Review

Molecular mechanisms of anti-cancer bioactivities of seaweed polysaccharides

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Abstract

Seaweed is a traditional Chinese medicine homologous to food, in which polysaccharides are responsible for anti-cancer by enhancing immunity, inducing cancer cell apoptosis, inhibiting cancer cell invasion and metastasis or directly scavenging oxidative free radicals that induce cancer cell changes. Among them, regulating immunity and promoting cancer cell apoptosis are intensively studied due to the important role in preventing cancer. Here we reviewed seaweed in the apoptosis-inducing signaling pathways including PI3K/AKT, ROS and JNK and discussed challenges in studying seaweed.

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Contents

1. Introduction .......................................................... 529
2. Enhancement of immune function .......................................................... 530
2.1. Promoting proliferation and activation of Mφ and improving phagocytic ability .................................................. 530
2.2. Activation of T and B lymphocytes .......................................................... 530
2.3. Promoting production of TNF-α, IL-2 and IFN-γ .......................................................... 530
3. Mechanism of inducing apoptosis of cancer cells .......................................................... 531
3.1. PI3K/AKT signal transduction pathway .......................................................... 531
3.2. ROS-mediated mitochondrial apoptosis pathway .......................................................... 532
3.3. JNK signal transduction pathway .......................................................... 531
3.4. Inhibition of lysosome-dependent autophagy .......................................................... 531
3.5. Inducing cell cycle arrest .......................................................... 532
4. Inhibition of cancer cell invasion and metastasis .......................................................... 532
4.1. Inhibition of VEGF expression .......................................................... 532
4.2. Down-regulation of EMP level .......................................................... 532
5. Scavenging free radicals .......................................................... 532
6. Discussion and perspectives .......................................................... 532
6.1. Tumor prevention is more important than treatment .......................................................... 532
6.2. Key development direction of seaweed in future .......................................................... 533
Declaration of Competing Interest .......................................................... 533
Acknowledgements .......................................................... 533
References .......................................................... 533

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1. Introduction

Cancer has become one of the most serious diseases that threaten human life and health. The radiotherapy or chemotherapy is usually used in modern medicine, but it has obvious side effects, which can destroy the normal hematopoietic organs and immune system, and lead to serious complications. Although the emergence of immunotherapy, targeted therapy and other new treatment methods, the therapeutic effect of some cancers has been continuously improved, but the complications of cancer patients have not been fundamentally solved, and the life cycle and quality of life of patients still need to be improved (Wang, Liu, & Lin, 2013). Traditional Chinese medicine has unique advantages in cancer treatment, which can improve patient tolerance, improve immune function, improve quality of life and reduce mortality (Zhu et al., 2018).

Seaweed, homologous to medicine and food, is a kind of marine plants with rich varieties, including brown algae, asparagus, porphyria, fucoidan and so on (Han, Zhang, & Liu, 2012; Liu, Sun, Zeng, & Zhou, 2015), as shown in Fig. 1. The medicinal use of seaweed has a long history, which can be seen in the Classic of Shen-nong Materia Medica, which tastes bitter, salty and cold, belongs to the meridians of liver, stomach and kidney, has the effects of softening, resolving phlegm, diuresis and detumescence, and is used in the treatment of gall cancer, testicular swelling and pain, phlegm edema and so on (Cao, Duan, Fan, Guo, & Su, 2014).

Historically, seaweed has been used to treat thyroid diseases, such as the end of the Warring States period, Lu’s Spring and Autumn recorded the relationship between goiter and regional existence, the book said: “Light water, many bald and gall people.” It is equivalent to the endemic goiter caused by modern iodine deficiency (Lu, 2003). The relationship between goiter and seaweed is described in the Classic of Shen-nong Materia Medica in the Qin and Han Dynasties, which records: “the seaweed is bitter cold, the main gall cancer gas, and the inferior cervical nucleus” (Ma, 2013). In the Tang Dynasty, Simiao Sun collected more than 20 kinds of prescriptions for treating gall, in which seafood such as Kunbu and seaweed were widely used (Lee & Chiu, 2021). The Materia Medica Chongyuan, which was continued by Shicong Gao, a physician in the Qing Dynasty, on the basis of his teacher Zhicong Zhang, further pointed out: “the gall cancer is gas, the neck hard nucleus is painful and swollen, it is the meridian disharmony and the disease is also external” and “seaweed dominates the meridians” (Zhang, 1997).

