



Shark Cartilage and Liver Oil Using Possibilities Against to the Cancer Formation

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Abstract

Cancer has been seen rarely or none in sharks, compare to the other organisms, and it is important to understand what the relationship of the shark's cancer-preventing immune system is that? A lot of different suggestions were made by the scientists. One of the important main explanation in that, the sharks cartilage and liver oil effections' against to the cancer formation. There are a lot of reasons to being cancer. But mainly, depends on the blood vessel developing status. One of the main differences between sharks and higher vertebrates; is that a shark's skeleton is made of cartilage. Cartilage is different from other types of tissue, meaning it does not contain any blood vessels. Recent research indicates there is a relation between the lack of blood vessels in shark cartilage and sharks anti cancer mechanism. It was determined that shark cartilage is a powerful inhibitor of tumor growth. Another important differences in sharks that their almost 10 times higher amount of liver oil content, compare to the other animals. The effective parts of shark liver oil have been determined as a group of ether-linked glycerols or in other saying alkylglycerols. The activation of protein kinase C, having a role in cell proliferation, can be prevented by alkylglycerols. Different studies indicated that, alkylglycerols have a multifunctional role and shark liver oil can be used in treatment of several types of cancer.

Key Words: shark, cartilage, liver oil, cancer.

INTRODUCTION

Cancer - uncontrolled growth of abnormal cells, is one of the major mortality factors for our country and worldwide. Cancer can develop in almost any organ or tissue of the body. It is important for cancer patients to maintain their immune system strong, especially if they are under chemotherapy or radiation. Many research have been carried out to find better cancer treatments. Because up to now it hasn't been found an effective treatments, some of these research based on new sources. In treatment of this illness, additional to standard methods, sharks, with their cartilage and liver oil, has been presented as a one of these new sources in this study [1,2].

Sharks have been seen in the earth's oceans for over 400 million years. Agains to many disasters, sharks have survived and become one of the most survival animals on our planet. One of the reason to that; they have powerful immune system. The reality of sharks get cancer very rarely, may help us in challenging, against to cancer. For years the scientists have been trying to understand shark's cancer-preventing immune system connection [3].

There are a lot of factors to being cancer. Some times it can be from deragements of cell differentiation, or can results from mutations that disrupt the regulatory mechanism of normal cell growth. There are several different types of control on the growth of normal cells. Some specific proteins, produced by different oncogens, take part in mechanism by which cells response to growth

factors. Abnormal cell colonies cause to solid tumor formation. As the tumor grows in size, it has to produce a network of blood vessels to provide it with an enough nourishment and blood supply. The generation of this new network of blood vessels is called angiogenesis.

A lot of different researches have been carried out for much better cancer treatments. It hasn't been found an effective treatments, even some of these research based on new sources. One of these sources is shark and related materials [1,3].

One of the main differences between sharks and higher vertebrates is that a shark's skeleton is made of cartilage, instead of true bony tissue. It has been thinking that this cartilaginous skeleton have a role on producing some substance that protect sharks against to cancer.

Cartilage is different from other types of tissue, like bones and muscles, meaning there is no any blood vessels. In spite of, badly torn cartilage cannot repair itself and must be surgically treated, broken bones or injured muscles, can heal in a few weeks with their rich blood supply. However, recent research indicates there is a relation between the lack of blood vessels in shark cartilage and sharks anti- cancer mechanism.

It was defined that shark cartilage is a powerful inhibitor of tumor growth. The extracted protein substance of shark cartilage have similar compound with bovine cartilage (from calves), which also inhibit the growth of tumors. Shark includes almost ten times as much of calfs bodys' cartilage. Also, large sharks are nearly ten times

heavier than calves. Which means 5 gram of shark cartilage is enough to produce the same amount of tumor-inhibiting factor with about 500 gm of calf cartilage. It means that shark cartilage one thousand times more powerful than bovine cartilage, and a large shark may contain up to one hundred thousand times more tumor-inhibiting factor than a calf [3].

Modern sharks are separated into several ordinal- or subordinal taxa. Cartilaginous fishes have developed several different successful adaptation techniques into the selection within the evolution. They can survive against to waves of extinction via producing enough level of offspring, can be specialise at various taxonomic levels with their morphological, behavioural, ecological and taxonomic diversity and can adapt their body to radiation. Also, they can be very efficient predators and they can successfully survive against to other predators attack with their delicate sensory system, brain and their special formed upper jaw and dentition [4].

In finding of effective treatment against to the cancer a lot of different alternative methods and materials were tested. Some of these new materials are related to the sharks. There are many researches, going on to find out relationship between some shark-related materials and their possible effect against to the cancer. This paper based on the sharks cartilage' and its liver oil' using possibilities against to cancer formation.

