

Physical, Chemical, and Biological Properties of Wonder Kelp—*Laminaria*

Se-Kwon Kim^{*,†,1} and Ira Bhatnagar^{*,‡}

| | | |
|----------|--|----|
| Contents | I. Introduction | 86 |
| | II. Physical Properties | 87 |
| | III. Life cycle of <i>Laminaria</i> sp. | 88 |
| | IV. Chemical Properties | 88 |
| | V. Biological Properties (Medicinal Applications of <i>Laminaria</i>) | 91 |
| | A. Alginate | 91 |
| | B. Fucoidan | 92 |
| | C. Laminarin | 94 |
| | D. Cardiolam | 94 |
| | VI. Concluding Remarks | 94 |
| | References | 95 |

Abstract

Laminaria is a kelp that finds its place in the brown algae family. It has been an area of study for past many years, and its wonderful biological properties have always attracted medical professionals and researchers to explore more and more from this wonder kelp. The constituents of *Laminaria* include iodine, potassium, magnesium, calcium and iron. Iodine compounds, TEA-hydroiodide in particular, are great lipolytic agents as they stimulate lipase activity. Laminarins on the other hand are used as a tumor angiogenic blocker.

* Department of Chemistry, Pukyong National University, Busan, Republic of Korea

† Marine Bioprocess Research Center, Pukyong National University, Busan, Republic of Korea

‡ Laboratory of Infectious Diseases, Centre for Cellular and Molecular Biology, Hyderabad, India

¹ Corresponding author: Se-Kwon Kim, E-mail address: sknkim@pknu.ac.kr

This genus of the kelps is also rich in algin, a high molecular weight polysaccharide that forms viscous colloidal solutions or gels in water leading to the use of kelp derivatives as bulk laxatives. It has great applications in cosmeceutical science, as well as some antibacterial properties have also been assigned to *Laminaria*. A deeper insight into the physical, biological, and chemical properties of this wonder kelp would lead to further exploitation of *Laminaria* for medicinal and cosmeceutical purpose.

I. INTRODUCTION

Our ecosystem is unique in its biodiversity. The most complex are the underwater ecosystems with ample of creatures and species, many of which are not yet discovered. We are unaware of many biological properties that may be buried deep in the oceans. Kelps are one such species which remain deep rooted in the marine environment. There are many varieties of kelps in underwater ecosystems that vary in size, shape and color. They are a major keystone species in this ecosystem, and without them, many organisms would die. They also possess ample of nutrients and minerals which make them highly bioactive. Anticoagulants, antibiotics, antiparasites, antihypertensives, reducers of blood cholesterol, dilatory drugs and insecticides are made with the help of such properties.

Sea kelp that grows on the bottom of the sea is especially rich in nutrients that are good for the human body. Beta carotene, fiber, chlorophyll, protein, enzymes, and amino acids are found in this ancient fruit of the sea. It contains a complex of sodium, potassium, iron, calcium, magnesium, phosphorus, and other minerals. The nutrients in sea kelp make for a perfect dietary recommendation (www.articleclick.com). Scientists believe that this ancient vegetable from the sea consists of many elements that are no longer present in the terrestrial soil on which we grow our vegetables. As a matter of fact, our body resembles in composition with the water found on deep levels of the sea and we share approximately 56 components in deep sea water that also circulate through our bodies. Thus, in sea kelp, the chemical composition resembles that of human plasma and consuming it contributes to regulate our internal balance.

In this chapter, we would like to deal with the physical, chemical, and biological properties of kelp taking *Laminaria* as the keystone species. We will try to explain the secret of this sea kelp. We would discuss the geographical distribution, life cycle, chemical composition, as well as the array of biological activity that *Laminaria* displays, may it be anticancer, antioxidant, antiviral, immunomodulatory or antihypertensive.

