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POTENTIAL HEALTH EFFECTS OF GREEN RIVER ALGAE (AONORI) OF THE LPP COMPLEX, WITH A REFERENCE TO ULVA PROLIFERA

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ABSTRACT

Marine resources have been attracting the attention of researchers as they provide healthy foods and may provide new drugs. Of more than a hundred Ulva (Enteromorpha) species found in the world, three (known as LPP complex) have been identified in Japan, where they are used as food: Ulva linza, Ulva clathrata (procera) and Ulva prolifera. This review paper reports on main compounds found in those green river algae (Aonori in Japanese) and highlights their potential prophylactic and therapeutic health effects. Scientific papers and reports on Ulva marine algae, their bioactive compounds and properties were collected using major scientific databases. Ulva species contain mainly ulvans (sulfated polysaccharides), phenolic compounds and flavonoids whose amount depends on species and the locations. In addition, terpenes and carotenoids have also been found in extracts from Ulva prolifera. A number of experimental studies have shown that extracts and ulvans from Ulva species have antioxidant, anti-inflammatory, anticoagulant, anticancer, antiviral effects. In particular, Ulva proliferaMüller, also known as 'Shimanto-nori' in Japan, exerts LDL-cholesterol lowering activity and increases adiponectin production. These health effects suggest that, apart from their nutritional value, Ulva bio materials may serve as source of natural prophylactic and therapeutic agents for cardiovascular and metabolic disorders. Further research is needed to confirm their beneficial health effects in humans.

KEYWORDS: Cardiometabolic Risks, LPP Complex, Ulva Prolifera, Ulva Linza, Ulva Clathrata (Varprocera)

INTRODUCTION

Recently, marine resources have been attracting attention in regard to the search for healthy foods and bioactive natural materials that may serve in the development of new drugs[1-3]. Considering the rapidly growing human population on the planet earth and the increasing demand of foods, marine environment could play an important role in solving problems related to shortage of nutritional resources.

Nowadays, marine algae have been marketed worldwide as constituents of dietary supplements due to their antimutagenic, anticoagulant, and antitumor properties as well as their high content of dietary fiber[4,5]. In Japan, marine algae (known as 'nori') have been extensively used as food since emperor Daigo's era in the first millennium (897-930)[6, 7]. Currently, tons of alga-based food products are manufactured and even exported annually, and Japan is known as one of the countries where the dietary intake of algal products is common. The first report on river Ulva species growing in Japan came from Nakura (1921)[6], based on alga collected in Aichi prefecture. Some decades later, Shimada and colleagues[6] conducted the first study that provided the genetic differences between Ulva species found in Japan. Of the 130 or more

Ulva species found in the world, currently three species, known as the LPP complex, have already been identified in Japan: Ulva linza, Ulva clathrata (varprocera) and Ulva prolifera. U. prolifera can be found in rivers located in Shizuoka, Okayama, Tokushima, Ehime and Kochi prefecture, although the distribution of U. Linza and U. clathrata (var procera)in the country is not yet well-known[6]. According to the work of Hayden and colleagues, Enteromorpha and Ulva represent the same genera and both terms are used[8].

Ulva proliferaMüller, 'Shimanto-nori' in Japanese, is an edible green alga that grows from the estuary to 7 km upstream[6] (Aosanori) and elsewhere (Aonori) in the Shimanto-river, Kochi prefecture (**Figure 1**).

Figure 1: Ulva (Enteromorpha) Prolifera, Shimanto-Nori, Being Harvested in Shimanto-River (A) and Dried (B) for its Commercialization in Kochi Prefecture, Japan (With the Courtesy of M. Kadota & U. Makoto)

It is said that water from the Shimanto River is one of the cleanest in Japan; thus, food resources from this river are regarded as of great value. Ulva prolifera Müller can also be found in some northern European countries such as Denmark[9]. However, the first report on Ulva species from Japan came from Nakurain the year 1921, based on alga collected in the prefecture of Aichi. Ulva clathratahas been previously considered as synonymous to U. linza[10], and the first scientific report to provide genetic differences between Ulva species that grow in river in Japan came from the work of Shimada and colleagues[6].

