

Marine Source Nutraceuticals

New Wave of Health from the Sea

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Sea vegetables offer untapped plethora of health benefits.

Much attention has been focused of late on the Asian diet, which appears to contain a wealth of protective health-promoting compounds. An examination of the Asian diet reveals that it is rich in sea vegetables. It should come as no surprise, therefore, that the long recognized traditional health benefits of certain sea vegetables are now being confirmed by modern scientific research.

Seaweed has long been used in the Japanese and Chinese diet. In 600 B.C., Sze Teu wrote in China, "Some algae are a delicacy fit for the most honored guests, even for the King himself." Some 21 species are used in everyday cooking in Japan, six of them since the eighth century. Seaweed accounts for some 10% of the Japanese diet and seaweed consumption reached an average of 3.5 kg per household in 1973, a 20% increase in 10 years. Most important are nori (*Porphyra* species), kombu (*Laminaria* spp.) and wakame (*Undaria* spp.).

In the West, seaweed is largely regarded as a health food and, although there has been an upsurge of interest in the last 20 years, it is unlikely that sea vegetable consumption will ever be more than a fraction of what it is in Japan. Among U.S. suppliers, all sea vegetables are known under a very general name "Pacific" and/or "Atlantic" kelp, which represents in most cases a "cocktail" of a dozen plant species harvested in the open ocean.

The focus of scientific inquiry has been directed at a sub-group of sea vegetables known as phaeophytes (brown seaweed). Powerful antioxidant activity was recently discovered in certain members of this class and this finding has resulted in an enormous increase in research on sea vegetables' metabolites and their activity against free radicals. The fruits of this research have shown that certain phaeophytes contain highly active polyphenols called phloroglucinols (1,3,5-trihydroxybenzene) that possess free radicals neutralizing activity.

Recently Japanese scientists discovered that phenolic compounds such as phloroglucinols possess 5-lipoxygenase activity. The products of arachidonic acid metabolism are not tumor promoters themselves, but play an integral part in the underlying mechanism of tumor promotion and 5-lipoxygenase is a key enzyme in the arachidonic cascade. Phytoactives present in brown sea vegetables possess antibacterial activity and

phloroglucinol is responsible for this effect. In addition phloroglucinols are moderate MAO inhibitors. This fact could contribute to their strong anti-depressant activity.

Sea Vegetables and Cholesterol

The Japanese have believed for many years that eating seaweed prolongs life. Since many deaths are due to heart disease, which may be linked with high plasma cholesterol levels and hypertension, the effect of seaweed on these physiological values have been investigated. Again, sea vegetables such as *Ascophyllum*, (*Cystoseira* and *Fucus* have been shown to lower significantly plasma cholesterol levels (Krotkiewski M., European Patent #90850263.6) and the active compounds have been identified: Fucosterol and the unsaturated fatty acids show hypocholesterolemic activity. This ability to reduce plasma cholesterol levels and to increase serum lipolytic activity may explain their use in the prevention of atherosclerosis. An antihypertensive activity of substances with sodium-binding properties, e.g. a polysaccharide, is obtained from brown seaweed fibers.

Sea Vegetables and Cancer

Certain sea vegetables have long been used in traditional Japanese and Chinese medicine in the treatment of cancer. Oxidative processes are involved in both the initiation of carcinogenesis and the promotion of tumor development (Pryor, 1987). Research of recent years provides strong evidence that the sea vegetables *Ascophyllum*, *Cystoseira* and *Fucus* showed antitumoral activity (IC₅₀mg/mL) against leukemia P-388 (Norte et al. 1995).

Based on epidemiological and biological data, consumption of sea vegetables are proposed as an important factor contributing to the relatively low breast cancer rates reported in Japan. It is well known that sea vegetables are the best source of nondigestible fiber, increasing fecal bulk and decreasing bowel transit time; it changes the posthepatic metabolism of sterols; it contains an antibiotic substance that may influence fecal ecology; it contains 1-3 beta glucan, which alters enzymatic activity of fecal flora and it stimulates the host-mediated immune response.