II. PHYSICAL PROPERTIES

Physically the kelps appear to be plants. The main body consists of a holdfast resembling roots that attaches to a substratum. While they remain attached, the body of the kelp remains floating and appears to be dancing on the tunes of ocean currents. The short branches like stipes resemble a stem whereas its blades appear to be the leaves. Kelp blades reach to the available light near the surface of the ocean through floats or pneumocystis which are gas-filled compartments otherwise known as gas bladders. *Laminaria japonica* is a common species of kelp that inhabits temperate and cold waters in the northern hemisphere and temperate waters in the southern hemisphere. It is known in China as “Kun Bu” and in Japan as “Kombu” (Fig. 7.1).

Genomic information has led to increased understanding of this group, and kelps are no longer considered as plants. Although structurally similar, kelps are functionally different from plants in certain aspects such as the use of root-like holdfast which only serves as an anchor and has no role in securing nutrition. Moreover, the task of mineral absorption is accomplished with the help of blades together with photosynthesis. Further, kelps use chlorophyll a during photosynthesis which appears to be a plant like feature. However, it also uses chlorophyll c, only present in chromists. A possible explanation for the use of chlorophyll c may be its

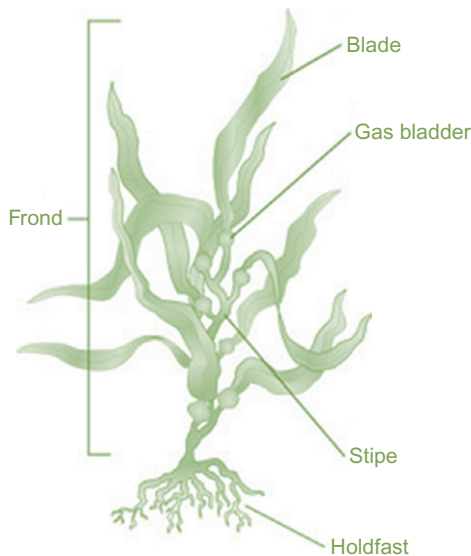


FIGURE 7.1 Generalized structure of *Laminaria* sp.

basis of fucoxanthin, a pigment that is most efficient in utilizing the blue-green light that penetrates the ocean. And that is one good reason for the brown coloration of kelp. Presence of fucoxanthin adds to the biological properties of kelps (discussed later in this chapter) as it is medically interesting and is under investigation for anticancer and anti-inflammatory properties.

III. LIFE CYCLE OF *LAMINARIA* SP.

The life cycles of many of the kelps are well characterized and can be controlled by environmental factors, and some have been used for significant molecular analyses (Billot *et al.*, 1998; Crepineau *et al.*, 2000; Yoon *et al.*, 2001). The order Laminariales is characterized by individuals with a heteromorphic alternation of generations, comprising two free-living life phases, a large diploid sporophyte and a microscopic haploid gametophyte generation (www.geol.utas.edu.au). *Laminaria* sp. consists of sori which are regions of epidermis along the length of the blade. The importance of these sori lies in the *unilocular sporangia* found inside them. These unilocular sporangia are in turn intermingled with sterile *paraphyses* that are filamentous structures found packed between sporangia or gametangia. In *Laminaria* sp., the unilocular meiosporangia produce 32 haploid *meiospores*. These meiospores produce the small filamentous *gametophyte* generation after settling to the substrate. The *male gametophytes* produce the motile, biflagellate *sperm* whereas the *female gametophytes* transform into elongated *oogonia* containing eggs. A single egg is released from the oogonium prior to fertilization. After fertilization, the *zygote* germinates to form a flat *proembryo* that subsequently differentiates into the mature *sporophyte* (Fig. 7.2).