CHEMICAL COMPOUNDS

Seaweeds in general, and in particular green river algae, contain a number of bioactive compounds that are currently subject to research due to their potential therapeutic use. Ulva species contain sulfated polysaccharides, ulvans, which resemble glycosaminoglycans and are soluble polysaccharides from the cell walls of these green algae; they are composed of repeating disaccharides with sulfated rhamnose and uronic acid[4]. Apart from ulvans, U. prolifera, U. linza and U. clathrata also contain other chemical compounds such as proteins, vitamins, minerals and polyphenols, including flavonoids[11-14]. In addition, terpenes and carotenoids have also been found in extracts of Ulva prolifera[15, 16]; however, though those chemical compounds may also be present in U. linza and U. clathrata. A number of bioactive compounds that are responsible of Ulva's health effects have been detected in algal biomaterials; however, their precise amounts in each of the above mentioned alga species are to be determined. That is one of the objectives of our ongoing research.

MEDICINAL PROPERTIES OF ULVA SPECIES OF THE LPP COMPLEX

Algal sulfated polysaccharides such as fucans, sacrans from Aphanothece sacrum and ulvans from Ulva species

exert antioxidant, anti-inflammatory, antiviral and immunostimulatory effects[14,17-20]. Moreover, ulvans from U. prolifera reduce a-amylase production, reduce LDL-cholesterol level and increase adiponectin production in experimental studies[21, 22] (**Table 1).** Through the reduction of alpha-amylase production, a decrease of the amount of food-contained sugar uptake by the body may occur, given that some sugars will not be divided into lighter sugar chains (disaccharides).

Obesity is strongly associated with metabolic and cardiovascular diseases. Previous studies found that low levels of adiponectin are associated conditions ischemic heart diseases, atherosclerosis, and peripheral artery disease[23-25]. Thus, adiponectin plays an important role in protecting cardiovascular tissues during stress, inhibiting pro-inflammatory and hypertrophic responses as well as the stimulation of endothelial cell thanks to its modulatory effects on signaling molecules such as AMP-activated protein kinase[23, 26]. Moreover, higher adiponectin levels are also associated with lower risk of type-2 diabetes[27, 28].

On the other hand, the reduction of triglycerides (TG) and LDL-cholesterol intestinal uptake or adsorption by ulvans from U. prolifera might justify the increase in HDL-cholesterol levels[22, 29]. This bioactive activity is to be investigated to determine ulvan's preferential effect on lighter fat, as it provides new biotechnology perspectives in the field of nutrition and health.

Table 1: Bioactive Compounds and Health Effects of Ulva Species of LPP Complex

Main Bioactive Compounds & Medicinal Properties	LPP Complex (Ulva Species) Ulva Prolifera	Ulva Linza	Ulva Clathrata (Procera)
Main Bioactive Compounds			
• Ulvans	yes	yes	yes
• Phenolic compounds	yes	yes	yes
• Flavonoids	yes	yes	yes
• Terpenoids	yes	yes	yes
• Carotenoids	yes	NI	NI
Main Medicinal Properties			
• Reduction of alpha-amylase	yes	NI	NI
• Increase of adiponectin production	yes	NI	NI
• Reduction of LDL-cholesterol and increase of HDL-Cholesterol	yes	NI	NI
• Immunity improvement	yes	NI	NI
• Antioxidant/anti-inflammatory	yes	yes	yes
• Anticoagulant activity	NI	yes	yes
• Anticancer activity	NI	yes	NI
• Antiviral activity	yes	NI	yes

***Footnotes**: NI, No Information; LPP, Linza, Prolifera, Procera.

Considering U. linza, it is reported to have anticancer and anticoagulant properties, whereas U. clathrata procera has demonstrated both antiviral and anticoagulant activities in experimental studies[11,22,30].

