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Study on Antihypertensive and Antihyperlipidemic Effects of Marine Algae

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A total of 26 species of seaweeds (1 green, 21 brown, and 4 red algae) and 6 polysaccharides were screened for their antihypertensive and antihyperlipidemic activities using rats in order to evaluate their potential application for the prevention of cardiovascular diseases. Although diets containing some pulverized seaweeds moderately elevated total cholesterol (TC), free cholesterol (FC), and low density lipoprotein (LDL), marked antihypertensive and antihypercholesterolemic activities were found in almost all seaweeds, some of which are commonly used as food. In addition, serum levels of high density lipoprotein (HDL) were enhanced 46.0% by seaweed powder diets. Six polysaccharides derived from active 'seaweed species were investigated, and appreciable suppression of hypertension and hypercholesterolemia was observed for all samples. They also markedly enhanced the serum level of HDL.

Key words: marine algae, polysaccharides, antihypertension, antihypercholesterolemia

Japanese edible seaweeds have proved to be antihypertensive in humans.[1] In 1960, Kameda[1] for the first time demonstrated that a brown alga *Laminaria* sp. was helpful in controlling human hypertension, and that the active substance was soluble in water but insoluble in diethyl ether. The same author[2] successively found that the water soluble fraction lowers the blood pressure of rabbits, and induces hypocholesterolemia in the animal. Takemoto *et al.*[3] isolated laminine, a basic amino acid, from *Laminaria angustata*, and Ozawa *et al.*[4] fround that its oxalate exhibits a weak hypotensive activity in rabbits anesthetized with urethane administrated intravenously. Kaneda *et al.*[5–8] reported the presence of several kinds of betaine in *Monstroma*. Among these, β-homobetaine can significantly decrease the artificially enhanced plasma level of cholesterol in rats. Subsequently, various investigations have reported that the seaweeds or the polysaccharides[9–14] isolated from them exhibit antihypertensive and or antihypercholesterolemic activities.

This paper deals with an evaluation of the effect of seaweeds and algal polysaccharides on the blood pressure and serum lipid level in rats fed with saline solution and cholesterol-rich diet.

Materials and Methods

Animals

Four-week-old female Wistar strain rats (Shizuoka Laboratory Animal Center, Hamamatsu) were used after being allowed to acclimate to laboratory conditions for 7 days.

Materials

Most of the 26 algae used were collected from the coast of Mie Prefecture, Japan. Some of them were obtained from seaweed retailers. After washing them with demineralized wateer, air-dried algae were powdered to 0.2 mm diameter by using a Retsch ultracentrifugal mill ZM-1.

Preparation of Polysaccharides

The polysaccharides used in the present study are listed in Table 1. Shilfated glucuronoxylorhamnan was extracted from *Monostroma nitidum.*[15] Porphyran was prepared from *Porphyra yezoensis*,[16] funoran from *Gloiopeltis tenax*,[17] fucoidan from *Sargassum ringgoldianum.*[18] and sodium alginate from *Analipus japonicus.*[19] Agar was a commercial product of Wako Pure Chemical Industries Ltd.

Determination of Blood Pressure

The animals were maintained in an environment of 37°C for 10–15 min. Systolic blood pressure (SBP) was measured indirectly in different groups of rats by the indirect tail-cuff method using a BP recorder, model MK-1000 (Muromachi Machine Co., Ltd., Tokyo).

Determination of Serum Lipid Levels

Total cholesterol (TC) levels in serum were assayed by the enzymatic method,[20,21] using NesuKouto TC kit-K (Nippon Shoji Ltd., Osaka), whereas free cholesterol (FC) levels were determined by the same method, using NesuKouto FC kit-K. Trigliceride (TG) levels were measured by the same method, using NesuKouto TG kit-K. High-density-lipoprotein cholesterol (HDL) levels were measured by using NesuKouto HDL kit-K, and low-density-lipoprotein cholesterol (LDL) was estimated from the following equation: LDL = TC-HDL. The antherogenic index (AI) was referred to as (TC-HDL)/HDL.

Statistical Analysis

Data were expressed as means $\pm$SE, and statistical analysis was performed with Student's t-test for unpaired groups. $p<0.05$ was considered of statistical significance.