IV. CHEMICAL PROPERTIES

Unlike plants where the main storage compound is starch, chromists store laminarin (hence the name *Laminaria*) in the form of chains of mannitol and glucose, and the organelles used for the storage are pyrenoids. Apart from the laminarin in pyrenoids, the cell walls of chromists contain algin, a gum used as a thickener and emulsifier in the food and cosmetics industry (www.biology-online.org). East Asian cultures have traditionally exploited kelp for food and medicinal values. On an average, 100 g of the dry kelp contains 17.1–32.0 g alginic acid, 8.46–28.48 g mannitol, 5.97–18.99 g crude protein, and 19.35–45.29 g ash, including 0.13–0.69 g iodine and 4.35–12.65 g potassium, yielding 262 kcal. Chemical analysis of the kelp shows that it may be regarded

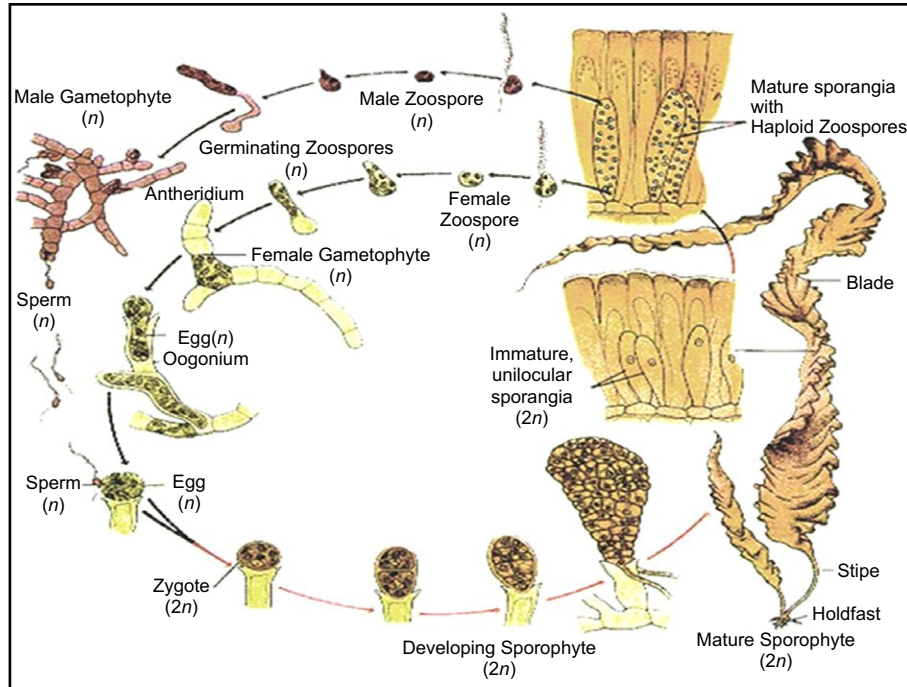


FIGURE 7.2 Life cycle of *Laminaria* sp.

as a "health food," especially desirable in the winter season in the north when green vegetables are comparatively scarce.

Owing to the balanced nature of the qualitative and quantitative composition of biologically active substances [amino acids, polyunsaturated fatty acid, alginate, vitamins (A, C, D, B1, B2, B3, B6, B12, E, K, PP), macro- and micronutrients (K, Na, Ca, Mg, I, S, Si, etc.)], *Laminaria*, the giant wonder kelp, is highly effective to ensure normal functioning of the body and aids in treating certain diseases. Minerals mainly present are water-soluble salts of potassium and sodium (chlorides, sulfates). It also possesses relatively large amounts of calcium. The cumulative effect of these substances in varied combinations provides a high therapeutic effect. Most of the medicinal properties of *Laminaria* are due to the presence of alginic acid. Content of alginic acid in algae ranges from 11 to 60%. This alginic acid is similar to pectin in its function that is present in the berries, fruits, and vegetables. Apart from the above-mentioned elements, *Laminaria* is also found to possess copper, antimony, lead, gold, chrome, etc.

The medicinal properties of *Laminaria* depend upon the content and qualitative composition of proteins and carbohydrates. Certain other properties that aid to its therapeutic use are the ability to absorb large amounts of water and increase in volume at the same time and the higher contents of various macro- and micronutrients as compared to the terrestrial plants. Also, possession of colloidal polymer contents such as agar, alginic acid, and others as well as mannitol, specific to the marine vegetation makes *Laminaria* a very potential medicinal food.

