SB - 4

Effect of Seaweeds on the Prevention of Lifestyle-Related Diseases

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In Japan, the consumption of meat, fat, and dairy products is increasing while the intake of cereals rich in dietary fiber is gradually decreasing. As a result, disease patterns are changing, and cases of ischemic heart disease, arteriosclerosis, carcinoma of the colon and other lifestyle-related diseases are increasing. This paper summarizes some of the seaweeds and seaweed products that are known to have positive effects on reducing the risks from these types of diseases.

Antitumor activity: Surgical treatment, chemotherapy and radiotherapy are the three main treatments for tumors, but occasionally biological response modifiers (BRMs) are used in a hospital setting. Interferon is a well-known BRM in clinical use. Another BRM is mushroom polysaccharides. These are effective against solid type tumors, but ineffective against ascites tumors. It has been reported that some seaweeds, namely *Ulva pertusa, Enteromorpha prolifera, Codium fragile, Scytosiphon lomentaria, Eisenia bicyclis, Laminaria japonica, Hizikia fusiformis, Sargassum thunbergii, Porphyra yezoensis, Eucheuma denticulatum, E. amakusaensis,* and *E. gelatinae,* are effective against Ehrlich ascite carcinomas in mice by oral administration of 1600 mg seaweed powder / kg body wt /day for 28 days at an inhibition rate between 35 and 70%. Sulfated polysaccharides from *Monostroma nitidum,* sodium alginate, fucoidan, kappa-carageenan, porphyran, and funoran inhibited the growth of Ehrlich ascite carcinomas by oral administration of 50-200mg /kg/day for 28 days. The mechanism of antitumor activity of fucoidan from *S. thunbergii* is the activation of host-mediated immune mechanisms by an increase in activated macrophages, helper T cells, cytotoxic T cells, and NK cells.

Antihypertensive activity: Laminine, a basic amino acid, from *Laminaria,* and angiotensin-I- converting enzyme (ACE) inhibitory peptides from *P. yezoensis* and *H. fusiformis,* are well known antihypertensive substances. The amino acid sequences of the most effective peptides from *P. yezoensis* and *H. fusiformis* are Ala-Lys-Tyr-Ser-Tyr and Gly-Lys-Tyr, respectively. The mechanism of action of these

peptides is the inhibition of ACE. Polysaccharides from *M. nitidum* and *Sargussum*, porphyran from *P. yezoensis*, funoran from *Gloiopeltis tenax* also strongly stimulate antihypertension. The mechanisms of antihypertension are the increase in urine volume, excretion of Na+ and Cl- in the urine, and a decreased Na+/K+ ratio in serum.

Antihyperlipidemic activity: Among 26 species tested, more than half of the species showed some antihypercholesterolemic activities against forced hypercholesterolemia of rats. In particular, *Laminaria longissima, U. pinnatifida, Heterochordaria abietina,* and *P. yezoensis* elevated HDL levels and depressed LDL levels. Polysaccharides from *M. nitidum,* fucoidan, sodium alginate, porphyran, and funoran showed the strongest activity. These polysaccharides also elevated HDL levels and depressed LDL levels. Therefore, in both seaweeds and seaweed polysaccharides, the Atherogenic Index {(TC-HDL)/HDL}, the rise of which is closely related to arteriosclerosis, was depressed. The mechanism of antihyperlipidemia is assumed to disturb the absorption of cholesterol and/or bile acid in the intestine.

Inhibition of diabetic complications: Ten percent of the people in Japan over 40 years old have diabetes. Insulin-dependent diabetes mellitus is common in Western countries. However, non-insulin-dependent diabetes mellitus is common in Japan. Aldose reductase (AR) is a key enzyme of the polyol pathway that catalyzes the reduction of glucose to sorbitol. Accumulated sorbitol causes diabetic complications. The AR inhibitory activity of water-soluble fractions was very strong in *E. bicyclis* > *Sargassum ringordianum* > *Ishige okamurai* > *Sargassum tortile.* The effective substance in *E. bicyclis* is dieckol (phlorotannin), with an IC50 of 6.4 ug/ml.

Blood anticoagulative activity : Algal polysaccharides are known to act as blood anticoagulants. The aggregation of platelets plays an important role in blood coagulation, and the enhancement of platelet aggregation accelerates the formation of thrombi, resulting in cerebral and myocardial infarctions and other diseases. Fucoidan is the most well known active substance. When a mixture of four edible seaweeds (*E. bicyclis, H. fusiformis, U. pinnatifida* and *P. yezoensis* (45:30:20:5 w/w)) was analyzed for platelet aggregation induced by ADP or collagen, the maximum aggregation was lowered to 89.0% and 85.5% of the control, respectively. D-cysteinolic acid, a sulfur-containing free amino acid, is known to inhibit platelet aggregation in rats. This amino acid is contained mainly in *Ulva, Monostroma,* and *Enteromorpha.* For the production of this amino acid, cultivation of sterile mutant of *Ulva* in deep-sea

water is the most effective.

Blood fluidity: To assess the usefulness of edible seaweeds for the prevention of cardiovascular disease, *Porphyra* and *Undaria* were examined for the improvement of deformability of erythrocytes. Rats were fed with a fat- and cholesterol-rich diet (control) or the control diet plus 10% *Porphyra* or *Undaria* powder for 30 days. In rats fed with *Porphyra*, deformability of erythrocytes improved approximately 11% compared to that of the control. Among n-3 and n-6 polyunsaturated fatty acids, which affected the deformability of erythrocytes, arachidonic acid content in erythrocyte membranes decreased ($p < 0.05$), while that of EPA increased 2.6-fold ($p < 0.01$) compared to the control. In rats fed with *Undaria*, the deformability of erythrocytes did not change significantly ($p > 0.05$). The arachidonic acid content increased significantly ($p < 0.05$), but that of EPA did not ($p > 0.05$). These results indicate that *Porphyra* is a promising alga for preventing cardiovascular diseases.