Table 1. Composition of diets (%)

Basal diets		Test substances	
CE-2	38.0	Seaweeds powder	5.0
Flour	10.0	Sulfated glucuronoxylorhamman	0.5
Casein	9.0	Fucoidan	1.0
Olive oil	16.0	Sodium alginate	1.0
Sucrose	25.0	Porphyran	1.0
Bile salts	0.5	Funoran	2.5
Cholesterol	1.5	Agar	2.5

Animal Experiment

Wistar rats of 5 weeks were used in the experiments. The animals were held in a temperature-(24 ± 2°C) and humidity-controlled (50 ± 10%) room. The rats were divided at random into groups of eight animals each. The control group was fed with 1.5% saline solution and synthetic diet (Table 1), and test groups were fed with 1.5% saline solution, synthetic diet, and seaweed powder or polysaccharide. SBP in the tail artery was measured by the indirect tail cuff method every 4 days.

At the end of feeding, they were starved for 12–14 hours prior to collection of blood from the heart. Serum lipid was determined as mentioned above.

Results

Antihypertensive Effect of Seaweed Powder and Their Polysaccharides

The animals were tested during a feeding period of 28 days. The body weight gain of 15 of the 26 test groups (58.0%) was slightly higher than those of the control at the end of the experiment (Table 2). During the experiment, there was no significant difference in the intake of food between the groups fed with seaweed powder and the control group.

As shown in Table 2, SBP of the control group was markedly higher than that of test groups throughout the feeding period. The decrease was particularly remarkable in the SBP of test groups fed with *L. ochotensis*, *G. tenax*, and *P. yezoensis* powder, and this trend was more evident from the 8th day of feeding ($p < 0.05$). On day 28, their SBP decreased to 88.0, 89.0, and 90.0% of the control group, respectively.

The rats fed with an algal polysaccharide-containing diet were examined for changes in their SBP every 4 days during the feeding experiments. The body weight gain of all test groups was slightly higher than that of the control at the end of the experiment (Table 3). During the experiment, there was no significant difference in the intake of food between the group treated with algal polysaccharides and the control group.

As shown in Table 3, the SBP of the groups fed with funoran, fucoidan, alginate, and porphyran were markedly lower than that of the control group, and the SBP of test groups on the 8th day of feeding were significantly lower ($p < 0.01$) than that of the control group. On the last day of feeding, their respective decreases in SBP were equivalent to 79.0, 84.0, 85.0, and 92.0% of the control group, respectively. Other polysaccharides showed no recognizable influence on the SBP.

Hypocholesterolemic Effect of Seaweed Powder and Their Polysaccharides

TC serum levels of the test groups (*M. nitidum*, *P. yezoensis*, *G. tenax*, *H. abietina*, *S. micracanthum*, *S. patens*, and *C. sisymbrioides*) were significantly lower than that of the control group as shown in Table 4. The other seaweeds caused no noticeable depression of the TC level as compared with that of the control group, but 14 of them increased the TC level to a considerable extent. For example, *E. cava* increased almost twice as high as that of the control. In the FC levels, this decrease was particularly remarkable with the following 7 species: *M. nitidum*, *P. yezoensis*, *G. tenax*, *H. abietina*, *S. micracanthum*, *S. patens*, and *C. sisymbrioides*. Other seaweed powder showed no recognizable differences in FC levels.

Most seaweed powders did not show any marked change in TG levels, with the exception of 2 species: *P. yezoensis* and *S. micracanthum* reduced TG to a degree as low as 73.0 and 84.0% of the control level, respectively.

Changes in LDL levels were markedly lower only with 3 species: *C. sisymbrioides* (43.0%), *H. abietina* (46.0%), and *S. patens* (51.0%). In contrast noticeable enhancements of the TG level were found in some seaweeds such as 135.0% of the control level for *E. cova*, 116.0% for *S. confusum*, and 180.0% for *H. fusiforme*.

Conspicuous enhancements of HDL levels were induced by the addition of powder of *L. diabolica* (165.0%), *S. ringgoldianum* (170.0%), *P. arborescens* (138.0%), *P. yezoensis* (164.0%), and *G. amansii* (159.0%). It must be pointed out that only *L. japonica* and *C. sisymbrioides* powder produced a noticeable depression of the HDL level.