Traditional Chinese medicine seaweed mainly contains seaweed polysaccharides, sodium alginate and seaweed polyphenols (Liu, Sun, Zeng, & Zhou, 2015). In recent years, experiments have confirmed that seaweed polysaccharides have immunomodulatory, anti-cancer, antioxidant and anticoagulant activities, among which the anti-cancer pharmacological activity is more prominent. It has a certain therapeutic effect on lung cancer, liver cancer, esophageal cancer, breast cancer, cervical cancer and other malignant cancers (Ali Shah, 2018). Seaweed polysaccharide is one of the important active components of traditional Chinese medicine seaweed. The well-known fucoidan, agarose, carrageenan, alginic acid, ulvan and fucoidan all belong to seaweed polysaccharide (Chudasama, Sequeira, Moradiya, & Prasad, 2021), as shown in Fig. 2. According to the literatures (Ling et al., 2021), seaweed polysaccharides play an anti-cancer effect by regulating immune mechanism, inducing apoptosis, blocking cell cycle progress, regulating transduction signal pathway, inhibiting cancer cell invasion and metastasis, inhibiting angiogenesis and antioxidant activity. Seaweed belongs to the same plant of medicine and food. Taking more seaweed food in daily life can enhance the immunity of the body and play a role in preventing the occurrence of cancer. At present, chemotherapy is the main treatment for malignant cancers, but the curative effect is limited by systemic toxicity and drug resistance of cancer cells. Traditional Chinese medicine has the
advantages of safety and little side effects, and can be used as an alternative therapy for cancer treatment. This paper summarizes the anti-cancer mechanism of seaweed polysaccharides, in order to excavate its anti-cancer effects and lay a foundation for the further development and clinical application of seaweed polysaccharides.

2. Enhancement of immune function

The immune system is an important system for the body to perform immune response and immune function, including immune organs, immune cells and immune factors. The occurrence and development of malignant cancer is closely related to the immune system. Cancer cells can achieve immune escape and induce immunosuppression through a variety of mechanisms.

Seaweed polysaccharides can promote the production of cancer necrosis factor-α (TNF-α), nitric oxide (NO), interleukin-2 (IL-2) and interferon-γ (IFN-γ) by activating macrophages (Mφ), T lymphocytes and B lymphocytes, and regulate the immune system, thus indirectly play an anti-cancer effect.

2.1. Promoting proliferation and activation of Mφ and improving phagocytic ability

Mφ is an important immune cell in the body, which has strong phagocytic ability and antigen presentation ability. Seaweed polysaccharides can stimulate Mφ and other immune cells to proliferate, activate and mature, exert their functions of immune surveillance and killing mutant cancer cells, and restore and strengthen the immune system of the body (Yan, Sun, Zhao, Zhang, & Liu, 2018).

Li (Li, 2015) used Mφ cell RAW 264.7 to explore the biological activity of porphyria polysaccharides and asparagus polysaccharides. MTT experiments showed that both polysaccharides could effectively promote the proliferation and enhance the cell activity of RAW 264.7. In the concentration range of 5 μg/mL, the proliferation effect of porphyria polysaccharides increased with the concentration of porphyria polysaccharides for 12 h, and the cell viability reached the highest at 40 μg/mL for 24 h, which was 2.7 times higher than that of the control group. Grazilactaria lanceolata polysaccharides could significantly enhance the viability of RAW 264.7 cells in the range of 12.5 μg/mL to 200 μg/mL, but there was no significant difference among different concentrations. Neutral red uptake test showed that porphyria polysaccharides and asparagus polysaccharides could significantly enhance the phagocytic ability of macrophages. The phagocytic ability of RAW 264.7 in porphyria polysaccharides treated with different concentrations (25, 50, 100 μg/mL) was 1.8, 2.1, 2.5 times higher than that in the control group, respectively. The phagocytic ability of RAW 264.7 treated with different concentrations (50, 100, 200 μg/mL) of asparagus polysaccharide was 1.7, 2.0 and 2.4 times higher than that of the control group, respectively. Therefore, the experimental results show that the polysaccharides purified from porphyria haita-nensis and asparagus can effectively activate RAW 264.7, promote cell proliferation and enhance phagocytosis.