As compared to other marine species, *Laminaria* has a greater ability to extract minerals from the sea water and hence accumulate a lot of elements, for example, 9–10-fold higher magnesium content, 17-fold higher sulfur, and 13 times higher bromine. Above all, 1 kg of kelp contains as much iodine as it is dissolved in 100,000 l of seawater. On the whole, the amount of iodine in kelp is several thousand times greater than in the terrestrial flora. Also, the boron in *Laminaria* is 90 times greater than in oats and four to five times higher than in the potato and beet. It contains an average of 0.43% phosphorus, whereas in the dried potatoes and dried carrots, it is almost half.

Laminaria accumulates not only large amount of various micro- and macronutrients but also many vitamins. Laboratory studies show that kelp contains a number of pro-vitamin A, which corresponds to its content in common fruits: apples, plums, cherries, oranges. As far as the content of vitamin B1 is concerned, kelp is no more inferior to the dry yeast. Reports suggest that about 100 g of dried *Laminaria* contains up to 10 µg of vitamin B12. *Laminaria* is considered of great interest as food ingredient, as it contains a fairly large amount of vitamin C (100 g of dry kelp contains approximately 15–240 mg). This content stands hand in hand with other citrus fruits of terrestrial origin such as orange,

pineapple, strawberries, gooseberries, green onions, and sorrel. In addition to the above vitamins D, K, and PP (nicotinic acid), pantothenic and folic acids are also found in *Laminaria* (www.authspot.com).

V. BIOLOGICAL PROPERTIES (MEDICINAL APPLICATIONS OF LAMINARIA)

Laminaria possesses remarkable properties that make it a wonderful component of dietary supplements. Due to its amazing medicinal benefits, it has been used in traditional Chinese medicine since centuries and is listed in the Chinese pharmacopeia. In general, *Laminaria* is considered as a cold, salty herb, prescribed to cleanse heat, resolve phlegm, and soften and disperse hard accumulations (e.g., goiters). It is often used to control edema, as an expectorant and antitussive, and as a remedy for testicular pain and swelling. Despite its salty character, the herb is slightly hypotensive.

As discussed under the chemical properties, a dietary supplement, *Laminaria*, is rich in several constituents that can be very beneficial to the health. Its high iodine content proves to be a great natural boon for the thyroid gland to prevent goiter. Apart from its high calcium, potassium, magnesium, iron, and trace minerals such as manganese, copper, selenium, and zinc, it provides vitamins B1 and B2 as well as chromium which is instrumental in blood sugar control and helps to keep diabetes in check. In Europe, *Laminaria* is basically harvested for a main source of alginate in the food industry, an emulsifying and binding agent used in the production of many foods like ice cream, toothpaste, cereals, and cosmetics as well as in paints and films (www.montereybayaquarium.org).

Dietary use of *Laminaria* dates back to the days of the First World War when it was used in raw form as a feed supplement for horses. It is used as a food, principally in Asian countries, where it is valued for its flavor, mineral content, and health giving benefits. The most important components with a medicinal point of view are *Laminaria's* polysaccharides. It contains alginates, laminarin, laminine, and fucoidan as well as a number of other polysaccharides and simple sugars.

A. Alginate

The alginates are binding agents that absorb toxic heavy metals and radioactive isotopes from the body by binding with them in the gastrointestinal tract when they are present in the bile. It operates as a pump, pumping out heavy metals and other toxins. It is suggested that if *L. japonica* is consumed on a regular basis for at least 4 months, levels of dangerous metals like mercury, lead, and aluminum can be significantly reduced. Alginate also prevents a person from harmful impact of

radiation emitted by TV-screens, computers, microwave ovens, and cellular phones. *Laminaria* alginate has been used with great success in treating radiation sickness in the victims of the Chernobyl, Russia disaster via this mechanism.