The effects of diets containing each algal polysaccharide on serum lipid levels in rats with hypercholesterolmia are shown in Table 5. Every test group significantly reduced the Atherogenic Index of serum as compared with that of the control group. For example, the Atherogenic Indices for sulfated glucuronoxylorhamnan, alginate, funoran, and porphyran were reduced to 47.0, 51.0, 57.0, and 73.0% of the control, respectively.

TC levels were also lowered by polysaccharide diets in the following order: funoran, sulfated glucuronoxylorhamnan, alginate, porphyran, fucoidan, and agar, the level for the last of these being almost in the same range as that of the control. The levels of reduction as compared with that of the control were 64.0, 65.0, 68.0, 77.0, 88.0, and 95.0%, respectively. FC concentrations were also lowered in a similar pattern to that of the TC levels. A particularly marked depression was noticed for the funoran diet (53.0% of control level).

The capicity of polysaccharide diets to lower the TG as well as the LDL level in serum shows similar patterns both in degree and in order. The most noticeable lowering of TG levels was by funoran and glucuronoxylorhamnan: they were in the range of 46.0 and 64.0% of the control level. Fucoidan and agar had the lowest capacity, the range being 80.0 and 98.0%, respectively.

In contrast to the above results, the levels of HDL were rather elevated by these polysaccharide diets. The highest increase was noticed with fucoidan, at 147.0% of the control level. However, the enhanced levels were only slight with funoran and porphyran diets. The other polysaccharide diets induced a moderate elevation (127.0% to 132.0% of the control level).

Discussion

In this work, we investigated the antihypertensive and antihyperlipidemic effects of seaweed powders and their polysaccharides using Wistar strain male rats fed with high concentrations of salt and cholesterol-rich diet. It was shown that many species of seaweed including edible algae were effective against hypertension in rats. For example, a diet containing *P. yezoensi* powder reduced it by nearly 90.0% of the levels of the control, and most seaweed powder diets had the same effect. In addition, diets containing each agal polysaccharide showed similar results. For example, porphyran, which is a sulfated galactan of *Porphyra*, also reduced nearly 92.0% of elevated blood pressure.

Table 2. Effect of seaweed powders on decrease in systolic blood pressure for 28 day-feeding (mmHg)