2.2. Activation of T and B lymphocytes

Lymphocytes are the main immune cells of the body, in which T lymphocytes are mainly involved in cellular immune response and B lymphocytes are mainly involved in humoral immune response. Studies have found that lymphoid T and B cells can protect the body from cancer damage. (Jia, 2016b) used mouse S180 sarcoma cells as coating antigen, serum as antibody, goat anti-mouse IgG-HRP as enzyme-labeled second antibody, and color reaction with substrate solution. When the antigen is excessive, the experimental results are proportional to the amount of antibodies in the serum, so as to compare the difference of antibody content in each group. The results showed that the IgG antibody in each group was significantly higher than that in the negative control group, and the content of IgG antibody in the model group and polysaccharide group was significantly higher than that in the blank group, and that in the polysaccharide group was significantly higher than that in the model group. The results showed that asparagus polysaccharide could induce specific humoral immune response in mice and produce a large number of specific antibodies, which could inhibit the proliferation of cancer cells and protect the body.

Zhang et al. (Zhang & Mou, 2016) compared different concentrations of seaweed sulfated polysaccharides into Kunming male mice with fluorouracil positive group. After the last administration, the thymus and spleen of mice were removed, the cancer was stripped and weighed, and the anti-cancer activity of seaweed sulfated polysaccharides was tested. The results show that it can inhibit the growth of cancer cells by improving the proliferation function of T-lymphocytes in mice. And the anti-cancer effect and administration dose were concentration-dependent (Liu et al., 2015).

2.3. Promoting production of TNF-α, IL-2 and IFN-γ

TNF-α is a type of cancer necrosis factor. As a multifunctional inflammatory cytokine, it can directly kill cancer cells without obvious cytotoxicity to normal cells, and has anti-infective and anti-cancer effects (Wang, Ren, Liu, Zhang, & He, 2017). Anti-inflammatory cytokines IL-2 and IFN-γ secreted by Th1 cells mainly participate in delayed anaphylaxis mediated by helper T cells and thus play an anti-cancer role.

Fan et al. (Fan, Zhang, & Nie, 2017) studied the inhibitory effect of spindle spirulina polysaccharide (SPS) on hepatocellular carcinoma in nude mice. After inoculating HepG2 hepatoma cells, the drug was intragastrically administered at 100, 200, 400 mg/kg weight for 28 d, and then the products in peritoneal macrophages and serum of cancer-bearing mice were detected. The results showed that SPS could significantly inhibit the growth of transplanted cancer of human hepatoma HepG2 cells in nude mice and significantly increase the level of TNF-α in serum of cancer-bearing mice. SPS can also promote the secretion of TNF-α by peritoneal macrophages of HepG2 cancer-bearing mice.

Ju et al. (Ju, Ye, Xie, & Chen, 2016) investigated the anti-cancer activity of polysaccharide from Gracilaria (GLP) on S180 sarcoma-bearing mice, and preliminarily discussed the anti-cancer mechanism of GLP by measuring the biochemical indexes of the immune system of mice. The results showed that the levels of IL-2 and IFN-γ in S180 cancer-bearing mice increased significantly. It is suggested that GLP can enhance the immune function of mice by increasing the levels of IL-2 and IFN-γ in peripheral blood.

3. Mechanism of inducing apoptosis of cancer cells

Apoptosis is an autonomous and orderly process of cell death controlled by genes (Wang et al., 2011). Different from cell necrosis, it is a kind of autonomous behavior of the body in order to better adapt to the surrounding environment. One of the characteristics of cancer cells is the lack of this programmed death process. Apoptosis includes a variety of signal pathways, including PI3K/AKT signal pathway, ROS-mediated mitochondrial apoptosis pathway, JNK pathway in MAPK signal transduction pathway and so on. When the pathway is affected, cells will proliferate infinitely and form cancers (Xu et al., 2018).
3.1. PI3K/AKT signal transduction pathway

It has been found that PI3K/AKT signaling pathway is maladaptation in most cancer cells, so it plays an important role in regulating the proliferation and apoptosis of cancer cells (Chen & Yang, 2017). PI3K/AKT signal transduction pathway can play a role in downstream apoptotic proteins such as aspartate-specific cysteine protease-9 (Caspase-9) and aspartic acid-specific cysteine protease-9 (Caspase-3), and mediate cell cycle regulatory proteins, stimulate their effects, and promote cancer cell apoptosis to inhibit the proliferation of cancer cells (Xu, Yang, Du, Xu, & Zhou, 2020).

