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Anticancer Properties of Krill Oil

Krill Yağının Antikanser Özellikleri

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Abstract

Krill which is a shrimp-like cold ocean creature is an important nutraceutical agent because it contains nutrient components (polyunsaturated fatty acids, astaxanthin, etc.) that have positive effects on health. Although its cardioprotective, neuroprotective and anti-inflammatory properties have been emphasized so far, it also has anticancer properties. It has been reported to inhibit the proliferation of cancerous cells, prevent metastasis and tumor growth, and induce apoptosis in cancer cells through various mechanisms such as regulation of the omega3/omega-6 ratio, inhibition of reactive oxygen species (ROS) formation, activation of caspase 3/9, and increasing mitochondrial membrane potential. It has been reported to induce apoptosis as well. It is believed that Krill can reduce the incidence of cancer and play an effective role in cancer treatment due to the above-mentioned properties

Keywords: Krill oil, Anticancer activity, Astaxanthin, Omega-3

Özet

Karides benzeri soğuk okyanus canlısı olan krill sağlık üzerinde olumlu etkiler yaratacak besin bileşenlerini (çoklu doymamış yağ asitleri, astaksantin vb.) içermesinden dolayı önemli bir nutrasötik ajan olarak gösterilmektedir. Kardiyoprotektif, nöroprotektif ve antiinflamutuvar özellikleri ile ön planda yer alsa da antikanser özelliği de bulunmaktadır. Omega3/omega-6 oranının düzenlenmesi, reaktif oksijen türleri (ROS) oluşumunun inhibe edilmesi, kaspaz 3/9'un aktivasyonu ve mitokondriyalmembran potansiyelini artırma gibi çeşitli mekanizmalar aracılığıyla kanser hücrelerinin proliferasyonunu inhibe ettiği, metastazı ve tümör gelişimini önlediği ve kanserli hücrelerde apoptozu indüklediği bildirilmiştir. Bahsi geçen bu özellikleri ile kanser insidansını azaltabileceği ve kanser tedavisinde etkin rol oynayabileceği düşünülmektedir.

Anahtar kelimeler: Krill yağı, Antikanser aktivite, Astaksantin, Omega-3

1. INTRODUCTION

Krill is a shrimp-like shellfish that feeds on plankton and algae in cold oceans. Frozen raw/boiled and peeled krill meat is used as a food source. It can also be consumed as a nutritional supplement in the form of krill oil. Krill oil is rich in carotenoid (astaxanthin) and polyunsaturated fatty acids such as omega-3 (n-3), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). It has positive effects on health due to these nutrient components (Bağcı&Can, 2015).

Through mechanisms such as their effect on cell membrane composition, potential and permeability, regulation of intracellular calcium concentration, regulation of intracellular pH, promoting cellular resistance to ROS damage, and changes in DNA and gene expression, EPA

and DHA in the composition of krill oil exhibit positive effects on cancer cells (reducing the number/size of tumors, preventing angiogenesis and metastasis, etc.) (Jayathilake, Kadife, Luwor, Nurgali & Su, 2019). The aim of the study is to determine whether krill oil has an effect on various cancer types and the possible mechanisms of action.

