

Pharmacological Activity of Deep-Sea Water: Examination of Hyperlipemia Prevention and Medical Treatment Effect

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When normal rabbits were administered various samples of deep-sea water, their biochemical values changed within normal limits, and no differences from distilled water administration (control) group levels were observed. Furthermore, no histopathological changes were observed in internal organs on the 28th day after administration. The serum total cholesterol (T-Cho) and low density lipoprotein cholesterol (LDL-Cho) levels of normal rabbits fed with a 1% cholesterol-containing diet simultaneously administered deep-sea water (desalinated water, hardness 28, 300, and 1200) increased with time up to about 1500 mg/dl. However, the degrees of increase were smaller than those of the control group, which received distilled water. Furthermore, when prepared hyperlipemia rabbits were administered deep-sea water (desalinated water, hardness 28, 300, and 1200), there were no significant changes in aspartate aminotransferase (AST), alanine aminotransferase (ALT), high density lipoprotein cholesterol (HDL-Cho), or triglyceride (TG) levels. On the other hand, T-Cho and LDL-Cho levels were reduced when the rabbits were changed to normal food, and the degree of reduction was more than that of the control group. In the liver and main artery bow, as the hardness of the deep-sea water increased, the accumulation of lipid and permeation of macrophages was reduced. This result was well in agreement with the results of the T-Cho and LDL-Cho levels. From these results, it is clear that deep-sea water controls the increase of serum lipid values (T-Cho and LDL-Cho) of cholesterol-fed rabbits, and promotes the reduction of serum lipid hyperlipemia rabbits. The minerals in deep-sea water greatly influence this effect.

Key words deep-sea water; hyperlipemia; total cholesterol; low density lipoprotein cholesterol; mineral

In recent years, deep-sea water has been applied not only in food production but in industry and the medical field in an attempt to utilize its properties,¹⁾ its wealth of inorganic materials, its purity and mineral content, which have attracted attention.²⁾ In particular, various minerals in their characteristic dissolved states, including indispensable trace elements abundant in deep-sea water have demonstrated their usefulness and attracted attention in each field, and various applications have been tried.³⁾

A major problem of insufficient minerals caused by the recent westernization of lifestyles and eating habits, has resulted in so-called lifestyle-related illnesses such as hyperlipemia, hypertension, and diabetes.⁴⁾ In order to prevent or treat these illnesses, it is important to adjust disorders in body functioning. However, although deep-sea water contains minerals used in the treatment of lifestyle-related illness and the production of health food, there is no scientific proof of its usefulness.

To examine the lifestyle-related illness, hyperlipemia, in which eating habit disorders are considered to particularly influence the development of symptoms, we medicated normal rabbits with deep-sea water (desalinated water, hardness 28, 300, and 1200) simultaneously with cholesterol loading, and examined its preventive effect on hyperlipemia. Furthermore, prepared hyperlipemia rabbits⁵⁾ carrying the same cholesterol load as normal rabbits, were administered deep-sea water, and its medical treatment effect on hyperlipemia was examined.

MATERIALS AND METHODS

Animals Male Japanese white rabbits weighing 1.8 to 2.0 kg (Shimizu, Kyoto, Japan) were used in this study. These animals were maintained on a 12 h light/dark cycle in a humidity- and temperature-controlled facility and allowed free access to food and water for 1 week during acclimatization before the experiment.

Deep-Sea Water Deep-sea water pumped up from a depth of 374 m off Muroto Cape (Kochi, Japan) was desalinated and concentrated by reverse osmosis. Various concentrations of water with eliminated sodium *etc.* were added to the desalinated water and deep-sea water samples of varying hardness (28, 300, 1200) were prepared. The mineral ingredient content of each deep-sea water sample is shown in Table 1.

Administration of Deep-Sea Water Normal rabbits were divided into four groups and administered 150 ml/d of deep-sea water (desalinated water, hardness 28, 300, and 1200) in a water supply bottle *ad libitum*, and fed normal food (CR-3, Clea, Osaka, Japan) for 4 weeks (Table 2). It was confirmed that the rabbits consumed the water each time.

Cholesterol-loaded rabbits were similarly divided into four groups and were each administered deep-sea water, and fed a 1% cholesterol-containing diet (CE-2, Clea, Osaka, Japan) for 4 weeks (Table 2).

Hyperlipemia rabbits fed a 1% cholesterol diet for 4 weeks and with a raised total cholesterol (T-Cho) level before this experiment, were similarly divided into four groups, admin-

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istered with deep-sea water and simultaneously fed normal food for 4 weeks (Table 2).

A distilled water administration group was used as the control. Body weight was measured weekly.

Measurement of Biochemical Values Blood samples were collected from the ear vein of each rabbit after 0, 7, 14, 21, and 28 d, and centrifuged to obtain sera. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) activities and levels of T-Cho, high density lipoprotein cholesterol (HDL-Cho), and triglyceride (TG) were measured using Fuji Dricchem (Fujifilm Medical Co. Ltd., Japan). The low density lipoprotein cholesterol (LDL-Cho) value was calculated from the presumed formula of Friedewald⁶ using the T-Cho, HDL-Cho, and TG values.