Species	Body weight gain (g)	0 day	4 day	8 day	12 day	16 day	20 day	24 day	28 day
Control	89.1±2.5*[1]	124.3±1.8	133.4±2.8	144.1±3.1	154.2±2.7	156.5±1.9	159.6±2.5	164.1±2.3	167.6±3.1
Green alga:									
Monostroma nitidum	94.4±2.9	124.1±2.3	125.3±1.9*	135.6±2.5*	137.5±2.1*	138.0±2.4*	150.4±2.8	150.1±1.7*	148.6±3.4**
Brown algae:									
Ishige okamurai	61.5±3.5	123.2±2.6	133.6±2.2	144.3±1.7	146.9±1.6*	161.3±2.8	149.1±1.3**	160.2±2.6	152.7±2.5*
Eisenia bicyclis	83.8±2.4	123.5±1.5	137.6±2.5	136.7±3.4	146.1±3.3	157.8±2.0	149.3±1.7*	157.5±3.1	161.5±1.9
Laminaria diabolica	98.0±1.5*	128.5±1.7	139.1±3.4	134.2±2.3*	147.3±1.9	138.5±3.5**	151.2±2.1	155.3±1.6*	154.4±1.8*
L. ochotensis	93.6±2.9	122.3±1.6	118.2±2.5*	129.8±2.6*	135.6±2.8*	140.3±3.1*	142.1±3.5**	143.7±1.9**	146.6±2.7**
L. japonica	87.3±2.1	124.2±3.0	130.0±2.0	135.8±1.8	137.7±2.3**	146.5±1.9*	146.6±2.8*	148.6±2.2*	156.3±2.5*
L. angustata	98.0±2.5*	131.1±1.3	131.5±2.3	146.5±1.5	156.2±3.8	145.5±2.3*	153.5±1.6	145.8±2.7**	161.8±3.5
L. longissima	88.2±1.9	127.5±2.0	133.5±1.7	133.3±2.6*	149.5±2.5	145.3±1.7*	151.5±3.9	159.8±3.7	150.5±5.1
Undaria pinnatifida	97.1±1.7*	125.5±1.8	132.1±2.1	144.6±3.2	154.9±2.9	156.7±3.3	155.8±1.5	157.6±4.6	165.5±4.2
Ecklonia cava	90.0±2.3	129.5±2.2	131.0±3.0	134.5±3.5*	161.0±4.3	141.5±3.1*	145.8±3.7**	153.2±1.8*	150.1±2.9*
Sargassum horneri	86.4±1.8	126.3±1.9	128.4±2.2	140.0±2.5	144.1±3.5	151.5±2.6	155.6±3.0	165.0±3.1	159.8±3.3
S. hemiphyllum	82.9±2.6	127.5±2.3	127.5±3.1	143.0±3.7	142.2±2.5*	152.5±1.9	151.6±3.2	170.1±2.9	158.3±5.4
S. thunbergii	78.4±2.0	125.4±3.1	133.5±1.8	147.9±3.0	153.5±4.7	153.2±2.0	145.3±1.9*	156.4±4.4	166.6±3.9
S. ringgoldianum	97.1±2.2*	124.5±3.5	132.9±2.5	139.8±2.7	145.1±3.0	140.1±3.6**	157.0±2.3	154.3±4.0*	152.5±2.1*
S. micracanthum	131.9±4.6**	125.3±3.0	134.4±2.9	140.1±3.5	149.5±2.8	157.5±4.5	153.6±2.9	152.6±3.0*	160.2±3.3
S. confusum	93.6±2.8	126.7±1.4	141.4±2.4	148.6±2.6	164.2±5.5	158.8±4.8	156.5±2.7	150.4±2.8**	163.5±2.5
S. patens	122.1±3.9**	126.5±1.7	145.2±3.5	152.3±4.0	153.5±4.8	159.5±5.0	161.6±4.7	161.4±5.6	162.3±3.8
Cystophyllum hakodatense	72.2±2.7	121.7±2.9	130.3±2.7	136.8±3.4	141.0±4.0	142.2±5.3*	147.8±3.6	153.1±4.2	161.5±3.5
C. sisymbrioides	95.3±2.6	128.4±2.3	132.3±1.5	139.2±3.0	146.5±3.3	152.6±2.4**	148.3±2.6*	167.3±3.4	160.8±4.7
Hizikia fusiforme	84.6±2.2	122.4±3.5	132.4±4.2	132.7±2.3	149.2±1.8	151.1±3.3	148.1±3.5	156.6±2.9*	151.3±2.7*
Heterochordaria abietina	93.6±2.8	122.0±1.5	130.2±2.6	137.0±3.2	148.3±2.4	150.5±2.8*	154.6±3.0	156.0±4.3	148.6±3.5**
Padina arborescens	85.5±3.0	121.5±2.6	128.5±3.0	132.5±2.8*	150.3±5.3	134.6±3.9**	141.5±3.3**	150.0±3.4**	151.1±4.0**
Red algae:									
Porphyra yezoensis	92.7±2.4	128.1±1.5	132.2±2.1	133.8±3.1*	143.9±1.8*	146.5±3.5*	143.1±2.9*	145.3±2.3**	151.5±2.7*
Gloiopeltis tenax	94.4±2.5	125.6±1.6	129.5±2.1	131.1±1.3*	140.2±1.8*	142.8±1.9*	148.3±1.9**	149.6±2.3*	148.5±2.5**
Gracilaria verrucosa	80.2±2.9	120.3±1.8	127.5±2.5	136.4±1.7	146.5±2.3	141.0±2.4*	147.6±2.0	152.3±3.5*	160.7±3.7
Gelidium amansii	91.8±1.9	123.4±2.3	123.3±1.9*	133.0±2.1	145.2±2.7	151.2±3.4	143.0±2.5**	148.3±2.4*	145.3±3.8**

*[1]: The values are expressed as mean±S.E. of 8 rats. $*p<0.05$, $**p<0.01$.