The Japanese dietary pattern, in general, has been reported to be associated with high serum adiponectin levels[31]. Considering the LDL-cholesterol lowering effect and the up regulation of adiponectin production by Ulvabio materials, they possess a potential to reduce cardiovascular and metabolic risks. Thus, dietary intake of specific food that have the above bioactive properties in combination with the reduction dietary and lifestyle related cardiovascular and metabolic risk factors would contribute to promoting a healthy life.

Alga-based food products and biomaterials are currently attracting the attention of both researchers and food

manufacturers. Findings from a recent work by Geamanu and colleagues[32] on a novel alga-based product suggest that algae may serve as a good source of dietary supplements, as they promote a well-balanced lipid profile. Marine green algae-derived sulfated polysaccharides or ulvans possess a great potential for the development of novel healthy food products and preventive and therapeutic agents[33-36]. Such health benefits will possibly contribute to improving lives, and possibly people's income, in countries where green algal biomaterials are available but their importance is ignored, especially in the developing world. For example, the antioxidant, anti-inflammatory, antiviral and anticancer potentials of ulvans[37-40]indicate that they are promising natural sources. Currently, we have launched an ongoing research aimed at determining the amounts of active molecules and confirm local LPP algal species' beneficial health effects in humans. Findings will culminate in new transitional researches would possibly put up additional value to marine green algae growing in Japan as they might lead to new dietary, pharmacological and biotechnological applications, especially in regard to the management of lifestyle and diet related disorders.

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CONFLICT OF INTEREST STATEMENT

None declared

REFERENCES

1. BelHadj S, Hentati O, Elfeki A, Hamden K. Inhibitory activities of Ulva lactuca polysaccharides on digestive enzymes related to diabetes and obesity. Arch PhysiolBiochem,2013; 119 (2): 81-87.
2. Huimin QI, Zhang QB, Zhao T, Chen R, Zhang H, Niu X, Li ZE. Antioxidant activity of different sulfate content derivatives of polysaccharide extracted from Ulva pertusa (Chlorophyta) in vitro. Int J BiolMacromol, 2005; 37(4): 195-199.
3. Sun HH, Mao WJ, Jiao JY et al., Structural characterization of extracellular polysaccharides produced by the marine fungus Epicoccumnigrum JJY-40 and their antioxidant activities. Mar Biotechnol, 2011; 13: 1048-55.
4. FedorovS, Svetlana P, Ermakova SP, Zvyagintseva TN. Stonik VA. Anticancer and cancer preventive properties of marine polysaccharides: Some results and prospects. Mar Drugs,2013;11: 4876-4901.
5. LahayeM.,Robic, A. Structure and functional properties of ulvan, a polysaccharide from green seaweeds. Biomacromolecules, 2007;8: 1765–1774.
6. Shimada S, Yokoyama N, Arai S, Hiraoka M. Phylogeography of the genus Ulva(Ulvophyceae, Chlorophyta), with special reference to the Japanese freshwater and brackish taxa. J ApplPhycol, 2008; 20: 979–89.
7. Miyashita A. The seaweed: the cultural history of material and human being. University of Hosie Press, Tokyo (in Japanese); 1974.
8. Hayden HS, Blomster J, Maggs CA, Silva PC, Stanhope MJ, Waaland JR. Linnaeus was light all along: Ulva and

Enteromorpha are not distinct genera. Eur J Phycol, 2003; 38:277–294.