Pathologic Histological Observation On the 28th day after deep-sea water administration, the rabbits were exsanguinated under general anesthesia (sodium pentobarbital, 20–30 mg/kg, i.v.). The liver, kidney, stomach, duodenum, large intestine, and main artery bow were collected at necropsy. Further, a portion of each liver and main artery bow was imbedded in paraffin, sectioned by microtome, and stained with HE.

Statistical Analysis All data are presented as the means±S.E.M. of 6 experiments. Statistical analysis was performed by analysis of variance (ANOVA) followed by the Dunnett's test. Differences were accepted as statistically significant at *p* values <0.05.

RESULTS

Weight Change of Rabbits during Deep-Sea Water Administration All the rabbits survived the experimental period. There were no remarkable differences in the body weights between the control and deep-sea water administration groups (data not shown).

Influence of Deep-Sea Water Administration on Normal Rabbits. Biochemical Values Changes in the biochemical values after deep-sea water administration in normal rabbits are shown in Fig. 1.

No differences were observed in AST levels between the administration groups on the measurement days. In the administration groups, no changes over time from the initial levels were observed, and any changes were within normal ranges. On the other hand, for ALT levels, significant differences were observed between the administration groups (*p*<0.001). Although the values changed within normal ranges, a low level was shown in the desalinated water administration group compared with other administration groups.

No differences of T-Cho, HDL-Cho, LDL-Cho and TG levels were observed in serum lipid between the administration groups in distributed analysis. Although all index levels changed within normal ranges from the initial levels, in the T-Cho and TG levels, differences were observed on the measurement days in distributed analysis (*p*<0.01).

Pathologic Histological Observations No visible gross changes such as swelling or bleeding were observed in any organ or tissue at necropsy on the 28th day after deep-sea water administration. No pathological changes were observed in the liver or main artery bow stained with HE.

Influence of Deep-Sea Water Administration on Cholesterol-Fed Breeding Rabbits. Biochemical Values Changes in the biochemical values after deep-sea water administration to 1% cholesterol-fed breeding rabbits are shown in Fig. 2.

No differences were observed in AST levels between the administration groups on the measurement days. In addition, no changes over time from the initial levels were observed, and the values changed within the normal ranges. On the other hand, for ALT levels, differences were observed between administration groups (*p*<0.01) on the measurement

Table 1. Mineral Ingredient Content of Each Deep-Sea Water

Mineral ingredient ^{a)}	Content (mg/l)			
	Desalinated water	Hardness ^{b)} of deep-sea water		
		28	300	1200
Na	4.2	49	58	44
Ca	N.D. ^{c)}	1.8	20	86
Mg	0.08	5.6	60	240
K	0.2	2.0	19	17

a) Measurement of analysis: Na, Ca, Mg; ICP atomic emission spectrometry, K; atomic absorption spectrophotometry. b) Hardness: Ca(mg/l)×2.5+Mg(mg/l)×4.1. c) N.D.: not detected.

Table 2. Experimental Design

Group (treatment)		Water (150 ml/d)	Diet	Time in weeks	Number of animals
Normal	A	Control (distilled water)	Normal	4	6
	B	Desalinated water	Normal	4	6
	C	Deep-sea water (hardness 28)	Normal	4	6
	D	Deep-sea water (hardness 300)	Normal	4	6
	E	Deep-sea water (hardness 1200)	Normal	4	6
Cholesterol (preventive effect)	A	Control (distilled water)	1% cholesterol	4	6
	B	Desalinated water	1% cholesterol	4	6
	C	Deep-sea water (hardness 28)	1% cholesterol	4	6
	D	Deep-sea water (hardness 300)	1% cholesterol	4	6
	E	Deep-sea water (hardness 1200)	1% cholesterol	4	6
Hyperlipemia (treatment effect)	A	Control (distilled water)	Normal	4	6
	B	Desalinated water	Normal	4	6
	C	Deep-sea water (hardness 28)	Normal	4	6
	D	Deep-sea water (hardness 300)	Normal	4	6
	E	Deep-sea water (hardness 1200)	Normal	4	6