Table 3. Effect of algal polysaccharides on decrease in systolic blood pressure for 20 day-feeding (mmHg)

Polysaccharide	Body weight gain (g)	0 day	4 day	8 day	12 day	16 day	20 day
Control	75.5±3.1*[1]	124.3±1.8	144.2±2.8	157.3±3.1	156.5±2.6	164.4±1.9	167.1±2.5
Sulfated glucuronoxylorhamnan	92.1±2.5*	125.4±2.1	133.5±1.9*	146.2±2.5*	136.7±2.4*	151.1±2.0*	156.8±3.3*
Fucoidan	80.0±2.9	134.2±2.6	143.1±3.5	136.3±1.4**	135.4±2.9**	137.6±3.7*	140.1±3.1*
Sodium alginate	92.9±2.5*	125.6±1.7	132.1±2.3*	145.5±2.6*	136.3±3.3*	141.1±1.6*	141.6±2.4*
Porphyran	81.5±3.9	128.3±2.6	138.1±3.1	145.6±1.9*	136.1±2.4*	147.5±3.0*	153.1±3.6*
Funoran	77.8±2.0	137.5±1.9	138.7±2.6	140.2±3.2*	140.4±2.7*	135.3±3.4*	132.4±2.8**
Agar	83.1±3.3	124.5±2.3	148.6±2.7	142.3±3.6*	144.5±3.5	145.9±4.3**	148.6±4.6*

*[1]: Values are expressed as mean±S.E. of 8 rats. * $p<0.01$, ** $p<0.001$.

Table 4. Effect of seaweed powder on serum lipid level in Wistar rats fed cholesterol-containing diet for 28 days

Spcies	Body weight gain (g)	TC (mg/d*l*)	FC (mg/d*l*)	HDL (Mg/d*l*)	TG (mg/d*l*)	LDL (mg/d*l*)	AI (TC-LDL)/HDL
Control	89.1±2.5*[1]	552.5±87.8	97.0±17.5	33.0±1.6	61.0±3.3	519.6±89.8	15.7±4.1
Grren alga:							
Monostroma nitidum	94.4±2.9	386.7±45.3*	55.8±14.7*	26.7±1.8	64.7±10.8	358.5±40.2*	13.4±3.3
Brown algae:							
Ishige okamurai	61.5±3.5	692.2±34.6	129.0±21.3	33.0±2.8	51.9±5.8*	662.1±39.1	20.1±2.6
Eisenia bicyclis	83.8±2.4	790.1±68.9	137.7±26.4	41.6±5.6	59.2±6.3	748.2±75.0	18.4±4.5
Laminaria diabolica	98.0±1.5*	607.8±52.3	100.9±15.5	54.5±4.8	62.8±3.7	561.1±49.8	10.3±2.3
L. ochotensis	93.6±2.9	812.2±73.5	183.3±33.3	41.6±5.4*	58.0±6.9	768.2±80.6	19.6±5.1
L. japonica	87.3±2.1	464.1±51.6	82.5±16.7	26.4±3.7	48.8±4.6	436.5±57.8	16.5±5.4
L. longissima	88.2±1.9	486.2±40.1	72.8±13.3	49.5±4.0*	60.4±3.6	446.9±36.8	9.0±2.0
L. angustata	98.0±2.5*	685.1±60.1	149.4±18.5	30.4±4.7	63.4±4.3	654.7±65.5	22.3±5.3
Undaria pinnatifida	97.1±1.7*	442.6±56.4	73.7±12.5*	40.3±6.3	45.1±5.5*	401.5±63.3*	10.0±3.5*
Ecklonia cava	90.0±2.3	944.8±71.0	295.9±45.9	43.9±5.6	82.4±6.4	898.9±78.7	21.4±4.4
Sargassum horneri	86.4±1.8	657.5±58.1	114.5±34.7	31.0±4.9	59.8±3.6	628.7±60.7	19.8±6.5
S. hemiphyllum	82.9±2.6	652.0±34.7	128.0±40.1	29.0±5.1	51.9±4.5	623.5±40.6	22.4±6.1
S. thunbergii	78.4±2.0	762.5±63.4	147.4±21.8	34.3±6.7	65.3±7.4	725.1±74.1	23.7±4.3
S. ringgoldianum	97.1±2.2*	613.3±43.2	98.9±18.0	56.1±7.5*	48.8±5.7*	550.8±52.1	9.8±2.6*
S. micracanthum	131.9±4.6**	364.7±19.5*	47.5±3.8*	26.7±1.7	51.2±1.8**	342.9±18.2**	12.8±1.7*
S. confisum	93.6±2.8	629.9±25.3	116.4±10.5	31.7±4.7	70.8±3.9	586.8±35.2	19.7±3.3
S. patens	122.1±3.9**	287.3±24.8*	35.9±4.2**	28.1±2.1	56.7±4.4	265.0±23.2**	9.4±1.6*
Cystophyllum hakodatense	72.2±2.7	475.2±55.5	73.7±11.7	30.4±5.2	50.0±8.9	425.6±82.9	16.8±4.4
C. sisymbrioides	95.3±2.6	254.2±24.3**	31.0±4.0*	26.1±1.6	56.1±5.1	223.4±30.3*	8.6±1.8*
Hizikia fusiforme	84.6±2.2	795.6±36.8	108.6±12.4	26.7±2.6	109.8±14.7	769.0±55.8	28.8±5.5
Heterochordaria abietina	93.6±2.8	276.0±14.4*	44.6±2.5*	44.0±1.7**	54.0±4.2	233.0±15.2*	5.3±0.7*
Padina arborescens	85.5±3.0	585.7±46.5	116.4±8.6	45.5±6.9	54.9±5.8	540.4±45.0	11.3±3.6
Red algae:							
Porphyra yezoensis	97.7±2.4	447.5±35.6*	75.6±4.8*	54.1±3.2**	44.5±1.2*	405.3±9.6*	7.5±0.6*
Gloiopeltis tenax	94.4±2.5	442.0±19.7*	54.3±6.2*	33.0±1.9	53.1±1.8*	405.6±25.7*	12.3±1.6*
Gracilaria verrucosa	80.2±2.9	403.3±28.2	126.1±18.2	31.7±4.3	68.3±3.9	374.1±30.1	11.8±3.2
Geliduim amansii	91.8±1.9	668.5±56.3	131.0±14.9	52.5±6.1*	63.4±3.6	613.1±65.2	11.7±2.5