Choo et al. (Choo, Lee, & Shin, 2016) treated DU-145 prostate cancer cells with 500 or 1000 g/ml fucoidan for 24 h, the phosphorylation level of PI3K/AKT decreased in a concentration-dependent manner, and decreased with the increase of time, indicating that fucoidan induced apoptosis of DU-145 prostate cancer cells by reducing the activation of PI3K/AKT.

Jiang et al. (Jiang, Zhu, & Liu, 2020) found that the expression of PI3K/AKT decreased in high-dose fucoidan group by Western blot detection, indicating that high-dose fucoidan had a significant inhibitory effect on proteins related to PI3K/AKT signal pathway and inhibited breast cancer genesis. This result is consistent with the research results of a previous research (Wang, Pu, Deng, & Lie, 2018).

Marcel et al. (Marcel, Hiroko, & Hidekazu, 2011) observed the effect of fucose sulfonated polysaccharide (FCS), an extract of sargassum, on the proliferation of melanoma B16 cells. It was found that the apoptosis induced by FCSs was characterized by asymmetric loss of cell membrane and translocation of membrane phospholipids, accompanied by the activation of Caspase-3. It is confirmed that FCSs may induce apoptosis through Caspase-3-activated cascade reaction, which plays a bioactive role in skin cancer cells.

After prostate cancer cells being treated with sodium alginate oligosaccharide (AOS), cleaved-Caspase-9 protein was detected by Western blot assay. The results showed that the expression of apoptosis-related protein cleaved-Caspase-9 in the treatment group was higher than that in the control group, indicating that AOS can induce apoptosis of prostate cancer cells by activating cleaved-Caspase-9 (Han, 2019).

3.2. ROS-mediated mitochondrial apoptosis pathway

Mitochondria are the control center of cell life activity, not only the center of cell respiratory chain and oxidative phosphorylation, but also the regulation center of apoptosis. When stimulated by internal (DNA mutation) or external stimulation, mitochondria release apoptosis factor ROS, to activate apoptosis signal pathway and promote apoptosis (Zheng, Yang, Yan, Tang, & Song, 2019). Excessive ROS, as a cellular signal molecule, can lead to DNA strand breakage, block cell repair and lead to apoptosis (Liang, Shan, Zhou, Xu, & Hou, 2019).

The hepatoma SMMC-7721 cells treated with fucoidan sulfate with probes were loaded, and detected the changes of ROS by flow cytometry. Firstly, the concentration of DCFH-DA was adjusted to 10 μmol/L, and the cells were incubated for 20 min and mixed upside down every 5 min. Finally, the cells were washed with serum-free cell culture medium for three times to fully remove the unloaded probes. The results of flow cytometry showed that the fluorescence intensity of M1 region gradually increased with the increase of concentration, and the ratio of M1 in the fucoidan sulfate group to the control group increased, indicating that fucoidan sulfate can induce apoptosis of SMMC-7721 cells through ROS-mediated mitochondrial apoptosis pathway (Yang, 2013).

3.3. JNK signal transduction pathway

JNK is called stress protein-activated kinase. As a member of the (MAPK) family of mitogen-activated protein kinases, the research on JNK pathway is mainly focused on post-injury stress response and promoting apoptosis.

Bai (Bai, 2020) explored the mechanism of apoptosis of HT-29 cells induced by fucoidan sulfate. Firstly, RT-PCR method was used to detect the signal molecule JNK, in the process of apoptosis. The results showed that compared with the control group, the expression of JNK in the experimental group increased with the increase of the concentration of fucoidan sulfate. At the same time, Western blot method was used to detect the expression level of related proteins in the process of apoptosis. The results showed that compared with the control group, the ratio of p-JNK/JNK in the experimental group increased from 2.9 to 5.2. Therefore, JNK signaling pathway plays an important role in the process of apoptosis induced by fucoidan sulfate.