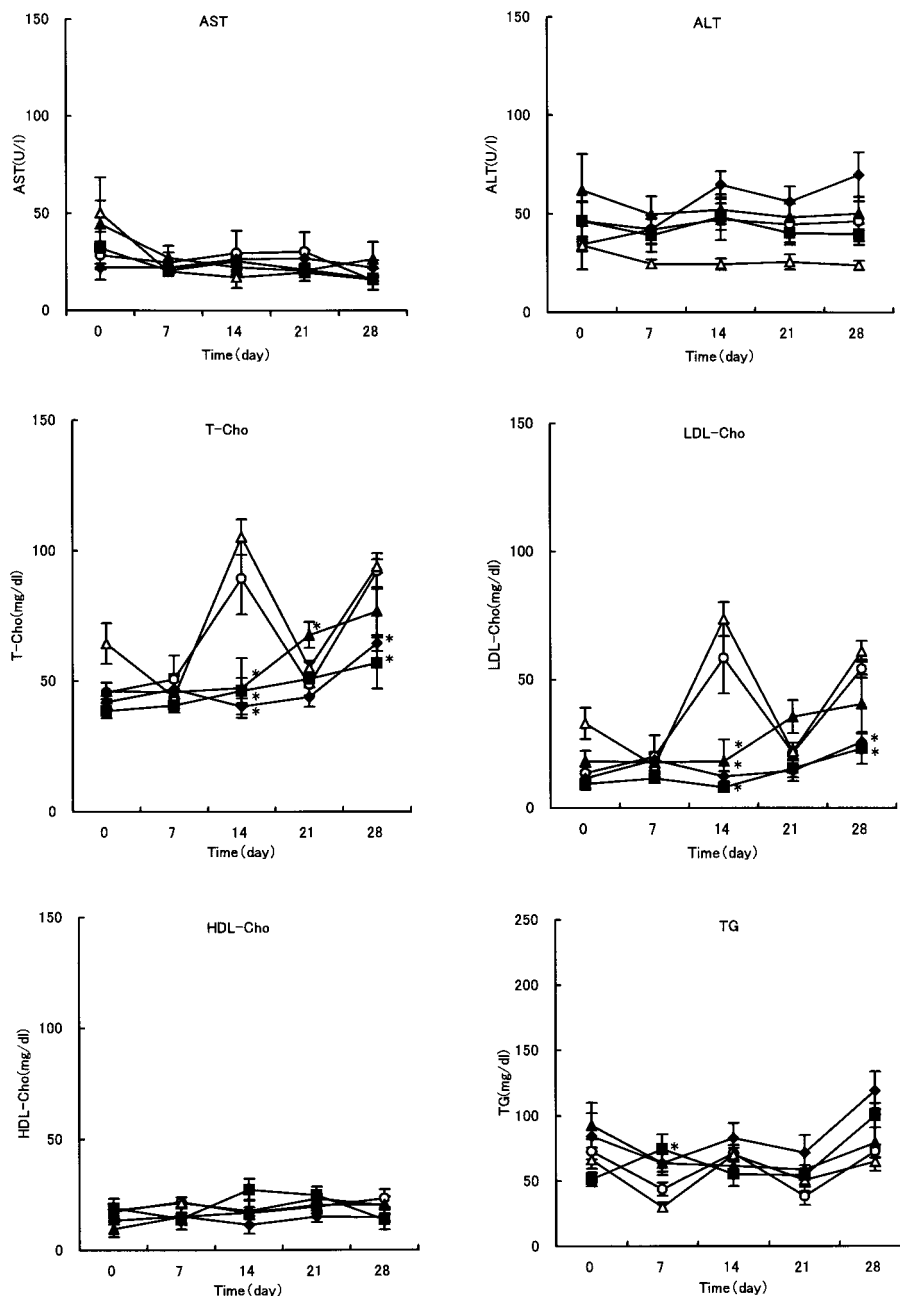


Fig. 1. Effect of Deep-Sea Water on Normal Biochemical Values

Rabbits received distilled water (○), desalinated water (△), deep-sea water (hardness 28) (▲), deep-sea water (hardness 300) (◆) and deep-sea water (hardness 1200) (■). Values are expressed as the means \pm S.E.M. ($n=6$). * $p < 0.05$, significantly different from the distilled water groups.

days ($p < 0.001$). The values showed a tendency to increase over time, and after the 14th day, a high value was shown in the control distilled water administration group.

Furthermore, in serum lipid, differences were observed between the administration groups ($p < 0.01$) on the measurement days ($p < 0.001$) in T-Cho and LDL-Cho levels. T-Cho and LDL-Cho levels of the 1% cholesterol diet breeding rabbits increased quickly from the initial level to 14 d after administration, and showed 1500 or more mg/dl on the 14th day. After the 14th day, it increased gradually. Furthermore, T-Cho and LDL-Cho levels on the 28th day after administration in the desalinated water group (1570.0 ± 48.8 , 1525.3 ± 51.2 mg/dl) and deep-sea water group for each hardness (hardness 28: 1697.5 ± 118.6 , 1659.0 ± 119.1 mg/dl,

hardness 300: 1613.3 ± 77.8 , 1570.9 ± 79.1 mg/dl, hardness 1200: 1688.3 ± 138.2 , 1654.4 ± 137.3 mg/dl) were lower than those of the control distilled water administration group (1727.5 ± 118.4 , 1672.0 ± 124.3 mg/dl).

On the other hand, although no differences in the HDL-Cho and TG levels were observed between the administration groups, differences were observed on the measurement days ($p < 0.001$). However, all index values changed within normal ranges from the initial level.

Differences in T-Cho and LDL-Cho levels were observed between each of the deep-sea water administration groups. In order to identify the speed of rise in each group after deep-sea water administration, logarithmic straight line approximation was performed and the time scale was compared