Summary of Some Researches

Shark cartilage papers

The first real important study was presented in a article in the journal *Science* titled "Shark Cartilage Contains Inhibitors of Tumor Angiogenesis," which indicated that "shark cartilage contains a substance that strongly inhibits the growth of new blood vessels toward solid tumors, restricting tumor growth" in 1983. After that, the initial studies were carried out with rabbits. A small amount of shark cartilage extract were placed next to small tumors in the corneas of the eyes of rabbits. As a controls, the same size of tumors were implanted into the other eye without cartilage at the same time. This study exhibited that shark cartilage prevented tumors from growing new blood vessels, hence restricting growth. This work showed that the effective substance within the shark cartilage does not act directly on tumors, but restrict their blood supply and nourishment.

Another study searched transplanted tumors without developing new capillaries. After two-week period, no tumor growth were seen [3].

After finding of some substance in shark cartilage have a tumor growth inhibiting ability in transplanted tumors, the next step was to determine of this antitumor factor' role in humans and other mammals. Also, it was important to find out this angiogenesis inhibitor from shark cartilage can be effective with orally, or can be administered only by injection.

The more research were carried out to determine these antiangiogenesis factor in shark cartilage possible effect on metastasis, the spreading of cancer. In 1988, Patricia D'Amore suggested that also metastasis may depend on the growth of new blood vessels and therefor inhibition of vascularization might be a solution to prevent the formation of metastases. In the explanation of this suggestion another study demonstrated and the result indicated that the prevention of a single capillary segment caused to the death or inhibition of a lot of tumor cells [3].

Cartilage is one of the new materials including avascular tissues where lack of angiogenesis in there indicating it could be used in designing therapies for treating cancer and related malignancies in humans through antiangiogenic applications. Cartilage includes some specific molecules such as; thrombospondin-1, chondromodulin-1, the type XVIII-derived endostatin, SPARC (secreted protein acidic and rich in cysteine) and the type II collagen-derived N-terminal propeptide (PIIBNP). Their antiangiogenic or antitumor properties have demonstrated in a trials without completely understood. For example thrombospondin-1, endostatin and the shark-cartilage-derived Neovastat preparation have been tested for different kinds of cancers, but still needs to improve to use as anticancer agents [5].

It has been determined that angiogenesis is a essential for the growth of a tumor and also antiangiogenic drugs can be useful in the treatment of angiogenesis-dependent diseases. Cartilage was evaluated as a possible natural source of antiangiogenic compounds due to its known avascular nature. Several studies were carried out to determine the antiangiogenic and antitumor compounds in bovine and shark cartilage. But, the potential utility of shark cartilage in the treatment of cancer and other angiogenesis-dependent diseases have not been totally accepted because of (i) the insufficient patient outcome from the test that have used shark cartilage in cancer patients, and (ii) the lack of data indicating, bioavailability of oral shark cartilage usage [6].

The anti-angiogenic activity was determined in the PG155, a novel polypeptide, extracted from cartilage of the shark, *Prionace glauca*, via guanidine-HCl extraction, acetone precipitation, ultra-filtration and chromatography. The anti-angiogenic effects of PG155 were demonstrated, using zebrafish embryos model in vivo. Using of 20 µg/ml PG155 in the treatment of the embryos, resulted with a significant reduction in the growth of subintestinal vessels (SIVs). A higher dose gave almost complete inhibition of SIV growth, obtained from endogenous alkaline phosphatase (EAP) staining assay [7].

Shark liver oil papers

Liver oil, obtained from sharks as a another anticancer source were searched as well. Fish oils, with including the essential fatty acids (EFA) of n-3 family, alkylglycerols and squalene, are very important for health maintenance. N-3 EFA has an important role in preventing of the atherosclerosis. Alkylglycerols and squalene are the main factors in struggle against to infections and cancer. Shark liver oil includes huge amounts of alkylglycerols and squalene, and moderate of n-3 EFA. Because of that, it can be used in cancer therapy, especially in radiotherapy, and in the treatment of infectious diseases [8]. In a similar research, it was determined that Squalene and Alkylglycerols; both of them have antitumor activity which are present in a high amount in Shark liver oils. This study showed that shark liver oil is useful in treatment of several types of cancer [9].

Fish oils include several active compounds that regulate cell activity and effect various functions of the human body. Shark liver oils are very rich in 1-O-alkylglycerols which have strong ability to induce human immune system. This study represents antitumor content of 1-O-alkylglycerols derived from fish oils and its effect in combined treatment of different types of cancer [10].