*[1]: The values are expressed as mean±S.E. of 8 rats. * $p<0.05$, ** $p<0.01$.

Table 5. Effect of algal polysaccharides on serum lipid level in Wistar rats fed cholesterol diet for 20 days

Polysaccharide	Body weight gain (g)	TC (mg/d*l*)	FC (mg/d*l*)	HDL (mg/d*l*)	TH (mg/d*l*)	LDL (mg/d*l*)	AI (TC-HDL)/HDL
Control	75.5±3.1*[1]	569.3±32.4	114.3±10.4	19.7±1.5	84.0±2.7	576.6±37.3	29.3±5.1
Sulfated glucuronoxylorhamnan	92.1±2.3*	385.6±38.4***	73.0±13.3*	26.0±5.2**	53.3±9.2***	359.4±42.5*	13.8±5.3**
Fucoidan	80.0±2.9	524.7±28.5	92.6±15.1*	29.0±6.7*	67.2±9.5*	490.3±41.6*	16.9±6.1
Sodium alginate	92.9±2.5*	405.6±28.2**	79.1± 5.7*	25.4±2.3	60.1±6.1**	380.3±29.2**	15.0±2.8*
Porphyran	81.5±3.9	456.7±33.2**	90.6± 8.3	20.4±1.0	60.7±2.9**	436.3±33.7**	21.4±2.7*
Funoran	77.8±2.0	381.6±43.3*	60.8± 2.0**	21.5±1.1	38.6±3.2**	366.3±38.8**	16.7±3.5
Agar	83.1±3.3	566.5±45.3	106.3±10.6	25.0±7.2	82.3±5.9	495.9±35.4	18.2±4.9

*[1]: The values are expressed as mean±S.E. of 8 rats. * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

The mechanism seems to be difficult to explain clearly. However, as has been reported previously,[22] the main factor may be the binding of sodium ions in diet to seaweed substances, particularly to its polysaccharides and their subsequent exeretion with feces.

Though in different degrees, all seaweed polysaccharides tested in the present study depressed TC, FC, TG, LDL, and AI in the blood of hypercholesterolemic rats. They moderately enhanced serum HDL levels. In contrast, the seaweed powders behaved in a different way: most of them enhanced HDL levels while some lowered TC, FC, TG, LDL, and AI levels, although the enhancement was rather irregular.

It seems difficult to explain the possible mechanism of these results. Apparently, as has been reported previously,[23] some seaweed powder as well as seaweed polysaccharides, (particularly polyinionic ones) may hold the cholesterol of the diet leading to excretion, and this may be related to the depression of blood cholesterol level. However, although it is difficult to explain why some of the seaweed powders did not reduce cholesteerol levels but rather enhanced them to considerably large extents, this may be explainable by the assumption that endogenous synthesis of cholesteerol, possibly in the liver, is enhanced and part of it is transported into blood to raise its level.