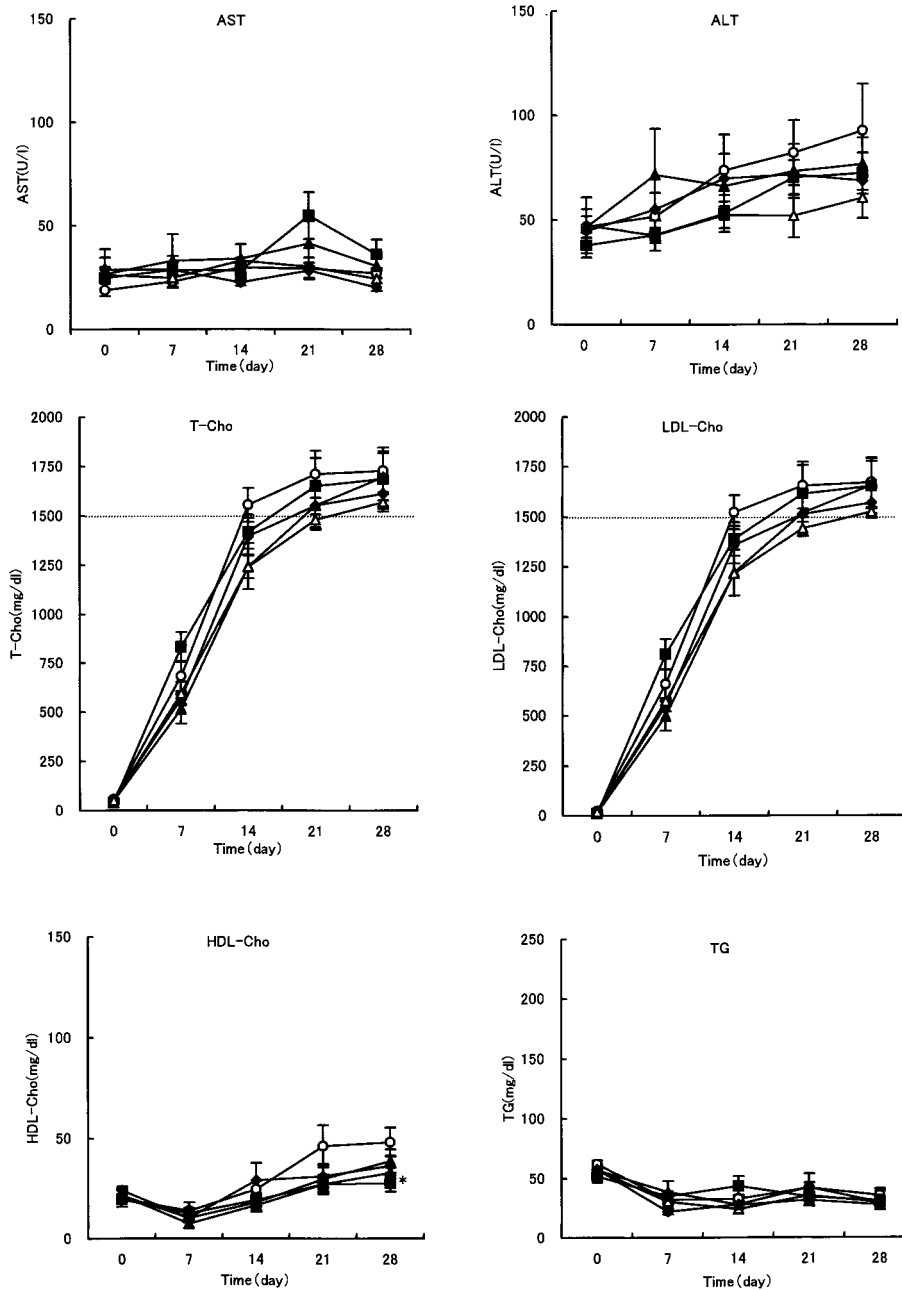


Fig. 2. Effect of Deep-Sea Water on Biochemical Values of 1% Cholesterol-fed Rabbits

Rabbits received distilled water (○), desalinated water (△), deep-sea water (hardness 28) (▲), deep-sea water (hardness 300) (◆) and deep-sea water (hardness 1200) (■). Values are expressed as the means ± S.E.M. (n=6). * p<0.05, significantly different from the distilled water groups.

($r=0.8909-0.9475$).

The rate constant of deep-sea water to 1% cholesterol-fed breeding rabbits, the days necessary to attain 1500 mg/dl of T-Cho and LDL-Cho levels, and the rate of rise control are shown in Table 3. For T-Cho and LDL-Cho, the rate constant had the largest contrast, and was in the order of hardness 1200, 28, and 300 and then desalinated water.

It is presumed from the table of transition time of these T-Cho and LDL-Cho levels that 1500 mg/dl was the balanced level. The desalinated water, hardness 28, and hardness 300 administration groups were 28.7 d, 25.5 d, and 24.6 d, respectively, and the days necessary to attain a T-Cho value of 1500 mg/dl increased compared with 18.5 d for the control group. However, in the hardness 1200 administration group

(19.8 d), the difference from the control group was small. Furthermore, desalinated water, hardness 28, and hardness 300 administration groups were 30.9 d, 27.1 d, and 25.0 d, respectively, and the days necessary to attain a LDL-Cho level of 1500 mg/dl increased compared with 20.1 d for the control group. However, in the hardness 1200 administration group (21.0 d), the difference from the control group was small.

The rate of rise control was calculated from the T-Cho and LDL-Cho levels of each deep-sea water group on the days (18.5 d, 20.1 d) when the T-Cho and LDL-Cho levels of the control distilled water administration group reached 1500 mg/dl from the approximation formula, and 1500 mg/dl calculated from the ratio with the control group. The rate of rise control showed the desalinated water administration

Table 3. Effect of Deep-Sea Water on T-Chol and LDL-Chol of 1% Cholesterol-fed Rabbits

Group	T-Chol		LDL-Chol	
	Time to attain 1500 mg/dl ^{a)} (Rate constant ^{b)}) (d)	Rate of rise control ^{c)} (%)	Time to attain 1500 mg/dl ^{a)} (Rate constant ^{b)}) (d)	Rate of rise control ^{c)} (%)
A Control (distilled water)	18.5 (1219)	—	20.1 (1205)	—
B Desalinated water	28.7 (1064)	13.6	30.9 (1059)	13.2
C Deep-sea water (hardness 28)	25.5 (1134)	10.6	27.1 (1133)	9.8
D Deep-sea water (hardness 300)	24.6 (1118)	9.2	25.0 (1113)	8.9
E Deep-sea water (hardness 1200)	19.8 (1171)	2.3	21.0 (1169)	1.5

a) Balanced value on T-Chol and LDL-Chol. b) Inclination of the straight line at the time of making a time scale to logarithm. c) The rate to 1500 mg/dl of each groups in the time of T-Chol and LDL-Chol reaching 1500 mg/dl in control group.

