oil

Considering the increased market of n-3 PUFA containing dietary supplements, supported by increased clinical evidence, there is a constant search for new n-3 PUFA sources and formulations [13].

Krill oil possesses several health benefits in clinical practice, in particular in cardiovascular disease risk factor management and in neurological diseases and inflammation [14]. It is commercialized in both the nutraceutical and pharmaceutical market in different dosage forms including soft gels, gummies, capsules and tablets.

However, despite many activities and functionalities that have been attributed to krill oil, the molecular pathways of actions are still in part unclear because few studies of pharmacodynamic are available and few have provided detailed information about molecular mechanisms of krill components such as astaxanthin, vitamin A, tocopherols, flavonoids, and minerals [15]. Most published RCTs do not provide any information regarding krill oil composition (except for the EPA and DHA content) [16]. In this regard, further studies are necessary to emphasize the relationship between krill oil components, mechanisms of action, health benefits and diversifying the different composition of krill oil for specific applications.

The importance of knowing the actions of the active components of krill oil is fundamental for the future development of new extraction techniques which could give rise to new chemical extract compositions for certain pathological conditions. To date, solvent and non-solvent extraction, super and subcritical fluid extraction and enzyme-assisted pre-treatment extraction represent the main technologies used for krill oil extraction, each of which have both advantages and disadvantages [17].

Among the active ingredients contained in krill oil, EPA and DHA constitute the main title of the products studied in clinical trials. EPA and DHA from krill oil are attached to phospholipids and to phosphatidylcholine. This composition promotes the efficiency of absorption of fatty acids into the blood when compared with omega-3 from fish oil [4]. However, the minor components contained in krill oil such as astaxanthin, alpha-tocopherol, vitamin A and flavonoids could exert pleiotropic activities and improve the bioaccessibility of EPA and DHA, even if data need to be clarified. Many studies on krill rarely detail the concentration in minor components, so it is hard to estimate their contribution to the final observed effects.

Krill oil products can be associated with other nutritional supplements to provide more benefits. Alvarez-Ricartes et al. demonstrated the efficacy of krill oil in addition to cotinine in the treatment of depressive symptoms in posttraumatic stress disorder people [18]. A study by Costanzo et al. found an association of krill oil with *Lactobacillus reuteri*, and vitamin D showed to reduce gut inflammation, reducing gut dysbiosis as well as increasing the epithelial restitution [19].

Currently, supplementation with krill oil is considered safe and well tolerated. Side effects are minimal or absent, and may include bloating, diarrhea and flatulence [20]. However, the available evidence is limited and further long-term RCTs, including many people, are needed to confirm both safety and efficacy of this nutraceutical. In addition, a cost/benefit analysis is necessary to better understand the implication of krill oil supplementation on health.

In conclusion, preliminary clinical data suggest that krill oil represent a valid supplement in the treatment of several conditions including CVDs, osteoarthritis, premenstrual syndrome and dysmenorrhea. Innovative technologies applied to improve krill oil purification and concentration could improve its cost-efficacy ratio.

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