Alkylglycerols (alkyl-Gro) are found largely in the liver of some elasmobranch fish species such as rattfishes and some sharks. Shark liver oil of *Centrophorus squamosus* (SLO), or alkyl-Gro mix obtained from this source, have several biological activities such as; stimulation of hematopoiesis and immunological defences, sperm quality improvement, or anti-tumor and anti-metastasis activities. Natural alkyl-Gro mix from SLO contains several alkyl-Gro, differed by chain length and unsaturation. In this study; six main components of natural alkyl-Gro mix, namely 12:0, 14:0, 16:0, 18:0, 16:1 n-7, and 18:1 n-9 alkyl-Gro, were synthesized and tested for anti-tumor and anti-metastatic activities on a model of transferred tumor in mice (3LL cells). It was determined that; 16:1 and 18:1 alkyl-Gro showed significant action in reducing lung metastasis number, while other alkyl-Gro had weaker or no specific effect [11].

Shark liver oil (SLOil) and fish oil (FOil), which are very rich in alkylglycerols (AKGs) and n-3 polyunsaturated fatty acids (PUFAs), have an ability to reduce the growth of some tumors. It is also known that FOil is able to increase apoptotic cells and lipid peroxidation of tumor cells and reduce proliferation rate. To test the effect of these components on tumor growth this study performed. For this study; weaning male Wistar rats were divided into 4 groups: fed regular chow (C), supplemented (1 g/kg body weight) with SLOil (CSLO), FOil (CFO) and both (CSLO+FO). After 8 weeks half of each group was inoculated with Walker 256 cells creating new groups (W, WSLO, WFO and WSLO+FO). Biochemical parameters of tumor weight, hydroperoxide content, proliferation rate and percentage of apoptotic tumor cells were obtained. In the result; fourteen days after inoculation, lower tumor weight (40%), greater tumor cell apoptosis (~3-fold), decreased tumor cell proliferation (35%), and higher tumor content of lipid hydroperoxides (40%) were obtained in WSLO rats especially; FOil showed more potent effects in the findings. The chromatographic results also indicated a potential incorporation competition between the n-3 fatty acids and the AKGs in the tumor cells' membranes. In the conclusion; it was suggested that the SLOil supplementation can be used as a supportive in the cancer therapy [12].

Alkylglycerols are natural etherlipids within the shark liver oil (SLO). A lot of different studies indicate the SLO have antitumor properties and it was described as an inhibitor of tumor neovascularization. It is known that both alkylglycerols and of fatty acids have potent biological properties but it is important to know which of them have more activities. To determine of this, another study carried out. In this study, a mouse model was used to investigate the antitumor effects of SLO and of alkylglycerols and both administered orally. In the findings; the alkylglycerol-treated mice, metastasis dissemination was reduced by 64 +/- 8%, whereas SLO effect was 30 +/- 9% below control. Purified alkylglycerols also decreased significantly plasmalogen content in tumors, whereas SLO had no such effect; suggesting that alkylglycerols were involved mainly and it has anti-angiogenic effect. In summary, there were decrease in the growth, vascularization, and dissemination of Lewis lung carcinoma tumors in mice when alkylglycerols were used. These findings suggest that the antitumor activity of SLO comes from mainly its alkylglycerols components [13].

It has been indicated that sharks are resistant to cancer and their liver oil can be used as anti-tumor drug. Shark liver oil includes 40% or more of squalene. Fish liver oil is also rich in squalene and polyunsaturated n-3 fatty acids.

This study based on determining of the anti-angiogenic and anti-tumor effects of these substances, in Balb/c mice after transplantation of syngeneic L-1 sarcoma. It was found that, all tested substances significantly diminished angiogenesis induced by tumor cells, and tumor growth [14].

CONCLUSION

A lot of massive researches are undergoing in cancer treatment and obtained very important benefits from the most of them, but still the certain treatment or cure is far from the applying into the practise. In this paper the importance of finding effective anti-cancer treatment and as alternative treatment materials, shark cartilage and liver oil were presented.

Several different studies were summarized and the conclusion can be done like that; shark cartilage is a powerful inhibitor of tumor growth and its extract has shown antiangiogenic and antitumor activities in animals and humans. It was found that oral administration of cartilage extract was effective in reducing angiogenesis [15].

On the other hand; shark liver oil can be used in treatment of several types of cancer with their alkylglycerol contents which have an multifunctional role, including anti-tumor and anti-metastasis activities in vivo. Shark liver oil has been used for over 50 years as a therapeutic and preventive agent, especially as an anti-cancer agent. It was determined that the intraperitoneal injection of shark liver oil (SLO) to tumor-bearing mice caused an increase T-cell infiltration into the tumor and lowered the tumor's volume, suggesting SLO is a good candidate and can be used in cancer therapy successfully without side effect [16].

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