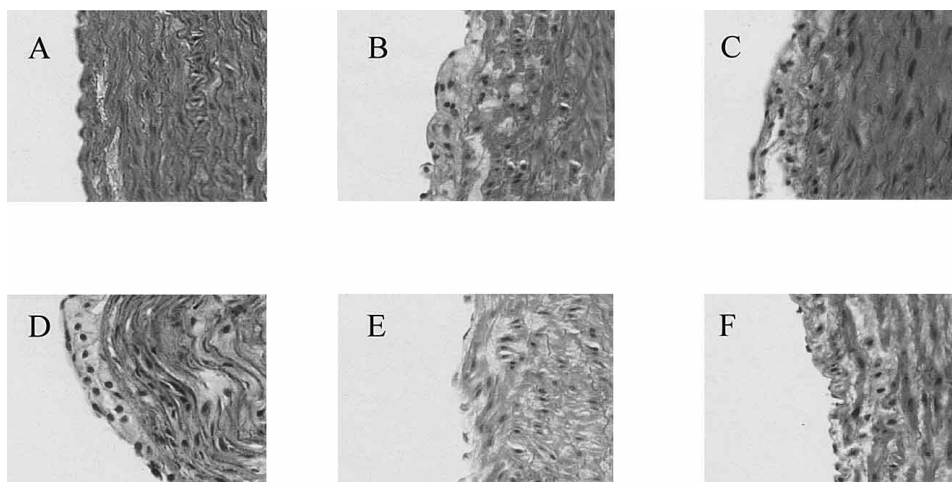


Fig. 3. Photomicrographs of the Main Artery Bow in 1% Cholesterol-fed Rabbits Administered Deep-Sea Water for 28 d

A: normal rabbit; B: distilled water (control); C: desalinated water; D, E and F: deep-sea water (hardness 28, 300 and 1200). HE stain, magnification $\times 200$.

group to be the largest at 13.6 or 13.2%, and was in the order of hardness 28, 300, and 1200.

Pathologic Histological Observations No visible gross changes such as swelling and bleeding were observed in any organ or tissue at necropsy on the 28th day after deep-sea water administration. No pathological changes were observed in the HE-stained liver.

However, in the main artery of all medicated groups, very small white droplets, which seemed to be lipid deposition, were observed.

Photomicrographs of HE-stained main artery bows after the 28th day of deep-sea water administration are shown in Fig. 3. In all administration groups, a slight permeation of macrophages, considered to be signs of arteriosclerosis, was observed. There were no differences among the groups.

Influence of Deep-Sea Water Administration on Hyperlipemia Rabbits. Biochemical Values Changes in the biochemical values after deep-sea water administration to hyperlipemia rabbits are shown in Fig. 4.

No differences were observed in the AST levels between the administration groups on the measurement days. In addition, for each administration group, no changes were observed over time from the initial levels, and the values changed within normal ranges. On the other hand, for the ALT levels, differences were observed on the measurement days ($p < 0.01$). The values in the administration group changed within normal ranges.

Differences were observed ($p < 0.001$) in T-Chol and LDL-Chol levels between measurement days. Although the index levels changed within normal ranges from the initial level, in T-Chol and TG levels, differences were observed on the measurement days ($p < 0.01$). The values decreased quickly until the 7th day after the initial value, and a subsequent tendency to dwindle was observed.

Furthermore, T-Chol and LDL-Chol levels on the 28th day after administration for the desalinated water group (110.2 ± 27.3 , 71.7 ± 27.5 mg/dl) and deep-sea water group of each hardness level (hardness 28: 82.7 ± 15.3 , 49.0 ± 13.1 mg/dl, hardness 300: 68.7 ± 16.1 , 31.3 ± 13.4 mg/dl, hardness 1200: 60.8 ± 9.7 , 31.2 ± 8.5 mg/dl) were lower than those of the control distilled water administration group (133.0 ± 26.7 , 98.5 ± 25.2 mg/dl).

On the other hand, for the HDL-Chol values, differences were observed on the measurement days between the administration groups in distributed analysis ($p < 0.01$ and $p < 0.01$). Although the values on the 7th day of administration were higher, they changed within normal limits from the 14th or subsequent days. As for TG values, differences were observed on the measurement days ($p < 0.01$). A transient rise was observed on the 7th day in the distilled water, desalinated water, and the hardness 28 deep-sea water administration groups.