9. Müller OF. Iconesplantarum; Florae danicae, vol. 5, fasc 13. Copenhagen; 1778.
10. World Register of Marine Species (WoRMS). Ulva linza. Available at: http://www.marinespecies.org/aphia. php?p=taxdetails&id=234474 (Accessed 08/05/2015).
11. Aguilar-Briseno JA, Cruz-Suarez LE, Sassi JF, Ricque-Marie D, Zapata-Benavides P et al. Sulphated Polysaccharides from Ulva clathrata and cladosiphonokamuranusseaweeds both inhibit viral attachment/entry and cell-cell fusion, in NDV infection. Mar Drugs 2015; 13(2): 697–712.
12. Cho ML, Yang C, Kim SM, You SG et al. Molecular characterization and biological activities of water soluble sulfated polysaccharides from Enteromorphaprolifera.J MolecBiotechnol,2010; 19(2): 522-533.
13. Qi X, Mao W, Chen Y, Chen, Y, Zhao C, Li N, Wang C. Chemical characteristics and anticoagulant activities of two sulfated polysaccharides from Enteromorphalinza (Chlorophyta). J Ocean Univ China,2013; 12: 175–182.
14. Farasat M, Khavari-Nejad RA, Nabavi SMB, Namjooyan F. Antioxidant activity, total phenolics and flavonoids contents of some edible green seaweeds from Northern coasts of the Persiangulf. Iran J Pharm Res, 2014; 13(1): 163–170.
15. Yamamoto M, Baldermann S, Yoshikawa K, Fujita A, Mase N, Watanabe N. Determination of volatile compounds in four commercial samples of Japanese green alage using solid phase microextraction gas chromatography mass spectrometry. The Scientific World Journal 2014; Available at: http://dx.doi.org/10.1155/2014/289780.
16. Alghazeer R, Whida F, Abduelrhaman E, Gammoudi F, Azwai S. Screening of anti-bacterial activity in marine green, red and brown macroalgaefrom the western coast of Libya. Natural Science, 2013; 5: 7-14.
17. Lee JC, Hou MF, Huang HW, Chang FR, Yeh CC, Tang JY et al.Marine algal natural pro- ducts with anti-oxidative, anti-inflammatory and anti-cancer properties. Cancer Cell Int 2013; 13: 55.
18. Ngatu NR, Okajima MK, Yokogawa M, Hirota R, Eitoku M et al. Anti-inflammatory effects of topical sacran, a novel polysaccharide from Aphanothece sacrum, on 2,4,6-trinitrochloro- benzene-induced allergic dermatitis in vivo.Ann Allergy AsthmImmunol,2012; 108(2): 117-122.e2
19. Kim JK, Cho ML,Karnjanapratum S, Shin IS, You SG.In vitro and in vivoimmuno- modulatory activity of sulfated polysaccharides fromEnteromorphaprolifera. Int J BiolMacromol,2011;49: 1051–1058.
20. Wei J, Wang S, Liu G, Pei D, Liu Y, Liu Y, Di D. Polysaccharides from Enteromorphaprolifera enhance the immunity of normal mice. Int J BiolMacromol, 2014; 64: 1-5.
21. Tang Z, Gao H, Wang S, Wen S, Qi S. Hypolipidemic and antioxidant properties of a polysaccharide fraction from Enteromorphaprolifera. Int J BiolMacromol, 2013; 58: 186-189.
22. Teng Z, Qian L, Zhou Y. Hypolipidemic activity of the polysaccharides from Enteromorphaprolifera. Int J BiolMacromol,2013, 62, 254–256.
23. Shibata R, Ouchi N, Murohara T. Adiponectin and cardiovascular disease.Circ J, 2009; 73: 608-614.
24. Okamoto Y, Kihara S, Ouchi N, Nishida M, Kumada M et al. Adiponectin reduces atherosclerosis in

apolipoprotein E-deficient mice. Circulation, 2002; 106: 2767-2770.