2. DEFINITION AND CONTENT OF KRILL OIL

Krill oil which is obtained from Euphausia superba, a crustacean organism, is rich in n-3 fatty acids, containing various nutrients important for health such as antioxidant carotenoid (astaxanthin), Vitamin A and Vitamin E (Tel Adıgüzel, Işgın & Pekcan, 2015). It has been identified as safe by the American Food and Drug Administration (EFSA, 2012). Krill oil is an important source of n-3 and is particularly rich in long chain polyunsaturated fatty acids EPA and DHA (Xiong et al., 2018). Krill contains 26.1% saturated fat, 24.2% monounsaturated fat, 48.5% polyunsaturated fat, 17.4% EPA, and 12.4% DHA (Tou, Jaczynski & Chen, 2007). Astaxanthin is a powerful antioxidant carotenoid that gives Krill its red color and is naturally present at different levels in salmon, shrimp, shellfish or some algae species. Krill oil contains approximately 0.5 mg/3 g astaxanthin (Georges et al., 2018). According to some sources, the esterified astaxanthin content is 1,000-1,500 mg/kg (EFSA, 2012). Krill oil contains high levels of phospholipids, flavonoids, Vitamin A, alphalinolenic acid, EPA, DHA, and astacin. 1 g krill oil has been found to contain at least 0.15 g EPA, 0.09 g DHA, and 0.3 g n-3 (EFSA, 2012). It has been reported that krill oil contains more EPA than fish oil and they are similar in terms of DHA content (Tou et al., 2007). In fish and fish oil, almost all of EPA and DHA are in triglyceride (TG) form, whereas in krill oil, the majority of EPA and DHA (65%) are in phospholipid form (Rundblad, Holven, Bruheim, Myhrstad & Ulven, 2018; Winther, Hoem, Berge & Reubsaet, 2011). It has been reported that EPA and DHA in krill oil are better incorporated into the tissues thanks to the phospholipid form and exhibit a stronger effect than the TG form (Xie et al., 2017). Although bioavailability of krill oil is reported to be higher than fish oil (Ramprasath, Eyal, Zchut & Jones, 2013), it is more advantageous than fish oil in that it further increases the content of unsaturated fatty acids in brain tissue (Ahn et al., 2018).

3. HEALTH EFFECTS OF KRILL OIL

It has been reported that krill oil may reduce the risk of diseases affecting the liver, kidney, cardiovascular system, muscle and brain by causing favorable changes in gene expression profiles and modulating endocannabinoid precursor suitability by regulating the cellular n-6/n-3 content. It has a particular role in reducing the risk of cardiovascular diseases and myocardial infarction, improving cognitive functions, preventing depression, and reducing the risk of inflammatory diseases such as rheumatoid arthritis and ulcerative colitis (Burri & Johnsen, 2015). Since astaxanthin is a powerful antioxidant and anti-inflammatory agent, krill oil has also been shown to be a therapeutic agent in the prevention of atherosclerosis (Fassett & Coombes, 2011).

It has important effects such as preventing the increase/damage of oxidative stress, preventing lipid peroxidation, preserving membrane integrity, strengthening immune system functions, and regulating gene expression (Ambati, Phang, Ravi & Aswathanarayana, 2014). Krill oil exhibits a neuroprotective effect on the neuron-like cell line (PC 12) by increasing cell viability, reducing protein expression of split caspase-3, reducing apoptotic rate, and increasing mitochondrial membrane potential. It has been reported that it can alleviate neurotoxicity by reducing apoptotic response and oxidative damage (Xiong et al., 2018). A recent genotoxicity study confirmed the safety of krill oil (Robertson, Burri & Berge, 2014). Thanks to the antioxidant (astaxanthin) in its composition, krill oil has positive effects such as inhibiting the formation of inflammatory and carcinogenic markers, slowing the aging process, and preserving the health of various organs (liver, heart, eyes, joints, etc.) (Arpacı & Ayaz, 2011).

4. ANTI-CANCER PROPERTIES OF KRILL OIL

Another emerging aspect of krill oil is its effective role in the prevention/treatment of cancer. It is reported that by regulating the n-3/n-6 ratio, krill oil may reduce the risk of many cancer types, particularly prostate cancer (Dindarlou & Mokhtari, 2015).It has been reported that it may have a positive effect on benign prostatic hyperplasia and prostate cancer through the inhibition of 5-cc-reductase enzyme (Arpacı & Ayaz, 2011). It is seen as an anticancer nutraceutical agent candidate because it can modulate cell proliferation and block malignant progression of transformed cells (Zhu, Shi, Qian, Cai & Li, 2008). It is thought to exhibit anti-cancer property by inhibiting/delaying the progression of malignant cells by regulating cell proliferation/differentiation (Zhu et al., 2008). EPA and DHA in the composition of krill oil have been reported to inhibit tumor cell growth via intracellular ROS at a better level than EPA/DHA in the composition of other sources. It is stated that this effect is due to the configuration difference in the composition of krill and the trans-double bond structure is more effective than cis-double bond structure (Zheng et al., 2017).