In the T-Chol and LDL-Chol levels, differences were observed between each of the deep-sea water administration

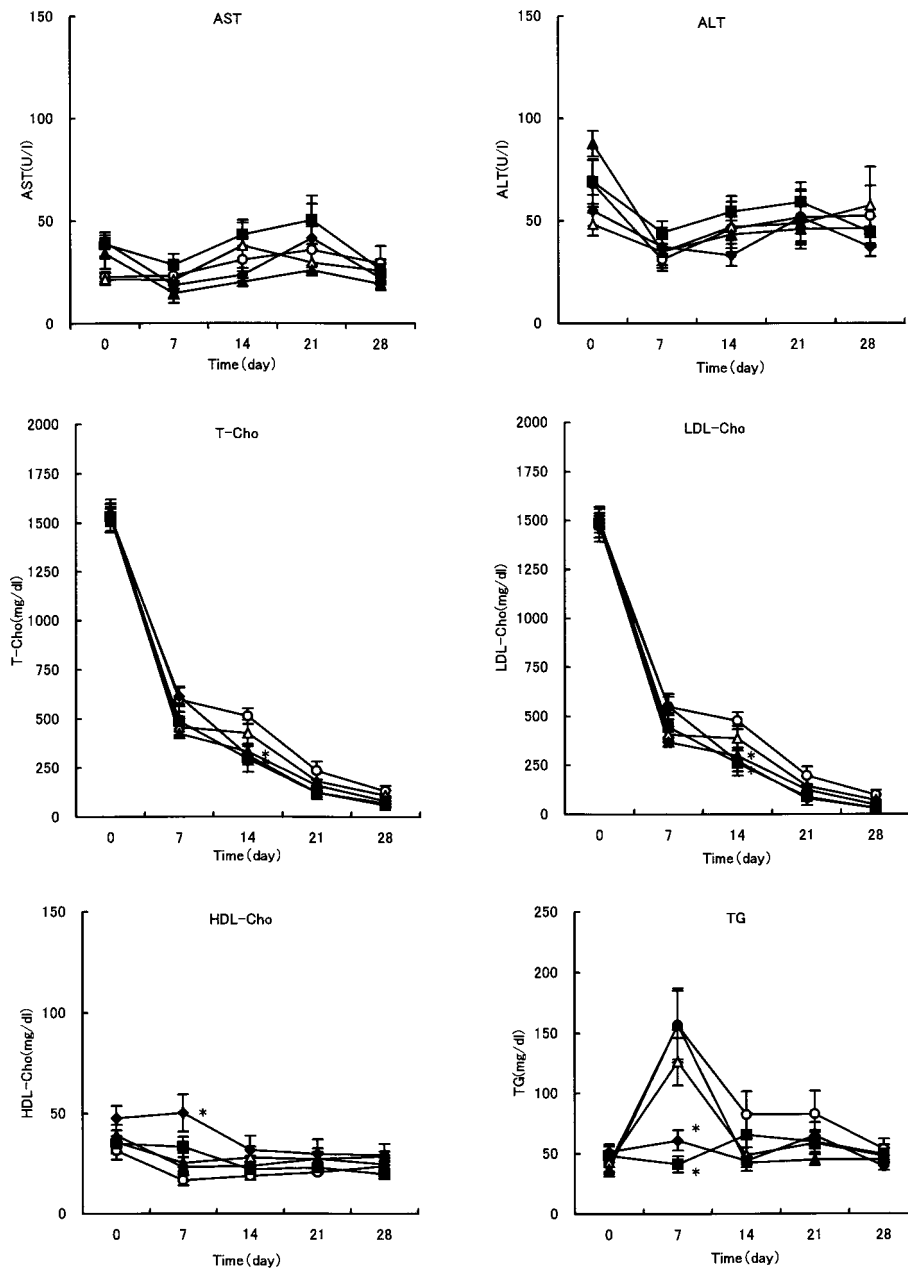


Fig. 4. Effect of Deep-Sea Water on Biochemical Values of Hyperlipemia Rabbits

Rabbits received distilled water (○), desalinated water (△), deep-sea water (hardness 28) (▲), deep-sea water (hardness 300) (◆) and deep-sea water (hardness 1200) (■). Values are expressed as the means ± S.E.M. ($n=6$). * $p < 0.05$, significantly different from the distilled water groups.

groups. In order to clarify the decline in kinetics in each group after deep-sea water administration, logarithmic, straight line approximation was performed and the time scale was compared ($r=0.9579-0.8769$).

In the rate constant of deep-sea water in hyperlipemia rabbits, the necessary days to attain 50 mg/dl T-Cho and 25 mg/dl LDL-Cho levels, and the rates of decline are shown in Table 4.

The negative rate constant of the various deep-sea water administration groups in T-Cho and LDL-Cho was large, in the order of distilled water, desalinated water, and hardness 28, 300, and 1200. The days required to attain normal T-Cho values calculated from each straight-line approximation formula and the LDL-Cho value varied little for the deep-sea water compared with the control group (distilled water ad-

ministration group). For T-Cho, the days needed to attain the normal value was shortest in the hardness 1200 administration groups (27.9 d) and prolonged in order of hardness 300, 28 and desalinated water. On the other hand, for LDL-Cho, in the hardness 300 administration groups, it was shortened (27.3 d) and prolonged in order of hardness 1200, 28 and desalinated water.

Pathologic Histological Observations No visible gross changes such as swelling or bleeding were observed in any organ or tissue at necropsy on the 28th day. Photomicrographs of the HE-stained liver and main artery bow on the 28th day are shown in Figs. 5 and 6.