B. Fucoidan

It is a sulfated fucopolysaccharide and is the subject of extensive research for its anticancer properties. Studies have shown fucoidan to be effective in stopping the growth of tumors, inducing cancer cell apoptosis (programmed cell death) in leukemia, stomach, and colon cancer lines, and in interfering with metastasis by inhibiting interaction between tumor cells and the host tissue basement membrane. Fucoidan from *Laminaria angustata* is composed mainly of fucose/galactose/sulfate (9/1/9) (Kitamura *et al.*, 1991). Fucoidan of *L. japonica* has anti-RNA and DNA virus functions. The antiviral effects of fucoidan on infection due to poliovirus III, adenovirus III, ECHO6 virus, Coxsackie B3 virus, and Coxsackie A16 are remarkable. Fucoidan can inhibit the development of cytopathic effect and protect cultural cells from infection caused by above viruses (Li *et al.*, 1995). Lu *et al.* (2007) added a “novel mechanistic profiling” of the previously reported sulfated polymannuroguluronate, a polysaccharide with an average molecular weight of 8.0 kDa isolated from the brown alga *L. japonica*, that has been reported to be in Phase II clinical trials in China as an anti-AIDS drug candidate (Mayer *et al.*, 2011). Fucoidan prevented concanavalin A-induced liver injury by mediating the endogenous interleukin (IL)-10 production and the inhibition of proinflammatory cytokine in mice (Saito *et al.*, 2006). The dietary fiber in edible brown seaweeds (*Laminaria* sp., *Sargassum fulvellum*, and *Eisenia bicyclis*) had the repressive effect against D-galactosamine (D-GalN)-induced hepatopathy, and the protective effect was caused at least in part by fucoidan (Kawano *et al.*, 2007a,b). Fucoidans from brown algae of Laminariales order have been also described as inhibitors of the complement (Zvyagintseva *et al.*, 2000).

Antitumor activity of many polysaccharides has been reported in recent years. Fucoidan from *L. japonica* is effective against sarcoma 180 (Song *et al.*, 2000). It can inhibit hepatoma QGY7703 cells into logarithmic phase *in vitro*, accordingly restraining the growth of tumor (Shi *et al.*, 2000). It can also restore the immune functions of immunosuppressed mice, and it acts as immunomodulator acting directly on macrophage and T lymphocyte (Wang *et al.*, 1994). It can also promote the recovery of immunologic function in irradiated rats through a mechanism associated with the arrest of lymphocyte apoptosis by fucoidan (Wu *et al.*, 2003, 2004). Japanese scientists found out that the lowest level of cancer in Japan was reported among population of Okinawa Island. They revealed

that Okinawa residents consume raw *Laminaria*, which contains great amount of fucoidan.

Lots of studies show that fucoidan presents significant antioxidant activity in experiments *in vitro*. It is an excellent natural antioxidant and has great potential for preventing free radical-mediated diseases. Fucoidan from *L. japonica* can prevent the increase of lipid peroxide in serum, liver, and spleen of diabetic mice obviously. However, no inhibition effect was found on both spontaneous lipid peroxidation of homogenates and that induced by Cys/FeSO₄ *in vitro* (Li *et al.*, 2002). This fucoidan had strong scavenging effect on superoxide radical, its effect on hydroxyl radical was weak, and it had less influence on 1,1-diphenyl-2-picryl-hydrazyl. It inhibited H₂O₂-induced hemolysis of rat erythrocytes effectively and showed significant protective effect on lipid peroxidation of liver homogenate in rat induced by FeSO₄-ascorbic acid (Zhang *et al.*, 2003).

Antioxidant activity relates to the molecular weight and sulfate content of fucoidan. Fucoidan fractions from *L. japonica* had excellent scavenging capacities on superoxide radical and hypochlorous acid, except the highly sulfated fraction L-B. In LDL oxidation system, low molecular weight fractions L-A and L-B exhibited great inhibitory effects on LDL oxidation induced by Cu²⁺; however, F-A and F-B had little inhibitory effects in this system due to their large molecular weights (Zhao *et al.*, 2005). Yoon *et al.* (2007) reported the purification of a complex and heterogeneous sulfated fucan from the brown alga *Laminaria cichorioides*. The purified polysaccharide had potent anticoagulant activity which is resulted from enhancement of thrombin inhibition by heparin cofactor II, within the same concentration range as the clinically used heparin (Yoon *et al.*, 2007).