Krill has been reported to specifically target malignant colon cancer cells. It has been suggested that krill oil inhibits the development of colon cancer by acting on resistant cancer cells (Zhu et al., 2008). Jayathilake et al. (2019) found that krill oil significantly inhibited cancer cell proliferation and ROS formation in human colorectal cell lines, increased mitochondrial membrane potential, and significantly increased the expression of active forms of caspase-3 and caspase-9. The anti-proliferative property of krill oil in colorectal cancer cells is associated with activation of caspase 3/9 (Jayathilake et al., 2019). It has been reported that krill oil can be used in conjunction with standard clinical practices to control primary tumor growth and metastasis (Su, Tanalgo, Bustos & Dass, 2018).

With its potential to induce apoptosis, krill oil is thought to be an effective chemotherapeutic agent in colorectal cancer. In a study on colorectal cancer cell lines, although the exact mechanism of the pro-apoptotic properties of krill oil extract has not been elucidated, it has been found to affect cancerous cells through mitochondrial pathways. In this study, a significant apoptotic activity was observed in the cell lines as a result of the application of krill extract, while the rate of cancer cell inhibition was found to be approximately 95%. Furthermore, mitochondrial membrane depolarization was found to be significantly higher after the treatment with krill oil extract (Jayathilake, Senior & Su, 2017). In support of this view, Jayathilake, Senior and Su (2016) found that krill oil suppresses cell growth and triggers apoptosis in human colorectal cancer cell lines (HCT-15, SW-480 and Caco-2).

Astaxanthin in the composition of krill oil is thought to have positive effects on gallbladder, colon, and breast cancer types by suppressing tumor development and stimulating immune response against antigens with its anti-inflammatory and oxidative stress reducing properties (Arpacı & Ayaz, 2011). In a recent study on a breast cancer cell line and epithelium, astaxanthin treatment was found to be effective in reducing the proliferation and migration of breast cancer cells (McCall, McPartland, Moore, Frank-Kamenetskii & Booth, 2018). Astaxanthin has been proven to exhibit anti-proliferative and anti-invasive effects through various pathways such as peroxisome proliferator activated receptor gamma (PPARγ), signal transducer and activator of transcription 3 (STAT3), and nuclear factor kappa light chain enhancer (NF-κB) of active B cells (Zhang & Wang, 2015). Since krill oil is a valuable source of astaxanthin, it can help in the prevention and treatment of cancer. Since krill is an important source of DHA as well as astaxanthin, it is reported that it can be also effective in breast cancer cell lines. Zheng et al. (2018) investigated the efficacy of krill oil application in breast cancer cell lines (MCF-7) and found that krill oil application significantly reduced the number of migrating and invasive MCF-7 cells. In addition, DHA in the composition of krill oil was found to increase the interaction between CD95 and caveolin-1. This increased interaction was found to inhibit cancer cell migration/invasion via the FAK/SRC/PI3K/AKT signaling pathway (Zheng et al., 2018).

5. CONCLUSION

Since krill oil contains valuable components such as EPA, DHA, and astaxanthin, it can help reduce cancer incidence and prevention cancer proliferation. It may be beneficial to use krill oil for nutraceutical purposes as an adjunct to clinical treatment in the prevention and treatment of cancer. Although significant positive effects of krill oil have been emphasized in various cancer types, it is a current and novel approach and should be further investigated. It will be beneficial to carry out sufficient studies to reveal the effects and mechanism of action of krill oil specific to different cancer types.

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