As shown in Fig. 5, in the liver, lipid accumulations were observed for each group. The degree of accumulation was small in the order of hardness 28, 300, and 1200. Further-

Table 4. Effect of Deep-Sea Water on T-Cholesterol and LDL-Cholesterol of Hyperlipemia Rabbits

Group	T-Cholesterol		LDL-Cholesterol	
	Time to attain 50 mg/dl ^{a)} (Rate constant ^{b)}) (d)	Rate of decline promotion ^{c)} (%)	Time to attain 25 mg/dl ^{d)} (Rate constant ^{b)}) (d)	Rate of decline promotion ^{c)} (%)
A Control (distilled water)	37.8 (-0.268)	—	39.5 (-0.311)	—
B Desalinated water	34.2 (-0.285)	17.1	34.8 (-0.343)	27.2
C Deep-sea water (hardness 28)	31.7 (-0.306)	37.8	32.4 (-0.367)	50.3
D Deep-sea water (hardness 300)	29.0 (-0.353)	48.3	27.3 (-0.465)	68.2
E Deep-sea water (hardness 1200)	27.9 (-0.355)	54.3	28.1 (-0.436)	68.3

a) Normal value of T-Cholesterol. b) Inclination of the straight line at the time of making a logarithmic time scale. c) The rate to 50 and 25 mg/dl of each groups in the time for T-Cholesterol and LDL-Cholesterol to reach for each control group. d) Normal value of LDL-Cholesterol.

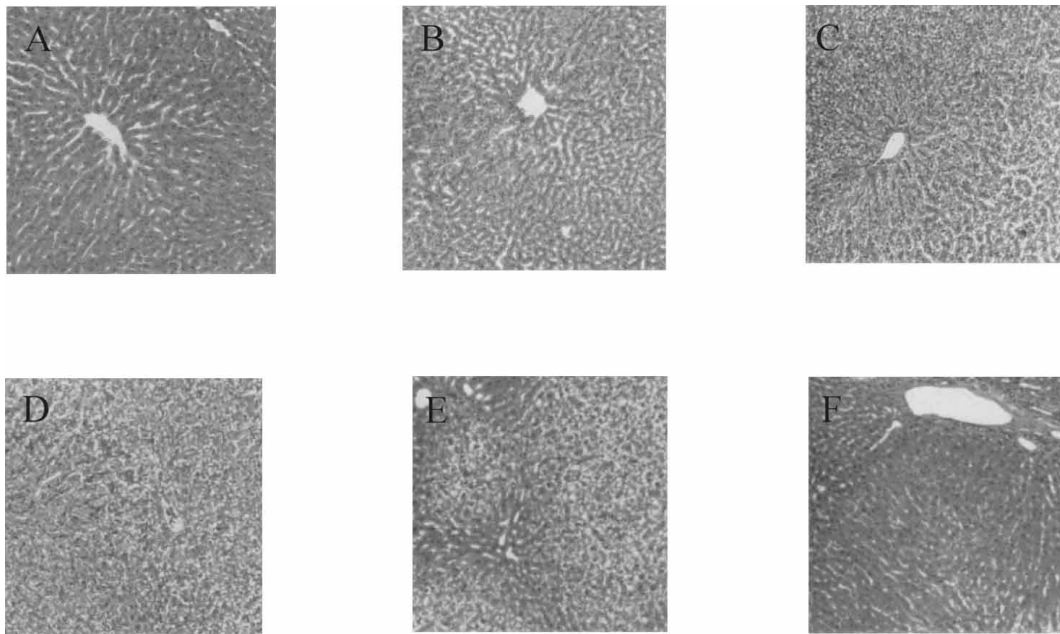


Fig. 5. Photomicrographs of Liver in Hyperlipemia Rabbits Administrated with Deep-Sea Water for 28 d
A: normal rabbit; B: distilled water (control); C: desalinated water; D, E and F: deep-sea water (hardness 28, 300 and 1200). HE stain, magnification ×50.

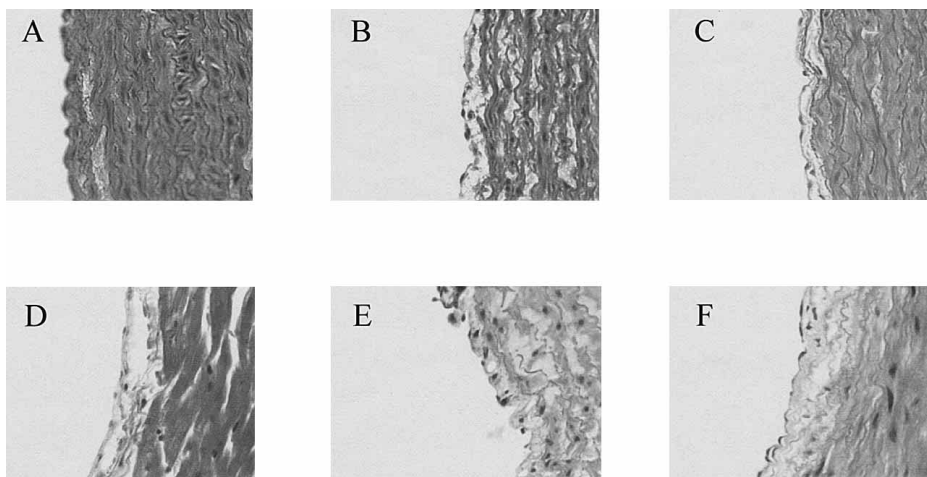


Fig. 6. Photomicrographs of the Main Artery Bow in Hyperlipemia Rabbits Administrated with Deep-Sea Water for 28 d
A: normal rabbit; B: distilled water (control); C: desalinated water; D, E and F: deep-sea water (hardness 28, 300 and 1200). HE stain, magnification ×200.

more, in all administration groups, a slight permeation of macrophages, considered to be a sign of arteriosclerosis, was observed. Macrophage permeation was least in the group administrated with hardness 1200 (Fig. 6).