It is suggested that Laminaria may play a role in preventing either the initiation of breast cancer or its promotion by endogenous physiological factors. Among mammary adenocarcinoma tumor-bearing animals, experimental rats had fewer individual adenocarcinomas. There was also an overall 13% reduction in the number of experimental rats with histologically confirmed adenocarcinomas (76% among the control rats compared to 63% among the experimental rats). Components of Laminaria, which might account for the observed difference in mammary tumor growth are varied and include the sulfated polysaccharide Fucans or fucoidan.

Fucans, sulfated polysaccharides extracted from brown seaweed, have been shown to have inhibitory effects on cell growth in various experimental models. These findings raise the possibility that brown seaweed may, have clinical value in the prevention of cancer metastasis.

Sea vegetables commonly eaten in Japan inhibit breast carcinogenesis. Anti-mutagenic activities were detected in polysaccharide and non-polysaccharide fractions from the extract of the other edible brown alga, *Undaria pinnatifida* (wakame in Japanese). These experimental results indicate that the hot water-soluble extract of *Laminaria japonica* or *Undaria pinnatifida* contains heterogenous antimutagenic activities against typical genotoxic substances.

The role of seaweed in breast cancer treatment was indirectly implicated at the inception of the low thyroid breast cancer hypothesis. Ancient Egyptians gave seaweed to breast cancer patients (Ebers Papyrus) and suggested that the iodine content in the seaweed was responsible for stimulating the thyroid. This hypothesis has generated many studies over the last 25 years, although none were able to establish a causal link between thyroid dysfunction and subsequent breast cancer. It has been observed that women with breast cancer who also have thyroid dysfunction have a poorer prognosis for both five and ten year survival. The most convincing data arguing against this theory is that as a result of iodized salt, endemic goiter rates have declined in the U.S., while breast cancer mortality rates have not. It is therefore intriguing to consider the alternative explanation -that it was the seaweed rather than the iodine content that lent efficacy to the Egyptian treatment. The existing data are supportive of the idea that sea vegetable consumption as well as terrestrial vegetables might be a protective factor.

Sea Vegetables and HIV

Anti-HIV-active and anti-herpes polysaccharides and polyphenols have been isolated in brown seaweed *Fucus vesiculosus* and red alga *Dumontia*. What about green sea vegetables such as *Ulva rigida* or sea lettuce, an edible alga containing the extraordinary potencies of soluble and insoluble dietary fiber and important minerals, as well as high potencies of vitamins, polysaccharides, chlorophyll and protein? *Ulva rigida* is a member of the group of green seaweeds *Monostroma* and *Enteromorpha*, which are called "annori" in Japanese.

Ulva has been used in salad and soups for many centuries; however, the recent discovery that xylofuranoglucuronan (Ulvan) and glucuronic acid are major constituents of *Ulva* dramatically increased interest in this seaweed. Glucuronic acid is a strategically important component of chondroitin (viscosity mucopolysaccharides that act as the flexible connecting matrix between collagen filaments in cartilage to form a polymeric system). To be able to synthesize enough chondroitin, the human body needs glucuronic acid and glucosamine. The lack of one of these components dramatically decreases the chondroitin synthesis.

Russian scientists provided strong evidence that the rate of C14 chondroitin sulfate synthesis de novo is much higher from I 4C glucuronic acid (*Ulva*) than from C14 chondroitin (Sidorov et al. 1977; *Applied Microbiology and Biotechnology*). We believe that chondroitin is hydrolyzed before it becomes bio-available in the body and that the rate of this hydrolysis not so high as to compete with free glucuronic acid (Sidorov et al. 1977). These results are not surprising, since glucuronic acid is an essential constituent of chondroitin. Beside glucuronic acid, *Ulva rigida* contains high proline and ascorbic acid required for collagen synthesis.

In the process of collagen synthesis two amino acids, proline and hydroxyproline, play a strategically important role. Collagen synthesis is initiated by hydroxylation of proline, which requires the presence of a sufficient amount of proline and ascorbic acid - a source of OH-groups needed to transform proline into hydroxyproline. *Ulva rigida* provides both proline and ascorbic acid.

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