Pei et al. (Pei, Sao, & Jie, 2016) studied apoptosis and cell cycle arrest of human gastric cancer MKN45 cells induced by algal polysaccharides. Before MKN45 cells were treated with polysaccharides (100 μg/ml), 5 μmol/L SP600125 (JNK inhibitor) was added for 1 h. The phosphorylation of JNK and p-JNK was detected by Western blotting. The result showed that the degree of phosphorylation decreased. It is suggested that the apoptosis and cell cycle arrest of gastric cancer cells induced by new algal polysaccharides may be the result of the regulation of JNK signal pathway.

3.4. Inhibition of lysosome-dependent autophagy

The main modes of cell death are programmed necrosis, apoptosis and autophagy (Hu et al., 2018). The killing effect of autophagy-promoting drugs is very good in the early stage of cancer, but it is easy to develop drug resistance in the late stage, which is beneficial to the survival of cancer cells. Inhibition of autophagy can improve the sensitivity of chemotherapeutic drugs to kill cancer cells. When autophagy is inhibited, the death mode of cancer cells will be transformed into apoptosis (Sung, Chung, & Kim, 2016).

Wu (Wu, 2018) compared Gracilaria brittle polysaccharides with 5-Fu group and 5-Fu single group. It was found that the fluorescence brightness and volume of lysosomes in 5-Fu cells increased significantly, while there was no significant change in Gracilaria brittle polysaccharides combined with 5-Fu. The results showed that Gracilaria polysaccharides could inhibit the fusion of autophagosomes and lysosomes, resulting in the accumulation of autophagy toxic proteins that could not be degraded, resulting in the death of ECA109 cells. After autophagy was inhibited, cancer cells showed apoptosis, and the degree of apoptosis was almost the same as that of autophagy inhibitor CQ. The experimental results show that the sensitizing effect of Gracilaria polysaccharide is to induce apoptosis of esophageal cancer cells by inhibiting lysosome-dependent autophagy and relieving autophagy of cancer cells. Which stage of Gracilaria brittle polysaccharides involved in the process of inhibiting autophagy and promoting apoptosis of esophageal cancer ECA109 cells remains to be further studied. The results show that Gracilaria brittle polysaccharides is expected to solve the problem of chemotherapeutic drug resistance and can be used as a chemotherapeutic drug sensitizer in the field of medicine (Wu, 2018).

It has been proved that Gracilaria polysaccharide can inhibit the growth of cancer cells by inducing cancer cell apoptosis (Ju, Cao, Chen, & Ye, 2016). It will be a research trend in the future to make good use of the relationship between apoptosis and autophagy to promote the apoptosis of cancer cells and improve the effect of anticancer (Yi et al., 2018).
3.5. Inducing cell cycle arrest

The animal cell growth cycle is divided into four cycles, in which G1 phase will affect cell division and then determine the cell fate. If an error occurs in G1 phase, it will destroy the normal cell cycle, resulting in unlimited proliferation and division of cells and then the formation of cancer (Ning & Geng, 2016). Therefore, changing the growth cycle of cancer cells may block the proliferation of cancer cells and play an anti-cancer effect.

The cell cycle and apoptosis rate of solid cancer cells in cancer-bearing mice were detected by flow cytometry PI staining (Jia, 2016a). The results showed that the apoptosis rate of solid cancer cells in the polysaccharide group was significantly higher than that in the model group ($P < 0.05$). The rest of the cells were blocked in G0/G1 phase and could not successfully enter S phase, while some S phase cells could successfully enter G2/M phase. In the polysaccharides group, the proportion of solid cancer cells in G0/G1 phase increased significantly, while the proportion of cells in S phase decreased significantly ($P < 0.05$), but there was no significant difference in the proportion of cells in G2 cycle M phase. It is suggested that asparagus polysaccharide can inhibit mouse cancer cells in G0/G1 phase and induce cancer cells to apoptosis and be absorbed by the body, thus making the cancer regression.

Yang et al. (Yang, Zhang, & Kong, 2015) determined the anti-cancer activity of fucoidan against diffuse large B cell lymphoma (DL-BCL) cells. The results showed that fucoidan could induce cell cycle arrest in G0/G1 phase, accompanied by up-regulation of cyclin kinase inhibitor p21 and down-regulation of cyclin CDK4 and CDK6.