25. Komai H, Shibata R, Juri M, Matsushita K, Ouchi N, Murohara T. Plasma adiponectin as a protective factor of survival after a bypass operation for peripheral arterial disease. J VascSurg,2009; 50 (1): 95–99.
26. Shibata R, Ouchi N, Kihara S, Sato K, Funahashi T., Walsh K. Adiponectin stimulates angiogenesis in response to tissue ischemia through stimulation of amp-activated protein kinase signaling. J BiolChem, 2004; 279: 28670-28674.
27. Yamamoto S, Matsushita Y, Nakagawa T, Hayashi T, Noda M, Mizoue T. Circulating adiponectin levels and risk of type 2 diabetes in the Japanese. Nutrition & Diabetes, 2014; **4**, e130
28. Li S, Joon H, Ding EL, van Dam RM. Adiponectin levels and risk of type 2 diabetes: a systematic review and meta-analysis. JAMA,2009; 302(2):179-188.
29. Wang X, Zhang Z, Yao Z, Zhao M, Qi H. Sulfation, anticoagulant and antioxidant activities of polysaccharide from green algae Enteromorphalinza. Int J BiolMacromol,2013;58: 225–230.
30. Zhang Z, Wang X, Yu S, Yin L, Zhao M, Han Z. Synthesized oversulfated and acetylated derivatives of polysaccharide extracted from Enteromorphalinza and their potential antioxidant activity. Int JBiol Macromol,2011;49: 1012–1015.
31. Guo H, Niu K, Monma H, Kobayashi Y, Guan L, Sato M, Minamishima D, Nagatomi R. Association of Japanese dietary pattern with serum adiponectin concentration in Japanese adult men. NutrMetabCardiovasc Dis, 2012; 22(3): 277-84.
32. Geamanu A, Goja A, Saadat N, Khosla P, Gupta SV. ProAlgazymesubfraction improves the lipoprotein profile of hypercholesterolemic hamsters, while inhibiting production of betaine, carnitine and choline metabolites. Nutrition & Metabolism, 2013; 10:55.
33. Devi GK, Manivannan K, Thirumaran G, Rajathi FAA, Anantharaman P. In vitro antioxidant activities of selected seaweeds from southeast coast i\of India. Asian Pacific J trop Med 2011; 4: 205-2011.
34. Domozych DS, Kiemle SN, Domozych CR, Sorensen I, Willats WG, Gretz MR. Differential occurrence of land plant extracellular polysaccharides in the charophycean green algae and implications for plant evolution. J Phycol 2007; 43: 27-28.
35. Qi X, Mao W, Gao Y, Chen Y, Chen Y, Zhao C, Li N, Wang C, Yan M, Lin C, et al. Chemical characteristic of an anticoagulant-active sulfated polysaccharide from Enteromorphaclathrata. CarbohydrPolym 2012;90: 1804-1810.
36. Jiao L, Jiang P, Zhang L, Wu M. Antitumor and immunomodulating activity of polysaccharides from Enteromorphaintestinalis. BiotechnolBioproEng2010;15: 421–428.
37. Wang L, Wang X, Wu H, Liu R. Overview on biological activities and molecular characteristics of sulfated polysaccharides from marine green algae in recent years. Mar Drugs 2014; 12(9): 4984–5020.
38. De Jesus Raposo MF, Bernardo de Morais AM, Costa de Morais RMS. Marine polysaccharides from algae with

potential biomedical applications. Mar Drugs 2015; 13(5): 2967-3028.

39. Smitt AJ. Medicinal and pharmaceutical uses of seaweed natural products: a review. J ApplPhycol 2004; 16: 245-262.
40. Wijesekara I, Pangestuti R, Kim SK. Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. CarbohydrPolym2011; 84: 14-21.
41. Senni K, Pereira J,Gueniche F, Delbarre-Ladrat C, Sinquin C, Ratiskol J, Godeau G, Fisher AM, Helley D, Colliec-Jouault S. Marine polysaccharides: A source of bioac- tive molecules for cell therapy and tissue engineering. Mar Drugs2011; 9:1664 - 1681.