Some epidemiological evidence and experimental studies have suggested that HDL may protect against the development of atherosclerosis.[24-27] High HDL then seems to be associated with increasing longevity as well as a lower incidence of coronary heart disease (CHD).[28] Low HDL levels may precede the onset of clinical CHD and increas the risk of CHD.[27,29] It is important, therefore, to know that the rise in Atherogenic Index is closely related to arteriosclerosis.[30]

Many diuretics increase serum TG and reduced serum HDL.[31] Our data demonstrated that seaweeds and their polysaccharides prevent the reduction of serum HDL and the increase of serum TG levels occurring after four weeks or 20 days of high cholesterol diet. In edible seaweeds, *M. nitidum*, *L. pinnatifida*, and *P. yezoensis* for example, HDL levels were higher (0.8, 1.2, and 1.6 times the control level) and their Atherogenic Indices were smaller than those of the control group (85.0, 64.0, and 48.0%, respectively). Thus, these edible seaweeds seem to be an ideal healthy seafood. From the present study it was concluded that these marine algae and their polysaccharides may play an important role as antihypertensive and antihyperlipidemic daily food.

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References

1) J. Kameda: Medical studies on seaweeds (I). Effect of extract of tangle on blood pressure. *Fukushima Igaku Zasshi*, **10**, 251–260 (1960).
2) J. Kameda: Medical Studies on seaweeds (II). Influence of tangle administration upon experimental rabbit atherosclerosis produced by cholesterol feeding. *Fukushima Igaku Zasshi*, **11**, 289–309 (1961).
3) T. Takemoto, K. Daigo, and N. Takagi: Studies on the hypotensive constituents of marine algae. I. A new basic amino acid "Laminine" and the other basic constituents isolated from *Laminaria angustata. Yakugaku Zasshi*, **84**, 1176–1179 (1964).
4) H. Ozawa, Y. Gomi, and I. Otsuki: Pharmacological studies on Laminine Monocitrate. *Yakugaku Zasshi*, **87**, 935–939 (1967).
5) T. Kaneda, S. Tokuda, and K. Arai: Studies on the effects of marine products on cholesterol metabolism-I. The effects of edible seaweeds. *Nippon Suisan Gakkaishi*, **29**, 1020–1023 (1963).
6) T. Kaneda and K. Arai: Studies on the effects of marine products on cholesterol metabolism in rats-IV. Fractionation of effective substances from purple laver (1). *Nippon Suisan Gakkaishi*, **31**, 152–156 (1965).
7) T. Kaneda, P. V. Kamasastri, and S. Tokuda: Studies on the effects of marine products on cholesterol metabolism-V. The effects of edible seaweed. *Nippon Suisan Gakkaishi*, **31**, 1026–1029 (1965).
8) S. Abe and T. Kaneda: Studies on the effects of marine products on cholesterol metabolism in rats-VI. Fractionation of effective substances from purple laver (2). *Nippon Suisan Gakkaishi*, **33**, 361–366 (1967).
9) E. Nishide: Biological activities of algal polysaccharides. *Seikagaku*, **61**, 605–609 (1989).
10) K. Tsuji, S. Oshima, E. Matsuzaki, A. Nakamura, S. Innami, T. Tezuka, and S. Suzuki: Effect of polysaccharides on cholesterol metabolism (Part 1). Studies on Konnyaku powder, sodium alginate, and pectin. *Eiyogaku Zasshi*, **26**, 113–122 (1968).
11) K. Tsuji, E. Tsuji, and S. Suzuki: Effect of polysaccharides on cholesterol metabolism (Part 3). Effect of several polysaccharides on serum cholesterol levels in cholesterol-fed rats. *Eiyogaku Zasshi*, **32**, 155–160 (1974).
12) K. Tsuji, E. Tsuji, and S. Suzuki: Effect of polysaccharides on cholesterol metabolism (Part 6). Effect of various polysaccharides on serum and liver cholesterol levels in cholesterol-fed rats. *Eiyogaku Zasshi*, **33**, 273–281 (1975).