4. Inhibition of cancer cell invasion and metastasis

In the process of cancer invasion and metastasis, there are some processes, such as cancer neovascularization, Embden-Meyerhof-Parnas (EMP) level increase and so on. A large number of experimental studies have shown that seaweed polysaccharides can act on these key processes of cancer cell invasion and metastasis, so as to achieve the purpose of anti-cancer invasion and metastasis (Wang & An, 2013).

4.1. Inhibition of VEGF expression

Vascular endothelial growth factor (VEGF) is the most important cancer-promoting factor known to mediate endothelial cell proliferation and migration, promote endothelial cell survival, and is a key factor in angiogenesis.

Chen et al. (Chen, Zhu, & Chen, 2014) adopted the model of implanted cancer mice inoculated with H22 liver cancer cell line, through intragastric administration of large, medium and low doses of seaweed polysaccharides on the growth of cancer cells in vivo, the positive group was given Polyposus umbellata polysaccharide, the model control group was given 0.9% sodium chloride injection of the same volume, and then the effect on the content of VEGF in peripheral blood serum of liver cancer mice was detected by ELISA method. It was found that all dose groups of seaweed polysaccharide could reduce the content of VEGF in peripheral blood serum of hepatoma mice, and the middle dose was the best. This is the same as the results of Zhu et al (Zhu & Chen, 2015).

The effects of different concentrations of Sargassum fusiforme polysaccharide (SFPS) on the proliferation of cancer vascular endothelial cells were monitored by real-time cell analysis system (Chen, Li, Chen, Kuang, & Guo, 2016). The secretion of VEGF-A in cancer cell culture supernatant was determined by ELISA method, and the level of cancer cell VEGF-A mRNA and cancer vascular endothelial cell VEGFR-2 mRNA were detected by real-time fluoroquantitative PCR. The results showed that SFPS at the concentration of 30, 100 mg/L could significantly reduce the content of VEGF in the medium supernatant of human gastric cancer MGC-803 cells and inhibit the proliferation of cancer vascular endothelial cells. The mechanism is related to the down-regulation of cancer cell VEGF-A and cancer vascular endothelial cell VEGFR-2 expression.

4.2. Down-regulation of EMP level

The level of EMP in cancer cells is often higher than that in normal cells. Cancer cells, as a metabolic disorder, can use EMP to produce energy in anoxic environment, and 50% to 70% of energy metabolism is dependent on EMP. Therefore, inhibiting the metabolic level of EMP is also the target of clinical drug development (Xin & Wise, 2015).

Feng et al. (Feng, Tang, Xu, & Tan, 2017) proved that seaweed polysaccharides can down-regulate the level of EMP metabolism in hepatoma cells Hep3B. After Hep3B cells were treated with different concentrations of seaweed polysaccharides for 48 h, the cells were collected, and the hexokinase (HK) activity, pyruvate kinase (competitive) activity and lactate acid content were determined. The results showed that when the concentration of seaweed polysaccharides was 10–100 mg/mL, the activities of HK and competitive enzymes decreased with the increase of seaweed polysaccharides concentration, suggesting that seaweed polysaccharides could inhibit the metabolism of EMP in hepatocellular carcinoma cells in a concentration-dependent manner.

5. Scavenging free radicals

Hydroxyl radicals, superoxide radicals and other highly oxidizing free radicals produce a series of harmful reactions to the human body, which can cause excessive oxidation of DNA, chromosome aberration, disorder of gene expression, and finally lead to cell carcinogenesis (Cao & Liu, 2018).

Wang et al. (Wang et al., 2010) tested the antioxidant activity of serum by intraperitoneal injection of seaweed sulfated polysaccharide (SP) into S180 cancer-bearing mice. SP samples were prepared with aspartic physiological sodium chloride solution, which were divided into low, middle and high dose groups (25, 50, 100 mg/kg), normal control group (physiological sodium chloride solution) and positive control group (fluorouracil 20 mg/kg). The results showed that SP could significantly reduce the activity of serum SOD in cancer mice, while the positive group had little effect on the activity of superoxide dismutase SOD. could significantly increase the activity of serum catalase (CAT) in cancer mice, while the activity of CAT enzyme in positive group decreased significantly.