Both molecular mass and sulfate content of fucoidan played very important roles in the effects on the azo radicals 2-2'-azobis (2-amidino-propane)dihydrochloride-induced LDL oxidation (Li *et al.*, 2006). The correlation between the sulfate content and scavenging superoxide radical ability was positive, the ratio of sulfate content/fucose was an effective indicator to antioxidant activity of the samples (Wang *et al.*, 2008).

Fucoidan is a kind of active material similar to sialic acid; it can enhance the negative charges of cell surface so as to effect the aggradation of cholesterol in blood, as a result of decreasing the cholesterol in serum. Fucoidan of *L. japonica* remarkably decreased total cholesterol, triglyceride, and LDL-C; increased HDL-C in serum of mice with hypercholesterolemia and rats with hyperlipidemia; and efficiently prevented the formation of experimental hypercholesterolemia in mice (Li *et al.*, 1999a,b, 2001). It can also remarkably reduce the contents of cholesterol and triglyceride in serum of patients with hyperlipidemia, without side effect of damaging liver and kidney (Wang and Bi, 1994). Low molecular weight sulfated fucan (average $M_w = 8000$ Da) prepared from *L. japonica* can distinctly reduce blood lipids of hyperlipidemic rats (Li *et al.*, 1999a,

b). Fucoidan oligosaccharides show good antihypertensive effects on renovascular hypertensive rats, and one of the mechanisms underlying the antihypertensive effects might be that they can inhibit the production of plasma angiotensin II (Fu *et al.*, 2004).

The elevated urinary protein excretion and plasma creatinine due to the induction of Heymann nephritis were significantly reduced by fucoidan from *L. japonica* by oral intubation. This indicated that fucoidan has a renoprotective effect on active Heymann nephritis and is a promising therapeutic agent for nephritis (Zhang *et al.*, 2005).

C. Laminarin

Another constituent has been found to assist with this process via a tumor angiogenesis blocking mechanism. Last but not least, *L. japonica* is great for the hair, skin, and nails, taken either internally or applied topically in masks and creams. Because of its high mineral content and polysaccharides, the seaweed helps by adding important nutrients to the skin, and by removing toxins. In its extract form, this seaweed can be easily incorporated into a range of skin care products to help give the skin a silky smoothness.

D. Cardiolam

Cardiolam is a commercial product made of *Laminaria* extract. It is a complex supplement for preventive health care with a profound therapeutic effect for those who are subjected to high blood pressure and various cardiovascular diseases. Besides, phytochemicals of this product ensure more efficient fat exchange by lowering cholesterol and sugar rates in the blood. It activates metabolic process in myocardium, improves feeding of cardiac muscle. A powerful antioxidant, it normalizes blood pressure, cholesterol, and blood sugar rates. It increases body resistibility to any physical and psychoemotional stresses (www.seabioresources.com).

VI. CONCLUDING REMARKS

As discussed in this chapter, kelps are indispensable species of deep oceans which forms the basis of an undersea ecosystem that provides food, shelter, and protection for a variety of marine organisms including plankton, sea urchins, mussels, fish, and sea otters. But owing to the danger caused to the *Laminaria* species because of environmental pollution and excessive harvesting for dietary intake, this species is under threat of extinction. Another factor effecting the growth and proliferation of *Laminaria* is global warming as it encroaches upon the cold water

habitat of the kelp. After understanding and unraveling the great bioactive potential of this medicinal kelp, we cannot afford to lose this species. The loss of *Laminaria* would be great loss to mankind. An analysis of the components of the algae showed that sea kelp is rich in vitamins and minerals, more than any other vegetable known by human (www.biol-ogy-online.org). Not only this, protecting this wonder kelp is further more important because of the economic potential and also because a kelp forest is one of the undersea wonders of the world. Quick measures such as that of diver quarantine have to be implemented, and efforts should be made for the proliferation of *Laminaria* sp. worldwide.