13) K. Tsuji, E. Tsuji, and S. Suzuki: Comparative cholesterol lowering activities of various kinds of propylene glycol alginate. *Eiyo to Shokuryo*, **31**, 485–489 (1978).
14) M. Koseki, K. Tsuji, M. Kazama, N. Kitabatake, and E. Doi: Interaction between dietary cholesterol or fatty acids and water-soluble fibers and increase in cholesterol excreation by pectin in rats. *Nippon Shokuhin Kogyo Gakkaishi*, **37**, 559–564 (1990).
15) Y. Iriki: Detection and identification of algal cell wall constituents, in "Research Methods of Algae" (ed. K. Nisizawa and M. Chihara), Kyoritsu Shuppan, Tokyo, 1979, pp. 602–612.
16) J. C. Su and W. Z. Hassid: Carbohydrates and nucleotides in the red alga, *Porphya perforata* I. Isolation and identification of carbohydrates. *Biochemistry*, **1**, 468–478 (1962).
17) S. Hirase, C. Araki, and T. Ito: Constituents of the mucilage of *Gloiopeltis furcata. Bulletin of the Chemical Society of Japan*, **29**, 985–987 (1956).
18) H. Mori and K. Nisizawa: Sugar constituents of sulfated polysaccharides from the fronds of *Sargassum ringgoldianum. Nippon Suisan Gakkaishi*, **48**, 981–986 (1982).
19) A. Haug: Methods in Carbohydrate Chemistry. Vol. V, Academic Press, New York. 1965, pp. 67–73.
20) W. Richmond: Preparation and properties of a cholesterol oxidase from *Nocardia* sp. and its application to the enzymatic assay of total cholesterol in serum. *Clin. Chem.*, **19**, 1350–1356 (1973).
21) C. C. Allain, L. S. Poon, C. S. G. Chan, W. Richmond, and P. C. Fu: Enzymatic determination of total cholesterol. *Clin. Chem.*, **20**, 470–475 (1974).
22) K. Ito: Dietary sodium restriction as nonpharmacologic treatment of hypertension. *Igakunoayumi*, **153**, 901–905 (1990).
23) S. Abe and T. Kaneda: Studies on the effects of marine products on cholesterol metabolism in rats-VII. The influence of dried purple laver on cholesterol levels of organs and cholesterol excretion in rats. *Nippon Suisan Gakkaishi*, **33**, 1050–1056 (1967).
24) G. J. Miller and N. E. Miller: Plasma-high-density-lipoprotein concentration and the development of ischaemic heart disease. *Lancet*, **1**, 16–19 (1975).
25) S. L. Hsia, Y. Chao, C. H. Hennekens, S. C. Yu, and W. B. Reader: Decreased serum cholesterol-binding researve in premature myocardial infarction. *Lancet*, **2**, 1000–1004, (1975).
26) T. E. Carew, S. B. Hayes, T. Koschinsky, and D. Steinberg: A mechanism by which high density lipopretins may slow the alterogenic process. *Iancet*, **2**, 1315–1317 (1976).

27) W. P. Castelli, J.T. Doyle, T. Gordon, C. G. Hames, M. C. Hjortland, S. B. Hulley, A. Kagan, and W. J. Zukel: HDL-cholesterol and other lipids in coronary heart disease: The cooperative lipoprotein phenotyping study. *Circulation*, **55**, 767–772 (1977).
28) C. J. Glueck, R. W. Fallat, F. Millett, P. Gartside, R. C. Elston, and R. C. P. Go: Familial hyperalphalipoproteinemia. Studies in eighteen kindreds. *Metabolism*, **24**, 1243–1259 (1975).
29) T. Gordon, W. P. Castelli, M. C. Hjortland, W. B. Kannel, and T. R. Dawber: High density lipoprotein as a protective factor against coronary heart disease. The framingham study. *Amer. J. Med.*, **62**, 707–714 (1977).
30) Y. Yano, N. Irie, Y. Homma, M. Tsushima, I. Takeuchi, N. Nakaya, and Y. Goto: High density lipoprotein cholesterol levels in the Japanese. *Atherosclerosis*, **36**, 173–181 (1980).
31) K. Hiwada: Diuretics: Reassessment of their tole in the long-term treatment of hypertension. *Igakunoayumi*, **153**, 922–926 (1990).