6. Discussion and prospects

6.1. Tumor prevention is more important than treatment

It is an eternal topic to treat and prevent diseases in people's daily life. The idea of prevention originated from the Internal Classic of the Yellow Emperor: “The sage does not cure the disease, but does not cure the disease, does not cure the disorder, which means that instead of carrying out treatment after the illness, it is better to start prevention before the illness occurs. In the Han and Tang dynasties, this kind of "thought of prevention" was further developed. Simiao Sun said in Thousand Golden Prescriptions that the superior doctor prevents illness, the mediocre doctor attends to impending sickness and the inferior doctor treats actual illness, indicating that the good at preventing illness is used to evaluate
ability of a doctor. He also pointed out that the meaning of pre-
vent illness is that he who is good at nourishing his nature cures
his disease (Sun, 1999). In the Song Dynasty, there were a large
number of thinkers, such as Anshi Wang and Liang Chen, who
abandoned the classic works that had always been regarded as
sacred, changed the habit of taking Dan medicine, which was pop-
ular in the previous generation, and made the concept of prevent
illness more scientific and it tends to be perfected gradually (Ni,
2021).

In modern times, with the development of immunology, people
realize that the occurrence and development of malignant tumor is
closely related to the immune system. The idea of prevention is
closely related to strengthening the immune system. As we all
know, T and B lymphocytes are the main cell groups that make
up the body’s immune system, which can protect the body from
tumor damage. As mentioned above, asparagus polysaccharides
and seaweed sulfated polysaccharides can activate T and B lymph-
ocytes and promote the secretion of immune factors, to a certain
extent, prevent the occurrence of tumor diseases. Seaweed belongs
to traditional Chinese medicine which is homologous to medicine
and food, which can be eaten directly in daily life. At present, there
are many kinds of health products and medicinal diets with sea-
weed as the main raw materials. Taking more seaweed in daily life
can also play a role in preventing the occurrence of cancer.

6.2. Key development direction of seaweed in future

With the enhancement of public health awareness, health prod-
ucts with seaweed as raw materials, medicine and food homolo-
gous products have received widespread attention (Gao et al.,
2021). Seaweed products can be used alone in daily life to “en-
hance immunity”; at the same time, seaweed can also be compat-
ible with other drugs to play the role of filling gas, filling blood,
nourishing yin, tonifying yang and so on. Personalized health care
is carried out according to personal conditions under the guidance
of clinical health care physicians.

The traditional extraction method to obtain the active compo-
nents of seaweed takes a long time and low efficiency. In recent
years, new processes such as ultrasound-assisted extraction,
enzyme hydrolysis-assisted extraction and enzyme digestion have
been developed on the traditional methods, which can retain the
activity and reduce the molecular weight at the same time. Not
only reduce the cost, but also more conducive to human absorp-
tion, to achieve the effect of health care, this technology may
become a cheaper and efficient preparation method after industri-
alization (Qin et al., 2021).

There are many kinds of seaweed with different shapes, and the
number of macroalgae is as high as 1277 species (Sun, Nan, Tang,
Jiang, & Hai, 2019). In order to ensure the effectiveness of seaweed
varieties, a quality control evaluation system based on “efficacy”
should be gradually established. For example, we should vigor-
ously develop the fingerprint technology of traditional Chinese
medicine, so that it can identify seaweed varieties more objectively
and obtain more accurate quality control.

The bioactive peptides in seaweed can inhibit the proliferation
of tumor cells and have no toxic side effects on normal cells, but
the activity has not reached the ideal state (Yang, Liu, Hu, Chen,
Wu, Li, Qi, Deng, & Yang, 2020). It is necessary to strengthen the
research in the future to clarify the amino acid sequence and
molecular structure of seaweed peptide to improve its anti-
tumor activity. In the study of mechanism, in addition to apoptosis
and necrosis, mediating immune and anti-angiogenic activity,
membrane receptors and other aspects may be the focus of research.

At present, the anti-tumor effect of seaweed extract is in the
ascendant, and it has great potential in tumor prevention and
treatment. There is a huge output of seaweed in China. The use
of seaweed preparation not only greatly reduces the cost of medi-
cation, but also has good safety and non-toxic effect on normal
cells. In the future, through the continuous efforts of researchers,
more seaweed-related preparations with strong activity and good
safety will be developed and applied in clinic.

Declaration of Competing Interest

The authors declare that they have no known competing finan-
cial interests or personal relationships that could have appeared
to influence the work reported in this paper.

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