REFERENCES

- Billot, C., Rousvoal, S., Estoup, A., Epplen, J. T., Saumitou-Laprade, P., Valero, M., and Kloareg, B. (1998). Isolation and characterization of microsatellite markers in the nuclear genome of the brown alga *Laminaria digitata* (Phaeophyceae). *Mol. Ecol.* **7**, 1778–1780.
- Crepineau, F., Roscoe, T., Kaas, R., Kloareg, B., and Boyen, C. (2000). Characterisation of complementary DNAs from the expressed sequence tag analysis of life cycle stages of *Laminaria digitata* (Phaeophyceae). *Plant Mol. Biol.* **43**, 503–513.
- Fu, X. Y., Xue, C. H., Ning, Y., Li, Z. J., and Xu, J. C. (2004). Acute antihypertensive effects of fucoidan oligosaccharides prepared from *Laminaria japonica* on renovascular hypertensive rat. *J. Ocean Univ. Qingdao* **34**, 560–564.
- Kawano, N., Egashira, Y., and Sanada, H. (2007a). Effect of dietary fiber in edible seaweeds on the development of D-galactosamine-induced hepatopathy in rats. *J. Nutr. Sci. Vitaminol. (Tokyo)* **53**, 446–450.
- Kawano, N., Egashira, Y., and Sanada, H. (2007b). Effects of various kinds of edible seaweeds in diets on the development of D-galactosamine-induced hepatopathy in rats. *J. Nutr. Sci. Vitaminol. (Tokyo)* **53**, 315–323.
- Kitamura, K., Matsuo, M., and Yasui, T. (1991). Fucoidan from brown seaweed *Laminaria angustata* var. *longissima*. *Agric. Biol. Chem.* **55**, 615–616.
- Li, F., Tian, T. C., and Shi, Y. C. (1995). Study on anti virus effect of fucoidan *in vitro*. *J. N. Bethune Univ. Med. Sci.* **21**, 255–257.
- Li, D. Y., Xu, Z., and Zhang, S. H. (1999a). Prevention and cure of fucoidan of *L. japonica* on mice with hypercholesterolemia. *Food Sci.* **20**, 45–46.
- Li, Z. J., Xue, C. H., and Lin, H. (1999b). The hypolipidemic effects and antioxidative activity of sulfated fucan on the experimental hyperlipidemia in rats. *Acta Nutriment. Sin.* **21**, 280–283.
- Li, D. Y., Xu, Z., Huang, L. M., Wang, H. B., and Zhang, S. H. (2001). Effect of fucoidan of *L. japonica* on rats with hyperlipidaemia. *Food Sci.* **22**, 92–95.
- Li, D. Y., Xu, R. Y., Zhou, W. Z., Sheng, X. B., Yang, A. Y., and Cheng, J. L. (2002). Effects of fucoidan extracted from brown seaweed on lipid peroxidation in mice. *Acta Nutriment. Sin.* **24**, 389–392.
- Li, L. H., Xue, C. H., Xue, Y., Li, Z. J., and Fu, X. Y. (2006). The effects of fucoidans from *Laminaria japonica* on AAPH mediated oxidation of human low-density lipoprotein. *Acta Oceanol. Sin.* **25**, 124–130.
- Lu, C. X., Li, J., Sun, Y. X., Qi, X., Wang, Q. J., Xin, X. L., and Geng, M. Y. (2007). Sulfated polymannuroguluronate, a novel anti-AIDS drug candidate, inhibits HIV-1 Tat induced angiogenesis in Kaposi's sarcoma cells. *Biochem. Pharmacol.* **74**, 1330–1339.