DISCUSSION

A recent large-scale epidemiology investigation showed that hyperlipemia, especially hypercholesterolemia, is the most important risk-factor for coronary artery disease.⁷⁾ A rise is observed every year in Japanese cholesterol values in serum due to the increased amount of fat ingestion accompanying the westernization of eating habits.⁸⁾ Therefore, by reducing the risk factors in lifestyle, such as eating, exercise, and smoking, it is thought that the risk of hyperlipemia and arteriosclerosis-type diseases can be greatly reduced.⁹⁾ To prevent hyperlipemia, lifestyle needs to be improved before medication is used.

In this study, we examined the prevention and medical effects of hyperlipemia of deep-sea water using normal rabbits, 1% cholesterol diet breeding rabbits, and hyperlipemia rabbits. With deep-sea water administration to normal rabbits, no differences in biochemical values and pathology organization images were observed between the control groups. From these results, it becomes clear that deep-sea water does not influence serum lipid, fat metabolism, or the function of digestive organs. In T-Cho and TG levels, although differences were observed on measurement days, the amount and the timing of diet influenced the T-Cho and TG levels. T-Cho and TG levels oscillated in the distilled and desalinated water administration groups. The body function changed because distilled and desalinated water do not contain any minerals. On the other hand, this phenomenon was not seen in the deep-sea water administration groups.

T-Cho and LDL-Cho levels of the 1% cholesterol diet breeding rabbits in all administration groups increased quickly from an initial level to 14 d after administration, and showed 1500 or more mg/dl on the 14th day. After the 14th day, it increased gradually. The increases of T-Cho and LDL-Cho levels of each of the deep-sea water administration groups were smaller than those of the control group. The days necessary for the desalinated water, hardness 28, and hardness 300 administration groups to attain T-Cho and LDL-Cho levels of 1500 mg/dl calculated from changes of T-Cho and LDL-Cho levels were more than that of the control group. Deep-sea water with low hardness seems to have a useful preventative effect because it controlled the rise of T-Cho and LDL-Cho levels. However, differences between the hardness 1200 administration group and control group were slight.

T-Cho and LDL-Cho levels of hyperlipemia rabbits in all administration groups decreased quickly from an initial level to 7 d after administration. After the 7th day, it decreased gradually. As the hardness was high, the rate of decrease was high compared to the control group. The days needed for the various deep-sea water administration groups to attain normal levels (T-Cho: 50 mg/dl, LDL-Cho: 25 mg/dl) were calculated to be about 10 d shorter than for the control group. Furthermore, in the liver and main artery bow, when hardness was high, the accumulation of lipid and permeation of macrophages was lower. The results were well in agreement with the results of the T-Cho and LDL-Cho levels, that is, when T-Cho and LDL-Cho levels are high, it is thought that prescribing deep-sea water with high hardness promotes the reduction of T-Cho and LDL-Cho levels for patients.

Hardness is calculated from the amount of calcium (Ca)

and magnesium (Mg). Ca supplementation causes beneficial changes in circulating lipids in normal older women.¹⁰⁾ Evans *et al.*¹¹⁾ reported that injections of Mg sulphate and ethylenediamine tetraacetic acid have a definite prophylactic effect on atherogenesis in cholesterol-fed rabbits, and may have some therapeutic value in the regression phase. Ouchi *et al.*¹²⁾ reported that dietary Mg prevents the development of atherosclerosis in cholesterol-fed rabbits by inhibiting accumulation in the aortic wall.

Kovanen *et al.*¹³⁾ reported that remarkable hypercholesterolemia was accelerated when LDL-Cho receptors in the livers of rabbits become saturated and suppressed as a result of cholesterol feeding. In this study, it is considered that deep-sea water suppresses cholesterol absorption in the alimentary canal, and that certain ingredients in deep-sea water affect LDL-Cho metabolism in the liver. Further detailed examination is necessary.

Since the influence of factors other than hardness should also be considered, Ca and Mg are added to distilled water, and water of the same hardness as deep-sea water prepared, and we consider that the same examinations are required. Furthermore, we intend to extend the administration period and to show the effects clearly.

Kobayashi *et al.*¹⁴⁾ examined the effect of simvastatin (Lipovas[®]; Banyu, Tokyo) on hypercholesterolemia induced by cholesterol feeding in rabbits, and reported that simvastatin inhibited the increase of serum lipid levels by about 80%. In conclusion, the treatment effect of deep-sea water on hyperlipemia is very small compared with commercial hyperlipemia improvement agents. However, it is considered that deep-sea water has a useful preventive effect when used as healthy drinking water. Furthermore, in the prevention of hyperlipemia, the combined use of deep-sea water and other hyperlipemia improvement agents or health foods should also be considered, and their interactions studied.

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