- Mayer, A. M. S., Rodríguez, A. D., Berlinck, R. G. S., and Fusetani, N. (2011). Marine pharmacology in 2007–8: Marine compounds with antibacterial, anticoagulant, antifungal, anti-inflammatory, antimalarial, antiprotozoal, antituberculosis, and antiviral activities; affecting the immune and nervous system, and other miscellaneous mechanisms of action. *Comp. Biochem. Physiol. C Toxicol. Pharmacol.* **153**, 191–222.
- Saito, A., Yoneda, M., Yokohama, S., Okada, M., Haneda, M., and Nakamura, K. (2006). Fucoidan prevents concanavalin A-induced liver injury through induction of endogenous IL-10 in mice. *Hepatol. Res.* **35**, 190–198.
- Shi, Z. Y., Guo, Y. Z., and Wang, Z. (2000). Pharmacological activity of fucoidan from *Laminaria japonica*. *J. Shanghai Fish. Univ.* **9**, 268–271.
- Song, J. Q., Xu, Y. T., and Zhang, H. K. (2000). Immunomodulation action of sulfate polysaccharide of *Laminaria japonica* on peritoneal macrophages of mice. *Chin. J. Immunol.* **16**, 70.
- Wang, S. Z. and Bi, A. F. (1994). Clinic observation of fucoidan on patients with hyperlipidaemia. *Med. J. Qilu.* **16**, 173–174.
- Wang, W. T., Zhou, J. H., Xing, S. T., and Guan, H. S. (1994). Immunomodulating action of marine algae sulfated polysaccharides on normal and immunosuppressed mice. *Chin. J. Pharm. Toxicol.* **8**, 199–202.
- Wang, J., Zhang, Q., Zhang, Z., and Li, Z. (2008). Antioxidant activity of sulfated polysaccharide fractions extracted from *Laminaria japonica*. *Int. J. Biol. Macromol.* **42**, 127–132.
- Wu, X. W., Yang, M. L., Huang, X. L., Yan, J., and Luo, Q. (2003). Effect of fucoidan on splenic lymphocyte apoptosis induced by radiation. *Chin. J. Radiol. Med. Prot.* **23**, 430–432.
- Wu, X. W., Yang, M. L., Huang, X. L., Yan, J., and Luo, Q. (2004). Effect of *Laminaria japonica* polysaccharides on radioprotection and splenic lymphocyte apoptosis. *Med. J. Wuhan Univ.* **25**, 239–241.
- Yoon, H. S., Lee, J. Y., Boo, S. M., and Bhattacharya, D. (2001). Phylogeny of Alariaceae, Laminariaceae, and Lessoniaceae (Phaeophyceae) based on plastid-encoded RuBisCo spacer and nuclear-encoded ITS sequence comparisons. *Mol. Phylogenet. Evol.* **21**, 231–243.
- Yoon, S. J., Pyun, Y. R., Hwang, J. K., and Mourao, P. A. (2007). A sulfated fucan from the brown alga *Laminaria cichorioides* has mainly heparin cofactor II-dependent anticoagulant activity. *Carbohydr. Res.* **342**, 2326–2330.
- Zhang, Q. B., Yu, P. Z., Zhou, G. F., Li, Z. E., and Xu, Z. H. (2003). Studies on antioxidant activities of fucoidan from *Laminaria japonica*. *Chin. Tradit. Herb. Drugs* **34**, 824–826.
- Zhang, Q. B., Li, N., Zhao, T. T., Qi, H. M., Xu, Z. H., and Li, Z. E. (2005). Fucoidan inhibits the development of proteinuria in active Heymann nephritis. *Phytother. Res.* **19**, 50–53.
- Zhao, X., Xue, C. H., Cai, Y. P., Wang, D. F., and Fang, Y. (2005). The study of antioxidant activities of fucoidan from *Laminaria japonica*. *High Tech. Lett.* **11**, 91–94.
- Zvyagintseva, T., Shevshenko, N., Nazarova, I., Scobun, A., Luk'yanov, P., and Elyakova, L. (2000). Inhibition of complement activation by water-soluble polysaccharides of some far-eastern brown seaweeds. *Comp. Biochem. Phys. C* **126**, 209–215.